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BIOCHEMISTRY AND PATOBIOCHEMISTRY OF THE KIDNEYS. URINARY SYNDROMES.

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The structure and function of the kidneys.

1. **The structure of the kidneys.** The kidneys are a paired organ weighing 120-150 g. The kidneys are located near the aorta and are intensively supplied with blood. In each kidney, the external cortical and internal medulla are distinguished. The structural and functional unit of the kidney is the nephron (Fig. 1). The kidneys contain about 2 million nephrons, of which only half work normally. Distinguish between superficial (cortical), mid-cortical and peri-cerebral (juxtagmedular) nephrons. The nephron consists of the renal corpuscle, the renal tubule system, blood and lymphatic vessels, and neurohumoral elements. Each section of the nephron has a high structural and functional specialization, which is determined by the histological and physiological characteristics of each element of the nephron. The renal corpuscle is formed by a glomerulus enclosed in a capsule. The glomerulus of the renal corpuscle (glomerula) consists of 3-4 intertwined capillaries originating from the afferent arteriole and flowing into the efferent arteriole. The filtration surface consists of 3 layers: capillary endothelium, basement membrane and epithelial cells. Epithelial cells at the exit site of arterioles are called podocytes. They face the inner surface of the nephron capsule. Endothelial cells have openings through which blood plasma can contact the basement membrane (fenestrated endothelium). The membrane, in turn, also has pores. Podocytes form outgrowths – pedicles, closely associated with the basement membrane. Kidney tubules. Distinguish between the proximal tubules located closer to the capsule, the nephron loop (Henle), in which the descending part, the knee of the loop and the ascending part, the distal, more distant from the capsule, tubules, and collecting ducts are distinguished. The latter end in the papillae, which open into the renal calyx, passing into the renal pelvis. This is followed by the urinary organs: ureters – one for each kidney, bladder, urethra. Juxtamedular nephrons are located on the border with the medulla, make up about 10% of the nephrons and contain special cells that are not found in other nephrons. These cells, together with the nephron, form the juxtaglomerular complex (JGC), which has secretory activity and forms renin. UGC affects the blood pressure level and the chemical composition of the ultrafiltrate (primary urine). The nephron is lined with a single-layer (renal) epithelium, the structure of which changes in different parts of the nephron, depending on the function. So, in the proximal tubule there is a cylindrical epithelium with a brush border, the descending part of Henle's loop contains a flattened epithelium, the ascending part is cubic or cylindrical, the distal tubule and collecting ducts are lined with cubic epithelium. In the epithelium of the collecting ducts, major and intercalary cells are distinguished, which differ functionally. Renal pelvis and the urinary tract is lined mainly with transitional epithelium, and the urethra in women and the lower third of the canal in men is lined with stratified squamous epithelium. The cortical substance of the kidneys is made up of glomeruli, the «upper» part of the proximal

and distal tubules. The medulla includes the nephron loop, the «lower» part of the proximal and distal tubules. The collecting ducts permeate the entire kidney tissue. To increase the suction surface, the epithelium of the proximal tubules has a brush border. The cells of Henle's loop have villi only in the descending part. The cells of the distal tubules do not have villi. In the kidneys of newborns, medullary and midcortical nephrons predominate. The development of the kidneys, their morphofunctional maturation is carried out due to the growth of cortical nephrons, which appear closer to the year of life. The development of new nephrons lasts up to 5 years.

The most intensive transformations of kidney functions correspond to 1-3 and 10-11 years with final stabilization in adolescence, however, the full use of functional reserves in the stress stage is possible only by 18 years. **2. The main functions of the kidneys.**

The following main functions of the kidneys are distinguished: 1. 2. 3. **Excretory** – the release of waste products of the body (urea, creatinine, etc.) and other water-soluble compounds, including those of exogenous origin (for example, drugs).

Homeostatic – maintaining the constancy of the volume and composition of the extracellular fluid (pH, osmolality, electrolytes).

Endocrine – the synthesis of hormones (erythropoietins and their inhibitors, renin, calcitriol). The functions of different departments and different types of nephrons are not the same, but their interaction allows you to maintain homeostasis – the constancy of the internal environment of the body, within fairly narrow limits.

The osmolality measured on the osmometer does not always match the calculated osmolarity, adjusted for 10 mOsm / L. An increase in the measured osmolality in comparison with the calculated one is associated with the presence of unmeasured osmotically active substances in the blood plasma (ethylene glycol, antifreeze, mannitol, glycerin, endotoxins, etc.) and an increase in the osmotic difference (more than 10 mosm / l). It is necessary to distinguish tonicity from osmolarity, i.e. the ability of a solution to induce movement of water into or out of the cage. The tonicity depends on the ability of the solute to pass through the semipermeable membrane. If the substance does not pass through the membrane, it has a high tonicity, since the solution molecules will be on one side of the membrane, and only water will move.

For example, Na + practically does not enter the cells, since the membrane is relatively impermeable to Na +, or sodium is removed from the cells using a Na +, K + pump (ATPase). NaCl solution has a high tonicity and is called osmotically effective substance. Urea, on the other hand, easily passes through most membranes, and water is distributed in accordance with the movement of the urea. Urea does not cause large flows of water and belongs to osmotically ineffective substances. When the cells are placed in a hypertonic solution, the water from the cells moves into the solution until the

osmolarity is equalized, the cells are dehydrated and shriveled. In a hypotonic solution, water enters the cells, the cells swell up to rupture of the membrane. Table 1 shows that the ionic composition of blood plasma differs from the interstitial fluid in the presence of protein, and it should be noted that proteins of body fluids, and, first of all, albumin, are charged, as a rule, negatively. The difference in the concentration of protein in blood plasma and intercellular fluid is associated with the lack of permeability of the vascular endothelium for protein during free diffusion of water and ions. Osmotic pressure due to the presence of protein is called colloid osmotic or oncotic pressure. It is not large and amounts to about 5%. However, in some cases, the presence of protein causes the movement of water from the interstitium into the blood. A decrease in plasma protein concentration can lead to fluid retention in the interstitial tissue and edema.

Formation of urine.

2. The normal functioning of the body is possible due to the following processes occurring in the nephron:

1. Glomerular filtration of blood plasma;

2. Reabsorption of the main part of the filtrate;

3.secretion in the tubules;

4.osmotic dilution and concentration of urine;

5. Ion exchange in the tubules. Glomerular filtration of blood plasma Filtration of blood plasma is carried out in the glomeruli by diffusion of substances dissolved in plasma and water under the action of filtration pressure. Filtration pressure represents the difference between hydrostatic pressure and the oppositely directed osmotic pressure of blood plasma.

Normally, the filtration pressure ranges from 10 to 24 mm Hg. Art. The filtering process is passive, i.e. does not require energy expenditure by the cell in the form of ATP. Filtration is possible when the systolic blood pressure fluctuates within 60-180 mm Hg. At higher and lower pressures, filtration is reduced until complete cessation due to vascular reaction. Only hydrophilic (water-soluble) substances and water pass through the glomerular filter, which consists of 3 layers – capillary endothelium, basement membrane and podocytes. Hydrophobic (fat-soluble) compounds are not filtered in healthy kidneys (Fig. 2). The endothelium of the capillaries has holes (fenestra) with a diameter of 40-100 nm. Its task is to detain the formed elements of the blood. Basement membrane provides size selectivity due to collagen fibers and charge selectivity for filtered substances. Due to the presence of heparan sulfate, a negative charge is formed on the membrane. The permeability of the membrane increases as the glomerular hydrostatic pressure rises. The processes or legs of podocytes (pedicles) form the so-called slit diaphragm with a filtration pore system of 5-12 nm. Easy. Small hydrophilic

molecules, regardless of the presence of charge, are filtered. The filtration of macromolecules, such as proteins, is limited by the relative molecular weight (RMM), the shape of the molecule and its charge. Usually, it is relatively easy to filter low molecular weight proteins with a BMM less than 70,000 D. These proteins include myoglobin (OMN 17000), hemoglobin (OMN 68000),-amylase (OMM 48000) etc. Proteins with a higher molecular weight practically do not pass through the renal filter, for example, immunoglobulin G (IgG, OMN 150,000 D). Albumin, despite the relatively low BMM 65000 D, is almost not filtered. Albumin, like the basement membrane, has a negative charge, which effectively prevents albumin from filtering. As the plasma moves along the capillary of the glomerulus, the capillary pressure of the plasma decreases, and the oncotic pressure, due to low filtration of proteins, increases, therefore the filtration pressure at the end of the glomerular capillary decreases. The result of filtration is the formation of 180-200 liters of primary (provisional) urine, which is 4.5 times the volume of the entire body fluid (Fig. 3). Primary urine is the liquid portion of blood plasma containing a small amount of low molecular weight protein. The composition of the primary urine depends entirely on the composition of the blood plasma. Only those substances that are contained in the blood plasma enter the primary urine, therefore a number of parameters of the primary urine coincide with those in the blood plasma. Thus, primary urine has the same pH (about 7.4) and the same osmolarity (about 300 mosm / l) as blood plasma. **Osmolarity** is an important indicator for both blood and urine. However, if the osmolarity of blood plasma can, in most cases, be calculated with a sufficient degree of reliability, it is almost impossible to calculate the osmolarity of urine, and osmometers are often not available, therefore in laboratories they usually use the measurement of an indicator that has a high correlation coefficient with osmolarity. This indicator is the density of urine. Density is the mass per unit volume of a substance, it is measured in g / l (for example, 1018 g / l), or in g / ml (for example, 1.018 g / ml). There is a formula for the transition from density to osmolality: osmolality = 33275 x density – 33270 Tubular reabsorption. Primary urine, which is the result of glomerular filtration of blood plasma, has characteristics similar to blood plasma: the same osmolality (300 mosm / kg) or density (1010 g / l), pH (7.4), but has a low protein content. The volume of primary urine is about 180 liters, which is 4.5 times the total fluid content in the body and 40 times the volume of blood plasma. The ultrafiltrate also contains a significant amount of substances necessary for the body, including glucose, amino acids, protein, electrolytes, etc. To return to the body water and substances dissolved in it, the process of reabsorption or reabsorption is carried out in the proximal tubules. The reabsorption process is active and requires energy expenditure in the form of ATP, which is formed in the mitochondria (MC) of the tubular epithelium. The process is called isoosmotic, since the reabsorption of solutes into the intercellular fluid and blood is accompanied by adequate movement of water, the osmolarity of urine does not change and remains equal to the osmolarity of blood plasma. The kidneys are the effector organ in the regulation of water metabolism, and water reabsorption is strictly regulated. Glucose is almost completely reabsorbed, as are amino acids and proteins.

However, the protein is reabsorbed by pinocytosis, i.e. the capture of protein molecules by the cell, followed by their splitting in the tubular epithelium cell to amino acids, the entry of amino acids into the blood and the formation of new protein molecules from them in the liver or other organ. The reabsorption of electrolytes is strictly controlled and depends on the needs of the body (see below). Water-soluble substances, the absorption of which is not regulated, for example, mannitol, antifreeze, water-soluble endotoxins, are filtered into the urine of their blood plasma and remain in the primary urine, increasing its osmolarity. The presence of such substances increases the volume of urine and the removal of water from the body. As a result of reabsorption processes, the volume of the ultrafiltrate decreases to 15% of the initial level (25-30 l), pH and osmolarity (density) of urine do not change.

Tubular secretion.

Secretion is a process that also occurs in the proximal tubules, and partially in the distal tubules, as a result of which a number of substances enter the urine through the wall of the nephron tubule. In this way, substances that are unnecessary for the body and are usually excreted in excess, for example, dyes (methylene blue), X-ray contrast agents, antibiotics, some salts, creatinine, especially when its level in the blood is high. If substances are secreted, then their content in the urine represents the sum of excretion as a result of filtration and secretion.

Osmotic dilution and concentration of urine.

It was previously indicated that the osmolarity of blood is 285-310 mosm / l, which corresponds to a density of 1009-1011 g / l, while the osmolarity of urine ranges from 50-1200 mosm / l (density 1001-1035 g / l). This fluctuation in urine osmolarity is necessary for the return of filtered water. Since water can move through membranes only passively, for its reabsorption it is necessary to remove solutes from the nephron (carry out osmotic dilution of urine), and then return the water to the intercellular fluid and blood (concentration of urine). Osmotic dilution of urine is carried out in the nephron loop (Henle) and, partially, in the distal tubules, and osmotic concentration is mainly in the collecting ducts. Osmotic dilution of urine in the loop of Henle and distal tubules is due to the entry of Na +, K + and Cl- into the interstitial tissue. The process is possible due to the low permeability of the ascending knee of the loop for water and the high ability to transport sodium chloride, as well as potassium, from the lumen of the nephron. The process of electrolyte transport is active, that is, it requires energy consumption in the form of adenosine triphosphate (ATP), which is formed in the cells of the loop epithelium in mitochondria (MC), and is cleaved with the release of chemical energy using the enzyme – Na +, K + ATP-ase, localized on the basolateral surface tubular cells. So, in the loop of Henle and in the distal tubules, an energy-dependent osmotic dilution of urine occurs due to the flow of electrolytes into the intestinal tissue and blood, while maintaining the bulk of water in the tubules. Osmotic concentration of urine is

characteristic of the collecting ducts. For osmotic concentration of urine, it is necessary to have a high osmolarity of the medullary interstitium, since the parts of the nephron responsible for osmolarity are located mainly in the medulla of the kidney, and the permeability of the collecting ducts for water must also be ensured, which determines both the concentration and the decrease in the volume of urine to normal values (about 1% of the original amount). High osmolarity of the medullary interstitium is created during the transport of ions and, in part, urea from the nephron loop and distal tubules into the interstitial tissue of the medulla. Thus, dilution of urine in the nephron is accompanied by an increase in the osmolarity of the interstitium and blood of the associated capillaries, which creates an osmotic gradient, which is the physiological basis for passive water transport. However, water transport is only possible if the collecting ducts are permeable to water, which in turn depends on the presence of antidiuretic hormone (ADH). ADH, aka vasopressin, is a peptide hormone (cyclic octapeptide) produced by the posterior lobe of the pituitary gland. The action of the hormone is directed at 2 loci: the smooth muscle cell of the vessel, which leads to its contraction, and the collecting ducts of the nephron. ADH ensures that the collecting ducts are permeable to water and allows water to move along an osmotic gradient from the lumen of the tubules into the blood vessels and be removed with the blood. Lack of antidiuretic hormone results in large volumes of dilute urine.

Table 2.

Osmolality (mOsm / kg) and density (g / l) of tubular fluid depending on the presence of antidiuretic hormone (ADH).

Nephron segment	**ADH is absent** **osmolality density**	**ADH maximum** **osmolality. density**
Proximal **tubule**	**300 -1010**	**300 -1010**
Gathering **tubule**	**50-100 1001-1003**	**300 1010**
The final **urine**	**50 1002**	**1200 1035**

An adult excretes from 0.6 to 2 liters of urine per day, about 2/3 of which is excreted in the daytime. With normal functioning of the renal tubules, the spread in the density of

individual portions of urine during the day can range from 1004 to 1035 g / l. Violation of the processes of urine formation is described in the following basic terms:

anuria - the release of less than 50 ml of urine per day;

oliguria - the release of less than 600 ml of urine per day;

polyuria - the release of more than 2 liters of urine per day;

nocturia - predominant excretion of urine at night;

isostenuria - the density of all portions of urine is equal to the density of blood plasma (1010 g / l);

hypostenuria - the density of all portions of urine is less than the density of blood plasma (<1010 g / l);

hyperstenuria - the density of all portions of urine is greater than the density of blood plasma (> 1010 g / l).

If the tubules are damaged, as a rule, the processes of urine concentration are first disrupted. This is probably due to the fact that the ability to concentrate urine appeared relatively recently. When comparing the structure of the nephron in fish, amphibians, birds and mammals, it turned out that all of these animals are able to dilute urine, but only birds and mammals, whose nephrons are equipped with a loop, are able to excrete urine with an osmolality exceeding that of blood plasma, i.e. concentrate it.

If a violation of the processes of urine concentration is detected, it is necessary to exclude the lack of ADH secretion.

In some cases, it is necessary to increase the volume of excreted urine. For this purpose, pharmacological drugs that increase diuresis are used - diuretics. There are several classes of diuretics with different mechanisms of action. So, osmotic diuretics are osmotically active water-soluble substances with low BMM, which are easily filtered in the glomeruli and either practically not reabsorbed in the nephron, or their reabsorption is limited by the capacity of the tubular apparatus (mannitol, etc.). Such diuretics interfere with osmotic dilution of urine, which reduces the passive movement of water along the osmotic gradient in the collecting ducts. The transport of Na +, K +, and Cl- ions is sensitive to “loop” diuretics, in particular to furosemide (lasix). The use of furosemide reduces the ability of the kidneys to maximize urine dilution, but at the same time promotes the excretion of K + ions. Thiazide diuretics reduce the excretion of Na + and Cl- in the distal tubule, which also prevents the formation of maximally diluted urine, but the diuretic effect is weaker and does not affect potassium levels.

Ion exchange in the tubules.

Sodium exchange.

The most important regulator of body fluid volume is sodium balance, since sodium is the main extracellular cation, and the kidney is the most important regulator of sodium balance. With a normal diet, the body receives 10 g of NaCl per day, of which 0.5 g is lost with sweat and excreted through the gastrointestinal (GI) tract, and the bulk of the balance is determined by the kidneys.

The main parameter that determines the excretion of sodium by the kidneys is the glomerular filtration rate (GFR). Small changes in GFR lead to marked changes in sodium filtration. To maintain body volume, filtered sodium must be transported from the tubule lumen to the renal interstitium. Sodium transport is carried out throughout the entire nephron, however, the amount of sodium returned and the mechanisms of reabsorption differ among themselves, although they are all energy-dependent (active transport) and are provided with energy, thanks to the work of the enzyme – Na +, K + ATP-ase, located on the surface of epithelial cells throughout the length of the nephron.

The movement of sodium from the lumen of the tubule into the cell can go in two ways:

- through the cell, transcellular path,

- between cells, paracellular path.

Sodium can move into the cell together with amino acids, glucose, phosphates, from the cell to the interstitium – with bicarbonates, through the intercellular space – with chlorides. The mechanism of exchange of sodium for a proton and sodium for potassium is very important. The latter mechanisms are competing; a decrease in the activity of one of them leads to an increase in the activity of the other. In the proximal tubules, up to 70-80% of filtered sodium is reabsorbed, in the rest of the nephron up to the collecting ducts, up to 90% of sodium is reabsorbed in total. The release of the remaining sodium depends on the needs of the body and is regulated by special mechanisms**.**

The regulation of sodium transport is provided by various biologically active substances. Increases sodium reabsorption high oncotic pressure in the efferent arteriole (v. Efferens), high reabsorption of sodium cotransporters (glucose, etc.), corticosteroids, estrogens, growth hormone, intrarenal factors. *Reduces sodium reabsorption*: atrial natriuretic factor, ouabain – a low molecular weight compound from the hypothalamus, progesterone, parathyroid hormone, glucagon, intrarenal factors. The most important extrarenal regulator of sodium reabsorption is aldosterone, a steroid hormone in the glomerular adrenal cortex. The hormone regulates the reabsorption of about 2% sodium, acts on the main cells of the collecting ducts of the cortex, opening sodium channels in the apical membrane facing the lumen of the tubule.

Increased sodium reabsorption leads to increased secretion of potassium into the lumen of the tubules. The secretion of aldosterone is regulated by the concentration of sodium and potassium in the blood plasma and the adrenocorticotropic hormone (ACTH) of the

pituitary gland, however, the greatest influence, providing the correction of volume disturbances extracellular fluid, renin – angiotensin II aldosterone system.

Table 3.

PHYSIOLOGICAL EFFECTS OF ANGIOTENSIN II.

Target organ	**the effect**
kidney	**Stimulates sodium reabsorption, reduces GFR by vasoconstriction of glomerular arterioles.**
Central nervous system	**Activates sympathetic nerves, increases secretion of ADH and a feeling of thirst.**
Vessels	**Reduces vascular smooth muscle, narrows arterioles.**
Adrenal glands	**Stimulates the secretion of aldosterone.**

GFR – glomerular filtration rate, ADH – antidiuretic hormone.

Renin is a proteolytic enzyme that is produced in the brain, uterus, and the juxtaglomerular apparatus (JHA) of the kidneys, but renal renin JHA is exclusively able to regulate the pressure and volume of extracellular fluid due to its ability to convert the liver-produced and plasma-derived angiotensinogen protein into the effector protein angiotensin II. Renin synthesis increases with a decrease in the volume of extracellular fluid and NaCl in the distal tubule, decreases with an increase in the volume of extracellular fluid and NaCl in the distal tubule or an increase in the level of angiotensin

II. Potassium exchange.

General information.

The intracellular potassium concentration is significantly higher than the extracellular one, which allows maintaining the potential difference of the cell membrane, on which the work of muscles and nerves depends. Abrupt changes in potassium homeostasis lead to dysfunction of muscles, heart, nervous system, often life-threatening. The normal potassium content in the blood is 3.5-5.4 mmol / L. A blood potassium content of less than 3.5 mmol / L is called hypokalemia, and more than 5.4 mmol / L is called hyperkalemia. Both disorders cause muscle weakness up to paralysis, decrease intestinal motility and cause cardiac arrhythmias, which in severe cases results in cardiac arrest.

Potassium balance is maintained in two ways:

1) by changing the distribution of potassium between intra- and extracellular segments,

2) by regulation of renal and extrarenal excretion of potassium ions.

The total potassium content in the body is about 3500 mmol, of which only 3% is localized in the extracellular space. Intracellular potassium concentration is 150 mmol / L, extracellular – 4 mmol / L. The concentration of extracellular potassium is regulated rather strictly, the distribution of potassium between the compartments is maintained by Na +, K + ATPase, which transfers 3 Na + ions from the cell in exchange for 2 K + ions into the cell.

The consumption of potassium by cells increases insulin, just as hyperkalemia stimulates, and hypokalemia inhibits insulin secretion; as well as catecholamines, aldosterone, etc. Potassium is excreted through the kidneys, gastrointestinal tract (about 10%) and a little with sweat. With diarrhea, the loss of potassium through the gastrointestinal tract can be significant. Violation work of the kidneys increases the release of cation through the gastrointestinal tract up to 75% of daily intake.

Renal mechanisms of potassium homeostasis.

Potassium, like other water-soluble substances, is filtered in the glomeruli and reabsorbed in the tubules. The excreted potassium usually makes up 10-15% of the filtered one, but in some cases its amount is more than the filtered one, therefore, potassium in the tubules can be both reabsorbed and secreted. Potassium is reabsorbed in the proximal tubule due to diffusion and the thick ascending knee of Henle's loop passively and with the participation of Na +, K + ATPase (main reabsorption). Potassium is secreted in the proximal tubule and the descending loop of Henle. However, the retention in the body or the excretion of potassium by the kidney is determined by the direction of ion transport by the main cells of the collecting ducts of the kidney cortex. The process is active, depending on the work of Na +, K + ATP-ase. With a high content of potassium, it is pumped from the interstitium into the cell, creating an excess concentration, and then through the luminal membrane facing the canaliculus, the epithelial membrane enters the tubule in exchange for sodium ions. With a decrease in potassium levels, the process is reversed. Aldosterone stimulates potassium secretion into the tubule lumen by activating Na +, K + ATPase and increasing the number of open potassium channels. Reabsorption of bicarbonates and secretion of protons. Acidification of urine. One of the main homeostatic functions of the kidneys is to maintain the concentration of hydrogen ions (H + protons). All body fluids and tissues are characterized by a certain pH, which is important for the processes of dissolution, complexation, neuromuscular conduction, enzymes, etc. In particular, the pH of arterial blood is maintained within a fairly narrow range – 7.35-7.45, and for a particular person, these limits are even narrower. However, normal physiological processes lead to the formation of 40-80 mmol of protons during the oxidation of amino acids, incomplete oxidation of energy substrates (lactic acid, keto acids), etc., which are ultimately excreted by the kidneys. The first stage of neutralization of acidic products is carried out in blood plasma due to the action of buffer

systems. Buffering systems of the blood include bicarbonate buffer, hemoglobin, protein, and finally phosphate buffer. The bicarbonate buffer, which is the basis of the buffering action, consists of weak carbonic acid, which, in accordance with the dissociation constant, partially dissociates into a proton and bicarbonate ion, and its sodium salt.

$H_2CO_3 = H^+ + HCO_3^-$

Carbonic acid is formed when carbon dioxide is dissolved in water, and with the participation of the enzyme carbonic anhydrase it can be split into carbon dioxide and water.

$H_2CO_3 = H_2O + CO_2$-

The role of carbonic anhydrase in our body is very great. Almost all organs and systems that are involved in maintaining the acid-base status or the formation of acidic or basic products have this enzyme: lungs, erythrocytes, kidneys, epithelium of the stomach and intestines. The enzyme allows regulate the content of carbonic acid, bicarbonates and protons. The content of bicarbonates in the blood is 25 mmol / l and ranks second after chlorides (100 mmol / l) in the amount of anions in the extracellular fluid. The hemoglobin buffer acts through the bicarbonate buffer, therefore the bicarbonate buffer is the main one. The role of phosphate buffer in the blood is extremely small, since phosphates are the main anions of the intracellular fluid, their content in the blood is low (about 1 mmol / L) and the buffer role is negligible. In urine, the main buffer is phosphate, since phosphates are excreted through the kidneys in amounts up to 70 mmol / day. At a certain stage, excess carbon dioxide is excreted by the lungs due to an increase in the number of breaths per minute (tachypnea), but protons are excreted only by the kidneys.

The excretion of protons by the kidneys is closely related to two other processes: reabsorption of bicarbonates and reabsorption of sodium from the renal filtrate. (GIVE DRAWING). It has been shown that the renal epithelium is impermeable to bicarbonates. In order for the filtered bicarbonates, which make up the basis of the bicarbonate buffer, to return to the blood, they must combine with a proton and form carbonic acid, which is split into water and carbon monoxide in the lumen of the tubule with the help of carbonic anhydrase. The latter enters the cells of the renal epithelium by diffusion, where, with the participation of the same enzyme, it forms bicarbonates through the stage of carbonic acid. With an excess of protons or a lack of bicarbonate, the kidneys can generate additional bicarbonate from carbon dioxide produced by metabolism. Reabsorption of bicarbonates is associated with sodium reabsorption and proton secretion, since sodium is exchanged for a proton. The secretion of the proton, in turn, is limited by sodium reabsorption, and by the capabilities of the urine phosphate buffer, since the proton is accepted by phosphate. In a balanced state, bicarbonates are almost completely reabsorbed, which is accompanied by the secretion of protons and acidification of the urine. Primary urine has the same pH as blood plasma, i.e. it is

slightly alkaline. When leaving the distal tubule, urine pH drops to 5.56.5 and it becomes slightly acidic. The process of urine acidification using this mechanism is most typical for cortical nephrons. In the medullary nephrons, the proton is released according to the ammoniogenesis scheme. In case of insufficiency of the above-mentioned proton secretion system, excess of protons in acidosis, as well as in newborns before the period of development of cortical nephrons, the process of excretion of ammonia plays a significant role in the process of excretion of hydrogen ions. The enzyme glutaminase is activated in the kidneys, which enhances the production of ammonia. Ammonia diffuses into the collecting ducts, where it is buffered by a proton to form an ammonium ion. The collecting ducts for the ammonium ion are impenetrable, there is no acidification of urine, therefore, urine in newborns is more alkaline.

NH3 + H + NH4 +

When assessing the contribution of the kidneys to the regulation of the acid-base state, one should not forget that the exchange of sodium ion for a proton and exchange of sodium ion for potassium ion are carried out in the distal tubules, and these processes are competing. So, with hypokalemia, the potassium ion will be retained in organism, and the exchange of sodium ion for a proton will increase. As a result, an increase in sodium reabsorption will automatically lead to an increase in the reabsorption of bicarbonates and alkalization of the blood – alkalosis, as well as an increase in the level of protons in the urine. Thus, in hypokalemic alkalosis, the patient will excrete acidic urine**.**

SOME SYNDROMES IN KIDNEY DISEASES AND THEIR LABORATORY DIAGNOSTICS.

All kidney diseases, regardless of etiology and pathogenesis, can be called a general term – nephropathy. In nephropathies, the renal parenchyma, represented by nephrons, is affected. The nephron is an indivisible structure. Despite the fact that the glomeruli and tubules perform different functions, they are morphologically and functionally related, and also have a common circulatory system. Nevertheless, depending on what is affected – the glomeruli or tubules, the nature and course of the disease is determined. So, for example, with a predominant lesion of the glomeruli, through which the blood plasma is filtered, there is a decrease in the glomerular filtration rate (GFR), a decrease in the volume of excreted urine (oliguria) and a retention in the blood of those substances that are excreted in the urine in a healthy person (urea, creatinine , potassium, phosphates, urates, etc.). If oliguria comes on quickly, within hours or several days, it is called acute. If in a short period of time it is not possible to cope with acute oliguria, it leads to impaired renal function, the so-called acute renal failure (ARF).

The following types of oliguria are distinguished:

1) Renal oliguria caused by kidney disease, for example, glomerulonephritis.

2) Oliguria caused by impaired circulation, for example, systolic blood pressure less than 60 or more than 180 mm Hg.

3) Congestive oliguria caused by impaired outflow of urine, for example, obturation with a stone.

With a predominant lesion of the tubules (poisoning with heavy metals, etc.), the reabsorption of water and solutes from the primary urine is impaired. This leads to an increase in the volume of urine (polyuria), increased excretion of electrolytes and some other substances in the urine, which can in some cases lead to a decrease in their concentration in the blood (for example, glucose in renal diabetes). In most cases, the entire nephron flows into the pathological process, and the nature of the disorders is determined by the predominant lesion of certain parts of the nephron. The degree of dysfunction is determined by the proportion of nephrons involved in the pathological process. In a healthy person, under normal conditions of life, homeostasis at a normal level is able to maintain about half of the available nephrons. When a small number of nephrons are affected, their function is compensated for by those nephrons that were «in reserve» before the appearance of the pathology. Renal impairment, assessed, for example, by the level of urea and creatinine, will manifest itself with a decrease in GFR to 30% of baseline and damage to more than half of the nephrons. This is due to high compensatory capabilities of the kidneys, formed in the process of phylogenesis, and the presence of a large reserve of "free" nephrons. With kidney disease, regardless of the cause, a number of syndromes are distinguished, which will be discussed below.

Acute renal failure (ARF) is a clinical syndrome characterized by a sharp drop in renal function. Usually reversible.

Chronic renal failure (CRF) is a clinical syndrome caused by irreversible, often progressive kidney damage.

Azotemia is a clinical syndrome associated with an increase in urea, creatinine and other nitrogen-containing blood compounds.

Uremia (urine in the blood) is the phase of renal failure in which there are signs of renal dysfunction. Terminal stage of renal failure is the stage at which there is a need for permanent replacement therapy in the form of hemodialysis or kidney transplantation.

Acute renal failure.

ARF is caused by a sharp drop in kidney function over a period of time from several hours to several days. The syndrome is characterized by azotemia and, in most cases, oliguria (urine output less than 600-400 ml / min). According to the reasons, there are three main types of arresters: 1. Prerenal (functional) arresters. 2. Renal (structural) surge arrester. 3. Postrenal (obstructive) ARF, Prerenal ARF is associated with a drop in renal blood flow of any etiology, for example, against the background of hypotension

(shock, blood loss, dehydration, edema). ARF is always characterized by oliguria up to anuria, as it is caused by a decrease in GFR. With timely treatment, it is reversible. Renal ARF is caused by acute tubular necrosis (TAT), which can be caused by kidney disease, renal ischemia, or exposure to nephrotoxic agents. PMC represents a segmental lesion of the nephron tubules and the exit of the filtrate from the nephron. Tubular damage is accompanied by impaired urine flow and the formation of damage to the cylinders distal to the site, which clogs the lumen of the tubule, and, as a result, causes a decrease in GFR ("filtrate leakage"). Fig.4 The reasons for renal ARF are as follows:

1. 2. Postischemic ARF (sepsis, operations on the heart, aorta, bile ducts, etc., nephrotoxic effect of endotoxins). ARF under the influence of nephrotoxic drugs:

A). Antibiotics. Kidney damage can be caused by water-soluble antibiotics such as aminoglycosides, which are secreted in the renal tubules. The accumulation of antibiotics to a critical dose occurs gradually, and the body cannot quickly get rid of the damaging factor. POC may develop 7-10 days after taking the medication and end after the medication is completely eliminated.

B). Drugs containing heavy metals that cause proximal tubular necrosis, such as cisplatin.

C). X-ray contrast agents.

D). Intravenous drug administration, causing the appearance of endogenous toxins. ARF in acute tubular necrosis can be non-oliguric (diuresis more than 400 ml / day). The course of the neoliguric POC is easier, the prognosis is better.

For the diagnosis of VOC and the prognosis of the disease, it is important to study the patient's history. The presence of kidney disease and the administration of nephrotoxic drugs confirm the diagnosis of POC. At the same time, acute renal failure against the background of known renal pathology is more severe and has a worse prognosis.

Postrenal ARF caused by a blockage of the urinary tract can be renal or extrarenal.

Intrarenal postrenal ARF is usually associated with acute urate nephropathy during chemotherapy for myelo- and lymphoproliferative diseases. It is characterized by oliguria up to anuria. In the blood serum, the uric acid content can increase up to 200 mg / l (12 mmol / l), i.e. 50-100 times more than the norm.

Extrarenal postrenal ARF can be caused by calculus, prostatic hypertrophy, tumor, pregnancy, and anatomical abnormalities. As a rule, ARF is accompanied by infection. The change in urine output is not constant: from normal to anuria. Arrester development phases. Regardless of the etiology, ARF goes through three developmental phases. Phase 1 of initial manifestations, usually oliguric. The phase is characterized by azotemia, acidosis, impaired exchange of water and electrolytes (Table 4).

Table 4

Biochemical changes in blood plasma in acute renal failure.

Enhancement	**Decrease**
Urea, creatinine **Protons** **Potassium, phosphates, magnesium** **Uric acid, urates**	**Sodium** **Bicarbonates** **Calcium**

Increases in urea and creatinine are associated with decreased GFR. Reduced proton excretion and the associated decrease in bicarbonate reabsorption lead to blood acidification - metabolic acidosis. Acidosis causes damage to cells and the entry of potassium, phosphates, and urates from the cells into the blood. A decrease in GFR causes an increase in the level of these substances in the blood. An increase in potassium concentration is most life-threatening in the early stages of acute renal failure, since a rapid increase in potassium levels can cause cardiac arrest.

Hyperkalemia is one of the reasons for the appointment of a hemodialysis patient in order to restore the potassium level compatible with life. Phosphate retention due to a decrease in GFR and leakage of intracellular phosphate lead to hyperphosphatemia, which, through a decrease in calcitriol and the parthyroid hormone leads to hypocalcemia. Magnesium levels rise due to decreased excretion.

The initial phase is 5-12 days. In the oliguric phase, a small volume of concentrated high-density urine with proteinuria and possible short-term high protein content (comparable to blood plasma) is observed.

Phase 2 - polyuric or diuresis phase. In this phase, GFR and diuresis increase, and the volume of urine excreted may exceed 5 L / day. An increase in urine volume is associated, on the one hand, with an increase in GFR, and on the other hand, with a decrease in the reabsorption of water and substances dissolved in it in the tubules. Although the glomeruli and tubules are inextricably linked, the restoration of tubular function is slower, therefore, the composition of urine is close to the protein-free part of blood plasma, and the kidney function is not restored. In the diuretic phase, the level of potassium decreases in the first days, and the content of urea and creatinine - only at the end of the second phase. Acidosis persists until tubular function is fully restored, and hypercalcemia may occur. The duration of the phase depends on the severity of the lesion, and, on average, is 5-10 days. 3 phase of recovery. The cells of the renal tubules gradually regenerate, the functions of the nephrons are restored, diuresis is normalized,

and the impairment of renal function disappears. Patients who survive the acute oliguric phase usually recover, but they still have residual renal impairment that is usually not detected by simple laboratory tests. ARF is usually reversible, which is apparently due to the fact that the architectonics of the kidney, as a rule, is not changed**.**

Laboratory parameters used for the diagnosis and treatment of acute renal failure

1. Determination of the concentration of urea in the blood and urine.

2. Determination of the concentration of creatinine in the blood and urine.

3. Determination of the concentration of uric acid.

4. Determination of the content of electrolytes (K +, Na +) in blood and urine.

5. Assessment of the acid-base state (CBS).

6. Assessment of the level of intoxication.

7. Measurement of urine osmolality.

8. Measurement of protein in urine.

9. Microscopy of urine sediment.

Based on the measured parameters, several more parameters can be calculated:

a) the ratio of urea / creatinine from 48.5: 1 to 80: 1 in mmol / l from 12: 1 to 20: 1 in mg / l;

b) excreted sodium fraction (FENa) FENa = UNa x PKP / UKP x PNa, where UNa - urine Na concentration UKP - urine creatinine concentration PNa - plasma Na concentration PKP - plasma creatinine concentration Sodium and creatinine should be measured in the same units. N = 1% Based on the data obtained, in some cases, differential diagnosis of prerenal and renal forms of ARF is possible

(Table 5, 6).

Parameters	Prerenal arrester	Renal Surge arrester		Parameters	Prerenal arrester	Renal Surge arrester
Urea, creatinine	>	>		Protein	+	+
Urea/	>80:1			Osmolal	>450	<350

Creatinine (mmol / l)				ness		
FE Na	<1	>1		Urine sediment	Hyaline and grainy cylinders	Epithelial nye, etc. cylinders
Creatinine urine / Creatinine plasma	<20	>40		Na of urine	<10	>20

Chronic renal failure (CRF)

CRF is a clinical syndrome caused by irreversible, often progressive kidney damage. In chronic renal failure, permanent damage to the kidney tissue occurs, in which normal kidney tissue is gradually replaced by scar tissue. **Causes of chronic renal failure**

1. Diabetes mellitus type I and II. It is histologically defined as nodular and diffuse glomerular sclerosis.

2. Hypertension (in 1/3 of patients it leads to nephrosclerosis and slowly developing renal failure).

3. Glomerulonephritis in its various manifestations.

4. Chronic interstitial nephritis (poisoning with pharmacological drugs, lead, with dysmetabolic nephropathies, etc.).

5. Hereditary pathology (polypous kidney disease, etc.).

Diseases that cause CRF initially damage one specific segment of the nephron and the surrounding blood vessels, glomeruli, tubules, and interstitium. When a small number of nephrons are damaged, the remaining intact nephrons compensate for the function of the lost ones, the kidney function is not impaired, and simple laboratory tests do not reveal any changes. With an increase in the number of nephrons involved in the pathological process, their replacement with collagen and a significant change in the architectonics of the organ, definable changes in their function appear. With the continuation of the process, the CKF decreases. In chronic renal failure, some nephrons do not function, others, which compensate for the missing nephrons, work in hyperfiltration mode and are damaged (focal glomerulonephritis). At a certain stage, with hyperfiltration, the tubular

reabsorption, resulting in temporary polyuria. With the progression of chronic renal failure, polyuria is replaced by oliguria, followed by azotemia and uremia.

The rate of progression of CRF varies from person to person. The development period is, on average, 1-10 years. Eliminating the cause of the disease does not stop the progression of the disease, but reduces the speed of this process.

Metabolic Effects of CRF In CRF, a reduced number of nephrons maintains extracellular fluid homeostasis.

In the course of the development of the disease, glomerular filtration may decrease without visible manifestations of renal failure, but against the background of the progression of the disease, the reserve capacities of the kidneys are limited, which are manifested in the following:

1) The ability of the kidneys to excrete salt load decreases, which, without limiting salt intake, can lead to sodium retention, an increase in the volume of extracellular fluid, hypertension and edema.

2) The ability to regulate water load decreases under conditions of water load and when water is deprived.

3) Potassium excretion is impaired, followed by hyperkalemia and the need for hemodialysis.

4) Protons are retained and metabolic acidosis develops. Compensation of acidosis with bone anions leads to bone pathology.

5) Mineral metabolism is disturbed, mainly with a violation of the exchange of calcium and phosphorus, which leads to damage to bones, deposition of salts in soft tissues (muscles, etc.).

6) The exchange of drugs is impaired, which is associated with their accumulation due to the limitation of glomerular filtration. An excess of drugs increases both their main action and the side effects. The ability of drugs to bind to proteins decreases. The kidneys are especially sensitive to aminoglycosides, penicillins, vancomycin, digoxin and allopurinol. To remove the toxic effect, it is necessary to reduce the dose and increase the interval of drug administration.

7) The endocrine function decreases, that is, the production of hormones such as calcitriol, erythropoietin. Thus, the changes that are observed in acute renal failure and chronic renal failure are similar. Both in one and in the other case, they are caused by impaired renal function, which are the same and do not depend on which disease develops - acute or chronic. However, the speed and sequence of the development of the pathological process depend on the cause and nature of the disease. So, acute renal failure begins, as a rule, with oliguria, followed by polyuria and restoration of renal

function. In chronic renal failure, polyuria represents the initial or intermediate stage, while oliguria marks the exit to the uremic and terminal stage, which is associated with irreversible damage to the nephrons and changes in the architectonics of the organ. With acute renal failure and chronic renal failure, all kidney functions are disturbed: water-electrolyte metabolism, acid-base status, excretory, including nitrogen-excreting function, calcium-phosphorus metabolism, hormonal function are disturbed.

Uremia

Uremia ("urine in the blood") is the phase of renal failure, characterized by the manifestation of renal dysfunction. It can also be observed with acute renal failure, and with chronic renal failure it is an obligatory stage in the development of the disease. Uremia is characterized by the accumulation of substances in the blood that are normally excreted in the urine, for example, urea and creatinine (impaired excretory function), the accumulation of endogenous toxins, in most cases unidentified, and impairment of all other functions, including hormonal. The patient complains of fatigue, poor sleep, decreased appetite, nausea and vomiting, that is, pronounced signs of intoxication. Objectively, there is a violation of the activity of all organs and systems of the body (Table 7).

In the presence of symptoms of uremia, the patient is shown replacement therapy in the form of hemodialysis. Symptoms of uremia appear when the GFR drops to 10 ml / min (at a rate of 90-130 ml / min). The basis for hemodialysis is the presence of clinical symptoms (vomiting, pruritus, tremor, pericarditis, etc.). Laboratory criteria for the need for hemodialysis can be:

a) an increase in creatinine of more than 80 mg / l or 700 μmol / l;

b) increased potassium levels.

Hemodialysis mimics the excretory function of the kidney. It consists in the exchange of water, electrolytes and low molecular weight substances between blood plasma and dialysis fluid through a semipermeable membrane. The composition of the dialysis fluid is selected in accordance with the most pronounced disorders. Water and small molecules, charged and uncharged, mostly water-soluble, pass through the membrane. Thus, the blood can be cleared of excess potassium and other ions, water-soluble ischemic toxins, urea, creatinine, and other substances.

Table 7

Dysfunctions of organs and systems in chronic renal failure

Organ or system	**Violations**	**Causes**
Nervous system	**Tremor, convulsions,**	**Accumulation of uremic**

	depression **consciousness (coma), peripheral** **sensory neuropathy**	**toxins**
System **hematopoiesis**	**Normochromic normocytic** **anemia** **Hemorrhagic diathesis** **Development of infections**	**Decreased hematopoietin,** **uremic toxins** **Impaired platelet function** **uremic toxins** **Immune and** **phagocytic functions of leukocytes**
Heart **vascular** **system**	**Hypertension, congestive heart** **failure** **Atherosclerosis** **Pericarditis**	**Retention of sodium and water, release** **renin** **Hyperlipidemia** **Uremic toxins**
Skeletal system	**Osteodystrophy** **Osteomalacia**	**Hypocalcemia, hyperthyroidism,** **metabolic acidosis** **Bone demineralization**
Skin and soft **fabrics**	**Calcification of soft tissues** **itchy skin**	**Hyperphosphatemia, uremic** **toxins**
Gastrointestinal **intestinal tract**	**Nausea, vomiting** **Mucosal hemorrhage**	**Uremic toxins** **Dysfunction of platelets,**
Endocrine **violations**	**Glucose intolerance,** **insulin resistance** **Decreased sexual function**	**Apparently ischemic toxins** **Decrease in testosterone,**

		estrogen

Control over hemodialysis is carried out according to the necessary and sufficient laboratory parameters: K +, Na +, Cl-, KOS, urea, creatinine, protein, glucose, etc. The level of uremic toxins cannot be controlled, since they are not identified and there are no available methods for their determination. The purification of blood from uremic toxins is indirectly judged by a decrease in the content of urea, creatinine, and substances of low and medium molecular weight (VL and SMM) from HMM up to 5000 D. **Determination of average weight molecules** is now widely used to assess the syndrome of endogenous intoxication. It is still unknown which substances are specifically responsible for intoxication. These substances include amino acids, nucleotides, polypeptides and even hormones. Some authors try to separate molecules in one way or another and identify toxic components. The method proposed by N.I. Gabrielyan et al, is the simplest, most accessible, and sufficiently informative. It consists in the precipitation of serum proteins with 10% TCA and the subsequent determination of the absorption of light by the solution in the ultraviolet region of the spectrum at a wavelength of 254 nm. In a healthy person, absorption is within 0.3 units. optical density (OD). This method was proposed for patients with renal disease and showed a good correlation between the patient's condition and the level of medium molecules. The results of scientific and practical work have shown that an increase in OP to 0.8 indicates a high level of intoxication, and more than 1 is rarely compatible with life.

Attempts to use this method for patients with other types of pathology, for example, with liver pathology, were not so encouraging. Even in patients with severe hepatic impairment, the level of MSM rarely exceeded 0.6 units. This situation becomes clear when considering the fundamentals of pathophysiology. The kidney is an organ that naturally secretes water-soluble compounds. During the precipitation of TCA proteins, low molecular weight hydrophilic substances remain in the supernatant, i.e. those that can be easily excreted by healthy kidneys. In case of impaired renal function, these substances accumulate, cause intoxication, and, according to laboratory tests, absorb light of the specified wavelength. In liver diseases, mainly fat-soluble substances accumulate, which are normally transported by albumin, metabolized in the liver and excreted in bile or urine. In the latter case, the liver, by conjugation with glucuronic acid or other compounds, converts hydrophobic substances, for example, drugs, similarly to bilirubin into a hydrophilic form that can be excreted in the urine. Therefore, when assessing hepatic intoxication, it is better to use other methods in parallel, for example, the method for determining the total and effective concentration of albumin. In case of kidney disease, it may be necessary to determine the indicators of the acid-base state and the content of electrolytes. These questions are a separate topic and are beyond the scope of this manual. However, some notes may be helpful.

1. In patients with damage to the renal parenchyma, various types of metabolic (non-respiratory) acidosis are observed.

2. Determination of the concentration of sodium ions can be carried out in serum or plasma and a single portion of urine.

3. Determination of the concentration of potassium ions can be carried out in serum or plasma and daily urine. An increase or decrease in the excretion of potassium per day can be a confirmation of the diagnosis of hyper- or hypokalemia, respectively. Sometimes a decrease in urinary potassium excretion is an earlier diagnostic criterion for hypokalemia than a decrease in serum or plasma potassium.

V. LABORATORY TESTS FOR NEPHRON DAMAGE

1. Tests for glomerular damage

1.1 Clearance methods It has been shown that the main function of the glomeruli is to filter blood plasma, therefore, tests to detect glomerular damage will be tests for changes in the glomerular filtration rate (GFR). GFR in each individual nephron is determined by

1) the amount of vascular blood flow,

2) the hydrostatic pressure gradient,

3) the oncotic pressure of blood plasma,

4) the ultrafiltration coefficient.

As each of these indicators grows, the GFR will increase. With a decrease in GFR, the content of substances such as urea, creatinine, etc., which are normally excreted by the kidneys, increases in serum and plasma. However, an increase is observed only when more than half of the kidney tissue is damaged, which is associated with the high compensatory ability of intact nephrons. Therefore, clearance methods are usually used to detect early pathology.

Clearance or cleansing factor is the amount of blood plasma that has been cleared of this or that substance in 1 min. If a substance is not reabsorbed, secreted or metabolized in the tubules, but only filtered, clearance is a measure of the glomerular filtration rate.

$$C = \frac{U}{P} \times V \text{ (ml/min)}$$

where C is the clearance,

U is the concentration of the substance in the urine,

P is the concentration of the substance in the blood plasma.

V - minute urine output in ml / min.

If the substance is reabsorbed, its concentration in urine decreases and clearance will be less than GFR (Table 8). If the substance is secreted, its concentration in the urine increases and the clearance will be greater than the GFR (Table 8). To match the GFR clearance, one that is only filtered is used as the analyte. The "gold standard" of GFR is the sugar clearance inulin, which is not synthesized in mammals, but is contained in plant products, for example, in Jerusalem artichoke. Patients have to inulin inulin intravenously, which is not always convenient.

Table 8

Ratio of clearance and GFR

Process	**Content in urine**	**Attitude to** **SCF**
Filtration	**const**	**C = GFR**
Reabsorption	**<**	**C <GFR**
Secretion	**>**	**C> GFR**

Rehberg proposed to use creatinine formed in the patient's body - endogenous creatinine - as an analyte. This method is called Rehberg's test, although recently it is more often called endogenous creatinine clearance. Clearance is an earlier criterion for a decrease in GFR than the level of urea and creatinine, since an increase in the level of creatinine is observed only after a decrease in clearance to 60 ml / min (the norm is 90-130 ml / min). Determination of endogenous creatinine clearance is available in any laboratory and is widely used in the clinic. However, creatinine is secreted in the tubules. With normal GFR, this difference is insignificant. With a decrease in GFR, the tubular secretion of creatinine is significant, and the GFR, determined by creatinine, turns out to be overestimated. At very low GFR, some of the creatinine released in the tubules is degraded, which also affects the study results. Thus, there must be a reasonable indication to determine the clearance.

The latter will include the following:

1) Examination of potential kidney donors to identify possible implicit dysfunctions of the organ.

2) Examination of patients with minimal impairment of renal function, when other more reliable indicators are within the normal range due to good compensation for impairment by healthy nephrons.

3) Determination of the dosage and the possibility of using nephrotoxic drugs. In some cases, the annotation to the drug indicates that when the clearance is reduced to a certain level, the use of the drug is not recommended. With a clearance above the critical, but below normal, the dose and time of administration of the drug is prescribed individually, since in patients with renal pathology, drug metabolism is reduced, and the toxic effect is increased.

4) Assessment of the function of the right and left kidney separately. In this case, urine is collected by a catheter from each kidney into a separate vessel, the clearance is calculated for each portion of urine, and the test result is compared with half the norm, or the clearance results are multiplied by 2, simulating the situation of two right and two left kidneys. The method is rarely used.

In the presence of a radioisotope laboratory, more reliable results are obtained with the elimination of ethylenediamine tetraacetate (EDTA) labeled with radioactive chromium 51Cr. EDTA is only filtered, but not reabsorbed or secreted. For most patients with established disease, it is recommended that renal function be assessed by serial measurements of urea and creatinine.

1.2 Determination of endogenous creatinine clearance:

Skreat = (Ucreate / Pcreate) x V (ml / min) x (1.73 m2 / S m2) Clearance is calculated based on several measured parameters: plasma creatinine Pkreat, which is sufficient for a given patient constant value, urine creatinine Ucreate, which depends on the concentrating function of the kidneys, minute urine output V (ml / min), which depends on the volume of excreted urine and the time of urine collection. There may be errors in the definition of each parameter. Consequently, several measured parameters increase the method error, which in ideal conditions is 10%, and in case of violations in urine collection, the result can increase by 2-3 times. Clearance is calculated based on a standard body surface of 1.73 m2. However, body surface area (S) varies from patient to patient. It can be calculated from the normogram or using a number of formulas. For the calculation, it is necessary to know the patient's body weight in kg and height in cm.

One of the formulas is as follows:

Sistm2 = 0.0167 □ height (cm) x m (kg)

To reduce the error in calculating clearance, it is necessary to standardize the methods of urine collection and determination of creatinine.

1. Creatinine of blood and urine, diluted 100 times, is determined by the same method in the same series of studies.

2. The greatest errors occur when the collection of urine is not correct.

Urine can be collected daily (24 hours in advance), nightly (8 hours in advance) or 2 hours. The most preferred daily urine collection. In this case, small changes in urine volume associated with incomplete emptying of the bladder do not play a big role. Errors are usually associated with storing urine, which must be kept in a cool, dark place to avoid contamination with bacteria that can use creatinine nitrogen as a substrate. Recently, it is more common to collect urine in 2 hours, which gives the largest error. The error is associated with incomplete emptying of the bladder before urine collection and after a 2-hour break. With a urine volume of up to 100 ml, an error of 5-10 ml during collection leads to altered results. Since it is believed that the kidneys are working optimally with a minute urine output of 0.5-2 ml / min, sometimes patients are given a water load (for example, 12 glasses of water) to increase urine output. This also leads to errors as water loading increases GFR and thus clearance. Consequently, the results will be overestimated. It is convenient to collect urine during the night and in the morning portion. For example, at 10 pm the patient emptied his bladder. Then he collects urine overnight and the last portion at 8 o'clock in the morning, for example, a total of 900 ml. Collection period urine will be 10 hours or 600 minutes. In the morning, blood is taken for creatinine.

Minute urine output V will be equal to:

V = D urine (ml) / t (min) = 900 ml / 600 min = 1.5 ml / min

Example of clearance calculation The patient collected urine for 10 hours (600 min) and collected 900 ml of urine ...

Patient weight 60 kg, height 160 cm.

Minute urine output V = 900 ml / 600 min = 1.5 ml / min

Blood creatinine = 100 μmol / L

Urine creatinine = 6000 μmol / L 6000 μmol / L C creatinine = ---- ---------- x 1.5 ml / min = 90 ml / min 100 μmol / L Body surface S = 0.0167 60 (kg) x 160 (cm) = 1.64 (m2) C = 90 (ml / min) x 1.73 (m2) / 1.64 (m2) = 90 x 1.05 = 95 (ml / min)

filtration and increases with an increase in GFR, for example, when diuresis is stimulated by water load or an increase in GFR with oral protein load. An increase in plasma creatinine levels leads to increased secretion of creatinine in the tubules. To avoid errors associated with urine collection, an estimate of GFR by blood creatinine (Cockcroft-Gault formula) is sometimes used. To do this, you need to know the age (years) and weight of the patient (kg). The results are evaluated in terms of a standard body surface.

(140-age) x Male weight: GFR = 1.23 x ---------- ----- ml / min Blood creatinine (μmol / L) (140-age) x Woman's weight: GFR = 1.05 x ---------- ml / min Blood creatinine (μmol / L)

1.3. Microalbuminuria.

Currently, microalbuminuria - the excretion of albumin in low concentrations in the urine - is recognized as a reliable criterion for damage to the renal glomeruli. It is expressed in mg / day (reference values 30300 mg / day), μg / min (reference values 20-200 μg / min), or mg / L, which is less reliable. Microalbuminuria can be expressed by the ratio of albumin / creatinine in the morning urine sample, which avoids collection of urine over a certain period of time (Table 9). The definition of microalbuminuria is relevant for patients with type 1 and 2 diabetes mellitus (insulin-dependent and non-insulin dependent), for patients with vascular pathology and for patients with glomerulonephritis in the early stages of the disease or with an exacerbation of the disease.

Table 9.

Classification of albuminuria

	morning a portion μg / min	**Per day mg**	**albumin in urine mg / l**	**albumen/ urine creatinine mg / mmol**
Normoalbuminuria	**<20**	**< 30**	**< 20**	**< 2,5**
Microalbuminuria	**20-200**	**30-300**	**20-200**	**2,5-25**
Macroalbuminuria	**> 200**	**> 300**	**> 200**	**> 25**

To determine microalbuminuria, radioimmunoassay methods, immunological methods (enzyme-linked immunosorbent assay, nephelometric and immunoturbidimetric methods) are used. The above methods require special equipment. In the absence of screening devices, immunochromatographic test strips can be used to determine the concentration of albumin in the urine semi-quantitatively.

1.4. Serial determination of blood urea and creatinine levels

As mentioned above, when kidney pathology is detected, serial determination of urea and creatinine levels is recommended. Both substances are fractions of residual blood nitrogen, that is, when serum proteins are precipitated by acid (trichloroacetic or perchloric), they remain in the supernatant (supernatant).

Urea

Urea is a low molecular weight hydrophilic compound with the formula (NH2) 2CO, which in a healthy person makes up about half of the total residual nitrogen fraction. As can be seen from the composition of the molecule, it is formed from 2 molecules of ammonia and 1 molecule of carbon dioxide. Ammonia, formed during the deamination of amino acids, combines with CO2 in the liver and forms a urea molecule. The process of urea formation is called the urea cycle, and it is closely related to the Krebs cycle, because the latter provides «intermediate» amino acids, CO2 and energy in the form of ATP. Urea synthesis, which is also a way to detoxify ammonia, is one of the most stable functions of the liver. It slows down only when about 85% of its volume is affected.

Urea enters the bloodstream is distributed between blood plasma and cells. So, erythrocytes contain about 80% of urea in comparison with blood plasma. In this regard, the results obtained when determining urea in blood serum and whole blood differ: in blood serum, taking into account hematocrit, urea is 8-10% higher. Urea is excreted through the kidneys: it is filtered through the glomeruli and reabsorbed in the tubules, therefore, urea clearance is less than creatinine clearance and less GFR.

Part of urea (about 10%) is secreted in the intestines, where, under the action of bacterial urease, urea is broken down to ammonia and carbon dioxide. (NH2) 2 CO + H2O urease 2NH3 + CO2

Ammonia and carbon dioxide are again absorbed in the intestines, with the blood of the portal vein they enter the liver, where they are again converted into urea. Reception adsorbents by patients with azotemia somewhat improves the patient's condition by absorbing ammonia, CO2 and reducing the load on the liver.

The norm of urea depends on age: in adults it is approximately 2.5-8.3 mmol / l, in children from 1.4 to 6.4 mmol / l, depending on age. In the elderly, especially in men, the urea level can increase to about 11 mmol / L, which is associated, on the one hand, with urea retention in the body, and on the other hand, with increased protein catabolism. An increase and decrease in urea is observed in the blood. The increase in blood urea is the main component of azotemia.

There are 2 types of azotemia:

1) Production, due to increased protein breakdown.

2) Retention, associated with the retention of urea in the body.

Production azotemias occur with an increase in the production (formation) of urea, which is usually caused by increased protein breakdown (consumption of large amounts of protein, gastrointestinal bleeding, increased catabolism - edema, tumor breakdown, myocardial infarction, stress, dehydration).

With production azotemias, urea usually increases by no more than 2 times (up to 16 mmol / l). Provided that the kidneys are not damaged, production azotemia is accompanied by an increase in the excretion of urea in the urine.

Retention azotemia occurs with impaired renal function and decreased GFR. It is associated with retention of urea in the body with acute oliguria, renal and extrarenal (decreased blood pressure, urinary stagnation), with chronic renal failure, obstruction of the urinary tract. With retention azotemia, the level of urea can increase 10 times or more. Since retention azotemia is caused by impaired renal function, urinary excretion of urea is reduced.

Uremia is often present with a urea content of about 50 mmol / L, but urea is not a criterion for uremia. Since urea easily passes through the dialyzer membranes, a decrease in its concentration in the blood plasma cannot be a reliable criterion for the removal of other toxic substances. In some cases, a decrease in the urea content is observed.

It can be associated: - - - - - -

with a diet that is poor in protein and rich in carbohydrates;

with increased utilization of protein (children, late pregnant women, excess growth hormone);

with malabsorption (celiac disease);

with drug poisoning;

with blood thinning, including early pregnancy;

with severe liver diseases, accompanied by impaired urea synthesis.

For the differential diagnosis of retention and production azotemia, it is useful to determine the content of urea in the blood, in daily urine, and the content of creatinine in the blood (Table 9).

Table 10

Differential diagnosis of azotemia.

Azotemia	**blood urea**	**urine urea**	**creatinine** **blood**
Production	>	>	**N**
Retention	>	**N**	>

> - increased, < - decreased, N - norm Reference limits of urine urea 12-20 g / day (430-710 mmol / day)

Methods for determining urea

Currently, the laboratory uses 3 groups of methods:

1. Determination with diacetyl monoxime, colorimetric method by the end point. During the analysis, it is necessary to boil a mixture containing carcinogens and sulfuric acid. The method is harmful to health, can be used if there is a fume hood with good ventilation.

2. End-point colorimetric urease methods available to any laboratory. Non-toxic, does not require boiling. Disadvantage: Ammonium ions can interfere with reaction results.

3. Kinetic urea, BUN (Binding Urina Nitrogen). The method is based on the urease reaction and the Warburg test using the enzyme glutamate dehydrogenase (GlDH). The method is sensitive and fast, it is recommended for automatic analyzers. Urine urea is determined by the same methods from the daily amount, taking into account urine output. Before testing, the urine is diluted 50 or 100 times.

Creatinine

Creatinine is formed primarily from muscle creatine phosphate (Figure 5). Its daily production is relatively constant and depends on the total muscle mass. Small amounts of creatinine come from meat-based foods. Creatinine is filtered and secreted by the renal tubules. With normal creatinine levels, the secretion level is low. With an increase in creatinine levels, secretion makes a significant contribution to the total creatinine in urine.

Normal creatinine values are 60-120 μmol / L, however, for a particular patient, the creatinine level is quite stable and varies within narrow limits. During the day, an almost constant amount of creatinine is excreted in the urine. The expected amount of released creatinine can be calculated, since it is shown that per day a man excretes 1 mg / kg / hour (88 μmol / kg / hour), and a woman - 0.8 mg / kg / hour (70 μmol / kg / hour) creatinine. By comparing the calculated results of the expected amount of excreted creatinine and the measured amount of excreted creatinine, the correctness of the collection of daily urine is checked. When the 24-hour urine is properly collected, the expected and measured creatinine levels are similar. Blood samples for creatinine should be taken on an empty stomach, as eating meat can overestimate the results.

With age, muscle mass decreases, which leads to a decrease in creatinine production. However, the age-related decrease in GFR compensates for the possible decrease in creatinine. During pregnancy, the formation of creatinine increases, but the increase in GFR allows creatinine to remain at the usual level. A decrease in the concentration of

creatinine can be during fasting, after surgery, during treatment with corticosteroids. However, the change in creatinine content for the above reasons rarely leads to diagnostic errors (Table 10). The main diagnostically significant reason for an increase in blood creatinine levels is a decrease in GFR. Although creatinine and urea rise at about the same time, the level of urea is influenced not only by the rate of excretion, but also by the rate of formation, and the level of creatinine is only affected by the rate of excretion, i.e. SCF. Creatinine levels are a more reliable measure of glomerular function and are unaffected by diet and liver disease.

Table 11

Change in the concentration of urea and blood creatinine

	Blood urea	**Blood creatinine**
>	**Protein diet** **Increased protein breakdown** **Dehydration** **Stagnant urine** **Decreased GFR**	**Fried meat (30% after 7h)** **Pregnancy** **(late dates)** **Decreased GFR**
<	**Protein-free diet** **Increased protein utilization** **(children, pregnant women, etc.)** **Severe liver disease** **Hemodialysis**	**Loss of muscle mass** **Operation** **Prolonged illness** **Corticosteroid treatment**

In case of kidney disease at the stage of the disease, characterized by an increase in nitrogenous substances (azotemia), it is sufficient to measure the concentration of urea and creatinine without determining the clearance. However, in accordance with the formula, clearance and blood creatinine are inversely proportional, therefore, in many clinics, the reciprocal of creatinine (1 / creatinine) is used to assess the patient's condition. The rate of decrease in this value shows the degree of dysfunction of the glomeruli. Determination of creatinine clearance with its high content in the blood gives unreasonably overestimated GFR values. The level of creatinine and urea in the blood is

one of the criteria for hemodialysis. Usually hemodialysis is performed with a creatinine content of more than 80 mg / L (700 μmol / L) and a urea content of more than 1 g / L (about 80 μmol / L). Determination of creatinine in urine is used to assess the correct collection of urine and when calculating clearance. In other cases, the determination of creatinine in urine as a separate test has little diagnostic value.

Methods for the determination of

Creatinine is most often determined by the reaction of Jaffe with picric acid. The reaction is characterized by low specificity. Picric acid, a nitro compound, reacts with all substances having double and triple bonds. Some of them are fast-reacting (in the first 30-60 seconds), some are slow-reacting (later 20 minutes), creatinine is in between. To obtain reliable results, it is necessary to strictly adhere to all conditions of the method.

In the laboratory, 2 main methods are used:

1. Determination of creatinine after precipitation of proteins at the end point. The method can be used in a laboratory equipped with FECs.

2. Determination of creatinine by a fixed time method without protein precipitation. The method is suitable for laboratories with appropriate equipment (programmable photometers or biochemical analyzers).

False increase is caused by: ischemia, hemolysis, ketoacidosis, temperature over 30 ° C. False underestimation causes jaundice. 2. Dysfunction of the tubules. Laboratory tests can assess the function of the proximal and distal tubules. To assess the function of the proximal tubules, those tests are used that assess the function of reuptake. These include a test for maximum glucose reabsorption, bicarbonate reabsorption. The appearance of glucose in the urine with its normal or low content in the blood, as well as an increase in the excretion of amino acids, indicates a violation of the function of the proximal tubules. Recently, urinary excretion of tubular enzymes and excretion of β2microglobulin have been used to assess distal tubular function. Tubular enzymes such as N-acetyl-β-D-glucosaminidase (NAG), β-glucuronidase and others have a high molecular weight and do not pass through the kidney filter in healthy people. The high activity of these enzymes in the urine without proteinuria indicates damage to the kidney tubules. An informative and accessible test for the reabsorption function of the proximal tubules is the determination of the β2microglobulin content. It is a low molecular weight protein that is freely filtered by the glomeruli and is almost completely reabsorbed and metabolized by the epithelium of the proximal tubules. An increase in the excretion of this protein in patients without proteinuria indicates a violation of the process of tubular reabsorption. The distal tubules are responsible for excreting water and acidifying urine.

Therefore, to assess the function of the distal tubules, a deprivation test, a test for acidification of urine with ammonium chloride, a test according to Zimnitsky or Reiselman, and free water clearance are performed. The test according to Zimnitsky or

Reiselman allows you to assess the function of osmotic dilution and osmotic concentration of urine by the kidneys. For correct interpretation of the sample, it is necessary to calculate the amount of liquid obtained, taking into account liquid and solid food. During the Zimnitsky test, the patient collects urine every 3 hours (a total of 8 servings). With the Reiselman test, which is more often used in pediatric practice, the patient collects urine during natural periods of urination with an indication of the time of urine collection.

The evaluation of the samples is the same. Namely:

 at least 65% of the resulting liquid should be released per day;

 about 2/3 of all urine should be excreted during the daytime;

 the spread of density in different portions of urine should be no lower than 7 g / l.

Greater variation indicates better kidney function. The determination of protein in each portion of urine is not included in the above sample, however, knowing its level is very useful from a clinical point of view. The sample is available to any clinical diagnostic laboratory, simple, cheap, informative, and therefore widespread. Determination of free water clearance (CH2o) has limitations, since it requires an osmometer. To carry out this test, it is necessary to measure the osmolality of blood plasma and urine at the freezing point.

Normal values of these indicators are 285-310 mmosm / l for plasma and 50-1500 mosm / l for urine. C osm = Uosm. / View x V,

where Sosm is osmotic clearance, Uosm is urine osmolality, Rosm is plasma osmolality, V is minute diuresis. If the osmolality of urine is equal to the osmolality of blood plasma (Uosm = Rosm), then the osmotic clearance is equal to the minute diuresis (Cosm. = V). In this case, the kidney does not do any of the work of regulating water exchange. If the osmolality of urine is greater than the osmolality of blood plasma (Uosm> Rosm), then the kidney concentrates urine. As a rule, the concentration function is impaired earlier. If the osmolality of urine is less than the osmolality of blood plasma (U osm <P osm), then the kidney dilutes urine. Osmotic dilution of urine is usually impaired later. The water excreted in the urine is conventionally divided into two fractions: 1. Water that provides the osmolality of urine equal to the osmolality of blood plasma, that is, the water that enters the urine according to the laws of osmosis without the active work of the nephron tubules.

2. Osmotically free water, free from salts.

CH2o = V - Cosm., Or V = CH2o + Cosm.

The clearance of free water makes it possible to assess the effectiveness of the renal excretory function. This method is often used when carrying out water loading. If the

urine is hyperosmolar, the reabsorption of osmotically free water (Tn2o) is determined. Тн2о = Cosm. - V Usually, the reabsorption of osmotically free water is assessed by performing a deprivation test (with fluid restriction). It should be remembered that the concentrating function of the kidneys changes during the day, which is associated with the daily rhythms of ADH secretion, as well as diet, ambient temperature, etc. The maximum concentration of urine is observed in the morning hours. In newborns and the elderly, the concentration function is reduced. Function concentration of urine, as mentioned earlier, is disturbed earlier than the function of osmotic dilution of urine.

Vi. EXAMINATION OF URINE

Urine examination is an informative and accessible method for the diagnosis of kidney diseases and monitoring of ongoing therapy. Distinguish between general urine analysis, determination of individual indicators, microscopy of urine sediment, urine analysis according to Nechiporenko, biochemical urine analysis and other special methods. The results of the analysis and their interpretation depend on many factors that are not always taken into account in real life. Many mistakes are associated with the collection and storage of biological material. For analysis, depending on the tasks, a single portion of a portion of urine is collected - morning or random, an average portion of urine, daily urine.

1. Rules for the collection and execution of urine analysis.

Screening (screening) methods for detecting kidney or urinary tract diseases is a general urine test. To standardize the conditions during the planned research and clinical examination of the population, the entire portion of urine is collected after the toilet of the external genital organs in the morning in one dish. A full portion of urine is needed in order to identify any pathology associated with both kidney disease and urinary tract diseases. If a pathology is detected, additional studies can be carried out aimed at establishing its localization. Urine should be examined no later than 2 hours after collection. With prolonged storage, urine becomes more alkaline, some of the salts, when cooled to room temperature, may precipitate, and some cellular elements, for example, erythrocytes, collapse. In practice, this rule is often violated not only among outpatients, but also among hospital patients, which leads to errors not related to the work of the laboratory (out-of-laboratory errors). In emergency situations, a random portion of urine can be examined, but some of its parameters may differ from the indicators of the morning portion. The urine collection container must be washed thoroughly. Traces of detergents (detergents) can lead to errors.

The analysis is accompanied by a direction in which the name, gender, age of the patient, the alleged diagnosis, and the therapy being performed are indicated.

This is due to the fact that:

 the norms differ in patients of different sex and age,

 the diagnosis in the direction helps more efficient and coordinated work of specialists from various departments of the CDL,

• a number of pharmacological drugs affect the results of laboratory tests, for example, ascorbic acid.

For urine analysis according to Nechiporenko, an average portion of urine is collected. Nephrologists advise to collect urine without interrupting the stream. It is believed that the first portion of urine reveals inflammatory processes in the urethra, the middle portion of urine reveals kidney pathology, and the last - pathology of the bladder. In a sense, this division is conditional, but the middle portion is more "clean". It is not recommended to take a urine test according to Nechiporenko on the same day with a general urine test, which in practice is constantly violated. Screening is a general urine test. If its indicators are not enough to diagnose and prescribe treatment, a urine analysis is performed according to Nechiporenko. Wrong assignment of analyzes leads to unreasonable expenditure of funds, burden of the laboratory with unnecessary work and inadequate interpretation of the results obtained. When collecting daily urine, the first morning urine portion, for example, at 7 o'clock in the morning, is poured out. Further, all portions are collected in one dish. The last portion is added at 7 a.m. the next day, i.e. exactly one day later. If a preservative, such as acid, needs to be added to the urine, it is added to the first portion of urine in the same container. Urine should be stored in a cool, dark place to prevent bacterial growth. Before sending it to the laboratory, you must make sure that the urine is well mixed and the volume is measured correctly, as poor mixing and incorrect volume measurement will automatically lead to an error in the results.

2. General analysis of urine.

The general analysis of urine consists of an assessment of the physical properties, chemical examination and microscopy of the sediment.

2.1. Physical Properties of Urine

The physical properties of urine include quantity, color, turbidity, and density.

The amount of urine depends on various factors, so pathology is assumed only for very small and large volumes. Normal urine color includes all shades of yellow. The red color of urine deserves special attention. If the urine is red and cloudy, this indicates gross hematuria ("the color of meat slops"). Red and clear urine can be found with hemoglobin, myoglobin, porphyrins, certain drugs, or food coloring. The reason for the red color of urine always needs to be found out. In rare cases, the color of urine when standing changes from yellow to red, which can be observed with a rare hereditary disease - Swedish-type hepatic porphyria due to the conversion of low molecular weight unstained porphyrin precursors (delta-aminoleulic acid and porphobilinogen) into red-colored porphyrins. Beer-colored urine is observed in the presence of direct bilirubin. Transparency. Freshly discharged urine is believed to be clear. Turbidity can be caused

by cells, salts, mucus, and bacteria. The assessment of transparency on a scale full - incomplete, involves reading a newspaper font through a test tube with urine. Experience shows that the font is not read in laboratories. Therefore, it is better to indicate transparent, dull or turbid on the form in accordance with visual assessment.

Density. The density of urine depends on the time of day, intake and loss of fluid, etc. As mentioned earlier, the spread of density during the day can be significant. The morning portion of urine is usually concentrated, therefore, its density is higher than that of blood plasma (> 1010 g / l). Density measurement in most laboratories is carried out with a urometer. Before measuring the density, before pouring it into the cylinder, urine must be thoroughly mixed to evenly distribute the formed elements throughout the urine volume. It is important to know at what temperature the urometer is calibrated, since a temperature change of 30 C changes the density by 1 g / l. As the temperature rises, the density decreases. The density of urine increases glucose (1% per 4g / l), protein (4g / l protein per 1g / l) and salt. Density is measured in g / l or g / ml, for example, 1018g / l corresponds to 1.018g / ml. With a small amount of urine, the density can be measured using a refractometer using the refractive index of light or using diagnostic strips.

2.2. Chemical examination of urine.

Mandatory chemical analysis of urine includes determination of pH, protein and glucose. Additional methods carried out according to indications include the determination of ketone bodies, bilirubin, urobilinoids, hemoglobin (Hb) and myoglobin (Mb), nitrites.

Chemical examination of urine is carried out in two main ways: 1). Determination of parameters by traditional chemical methods.

2). Determination of parameters using diagnostic strips.

Each of these methods has its own advantages and disadvantages, which will be outlined below. When determining chemical parameters by traditional methods, urine must be mixed, centrifuged (1500 rpm, 10 min) and the required parameters must be determined in the supernatant fluid (supernatant). After centrifugation, mucus and cellular elements are precipitated, the transparency increases and the possibility of error in the determination is reduced. If the urine is acidic, then the remaining parameters are determined according to the method. In alkaline urine, that part of the supernatant that is used for chemical research must be acidified with a few drops of weak acetic or hydrochloric acid. This is due to the fact that in alkaline urine, a number of indicators (protein, bilirubin, etc.) can be false negative, since the chemical reaction is designed for normal weakly acidic urine. Acidifying or alkalizing urine also dissolves a number of salts. Reaction (pH) of urine. Since the kidneys perform a special function of acidifying urine, in a healthy person, urine is usually slightly acidic (pH 5.5-6.5) However, in some situations, urine can be either more acidic or alkaline, and the urine reaction does not always correspond to the plasma reaction blood, for example, with hypokalemia, acidic

urine is released against the background of an alkaline reaction of the blood (alkalosis). Usually, urine alkalizes over time. In renal tuberculosis, urine pH is stable acidic throughout the day (Table 10).

The pH of urine is determined using indicator strips, which is simple and accurate enough. Andreev's reagent allows you to roughly determine the reaction of urine - acidic, neutral, alkaline.

Table 12

Urine reaction	Clinical situations
Sour	Protein food, diabetic coma, feverish conditions, diseases of the renal parenchyma, renal tuberculosis, leukemia, excess uric acid and urate, hypokalemia
Alkaline	Carbohydrate and vegetable diets, kidney and urinary tract infections pathways, diarrhea, resorption of edema.

Protein in the urine. The determination of protein in urine is one of the most important indicators in the diagnosis of kidney disease. This parameter is determined in any laboratory, but it is with it that the greatest number of difficulties arise.

Each person secretes a small amount of protein at any time of the day. It was found that from 50 to 150 mg of protein (0.05-0.15 g / day) is excreted in the urine per day. More protein is released during the daytime, especially in the presence of physical activity, less - at night in a calm state. The release of protein is associated with the work of the nephron, since proteins are filtered in the glomeruli, then reabsorbed in the tubules. With all the perfection of the reabsorption mechanism, the kidneys are not able to completely return the filtered substances from the urine. A small amount necessarily remains in the urine. Consequently, all compounds that are in the urine enter the lumen of the tubules from the blood plasma. All substances that have entered the filtrate are necessarily present in the final urine, but sometimes in such a small amount that it cannot be determined by conventional chemical methods. These substances include protein, glucose, amino acids and some others. In addition, a small amount of protein is excreted into the urine by the cells of the renal epithelium.

The urine protein of a healthy person consists of:

A). Proteins that are not reabsorbed (40% is albumin).

B). Protein of the urinary tract (Tamm-Horgfall).

C). Certain other proteins.

Protein filtration is limited by HMM (<70,000 D), molecular shape and negative charge. Albumin (OMM 65000 D), which makes up about half of the proteins in the blood plasma, is a tiny fraction in the urine, since no more than 1% of albumin is filtered. The low content of albumin in primary urine is due to the fact that albumin is practically not filtered due to the presence of a negative charge of the molecule and a negative charge of the basement membrane, which are mutually repelled. With minimal damage to the glomeruli at the initial stages of kidney disease (diabetes mellitus, hypertension, glomerulonephritis, etc.), the negativity of the membrane charge decreases, which is accompanied by an increase filtration of albumin. The patient develops microalbuminuria, which is an informative test for detecting the initial stage of kidney disease. In particular, according to the materials of the World Health Organization (WHO), the determination of microalbumin is a mandatory test for patients with diabetes mellitus. , myoglobin (17,000 D), hemoglobin (68,000 D), alpha-amylase (48,000 D), etc.

The proteins that have entered the primary urine are almost completely reabsorbed by pinocytosis, and only a small part remains and is excreted in the urine.

In Russia, it is customary to take the amount of protein equal to 0.033 g / l for traces. This value is controversial, established by such methods that do not allow guaranteeing the degree of accuracy up to the 3rd decimal place. In a number of countries, a value of 0.1 g / l is taken for traces of protein. If the protein level exceeds the allowable value, the patient is diagnosed with proteinuria (Table 11).

There are two main types of proteinuria.

1. Functional, not associated with organic damage to certain organs.

2. Organic, associated with structural or metabolic damage to certain organs. Organic proteinuria is divided into:

2.1 Prerenal proteinuria associated with an excess of low molecular weight protein in the blood plasma.

2.2 Renal proteinuria due to kidney disease.

2.3 Postrenal proteinuria accompanying inflammatory diseases of the urinary tract (MEP), genital organs or caused by impaired urine outflow.

An example of functional proteinuria is stress proteinuria, for example, during hard physical work, proteinuria with hyperthermia, orthostatic proteinuria associated with a change in body position. In case of proteinuria with hyperthermia, the analysis must be

repeated after normalization of body temperature. Orthostatic proteinuria, which often occurs in adolescence, needs monitoring, since in 15-20% of cases it can be associated with anatomical or histological abnormalities of the kidneys. Organic proteinuria is not only associated with kidney disease. So, with prerenal proteinuria, an increase in protein in the urine is due to an increase in its blood filtration due to an increased content of low molecular weight protein in the blood plasma. For example, with multiple myeloma, plasma accumulates a large amount of immunoglobulin light chains with a GMM of 17,000 D, which easily pass into the urine. With prolonged crush syndrome, low molecular weight myoglobin is filtered, which accumulates in the tubules, creating a mechanical obstruction to the outflow of urine, and then can cause acute tubular necrosis.

Postrenal proteinuria is observed with cystitis, blockage of the ureter by a tumor, some diseases of the genital organs, etc.

Renal proteinuria is associated with kidney disease. It may be associated with increased protein filtration (glomerular), with impaired protein reabsorption (tubular), or with both at the same time (mixed). Glomerular proteinuria is most pronounced. So, with acute renal failure, the protein content in the urine can briefly exceed the level of protein in the blood plasma (the norm of protein in the blood plasma is about 65-85 g / l).

Table 13

Types of proteinuria.

Functional	**Органическая**		
Orthostatic **Voltage** **Hyperthermia**	**Prerenal -** **excess** **low molecular weight** **protein (myeloma,** **Crash syndrome, etc.)**	**Renal -** **glomerular,** **tubular,** **mixed** **(kidney disease)**	**Post-renal** **(inflammatory** **diseases of the MEP and** **genitals)**

Depending on the amount of protein secreted per day, moderate proteinuria up to 1 g / day, moderate proteinuria, severe proteinuria up to 3 g / day, more than 3 g / day are distinguished.

If the amount of protein secreted exceeds 3.5 g / day, the patient is diagnosed with nephrotic syndrome, i.e. a syndrome characterized by severe proteinuria, hypoproteinemia, hyperlipidemia and edema. The first two signs are required.

Hypoproteinemia is caused by proteinuria - the loss of protein through the kidneys. A decrease in the level of protein, especially albumin, in the blood plasma leads to a decrease in oncotic pressure and water retention in tissues, or, in other words, edema. Edema in nephrotic syndrome is classified as protein-free. The cause of hyperlipidemia has not been definitively established. One hypothesis is an increase in lipid content to compensate for a decrease in protein.

The causes of nephrotic syndrome (NS) can be:

1. Kidney disease (glomerulonephritis, lipoid nephrosis, nephropathy of pregnant women, etc.).

2. General systemic diseases with a periodic course (amyloidosis, systemic lupus erythematosus, rheumatism, sickle cell anemia, diabetes mellitus, etc.).

3. Infections (syphilis, malaria, tuberculosis, etc.).

4. Toxic agents (heavy metals, antiepileptic drugs, etc.).

5. Allergic influences (snake venom, vaccination, administration of serums).

6. Violation of blood circulation (extremely rare).

NS can occur in people of any age, but more often it occurs in children under 5 years of age and in adults under 35 years of age. The amount of protein secreted can range from 3.5-6 to 20-50 g / day. The prognosis of the disease depends on which protein is released - low molecular weight or high molecular weight. If a low molecular weight protein, for example, albumin, is excreted in the urine, the prognosis of the disease is favorable, and proteinuria is classified as selective (selective). This means that the kidneys filter the protein that easily passes through the kidney filter. If high molecular weight protein, such as alpha-2-macroglobulin, immunoglobulins, is excreted in the urine, the prognosis is poor and proteinuria classified as non-selective. This means that the kidneys filter any protein, the selectivity of the kidney filter is impaired. To assess the selectivity of proteinuria, clearance methods and protein electrophoresis are usually used. In our country, electrophoresis of urine proteins is often performed in parallel with electrophoresis of serum proteins. Typically, the urine protein electropherogram complements the serum electropherogram. Urine protein electrophoresis is a laborious and time-consuming procedure, since it includes the stages of urine dialysis, urine concentration and directly electrophoresis of urine proteins and blood serum. Currently, devices for electrophoresis of urine proteins have appeared, which allow separation of fractions without dialysis and concentration. These are highly sensitive tests to detect glomerular, tubular, and mixed proteinuria. In addition, using electrophoresis, you can determine the Benz-Jones protein, which is found in multiple myeloma and similar diseases. Other methods for the determination of this protein are not standardized.

Methods for the determination of protein in urine are divided into qualitative, semi-quantitative and quantitative. First, it is recommended to carry out a qualitative determination of the protein, and then in samples with a positive result - a quantitative one. When determining protein in urine, all soluble protein that has entered the urine is measured. The task of the laboratory is to identify the protein, and then using additional methods to determine the source of its origin. The most sensitive qualitative method is the 20% sulfosalicylic acid sample. The sample is simple, fast, reliable, cheap and available to any clinical diagnostic laboratory. When acid is added, the protein coagulates, the solution becomes cloudy. The result is assessed visually against a dark background in comparison with intact urine. An alkaline urine sample must be acidified to rule out false negative results. The analysis is performed in urine after centrifugation. In the presence of significant amounts of hemoglobin and myoglobin, the protein precipitate will have a brown tint. Semi-quantitative methods include the determination of protein by layering 50% nitric acid or Larionova's reagent on a urine sample, as well as the determination of protein in urine using diagnostic strips. Layering results are dependent on lighting, sample evaluation time, visual acuity, integrity and experience of the technician. The appearance between the second and third minutes of a thin ring of precipitate at the interface between the two media theoretically corresponds to 0.033 g / L of protein in the sample. This value is to a certain extent arbitrary, but we have accepted it. If the ring is wide or appeared earlier, the urine is diluted until the initial conditions are met. In this case, 0.033 g / L is multiplied by the dilution. The method is subjective and can be used in laboratories that are not equipped with photometers. Currently not unified. The quantitative methods include the determination of protein in urine by the biuret method, which is very laborious and is not usually used in laboratories, by the method of turbidimetry on a photometer with 3% sulfosalicylic acid, and with pyrogallol red. Determination of protein with sulfosalicylic acid is the most accessible and widespread method, given in almost all manuals. To obtain reliable results, it is necessary to correctly construct a calibration graph, accurately maintain the incubation time, noting the beginning of incubation for the first sample, stir the reaction mixture before measuring, put a sample blank (urine sample with saline). The most sensitive and reliable is the determination of the protein with pyrogallol red, since the dye reacts equally well with proteins of various classes. As a result of the complexation reaction of the reagent with the protein, the red color of the solution turns into blue. The method is also recommended for the determination of protein in the cerebrospinal fluid. Glucose in the urine. Determination of glucose in urine belongs to the category of mandatory chemical research. Glucose, being a low-molecular water-soluble compound, is easily filtered in the glomeruli, then reabsorbed in the tubules. Filtration of glucose in the intact glomerulus is practically not limited by anything. Reabsorption is a complex process. It depends on the availability of energy (ATP), enzyme activity, ionic composition, etc. Therefore, glucose reabsorption is limited by the capabilities of the tubular apparatus. In a healthy person, the ability of the tubules to reabsorb glucose is much higher than the amount of its intake, therefore, almost all glucose returns to the blood. As mentioned

earlier, despite the uniqueness and perfection of the nephron, the kidney cannot completely reabsorb glucose, like other substances, therefore, glucose is present in the urine of any person, but its level is very low and is approximately 0.1-0.8 mmol / l and no more than 2.78 mmol / day. The physiological level of glucose in urine is not determined by conventional laboratory methods, so tests are negative. The appearance of detectable glucose in the urine may be associated with an increase in the level of glucose in the blood (hyperglycemia), with a decrease in the reabsorption of glucose in the kidneys. Normal fasting blood glucose is approximately 3.56 mmol / L. The glucose level depends on age (increases), the method of determination and on the biological material in which the study is carried out. So, in serum and blood plasma, the glucose content is 8-10% higher than when determined in whole blood. In a patient on a mixed diet, the blood glucose level rises after a meal, reaching a maximum after about an hour. However, with normal consumption of glucose by the liver, muscles and other organs, it usually does not increase by more than 1.7-1.8 times and does not exceed the level of 9-10 mmol / L. With an increase in the level of glucose in the blood, its filtration also increases, but the reabsorption capacity of the kidneys is sufficient to return the filtered glucose to the blood, therefore, the level of glucose in the urine remains normal and cannot be determined by conventional methods. With a higher content of glucose in the blood (hyperglycemia), it is also easily filtered, but the energy or enzymatic capacity of the kidneys becomes insufficient to return glucose to the blood.

Glucose appears in the urine and is determined by standard laboratory methods. The patient has glucosuria. The limit for blood glucose at which it appears in urine is called the renal threshold for glucose, and glucose is called the threshold. The renal threshold for glucose is individual. In a child, it is higher: 10.5-12.5 mmol / l, in an adult - 9-10 mmol / l. In a number of patients with diabetes mellitus the renal threshold rises significantly, and urine glucose is not always detected with elevated blood glucose values. Since glucose belongs to osmotically active substances, it acts in the urine as an osmotic diuretic, increasing the volume of excreted fluid. Polyuria is characteristic of patients with glucosuria.

Hyperglycemia above the renal threshold always causes glucosuria, regardless of etiology. Consequently, pancreatic hyperglycemia (diabetes mellitus, pancreatitis), and extra-pancreatic hyperglycemia (alimentary, nervous, hormonal, with liver diseases) are accompanied by glucosuria. Alimentary (food) hyperglycemia occurs after taking more than 100 g of glucose at a time. Practice shows that they often forget about another type of glucosuria associated with a decrease in glucose reabsorption in the tubules, the so-called renal (renal) glucosuria. With congenital (primary) or acquired as a result of organic damage to the kidneys (secondary) disruption of the enzyme systems, or, less often, lack of chemical energy, the ability of the kidneys to reabsorb glucose decreases, which is expressed by a decrease in the renal threshold for glucose and the appearance of glucose in urine at normal or low levels blood glucose. According to literature data, the

renal threshold can be reduced to 6-0.8 mmol / l. Since blood glucose is determined by dietary glucose intake, tissue glucose uptake and renal excretion of glucose, a sharp decrease in renal threshold leads to significant excretion of glucose in the urine and a decrease in blood glucose levels. Thus, glucosuria can be the cause of hypoglycemia (Table 12).

From the above, it follows that the urine glucose test cannot play a diagnostic role in detecting diabetes mellitus, since there are a number of other causes that cause glucosuria. On the other hand, the test is very important in the chemical study of urine, since it allows you to determine the tactics of examining the patient. The qualitative determination of glucose in urine is carried out with the Guines reagent. The method is unified, although it does not differ in high sensitivity and reliability.

Recently, the determination of glucose in urine is carried out semi-quantitatively using diagnostic strips. The sensitivity of the strips from different manufacturers may differ, but on average it is about 2 mmol / l and does not determine the physiological concentration of glucose in the urine. A number of substances, for example, ascorbic acid, can affect the test results, so you should carefully read the instructions.

Quantitative determination of glucose can be carried out by the polarimetric method and chemical enzymatic methods, which are used to determine glucose in the blood (glucose oxidase, hexokinase). Determination of glucose concentration using a polarimeter is based on the property of sugars to rotate the plane of polarized light to the right. The degree of deflection of the beam is used to determine the glucose content in the urine. A prerequisite for determining is the transparency of urine. Acidified lead acetate is added to the cloudy and colored urine and filtered. Some pharmaceuticals, such as tetracyclines, also have optical activity and can give false positive results.

With the quantitative determination of glucose by enzymatic methods, the urine sample is diluted 10-20 times nat. solution, then the result is multiplied by the dilution.

The formula for converting

glucose concentration from mmol / L to g / 100 ml (%): C glucose g / 100 ml (%) = C glucose mmol / L x 0.018

The formula for converting glucose

concentration from mmol / L to g / L: C glucose g / l = C glucose mmol / l x 0.18 When determining glucose in daily urine, it is necessary to add a preservative (thymol, toluene, etc.) to prevent the consumption of glucose by bacteria. The urine should be stored in a cool, dark place. Ketone bodies. Ketone bodies are formed in the liver from lipolysis products and ketogenic amino acids, as well as by-products of fatty acid oxidation. Ketone bodies enter the bloodstream and then are filtered into urine. During the day, 20-50 mg of ketone bodies are released. (Table 13).

The accepted method for the determination of ketone bodies is a sample with sodium nitroprusside (Legal's reaction).

The sensitivity of the method is about 50 mg / l. The peculiarity of the study is that this method allows you to determine the presence of acetoacetic acid and acetone, and the sensitivity of the sample to acetone is 20-30 times lower than the sensitivity to acetoacetic acid.

β -hydroxybutyric acid is not determined using this test, although it constitutes the main part of ketone bodies and is formed in large quantities during decompensation of diabetes mellitus. When treating diabetic patients with insulin, β-hydroxybutyric acid is converted into acetoacetic acid, which indicates the effectiveness of treatment, but according to Legal's test, the level of ketone bodies increases, since acetoacetic acid is determined by this method. An increase in the level of ketone bodies is observed in a number of diseases associated with metabolic disorders, especially lipid metabolism. So, the level of acetoacetic acid increases with diabetic ketoacidosis, excessive insulin administration, prolonged fasting, strict restriction of carbohydrates in the diet, with persistent vomiting, after anesthesia, with an increase in the metabolic rate (fever, thyrotoxicosis), pregnancy, stress.

Some medications (cysteine, levodopa, etc.) can lead to false positive results. β -hydroxybutyric acid increases in alcoholic ketoacidosis, lactic acidosis, shock, liver disease, infections, phenformin and salicylate poisoning. The high level of β-hydroxybutyric acid observed in diabetic ketoacidosis decreases with insulin treatment against the background of an increase in the concentration of acetoacetic acid. Determination of β-hydroxybutyric acid is a more reliable test in monitoring the treatment of patients with diabetic ketoacidosis, but for its determination it is necessary to use an enzymatic method, which is not available in every laboratory. Acetone levels increase in diabetic and hungry ketoacidosis, malnutrition, severe carbohydrate restriction, and isopropanol poisoning. Legal's breakdown of acetone is determined, but with a lower sensitivity, the recommended method is gas-liquid chromatography. In diabetic ketoacidosis, the appearance of ketone bodies is combined with the presence of glucose in the urine. In patients with severe alcohol intoxication, Legal's test may be negative, since ketone bodies are represented mainly by β -hydroxybutyric acid, which is not detected by this test.

Bile pigments.

Bile pigments detected in urine include bilirubin and urobilinoids or urobilin bodies. Bilirubin is formed during the cleavage of heme in the cells of the reticulo-hysteocytic system and is called free bilirubin. It does not give a direct reaction with diazosmeya, therefore the accepted name for bilirubin is indirect bilirubin. Indirect bilirubin is a toxic fat-soluble substance that easily passes into those organs and tissues that are most permeable to hydrophobic substances, namely, into nerve cells and adipose tissue.

Indirect bilirubin does not pass through the renal filter, which is permeable only to hydrophilic compounds. The exception is newborn children up to 7-10 days of age, whose kidneys in some cases can pass indirect bilirubin. In the liver, glucuronic acid is added to indirect bilirubin, which changes the properties of bilirubin: it becomes hydrophilic and loses its toxicity. Bilirubin with glucuronic acid is called conjugated, it is secreted into bile, and since it gives a direct reaction with a diazo mixture is called direct bilirubin. Direct bilirubin passes through the kidney filter. The usual concentration of bilirubin in the blood is very low (less than 21 μmol / L), and direct bilirubin can make up from 0 to 25% of the total bilirubin. Since only direct bilirubin is filtered through the kidneys, of which there is an insignificant amount in the blood, there is practically no bilirubin in the urine. An increase in the level of direct bilirubin in the blood above the renal threshold leads to the appearance of direct bilirubin in the urine. The urine takes on a "beer color". All diseases accompanied by the growth of direct bilirubin cause the appearance of bilirubin in the urine. Such diseases include obstructive and parenchymal jaundice, Dabin-Johnson and Rotor syndromes.

Urobilinoids are products of the conversion of bilirubin in the biliary tract or intestines under the influence of intestinal flora. There are 4 known urobilinoids, but in practice we have to meet with two: urobilinogen and stercobilinogen.

Urobilinogen is formed in the biliary tract, absorbed in the intestine and returns to the liver with the blood of the portal vein, where it is destroyed to pyrroles. In a healthy person, urobilinogen does not enter the general circulatory system, is absent in the blood and, accordingly, in the urine. An increase in the level of urobilinogen in the blood and urine is observed in liver diseases, for example, hepatitis, and some hereditary bilirubinemia (Dabin-Johnson and Rotor syndromes).

Stercobilinogen, formed in the intestine, is partially absorbed through the hemorrhoidal veins into the bloodstream and excreted in the urine. The approximate level of stercobilinogen in urine is 5-17 μmol / L. The bulk of unstained stercobilinogen in the rectum under the influence of atmospheric oxygen is converted into colored stercobilin and provides a normal color of feces. With cholestasis, the flow of bile into the intestine is disrupted and the content of stercobilinogen decreases up to a complete absence in feces (acholic feces) and urine. With hemolytic jaundice, accompanied by excessive release of bilirubin into bile, the level of stercobilinogen in both feces and urine increases. The urobilinoid found in urine is often called urobilinogen because it is excreted in the urine, although it is a stercobilinogen by its chemical structure. The separation of urobilinoids requires high performance liquid chromatography, which is inaccessible to conventional clinical diagnostic laboratories. The methods that are actually used do not allow separating urobilinoids by chemical structure and determine their total amount. Direct bilirubin secreted by the kidneys stains urine "beer-colored".

Urobilinoids can give a reddish tint to urine in large quantities, but, as a rule, no noticeable discoloration is observed. For the appearance of a reddish color, it is necessary - the release of stercobilinogen in quantities tens of times higher than the normal value, for example, in hemolysis associated with the transfusion of incompatible blood, - urine must stand in the air for several hours so that unstained stercobilinogen under the influence of atmospheric oxygen turns into colored stercobilin.

Analysis of urine for bile pigments involves two studies: determination of bilirubin and urobilinoids, while urobilinoids rarely stain urine. The combination of bilirubin and urobilinoids in urine can be very different depending on the nature of the disease. In many hospitals there is a tendency to equate urinalysis for bile pigments with urinalysis for bilirubin. The examples in Table 14 will help you understand this misconception.

Methods for determining bilirubin. The most sensitive test for bilirubin is Fouche's test. The quality of the sample depends on the pH of the urine; therefore, alkaline urine must be acidified before determination. A simpler and more common, but less sensitive, test of Rosin with Lugol's solution. Methods for the determination of urobilinoids. Chemical methods for the determination of urobilinoids require the use of solvents, special glassware and depend on the quality of workmanship; therefore, it is better to determine urobilinoids using diagnostic strips.

Hemoglobin.

Hemoglobin belongs to the group of hemoproteins and consists of heme containing iron and globin protein. With the natural destruction of erythrocytes, a small amount of hemoglobin enters the blood plasma, not exceeding 40 mg / l. Since hemoglobin has a HMM of 68,000 D, it passes through the renal filter. In blood plasma, it combines with the protein haptobin, which increases the BMM to 160-320 kD and limits the filtration of hemoglobin. In case of intravascular hemolysis of various origins and excess of the content of free hemoglobin in the blood plasma of the reserve capacity of its binding by haptoglobin, it accumulates in the blood plasma and is filtered into the urine. In such patients, both blood plasma and urine become red in color, and free hemosiderin can be found in the urine. Hemoglobin in urine can also come from destroyed or altered (lost hemoglobin) red blood cells.

Methods for determining hemoglobin.

A qualitative method for determining hemoglobin can be any method for traces of blood. For instance, benzidine test or orthotolidine reaction. To determine hemoglobin, urine protein electrophoresis is used. Myoglobin. Myoglobin also belongs to the group of hemoproteins and consists of heme containing iron and globin protein. Myoglobin is found in skeletal muscle and myocardium, and its function is to store oxygen. In a healthy person, myoglobin levels are very low. When muscle tissue is damaged,

myoglobin enters the bloodstream (myoglobinemia), and from the blood into the urine (myoglobinuria). The OMM of myoglobin is only 17,000 D, so it is easily filtered in the glomeruli. Myoglobin in urine is detected if its concentration in the blood reaches a level of 9-12 μmol / l (20-25 mg%). Myoglobinuria can be idiopathic, associated with ischemia or crushing of muscle tissue (heart attack, thrombosis, prolonged crush syndrome), toxic (snake, wasp, hemlock root), marching, caused by cooling and positional pressure, etc. Massive myoglobinuria leads to blockage of the lumen by myoglobin tubules, to acute necrosis of tubules and acute renal failure. The urine of patients with severe myoglobinuria has a red color, which turns brown after 2-3 hours, the reaction is sharply acidic, proteinuria and often cylindruria are detected. In myoglobinuria, blood plasma is not colored (Table). A qualitative reaction to myoglobin is based on the ability of myoglobin to form red-brown compounds with ammonium sulfate. 2.8 g of crystalline ammonium sulfate are dissolved in 5 ml of urine and filtered. A colored filtrate indicates the presence of myoglobin in the urine. The absence of color in the filtrate is observed in the presence of hemoglobin, 80% of which is precipitated by the reagent. Quantification is carried out by immunological methods.

2.3. Microscopy of urine sediment.

Preparation of urine sediment.

Urine sediment microscopy is an analysis that is performed in almost all laboratories. However, the results obtained in different laboratories do not always coincide. This is due, in most cases, to improper preparation of drugs. To obtain comparable results, it is necessary to standardize as much as possible the method of preparing biological material.

Before centrifugation, the urine is thoroughly mixed, poured into a 10 ml tube and centrifuged for 10 minutes at 1500 rpm. The supernatant is decanted, if necessary, for chemical analysis, the tube is shaken gently to get rid of excess drops of supernatant. The content of the precipitate is stirred with a plastic pipette, which is then applied to a drop on a glass slide. A drop applied with a pipette has a standard volume. Then the drop is covered with a cover glass. If a standard drop is covered with a standard glass, the thickness of the preparation will be approximately the same, and the number of shaped elements in the field of view will be the same for different performers. The specimen is first microscoped at low magnification, and then at high magnification: for a monocular microscope objective 40, eyepiece 10, for a binocular microscope objective 40, eyepiece 7.5. Distinguish between organized (cells, cylinders) and unorganized urine sediment (salt crystals).

Organized urine sediment.

In the organized sediment of urine, cells of 3 types of epithelium are distinguished - squamous, transitional and renal, erythrocytes, leukocytes, casts, fungi and bacteria.

Squamous epithelium. In men, squamous epithelium is found only in the lower third of the urethra, it is little exfoliated, and it practically does not occur in the urine of healthy men. In women, squamous epithelium lines the entire urethra and vagina, so in women it is almost always present in the urine. With a poor toilet of the external genital organs, the amount of squamous epithelium can be so significant that other elements of the sediment become invisible. In this case, the analysis must be retaken. Squamous epithelium is a large polygonal or rounded cell with a small nucleus, not stained and not containing granularity or inclusions. In girls before puberty, the squamous epithelium, which got from the walls of the vagina, is smaller and its nucleus is larger, which sometimes leads to microscopic errors, since the squamous epithelium is mistaken for transitional. Layers of squamous epithelium in women may be an indirect sign of squamous cell metaplasia, and in the treatment of prostate cancer in men with estrogens, it may indicate the adequacy of the dose.

The transitional epithelium lines in men the renal pelvis, ureters, bladder, 2/3 of the urethra and prostate ducts. In women, the renal pelvis, ureters and bladder.

The epithelium is 3-6 times larger than the leukocyte in size and is characterized by pronounced polymorphism. In different parts of the urinary tract, it differs in size, cell shape, number of nuclei (Fig.). So, the cystic epithelium is large rounded cells containing from 1 to 3 nuclei, the epithelium of the ureters is represented by elongated cells, etc. Common signs are a slight yellowish staining of the cytoplasm as a result of contact with urine urochromes and the presence of fine granularity. Vacuoles and fat droplets may appear. The norm is made up of single cells in the preparation. The parameter is estimated by the number of cells in the field of view. An increase in content is observed in inflammatory diseases of the urinary tract, prostate gland, with intoxication or after anesthesia. When a large amount of transitional epithelium is found, do not confirmed by the diagnosis, it is recommended to conduct a cytological study for the presence of atypical cells.

Renal epithelium. The renal epithelium lines the nephrons. Morphologically, it represents small cells 1.5-2 times larger than a leukocyte, irregularly rounded, quadrangular or oval in shape with a fairly large nucleus. The renal epithelium is never a regular round shape, there are always elements of angularity (Fig.). Since the epithelium has long-term contact with urine urochromes, it is colored in various shades of yellow: from light yellow to brownish yellow. In the cells of the renal epithelium, elements of dystrophy are expressed, which are manifested by large granularity, often covering the nucleus, the presence of vacuoles and fat droplets. Fatty degeneration of the renal epithelium indicates the severity of the lesion. In urine containing bilirubin, the cells of the renal epithelium swell and appear larger, rounded, and pigmented. In the urine of a healthy person, the renal epithelium is never found. It appears as a result of damage to the renal parenchyma in kidney disease, with intoxication and after anesthesia.

The most common laboratory errors are related to the detection of renal epithelium. To be confident in the test results, it is necessary to compare the detection of renal epithelium with other parameters, such as protein in the urine and the presence of casts, as well as with the history or diagnosis. Protein in the urine, casts, especially epithelial casts, desquamation of the chains of renal epithelium cells and a history of kidney disease, the presence of intoxication or anesthesia confirm the presence of renal epithelium in the urine. If there are difficulties in the differential diagnosis of urine sediment cells, it is recommended to use the "Urine sediment" set, which allows you to distinguish cells by color.

Leukocytes.

In the urine of healthy people, leukocytes are almost always found. These are small round colorless or grayish cells, 1.5-2 times more red blood cells. As a rule, leukocytes in urine are represented by segmental-nuclear neutrophils (95%), less often - lymphocytes or eosinophils. The number of leukocytes depends on gender and age: in boys until puberty, they may not occur, in men 0-3 in the field of vision, in women - 0-5 in the field of vision. Leukocytes in urine increase in diseases of the kidneys and urinary tract of an infectious and inflammatory nature. The detection of a high content of leukocytes against the background of bacteriuria indicates pyuria (pus in the urine). In the preparation, leukocytes can be located separately or in the form of clusters. The presence of clusters must be noted on the test form. In low-density urine, leukocytes may swell and, under conditions of alkaline urine, collapse.

With some infectious and allergic diseases, as well as with dysmetabolic nephropathies, the content of lymphocytes and eosinophils can significantly increase and make up more than 15% of all leukocytes. Differential leukocyte counting helps in diagnosing and assessing the prognosis of the disease, but is difficult in a native preparation. In order to calculate the leukoformula of urine, an uroleukocytogram is prepared. The urine is centrifuged to obtain a precipitate. In the absence of visible sediment, it is enriched, i.e. the entire volume of urine is centrifuged in one test tube in several stages. A drop of serum or blood plasma is added to the resulting sediment as a protein source, mix and smear on a slide. The smear is fixed and stained with dyes for staining a blood smear, but the exposure time is reduced by 2 times in comparison with blood. The smear is dried, microscoped and evaluated as a blood count.

Red blood cells.

In the urine of healthy people, the presence of single erythrocytes in separate portions of urine is allowed. Erythrocytes are found unchanged and altered. Unchanged erythrocytes are similar in shape to yellowish-greenish discs, contain hemoglobin, and become opalescent in the preparation. Modified erythrocytes are erythrocytes that have lost hemoglobin. They look like rings. Altered red blood cells are found in acidic urine. In sharply alkaline urine, erythrocytes are destroyed. Previously, it was believed that

unchanged (fresh) erythrocytes enter the urine from the urinary tract, and altered ones - from the renal parenchyma. However, experience has shown that red blood cells from the urinary tract can also lose hemoglobin if they are in acidic urine for a long time, for example, in the bladder or urine collection container. The division of erythrocytes into altered and unchanged ones is important if a portion of urine is random, was in the bladder for no more than 2-4 hours, and was examined immediately after urination. Since these conditions are not met in most cases, laboratory staff are advised to note the total number of erythrocytes without dividing them into changed and unchanged to avoid misinterpretation of the results. The shape of red blood cells depends on the osmolality (density) of the urine. In urine with a low density, erythrocytes increase in diameter, in some cases hemolysis may occur. In urine with a high density, red blood cells decrease in size, the membrane has a folded structure (shrinks). With a large number of altered red blood cells in the urine, hemoglobin can be detected.

The appearance of red blood cells in the urine is called hematuria. Blood in the urine detected with the naked eye (urine of the color of "meat slops") indicates gross hematuria. The detection of erythrocytes in an amount of more than 3 in the field of view or more than 1000 / ml (106 / l) according to Nechiporenko allows the diagnosis of microhematuria. The main causes of hematuria:

1. Diseases of the renal parenchyma.

2. Inflammatory processes in the urinary tract.

3. Kidney stone disease.

4. Dysmetabolic nephropathy.

5. Violation of blood coagulation processes.

Hematuria associated with impaired blood coagulation processes is often observed in patients with an overdose of indirect anticoagulants (vitamin K antagonists - neodikumarin, phenylin, syncumar, omefin, etc.). Vitamin K antagonists interfere with the synthesis in the liver of vitamin K-dependent coagulation factors, such as V, VII, X. With a deficiency of factors, the blood coagulation process slows down. Control over the processes of coagulation is carried out by determining the prothrombin index (PTI) or prothrombin time according to Quick. In case of an overdose of indirect anticoagulants, PTI decreases sharply, and the patient may experience diapedetic bleeding, in particular, in the kidneys, which is manifested by microhematuria.

Cylinders. The cylinders are protein and cell casts of the renal tubules. At the heart of any cylinder is protein, which acts as an adhesive. The protein in the cylinders is changed and represented by a hyaline-like mass. Cylinders are usually found in acidic urine. The cylinders dissolve in alkaline urine.

For the formation of cylinders, the following conditions must be met:

the presence of protein in the urine,

an acidic reaction of urine, impaired outflow or stagnation of urine.

There are several types of cylinders.

Hyaline cylinders are homogeneous, translucent, with rounded edges. Salts characteristic of acidic urine (mainly urates), bacteria, leukocytes, erythrocytes, and renal epithelium can be deposited on the surface of the cylinders. Hyaline casts, single in the preparation, can be found in the urine of a healthy person.

Granular cylinders are formed either by protein altered as a result of coagulation or by decay products of cellular elements. Normally they are not found. Pigment casts are yellow-brown granular casts formed as a result of coagulation of hemoglobin or myoglobin. Normally, no.

Waxy casts are formed from hyaline and granular casts during their long stay in the tubules. The cylinders are yellowish in color, have uneven edges, cracks and indicate severe damage to the renal parenchyma. Normally they never meet.

Epithelial casts are formed by cells of the renal epithelium. Epithelial casts confirm the presence of renal epithelial cells in the urine sediment.

Leukocyte casts are formed by leukocytes, are observed in pyuria and confirm the renal origin of leukocyturia.

The erythrocyte casts are composed of erythrocytes and confirm the renal origin of hematuria. Fat casts are made up of droplets of fat and strongly refract light. Usually found against the background of fatty renal epithelium and indicate the severity of the damage.

For kidney disease, a triad of changes is characteristic:

1. The presence of detectable protein in the urine.

2. The presence of cylinders.

3. Presence of renal epithelium.

Intermittently, but often, microhematuria is also found. However, in some cases, there is a discrepancy between the presence of casts and the protein content in the urine. If there are no conditions for the formation of casts, only soluble protein can be found in the urine. If the processes occurring in the tubules are such that practically all the protein coagulates and turns into cylinders, the amount of dissolved protein is so small that it cannot be detected by conventional laboratory methods, i.e. is within normal limits. In

this case, the cylinders can be detected against the background undetectable dissolved protein. Thus, all the situations shown in table. are real.

3. Study of urine according to Nechiporenko.

The study of urine according to Nechiporenko refers to quantitative methods for assessing the content of urine formed elements. The method is used to diagnose the initial stages of kidney disease. The method allows detecting microhematuria, an increase in the content of leukocytes and cylinders. Sometimes the method is used to assess the effectiveness of a treatment. For urine analysis according to Nechiporenko, an average portion of morning urine is used. Stir the urine thoroughly. 10 ml of urine is poured into a measuring centrifuge tube and centrifuged for 10 minutes at 1500 rpm. After centrifugation, the upper layer of urine is collected so that 1 ml remains in the test tube. Thus, the concentration of the shaped elements occurs 10 times. Remaining in the test tube, the urine is mixed and the counting of the formed elements is made in the Goryaev chamber, which has a volume of 0.9 μl.

Counting can be done in two ways.

1. Shaped elements are counted in 100 large squares (according to Pytel). The result obtained is multiplied by 250 to obtain the number of formed elements in 1 ml, or by another 1000 to obtain the number of formed elements in 1 liter (since 1000 ml in 1 liter).

2. Shaped elements are counted throughout the Goryaev chamber (unified method). The result obtained is multiplied by 111 to obtain the number of formed elements in 1 ml, or by another 1000 to obtain the number of formed elements in 1 liter. The content of formed elements is normal: Erythrocytes up to 1000 / ml Leukocytes Cylinders up to 2000 / ml up to 20 / ml 106 / l. 2x106 / l. 2x104 / l.

If 2 or more cylinders are found in the preparation or if they are absent, the calculation is carried out as indicated above. If there is one cylinder in the preparation, it is advisable to look at another Goryaev chamber and 2 Fuchs-Rosenthal chambers with a volume of 3.2 μL for cylinders, only for the presence of cylinders. This is due to the fact that hyaline casts may be present in the urine of a healthy person. The calculation according to the usual scheme will immediately show a pathology of 100 cylinders / ml. The presence of one cylinder in 2 Goryaev chambers and 2 Fuchs-Rosenthal chambers, which approximately corresponds to 8 Goryaev chambers, will show the presence of only 12 cylinders, i.e. normal quantity. This approach allows you to distinguish between normal or borderline condition from pathology.

If the collected urine is less than 10 ml in volume, it must be concentrated 10 times. For example, take 8 ml for centrifugation and leave 0.8 ml for microscopy. When collecting urine from a child with a volume of 1-2 ml, it must be mixed and microscoped without

centrifugation. Since there is no 10-fold concentration of urine, the results of microscopic examination are multiplied by 2500 (according to Pytel) and 1110 for the unified one.

VII. DETERMINATION OF URINE PARAMETERS USING DIAGNOSTIC STRIPS.

Currently, the simplest way to study urine is to determine its parameters using diagnostic strips. There are a number of manufacturers that produce urine test strips. The principle of determining the parameters is in most cases the same, however, the sensitivity, the influence of various factors, exposure time, possible errors, etc. may differ. Therefore, before working with the strips, you must carefully read the instructions, paying attention to each determined parameter, the number of which ranges from one, for example, glucose, to eleven. These include: pH, protein, density, glucose, ketone bodies, bilirubin, urobilinogen, blood, leukocytes, nitrites, and ascorbic acid or reducing substances. The study of urine using diagnostic strips is a screening (selection) method for detecting a particular pathology. So, the appearance of glucose in the urine may be a sign of diabetes mellitus or a decrease in the renal threshold for glucose, an increase in the level of ketone bodies indicates an increase in ketogenesis, pathological values of the content of bilirubin and urobilinoids - a violation of the exchange of bile pigments.

Determination of ascorbic acid is associated with the influence of its excess on the quality of studies of a number of other parameters.

To identify pathology of the kidneys and urinary tract, the following indicators are used: pH, protein, leukocytes, erythrocytes, nitrites. If the above indicators are within normal limits, then microscopy of urine sediment can be omitted during medical examinations. If kidney disease is suspected, microscopy of the urine sediment is required. Research evaluation involves visual and instrumental recording of research results. By visual assessment, semi-quantitative data can be obtained based on a comparison of the color of the working strip with the color scale attached to the tube where the strips are stored. The test results are influenced by the exposure time, so it should be noted using a stopwatch or laboratory clock. Urine analyzers evaluate the same parameters, but using an objective method - reflective photometry.

The analyzers strictly adhere to the exposure time, it can automatically correct some determination results, for example, those related to urine pH, and simplifies the registration of results. When the analyzer is connected to a computer, the research results can be entered into the database. But the sensitivity of the method and errors associated with improper sampling and preparation of samples are not corrected by the analyzer.

To avoid errors in determining chemical parameters using diagnostic strips, the urine is thoroughly mixed, and the strip is dipped into it immediately after mixing. Then the strip is placed on horizontal surface and is assessed after the exposure time, which is specified in the method and is usually 60-120 sec. Thorough mixing of urine is especially

important when assessing the content of cellular elements - erythrocytes and leukocytes. Poor mixing is a common cause of in-laboratory errors. For a successful study with a visual assessment method, it is advisable to purchase strips with the lightest background, do not use the strips later than the expiration date, store the strips in a tightly closed tube at the specified temperature. Urine before examination can be stored for no more than 2 hours.

Defined parameters.

RN. The reaction of urine is determined using a universal indicator or a mixture of indicators and usually does not cause difficulties. Normal pH 56. The results of the reaction are influenced by disinfectants and detergents and long-term storage of urine, since during storage the pH of urine rises.

Protein. The determination of protein is based on a change in the color of an acid-base indicator in the presence of a protein. The measurement technique is designed for the main urine protein - albumin. The presence of other proteins in the urine, for example, Benz-Jones myeloma protein, myoglobin, hemoglobin, may not be detected using diagnostic strips. Protein sensitivity varies from manufacturer to manufacturer and is typically 0.10.3 g / L. The smallest visible color change can be regarded as the presence of protein no less than the sensitivity of the strip. This means that the test results for patients with a protein below the sensitivity of the strip or a protein other than albumin will be assessed as negative. High quality strips can have a sensitivity of 0.15 or even 0.1 g / L, but these figures also exceed the accepted value of 0.033 g / L.

The strips are recommended for use in mass examinations to identify gross pathology. However, when using diagnostic strips, it is recommended to carry out a qualitative determination of the protein by the chemical method - with 20% sulfosalicylic acid for all patients with negative protein analysis on the strips. The use of a urine analyzer standardizes the determination and recording of results, but does not change the sensitivity of the strips. If the instructions do not indicate the sensitivity of the strips, it can be easily determined by the color scale. The value of the window with the first positive result determines the real sensitivity of the strip. The results of the study are influenced by the drugs indicated in the instructions, and the sharply alkaline reaction of urine.

Density. Density determination is based on the ion exchange technique and correlates well with the refractometric method. Test strips usually measure density at 5g / L intervals. In alkaline urine, as a rule, the density measured with strips must be corrected. Usually 0.005 is added to the result. A number of urine analyzers automatically correct for pH. The possible effect on the density of protein, keto acids, ascorbic acid and glucose is indicated in the attached method, which must be carefully studied before work.

Glucose. Glucose is usually determined by the glucose oxidase method with a sensitivity of about 2 mmol / l (40 mg%). The analysis results may to influence pH, density, the presence of ascorbic acid, salicillates and detergents, which should be indicated in the methodology passport.

Ketone bodies. The determination of ketone bodies is based on the Legal reaction, which determines acetoacetic acid and, with a lower sensitivity, acetone. The sensitivity of the method is usually about 0.3-0.5 mmol / L, which includes the content of ketone bodies in the norm. It is known that drugs and diagnostics containing sulfhydryl groups, phthaleins, phenyl ketones can color the reaction zone orange. The influence of various agents should be indicated in the method passport.

Bilirubin. The reaction is based on the interaction in an acidic medium of direct bilirubin with a diazonium salt or triazene with the formation of a pink product. Sensitivity and influencing factors must be determined according to the methodology passport. Urine components can give a yellow coloration of the reaction zone.

Urobilinogen. The reaction is based on the interaction in an acidic medium of urobilinogen with a stable diazonium salt with the formation of a red product. Red substances in the urine can cause a false positive reaction. In reality, both urobilinogen and stercobilinogen are determined by strips, which is present in urine normally at a concentration of 5-17 μmol / l. Bilirubin can give an irregular color (blue or green). Sensitivity and influencing factors must be determined according to the method. Since the determination of urobilinoids by chemical methods is laborious and depends on many factors, the determination of the indicator using diagnostic strips is preferable.

Blood. The reaction is based on oxidation by hemoglobin and myoglobin through the formation of colored indicator hydroperoxides. With the help of the strip, hemoglobin, myoglobin and erythrocytes are detected. Hemoglobin and myoglobin give a uniform coloration of the field, erythrocytes give a point coloration. It is impossible to distinguish between hemoglobin and myoglobin using this method. The sensitivity of the sample is 5-10 erythrocytes / μl (5,000 - 10,000 / ml). The influencing factors must be viewed in the methodology passport. When red blood cells are destroyed in alkaline or hypoosmolar urine, the results of the study on the strips may not coincide with the results of microscopy, since the strips can determine the hemoglobin that has entered the urine from the destroyed red blood cells, while the red blood cells in the urine sediment are absent or are contained in a smaller amount than shown strip results.

Leukocytes. The method is based on the cleavage of the indoxyl ester by granulocyte esterase and the subsequent interaction of indoxyl with the diazonium salt and the formation of a violet color. The presence of bacteria, Trichomonas and erythrocytes does not affect the reaction. However, an admixture of vaginal discharge to the urine, or a large number of destroyed leukocytes, can give a positive reaction due to esterase activity, which will not correspond to the results of microscopy, since the destroyed cells cannot be seen in a microscope. The high concentration of protein and glucose slows down the color development. The sensitivity of the method is about 15 leukocytes / μl (15,000 / ml). Other limitations of the method and influencing factors are indicated in the method of analysis.

Nitrite. The determination is based on the Griss reaction - the reaction of azo coupling of nitrites with sulfanyl and the subsequent interaction with a quinoline derivative with the appearance of a pink coloration. Determination of nitrites is a screening test for latent bacteriuria, since most bacteria (E. coli, Proteus, Salmonella, etc.) reduce nitrates to nitrites. A positive reaction of diagnostic strips was found in 90% of cases of all infectious diseases of the urinary tract and corresponds to the content of more than 105 microorganisms / ml. Staphylococci, streptococci, enterococci, pseudomonas and some other bacteria do not form nitrites. This means that if bacteriuria is detected with these pathogens, the nitrite test will be negative. False positive results can be obtained with prolonged storage of urine in a warm place due to exogenous growth of bacteria. False negative results can be associated with the presence of nitrite-reducing microorganisms, or with a short period of urine in the bladder.

To obtain reliable results, use either the morning urine portion or the urine collected after a 4-hour break. The study should be carried out within 4 hours. 3 days before the analysis, it is necessary to cancel antibiotics and vitamin C preparations. Other influencing factors are indicated in the analysis method. If bacteria are present, urine culture is helpful to identify the pathogen. Thus, the use of diagnostic strips with a visual or instrumental method of evaluating the results greatly simplifies and speeds up urine analysis and is a screening research method that is convenient for mass examinations and urgent analyzes. However, in order to obtain correct results, it is necessary to carry out the analysis correctly and familiarize yourself with the probable errors of the method in the method passport. The results of some tests, primarily protein, need to be checked chemically if the value is negative. Regardless of the results of the analysis, it is recommended to carry out microscopy of the urine sediment, since in some cases the number of formed elements may not coincide. It is recommended that quality control of urine analysis be performed using control material available from the Federal Center for Quality Control.

VIII INORGANIZED SEDIMENT OF URINE

1. **Crystalluria.**

Urine, as you know, is an aqueous solution of salts and organic compounds that enter the urine by filtration in the glomeruli and secretion in the tubules. Also, urine contains a small amount of cellular elements. Starting with the filtration of urine in the glomeruli, up to urination, salts in the urine are in a dissolved state. This is ensured by a number of factors: salt concentration lower than saturation, slightly acidic reaction of urine, temperature, absence of heterogeneous nuclei of crystal formation, release of anti-crystal activity.

In a healthy person, urine salts, both in the urinary tract and in freshly released urine, are in a dissolved state and do not form crystals. Normally, the appearance of up to 10 small crystals in the field of view is allowed. With more crystals, crystalluria is identified. Crystals may form and enter the urine from the urinary tract, or salts may form crystals in urine after urination when urine is stored. These two processes can be separated by examining urine immediately after urination. When conducting an analysis a few hours after urine excretion, it is almost impossible to determine the nature of the formation of crystals, since external influences are added that affect the process of crystal formation. C

ertain factors are known that affect the crystallization process:

1). The concentration of salt or organic matter in the urine.

2). Reaction (pH) of urine.

3). Body fluid temperature.

4). The time elapsed from the moment of urination to the urine test.

5). The presence of promoters (activators), for example, acidic mucopolysaccharides, and inhibitors of crystal formation, for example, pyrophosphates, heparin.

When assessing crystal formation, it is useful to remember that

1. Crystals of those salts are more often formed, the concentration of which is close to saturation. For example, uric acid and its urate salts. But sometimes crystals of salts are formed, the concentration of which is less, but there are conditions for their crystallization.

2. Some salts form crystals in acidic urine (for example, urates), others - in alkaline urine (phosphates), since the solubility of salts depends on the pH.

3. The solubility of salts, as a rule, increases with increasing temperature. Cooling urine promotes the precipitation of crystals.

4. During storage of urine, the pH changes to the alkaline side due to the release of ammonia and other volatile components, and, accordingly, the solubility of salts changes.

5. The presence of promoters and crystallization inhibitors is determined by the characteristics or metabolic disorders.

Unfortunately, the conditions that lead to the formation of this or that type of crystal are still unknown. For example, uric acid can form crystals of various shapes and sizes, which are identified even in a conventional microscope. It should be noted that the processes of crystallization are not always subject to substances, of which there are more, rather those for the crystallization of which there are conditions. Only cystine crystals indicate cystinuria and the possible formation of cystine stones. Persistent crystalluria, regardless of the nature of the crystals, is a possible sign of metabolic (metabolic) disorders, which are accompanied by increased excretion of salts, kidney damage or the development of kidney stones. Salt crystals that are found on microscopic examination of urine sediment are termed "unorganized urine sediment". The main compounds that form crystals in urine are: oxalic acid, its salts, oxalates, mainly calcium, - uric acid and its salts, urates, - salts of phosphoric acid (phosphates) - ammonium, magnesium and calcium.

Rarely in acidic urine are crystals of calcium sulfate, cystine (cystinosis, cystine stones), tyrosine and lecine (phosphorus poisoning, liver disease), cholesterol (cholesterol stones, fatty degeneration of the renal epithelium), bilirubin (phosphorus poisoning, liver disease), hematoid chronic bleeding, etc.), hemosiderin (intravascular hemolysis), xanthine (xanthine stones), amidopyrine. Calcium carbonate salts are sometimes found in alkaline urine. Crystals of sulfonamides are found in both acidic and alkaline urine and indicate an overdose of the drug.

On the basis of the detection of crystals in the urine, in most cases it is impossible to make any diagnosis. Crystals of salts, especially of uric acid, are very beautiful, and sometimes their identification takes an unreasonable amount of time, especially for young specialists, and the diagnostic value is rather arbitrary. Salts in urine sediment, of course, are identified both by the shape of the crystal and by the solubility in acids and alkalis, which is described in numerous manuals. It should be remembered that when acid or alkali is added to urine, not only salt crystals dissolve, but also urine formed elements are destroyed. Amorphous urates dissolve by heating at 37 ° C without morphological consequences. When microscopying the sediment, special attention should be paid to the number and size of crystals. In patients without metabolic disturbances, the crystals are usually small. Large crystals and conglomerates of salts are found mainly in pathology. A patient with severe and persistent crystalluria needs repeated tests and a more detailed examination, including a biochemical study of blood and urine, measurement of hormone levels, detection of inflammatory diseases, etc.

2. Processes of formation of kidney stones. Kidney stone disease.

Recently, more and more people suffer from nephrolithiasis (PKD). Renal colic associated with urolithiasis processes is increasingly common among children. There are known cases of urolithiasis in infants. Statistics have shown that about 30% of renal patients suffer from dysmetabolic nephropathies - metabolic diseases in which the target organ is the kidney. The formation of kidney stones, as well as in other organs and tissues of a person, differs from the processes of a spontaneous crystallization process caused by external environmental factors.

Firstly, at the heart of any stone is a protein matrix, which is the center of crystallization, determines the growth of the crystal and at the same time performs the functions of a "cementing" material.

Secondly, the stone in some cases is formed not by the salts that are more in the urine, but by those that interact with the protein matrix. For example, with the formation of oxalate stones, oxaluria is practically absent. The exact composition of the urinary stone can be judged after a chemical study of a particular stone.

Thirdly, the processes of stone formation are not always constant. As a rule, periods of active stone formation are replaced by periods of attenuation of the process. Moreover, with the subsequent activation of the process, to change the composition of the stone, as evidenced by the structure of stones isolated by the patient spontaneously or obtained as a result of surgery.

Fourthly, the processes of stone formation are influenced by such external and internal factors as climate, drinking water, unhealthy diet, hypovitaminosis, metabolic disorders, the presence of infectious and inflammatory processes, changes in the viscosity of the medium, the formation of immune complexes, the presence of tissue degradation products, impaired urine outflow, etc.

chemical composition distinguishes the following types of stones: oxalates, phosphates, urates, carbonates, and more rarely cystine, xanthine, cholesterol and protein stones. The cause of the formation of cystine kidney stones can be cystinuria, a disease associated with a congenital disorder of the reabsorption of dibasic amino acids: cystine, ornithine, arginine and lysine. The high excretion of these amino acids with their low solubility leads to the formation of cystine stones and contributes to the development of Fanconi's syndrome (a defect in the reabsorption of phosphates, glucose, amino acids).

Separately, coral-shaped kidney stones are distinguished, which represent an impression of the calyx-pelvis system.

From 70 to 90% of stones are oxalate and phosphate stones, and about 10% are urate stones, which consist of 97% of uric acid, and only 3% of urates. The composition of these main types of stones after their isolation can be determined in any clinical diagnostic laboratory using simple available methods.

3. Pathogenetic method for the diagnosis of kidney stones.

The number of patients with kidney stones is growing and the disease is "getting younger". There are known cases of detection of kidney stones in infants. The reasons may be high mineralization of drinking water, unfavorable environmental factors, an increase in metabolic diseases, etc. Therefore, early diagnosis and monitoring of stone formation will allow the necessary measures in order to slow down or stop the process, or solve the issue more radically with the help of lithotripsy (crushing stones) or removing stones by surgery.

Unfortunately, until recently, there were no reliable and accessible tests for assessing the processes of stone formation, and the chemical composition of the stone could be determined only after its removal. The appearance of a certain type of salt crystals in the urine, as well as the biochemical determination of the amount of excreted salts per day, does not give an idea of the activity or presence of stone formation processes, or the composition of urinary stones. One of the main landmarks was the presence or absence of an inflammatory process.

At the end of the 90s of the last century, Academician V.N. Shabalin and Professor S.N. Shatokhina proposed a simple and original method for assessing the processes of stone formation in the kidneys, which received the commercial name "Litos-system". The method is based on the assessment of the crystallization of a drop of urine during its drying (according to the authors' terminology - wedge-shaped dehydration). Before the study, the content of protein and glucose in the urine is determined and a standard amount of albumin is added.

A drop of protein-containing urine from a healthy person during dehydration under the influence of osmotic forces acquires a certain structure: salts crystallize in the central zone of the drop, and protein components form a peripheral amorphous marginal zone.

In patients with kidney stones, salt complexes are found within the marginal protein zone. Moreover, the more active the processes of stone formation, the more salt crystals are in the protein zone. In some cases, with hyperactivity of stone formation processes, the salt content in the protein zone exceeds their amount in the center of the drop. According to the results of the analysis of a drop of dehydrated urine, activation of stone formation processes can be detected earlier than stone formation, i.e. diagnosis of kidney stone disease is carried out before the formation of kidney stones. The results of the analysis can be assessed visually or under a binocular loupe, which makes the method accessible to any CDL. When measuring the content of various chemical elements from different zones of a dried droplet (for example, the marginal protein and central zone), it is possible to determine the type of stone without removing it from the body. Stone identification requires special X-ray equipment, microanalysis, and specialized institutions. for example, equipment for and can be carried out in the only contraindication of the method is the presence of glucose in the urine. With glucosuria, a

dried drop of urine looks like a glassy film, since at a high concentration glucose does not crystallize itself and prevents the crystallization of salts. Before the study, it is necessary to determine glucose in the urine using a diagnostic strip.

The authors' dynamic observation of stone formation processes in patients with calcium, urate or mixed stones made it possible to determine the following features of their course:

 the transition of the active stage of urolithiasis to the stage of remission occurs gradually with a decrease in the activity of the stone formation process,

 the stopping of the stone formation process is accompanied by the release of stone-forming and other salts with urine or the rejection of calculus,

 the release of salts occurs in the absence of protein in the urine.

Assessment of the activity of stone formation processes using the "Lithossystem" allows you to choose the safest time for lithotripsy or surgical stone removal, as well as to individually select a diet or drug treatment for the patient. Lithotripsy and surgical stone removal are the most effective and are accompanied by fewer complications in the absence of stone formation. Analysis of the dried drop of the morning portion of urine makes it possible, by the presence or severity of crystallization areas in the protein zone, to determine substances-inducers of stone formation, protective substances of

stone formation, to check the effect of drugs and food products on the process, to select complex therapy individually for each patient. Thus, the use of the above method, even within the limits available for each CDL, allows using a non-invasive method period for lithotripsy in order to prevent recurrence of the disease.

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