Vyšetření močového sedimentu

Morphological components of urine can be detected **by microscopic examination** of the urinary sediment and, more recently, by **flow cytometry .**

Urine sediment analysis is not a screening procedure. We approach its analysis in the following **indications:**

- in case of a positive finding of a chemical examination of the urine (positive erythrocytes , protein , nitrites);
- if the leukocyte test is positive with diagnostic strips;
- in clinical suspicion of kidney and urinary tract disease;
- during follow-up examinations of patients with nephrological or urological diseases.

Orientation examination of urinary sediment

As an indication , erythrocytes, leukocytes and ***bacteriuria*** can be detected indirectly by the nitrite test (Table 1). If the strips are found to be positive, a more demanding microscopic examination must be performed . However, the use of diagnostic strips will reduce unnecessary microscopic evaluation requirements. The strips are also used when the cell elements break down due to low osmolality or high urine pH , when the sample is standing for a long time or at a higher room temperature. The finding in the urinary sediment is negative, but the presence of disintegrated erythrocytes and / or leukocytes may be indicated by a positive finding when tested with a test strip. Pseudoperoxidase activity of hemoglobinor the activity of leukocyte esterases persists for several hours after release from the cells.

Tab. 1 Orientation examination of urinary sediment using diagnostic strips

Diagnostic strip (reaction zone)	Microscopic equivalent
Blood (hemoglobin / erythrocytes)	Erythrocytes, erythrocyte cylinders
Leukocytes	Leukocytes, leukocyte cylinders
Protein	Hyaline, waxy, granular cylinders
Dusitany	Bacteria

Microscopic examination of urinary sediment

Microscopic examination procedure

Urine sample preparation

- A middle stream of the first or second morning urine is taken for microscopic examination of the urine sediment. The second morning urine is recommended because the cell elements in the first morning sample are often damaged or broken. Also, a significant reduction in urine osmolality and alkaline pH reduces the occurrence of formed elements due to their lysis.
- For examination of urinary sediment, it is necessary to process *fresh urine within 1 hour after collection.* Prolongation of the interval between urine collection and examination of urinary sediment is accompanied by cell breakdown and death.
- Mix the urine sample well and then measure 5 ml or 10 ml of urine into a test tube. Centrifuge at 400 g for 5 minutes, preferably at 4 ° C. Then carefully aspirate 9 parts of supernatant ; that is, the sediment is 10 times concentrated. If we work with a stained preparation (see below), we add the dye in an amount that corresponds to 10% of the total volume.

Staining procedure

1. Dilute 50 µl of the staining solution (alcian blue and pyronin B in a ratio of 1: 1) in 0.5 ml of urine sediment and mix gently.
2. After 5 minutes, transfer 13 µl of stained sediment to a slide and cover with an 18 × 18 mm coverslip. A larger volume of stained sample with the appropriate size of coverslip can also be used.

- We first view the sample at a magnification of 100–200 ×, when we can assess the uniform distribution of the elements and notice rare particles such as cylinders and epithelial cells. Then we proceed to the counting of elements at a magnification of 400 × in at least 10 randomly selected fields of view. After conversion to the original urine volume, the results are reported as the average number of particles in 1 µl of urine. Higher accuracy of element counting is achieved by using a chamber (Bürker or other chamber).

Possibilities of microscopic examination

Transmitted light microscopy and phase contrast techniques are used for microscopic examination of urinary sediment, and in special cases also polarization filter microscopy.

1. **Transmitting light microscopy**
   Allows rough orientation or search for pathological findings. Using light microscopy , ***unstained specimens*** may escape hyaline warfare and bacteria during evaluation . Accurate identification of leukocytes, macrophages and renal tubular cells is very difficult in unstained preparations. ***Supravital staining*** is recommended for reliable determination of urinary element morphologythat highlights some cellular details. By supravital staining we mean staining a wet unfixed preparation in which some cells still survive. Sternheimer staining using blue and red color contrast with alcian blue and pyronine B is recommended. Due to its strong affinity for mucopolysaccharides, alcian blue stains the surface of cells and elements, pyronin B penetrates inside the cells and stains the cytoplasm in particular.

2. **Phase contrast microscopy**

   It is a suitable method for rapid evaluation of unstained slides. It is used for more detailed assessment of sediment, especially better recognition of leukocytes, cylinders and crystals and differentiation of erythrocytes, including morphological changes of membranes. A better display of details allows you to increase the contrast, which is achieved by shifting the phase of the light wave of part of the rays.

3. **Polarizing filter microscopy**

   It is suitable for better identification of crystals and fat bodies.

Components of urinary sediment and their evaluation

In the urinary sediment, we assess ***organ*** components, mainly represented by cells, or cylinders, and non- ***organs*** , among which we include crystals. We also notice the presence of microorganisms and various artifacts may occur. The main components of urinary sediment are summarized in Table 2.

Tab. 2 Overview of the main components of urinary sediment

		erytrocyty
Cellular elements	blood cells	erythrocytes
		leukocytes
		lymphocytes
		macrophages
	epithelium	renal tubular cells
		transitional epithelial cells
		squamous epithelium
	tumor cells	
Rollers	cellless	hyalinní
		granular
		waxy
		fat
	cellular	erythrocyte
		leukocytové
		epithelial
		bacterial
Microorganisms	bacteria	
	yeast	
	trichomonády	
	mold	
Crystals		

Cellular elements

Leukocytes

- *Polymorphonuclear granulocytes* are the most frequently detected . They are round cells (average size 10 μm) with granular cytoplasm. The nucleus is segmented, but is often subject to degenerative changes and in this case is difficult to distinguish from the cytoplasm. Sometimes it stains badly; when stained, it is markedly blue, while the cytoplasm tends to turn red and reddish brown. The appearance of granulocytes is also affected by urine osmolality. They often gather. The finding is characteristic of a urinary tract infection, if erythrocytes are present at the same time, it may affect the glomeruli. Bacteria are also found in about 50% of leukocytes. Eosinophilscan only be demonstrated using special staining. A false positive finding may be due to urinary contamination (vaginal secretion, failure to follow urine collection instructions - first stream).

- The occurrence of *lymphocytes* in the urine is mostly associated with chronic inflammation of the kidneys , sometimes with viral infections and further with kidney rejection after transplantation . Lymphocytes have a homogeneous nucleus with a thin cytoplasmic margin. The ratio of nucleus to cytoplasm and the smooth structure of the cytoplasm are best distinguished from renal tubular cells.
- Sometimes we can also meet *macrophages* . Their finding is relatively common in urinary tract infections.

- **Reference values**

  - ≤ 10 leukocytes/µl urine,
  - approximately < 5 leukocytes/field of view.

Erythrocytes

- The presence of erythrocytes in the urine is usually a symptom of kidney or urinary tract disease. Erythrocytes are smaller than leukocytes. They appear as non-nuclear discoid bodies with an average size of about 6 µm. In hyperosmolar urine, where erythrocytes easily lose intracellular fluid , their diameter decreases and they become creped to spiny. Conversely, in hypoosmolar urine, fluid enters erythrocytes, enlarges and may disintegrate. With a low hemoglobin content , they are difficult to recognize and appear as so-called shadows.
- From the appearance of red blood cells we can deduce their origin. With significant damage to the glomerular membrane, penetration of not only proteins but also erythrocytes is possible. As the erythrocyte passes through the glomerular membrane, the shape is deformed and the structure changes. Erythrocytes that show deviations from the discoid shape are termed *dysmorphic.*Sometimes they have the shape of "tires" (so-called ring or annular erythrocytes), other times the membrane of erythrocytes extends into the vesicles, in this case we are talking about acanthocytes. An increased incidence of dysmorphic erythrocytes is typical of renal glomerular involvement. The proportion of dysmorphic erythrocytes in more than 80% indicates glomerular hematuria and we usually find proteinuria at the same time. If isomorphic erythrocytes are present in more than 80%, this is non-glomerular hematuria, where the source of erythrocytes is bleeding from the urinary tract or bleeding from ruptured blood vessels in kidney tumors or urolithiasis. Phase contrast microscopy is required to identify dysmorphic erythrocytes.
- The causes of haematuria must always be clarified, in particular cancer or severe glomerulopathy (glomerulonephritis) must be ruled out.
- The cause of the increased number of erythrocytes in the urinary sediment can also be extreme physical exertion, the use of anticoangulants or the admixture of menstrual blood .

- **Reference values**

  - < 5 erytrocytes/µl urine,
  - approximately < 5 erytrocytes/field of view.

Epithelium

They come from the epithelial lining of the renal tubules and urinary tract.

Renal tubular cells

- Their occurrence in urinary sediment is *always a pathological finding* and indicates serious kidney damage, especially for diseases affecting the tubules (acute tubular necrosis , acute interstitial nephritis). They are relatively small cells (average size 13 µm) only slightly larger than leukocytes, either round, irregularly polygonal, cubic or faceted with a smooth, usually eccentrically placed (dark blue in the colored sample) round nucleus, without nucleoli. They are characterized by a granular cytoplasm, red in the stained sample. They usually occur alone, sometimes in clusters or can form cylinders.
- In the unstained preparation, they are difficult to distinguish from transitional epithelial cells. Therefore, the term "small round epithelial cells" is sometimes used in laboratory practice. They can also be mistaken for leukocytes.

Transient epithelial cells

- They come from the superficial or deeper layers of the transitional epithelium lining the urinary tract. It is not possible to locate them in a certain part of the urogenital tract. A more common finding is surface layer cells that are round or ovoid with a round or ovoid nucleus located centrally or slightly eccentrically with a visible nucleolus and a cytoplasm that is usually finely granulated (less than tubular cells), granulation is usually on the periphery of the cell, rarely around the core. The average size is around 30 µm. Their findings usually indicate an infection of the lower urinary tract, especially in the presence of leukocytes. They can also be found in the urine of healthy people.
- Cells from deeper layers are smaller (average size 17 µm), ovoid and their shape is much more variable (shape of clubs, hammers or cells with tails). Dual-nuclear cells are a common finding. We encounter them in the urine of patients with urothelial carcinomas or urinary stones .

Squamous epithelium

- They are the largest cells in the urinary sediment (average size 55 µm), rectangular to polygonal in shape with a small nucleus and rich cytoplasm. They come mostly from the urethra or vagina and their amount depends on the quality of the urine sample. They are usually found in the urine of women when poorly contaminated, ***they have no diagnostic significance* .**

Tumor cells

- Tumor cells can be released into the urine in tumors of the kidneys, urinary tract and accessory organs (eg prostate). They are characterized by an irregular shape of the nucleus, which is usually significantly larger in relation to the cytoplasm. Without staining, the presence of tumor cells is difficult to detect (Table 3).

Tab. 3 Basic morphological characteristics of urinary sediment cells

Cell type	Kernel	Cytoplazma
Erythrocyte	bezjaderný element	discoid bodies
Granulocyt	segmented, multilobed, bright blue, sometimes poorly colored	granular, usually colored red
Macrophage	often broken blue nuclei, inhomogeneous chromatin	granular, usually contains parts of erythrocytes or other phagocytosed material
Lymphocyte	large, smooth nucleus, filling almost the entire cell	thin edge of cytoplasm without granulations
Tile cell	degenerate, small (polygonal) located in the middle	indistinctly rich
Superficial transitional epithelial cells	oval or round, usually deposited in the center of the cell, chromatin finely granulated, occasionally nucleolus occurs	finely granulated cytoplasm, granulation more often at the periphery of the cell
Transient epithelial cells deep	well defined, distinct nucleoli	numerous granules may be dark red
Renal tubular cell	homogeneous clear, spherical or oval, usually eccentrically arranged	the coarser granulated dense cytoplasm, often dark red, may contain fat particles inside

Rollers

The cylinders are cylindrical structures formed in the distal tubules and collecting ducts of the kidneys. The matrix is made up of ***Tamm-Horsfall protein*** , which is produced by the tubular epithelial cells whose surface it protects. Under certain circumstances, such as low pH , high osmolality , high protein concentrations, Tamm-Horsfall protein can precipitate and form casts of tubules that are released into the urine. On microscopic examination, they are described as cylinders. During the precipitation, other material can be incorporated into the cylinder matrix, eg cellular elements (leukocytes, erythrocytes, renal cells), pigments (hemoglobin, bilirubin), crystals and plasma proteins. Cylinders are the only elements that are ***always of renal origin***, cannot come from the urinary tract. The morphology of the cylinders depends on the diameter of the tubules in which they form. If the tubule in which the cylinder is formed is enlarged due to atrophy or obstruction, wide cylinders, typical of kidney failure, form .

According to their appearance, the cylinders are classified into:

- ***cellless***

  hyalins,
  granular,
  waxy,
  fat;

- ***cellular*** (the area of the cylinder is more than 1/3 covered by cells)

  erythrocyte,
  leukocyte,
  epithelial,
  bacterial.

Demonstration of cell cylinders in urinary sediment is always a sign of a pathological process in the kidneys (Table 4).

Tab. 4 Overview and diagnostic significance of individual types of cylinders in urinary sediment '

Cylinder designation	Characteristics	Diagnostic significance
Hyalinní	▪ pure protein castings of tubules ▪ made of Tamm-Horsphall protein, they refract light little, they do not always absorb the dye	▪ they may occasionally occur in people without kidney disease, such as after increased physical activity, fever or dehydration ▪ in larger numbers, their finding may be a manifestation of proteinuria
Granulated	▪ granules that are deposited in the form of drops in the hyaline matrix ▪ they arise as a product of the breakdown of cells (tubular or blood) or proteins	▪ they occur in patients *with proteinuria* or *tubular cell damage* ▪ pathognomonic for glomerular and tubular kidney diseases
Wax	▪ they are formed from the originally granulated cylinder by the complete decay of the cell debris, so that it loses any internal structure ▪ the development of the wax cylinder takes several hours ▪ they have a homogeneous structure, they are wide, with clearly broken ends, they strongly refract light	▪ typical of patients with renal failure or renal insufficiency ▪ "Renal failure wars" ▪ *indicator of severe proteinuria*
Grease and fat cell cylinders	▪ on the surface are fat bodies formed by triacylglycerols or cholesterol ▪ with more significant damage to the glomerular membrane, lipoproteins can also pass into the urine, which are taken up by tubular cells, they degenerate and form fat bodies, which can be incorporated into the cylinder matrix	▪ typical of glomerular damage ▪ *in nephrotic syndrome*
Epithelial	▪ epithelium peeled from the renal tubules is trapped on the surface of the hyaline matrix	▪ they occur in patients with *tubular damage*
Erythrocytes	▪ erythrocytes are glued to the surface of the matrix ▪ erythrocyte degeneration can turn into hemoglobin cylinders	▪ indicates *hematuria of renal origin* , because cylinders are formed only in the renal tubules
Leukocytové (granulocytové)	▪ mainly granulocytes are trapped on the surface of the hyaline matrix	▪ their presence is typical for *inflammatory kidney diseases of* bacterial or non-bacterial origin ▪ evidence of renal leukocyte origin
Bacterial	▪ clearly granular, very brittle	▪ are evidence of renal origin of bacteria ▪ very rare, as they require a large amount of bacteria in the kidney

Microorganisms

Bakteria

- Under physiological circumstances, the urine contains bacteria in an amount of less than 10 5 / ml. They have the appearance of small coccal or rod-shaped formations, which differ from other elements.
- The presence of bacteria can also be a sign of non-sterile urine collection, as the bacteria multiply rapidly when the sample is allowed to stand for a long time.

Trichomonades

- They have a round or oval shape with whips, they are characterized by fast irregular movement when alive. Their frequent finding is in concomitant inflammation of the vagina.

Yeast

- They are slightly smaller than erythrocytes, oval but of various sizes. We find them in groups and sometimes grouped in the form of chains. They are common in diabetics, in patients treated with immunosuppressive drugs and sometimes after antibiotics.

Crystals

Examination of the crystals must be performed in the morning urine immediately after its collection. The finding of crystals, which occur relatively frequently in the urinary sediment, cannot be overestimated. The presence of crystals may be due to transient urinary supersaturation, eg when eating food rich in urates or oxalates, and is a signal for increased fluid intake. *Crystals form in vitro* as the urine sample cools or the pH changes. The finding of crystals in these circumstances is clinically insignificant.

- ***Uric acid crystals and amorphous urates*** in acidic urine and ***ammonium magnesium phosphate*** in alkaline urine in urinary tract infections are common .
- Crystal detection is important in patients with urolithiasis. Their ID can indicate what kind of stones it is. However, it is not possible to conclude from the findings of crystals in the urine that there is a concrete of the same chemical composition in the urinary tract. Repeated detection of crystals is especially important in the control of patients after removal of the stone or in patients with recurrence of urolithiasis.
- Identification of hexagonal ***cystine*** crystals will support the diagnosis of cystinuria.
- The finding of ammonium magnesium phosphate crystals together with high urine pH indicates the probability of struvite stones.
- Flooding of ***calcium oxalate crystals*** is a characteristic finding in ethylene glycol poisoning, otherwise these crystals are a common finding especially in people with a higher intake of plant foods and are not related to the formation of stones. Another example is uric acid crystals in urate nephropathy.
- ***The presence of leucine and tyrosine*** crystals accompanies severe liver disease. Also, some drugs may be excreted in the form of crystals, especially in overdose, dehydration or hypoalbuminemia. Urine pH also affects the nature of the drug.
- ***Cholesterol crystals*** are a sign of severe glomerular membrane damage (Table 5).

Tab. 5 Selected crystals in urinary sediment

Kind of crystal	Typical shape	Urine pH			Clinical significance
		Sour	Alkaline	Variable	
Urine	amorphous	+			▪ in healthy individuals
Uric acid	various shapes, "kegs", "rosettes"	+			▪ in healthy individuals ▪ in chemotherapy ▪ in days
Ammonium urea	balls, "thorn apples"		+		▪ in healthy individuals ▪ in old urine
Calcium carbonate	balls arranged in the shape of a dumbbell		+		▪ healthy individuals
Ammonium magnesium phosphate (triple phosphate)	coffin lid shape		+		▪ in urinary tract infections ▪ struvite stones
Calcium oxalate	"Envelopes" (dihydrate), "biscuits" - (monohydrate)			+	▪ in healthy individuals ▪ ethylene glycol poisoning
Cholesterol	flat plates with broken corner			+	▪ damage to the glomerular membrane
Cystin	hexagonal prisms	+			▪ cystinurie
tyrosine	thin needles in bundles or rosettes			+	▪ liver disease ▪ aminoaciduria
leucine	oily balls			+	▪ liver disease ▪ aminoaciduria

Lipids

- Lipids can enter the urine through the damaged glomerular membrane in the form of plasma lipoproteins.

Lipoprotein particles are larger than the proteins themselves, and therefore lipiduria is associated with severe proteinuria and signals severe kidney damage.
- Lipids occur in the form of loose droplets isolated or in clusters; in this case, their presence may be caused by contamination, such as suppositories. Intracellularly localized fat inclusions are a sign of degenerative cell changes. Another form is cholesterol crystals or fat cylinders.

Other findings

- In the urinary sediment, we can also notice motile spermatozoa with a long thin flagellum, mucus and fibrin fibers and various contaminating formations, such as fibers of toilet paper or various textiles.

Quantitative examination of urinary sediment according to Hamburger

In indicated cases, a quantitative examination of urinary sediment according to Hamburger can be performed, which is used to monitor the rate at which erythrocytes, leukocytes and cylinders are excreted in the urine. The patient collects urine for 3 hours. As a last resort, a deviation of ± 30 minutes is tolerated, which must be taken into account in the calculation. At the end of the collection, the entire volume of collected urine is delivered to the laboratory within 1 hour. At the same time, it is necessary to state the collection time to the nearest minute. The number of erythrocytes, leukocytes and cylinders in the 5 large squares of the Bürker chamber is evaluated in the sediment.

References values

- Erythrocytes up to 2000/min, ie. 33 Er/s.
- Leukocytes up to 4000/min, ie. 67 Leu/s.
- Cilinders up to 60–70/min, ie. 1 válec/s.

Automatic analysis of urinary sediment

Devices for automated examination of urinary sediment are currently available. They work on the principle of flow cytometry or digital particle sensing.

Flow cytometry

Flow cytometry is a laboratory method that allows the simultaneous measurement of a number of parameters in a large number of particles. In addition to hematology, its application in the examination of urinary sediment is gradually expanding, which has hitherto significantly burdened laboratories and, in addition, has been burdened with subjective error. In flow cytometry, the particles are labeled with different fluorophores and then the cell suspension is driven through a narrow capillary. As they pass through the capillary, the particles encounter a beam of light, usually from a laser, which excites the fluorescence of the fluorophores. The laser light is scattered by the cell. The most frequently measured parameters are *light scattering at a small angle* , which is directly proportional to the size of the cells - the so-called forward scatter, *light scattering to a large angle*so-called side scatter, which provides information about the internal structure of particles, and fluorescence of different wavelengths. The flow cytometer is a fully automated analyzer for the analysis and identification of cells and other elements of native urine samples.

Analysis procedure

- When examining the urine sediment by flow cytometry, the urine is aspirated (0.8 ml) after mixing, diluted and the conductivity is measured.
- This is followed by automatic staining of the urinary elements with two different fluorescent dyes. The phenanthridine dye stains nucleic acids (orange fluorescence). The second dye used - carbocyanine is intended for staining of negatively charged cell membranes, nuclear membranes and mitochondria (green fluorescence).
- The colored particles pass through the capillary and are irradiated with a laser beam, which is both scattered by the cell and excited by the ***fluorescence of*** the fluorophores. ***At the same time, the electrical conductivity*** of the particles in the capillary is measured . Identification and counting of elements is made possible by evaluating the fluorescence of both dyes together with measuring the scattering of the radiation emitted by the laser and the measured conductivity.

All cell elements - erythrocytes , leukocytes , bacteria and epithelial cells - can be diagnosed using a flow cytometer . In addition, it is able to differentiate some clinically significant modifications such as ***isomorphic and dysmorphic erythrocytes*** . Provides information on the presence of ***pathological cylinders***, which, however, need further microscopic examination. It also demonstrates crystalline structures, but does not distinguish between different types of crystals, in which case microscopic refinement is required. The flow cytometer is unable to differentiate trichomonads. The number of erythrocytes, leukocytes, bacteria, flat epithelium and cylinders is given in elements / µl. To increase the accuracy of urinary sediment analysis, it is possible to automatically compare the results of chemical analysis using diagnostic strips, which is evaluated by a reflection photometer, and analysis by flow cytometry, so-called cross-check. Conformity of flow cytometry with microscopy ranges from 80-90%, agreement with diagnostic strips in 72-96%. Flow cytometry significantly reduces the need for microscopic analyzes, improves measurement accuracy and facilitates standardization of results.

Digital particle sensing

In this method of automatic urine sediment analysis, a sample of uncentrifuged urine is injected into a planar cuvette. Particles present in the urine are scanned multiple times using a digital camera and their images are compared based on their size, shape and structure with a database that is part of the device software.

Urine test reference values

Chemical examination

- pH 5–7.
- Relative density 1,016–1,022.
- Protein up to 0.3 g / l.
- Glucose negative.
- Ketone bodies negative.
- Bilirubin negative.
- Urobilinogen 3,2–16 µmol/l.
- Blood up to 5 / µl.
- Leukocytes up to 10 / µl.
- Nitrite negative.

Sediment (quantitative)

- Erythrocytes <33 / s.
- Leukocytes <67 / s.
- Cylinders <1 / s, only hyaline.

Links

Externí odkazy

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