**LABORATORY DIAGNOSIS OF KIDNEY DISEASES**

Kidneys are a pair of bean-shaped organs with a weight of 120-200 grams and a length of 10-15 cm. It is located on both sides of the spine, at the level of XI-XII thoracic, II-III lumbar vertebrae. The kidneys, which maintain the stability of the internal environment of the body, implement *excretory* and *incretory* functions.

Based on the *excretory* *function*, the points which are mentioned below are ensured:

• regulation of water balance;

• regulation of volume of blood, intracellular and extracellular fluid;

• stable maintenance of the osmotic pressure of the internal environment;

• maintaining a stable pH;

• metabolic function (regulation of protein, fat and carbohydrate metabolism);

• regulation of internal environment stability (homeostasis) of the body;

• excess amount of fluid, organic and inorganic substances, harmful and toxic products are removed from the organism.

Based on the *incretory function* the points which are mentioned below are synthesized:

• renin (renin-angiotensin system);

• erythropoietin (erythropoiesis);

• urokinase (hemostasis, plasminogen activator);

• calcitriol (metabolite of vitamin D3);

• bradykinin (vasodilator);

• prostaglandins.

The most common kidney pathologies are urolithiasis, glomerulonephritis, pyelonephritis, urolithiasis, kidney polycystosis, pregnancy nephropathy, hydronephrosis, nephrosclerosis, kidney tumor, kidney failure. In most cases, patients complain of various localized pain, urination disorders, edema, headache, dizziness, fever. Most kidney diseases are asymptomatic. This, in turn, complicates the diagnosis of nephrological diseases. Sometimes kidney pathologies are discovered accidentally during medical examinations for other reasons. Carrying out specific laboratory examinations allows timely detection of disturbed functions of the kidney and effective treatment.

The initial stage of detecting kidney pathology consists of collecting anamnesis from the patient (questioning), palpation and percussion of the kidney area. Laboratory and instrumental examinations should be performed to confirm the initial diagnosis. Laboratory diagnosis of kidney diseases includes:

• general examination of urine;

• urine culture;

• general and biochemical examination of blood.

The general examination of urine must be included in the laboratory examination plan of patients. This is the simplest examination method performed initially in all patients who are suspected of having kidney disease. Examination of urine consists of studying its physical examination of urine, chemical composition, microscopic examination of urine sediment.

**PHYSICAL** **EXAMINATION** **OF** **URINE**

The physical urine examination consists of assessment of urine volume, color, its transparency, odor, specific gravity and also measurements of its pH,

*Volume of urine.* Daily diuresis is equal to 800-2000 ml. During the day, the frequency of urination is 4-7 times, and the volume of urine excreted on each time is 200-300 ml. Volumes less than 500 ml of daily diuresis and more than 2000 ml daily diuresis are considered pathological and are called oliguria and polyuria, respectively.

*Color of urine.* Normally, the color of urine is straw-yellow (up to orange-yellow) due to presence of urochrome pigment produced as a result of hemoglobin degradation. The change of its color can be observed both physiological and pathological conditions. Physiologically, certain nutrients (for example, beetroot, carrot and etc.), a number of drugs (amidopyrin changes the color of urine to red, acetylsalicylic acid changes its color to pink and etc.) are excreted with urine and may change its color. Pathologically, the color of urine can change because of diseases of the kidney and urinary tract, as well as diseases of the other organs and systems *(table 1)*. For example, urine in the color of "meat red" (indicating blood in urine) is found in glomerulonephritis. When this kind of urine remains, it turns dark brown. This is due to the conversion of hemoglobin into methemoglobin in the acidic urine. "Beer" colored urine is observed in parenchymatous and mechanical jaundice, black colored urine is observed during hemoglobinuria (hemolytic anemia), alkaptonuria, melanosarcoma. The red-brown color of urine indicates the presence of myoglobin in its composition. When bile pigments are present in the urine, it turns to brownish-yellow or brownish-green. Hiluria, meaning that the color of urine changes to milky, occurs when there are fat drops or lymph in the urine. Lymphatic fluid can pass into the urine as a result of injury during obstruction of the renal lymphatic drainage or when a fistula is formed between the retroperitoneal lymphatic outflow and the urinary tract (tumor diseases, tuberculosis, trauma, etc.). Dark yellow urine is observed in case of kidney congestion, burns, vomiting, diarrhea, drinking less water, and colorless or light yellow urine is observed in diabetes mellitus and diabetes insipidus, drinking more water.

*Table 1: Characteristic changes in urine color*

|  |  |  |
| --- | --- | --- |
| Color | Causing substance | Occurrence |
| Yellow to colorless |  | • increased diuresis in excessive drinking  • diuretic drugs  • diabetes mellitus  • diabetes insipidus  • polyuric phase of renal failure |
| Brown | Bilirubin | • diseases of liver and biliary tract |
| Green-brown | biliverdin (originates  from bilirubin by oxidation on air) | • diseases of liver and biliary tract |
| Yellow-orange | riboflavin, carotenes | • exogenous intake |
| Meat red  (without turbidity) | Hemoglobin  myoglobin  porphyrins  beetroot | • intravascular hemolysis  • burns  • necrosis of muscles  • inflammation of muscles  • porphyrias  • exogenous intake |
| Meat red  (with turbidity) | blood in urine –  macroscopic hematuria | • diseases of kidney and urinary tract  • disorders of hemostasis  • bleeding to urinary tract |
| Dark | Melanin  homogentisic acid | • melanoma  • alkaptonuria |
| Light red | Urates | • hyperuricosuria |

*Transparency of urine.* Normally, urine is transparent, but in a number of pathologies, urine loses its transparency. Turbidity of urine usually can occur due to presence of bacteria, mucus, lipids, and cellular elements. When urine is retained, its turbidity indicates the presence of salts in the urine. This can also be determined through some tests. If urine loses its turbidity when turbid urine is heated (60⁰C), this indicates the existence of uric acid and urates in urine. If urine loses its turbidity when 10% acetic acid is added into urine, it indicates the presence of phosphate salts. If cloudy urine becomes clear when adding HCl acid, it indicates the presence of oxalate salts in urine. If urine losses its turbidity due to addition of ether and ethanol into urine, it indicates the presence of fats in the urine. If the urine does not become transparent due to the conducted tests, a judgement can be made about the cause of the cloudy urine through microscopic examination.

*The odor of urine.* Normally, urine has faint odor. As a result of the decomposition of urea due to bacteria in the urine, it may smell of ammonia (for example, during cystitis, the breakdown of tumor, etc.). When there are ketone bodies in the urine, it smells like overripe apples, which is especially characteristic of diabetic comas *(table 2).*

Table 2: Causes of changes in the odor of urine

|  |  |  |
| --- | --- | --- |
| **Smell** | **Cause** | **Occurrence** |
| **Ammonia** | bacteria producing urease | Old urine sample  Infections of urinary tract  Diseases with chronic urine  Adenoma of prostate |
| **Acetone**  **(overripe apples)** | excretion of acetone in  ketoacidosis | Diabetes mellitus  Starvation |
| **Maple syrup** | branched chain carboxylic oxoacids (especially 2-oxoisocapronic, 2-oxoisovaleric acids) | Leucinosis  (maple syrup disease) |
| **Hydrogen sulfide** | bacterial decomposition of proteins releases H2S from sulfur-containing amino acids | Infections of urinary tract  associated with proteinuria  Cystinuria, homocystinuria |
| **Mouse** | phenylacetate | Phenylketonuria |
| **Fish** | tyrosin | Tyrosinemia |

*Specific gravity of urine.* The specific gravity of urine depends on its amount and the concentration of organic and inorganic substances and it ranges from 1.015 to 1.025 during a day. The main components that, normally, determine the specific gravity of urine are sodium and chloride ions, as well as urea and creatinine. In pathological situations, the presence of glucose, ketone bodies, and protein in the urine can affect the specific gravity of urine. If the specific gravity of urine is more than 1025, it is called hypersthenuria, and if it is less than 1008, it is called hyposthenuria. When the specific gravity of urine equals to the specific gravity of the primary urine (1008-1010) during a day, it indicates the disorders of reabsorption in the renal tubules and it is called isosthenuria which is observed in acute and chronic kidney failure.

The specific gravity of urine decreases in the following pathologies in:

- taking diuretics;

- tubulopathies;

- excessive intake of water;

- deficiency of antidiuretic hormone – diabetes insipidus;

- unsalty, protein-free diet and etc.

The specific gravity of urine increases in the following pathologies in:

- diabetes mellitus (due to glucosuria);

- nephrotic syndrome (due to proteinuria);

- dehydration (vomiting, diarrhea, severe sweating and etc.);

- decrease in water intake;

- inappropriate secretion of antidiuretic hormone (or Parkhon's syndrome) and etc.

*Urine reaction.* Urine has a weak acid reaction and its pH varies between 5.0-7.0. Food intake affects urine pH. The acidic reaction of the urine is observed when eating too much meat and the tendency towards alkalinity is observed during a vegetable-dairy diet. Also during pathologies, the pH of urine can change to acidity or alkalinity *(table 3).*

*Table 3. Changes in urine pH during pathologies*

|  |  |
| --- | --- |
| ***İncreased of pH*** | ***Decreased of pH*** |
| Vegeterian diet | Protein diet |
| Metabolic and respiratory alkalosis | Metabolic and respiratory acidosis |
| Vomiting, diarrhea, taking drugs - carbonic anhydrase inhibitors (diacarb), hypokalemia | Diabetic coma, heart failure, podaqra, dehydration, fever |
| Chronic urinary tract infection, cystitis, pyelitis | Kidney failure, acute nephritis, renal tuberculosis |
| Primary hyperaldosteronism, Cushing syndrome | Phenylketonuria, alkaptonuria |

In chronic infections of the urinary tract, the cause of the increase in pH of urine is due to the conversion of urea into ammonia in the urine by microorganisms which synthesize the urease. A long-term change in urine pH to alkalinity leads to the formation of phosphate-containing stones, and a change to acidity leads to the formation of urate and uric acid-containing stones. From this point of view, the determination of pH is important in the identification of crystals in microscopic analysis, as well as in the determination of therapy.

**CHEMICAL EXAMINATION OF URINE**

Chemical examination of urine consists of determination of protein, glucose, ketone bodies, bile pigments, urobilinoids and other ingredients in urine.

*Protein in the urine*. Protein is not observed in the urine of a healthy person. Proteins passing into the glomerular filtrate are completely reabsorbed by the tubular epithelium. Detection of protein in the urine is called proteinuria. Qualitative (sulfosalicylic acid and nitric acid test) and quantitative methods based on protein denaturation and precipitation are used to determine proteinuria. In renal pathologies accompanied by proteinuria, the level of protein excretion in urine changes during a day. In this regard, determination of daily proteinuria is of great importance. Daily proteinuria is calculated by the following formula:

Ps = P × V

Ps – daily proteinuria (in grams); P – protein in daily urine (g/l); V – daily diuresis.

Proteinuria is divided into two groups: true and false. The following types of true proteinuria are distinguished:

• *Functional (physiological) proteinuria.* It is mainly observed during heavy physical work (stress proteinuria), emotional stress, fever, congestion in blood circulation (congestion proteinuria) and etc. At this time, as a result of increase in permeability of glomerular capillaries, there is protein in the urine. During functional proteinuria, the kidney and urinary tracts are not damaged, and when the reason of observing proteinuria is prevented, protein is not observed in urine. the amount of protein in the urine does not exceed 1g/l per day. Orthostatic proteinuria occurs in teenagers when they stand and walk a lot.

• *Pathological (organic) proteinuria*. It is caused by damage of nephrons. It appears in acute and chronic glomerulonephritis, acute and chronic pyelonephritis, renal amyloidosis, systemic diseases of the connective tissue accompanied by kidney damage and other pathologies. Selective and non-selective forms are distinguished. During selective proteinuria, small molecular proteins, meaning that albumins, pass through the glomerular basement membrane. Non-selective proteinuria is accompanied by the loss of proteins of different molecular weight and all plasma proteins are detected in the urine.

Protein on the background of hematuria and leukocyturia ((pyuria)) is called false proteinuria. It is obtained during the breakdown of shaped elements. It is found in vulvovaginitis.

*Prerenal, renal* and *postrenal* types of proteinuria are distinguished depending on the cause of development. Prerenal proteinuria is the result of the breakdown of tissue proteins. It appears on hemolysis of erythrocytes (breakdown products of hemoglobin), myeloma disease (Bens-Jones protein), burns, oncological diseases and other pathologies. Renal proteinuria develops on the background of damage of glomeruli or tubules or both of their damage at the same time. Glomerular proteinuria is associated with a decrease in the negative charge in the basement membrane of glomerulus, as well as damage of the basement membrane by immune complexes. It is observed in glomerulonephritis, renal amyloidosis, diabetic glomerulosclerosis, thrombosis of renal veins and etc. Tubular proteinuria occurs when protein reabsorption is impaired in the proximal convoluted tubules or when Tamma-Horsfall glycoprotein (hyaline) secretion increases. It is detected in acute tubule necrosis, congenital and acquired anomalies of tubules, interstitial glomerulonephritis and other pathologies. Proteinuria becomes massive during nephrotic syndrome, kidney tumor, shock kidneys, Fanconi’s syndrome. Postrenal proteinuria is associated with inflammatory diseases of the urinary tract, bladder tumors, adenoma of the prostate gland and other pathologies.

*Microalbuminuria*. Through usage of immunochemical methods, it is possible to determine a low concentration of albumin (<200 mg/l), which is important in monitoring the development of vascular complications of diabetes mellitus. The term "microalbuminuria" is defined as the excretion of albumin in the urine in the amount of 30-300 mg/day or 20-200 μg albumin/min. Microalbuminuria is the earliest criterion for the development of diabetic nephropathy (before the onset of proteinuria). Currently, diabetic nephropathy is the leading cause of high disability and death in patients with diabetes, with an incidence of 40-50% in type 1 diabetes and 15-30% in type 2 diabetes. The occurrence of permanent microalbuminuria in a patient with diabetes mellitus indicates a rapid development (within the next 5-7 years) of a significant stage of diabetic nephropathy.

*Glucose in the urine*. The cells of the proximal renal tubules reabsorb most of the glucose from the glomerular filtrate. Glycosuria develops only when the amount of glucose in the glomerular filtrate significantly exceeds the reabsorption capacity of the renal tubules. This situation can occur in the following cases:

• the concentration of glucose in blood plasma and glomerular filtrate exceeds 10 mmol/l (renal threshold), which significantly exceeds the reabsorption capacity of healthy renal tubules;

• as a result of enzyme (hexokinase and glucose-6-phosphatase) deficiency, the reabsorption capacity of renal tubules decreases, which leads to glucosuria at a glycemic level below the renal threshold (renal glucosuria or renal diabetes).

Glucosuria can be physiological and pathological. Physiological glucosuria can appear after excessive intake of carbohydrates, after emotional stress, after taking drugs (corticosteroids, adrenaline, caffeine). Pathological glucosuria is more often observed in diabetes mellitus, and less frequently in Itsenko-Cushing's syndrome, thyrotoxicosis, liver cirrhosis.

*Ketone bodies in the urine*. Ketone bodies (acetoacetate, acetone, and β-hydroxybutyrate) are products of free fatty acid catabolism. Ketone bodies are not detected in urine in healthy people. When lipid and protein metabolism is disturbed, ketone bodies are found in the urine. The presence of ketone bodies in the urine is called ketonuria and it is mainly observed during diabetes mellitus, starvation, alcohol intoxication, long-term fever, carbohydrate-free but fat-rich diet, hormonal dysfunctions (thyrotoxicosis, Cushing's disease, acromegaly and etc.), pregnancy toxicosis.

False-positive results may be obtained when detecting ketonuria on the background of a high concentration of urine or during the use of certain drugs (for example, angiotensin-converting enzyme blockers).

*Hematuria.* The presence of blood in the urine is called hematuria. Two types of hematuria are distinguished:

- *microhematuria* - erythrocytes are detected only during examination of the sediment under a microscope. This is also called erythrocyturia;

- *macrohematuria* - blood in the urine is determined macroscopically.

Hematuria can be of renal or non-renal origin. Renal origin of hematuria is observed in glomerulonephritis, kidney tumor, tuberculosis, heart attack, traumatic injury, hydronephrosis, kidney polycystosis, urinary tract diseases, and non-renal origin of hematuria is observed during hemophilia, thrombocytopenia, DIC-syndrome, treatment with anticoagulants and etc.

From a practical point of view, glomerular and non-glomerular hematuria are distinguished. Glomerular hematuria is the result of renal glomerular pathology, it is stable and often accompanied by proteinuria and erythrocyte casts. During the microscopic examination of the sediment, erythrocytes with changed morphology (dysmorphic erythrocytes) are detected. The causes of non-glomerular hematuria are renal pelvis stones, bladder and ureter stones, malignant tumors of the bladder and tuberculosis. It is mainly intermittent in nature (periodically increases and decreases).

In hematuria, the three-cup test is used to identify the source of the blood.

If the blood is present at the beginning of urination, meaning that, the urine in the first cup is bloody, and the urine in the second and third cups is clean, then the source of hematuria is considered to be the urethra. This is called initial hematuria.

If the blood is present at the end of urination, meaning that, the urine in the first and second cups is clean, and the urine in the third cup is bloody, the source of hematuria is considered to be pathological processes in the urethral neck (cancer of the urethral neck, adenoma and cancer of the prostate gland). This is called terminal hematuria.

In case of total hematuria, the urine in all three cups is bloody. The source of such hematuria is the urinary tract, upper urinary tract and kidneys. It is mainly observed on tumors, stones, and other diseases of the urinary tract and upper urinary tract.

Immunoselectophoresis is used to differentiate hematuria from hemoglobinuria and myoglobinuria. In contrast to macrohematuria, in hemoglobinuria and myoglobinuria, the transparency of urine is preserved, but only the color changes.

*Bilirubin in the urine*. Normal urine does not contain bilirubin. Only conjugated bilirubin is excreted in the urine, unconjugated bilirubin cannot pass into the urine because it is not soluble in water. Excretion of bilirubin with urine is called bilirubinuria which is observed in parenchymatous and mechanical jaundice. Bilirubinuria is determined through qualitative tests. These tests are based on the conversion of bilirubin to green biliverdin with the help of oxidizing agents (iodine, nitric acid and etc.).

*Urobilinogen in the urine*. Urobilinogen bodies are derivatives of bilirubin. Urobilinogens are colorless substances, but urobilins are colored, yellowish-brown. The upper limit of the physiological concentration of urobilinogen in urine is 17 μmol/l (1 mg per 100 ml). An excess of urobilinogen bodies is called urobilinogenuria and is observed on hemolytic conditions, damage to the liver parenchyma and intestinal pathologies. In intestinal diseases, the reabsorption of urobilinogen from the mucous membrane of the large intestine increases and as a result, its amount in the urine increases. This type of urobilinogenuria is more often observed in children (in case of colitis, constipation, intestinal obstruction). The level of urobilinogen in the urine increases during portal cirrhosis of the liver, thrombosis of the portal vein and etc. If the patient does not have hemolysis and intestinal disease, urobilinogenuria is a sign of damage of the liver parenchyma. During liver tumor, abscess, echinococcosis, urobilinogenuria is observed when the pathological process affects only most of the organ and disrupts the function of the liver.

**MICROSCOPIC EXAMINATION OF URINE SEDIMENT**

Microscopic examination of urine sediment consists of the detection of blood-shaped elements (leukocytes, erythrocytes), cylinders, epithelial cells, as well as bacteria and salts. Microscopic elements observed in urine sediment are divided into two groups, organic and inorganic. Organic deposits of urine, unlike inorganic ones, do not dissolve under the influence of temperature and weak acids.

*Organic elements of urine sediment*. Squamous and keratinized epithelial cells, transitional epithelial cells, leukocytes and mucus belongs to organic elements of urine sediment.

A small amount of organic elements of sediment is found in normal urine sediment. The following forms of organic elements can be found in pathological urine sediment.

*Epithelial cells*. Different types are distinguished according to their origin: squamous epithelial cells, transitional epithelial cells and renal epithelial cells. *Squamous epithelial cells* are large, wide, round and oval, mononuclear and have small granules in the cytoplasm. It enters the urine through the uterus, external genitalia and urethra.

*Transitional epithelial cells* are cells with a yellowish tinged round nucleus. It enters the composition of urine as a result of the rupture of the mucous membrane of the urinary canal, bladder and renal pelvis.

*Kidney epithelial cells* are small, round or cube-shaped cells, the nucleus is large, the cytoplasm is slightly granular and vacuolated. It enters the urine through the epithelium of the urethra.

Normally, in the urine sediment, individual squamous and transitional epithelial cells are found. An increase in their amount does not have important diagnostic significance. If the increase of renal epithelial cells is accompanied by leukocyturia, cylinduria and hematuria, this is an indicator of damage to the renal tubules (pyelonephritis, acute tubule necrosis, malignant nephrosclerosis, poisoning with heavy metal salts and etc.) and is considered an important diagnostic criterion. Renal epithelial cells can also be found in healthy people (singly in the field of vision).

*Leukocytes*. Normally, during the examination of urine sediment, 0-2 leukocytes in men and 4-6 leukocytes in women in the field of vision and mainly neutrophils are detected. They are round-shaped, small gray granular cells. The nucleus consists of several segments, the granularity of the cytoplasm is clearly distinguished.

Morphology of leukocytes varies depending on urine pH, specific gravity and residence time. In the cytoplasm of leukocytes *in a weak acidic urine*, granularity is clearly noticeable and as a result, the nuclei are difficult to distinguish. In hypotonic urine with an alkaline reaction (pH 8.0 - 9.0), leukocytes swell, Brownian movement of neutrophil granules is detected in the cytoplasm. Such leukocytes are called *activated* or *Sternheimer-Malbin cells*. It is detected in inflammatory processes of the kidney and urinary tract. This is due to hypo- and isosthenuria. During inflammatory processes, when adding a few drops of distilled water to urine, it is possible to detect leukocytes as the relative density of urine decreases. When a leukocyte is alive, water passes through its semipermeable membrane according to the law of osmosis. As a result, leukocytes swell, granularity and Brownian movement begin in their cytoplasm. On the contrary, *in urine with an acid reaction*,the size of leukocytes decreases, polymorphic nuclei are clearly visible inside of the cytoplasm, granularity and Brownian movement are lost in the cytoplasm. Sometimes, because the membranes of neutrophils are broken (when they remain in the urine with bacteria for a long time), free neutrophil nuclei are found.

If the number of leukocytes in the urine sediment exceeds 5-6 in the field of vision, it is called *leukocyturia*, and if leukocytes cover the entire field of vision, it is called *pyuria*. Pyuria (leukocyturia) is the main characteristic symptom of the infectious and inflammatory process in the kidneys and urinary tract. Leukocyturia is more common in women than in men, which is associated with diseases of the urinary tract and the possibility of contamination of urine with vaginal leukocytes. Leukocyturia and bacteriuria are characteristic of acute and chronic pyelonephritis. Lymphocyturia is characteristic of kidney diseases of immune origin, chronic glomerulonephritis, lupus nephritis and the delayed stage of chronic lymphocytic leukemia. Eosinophils appear in the urine during chronic pyelonephritis of tuberculosis origin, cystitis, urethritis of allergic etiology.

In case of leukocyturia, the two-cup test is used to determine the source of inflammation. In the morning, the initial portion of urine is collected in the first cup, and the next portion is collected in the second cup. If leukocytes are found in the first portion of urine, the source of inflammation is considered to be the urethra, if it is found in the second portion, the source of inflammation is considered to be the prostate gland, and if it is found in both portions, the source of inflammation is considered to be the urethra and kidneys.

*Erythrocytes*. In normal urine sediment, there does not exist erythrocytes or it is found singly. The color and shape of erythrocytes depends on the pH and relative density of urine. In the urine sediment, erythrocytes are yellowish-green or reddish color, appear as a small circle cells, are in the form of a two-contour ring, and are not granular. *In urine with weak acid reaction* and normal relative density, erythrocytes appear light yellow, retain their shape and pigment for a long time, and do not change. Such erythrocytes are called *"fresh"* or *unchanged erythrocytes*. Erythrocytes can take the form of stars in solid *urine with an acid reaction*. The sizes of erythrocytes found in urine with a weak alkaline reaction are larger than those of normal erythrocytes. *In urine with an alkaline reaction*, they break down quickly, and if it remains in urine with a low relative density for a long time, erythrocytes lose their pigment and as a result, it turns into colorless, different-sized, sometimes jagged contoured and thin-membrane cells. Such erythrocytes are called *"alkalized"* or *altered erythrocytes*. Usually, in the case of hematuria caused by the damage of the kidney glomeruli, changed erythrocytes are detected in the urine, and in the case of hematuria caused by the damage of the ureters, unchanged erythrocytes are detected.

*Cylinders*. They are protein particles that have taken the shape of the distal part of the renal tubules (cylindrical shape). It has an elongated or spiral shape and different sizes. Their protein base consists of uroprotein and aggregated plasma proteins. Cylinders are of pure protein origin (hyaline, wax-like) or have various additions mixed with protein. Normally, there is no cylinder in urine, it is mainly found in kidney pathologies. In acidic urine, they are reamined unchanged for a long time, and in alkaline urine, they are quickly broken down.

Several types of cylinders are distinguished:

• *hyaline cylinders* – observed in kidney diseases accompanied by proteinuria (eg, nephrotic syndrome). They are pale colored transparent particles formed from coagulated proteins. When the concentration of protein in the lumen of the proximal tubule is high, as well as in acidic urine, the proteins are denatured and take the shape of the distal branch of the lumen of the renal tubules (cylindric). Hyaline cylinders are not formed in urine with an alkaline reaction. In general, the finding of hyaline cylinders in the urine sediment indicates the increase of glomerular capillary permeability.

• *wax-like cylinders* - light yellow particles with rough contours. They are larger than hyaline cylinders. It is detected during severe acute and chronic damage of kidneys.

• *leukocyte cylinders* - covered with leukocytes, formed of coagulated protein, having a cylindrical shape. It is mainly characteristic for purulent-inflammatory processes of the kidneys accompanied by leukocyturia and pyuria.

• *epithelial cylinders* – are epithelial cells of kidney tubules and cylinders composed of protein. Finding them in the urine sediment indicates damage of the renal tubule. It is observed in tubular necrosis, poisoning with heavy metal salts and salicylates, nephrotic syndrome.

• *granular casts* – consist of altered (destroyed and fragmented) renal epithelial cells. A characteristic feature is that their surface has a granular appearance. If there are blood pigments in the urine, it will be red-brown, and if there are bile pigments, it will be yellow. It is found in glomerulonephritis, pyelonephritis, renal amyloidosis, diabetic glomerulosclerosis and other pathologies.

• *fat cylinders* – formed from epithelial cells that have undergone fat degeneration.

• *erythrocyte cylinders* – consist of protein derivatives covered by modified erythrocytes. It is formed during hematuria of renal origin, it indicates the damage of renal glomeruli. They are found in glomerulonephritis, kidney tumor, heart attack, thrombosis of renal veins and etc. The blood that coagulates in the renal tubules and takes a cylindrical shape is also referred to erythrocyte cylinders.

• *false cylinders* - they look like a cylinder, but they have longitudinal stripes. False cylinders include bacteria, myoglobin and uric acid salts.

*Mucus and bacteria* – mucus appears under the microscope as grayish particles with a homogeneous or fibrous structure. Normal urine does not contain mucus. It is detected during diseases of the urinary tract (cystitis, urethritis, kidney stone disease, prostatitis).

Normally, urine does not contain more than 1×105/ml bacteria. Exceeding this indicator is called bacteriuria, it is observed in inflammatory diseases of the kidneys and urinary tract.

*Fibrin* is a group of light brown fibers.

*Lecithin* *grains* are globular shiny derivatives, slightly smaller than erythrocytes.

In addition to these, the organic elements of pathological urine sediment include urethral rods, giant Langhans cells and tumor cells.

*Inorganic urine deposits.* Inorganic elements of urine sediment include crystals and salts. Their characters depend on the colloidal state of urine, pH and other characteristics. Uric acid crystals and urates are observed in the contain of acidic urine. Crystals of oxalic acid, calcium and magnesium salts of phosphoric acid, and ammonium salts of uric acid are found in urine sediment with an alkaline reaction. Calcium sulfate, hippuric acid, calcium-carbonate, calcium-phosphate, magnesium-phosphate belong to inorganic sediment elements that are found relatively rarely in urine. Sometimes cystine, tyrosine, leucine, cholesterol crystals are found in urine sediment. This is mostly observed in phosphorus poisoning and subacute dystrophy of the liver.

Some of the inorganic sediment elements can be seen with eyes. For example, the precipitate of uric acid is brick-red, the precipitate of urate is pink, and the precipitate of amorphous phosphate is whitish.

**URINE CULTURE**

Urine culture is an examination to detect and identify microorganisms (usually bacteria) that cause urinary tract infections. Urine is usually sterile in the bladder, meaning that, it does not contain bacteria or other microorganisms (such as fungi). But bacteria can get into the urethra and cause an infection. The urine sample is stored in an environment that is favorable for the growth of bacteria and other microorganisms. If there is no growth of microorganisms in the urine, then the result is negative. The result of the examination is positive if the infectious microorganisms grow in large quantities, that is, to the point of causing infection. The type of infecting microorganisms is identified by microscopy and chemical testing. Urinary tract infections are more common in women and girls than in men. Thus, the female urethra is shorter than that of men and closer to the anus, which allows bacteria to fall from the intestine into the urethra. Men's prostate gland contains an antibacterial substance, which reduces the risk of developing urinary tract infections.

If the urine culture is positive, an antibiotic sensitivity test is performed to determine which antibiotic to use for treatment.

**LABORATORY DIAGNOSTICS OF THE EXCRETORY FUNCTION OF THE KIDNEYS**

***Determination of glomerular filtration***. Quantitative assessment of glomerular filtration, reabsorption and secretion levels in tubules are nesessary diagnostic importance during a number of kidney diseases. Modern methods of determining the functions of the kidneys are based on the calculation of clearance.

Clearance is the volume of blood plasma completely cleared from any endogenous or exogenous substance during 1 minute passing through the kidneys. The clearance of any substance excreted in urine is calculated according to the following formula:

C = U x V / P (ml / min);

C - clearance; U – concentration of the researched substance in urine;

P - the concentration of the researched substance in the blood plasma;

V - the amount of urine excreted in 1 minute (minute diuresis).

Glomerular filtration (GFT) is the volume (in ml) of the liquid part of blood that passes through the glomerular filter into the cavity of the Shumlyansky-Bowman capsule in 1 minute. The level of glomerular filtration rate (GFR) is an important indicator of the onset of kidney failure, as well as the risk of developing complications of chronic kidney diseases. In addition, in clinical practice, the calculation of GFR allows determining the correct dose of drugs excreted by glomerular filtration in order to prevent their toxic effects.

Inulin clearance fully reflects the state of glomerular filtration. Because the size of inulin molecules is smaller than the diameter of the pores in the basal membrane of the glomerular capillaries, they can easily pass into the cavity of the capsule. As a result, the concentration of inulin in the glomerular filtrate completely corresponds to the concentration in the blood plasma. The average clearance of inulin in healthy young men is 127 ml/min and it is 118 ml/min in women. After age of 20, GFR decreases by about 1.0 ml/min per year. However, inulin clearance was not widely used in clinical practice due to the fact that this substance was administered intravenously by infusion during the research, as well as due to the high probability of developing allergic reactions. This situation has led to the development of alternative methods for evaluating GFR.

Currently, the most commonly used method for evaluating GFR in clinical practice is based on determination of endogenous creatinine clearance. This method was proposed by P.Reberg in 1926. Reberg administered exogenous creatinine intravenously by infusion and determined its clearance. Laterly, it was found that the concentration of creatinine in the blood plasma remains constant throughout the day. Considering this, E.M.Tareyev proposed to use endogenous creatinine concentration in 1936. An important condition for the reliability of the research is the strict calculation of the time when urine was collected. The most reliable results of determination of GF are obtained when the minute diuresis is between 1.5-2 ml. If the minute diuresis is less than 1 ml, the GF decreases, and if it is more than 2.5 ml, the GF increases. The essence of the research is to collect daily urine, to determine the concentration of creatinine in the blood and urine, to calculate the minute diuresis and to determine the clearance according to the above mentioned formula. Normally, creatinine clearance is 80-120 ml/min in men; it is 70-110 ml / min in women.

***Determination of reabsorption in renal tubules*.** Normally, renal tubule reabsorption is 96-99% (under conditions of normal fluid intake). In tubulointerstitial pathologies (hydronephrosis, pyelonephritis, polycystic kidneys, etc.), the decrease in reabsorption is observed in the early stages of the disease. However, it occurs later in diseases accompanied by glomerular damage. Renal tubule reabsorption indicator is calculated by the following formula:

R= F-V ×100%;

V

R – tubule reabsorption;

F – glomerular filtration;

V – minute diuresis.

Tubular reabsorption is reduced in the following pathologies:

- when taking diuretics,

- diabetes insipidus,

- excessive fluid intake (hyperhydration),

- primary (chronic glomerulonephritis and pyelonephritis) and secondary (diabetic nephropathy, hypertension) kidney shrinkage,

- acute and chronic pyelonephritis.

***Secretory function of the kidneys*.** The assessment of this function is based on the determination of the clearance of exogenously administered phenolroth. 94% of phenol rot is removed from the body through secretion.

In the morning, on an empty stomach, the patient is suggested to drink 400 ml of water and urinate after 15-20 minutes. Then, 1 ml of 6% phenolroth solution is injected into the patient intramuscularly, one and two hour portions of urine are collected in separate containers. In each portion, the concentration of phenolroth is determined based on the color reaction of sodium-bicarbonate using the colorimetric method. When the secretory function of the tubular epithelium is normal, 40-60% of the dye matter is excreted in the urine during the first hour, and an additional 20-25% of the dye matter is excreted in the urine during the second hour (60-85% in total). When the secretory function of the kidney tubules is weakened, the excretion of the dye matter slows down, the maximum limit of the excretion of phenolroth is determined in the second portion of urine, not in the first portion.

In addition to phenolroth, other substances such as paraaminohippuric acid, diodrast and etc. are used to research the secretory function of the kidneys.

**GENERAL AND BIOCHEMICAL EXAMINATION OF BLOOD IN UROLOGY DISEASES**

In the case of kidney pathologies, leukocytosis, an increase in the concentration of C-reactive protein and an increase in ESR (especially in the case of inflammatory diseases of the kidneys and urinary tract) are observed in the general analysis of blood. The amount of creatinine, urea, residual nitrogen is determined in the biochemical examination of blood.

*Creatinine* is mainly produced by the metabolism of creatine in muscles, and its production is proportional to the total muscle mass. As a result, the average rate of creatinine formation is higher in men than in women, and is higher in young people than in older people. This condition causes differences in serum creatinine concentrations depending on age and gender. It is mainly considered as a source of energy for muscle building. Creatinine refers to substances that do not have a kidney limit. It is removed only by filtration from the glomeruli, it is not secreted or reabsorbed in the tubules. Normally, blood level is 80-115 μmol/l in men, 53-97 μmol/l in women, 18-35 μmol/l in newborns, 35-110 μmol/l in children up to 14 years old. The amount of creatinine in the blood increases during acute and chronic kidney failure, pyelonephritis and glomerulonephritis. In addition, the amount of creatinine increases during hyperthyroidism, acromegaly, fever, dehydration, excessive consumption of meat products in the food ration, and decreases during long-term starvation (protein-calorie starvation) or restriction of meat products intake (protein-free diet) and hyperhydria.

*Urea* is one of the end products of protein catabolism, it is formed in the liver. Normally, the amount of urea in blood plasma is 4.2-8.3 mmol/l, 1.4-4.3 mmol/l in newborns, 1.8-6.4 mmol/l in children up to 14 years old. When the function of the kidneys is disturbed, the amount of urea in the blood plasma increases, and when the liver is damaged, it decreases.

The amount of *residual nitrogen* in the blood is 14.3-28.6 mmol/l. Its increase can be of production and retention origin. Production azotemia occurs as a result of increased synthesis of residual nitrogen in the fever and at the stage of tumor tissue destruction, regardless of kidney function. Retention azotemia is caused by impaired kidney function. Secretory and excretory retention azotemia are distinguished. Secretory azotemia occurs as a result of a violation of the secretory function of kidneys and excretory azotemia occurs as a result of a violation of the excretory function of kidneys.

The amount of residual nitrogen decreases in liver failure and increases in urological diseases.