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WATER-SALT AND MINERAL METABOLISM. URINARY FUNCTION OF KIDNEYS. NORMAL AND PATHOLOGICAL COMPONENTS OF URINE

Textbook
for students of general medicine and dentistry

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

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ВОДНО-СОЛЬОВИЙ ТА МІНЕРАЛЬНИЙ ОБМІН. СЕЧОУТВОРЮВАЛЬНА ФУНКЦІЯ НИРОК. НОРМАЛЬНІ ТА ПАТОЛОГІЧНІ КОМПОНЕНТИ СЕЧІ

Навчальний посібник
для студентів медичного
та стоматологічного факультетів

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N18 Water-salt and mineral metabolism. Urinary function of kidney. Normal and pathological components of urine. Textbook for students of general medicine and dentistry / O. A. Nakonechna, S. A. Stetsenko, A. V. Bondareva.– Kharkiv : KhNMU, 2020. – 64 p.

The textbook contains the issues of water-salt and mineral metabolism, their regulation and disturbance, as well as biochemistry of kidney and biochemistry of urine with a detailed examination of normal and pathological components of urine in accordance with the curriculum in the specialty "Medicine" and "Dentistry". The textbook is recommended for students of medical and dentistry faculties of medical universities.

Н18 Водно-сольовий і мінеральний обмін. Сечоутворювальна функція нирок. Нормальні та патологічні компоненти сечі : навч. посібник для студентів мед. та стомат. факульте / О. А. Наконечна, С. А. Стеценко, А. В. Бондарева. – Харків : ХНМУ, 2020. – 64 с.

У підручнику зібрані питання водно-сольового та мінерального обміну, їх регуляція та порушення, а також біохімія нирок та біохімія сечі з детальним вивченням нормальних та патологічних компонентів сечі відповідно до навчальної програми зі спеціальності "Медицина" та "Стоматологія". Підручник рекомендовано студентам медичних та стоматологічних факультетів медичних університетів.

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CONTENT

INTRODUCTION

The human body contains inorganic substances - water and nutrients that are not sources of energy, but their role for the vital activity of the body is quite large. The concepts of water-salt and mineral metabolism are ambiguous.

Water-salt metabolism is considered as the exchange of water and mineral salts. Water and mineral salts dissolved in it constitute the internal environment of the human body, creating conditions for the biochemical reactions occurrence. The hormones regulating the work of the kidneys (vasopressin, aldosterone, atrial natriuretic factor, renin-angiotensin system) play an important role in maintaining water-salt homeostasis. The water-salt balance in the human body is supported by the supply of water and minerals, their excretion with sweat, urine and faces. Osmotic pressure, pH and circulating fluid volume are the main parameters of the body fluid. Maintaining homeostasis is ensured by the constancy of osmotic pressure, pH, the volume of intercellular fluid and blood plasma. Disorders of water-salt metabolism, the main parameters of the body's fluid environment include: tissue dehydration, edema, increase or decrease in blood pressure, shock, changes in the pH of the medium (acidosis, alkalosis).

Mineral metabolism is considered as the exchange of any mineral components of the body, including those that do not affect the basic parameters of the liquid medium, but perform various functions (catalytic, regulatory, transport, depositing, etc.). Knowledge of mineral metabolism and methods of studying it underlie the diagnosis, treatment and prognosis of exogenous (primary) and endogenous (secondary) microelementoses.

The kidneys occupy a special place in the mechanism of central neurohumoral systems action. The kidneys are the most important organs, the main purpose of which is to maintain the dynamic constancy of the internal environment of the body. The kidneys are involved in the regulation of water and electrolyte balance, blood pressure, maintaining the acid-base state, osmotic pressure of body fluids; stimulation of erythropoiesis, etc. The kidneys form urine from the components of blood plasma. Up to 150 various substances are excreted in urine (urea, creatinine, uric acid, ammonium salts, hormone metabolites, etc.). On average, about 40 g of organic matter and about 20 g of inorganic matter are contained in daily urine. Clinical and biochemical examination of urine plays an important role in the clinic for the diagnosis and prognosis of diseases, monitoring the effectiveness of the treatment.

Purpose of training manual: To get acquainted with the chemical structure, properties and functions of water in the life processes of the body. To study the content and distribution of water in cells, tissues and organs; water condition and its exchange. Have an idea of the water pool (ways of entry and excretion from the body); endogenous and exogenous water, water content in

the body, its daily requirement, age characteristics. To study the regulation of water content, its distribution between individual fluid spaces in the body and possible disturbances. To study the biogenic elements classification, to be able to characterize the macro-, oligo-, micro- and ultramicrobiogenic elements, their general and specific functions; electrolyte composition of the body; biological role of the main cations and anions. To get acquainted with the phosphoric-calcium metabolism, its regulation and violation. Determine the role of iron, copper, cobalt, zinc, iodine, fluorine, selenium and other biogenic elements. To study the daily need of the body for mineral substances, their absorption, excretion and deposition, the clinical manifestations of metabolic disturbances of the main biogenic elements.

Familiarize yourself with the basic physicochemical properties (pH, density, color, clarity, odor) and chemical composition of normal urine. Get acquainted with the methods of clinical and biochemical analysis of urine. Remember some physico-chemical constants and biochemical indicators of urine are normal with the purpose of their use for the diagnosis of diseases, the correct assessment of deviations from the norm. To study the pathological components of urine (blood, protein, glucose, keto-new bodies, bile pigments, etc.), the reasons for their appearance in the urine, and qualitative reactions to these components.

CHAPTER I
WATER-SALT METABOLISM

Water and substances dissolved in it, including mineral salts, create the internal environment of the body, the properties of which remain constant or change when the functional state of organs and cells is disturbed. Among the inorganic components of the body, an important role is given to water, which constitutes 55–65 % of the body weight of an adult.

Physico-chemical properties of water. The important and diverse functions of water in the body are due to its unique physicochemical properties, the dipole nature of molecules. High heat of evaporation and high heat capacity provide thermoregulation mechanisms. The high dielectric constant and strongly pronounced ability to form hydrogen bonds make water a universal solvent. A low viscosity of water determines its rapid movement and distribution in the body.

The main functions of water in the body.

1. Essential nutritional factor (losing 12–25 % of water leads to deth).
2. Universal solvent of organic and inorganic substances (being a neutral medium, water does not alter the chemical properties of the substances dissolved in it; ensures their dissociation and, thus, activation of a number of biomolecules).
3. The basis of the internal environment of the body (2/3 of the body weight of an adult person is water).
4. Structural component of tissues (most functioning fabrics contain more water).
5. Takes part in the structural organization of biomembranes and their bases, a double lipid layer in which the hydrophilic surfaces of each monolayer interact with water.
6. Performs the role of hydrate shell of biopolymers and cellular organelles (for example, the interaction of water with proteins ensures their conformation).
7. The transport role is the transfer of substances both within the cell and in the surrounding extracellular space, between the organs.
8. Participation in biochemical reactions (hydrolysis, redox).
9. Regulation of osmotic pressure (isosmia).
10. Maintaining of body temperature (isothermia); water evaporation by the skin is a device for constant body temperature maintaining.
11. Regulation of pH.

Mechanical (weakens friction between articular surfaces, ligaments, muscles).

The water content in the body depends on: age (in embryos – 94 %, in newborns – 80 %, in elderly people – 45 %); sex (in the female body contains less water than men, due to the high content of adipose tissue). In people with obesity, the water content is reduced due to the hydrophobic properties of adi-

pose tissue. All water in the body is updated within a month, and intracellular - in a week. The water content is uneven in different organs and tissues: the liver, the white matter of the brain – 70–85 %; muscle tissue, myocardium – 76–80 %; kidneys, lungs – 80–82 %; bone and adipose tissue – less than 30 %; blood plasma, lymph, cerebrospinal fluid, urine, tears – at least 90 %.

The body's need for water. The daily requirement for water is 1.5–2 liters (adults 40 ml/kg body weight, children – 100–150 ml/kg body weight). The body's need for water depends on: age, intensity of metabolic processes, physical activity, the functional state of the kidneys, body temperature and the environment, the nature of nutrition. Absorption of water occurs throughout the gastrointestinal tract, most of it is reabsorbed in the small intestine.

A pool of water in the body. The main routes of entry and removal of water from the body is presented on *Fig 1*.

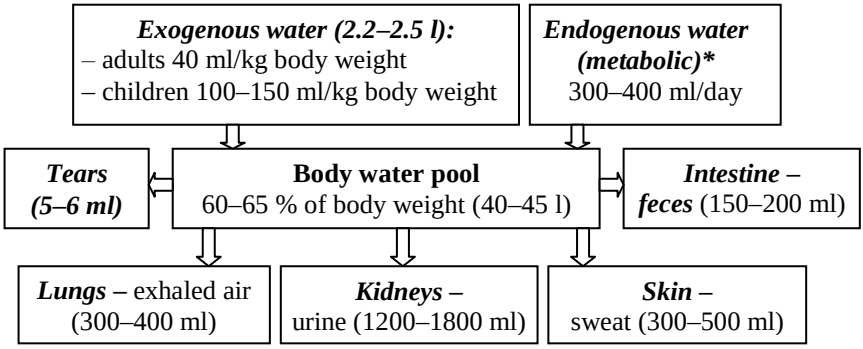


Fig. 1. A pool of water in the body.

****–-*** *The amount of endogenous (metabolic) water depends on the nature of the decomposing substrate: thus, upon oxidation of 100 g of fat, 107 ml of water are formed, 100 g of protein – 41 ml of water, 100 g of carbohydrates – 55 ml of water.*

The kidneys are the main organ of excretion of water and electrolytes.

Water losses in the body are divided into: obligatory (the smallest amount of liquid with which the final products of metabolism are released at maximum concentration) - 0.5 l / day; adjustable depending on the amount of water injected - 0.8-1.3 l.

The distribution of water in the body. Intra- and extracellular fluids are distinguished in the body. This division is based on the fact that the extracellular fluid forms a single phase in all parts of the body. In addition, both body fluids differ in electrolyte composition: in the extracellular fluid, sodium prevails from cations, and from anions - chlorides, bicarbonates; the intracellular fluid from cations contains potassium, magnesium, as well as proteins and phosphates. In adults, 2/3 of the body's water accounts for intracellular fluid,

and 1/3 for extracellular fluid (*Fig. 2*). The distribution of water between cells and the extracellular space depends on the difference in osmotic pressure of intracellular and extracellular fluid. The distribution of water in the body depends on age. Thus, in infants, extracellular fluid forms most of the body mass.

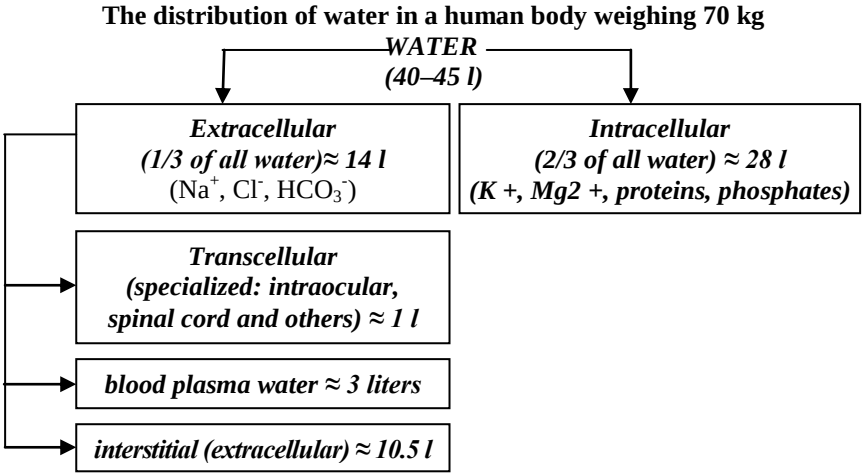


Fig. 2. The distribution of water in the human body weighing 70 kg

Fractions of water in the body.

1. Unorganized water (moves freely in the extracellular space), labile, mobile.

2. Organized (associated with the structures of the extracellular space – with collagen, mucopolysaccharides).

3. Constitutional (part of the molecules of proteins, lipids, carbohydrates).

Intensive exchange between the body's main water basins, they are separated from each other by semipermeable membranes. Water is constantly moving, constantly sharing with other secrets and the external environment. With an average body weight of 70 kg, the volume of free water and bound hydrophilic colloids is about 60–65 % of body weight.

Water-salt metabolism and secretion of digestive juices. In particular, the movement of water is carried out, thanks to the release of digestive juices. The daily secretion of all digestive glands is 7–8 liters (*Table 1*). Secrets differ in their specific ionic composition. In the normal functioning of the body, secretions of the digestive glands are absorbed back into the small intestine, and about 2 % (150–200 ml) is lost with feces. A large amount of water and electrolytes may be lost in violation of the reverse suction. For example, in pathological conditions involving vomiting and diarrhea, the volume of extracellular fluid decreases, tissue dehydration occurs. This leads to an increase in the blood plasma and intercellular fluid albumin content, which leads to an increase in

pressure in the intercellular space, thickening of the blood and impaired hemodynamics. Diarrhea in acute intestinal infections (salmonellosis, dysentery, etc.) is usually caused by increased secretion of digestive juices through activation of adenylate cyclase (since the regulation of the production of the intestinal juice occurs through the adenylate cyclase mechanism).

Table 1

Quantitative characterization of secretions of the digestive glands

Secrets of the digestive glands	Amount (l)
Saliva	1,5
Gastric juice	2,5
Bile	0,5
Pancreatic juice	0,7
Intestinal juice	3,0

The main parameters of the body fluid: osmotic pressure, pH and volume.

Osmotic pressure is provided by the concentration of electrolytes and non-dissociated substances dissolved in cellular and extracellular fluids; depends on the total number of ions and molecules in the solution; expressed as osmolarity or osmolality (osmolarity is the number of mmol per 1 l of solution; osmolality is the number of mmol in 1 kg of solvent). The osmotic pressure of the extracellular fluid is largely dependent on sodium chloride, which is contained in this fluid in the highest concentration. Therefore, the main mechanism of regulation of osmotic pressure is associated with a change in the rate of release of either water or sodium chloride. Osmotic pressure and pH of the extracellular fluid and plasma are the same; they are also the same in the intercellular fluid of different organs.

The pH value inside the cells of different tissues may be different, which is associated with the features of metabolism, mechanisms of active transport, selective permeability of membranes, etc. But at the same time, the pH value characteristic of a certain cell type is maintained at a constant level; an increase or decrease in pH leads to impaired cell functions.

Maintaining the constancy of the intracellular environment is ensured by the constancy of the osmotic pressure, pH, volume of the intercellular fluid and blood plasma (extracellular fluid). The constancy of extracellular fluid parameters is determined by the functional ability of the kidneys and hormones that regulate their function.

CHAPTER 2
MINERAL EXCHANGE

Mineral components should be approximately 4–16 % of the dry weight of the food. They are considered as essential nutritional factors along with vitamins, essential amino acids, polyunsaturated fatty acids.

Biogenic elements make up about 5–6 % of body weight.

Classification of nutrients in the body:

– macrobiogenic (1 % or more): O, C, H, N, P, Ca;

– oligobiogenic (0,1–1 %): K, Na, Cl, Mg, Fe, S;

– microbiogenic (0,01–0,1 %): Zn, Mn, Cu, Co, Br, F, J;

– ultramicrobiogenic (less 0,01 %): Li, B, V, Cr, Ni, Al, Si, Sn, As, Se, Ti.

The main functions of biogenic elements:

– structural (for example, the calcium content in bone tissue in an adult is 1.0–1.5 kg, phosphorus – 500–900 g, magnesium - up to 10 g; Ca, P, Mg, F, Si – create the mineral matrix of the bone, enamels, dentin; ions Ca, PO4, Co, Mg, F – the most important elements of dentin; Ca, P – are included in the structure of carboxy and fluorapatite (Ca10(PO4)6(OH)2, Ca10(PO4)F2) tooth);

– an integral part of biologically active substances (for example, zinc is bound to insulin; iron is a component of hemoglobin, myoglobin, cytochrome, catalase, peroxidase; iodine is part of the structure of thyroid hormones);

– regulatory (for example, Na, Cl – participate in the regulation of osmotic pressure; Na, Cl, Fe, Mg, Mn, Cu, K, etc. – participate in the regulation of enzyme activity; participate in the regulation of acid-base equilibrium in buffer systems blood);

– cofactor (for example, Mn^{2+} – arginase cofactor, – xanthine oxidase cofactor; $Fe^{2+,}$ Cu^{2+} – cytochrome oxidase aa3 cofactors);

– transport (for example, metal-dependent ATP-ases);

– energy (ADP + Pi → ATP);- hemostatic (Ca);

– participation in blood formation processes (Fe, Cu, Co);

– participation in tissue respiration (Fe, Cu);

– participation in the creation of the difference of the bioelectric potential on the membrane and the transmission of excitation through the neuromuscular fiber (Na, K, Ca);

– biopolymer structure stabilizers (for example, Mg^{2+} stabilizes the tertiary structure of RNA).

General characteristics of the main biogenic elements in human body

Potassium. The body contains about 160 g; in erythrocytes is 20 times more (95–96 %) than in blood plasma; the main intracellular cation (98 % is inside the cells); sodium synergist and calcium antagonist; 85 % is excreted in the urine, the rest is excreted in sweat and feces; completely reabsorbed by proximal renal tubule cells from primary urine.

The concentration of potassium in the blood is 3.5–5.3 mmol/l, in the erythrocytes – 77.8–95.7 mmol/l; daily requirement – 2–4 g.

The role of potassium.

1. Maintenance of osmotic pressure and acid-base homeostasis (the concentration of potassium increases with acidosis and decreases with alkalosis).

2. Participation in the distribution of water in the body; reduces the hydrophilicity of tissue colloids, contributes to the loss of water.

3. Participation in the provision of transmembrane potential difference.

4. Participation in the biosynthesis of protein, glycogen, hemoglobin gas transport function as a cofactor.

5. Stimulates the formation of acetylcholine, regulates the conduction of excitation in synapses.

6. Participation in muscle contraction.

7. Participation in glucose phosphorylation, the synthesis of high-energy compounds - creatine phosphate, acetylcholine.

8. Participation in the energy exchange.

9. Activator of enzymes catalyzing the transfer of phosphate groups (kinases).

10. Participation in the formation of short-term memory.

11. Participation in the activities of the cardiovascular system, gastrointestinal tract and kidneys.

12. Participation in the regulation of the synthesis of DNA, RNA and protein.

13. Strengthens the functioning of the parasympathetic nervous system, reduces the stimulating effect of sodium on muscle tissue.

Regulation of exchange of potassium. The pH of extracellular fluid, as well as hormones (insulin, aldosterone) affect the distribution of potassium between extracellular and intracellular fluid. The maintenance of potassium in the human body depends on the regulation of its excretion by the kidneys. Most of the potassium is reabsorbed in the proximal part of the renal tubules and the loop of Henle from the primary urine. Potassium is secreted in exchange for sodium ions under the influence of aldosterone, insulin reduces potassium excretion by the kidneys, and promotes its transport into cells in the proximal tubule. The renal mechanism of regulation effectively prevents hyperglycemia.

Hypokalemia – decrease of blood potassium concentration below 3.5 mmol/l. The main causes of hypokalemia are prolonged starvation, potassium loss through the gastrointestinal tract as a result of vomiting, diarrhea, malabsorption, pylorostenosis, administration of potassium-non-sparing diuretics, renal diseases, aldosterone hyperproduction, adynamia, asthenia, apathy.

The main clinical symptoms of hypokalemia are: fatigue, muscle weakness, nausea, vomiting, constipation, weak irregular pulse, dryness of the skin, weakening of muscle contractions, tendon reflexes, tachycardia, low blood pressure, arrhythmia.

Hyperkalemia – increasing the concentration of potassium in the blood of more than 5.3 mmol/l. The main causes of hyperkalemia are: the release of potassium from cells in case of tissue damage (burns, purulent-septic diseases, tumors) and a violation of its excretion with urine, intravenous administration of potassium-containing solutions.

The main clinical symptoms of hyperkalemia: irritability, anxiety, spasmodic abdominal pain, nausea, vomiting, diarrhea, weakness, paresthesia, bradycardia, arrhythmia, up to cardiac arrest (with a potassium content of 7.5–10.0 mmol/l.

Foods rich in potassium: apricots, avocados, bananas, carrots, legumes, tomatoes, melons, nuts, oranges, potatoes, raisins, pumpkins, spinach, turnips.

Sodium. In total, the body contains 70–110 g of sodium; is the main extracellular cation; inside the cell, the sodium content is between 2.5 and 9 %, in bone tissue – about 40 %; Sodium salts are predominantly dissolved in blood plasma and lymph.

Sodium concentration in blood plasma is 130.5–156.6 mmol/l, in erythrocytes – 13.48–21.75 mmol/l; daily requirement – 4–6 g.

The role of sodium.

1. Maintaining the composition and volume of extracellular fluid.
2. Participation in osmoregulation; determines the osmolality of blood plasma and extracellular fluid.
3. Participation in maintaining acid-base balance (bicarbonate buffer system).
4. Participation in the generation of membrane potential and action potential on the plasma membranes of excitable cells.
5. Enzyme activators (eg, saliva alpha-amylase).
6. Participation in the regulation of cell volume.
7. Participation in the active transport of ions, monosaccharides, amino acids, etc.
8. Participation in the regulation of the synthesis of DNA, RNA, proteins.
9. Participation in the regulation of vascular tone (through the potentiation of the action of adrenaline).

Regulation of sodium metabolism. The main hormones that regulate the concentration of sodium in the blood are aldosterone, a natriuretic factor, and the renin-angiotensin system.

Aldosterone stimulates the reabsorption of sodium ions by the epithelial cells of the distal kidney tubules in exchange for potassium ions or hydrogen ions while reducing the osmolarity of extracellular fluid. Mineralocorticoids cause sodium retention and loss of potassium in the salivary and sweat glands, the mucous membrane of the large intestine.

The renin-angiotensin system reacts to a decrease in circulating blood volume, which causes a decrease in renal blood flow and leads to the secretion of renin, the formation of angiotensin II. Angiotensin II, in turn, stimulates the secretion of aldosterone and causes vasoconstriction.

The atrial natriuretic hormone is formed and secreted into the blood in response to an increase in circulating blood volume, an increase in blood pressure. The hormone inhibits sodium reabsorption in the renal tubules. The volume of circulating blood decreases, blood pressure decreases due to increased excretion of sodium and water from the body.

Hyponatremia – decrease in blood sodium concentration below 130.5 mmol/l. Observed with excess water or loss of fluids rich in sodium. *The main clinical symptoms of hyponatremia:* irritability, fatigue, dizziness, hypotension, dry mucous membranes, tremor, convulsions, fatigue, apathy, nausea, vomiting, tachycardia, loss of appetite.

Hypernatremia - an increase in the concentration of sodium in the blood above 156.6 mmol/l. It develops as a result of water loss or an increase in sodium intake from food or perfusion solutions, as well as in aldosteronism, kidney disease, and intake of glucocorticoid drugs. *The main clinical symptoms of hypernatremia:* hypertension, causing the release of fluid from the cells (cell dehydration), edema, severe thirst, fatigue, anxiety, agitation, tachicardia, coma.

Foods rich in sodium: sea kale, mussels, flounder, salt, caviar, olives.

Calcium. In bone tissue, dentin, tooth enamel contains 90–99 calcium; the concentration in the extracellular fluid is approximately 1.3×10^{-3} mol/l, in the cytoplasm $–10^{-7}$ mol/l; the calcium cell contains more in the mitochondria and the endoplasmic reticulum; in blood plasma, calcium present in three forms: ionized, bound, and complex; at normal blood pH, about half of the total plasma calcium is in ionized form; a slightly smaller amount of calcium is associated with proteins (albumin), the rest forms complexes with anions.

The concentration of calcium in serum is 2.25–2.75 mmol/l; daily requirement – 0.8–1.2 g

The role of calcium.

1. Participation in the processes of neuromuscular excitability (in hypercalcemia – inhibited, and in hypocalcemia – increased neuromuscular excitability).
2. Participation in the processes of muscle contraction, contractile ability of the myocardium.
3. Participation in the process of blood coagulation (protein binding – plasma factors II, VII, IX, X).
4. Reduced capillary permeability.
5. Activation of enzymes (trypsinogen, lipase, amylase, ATP-ase).
6. Performing the role of a secondary mediator in the transmission of hormonal signal, promotes the secretion of mediators, the release and physiological action of hormones.
7. Participation in the regulation of protein phosphorylation.
8. Structural function (for example, calcium salts provide a rigid structure of bones and teeth; calcium is associated with phosphorus and forms mineral salts of bones and teeth).

Regulation of calcium metabolism. It is carried out by thyroid and parathyroid hormones, as well as vitamin D. Parathyroid hormone and vitamin D3 (active form $1.25(OH)_2D_3$) increase the concentration of calcium in the blood, and calcitonin, on the contrary, reduces.

Parathyroid hormone stimulates the mobilization of calcium from bone tissue; stimulates calcium reabsorption in the distal tubules of the kidneys; activates the synthesis of calcitriol in the kidney, which leads to an increase in calcium absorption in the intestine (*Fig. 3*).

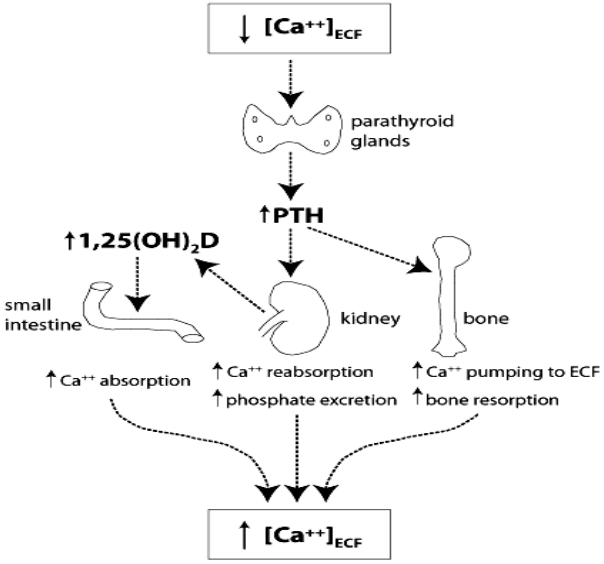


Fig. 3. Regulation of calcium metabolism by parathyroid hormone

The active form of vitamin D_3 is a synergist of parathyroid hormone in action on bone tissue - calcitriol ($1.25(OH)_2D_3$). Calcitriol induces the synthesis of calcium-binding proteins in the intestine, which provide calcium absorption; stimulates calcium reabsorption in the distal tubules of the kidneys; promotes the mobilization of calcium from bone tissue. It should be noted that calcitriol maintains such concentrations of calcium and phosphate, which are necessary for the formation of hydroxyapatite crystals deposited in bone collagen fibrils. If the calcitriol synthesis is violated, the formation of new bones is slowed down and the bone tissue renewal is disturbed.

Calcitonin inhibits the release of calcium from bone tissue, reducing the activity of osteoclasts; reduces calcium reabsorption in kidney steel tubules. *Hypocalcemia* – a decrease in blood calcium less than 2.25 mmol/l. It develops with: insufficient intake of vitamin D (rickets) or calcium, renal failure, impaired

hormonal regulation processes (hyperthyroidism, hypoparathyroidism). *The main clinical symptoms of hypocalcemia:* numbness and tingling in the limbs, increased neuromuscular excitability up to the development of clonic-tonic seizures.

Hypercalcemia – an increase in blood calcium more than 3.0 mmol/l. The main causes of hypercalcemia: increased secretion of parathyroid hormone, hypervitaminosis D, sarcoidosis, hypothyroidism. *The main clinical symptoms of hypercalcemia:* the formation of renal nodules, depression, neuromuscular excitability, increased blood clotting, anorexia, nausea, vomiting, pruritus, polyuria, asthenia, adynamia, and arhythmia.

Calcium-rich foods: dairy products (yoghurt, cheeses), nuts, legumes, spinach, cabbage.

Phosphorus. About 1 % of human body weight (up to 1 kg) is inorganic phosphates; mainly localized in bone and teeth; distributed in the body as follows: 85 % – bones, teeth; 14 % – soft tissue, 1 % – extracellular fluid; the main intracellular element. Phosphorus metabolism is closely related to calcium metabolism.

The concentration of phosphate in the blood plasma is 0.8–1.4 mmol/l; daily requirement is 1–2 g.

The role of phosphorus.

1. Structural (part of the bone tissue of the teeth, a component of other tissues of the body; the structural element of phosphoproteins, phospholipids – the main components of cell membranes).

2. Participation in energy transfer in the form of high-energy bonds (ADP, ATP).

3. Participation in the phosphorylation of organic compounds.

4. Participation in the regulation of acid-base balance (phosphate buffer system).

5. Participation in the processes of growth, cell division, storage and use of genetic information (as part of nucleic acids).

Regulation of phosphorus metabolism. It is performed by thyroid and parathyroid hormones, Vitamin D. Parathyroid hormone stimulates the functional activity of osteoclasts, releases phosphates and removes into the blood; in the kidney reduces phosphate reabsorption and leads to phosphaturia. Calcitonin inhibits the functioning of osteoclasts; as a result, the resorption of both the organic and inorganic components of the bone matrix is inhibited, which leads to a decrease in the intake of phosphate in the blood. Vitamin D and its metabolites enhance the absorption of phosphorus in the intestine.

Changes in the phosphorus content, even in a wide range, usually do not cause clinical manifestations. Phosphorus deficiency is rare.

Hypophosphatemia – a decrease in blood phosphorus below 0.8 mmol/l. It is noted in violation of the absorption in the intestines, alcoholism, vomiting, diarrhea, loss of phosphate in the urine, hyperparathyroidism, vitamin D-resistant rickets, osteomalacia, Fanconi syndrome.

The main clinical symptoms of hypophosphatemia: memory impairment, bone pain, cramps, muscle weakness, muscle pain, numbness and tingling in the fingertips, poor coordination of movements.

Hyperphosphatemia – an increase in the phosphorus content in the blood above 1.4 mmol/l. It is marked with excessive intake, cell destruction, damage to the renal glomeruli, hypoparathyroidism, acromegaly, and diabetes mellitus. *The main clinical symptoms of hyperphosphatemia:* anorexia, nausea, vomiting, muscle weakness, hyperreflexia, tetany, tachycardia.

Foods rich in phosphorus: fish, meat, eggs, nuts, seeds.

Magnesium. An adult's body contains 20–25 g of magnesium, half of which (50–60 %) are deposited in the bones, and 1/3 in the muscles; in the gastrointestinal tract only 30–40 % of magnesium supplied with food is absorbed; about 25 % of magnesium is bound to plasma proteins, a small part forms complex compounds, and the rest is free, ionized; main intracellular cation.

The concentration of magnesium in serum is 0.7–1.0 mmol/l; daily requirement – 300–500 mg.

The role of magnesium.

1. Structural (composed of bones, tooth tissues).
2. It acts as a cofactor and activator of enzymes (for example, Mg^{2+} – dependent ATPases, acetylcholinesterase).
3. Participation in reactions of glycolysis.
4. Participation in the exchange of macroergic compound (ATP cleavage).
5. Influence on the contractility of the myocardium and smooth muscles (determines neuromuscular excitability).
6. It has a depressive effect on the central nervous system.
7. Participation in the metabolism of cholesterol, nucleotides, protein biosynthesis.
8. Stabilization of the structure of nucleic acids, ribosomes, chromatin.
9. Regulatory function (maintains the level of potassium in the cell).

The regulation of the magnesium exchange is carried out by changing the reabsorption in the renal tubules. There is no specific hormonal regulation system for this process. *Hypomagnesemia* - a decrease in the blood magnesium content below 0.7 mmol/l. The main causes of hypomagnesemia: profuse vomiting, diarrhea, chronic alcoholism, malabsorption syndrome, infusion therapy with a low content of magnesium, cardiovascular diseases (ischemic heart disease, atherosclerosis), kidney and thyroid diseases, hyperadosteronism, diabetes mellitus (removal of magnesium with urine due to glycosuria), the use of diuretics, reduced intake of magnesium from food, loss with feces and urine. *The main clinical symptoms of hypomagnesemia:* apathy, leg muscle cramps, insomnia, mood changes, hallucinations, confusion, anorexia, nausea, paresthesia, dysphagia, tachycardia.

Hypermagnesemia – an increase in the blood magnesium content of more than 1.0 mmol/l. The main causes of hypermagnesemia: acute and chronic kidney failure, Cushing's disease, the use of magnesium-containing drugs. *The main clinical symptoms of hypermagnesemia:* nausea, vomiting, skin hyperemia, mental disorders, drowsiness, muscle weakness, hypotension.

Magnesium is used in medical practice for treatment of pregnant women hypertension, coronary heart disease, arrhythmias, central nervous system diseases.

Foods rich in magnesium: chocolate, cheese, fish, cottage cheese, eggs, carrots, cabbage, beets, tomatoes, rye bread, buckwheat, wheat bran, spinach.

Iron. The iron content in the human body is 3–4 g.

Basic funds iron in the body.

1. Heme (cell) – is a part of hemoglobin, myoglobin, enzymes (cytochromes, catalases, peroxidases), metalloproteins (aconitases, etc.).

2. Non-heme iron.

3. Extracellular: free iron of plasma and iron-binding proteins (transferrin, lactoferrin) involved in iron transport.

4. The iron depot is located in the body in the form of two protein compounds – ferritin and hemosiderin.

The role of iron.

1. Structural (part of the iron-containing proteins: hemoglobin, myoglobin, cytochrome, etc.).

2. Used for the synthesis of hemoproteins and other iron-containing proteins.

3. Participation in redox reactions in the composition of cytochromes and iron-sulfur proteins (electron transfer through the respiratory chain).

4. Transport (as part of hemoglobin carries oxygen and carbon dioxide).

Iron absorption in the intestine is an active process. Iron penetrates cell membranes only in the form of Fe^{2+}. Ascorbic acid (vitamin C) improves the absorption of iron. In women, iron absorption is increased, due to the loss of iron during period. In blood plasma, iron is in the oxidized form of Fe^{3+} and is associated with transferrin.

The concentration of free iron in serum is 12.5–30.4 μmol /l. Almost all serum iron is found in transferrin. The iron deficiency in the body is accompanied by an increase in the transferrin content (normally 0.4 g/l). Transferrin transports iron to the bone marrow and other tissues for the purpose of depositing or using as needed. Storage of iron in the body - liver, spleen, red bone marrow. The daily requirement for iron depends on age, gender, and on average is 10–15 mg. Iron metabolism in the body is shown in *Fig. 4*.

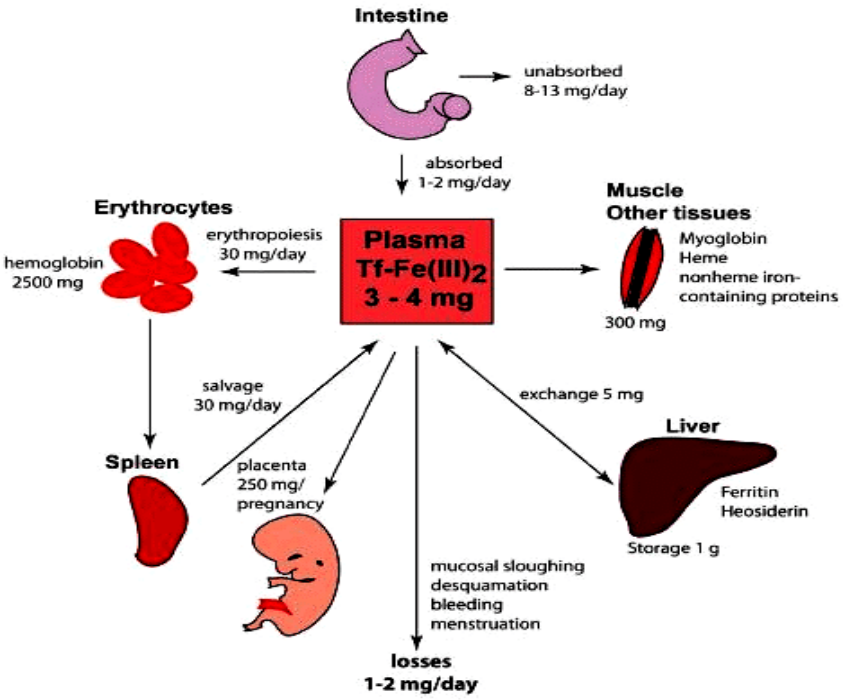


Fig. 4. Metabolism of iron in the body

The role of iron-containing proteins.

1. Transport and storage of oxygen (hemoglobin, myoglobin).
2. Participation in redox reactions (oxidases, cytochromes, peroxidases, etc.).
3. Participation in the process of blood formation.
4. Regulatory (participation in the regulation of immune processes, ensuring the activity of interferon and killer cells).
5. Participation in the detoxification processes in liver.
6. Participation in cell division.
7. Participation in biosynthetic processes (for example, in DNA synthesis).
8. Participation in the metabolism of biologically active compounds (catecholamines, collagen).
9. Participation in energy metabolism (through the enzymes of the tricarboxylic acid cycle containing iron).

The decrease in the iron content in the body occurs when there is an inadequate intake with food, poor absorption in the gastrointestinal tract (anacid and hypoacid gastritis, gastric and intestinal resections); increased utilization of organs and tissues (pregnancy, body growth in childhood, increased physical

exertion), loss (bleeding), redistribution (systemic diseases of connective tissue: collagenosis, rheumatism, rheumatoid polyarthritis; and chronic leukemia, chronic hepatitis, cirrhosis, myocardial infarction). *A decrease of the iron content in the body* is accompanied by hypochromic microcytic anemia (color indicator – 0.8 or less), trophic disorders in organs and tissues, mental disorders, and a decrease in immune resistance.

Increasing the iron content in the body occurs: an excess of intake, insufficient use in the blood-forming organs; accompanied by hepatosis with cirrhosis, splenomegaly, the development of copper and zinc ions deficiency. Excess iron is deposited in the parenchymal organs in the form of hemo-sederin; deposition in the liver leads to cirrhosis, pancreas – diabetes, skin – pigmentation.

Foods rich in iron: green apples, liver, pine nuts, spinach, oatmeal, legumes, lentils.

Copper. About 100 mg of copper is contained in the body of an adult; copper is concentrated in the liver, brain, blood mainly; almost 90 % of copper is as a part of ceruloplasmin.

The concentration of copper in the blood is: 11–22 μmol/l; daily requirement – an average of 2.5 mg.

The role of copper.

1. Participation in tissue respiration (part of cytochrome oxidase).
2. Participation in the oxidative deamination of amines.
3. Participation in the formation of cross-links in collagen and elastin (lisoxidase).
4. Participation in the synthesis of norepinephrine (part of the dopamine-β-monooxygenase).
5. Participation in the synthesis of melanin (part of tyrosinase).
6. Antioxidant function (inactivates superoxide radical in the cytoplasm, being part of superoxide dismutase).
7. Participation in erythro-and leukopoiesis.
8. Participation in the synthesis of female sex hormones.
9. Participation in immune processes.
10. Participation together with iron and vitamin C in the synthesis of hemoglobin.
11. Participation in the metabolism of bile acids, steroids, unsaturated fatty acids.
12. Participation in the neutralization of xenobiotics.
13. Participation in the synthesis of myelin.

Hypocupremia - a decrease in the copper content in the blood below 11 μmol/l. *Hypocupremia is observed in*: Konovalov-Wilson disease, burns, coronary heart disease, iron deficiency anemia. *The main clinical symptoms of hypocupraemia*: fatigue, frequent headaches, depression, hypochromic anemia, skin rash, diseases of the nervous system, osteoporosis.

Hypercupremia – increase in the copper content in the blood above 22 μmol/l. Hypercupremia occurs with excessive copper intake in the body, metabolic disturbances, multiple hemodialysis sessions, aplastic and megaloblastic anemia, thalassemia, Hodgkin's lymphoma, hepatitis, cirrhosis). *The main clinical symptoms of hypercupraemia:* depression, pain in muscles and joints, insomnia, irritability, dyspepsia (vomiting, nausea, diarrhea, abdominal pain), metallic taste in the oral cavity, neurological disorders (increased salivation, impaired behavior, speech, epileptic seizures).

Foods rich in copper: spinach, buckwheat, nuts, liver, rye bread, legumes, seafood, apricot, avocado.

Molybdenum. An adult's body contains about 9 mg, of which 5 mg is in the bones, 2 mg is in the liver. Daily requirement is 0.2–0.3 mg.

The role of molybdenum.

1. Participation in the decay of purine nucleotides (part of the xanthine oxidase) and the removal of uric acid from the body with urine.
2. Normalizes sexual function.
3. Stimulates growth.
4. Strengthening of dental tissue (retains fluoride in the body, helps prevent tooth decay).
5. Participation in the synthesis of ascorbic acid.
6. Antitoxic factor (affects the decay of sulfides, alcohol).

Molybdenum deficiency is extremely rare.

Excessive intake of molybdenum in the body activates the synthesis of xanthine oxidase, increases the formation of uric acid and, as a result, the disease "molybdenum gout" occurs.

Foods rich in molybdenum: beans, dogrose, beef liver, lentils, cocoa.

Zinc. An adult's body contains 1.4–2.3 g of zinc, of which 20 % is in the bones, 65 % is in the muscles, 9 % is in the blood, and the rest is in the liver and prostate gland. The daily requirement is 10–20 mg.

The role of zinc.

1. Participation in the growth and metabolism of cells.
2. Participation in protein biosynthesis.
3. Wound healing effect.
4. Activator of immune responses.
5. Participation in maintaining and improving memory.
6. Participation in the maintenance of taste and olfactory sensitivity.
7. Participation in reproductive function.
8. Participation in the transfer and implementation of genetic information (in the composition of DNA and RNA polymerases, polyadenylate polymerase).
9. Participation in the deposit of insulin in the Langerhans' cells (zinc-insulin complex).

Zinc deficiency in the body is associated only with poor nutrition, leads to growth retardation, development of reproductive function, poor wound healing, memory loss, brittle nails (white spots - leukonychia), hair loss, dermatitis, immunodeficiency states, impaired taste and odor perception.

Foods rich in zinc: meat, liver, eggs, nuts, pumpkin seeds, bran.

Iodine. The human body contains 20–35 mg of iodine. The distribution in the body is: it is least concentrated in the blood and kidneys, most of all in the thyroid gland (about 10–15 mg). Iodine in the human body is predominantly in organic form. A-cells of the thyroid gland selectively capture iodides from the blood flowing through the gland and form the hormones T3, T4 and thyroglobulin, which is a reserve form of thyroid hormones and contains about 90 % of the total iodine present in the thyroid gland.

The content of iodine in the blood during its normal entry into the body is 10–15 μg /l, while the total extracellular reserve of iodine is about 250 μg. Most of this stock is iodine, absorbed in the intestines. In addition, the same stock includes a small amount of iodine, which is secreted by thyrocytes, as well as iodine formed during the exchange of thyroid hormones in peripheral tissues.

Daily requirement – 100–150 mcg.

The role of iodine.

1. Participation in the thyroid hormones synthesis.

2. Participation in the processes of growth and development of the body, the production of heat (as part of thyroid hormones).

Iodine-deficient diseases, such as iodine-deficient hypothyroidism, diffuse non-toxic goiter, endemic goiter occur when iodine is insufficiently ingested with food. *The main clinical symptoms of iodine deficiency in the body:* feeling of cold, an increase in the size of the thyroid gland, shortness of breath, painful sensations in the heart, weakness, drowsiness, hearing loss, weakening of memory, pallor and dry skin, dull hair.

An excess of iodine usually occurs when working in hazardous industries. *The main clinical symptoms of iodine excess in the body:* muscle weakness, irritability, hyperthermia, depigmentation of the skin, premature graying of hair.

Foods rich in iodine: seafood, iodized salt, black currant, grapes, black chokeberry, tomatoes, spinach, asparagus, carrots, radish.

Cobalt. The human body contains 0.5–1.5 mg of cobalt; 14 % is in the bones, 43 % is in the muscles and the rest is in the soft tissues.

Daily requirement – 20–50 mg.

The role of cobalt.

1. Participation in the synthesis of vitamin B_{12}.

2. Participation in the processes of blood formation and maturation of red blood cells, the synthesis of amino acids, proteins, DNA, RNA (as part of vitamin B_{12}).

3. Participation in redox reactions (as part of oxidoreductases), hydrolysis reactions and transfer of chemical groups.

4. Stimulates the growth of bone tissue.

5. Participation in the formation of thyroid hormones.

6. Antiatherosclerotic effect.

7. Participation in the synthesis of insulin.

Reduction of cobalt in the body occurs with a decrease in dietary intake, impaired absorption in the intestine, the formation of transcobalamin in the blood, B_{12} metabolism in the tissues, as well as increased removal of vitamin B_{12}, protein-bound and free cobalt. *Reducing the content of cobalt in the body* leads to the development of vitamin B_{12}-dependent hyperchromic anemia, leukopenia, thrombocytopenia, decreased cells' division, cell renewal (especially mucosal cells of the digestive tract and skin), impaired central nervous system, reduced thyroid hormone-biosynthesis.

An excess of cobalt is possible only in people employed in industry; accompanied by damage to the respiratory system, impaired blood formation, disorders of the central nervous system, dyspeptic disorders, impaired sense of smell, chronic rhinitis, pharyngitis.

Food products rich in cobalt: beets, radishes, cabbage, potatoes, onions, legumes, grains, pears, apricots, hearts, beef, eggs, cod, sardines.

Fluorine. The adult body contains 2.5–3 g; in tooth enamel – 90 %, in other tissues of the tooth and in bone tissue – 9 %. Fluorine is excreted mainly with urine. Daily requirement is 1.5–5 mg.

The role of fluoride.

1. Participation in the formation and strengthening of bone tissue and tooth enamel (with phosphorus and calcium); Included in the fluorapatite bone and tooth, which increases the resistance of enamel to destruction.

2. Participation in the activation of hemopoiesis.

3. Participation in the elimination of heavy metal salts from the body.

4. Reduces the activity of acid-forming bacteria.

5. Fluorides increase alkaline phosphatase activity.

A decrease in the fluorine content in the body leads to the development of dental caries, osteoporosis. Fluorosis (mottling of teeth), chronic poisoning development with an *excess of fluoride.*

Foods rich in fluorine: tea, nuts, grains, onions, potatoes, apples, rice, spinach, seafood, milk, eggs, meat.

Selenium. The content in the body is about 20 mg (mainly in the spleen, liver, kidneys, heart, testes).

Daily requirement – 20–70 mcg.

The role of selenium.

1. Antioxidant (as part of antioxidant enzymes, for example, glutathione peroxidase).

2. Participation in immune responses.

3. Participation in the metabolism of thyroid hormones.

4. Enhance reproductive function in men.

Manifestations of a decrease in the content of selenium in the body: a sharp decrease in performance (physical and mental), cellular and humoral immunity, frequent colds or skin pustular diseases, slow regeneration after injuries, increased tendency to cardiovascular, infectious, gastroenterological, malignant diseases, impaired vision (acuity, accommodation), the emergence of sexual weakness.

CHAPTER 3
FEATURES OF THE WATER-SALT AND MINERAL METABOLISM IN CHILDREN'S BODY

The tissues and organs of a child's body contain significantly more water than an adult. The water content in newborns is 80 %, in children of the first five years – 70 % of body weight. At physiological lowering of body weight (in the first days after birth), the child loses water (8.7 % of body weight) by evaporation from breathing, from the skin surface, with urine and meconium. The removal of water by evaporation amounts to 52–75 % of the total value. With age, changes in the content of intra- and extracellular fluid occur (*Table 2*). Children have large body surface and kidney immaturity. Extrastropanal water loss in children is 1 ml per kg of body weight per hour (in adults – 0.45 ml/kg). Water loss by perspiration – up to 30 ml/kg.

Table 2

Total water content (%) and ratio in the distribution of fluid depending on age

Indicator	Newborns	1–6 months	6 months – 1 year	1-5 years old	Adult
Total water	75–80	70	70	60–65	60–65
Intracellular	30−40	30	35	35–40	40–45
Extracellular					
Interstitial	32–44	34,5	30	25	17
Plasma	6	5,5	5	5	5

In childhood, water exchange is more intense than in adults. Young children have high permeability of cell membranes, and fixation of fluid in cells and intercellular space is weak. A child has almost the same volumes of chloride (extracellular water) and inulin space (labile water) are and make up 41 and 40 % of body weight, respectively (in an adult – 26.4 % and 16 %). Children has labile water metabolism, due to the mobility of extracellular water. During dehydration (loss of fluid) there is a significant decrease in both extra- and intracellular fluid.

The water needs of children are much higher than in adults: from 10 days of life to 5 years it is 130–150 ml/kg body weight.

Sodium. The sodium content in the serum of the newborn is the same as in the mother's blood (≈ 142 mmol/l). The intracellular content of sodium in children is higher, which is associated with the maturation processes of the "sodium pump" in the cells.

Potassium. The potassium content in newborns is up to 6.6 mmol/l. The content of potassium in the blood of more than 6 mmol/l is dangerous for the life of children older than 1 month. The daily need for potassium is higher than that of adults. The lack of potassium in the children's body inhibits the growth and development of the child.

Calcium. Enters the fetus transplacental through active transport. In the last months of pregnancy, up to 100–150 mg of calcium per kg of fetus weight is daily applied. The body of the newborn contains 30 g of calcium. Up to 4 months there is a rapid growth and mineralization of bone tissue. To ensure this process, the child needs to receive 500 mg of calcium daily. The children's body of the first year contains 400 mmol/kg body weight of calcium. The calcium content in the blood of full-term newborns is 2.25–2.45 mmol/l, the first year of life and older is 2.5–2.8 mmol/l. Healthy children with urine emit 0.1–0.3 g/day of calcium; much of it is excreted in the feces.

Magnesium. Every day, the fetus receives 3–4 mg of magnesium. The concentration of magnesium in serum is 0.66–0.99 mmol/l, 2/3 of magnesium is in ionized form. Pediatric hypomagnesemia is manifested by increased neuromuscular excitability, prolonged diarrhea. Hypermagnesemia is observed with children receiving large doses of vitamin D.

Phosphorus. Enters the fetus against the concentration gradient. The concentration of phosphorus in the blood serum of the first year of life is 1.29–2.26 mmol/l, from 2 to 4 years old – 0.65–1.62 mmol/l.

The age-related features of calcium, magnesium and phosphorus metabolism are determined by the state of the neuroendocrine regulation of homeostasis and bone mineralization.

The effect of antidiuretic hormone and aldosterone on the body of a child of the first year of life is much less pronounced than in children over 1 year.

CHAPTER 4
STRUCTURE AND FUNCTIONS OF KIDNEYS

The kidneys are a paired organ, necessary for maintaining homeostasis and excretion of end products of metabolism. The kidneys are directly involved in the regulation of water-salt and mineral exchanges, as well as the acid-base state, the excretion of nitrogen-containing slag, the osmotic pressure of body fluids, blood pressure and erythropoiesis.

The kidneys consist of two layers: the outer - cortical substance and the inner - brain (*Fig. 5*). Cortex substance in the form of pillars penetrates into the medulla. Between the pillars, the medullary substance forms pyramids (from 4 to 16), which by their bases are directed to the cortical substance. The tops of the renal pyramids, connecting by two or three, end in the papillae, which are surrounded by small renal cups. Small cups, merging, form large cups from which the renal pelvis is formed. The functional unit of the kidney is the nephron. Their number is about two million. Nephrons consist of a renal body and a system of renal tubules. There is a vascular glomerulus (a glomerulus of the renal corpuscles) in the renal body and a capsule enveloping it. The capillaries of the glomerulus originate from the afferent arterioles and are collected in the efferent, which further disintegrates into the capillary network supplying blood to the tubule segments. In the vascular glomerulus of the renal corpuscles there are about 50 capillary loops anastomosing among themselves. The capsule of the glomerulus consists of two leaves: the inner, adjacent to the glomerular capillary network, and the outer, passing into the wall of the tubules of the nephron. Between the sheets there is a cavity that passes into the nephron tubules wall. Albumin molecules and immunoglobulins can pass through the pores of the basement membrane, but their penetration is limited by the presence of the glyco-complex of the basement membrane and its negative charge. The structural element of the kidney is the juxtaglomerular complex, which plays an important role in the production of renin, erythropoietin and in the regulation of arterial blood pressure. Brain substance interstitial cells of the kidney produce prostaglandins, which have a hypotensive and antidiuretic effect at the level of the microvasculature. Renal tissue contains a lot of water (up to 84 %), which indicates a high level of metabolic processes. The kidneys are able to absorb up to 10 % of all oxygen. The main energy material in the kidneys - carbohydrates. The kidneys form an active form of vitamin D_3 and kallikrein, which cleaves kinin from kininogen. Renal kinins (eg, bradykinin) have a pronounced vasodilator effect on both cortical and juxtaglomerular blood flow.

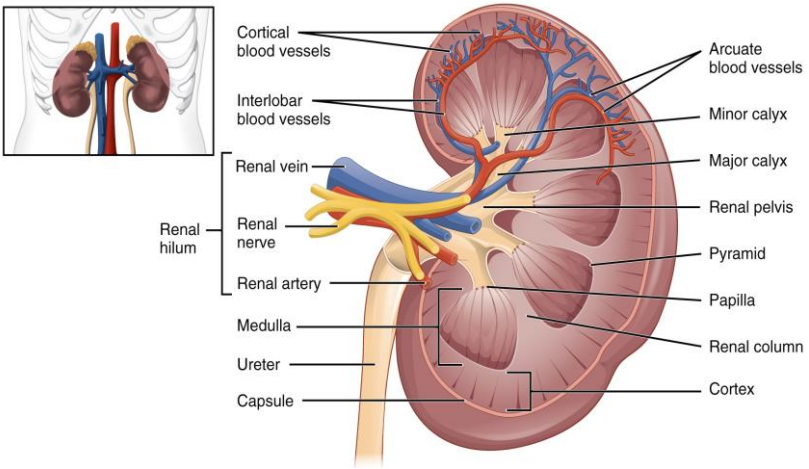


Fig. 5. The structure of the kidneys

Functions of Kidneys.

1. Urinary (in the nephrons about 180 liters of fluid per day is filtered and reasorbed**).**

2. Excretory – excretion of end products of metabolism with urine (urea, uric acid, ammonium salts, indican, etc.).

3. Regulatory:

– volume regulation (maintaining a certain amount of water)

– osmoregulation (maintaining a certain concentration of osmotic active substances through the allocation of water, electrolytes or reabsorption of these substances)

– regulation of acid-base balance (through the exchange of sodium ions to hydrogen ions in the distal part of the tubules with the participation of carbo-anhydrase; reabsorption of sodium is accompanied by a change in the urine reaction to the acidic side; the level of alkaline reserves in the body remains; hydrogen; the release of ammonia produced from glutamine by the glutaminase enzyme by the distal part of the tubules contributes significantly to the preser-vation of alkaline reserves; kidneys can be a source of $HCO^{3-,}$ resulting from the oxidation of metabolites)

– regulation of blood pressure (renin-angiotensin system).

4. Endocrine: synthesis of erythropoietin, calcitriol.

5. Metabolic:

– ATP synthesis

– in the kidneys actively proceeds gluconeogenesis, glycolysis, aerobic oxidation of glucose; aerobic type of metabolism prevails in the cortex; in the brain – anaerobic

– synthesis of calcitriol, phospholipids, triacylglycerols, prostaglandins, ketone bodies (ketogenesis), and ketolysis intensively proceeds

– synthesis of biologically active substances - renin, erythropoietin

– processes of trans-and deamination of amino acids with the release of ammonia and the formation of its transport forms - glutamine and asparagine

– creatine synthesis

– the presence of specific enzymes: $LDH_{1,2}$ (cortical substance), $LDH_{3,4}$ (medulla), alanine aminopeptidase isoform – AAP_3, transamidinase (the appearance of these enzymes in the blood and urine indicates damage to the kidney tissue).

Theory of urine formation. The most common theory of urine formation is filtration-reabsorption-secretion. According to this theory, about 180 liters of primary urine, which is concentrated in the tubules of the nephrons (Keshne theory), is filtered in the renal corpuscles per day. Glomerular filtration is a passive process that results in the formation of primary urine. Filtration is carried out through complex structural formations – glomerular capillary walls. This process is based on a hydrostatic pressure gradient. In the bringing artery, the hydrostatic pressure is 65–70 mm Hg, and in the carrying artery – 15–20 mm Hg. Glomerular filtration strength is about 20 mmHg. Under this pressure, the glomerulus membrane freely passes water and non-colloid plasma components. The filtered liquid portion of blood enters the lumen of the glomerulus capsule. The most important in filtration is the basement membrane. Filtering occurs the faster, the higher the arterial and lower colloid-osmotic pressure. The pressure in the glomerular capillaries is 9.3–10.7 kPa (70–80 mm Hg), and the colloid osmotic pressure of plasma proteins is 3.3–4.0 kPa (20–30 mm Hg). The decrease in pressure in the glomerular capillaries below 6.7 kPa is accompanied by a violation of filtration processes. The pressure in the glomerular capillaries is regulated by the reduction of the adducting and discharging arterioles.

Primary urine is identical to protein-free blood plasma and contains glucose, phosphates, urea, uric acid, creatine, and occasionally other fine proteins with a molecular weight below 70,000 Da (up to 0.15–0.2 g/l). The relative density of the primary urine – 1,010, pH – 7.4. In the tubules of the nephrons, primary urine undergoes reabsorption, as a result of which substances necessary for the body (glucose, amino acids, bicarbonates, finely dispersed proteins, salt, water) flow back into the blood. Some elements of the filtrate (creatine, inulin and a number of other polysaccharides) are not reabsorbed at all. On the basis of nonidentical transport of substances in the canalicular apparatus in the primary urine, Keshne divided all substances into threshold (subject to reabsorption) and thresholdless (creatine, sulfates). Urea, uric acid, phosphates are partially absorbed by simple diffusion. Glucose is completely reabsorbed if its concentration in the plasma does not exceed the threshold (more than 10 mmol/l). With a threshold increase in the concentration of glucose in the blood, it is partially excreted in the urine (glycosuria). In the proximal part of the nephron canaliculi, water is constantly reabsorbed passively, along with the active reab-

sorption of other substances, which creates isosmia of urine. In the distal part of the tubules, water reabsorption is regulated by an antidiuretic hormone (vasopressin) and is therefore not constant. Sodium reabsorption in the proximal part of the tubules is active and constant, and in the distal - non-permanent and regulated by aldosterone. Sodium reabsorption is reduced and hyponatremia develops with insufficient production of this hormone. Ultrafiltration in the glomeruli, as well as reabsorption and secretion in the tubule occurs in the nephron. Thus, it absorbs all substances from the proximal tubule through the epithelium of the proximal tubule. Regulation of osmotic pressure and acid-base balance occurs mainly in the distal part of the tubules. Absorption is carried out independently of the osmotic gradient. At the same time, the tubular epithelium reabsorbs some of the elements from urine into the blood. 99 % of water, potassium, chlorine, sodium, and urea are reabsorbed in the tubules. As a result of reabsorption, secondary urine is formed, which enters the renal pelvis and enters the bladder.

The modern theory of urine formation suggests that the formation of the final primary urine occurs through the return transport in the tubules of water and substances dissolved in it.

Secretion is an active process and is associated with the functioning of the tubule cells. Reabsorption processes can occur actively with the participation of enzymes, energy expenditure and passively – by simple diffusion. In addition, the epithelium of the nephron tubule secretes certain substances (drugs, acids, alkalis).

The secretion processes (flow of blood and lymph into the tubules of certain substances: creatinine, etc.) are important in the formation of secondary urine.

Functional features of urine formation in childhood.

1. Structural features of the glomerulus: small size, low hydrostatic pressure.

2. The plasma in the young childrens' kidney (the first year of life) is slightly less than in adults. Low glomerular filtration rates.

3. Young children has a low hydrostatic and oncotic pressure (due to hypoproteinemia).

4. Clearance in children of the first year of life is significantly lower than in adults.

5. Compensatory opportunities of children are limited.

6. The kidneys of newborns are not able to quickly release the body from excess water.

7. The osmolar concentration of urine is much lower in children.

8. The formation of the osmoregulation function takes place by the second year of life.

9. The reabsorption of glucose while first months of life is 25 % of the adult rate.

10. Only in the second year of life the childs' body is capable of concentrating chlorides.

11. At an early age, the mechanisms of renal regulation of acid-base balance are imperfect, which leads to the development of acidosis in various diseases.

12. The immaturity of the renal tubules in the first weeks of life leads to the restriction of ammonia production.

13. Sodium ions are reabsorbed with greater speed in children.

14. Insufficient reabsorption function of the kidney tubular apparatus is noted. In the first year of life, the child's body does not respond to the introduction of antidiuretic hormone, mineralocorticoids.

15. In children, in the renal tubules, the secretion process is slower.

Regulation of urination. Urination is regulated by nerve and reflex mechanisms. The kidneys are innervated by sympathetic and parasympathetic fibers.

CHAPTER 5
HUMORAL REGULATION AND VIOLATION WATER-SALT EXCHANGE

The main hormones involved in the humoral regulation of water-salt metabolism are the antidiuretic hormone, aldosterone, atrial natriuretic factor, and the renin-angiotensin system.

ANTIDIURETIC HORMONE (VASOPRESSIN)

It is synthesized in the supraoptic and paraventricular cores of the hypothalamus, is transported via the supraoptic-pituitary tract to the neurohypophysis and is secreted into the blood. By chemical nature, it refers to protein-peptide hormones, is a nano-peptide. Target organs are vessels, distal tubules of the kidneys. The mechanism of action is membrane-intracellular. It is responsible for osmoregulation and the volume of fluid, regulates water balance, has a vasoconstrictor effect, regulates the function of the cardiovascular system.

Effects of antidiuretic hormone (ADH):

1) antidiuretic hormone (interacts with V_2 receptors in the renal tubules, increases the level of cAMP, phosphorylates proteins, increases the permeability of membranes to water and its reabsorption):

increase of osmotic pressure of blood plasma
↓
excitation of the hypothalamus osmoreceptors
↓
secretion of ADH from secretory granules
↓
distal tubules of the kidneys
(activation of hyaluronidase)
↓
hyaluronic acid depolymerization
↓
increased water permeability of the distal tubules
↓
decrease of diuresis (water is retained in the body)

2) regulation of arterial pressure (interacts with V_1-receptors of smooth muscle cells in vessels, increases calcium concentration in cells, causes muscle contraction, narrowing of blood vessels and increase in blood pressure);

3) participates in the mechanisms of memory, namely in fixing the memory, mobilizing information.

Diabetes insipidus is a chronic disease of the hypothalamic-pituitary system, which is based on ADH deficiency. It is characterized by the release of a significant amount of urine with a low specific weight. Main symptoms: polyuria (more than 5–6 l), polydipsia, hypostenuria (low specific weight of urine),

fatigue, decrease in body temperature, dry skin. Allocate the central (neurogenic) and peripheral (nephrogenic) forms of diabetes insipidus. *The neurogenic form* is the primary violation of ADH production (infectious or toxic lesions of the hypothalamus, head injuries, impaired patency of the portal system of the pituitary by the tumor). *Nephrogenic form* – occurs as a result of reducing the sensitivity of the renal tubules to the action of ADH; reabsorption of water is disturbed, which leads to the elimination of water in large quantities; osmotic pressure of plasma increases, the center of thirst is irritated.

Diagnosis of diabetes insipidus:

– polyuria;

– hyposthenuria – low specific weight of urine (1,000–1,005);

– blood clots: an increase in the number of red blood cells, hematocrit;

– a decrease in the content of ADH in the blood plasma (the norm is 0.6–4.0 ng/l);

– increase of osmolarity of blood plasma (norm – 285 mmol/l).

Treatment of diabetes insipidus: substitution therapy with vasopressin (adiurecrin, adiuretin).

Parhon's syndrome is a rare disease associated with hyperproduction of ADH, despite of a decrease in the blood plasma osmotic pressure; it releases concentrated urine, which leads to an increased retention of fluid in the body. Symptoms: oliguria, weight gain, peripheral edema, headache, dizziness, drowsiness, apathy, disorientation, psychosis, muscle spasms, convulsions, decrease in body temperature, nausea, lack of appetite.

ALDOSTERONE. Synthesized and secreted by the glomerular layer of the adrenal cortex (angiotensin II, corticotropin, hyperkalemia, hyponatremia stimulate synthesis and secretion; dopamine, atrial natriuretic factor inhibit synthesis). By chemical nature – a steroid with an aldehyde group. The target organ is the kidney. The mechanism of action is cytosolic. Responsible for the constancy of the body electrolyte composition, affects sodium retention and excretion of potassium from the body:

decrease NaCl in blood

↓

aldosterone secretion

↓

increase the rate of sodium and chlorine reabsorption in the tubules of the nephrons

↓

the delay of NaCl in the body

Hyperaldosteronism (Conn's syndrome) is a violation of water-salt and mineral exchanges associated with excessive production of aldosterone due to a tumor of the glomerular cells of the adrenal cortex (adenoma):

increased aldosterone production

↓

sodium and chlorine retention

↓

increased osmotic pressure of extracellular fluid

↓

vasopressin release

↓

water reabsorption

↓

water retention (hypervolemia), hematocrit changes

↓

loss of potassium and hydrogen with urine

↓

decrease in sensitivity of cells to ADH

↓

development of secondary diabetes insipidus

Clinical symptoms of Conn's syndrome: persistent increase in arterial pressure (hypertension), polydipsia, neuromuscular syndrome (headache, muscle weakness, convulsions), changes in daily diuresis. In the biochemical analysis of blood - hypokalemia, hypernatremia, intracellular acidosis, extracellular alkalosis. The resulting potassium deficiency is accompanied by disturbances in the distal tubules of the kidneys, skeletal and smooth muscle tissue, the central nervous system, and sodium retention leads to hypovolemia, a decrease in the synthesis of renin and angiotensin II.

Diagnosis of Conn's syndrome: hypertension, hypokalemia, hypernatremia, increase in the Na / K ratio, increase in the content of aldosterone (3–4 times); MRI (tumor detection).

Treatment: operative; with idiopathic – conservative treatment.

RENIN-ANGIOTENSIN SYSTEM – the main mechanism of aldosterone and ADH secretion regulation. The irritation of the juxtaglomerular apparatus with the production of renin in the blood occurs with a decrease in the volume of intravascular fluid (hypovolemia), a decrease in blood pressure with a change in local hemodynamics, a decrease in blood circulation of afferent arterioles. Renin is a proteolytic enzyme that is synthesized in the juxtag-carbonular cells of the kidneys – receptors for stretching the arteriole wall. The substrate for the action of renin is a glycoprotein, an angiotensin gene that is synthesized in the liver. Renin cleaves a peptide bond in an angiotensinogen molecule with cleavage of inactive angiotensin I. Under the action of carboxy-dipeptidyl peptidase in the endothelium of blood vessels, angiotensin I is converted to angiotensin II. The latter has a powerful vasoconstrictor effect, increases blood pressure, stimulates the synthesis and secretion of aldosterone and vasopressin.

The renin-angiotensin system plays an important role in restoring circulating blood volume during bleeding, profuse vomiting and diarrhea. Inadequately high renin secretion (for example, as a result of renal artery stenosis) leads to the development of renal hypertension.

Reduced blood volume, blood pressure
↓
irritation of the volumoreceptors of the kidney's juxtaglomerular apparatus
↓
decrease of perfusion pressure in the glomeruli
↓
renin secretion
↓
angiotensin I
↓
angiotensin II (octapeptide) → vasoconstriction
↓
release of aldosterone (NaCl delay),
vasopressin (water reabsorption)

The role of the renin-angiotensin system:

– restoration of blood volume (especially after bleeding, vomiting, diarrhea) by: a) vasoconstriction; b) the retention of water and sodium chloride from food and drink;

– strengthening the filtering ability of the kidney's glomerular apparatus;

– an increase in the formation of urine;

– influence on the production of natriuretic factor.

ATRIAL NATRIURETIC FACTOR. (Peptide).Place of production – cardiomyocytes of the atria and ventricles of the heart. The target organ is kidneys. It is produced in response to atrial stretching, β-adrenoreceptor stimulation, hypernatremia, hypertension. The hormone stimulates the activation of plasma membrane guanylate cyclase, the synthesis of cGMP; strengthens the filtering ability of the glomerular apparatus of the kidneys, increases the formation of urine; is a powerful vasodilator; reduces the amount of water, the reabsorption of sodium in the renal tubules, the concentration of sodium in the blood, the volume of circulating blood and blood pressure; increases the pressure in the glomerular capillaries and increases the volume of glomerular filtration; inhibits renin secretion, reduces aldosterone secretion. The effects of the atrial natriuretic factor are opposite to the effects on the organism of the renin-angiotensin system.

VIOLATIONS OF THE EXCHANGE OF WATER, SODIUM AND CHLORIDE – changes in the qualitative and quantitative ratio of the intracellular and extracellular aquatic environment of the body. Water metabolism changes are closely associated with impaired electrolyte metabolism. *A positive water balance*, characterized by tissue hydration, appears when water is retained in the body or when the water supply prevails over excretion. A negative

water balance, characterized by dehydration of tissues, occurs with an increase in the excretion of water from the body.

Dehydration (exsiccosis, dehydration). It develops with insufficient intake of fluid in the body or with its significant losses (vomiting, diarrhea, extensive burns), endocrine disorders (sugar, diabetes insipidus). There is a redistribution of fluid in the body. Interstitial fluid enters to the blood plasma. Significant water losses lead to a decrease in the content of intracellular fluid.

Clinical symptoms:

– weight loss of 5 % or more

– dry skin, sunken eyes, reduced tissue turgor, dry sclera and cornea

– changes in cardiovascular activity as a result of a decrease in circulating blood volume; heart sounds are muffled.

Types of dehydration:

– *hypoosmolar* – occurs as a result of fluid loss with a high salt content; observed in patients with prolonged fever, workers in hot workshops, at high ambient temperatures; NaCl is then lost, extracellular dehydration leads to the movement of a part of the fluid into the cells; symptoms - dry skin and mucous membranes, muscular hypotonia, headache, hypovolemia, blood clots;

– *hyperosmolar* – occurs as a result of a greater water loss than salts; in the extracellular space, osmotic pressure rises, the fluid moves from the cells into the intercellular space (dehydration of the cells); potassium and acid metabolites with water are released from cells, acidosis and hyperkalemia occur (this condition occurs in Conn's syndrome, diabetes mellitus and diabetes mellitus); symptoms – thirst, dry skin and mucous membranes, oliguria.

– *Isoosmolar* – occurs when bleeding, burns, peritonitis, exudative processes; accompanied by the loss of water, salt, protein; water moves from the vascular bed to the extracellular space, which leads to hypovolemia, extracellular water enters the cells, which leads to blood thickening; symptoms – headache, vomiting, lethargy, weakness.

Hyperhydration (water intoxication). Occurs with an excessive flow of water into the body or with insufficient excretion of it; chronic kidney disease (chronic nephritis), salt-free diet, long-term infusion therapy. There is hyponatremia and chlorpyemia. Symptoms: headache, mental disorders, muscle contractions, convulsions, brain swelling, coma. Hypoosmia, hyponatremia and hyperkalemia are noted in blood plasma. Liquor hypertension occurs, followed by swelling of the brain.

Types of overhydration:

– *extracellular (edema)* – a fluid increase in the intercellular space due to hypoproteinemia (proteinuria), hypodynamic edema; hypovolemia causes the secretion of renin, and then the secretion of aldosterone; sodium retention occurs, osmolarity increases, water retention and an increase in edema;

– *cellular* – occurs as a result of excessive drinking, the introduction of hypotonic solutions, insufficient removal of fluid from the body.

CHAPTER 6
BIOCHEMISTRY OF URINE

Urinalysis is important for the diagnosis of the kidneys diseases, urinary tract, as well as diseases of other organs and systems. Clinical analysis of urine includes the determination of physical properties, chemical and microscopic examination.

The main physico-chemical indicators of normal urine are: the amount of urine, color, density.

The amount of urine. It is measured in graduated cylinders or test tubes. Determining the daily amount of urine is a valuable indicator of renal excretory function and water metabolism. *Diuresis* - the allocation of urine per unit of time. Daily diuresis in adult is 1.2–1.8l, the child's diuresis depends on his age. The ratio of daytime diuresis to night is 3 : 1.

Change in the amount of urine.

Polyuria – diuresis more than 2 liters; noted when taking a large amount of fluid, resorption of transudates and exudates, edema, after fever in the recovery period, with nephrosclerosis, diabetes insipidus and diabetes mellitus, taking diuretics.

Anuria – total cessation of urine separation; noted with severe acute renal failure, severe nephritis, meningitis, severe poisoning, peritonitis, blockage of the urinary tract tumor or stone (retention anuria); physiological anuria is observed in newborns on the first day after birth. Thus, anuria is isolated: 1) false – excretory (obstruction to urination (urolithiasis, tumor), 2) true – secretory (violation of renal excretory function – acute renal failure).

Oliguria – excretion of less than 500 ml of urine per day. In adults, oliguria occurs with insufficient fluid intake, an increase in edema, fever, vomiting, diarrhea, diseases of the cardiovascular system, toxicosis, acute renal failure, nephritis. In infants, in the absence of another pathology, oliguria may indicate underfeeding.

Oliguria is: 1) prerenal – insufficient renal perfusion – a decrease in the volume of extracellular fluid as a result of vomiting, diarrhea, burns, sweating, etc; 2) renal – accompanies kidney disease (glomerulonephritis, acute interstitial nephritis); 3) postrenal – obstruction of the urinary tract (urolithiasis, tumor, stricture of the urethra).

Dysuria is a common name for urinary disorders; painful urination in the inflammatory process of the urinary system, urolithiasis, vulvovaginitis.

Nocturia – the predominance of nighttime diuresis over daytime; observed in cystitis, prostate adenoma, impaired concentration ability of the kidneys, production of ADH, etc.

Ischuria – delayed urine output; observed with spinal cord injuries (the patient cannot empty the bladder).

Pollakiuria – increased urination (over 6 times a day); observed in cystitis, prostate adenoma, urethritis, and others., as well as hypothermia, nervous disorders.

Olachiuria – rare urination; observed with neuro-reflex disorders.

Enuresis – urinary incontinence; it can be long (in case of diseases of the central nervous system) or temporary (in inflammation of the urinary tract, severe diseases accompanied by fever, seizures); night urination can be observed in children with neurasthenia.

Relative density of urine. Pots in various conditions can excrete urine with a relative density of 1.001 to 1.040. Normally (with a normal water load), the relative density of morning urine is most often equal to 1,015–1,024. It is determined by the urometer with graduations from 1.0 to 1.06. It depends on (for healthy person): the concentration of substances dissolved in the urine, the composition of food, the ambient temperature., The sum of the first two digits of daily diuresis and the last two digits of density in healthy people is 30. If the daily diuresis is 1 100 ml and the density is 1019 g/l, then 11 + 19 = 30. Relative urine density in children: newborns – 1018; 5–6 days – 2 years – 1002–1005; 2–3 years – 1010–1017; 4–5 years old – 1012–1020; 6–12 years old – 1011–1025. Relative density varies with different pathological conditions. Thus, its sharp decline (hypostenuria) observed at polyuria arising in diabetes insipidus. The discrepancy between the relative density and the amount of urine is observed in diabetes mellitus, when the relative density remains high (hypertensuria), despite of the large amount of urine. The presence in the urine of protein and glucose also affects the relative density. The presence of 0.1 g/l glucose increases the relative density of urine by 0.004, and 0.4 g/l of protein increases by approximately 0.001.

The Zimnitsky test is carried out to detect variation in the relative density of urine. Indicators of renal function in the study of urine Zimnitsky in healthy people are: daily diuresis is about 1.5 liters (50–80 % of the total fluid consumed is allocated); daytime – about 1 l (predominantly prevails), night – about 0.5 l. The amount of water in individual portions ranges from 50 to 400 ml, the relative density from 1.003 to 1.028. When conducting a Zimnitsky test in healthy people, the relative density of various urine samples varies considerably. The ability of the kidneys for dilution and concentration decreases with subacute and chronic nephritis, nephrosclerosis and is lost in severe forms of renal disease. Prolonged excretion of such urine is called isostenuria, which indicates an extreme stage of kidney damage.

The maximum upper limit of the relative density of urine in healthy people is –1.028, in children up to 3–4 years –1.025. Lower maximum urine density is a sign of impaired concentration of the kidneys. It is considered that the minimum lower limit of the relative density, component 1,003–1,004, indicates a normal function of the dilution of the kidneys.

Changing the density of urine

Hyperstenuria – an increase in the relative density of urine more than 1.025 g/l; observed with insufficient drinking regime, profuse vomiting, diarrhea, increased edema (acute glomerulonephritis), diabetes mellitus (glycosuria), acute glomerulonephritis (proteinuria).

Hypostenuria – decrease in the relative density of urine less than 1.015 g/l (indicates a significant damage to the kidneys while maintaining their functional ability); observed with diabetes insipidus, chronic renal failure, acute pyelonephritis, polycystic kidney disease, resorption of edema, and abundant fluid intake.

Isostenuria is a constant excretion of primary urine with a density of 1.010–1.011 g/l (indicating a complete loss of the concentration ability of the kidneys).

Urine color. Normally straw yellow; due to the presence of pigments: urochrome (dark yellow), urobilin (pale pink), uroerythrin (reddish), urorosein, hematoporphyrin, etc. Impurities of different origin can also change the color of urine. Intensive urine coloring is observed in liver pathology, hyperthyroidism, hemolytic processes, cardiovascular diseases, as well as in the release of more concentrated urine as a result of dehydration (in case of diarrhea, toxicosis, vomiting, sweating, fever, etc.). Poorly colored urine is observed in severe kidney failure (relative density of 1.010 and characteristic changes in sediment microscopy), since the kidneys lose their ability to secrete pigments and convert chromogens to pigments. Lighter urine is excreted in polyuria (diabetes mellitus and diabetes insipidus).

Discoloration of urine

A red color or shade of urine is observed in hematuria (urolithiasis, kidney infarction, traumatic lesions) and hemoglobinuria, indicating organic kidney damage or hemolysis. The presence of blood pigments paints urine pink or brown. Urine is colored red with porphyrinuria. The reaction of Ehrlich is carried out to identify porphyrinuria. This shade is also observed during uric acid diathesis, after taking certain medications (antipyrine, sulfa drugs, vitamins). Carrot and beetroot pigments can stain urine pink.

Brown urine is usually caused by a large amount of bile pigments, broken blood (methemoglobin) or the use of certain drugs (phenol, etc.). The appearance of yellow-colored foam after agitation of urine is characteristic of bilirubinuria.

Brownish urine is usually associated with the presence of urates and oxalates.

The black color of urine is associated with the presence of black pigments of alcaptones that appear when urine is standing with a high concentration of homogentisic acid (alkaptonuria), as well as in the presence of melanin (melanosarcoma), hemoglobinuria (acute hemolytic kidney), and phenol poisoning, cresol.

Green tint of urine appears when bile pigments and methylene blue are excreted, after eating rhubarb, senna leaves, chrysophanic acid preparations, as well as strengthening the process of rotting in the intestines; in the presence of pus, urine is opalescent.

Greenish yellow urine is observed with obstructive jaundice.

The greenish-brown color of urine is observed in bilirubinuria.

The color of the dark "beer" is observed in urobilinogenia (felinechymatic jaundice, hemolytic anemia).

Green-blue color of urine is observed in bacteriuria; excessive content of indican in it, which turns into indigo blue; eating rhubarb, senna extract; using methylene blue.

The grayish-milky color of urine is usually associated with an increased amount of phosphate in the urine.

A milky-white shade of urine is observed in pyuria, the release of a large amount of phosphates, of lipuria**.**

Pale (colorless) color of urine occurs with a decrease in its density, sugar and diabetes insipidus, chronic renal failure.

The urine color of the newborn changes during the first week of life: after birth it is colorless, in the next 2–4 days it is dark amber brown, turbid (the presence of uric salts), and from 5–6 days it is light straw. In infants, urine is lighter than in adults.

Transparency of urine. Normal urine is clear, and after a short standing, a small cloud is formed, which contains homogeneous mucus, single white blood cells and the epithelium of the mucous membrane of the bladder, and in women also flat squamous epithelium of the external genitalia. Blood, protein, salts, bacteria, lipids contribute to the appearance of turbidity, which, in turn, indicates the pathological processes occurring in the kidneys and urinary tract. The turbidity observed when standing urine, due to bacterial decomposition of urea with the release of ammonia.

If the turbidity does not disappear when heated, add a few drops of acetic acid - the disappearance of turbidity indicates an excess of phosphate, hissing indicates the presence of carbonates.

Smell of urine. Fresh urine does not have an unpleasant odor, but when standing, it acquires a strong smell of ammonia, which is formed due to the splitting of urea by urease of microorganisms. This smell accompanies fresh urine in cystitis, pyelitis, pyelonephritis, etc. When gangrenous processes in the urinary tract, in particular in the bladder, urine becomes smell of rot. Fragrant food substances or medicines (garlic, horseradish, asparagus, corvalol, validol, etc.) can give urine an inherent odor. The urinary odor acquires diagnostic value in diabetes mellitus (the smell of unripe apples), inherited disorders of amino acid metabolism (mold smell in phenylketonuria, the smell of maple syrup in branched-chain amino acid metabolism).

Reaction of urine. Depending on the diet, the pH can range from 4.0 to 8.0 (on average 5.3–6.5). The reaction of urine should be determined immediately after its delivery to the laboratory, as it may change upon standing. The most convenient and quickest way is to determine the response by a universal indicator, by comparing the change in color of indicator paper with a standard colorimetric

scale. In the case of the mixed nature of food, the reaction of an infant in an adult is weakly acidic or neutral (pH 5.3–7.5, on average - 6). The reaction of urine in newborns is acidic (pH 5.4–5.9), after a few days it reaches 6.9–7.8; after a year – 5.5–6.5.

Alkaline urine can be released by consuming vegetable food, taking alkaline drugs (blemen), metabolic or respiratory alkalosis, chronic renal failure, bacterial inflammatory processes of the urinary system, urolithiasis with the formation of alkaline stones, after abundant acid vomiting. Acidic urine is observed in patients with diabetes mellitus, metabolic or respiratory acidosis, dehydration, fever, hypokalemia, severe renal insufficiency (not produce ammonia, neutralizes urine), urolithiasis, Used meat used cranberries, blueberries, reception salicylic acid, gasoline acid significant quantities muscle load. Some drugs may affect urine pH, in particular, some diuretics, sodium salts alkalize urine, and phosphate salts, methionine, furosemide, and ascorbic acid are acidified at therapeutic doses.

Various organic and inorganic substances ***are found in the urine.*** Some of them are dissolved, others form the basis of urinary residues: unorganized (salts, organic compounds, medicinal substances); organized (epithelial cells, shaped elements). The nature of the salt depends on the reaction of urine. Uric acid, urate, calcium phosphate, calcium oxalate precipitate in acid urine. Triplephosphate, ammonium urate, calcium carbonate, calcium oxalate precipitate in an alkaline medium. The diagnostic value of salts that are found in the urine is ambiguous: the appearance of some is not associated with pathology.

Chlorides. A person excretes with urine an average of 8–15 g of chlorides per day. The amount of chlorides depends on the intake of salt from food. Chlorides in the urine are easily detected by the formation of a cottage cheese of silver chloride (when 2 % $AgNO_3$ is added to the urine, silver chloride precipitates).

***Sulfates*.** On average, about 2.5 g of sulfate per day is excreted in the urine, which is formed due to the oxidation of sulfur cysteine, cystine and methionine. The release of sulfates is associated with the development of acidosis. To identify sulfates in the urine can be through reaction with barium chloride; when the latter is added to the urine, an insoluble barium sulfate precipitates.

***Phosphates*.** Phosphates are found in small amounts during normal kidney function. They are detected in children under 5 years old, and may indicate such a disease as rickets. The appearance of salts is also associated with changes in diet (vegetable food, dairy products, fish).

The number and chemical composition of urine in children at different periods of age are different (Table 3). The peculiarity of urination in children is the low density of urine.

Table 3

The amount and chemical composition of urine in children depending from age

Age	Diuresis, ml	Density of urine	Diuresis, ml/kg	The amount per 1 kg of body weight per day						
				Sodium, g	Potassium, g	Chlorides, g	Phosphorus, g	Calcium, g	Sulfur, g	Urea, g
Premature	90–125	1005	50	–	–	–	–	–	–	–
Newborns	–	1012	–	–	–	0,013	0,001	–	–	1,4
Week 1	250	1009	75	–	–	0,033	–	–	–	20–40
1 month	320	1009	80	0,001	0,02	0,25	0,003	–	2–7	–
6 month	–	1012	–	0,001	0,06	0,05	0,06	–	2–8	–
12 month	450	1014	45	0,02	0,08	0,06	0,08	2-6	11	15
2–5 years	520	1015	40	0,1	0,1	0,18	0,08	-	20	10
5–8 years	700	1016	36	0,1	0,1	0,25	0,01	-	50	10
8–11 years	850	1017	36	0,1	0,07	0,025	0,1	-	60	10
11–15 years	1100	1018	30	0,1	0,07	0,25	0,1	-	60	–
Adults	1500	1018	20	0,1	0,04	0,25	0,1	-	45	15

Sediment microscopy. Microscopy of sediment should be carried out on fresh urine samples. Prolonged storage of urine leads to lysis of the cylinders, cells and dissolution of crystals. Up to 50 % of cells and almost all cylinders are destroyed when urine is stored at room temperature for 2–3 hours. If it is impossible to immediately take a microscopy of urine, then it should be cooled or add a few drops of 40 % formalin. Urine microscopy is performed by two methods – direct microscopy and sediment microscopy. Fresh non-centrifuged urine is examined in the case of direct microscopy. A fresh urine sample is thoroughly mixed. A drop of urine is applied with a pipette onto a glass slide and covered with a coverslip. Examine ten fields of view using a lens with a magnification of 40. In the case of microscopy of the centrifuged sediment, a fresh urine sample is thoroughly mixed. 5 ml of urine is poured into a centrifuge tube with a sharp end and centrifuged at 1 000–1 500 rpm for 5minutes. The supernatant is transferred to another tube, it may be necessary for differential analysis. The precipitate (approximately 0.5 ml) is thoroughly mixed and examined under a microscope.

Microscopic examination of urine sediment is one of the main components of urine analysis, especially in the diagnosis of diseases of the kidneys and urinary tract. The first morning urine is subject to microscopic examination. Microscopic examination of urine helps to establish a violation of the kidney's functions, to identify elements characteristic of inflammation and other pathological processes in the urinary organs. Red blood cells, white blood cells, epithelium and cylinders are the main elements of the organized sediment.

Elements of organized sediment

White blood cells. Neutrophilic granulocytes often found in the urine. Normally, for males – 2–3 in sight, and for females – up to 5 copies in sight. Their appearance in large numbers indicates an inflammatory process in the urinary tract. Lymphocytes can be found in the urine in the later stages of lymphocytic leukemia due to leukemic infiltration of the kidneys, as well as in kidney diseases, the etiology of which is associated with immune factors (glomerulonephritis).

Erythrocytes. In the first morning portion of urine there is no normal red blood cells, but there may be isolated unchanged specimens that got into the urine as a result of scratching during itching of the external genital organs, due to injuries of the urinary tract of salt crystals. The presence of red blood cells in the urine (hematuria) indicates bleeding in the urogenital system. Distinguish gross hematuria (urine color "meat slop") and microhematuria (urine color is not changed).

Epithelial cells. In a urine sediment in a healthy person, usually separate epithelial cells of the mucous membrane of the bladder and flat epithelial cells of the mucous membrane of the vagina occur. A more significant content of epithelial cells is observed during inflammatory processes, and the localization of the pathological process (ureter, renal tubules, renal pelvis, etc.) can be determined by the nature of the epithelium. In pathological conditions, desquamation of epithelial cells occurs under the influence of various agents (toxins, etc.), which leads to changes in the physicochemical state of the environment. This study allows to detect various salts, various forms of epithelial cells, blood cells, bacteria, fungi, parasites.

Elements of unorganized sediment. Urine sediment, consisting mainly of salts, is called unorganized. The whitish sediment consists of amorphous phosphates; pinkish – from amorphous urats; brick red - from uric acid; crystalline whitish – from triplephosphates.

Diagnostic criteria for microscopic examination of salts in the urine:

– detection of a large number of uric acid crystals in the form of spikes in the urinary sediment (uric acid diathesis);

– in the first days of life, uric acid crystals are present in the urine of a newborn, urates, the color of urine is brick-red; it is a "transient" state;

– detection in significant quantities of ammonium urate salts; in childhood – the basis of kidney and cystic stones;

– detection of calcium oxalate crystals with exclusion from the diet of foods containing oxalic acid (sorrel, spinach, mats, asparagus, apples, oranges, tea, coffee, cocoa);

– detection of phosphates with triplex phosphate crystals - in case of metabolic disorders, disorders of the central nervous system;

– in pathological conditions, crystals of cistin, xanthine, leucine, tyrosine, cholesterol, bilirubin, crystals of fatty acids are found;

– when cystinosis in the urine crystals of cystine are found in significant amounts (cysteine stones in the kidneys can also be formed).

Crystallographic analysis of urine. At present, the urine crystallographic method is very promising (*Fig. 6, 7*). The urine is pre-centrifuged at 100 rpm for 10 minutes. For the study is taken supernatant. To 2 ml of the test substrate, 10 ml of a 2 % alcohol solution of copper chloride are added dropwise with continuous shaking. The resulting mixture is left in a glass cup under normal conditions at room temperature for 15 minutes, then passed through a fine-pored ashless filter. The resulting filtrate is poured into a Petri dish and put in thermo-stat. Growing crystals occurs in a thermostat at 37 °C and constant humidity created by the dynamic system for 5–6 hours. To control the thermostat in parallel put 10 ml of pure alcohol solution of copper chloride in a Petri dish. The crystals formed in the Petri dishes are studied macro- and microscopically. The number of crystallization centers and the nature of the crystallographic pattern are macroscopically noted. Microscopically study the structure of crystals and its change. Photographing is performed through a microscope using a photomount with a magnification of 60 times.

A human urine crystallogram of a healthy person is characterized by dark cylindrical rays emanating from crystallization centers, but more coarse and wider than in the cerebrospinal fluid crystallogram. The number of crystallization centers is from 5 to 20.

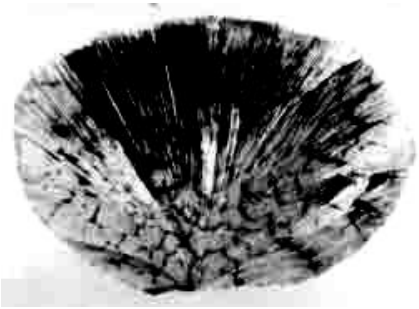
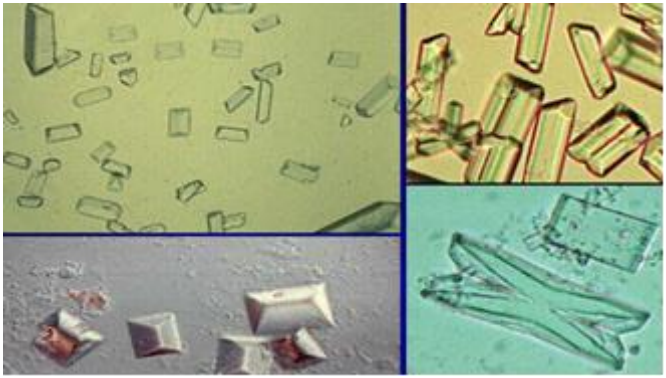


Fig. 6. Crystallographic picture of the healthy person urine

Fig. 7. Crystallographic picture of the patient's urine with acute leukemia

Triplex phosphates (struvites, ammonium magnesium phosphates). Form a crystalline-whitish precipitate, easily soluble in acids. Found in 95 % of cases of urolithiasis. These crystals are found in the form of three- or six-sided prisms or in the form of a leaf of an armpit. Struvites are more common in alkaline urine, but can also form in slightly acidic (pH 6.5). Crystals can be of different sizes, small and short crystals can be easily confused with oxalates, especially since oxalates can also be formed not only in acidic, but also in weakly acid urine. Therefore, some experience is needed to correctly determine the type of crystals.



Struvites appear in the urine not only with the development of urolithiasis, but also with bacterial inflammatory processes of the urinary tract, the consumption of plant foods, and mineral water (*Table 4*). This division is conditional, in cases of mild bacterial cystitis, ammonia smell may be absent, and in the treatment of urolithiasis with diuretic preparations, the number of crystals may be insignificant. In addition, struvite urolithiasis can be complicated by secondary bacterial cystitis, and bacterial inflammatory processes in the bladder can lead to secondary urolithiasis. Therefore, you should always take into account the complex of clinical signs and laboratory data (including the results of ultrasound, x-ray, complete blood count, etc.).

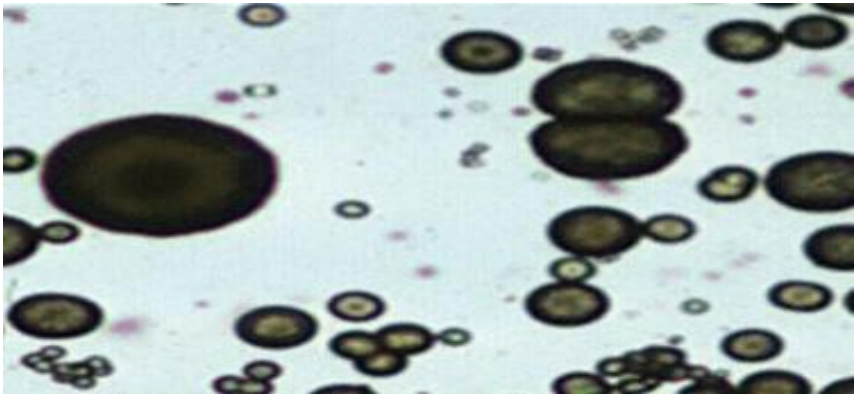
Table 4

Clinical signs in the development of urolithiasis and bacterial inflammatory processes

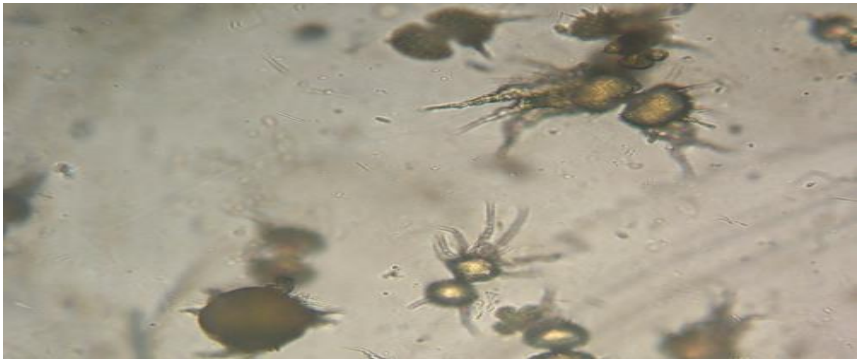
Urolithiasis disease	Bacterial inflammatory process
pH 6.5–8	pH greater than 8 (up to 10)
urine smell strong peculiar	the smell of urine is strong ammonac
single crystals or in large quantities	secondary urolithiasis

Calcium phosphate). It is found in alkaline, amphoteric and slightly acid urine. It is found in the form of needles or thin prisms. Forms phosphate-calcium uroliths. Often found together with struvites, forming mixed uroliths.

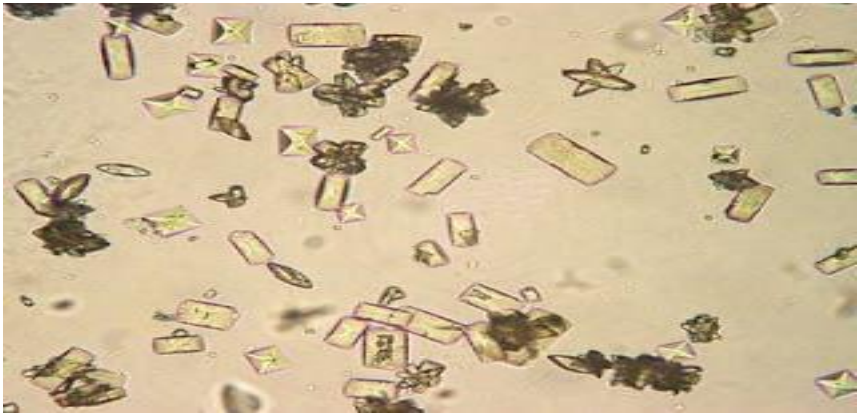
Calcium carbonate). The crystals are colorless, have the appearance of concentric balls of various sizes, are folded in the form of gymnastic weights, crossed drum sticks. It is dissolved in acids with the release of CO_2.

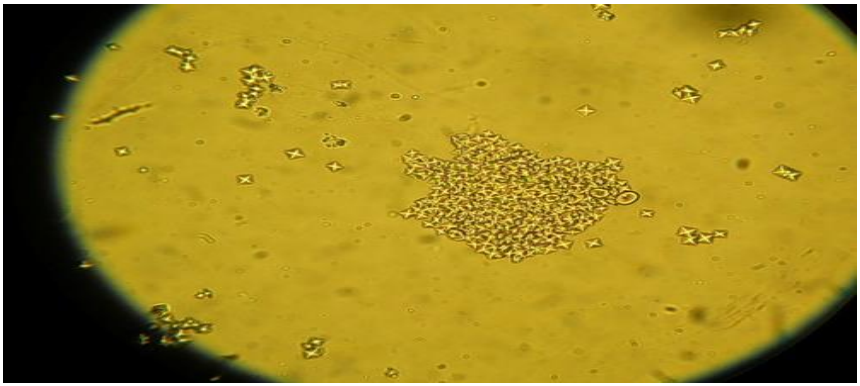


Ammonium urine. It is found in the form of yellow-brown balls with spikes on the surface. These salts can form uroliths, but they also occur in purulent bacterial cystitis, pyelitis, pyelonephritis. When heated dissolves, and when cooled – again precipitates. In neutral or acidic urine occurs in newborns and infants.

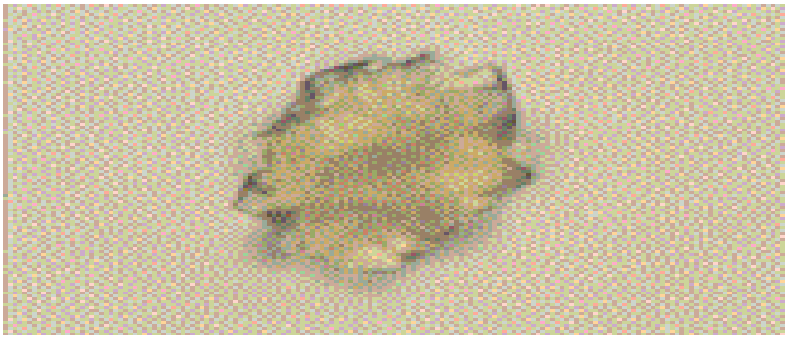


Oxalate can occur in acidic and alkaline urine. Their crystals most often have the form of colorless, strongly refracting light octahedra (in the form of post envelopes) of various sizes, often very small. Crystals resembling a sand-colored clock, as well as round and oval, are less commonly observed. Sometimes you can find larger crystals with radial striation - intergrowth of oxalates. In the urine with bile pigments, oxalates, as well as shaped elements, are painted in a yellowish-brown color. These salts dissolve in hydrochloric acid and do not dissolve in alkalis and in acetic acid. They are often found in the urine of healthy people after eating foods rich in oxalic acid (tomatoes, sorrel, spinach, asparagus, green beans, beets, grapes, apples, oranges, etc.).

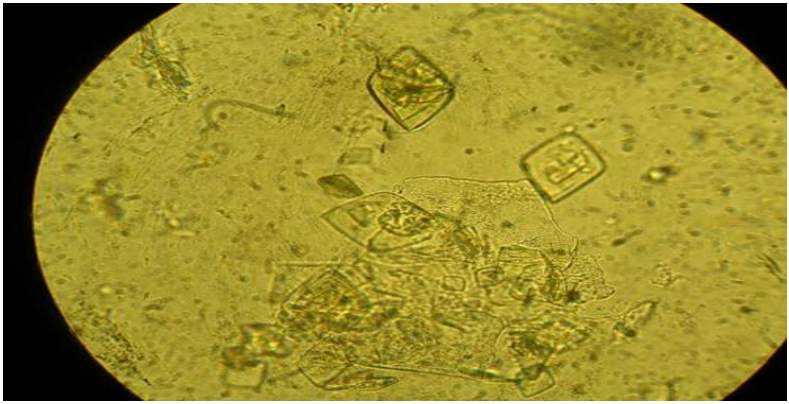




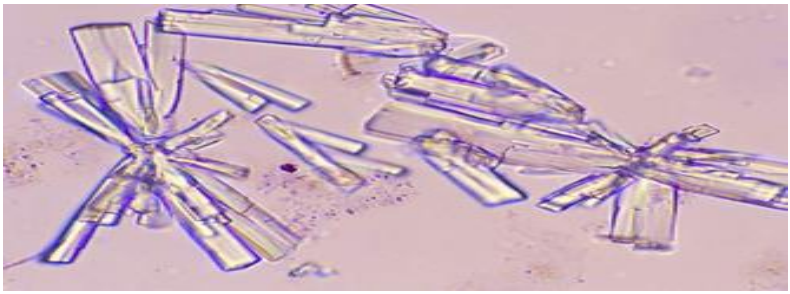
Calcium sulfate. It is very rare and only in highly acidic urine.



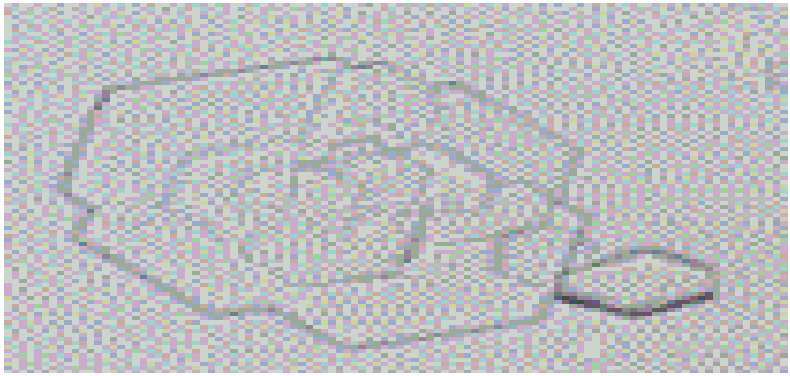
Uric acid. Occurs in acidic urine. It has the appearance of yellow-brown crystals, resembling an hourglass in its form. Uric acid crystals are impregnated with urochrome and painted in brick-red or golden-yellow color. Easily soluble in alkalis, not soluble in hydrochloric and acetic acids and when heated.

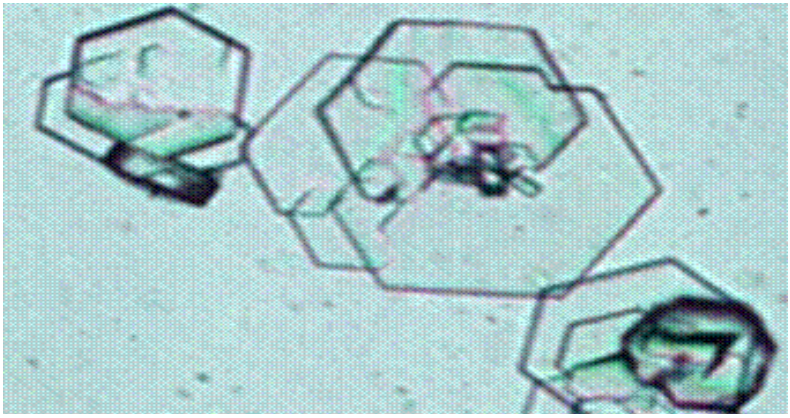


Urata. Have the appearance of round small grains, collected in piles. These salts form urate uroliths. A large number of urates can also be observed with abundant protein nutrition. That is how urats look under a microscope. The picture is generally incomprehensible. As a rule, urine containing a large amount of urats is very turbid. A simple test is used to facilitate diagnosis. To 0.5 ml of urine sediment add a few drops of 10 % KOH solution. In the presence of turbidity due to urata, the urine is instantly translucent. If the turbidity of urine is caused by the presence of pus, a jelly-like mass is formed, if the turbidity is caused by mucous secretions, then white flakes appear. To diagnose urates, you can also heat the urine above the burner flame. Urine becomes transparent when heated, again becomes turbid when cooled.



Cystine has the appearance of a grayish-white mass, which are flat, transparent hexagonal plates. The crystals are insoluble in water, alcohol, ether, acetone, acetic acid, but soluble in mineral acids. Cystine appears in hereditary cystinuria. Muddy urine is greenish-yellow in color.





For the differentiation of crystals of different salts, you can apply diagnostic tests using simple chemical reagents **(***Table 5*).

Table 5

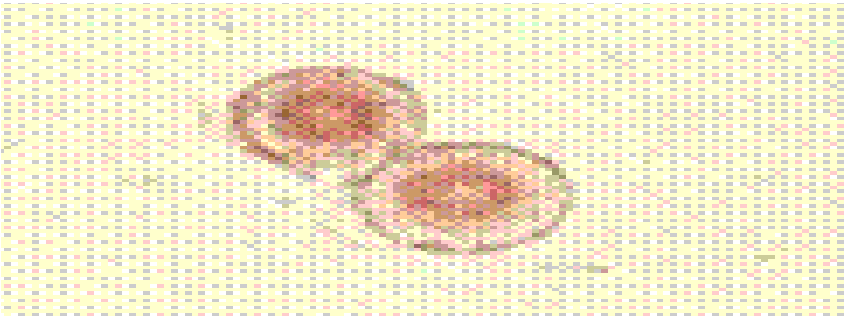
Differentiation of crystals of different salts

10 % Acetic acid		10 % Hydrochloric acid		10 % Caustic potash
dissolve	do not dissolve	dissolve	do not dissolve	dissolve
Calcium carbonate (with gas bubbles)	oxalates	Calcium carbonate	calcium sulphate	uric acid
Struvites (without gas)	calcium sulphate	struvites	cholesterol, bilirubin	urats
Biurats	tyrosine	oxalates	fat	
	urinary acid	leucine, tyrosine	uric acid	

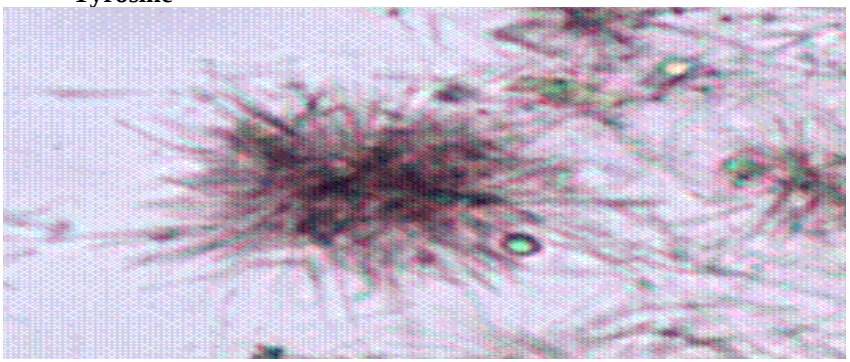
Also, crystals of other metabolites may be present in the urine, they are not the cause of urolithiasis, but can help in the diagnosis of other diseases.

Leucine and tyrosine crystals in urine sediment are usually observed simultaneously, they are not found in normal urine. Detected in acute atrophy of the liver, leukemia and other pathological conditions.

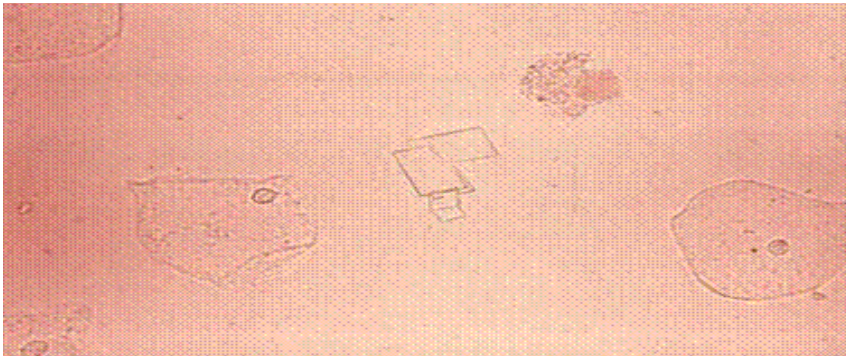
Leucine



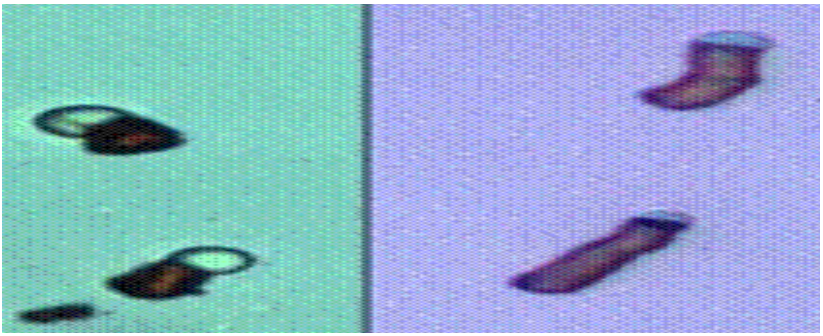
Tyrosine



Cholesterol crystals are sometimes found in the urine with amyloid and lipoid degeneration of the kidneys, urinary tract tumors.

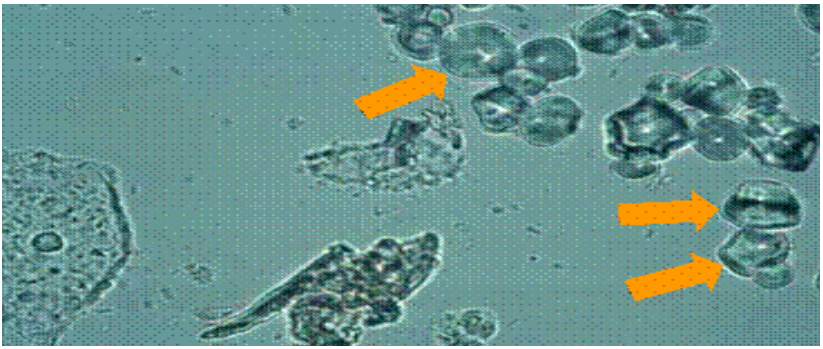


Bilirubin in the form of needle crystals of yellowish-brown color.

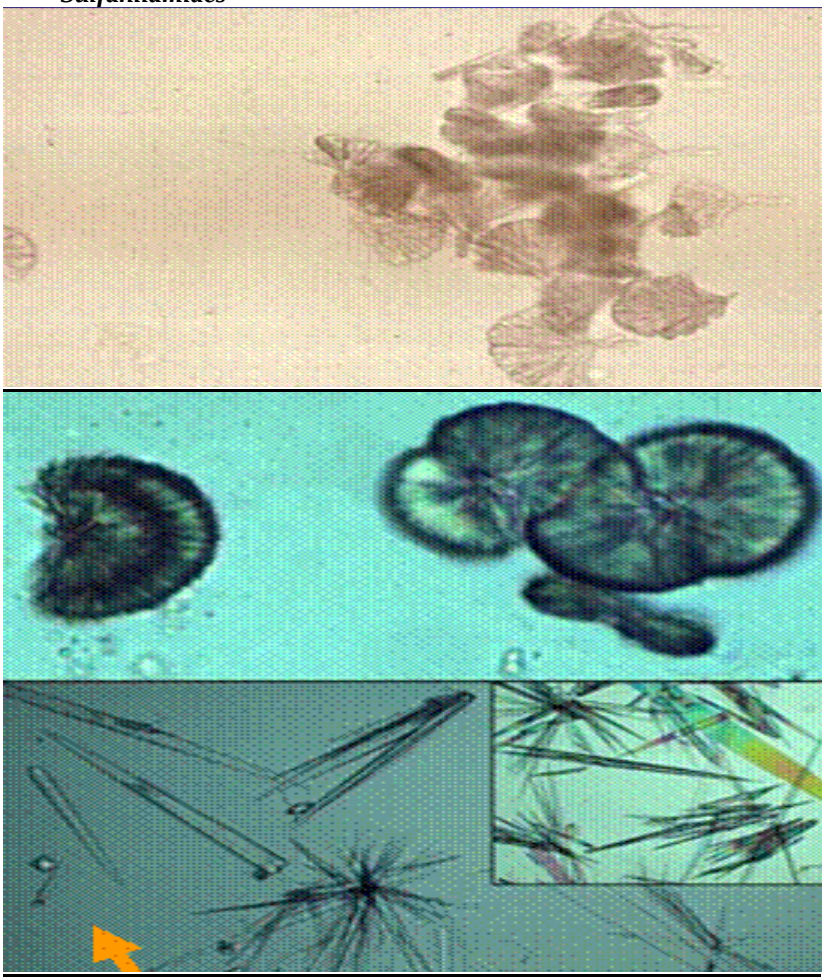


Crystals of medicinal substances may also be present.

Talc



Sulfanilamides



Pathological components of urine

Protein

Normal urine contains almost no protein (traces of it can be found). The kidneys are actively involved in maintaining protein homeostasis. Albumin molecules are reabsorbed in the proximal tubule. Protein in the urine is determined by the coagulation reaction. First, a qualitative test is carried out on the block, and then its quantity is determined.

Proteinuria – detection of protein in the urine, is observed in many diseases. Types of proteinuria: physiological and pathological proteinuria.

Physiological proteinuria is observed with increased physical exertion, hypothermia, as well as in newborns.

Extrarenal proteinuria: caused by the admixture of urine protein, released during inflammatory processes in the urinary tract and genital organs, cystitis, pyelitis, urethritis, prostatitis, vulvovaginitis and other diseases.

Renal proteinuria is more common. Can be organic and functional. The cause of organic proteinuria is damage to the structure of the kidney parenchyma. Characteristics of acute and chronic glomerulonephritis, nephrosis, congestion in the kidneys, infectious, allergic and toxic lesions of the glomerular apparatus of the kidneys, as well as their abnormalities, for example, polycystic kidney. The highest amount of protein in the urine is observed in nephrotic syndrome (up to 60–80 g/l). Functional renal proteinuria occurs due to an increase in renal permeability of the filter or a slowing down of blood flow in the glomeruli in response to strong external stimuli. Alimentary – when taking a large amount of protein foods; orthostatic – in children under 18 only in the standing position. In newborns, proteinuria is observed relatively often and is due to the presence of a functionally non-kidney filter that has not formed yet. Prolonged blood stasis can cause organic kidney damage, and in such cases organic renal proteinuria occurs. Protein bodies of Bens-Jones are low-molecular paraproteins with a molecular mass of 45×10^3 Da, due to which they easily penetrate through an intact kidney filter. The definition of these proteins by electrophoresis is the most reliable method for the detection of multiple myeloma, Waldenstrom's disease, etc. Sometimes the appearance of protein is observed in the daily portions of urine, while the morning and evening portions do not contain protein. This phenomenon of cyclic proteinuria is associated with various infectious diseases, but is not associated with kidney disease.

It is important to remember that proteinuria must be interpreted in light of the relative density of urine. The amount of protein up to 0.4 g/l is considered normal if the urine density is more than 1.035. With a relative urine density of less than 1.035, any amount of protein is potentially abnormal. To accurately determine the severity of protein loss in the urine, the ratio of urine protein to urine creatinine is calculated. This test is carried out in laboratories, it requires any urine sample and the presence of a photometer, by which the concentration of protein and creatinine in the urine is measured.

Table 5

Diagnostic value of protein/creatinine ratio

Attitude protein/creatinine	Value
Less than 0.5	Normal urine
From 0.5 to 1.0	It may be normal, but a mild form of the disease is assumed. Repeat analysis after 2–3 days.
1.0 to 5.0	Small loss of protein.
5.0 to 13.0	It is assumed prerenal disease.
Over 13,0	The average protein loss. Postrenal disease.

Glucose

It is found in the urine of a healthy person in a very small amount (0.17–0.28 mmol/l) and is not determined by research methods adopted in clinical laboratories. Qualitative and quantitative samples are used to determine glucose in urine, which in most cases are based on the reducing ability of the aldehyde group of glucose to reduce heavy metal salts in an alkaline medium.

Glycosuria - can be physiological and pathological.

Physiological (alimentary) glycosuria – observed when large amounts of carbohydrates are ingested with food. In these cases, the level of glucose in the blood is above 9.99 mmol/l, i.e., it exceeds the renal threshold of glucose reabsorption.

Pathological glucosuria – can be renal and extrarenal. Renal glucosuria is due to impaired glucose reabsorption in the tubules of the nephrons, and the blood glucose level is normal or even slightly reduced. It is observed in chronic nephritis, glycogenosis, and acute renal failure. Pathological extrarenal glucosuria often caused by metabolic disorders and diabetes occurs, rarely with pituitary disease (acromegaly, gigantism, Cushing's disease), thyrotoxicosis, cirrhosis, overdose glucocorticoids, pheochromocytoma, renal cancer, central nervous system trauma. Determining the amount of glucose in diabetes mellitus in the daily volume of urine is very important for prescribing a diet and treating these patients. In addition to glucosuria, an increase in blood glucose is observed in all the above cases. If blood glucose is normal, the presence of glucose in the urine indicates renal glucosuria due to renal tubular damage, for example, in acute renal failure, chronic nephritis, or due to the toxic action of aminoglycosides.

Other carbohydrates in the urine are rare.

Galactosuria and lactosuria are found most often in children after ingestion of a large amount of these sugars with food.

Galactose takes part in the metabolism of carbohydrates only after its phosphorylation in the liver. In diseases of the liver, galactose is not absorbed by the body and is excreted in the urine. Galactosuria can be observed in addition to liver diseases in cases of hyperthyroidism, digestive disorders and galactosemia in early childhood or in the case of inborn insufficiency of galactose metabolism (Tollens's test).

Fructose in the urine is observed in diabetes mellitus (with glucose), metabolic disorders, deficiency of hexokinase and deficiency of fructose phosphate aldolase.

Ketone (acetone) bodies

Ketone bodies include acetone, acetoacetic acid and hydroxy-butyric acid. Ketone bodies appear in the urine during metabolic disorders. Normally, carbohydrates, lipids and proteins are cleaved through intermediate stages to acetyl coenzyme A, which in the body turns into CO_2 and H_2O. For its combustion in the Krebs cycle, the presence of oxaloacetate is necessary. With a lack of carbohydrates, the quantitative ratio between acetyl coenzyme A and oxaloacetate is disturbed, and there is a lack of oxaloacetate. The accumulation of

acetylcoenzyme A and the condensation of its molecules further lead to the formation of ketone bodies. In the urine, ketone bodies appear during ketonemia. To identify them, the Lange, Legal, and Liben reactions are used. The property of ketone bodies to give in an alkaline medium a color reaction with sodium nitroprusside is the basis of these reactions (the formation of complex compounds of red-brown color).The urine of a healthy person contains the minimum amount of ketone bodies, which are not detected by the above methods. Ketone bodies appear during diabetes, fasting, fever, carbohydrate-free (ketogenic) diet, in the postoperative period, as well as glycogenosis, renal glycosuria (loss of carbohydrates), acromegaly, Cushing syndrome. Ketonuria of central origin occurs in subarachnoid hemorrhage, traumatic brain injury, severe irritation of the central nervous system (ketonemic vomiting in children), vomiting and diarrhea.

Normally, the ketone body test should be negative. Ketonuria in combination with glycosuria is a sign of diabetes mellitus. Ketonuria without glucose is evidence of excessive fat splitting and is observed with severe depletion and prolonged fasting. Unbalanced diet with excess lipids in the diet also leads to ketonuria. Minor ketonuria can also be observed in severe poisoning and anorexia.

Bilirubin

In humans, bilirubin is formed during the breakdown of hemoglobin in the system of mononuclear phagocytes (80–85 % of the total hemoglobin). Bilirubin can also be formed from non-hemoglobin sources: myoglobin, catalase, peroxidase, cytochrome c during their decomposition (5 % of the total bilirubin). Normally, serum contains on average 17 μmol/l of total bilirubin, of which only 20–25 % is part of the direct fraction. Indirect bilirubin cannot pass through the renal corpuscles, and therefore the urine of a healthy person does not contain this pigment. The appearance of bilirubin in the urine indicates an increase in the blood of its direct fraction and, as a rule, is a sign of impaired excretion of bile pigments (parenchymal and mechanical jaundice). Rosina's reaction is a qualitative test for bilirubin in the urine, based on the oxidation of bilirubin in urine to biliverdin under the action of a 1 % alcoholic solution of iodine. Pathological bilirubinuria is observed in parenchymal and mechanical jaundice.

By the nature of the violation of bilirubin metabolism and the mechanism of occurrence, four main types of jaundice are distinguished: parenchymal, mechanical, hemolytic, and conjugative, or enzymatic.

Both direct and indirect fractions of bilirubin are elevated in the blood during parenchymal jaundice. The amount of bilirubin in the blood and urobilin in the urine is increased, and the amount of stercobilin in the feces decreases to varying degrees and depends on the period of the disease and its severity. The leading mechanism of bilirubin metabolic disorders and its derivatives in parenchymal jaundice is a violation of the excretion of bile pigments into the intestine (a decrease in the activity of glucuronyltransferase, which ensures the conjugation of bilirubin, although it is observed, but not the leading factor). The

identification of urobilinuria in diseases of the liver parenchyma has great diagnostic importance. In viral hepatitis, urobilinuria appears even in the preichelous stage and increases in the first days of jaundice. In the midst of the disease with severe jaundice and acholic feces (intrahepatic congestion), it disappears, reappearing with recovery. In mild cases of infectious hepatitis, urobilinuria biphasic does not occur. Urobilinuria disappears in 8–24 days. Long-term urobilinuria occurs in chronic hepatitis, cirrhosis of the liver.

In obstructive jaundice, hyperbilirubinemia is observed in the blood due to an excess of direct and indirect bilirubin. The amount of direct bilirubin in the urine increases, and urobilin does not change. The content of stercobilin in feces is significantly reduced or it is completely absent. The main mechanism of violation of the exchange of bile pigments is the block removing them into the intestines.

The content of indirect bilirubin increases with hemolytic jaundice as a result of increased destruction of red blood cells in the blood. There is no bilirubin in the urine. Since conjugation and excretion of bilirubin occur at maximum speed, the content of stercobilin in the feces reaches significant values (up to 1 800 mg per day), and the level of urobilin in the urine may also increase.

With hemolytic anemia, urobilinuria is an important sign of hemolysis, since if it stops, it disappears. Urobilinuria of the hemolytic type occurs under hemoglobinuria, malaria, scarlet fever, extensive myocardial infarction, and the resorption of large hemorrhages.

Conjugation jaundice develops as a result of insufficient conjugation in the liver. Indirect bilirubin accumulates in the blood (up to 171 μmol/l). There is no bilirubin in the urine, urobilin is in the normal range, the content of stercobilin in the feces is reduced.

Physiological jaundice of the newborn is not accompanied by urobilinuria. Urobilinuria is a characteristic sign of congestion in the liver (decompensated heart activity).The absence of urobilin in the urine with severe forms of jaundice may indicate acute yellow atrophy of the liver. Urobilin is absent in the urine with obstructive jaundice.

The resorption of urobilinogen through the intestinal mucosa is increased and an increase in urobilinuria is observed with enterocolitis, intestinal inversion as a result of an enhanced decay process.

Bile acids

When bile enters the urine, bile bilirubin contains bile acids in it. There are qualitative and quantitative tests for determining bile acids in the urine (samples of Guy and Petenkofer). Quality tests are based on the property of these acids to lower the surface tension of liquids. The determination of bile acids in the urine is a diagnostic criterion for parenchymal jaundice.

Blood and blood pigments

There are renal (renal) and extrarenal (extrarenal) hematuria.

Renal hematuria can be organic and functional. Organic renal hematuria is noted in acute diffuse nephritis. Hematuria is negligible with focal nephritis. Chronic nephritis is accompanied by moderate hematuria. The occurrence of hematuria in infectious diseases indicates a violation of renal function. Hematuria also occurs in acute kidney failure, renal vein thrombosis, systemic diseases of the connective tissue, accompanied by kidney damage. With decompensation of the heart activity, congestive hematuria can be observed, which disappears with an improvement in heart function. Functional renal hematuria occurs very rarely when the body is exposed to extremely strong stimuli.

Extrarenal hematuria appears in inflammatory processes in the urinary tract and during their injury. It is accompanied by pyuria and bacteriuria for pyelitis and pyelocystitis. In urolithiasis, uric acid infarction of the kidneys, nephroblastoma, hydronephrosis, congenital anomalies of the kidneys, hypovitaminosis C, hematuria has a different origin.

Hemoglobin

Hemoglobinuria occurs with hemoglobinemia. The renal hemoglobin plasma threshold is 0.06 mmol/l. To detect hemoglobinuria, a chemical reaction should be conducted for the presence of hemoglobin in the urine and by means of microscopic examination of urine sediment to establish the absence of red blood cells. Hemoglobinuria is observed during intrasostoid hemolysis of erythrocytes. There are primary and secondary hemoglobinuria.

Primary hemoglobinuria includes cold, marching, primitive, with paroxysmal nocturnal hemoglobinuria (Marchiafava-Micheli syndrome), etc.

Secondary hemoglobinuria appears after transfusion of incompatible blood, in case of poisoning with aniline dyes, sulfanyl-amide preparations, fungi, chloroform, strichinine, potassium chlorate, and other substances, as well as in severe infectious diseases (sepsis, scarlet fever, malaria), severe injuries, some types of hemolytic anemia, allergic diseases, acute yellow liver atrophy.

If the result of the test for blood pigments is positive, it is imperative to examine the urine sediment. When detected in the sediment of erythrocytes talk about hematuria. After centrifugation, the color of the supernatant is characteristic of normal urine. If there is no red blood cells in the sediment, and the color of urine after centrifugation is red, brown or pinkish, then hemoglobinuria should be assumed, a complete blood count should be performed, hematocrit and plasma color should be determined. Hemoglobinuria is observed in diseases associated with erythrocyte hemolysis. In the absence of the above signs of hematuria or hemoglobinuria, the likelihood of myoglobinuria should be considered. It is recommended to conduct a study of serum creatinine-phosphokinase activity.

Hemosiderin

Hemosiderinuria occurs as a result of a prolonged increase in serum iron levels and the development of kidney hemosiderosis. Hemosiderin is formed by enhanced hemoglobin breakdown, it is deposited in the cells of various parenchymal organs, including kidney epithelial cells in the form of dark granules

containing ferric iron. The renal epithelium, saturated with hemosiderin, undergoes degenerative changes, is exfoliated, enters the urine and at the same time partially collapses. Hemosiderin is insoluble in urine. To identify hemosiderinuria examine the urine sediment. Hemosiderinuria is observed in chronic hemolytic anemia, multiple red blood cell transfusions or whole blood, an overdose of preparations containing iron, etc.

Porphyrins

Porphyrinuria may be primary or secondary.

Primary porphyrinuria occurs in congenital disorders of the metabolism of porphyrins, secondary appears against the background of existing diseases. Most porphyrins enter the body with food (meat, vegetables), i.e. it has an exogenous origin. The endogenous source of porphyrins is their synthesis from glycine and succinyl CoA. In porphyrinuria, urine is red because porphyrins are pigments. Porphyrinuria is observed in acute intermittent porphyria, Gunther's disease, chronic porphyria.

Secondary purpurinuria found in acute hepatitis, liver cirrhosis, severe febrile disease, some anemia (aplastic, hemolytic) and leukemias, beriberi (B_1, PP, B_2, B6), lead poisoning, acetylsalicylic acid, sulfanilamide preparations, aniline dyes, etc.

Myoglobin

Appears in the urine as a result of muscle breakdown. It is a muscle pigment, similar to hemoglobin in chemical structure; renal threshold of about 0.15 g/l. Myoglobinuria is observed in severe injuries with crushing of muscle tissue, electrical injury. Non-traumatic myoglobinuria occurs in muscular atrophy, myocardial infarction, myositis, carbon monoxide poisoning, thrombosis of muscle vessels, etc.

Indican

Indican is formed in the small intestine from tryptophan. In tissues as a result of protein decay, indole is oxidized, turning into indoxyl. As a toxic substance, indoxyl is neutralized by sulfuric and glucuronic acid. Indican excreted in urine. In normal urine traces of indican are detected. With a high relative density of urine, indican concentration increases. Indican in the urine is detected by the use of meat food, with constipation of various etiologies, and especially with obstruction of the small intestine, with increased processes of decay in the large intestine.

Melanin

The kidneys secrete colorless melanogen. Urine containing melanogen darkens in the air due to the transition of melanogen to melanin. Melanogen in the urine is found in patients with melanoma (especially in large quantities with metastasis of melanoma in the liver), as well as in some cases of poisoning.

CHAPTER 7. TASKS FOR FOR SELF STUDY CONTROL QUESTIONS

1. The biological significance of water and its content, daily requirements. Exogenous and endogenous water.

2. Properties and biochemical functions of water. The distribution and state of water in the body.

3. Metabolism of water in the body, age-related features, regulation.

4. Water balance of the body and its types.

5. Functions of mineral salts in the body.

6. Neurohumoral regulation of water salt metabolism.

7. Electrolite composition of liquids in the body, its regulation.

8. Minerals of the human body, their content, role.

9. Classification of biogenic elements, their role.

10. Functions and metabolism of sodium, potassium, chlorine.

11. Functions and metabolism of iron, copper, cobalt, iodine, zinc, fluorine, selenium.

12. Phosphate-calcium metabolism, role of hormones and vitamins in its regulation. Inorganic and organic phosphates. Phosphates in the urine.

13. The role of hormones and vitamins in the regulation of mineral metabolism.

14. Pathological conditions associated with metabolic disorders of mineral substances.

15. Renal functions and features of metabolism in kidneys.

16. Biochemical regulatory mechanisms of renal functions.

17. General properties and chemical composition of normal urine. Significance of urinalysis in clinical practice.

18. Organic and inorganic components of normal urine. Aging-related changes.

19. Physical and chemical properties of urine: urine output, specific gravity, pH, odor, color, and transparency. Significance of their investigation. Possible deviations from the normal ranges.

20. Clinical and diagnostic significance of quantitative and qualitative analysis of urine.

21. Proteins as pathological components of urine. Possible causes of their occurrence. Methods of determination. Types of proteinuria.

22. Glucose as a pathological component of urine. Causes and types of glycosuria. Methods of determination.

23. Creatine as a pathological component of urine. Possible causes of its occurrence. Methods of determination. Physiological creatinuria.

24. Ketone bodies as pathological components of urine. Possible causes of ketonuria. Methods of determination.

25. Blood pigments (hemoglobin, methemoglobin) as pathological components of urine. Possible causes of their occurrence. Methods of determination.

26. Bile pigments as pathological components of urine. Possible causes of their occurence. Methods of determination.

27. Indican as a component of urine. Possible causes of its increased urinary excretion. Methods of determination.

TESTS FOR SELF-CONTROL

1. Addison-Biermer's disease (pernicious hyperchromic anemia) develops due to vitamin B_{12} deficiency. Choose a metal incorporated to this vitamin:

A. Zink. B. Cobalt. C. Molybdenum. D. Magnesium. E. Iron.

2. During the thyroid surgery, parathyroid glands had been mistakenly removed from a patient with a diffuse toxic goiter. There were cramps, tetany. Which bioelement metabolism is affected?

A. Magnesium. B. Potasium. C. Iron. D. Sodium. E. Calcium.

3. It has been known that in some biogeochemical areas endemic goiter is widespread. Which bioelement deficiency can cause this disease?

A. Iron. B. Zinc. C. Iodine. D. Copper. E. Cobalt

4. Against the background of treatment with diuretics, a patient who abuses alcohol has a strong muscle and heart weakness, vomiting, diarrhea, blood pressure – 100/60 mm. Hg, depression. The cause of this condition is a higher urinary excretion of:

A. Sodium. B. Potassium. C. Chlorine. D. Calcium. E. Phosphates.

5. Microelement selenium deficiency manifests by cardiomyopathy. The likely cause of this condition is a decrease in the activity of the selenium-containing enzyme called:

A. Catalases.
B. Cytochrome oxidase.
C. Succinate dehydrogenase.
D. Lactate dehydrogenase.
E. Glutathione peroxidase.

6. Biochemical blood serum tests of a patient with hepatolenticular degeneration (Wilson disease) revealed a decrease in the content of ceruploplasmin. Which ion concentration will be increased in the serum of this patient?

A. Copper. B. Calcium. C. Phosphorus. D. Potassium. E. Sodium.

7. Excessive formation of angiotensin II is observed in a patient with a pathology of the cardiovascular system. It is synthesized with the participation of the enzyme called:

A. Kallikrein.
B. Kininase.
C. Urokinase.
D. Angiotensin-converting enzyme.
E. Cyclooxygenases.

8. What is the normal blood calcium level?

A. 1.50–1.75 mmol/L.
B. 1.75–2.00 mmol/L.
C. 2.25–2.75 mmol/L.
D. 3.0–4.5 mmol/L.
E. 0.65–1.60 mmol/L.

9. Prolonged vomiting in a patient led to dehydration. Which hormone oversecretion contributes to water retention in the body?

A. Vasopressin. *C. Somatostatin.* *E. Thyroxine*
B. Calcitonin. *D. Aldosterone.*

10. A female patient complained of general weakness, drowsiness, apathy, and edema. After the examination, endemic goiter was diagnosed. Which element deficiency can lead to this pathology?

A. Iron. *B. Fluorine.* *C. Calcium.* *D. Magnesium.* *E. Iodine.*

11. A patient has reduced vasopressin synthesis, which leads to polyuria and, as a result, to severe dehydration. What is the mechanism of polyuria development?

A. A decrease in tubular reabsorption of sodium ions.
B. Increased glomerular filtration rate.
C. A decrease in protein tubular reabsorption.
D. Decrease in tubular water reabsorption.
E. Decreased glucose reabsorption.

12. A patient complains of thirst and polyuria. Urinalysis revealed: daily diuresis is 10 L; urine density is 1.001. Which disease causes such changes?

A. Diabetes mellitus. *C. Thyrotoxicosis.* *E. Diabetes insipidus.*
B. Steroid diabetes. *D. Acromegaly.*

13. A patient with liver cirrhosis has edema. What is the cause of its appearance?

A. A decrease in blood albumin content.
B. Reduction in the content of haptoglobin in the blood.
C. Increased blood transferrin.
D. An increase in the blood content of gamma globulins.
E. Decreased blood glucose.

14. A tourist exposed to the heat for a long period of time experienced a significant loss of water, which was accompanied by a sharp decrease in diuresis. Which hormone is secreted excessively in this case?

A. Glucocorticoids and insulin. *D. Serotonin and dopamine.*
B. Vasopressin and aldosterone. *E. Adrenaline and norepinephrine.*
C. Thyroxine and triiodothyronine.

15. A young man had an increased amount of potassium in the secondary urine. Which hormone oversecretion could cause such changes?

A. Oxytocin. *C. Glucagon.* *E. Testosterone*
B. Adrenaline. *D. Aldosterone.*

16. The main symptoms of primary hyperparathyroidism include osteoporosis and kidney damage with the development of urolithiasis. Which substances form stones in case of this disease?

A. Uric acid. *C. Calcium phosphate.* *E. Cholesterol.*
B. Cystine. *D. Bilirubin.*

17. In toxic damage to hepatocytes with their abnormal protein-synthesizing function, the albumin content in plasma and the oncotic plasma pressure decrease sharply. What will be observed?

A. A decrease in diuresis. *D. An increase in the volume of circulating blood.*
B. Edema. *E. High blood viscosity.*
C. Low ESR.

18. Calcium ions are referred to as second messengers in cells. They activate glycogen catabolism by interacting with:

A. Calmodulin. *C. Calcipherol.* *E. Phospholipase C.*
B. Calcitonin. *D. Glutamine.*

19. Daily water requirement for adults is:

A. 30–50 ml/kg. *B. 75–100 ml/kg.* *C. 75–80 ml/kg.* *D. 100–120 ml/kg.*

20. Which pH and density urine indices are normal in adults?

A. pH=4.8; density 1.001. *D. pH=3.5; density 1.020.*
B. pH=8.0; density 1.040. *E. pH=6.0; density 1.021.*
C. pH=8.5; density 1.029.

21. How can be called the pathological state of adults when the urine excretion is absent?

A. Enuresis. *B. Oligouria.* *C. Anuria.* *D. Nicturia.* *E. Dysuria.*

22. How can be called the pathological state of adults when the daily diuresis is below 500 ml?

A. Anuria. *B. Polyuria.* *C. Nicturia.* *D. Oligouria.* *E. Pollakiuria.*

23. A patient has impaired renal function. To assess the state of the renal filtration capacity, a clearance of one of the following substances should be measured:

A. Creatinine. *C. Uric acid.* *E. Hydrocarbonate.*
B. Glutamine. *D. Indole.*

24. The part of dietary proteins is not broken down in the gastrointestinal tract and is exposed to microorganisms in the large intestine. This process is called protein putrefaction. Which substance in urine indicates the intensity of putrefaction?

A. Protein. *B. Urea.* *C. Creatine and creatinine.* *D. Urates.* *E. Indican.*

25. When the excretion of ketone bodies is observed?

A. Diabetes insipidus and bronze disease. *D. Hemolytic anemia.*
B. Rickets and pellagra. *E. Obstructive jaundice.*
C. Diabetes mellitus and starvation.

26. Alkaponuria leads to deviations from the normal composition of urine. Which acid concentration increases in the urine?

A. Acetoacetic acid. *C. Homogentisic acid.* *E. Pyruvic acid.*
B. Phenylpyruvic acid. *D. Oxalic acid.*

27. A patient has reduced blood indican levels. Its daily urinary excretion is also low. Which organ functions improperly?

A. Kidney. *B. Heart.* *C. Lung.* *D. Liver.* *E. Pancreas.*

28. A newborn child was diagnosed with phenylketonuria in the maternity hospital. Which metabolite should be determined in the urine to confirm the diagnosis?

A. Phenylpyruvate. *C. Hydroxyphenylpyruvate.* *E. Fumarate.*
B. Fumaryl acetoacetate. *D. Homogentisic acid.*

29. Amylase activity is increased and trypsin is present in the patient's urine. Amylase activity is also increased in the blood. Which organ pathology can be suspected?

A. Pancreas. *B. Liver.* *C. Stomach.* *D. Kidney.* *E. Intestine.*

30. Analysis of urine from a 24-year-old man revealed the following changes: daily diuresis – 10 l, relative density - 1,001, qualitative alterations are absent. A patient complains of excessive thirst, frequent urination. What is the most likely cause of this disease?

A. Glucocorticoid hypersecretion. *D. Relative insulin insufficiency.*
B. Vasopressin hyposecretion. *E. Aldosteron hypersecretion.*
C. Vasopressin hypersecretion.

Testimonials

1	B	**16**	C
2	E	**17**	B
3	C	**18**	A
4	B	**19**	A
5	E	**20**	E
6	A	**21**	C
7	D	**22**	D
8	C	**23**	A
9	A	**24**	E
10	E	**25**	C
11	D	**26**	C
12	E	**27**	D
13	A	**28**	A
14	B	**29**	A
15	D	**30**	B

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