

Strategy and interpretation of paraclinical investigations in renal diseases

Kidney disease is a pathology commonly encountered in family physician practice. In addition, the investigation of renal function is also useful to assess organ damage in various diseases: HTA, diabetes, autoimmune diseases (spondylitis, rheumatoid arthritis), infectious diseases. Therefore, exploring the renal system is part of the skills that the family doctor must acquire.

Urine examination - It is performed routinely to all patients, quantitative, semi-quantitative or qualitative determinations can be made. Use dipsticks (urinary strips), semi-quantitative method, presents the advantage of the immediate results, but to the individuals who present. Symptoms of the urinary tract are required to perform quantitative tests, microscopic examination of urinary sediment, uroculture.

Harvesting is done in the morning urine, after the first toilet of the urogenital region, from the middle of the urinary stream. In special situations, the urine can be harvested using a syringe adapted to the urinary probe or to the suprapubic puncture (when it cannot be collected from the urine spontaneously or to children).

a. Quantitative evaluation

- normal motions 600-1.800 ml / day
- oliguria <400 ml / day
- anuria <100 ml / day
- polyuria > 2,500 ml / day

b. Macroscopic examination (color, appearance, smell)

Appearance

- Clear (normal urine)
- Blurred (leukocytes, mucus, fats, salts),

Color

- Intense yellow (high doses B2, phenacetin)
- Orange (concentrated urine, bilirubin, urobilinogen)
- Yellow-green (biliverdin, pseudomonas)
- Greenish blue (methylene blue, pseudomonas)
- Red (hematuria, myoglobinuria, porphyria, beet, pyramid)
- Reddish-brown (methemoglobin)
- Brown-black (methemoglobin, alcaptonuria, porphyria, methyldopa, L-dopa)

The smell

- Normal urine - aromatic odor, fad
- Ammoniacal - urinary tract infections, renal tumors
- Rotten - infections with anaerobic germs
- Acre apples - diabetes

c. Physical examination

Density

- normal = 1.015-1.030
- hyposthenia <1,015 (reducing the concentration capacity of urine) - tubular or tubulointerstitial impairment, IRC)
- Hypertension > 1,030 (reduced fluid consumption)

Normal osmolarity = 800-1,200 mOsm / kg water

- Increased - hyponatremia, Addison disease, heart failure, cirrhosis, inadequate secretion of ADH

- Low - diabetes insipidus, hyperaldosteronism, excessive ingestion of water, polyuria (diabetes, CKI)

Normal pH = 5.8-7.4

- acid pH - uric lyticase or cysteine calculations, hyperprotein diet, dehydration (fever, diarrhea), diabetes mellitus, metabolic acidosis, distal tubular renal acidosis, phosphomycin, methanol poisoning

- Alkaline pH - phosphate-magnesian lithiasis, vegetarian diet, urinary infections with urease-producing germs (*Proteus mirabilis*, *Klebsiella*, *Pseudomonas*), metabolic alkalosis (vomiting, hyperventilation), sodium bicarbonate.

d. Chemical examination - detection of the presence in the urine of some compounds: proteins, carbohydrates, ketones, bile pigments, urobilinogen, porphyrins.

Chemical determinations can be performed by dipstick, semi-quantitative method, or by quantitative dosing in the morning urine or 24 hour urine.

- Urinary protein - physiologically <150 mg / 24 hours; may increase after physical exertion, prolonged or pathological orthostatism, especially in glomerular, tubular disorders.

- Values of albuminuria (normally <30 mg / 24 hours) in the range 30-300 mg / 24 hours are considered microalbuminuria and represents the first sign of glomerular impairment, being a parameter mandatory to be monitored annually in all diabetic and hypertensive patients (it is considered a sign of subclinical organ damage).

- Albuminuria values > 300 mg / 24 hours are considered clinical organ damage.

Proteinuria is considered

- mild (0.3-1 g / 24 hours) being found in tubulointerstitial nephropathies, intrinsic IRA, glomerulopathy remission phase,
- moderate proteinuria (1-3 g / 24 hours)
- severe proteinuria (urinary protein ≥ 3.5 g / 1, 73 m² / day) which is a criterion in the diagnosis of nephrotic syndrome.

Tubular proteinuria occurs in acute and chronic tubulointerstitial nephropathies through resorption defect and is characterized by low albumin content (10-20%) and globulin predominance. Postrenal proteinuria (usually <1 g / 24 hours) that may accompany a urinary tract infection, renal lithiasis, renal tumors. Overload protein, in which large amounts of pathological proteins produced in excess are eliminated: multiple myeloma, rhabdomyolysis (myoglobinuria), intravascular hemolysis (hemoglobinuria), acute myelocytic leukemia.

Qualitative methods for detecting urinary proteins its use when tracking pathological proteins in urine and protein electrophoresis is performed (Bence protein-Jones, monoclonal gamapati, amyloid) in systemic diseases.

If you cannot harvest urine for 24 hours you can use it **urinary protein / urinary creatinine ratio** made from morning urine:

- <1 is considered mild proteinuria
- = 1-3 we talk about moderate proteinuria,
- > 3 we are facing a severe proteinuria.

Urinary glucose <0.5 g / 24 h physiologically; increases in diabetes, proximal tubular disorders (Fanconi), heavy metal poisoning. In diabetes mellitus glycosuria normally occurs at blood glucose levels > 180 mg / dl; if it occurs at low blood glucose levels it means the association of a tubular impairment. The strips can be used for semi-quantitative evaluation or quantitative determination can be performed in the urine for 24 hours. High glycosuria can be found in conditions other than diabetes: Cushing's syndrome, hyperthyroidism, STH hypersecretion, pancreatic disorders or kidney disease that causes glycosuria without proper hyperglycaemia (tubulopathy, Fanconi syndrome, Wilson's disease);

- **Ketonuria** is identified in the case of diabetic ketoacidosis or after a long period of fasting. False positive results may be obtained in patients treated with drugs containing sulfhydryl group (captopril, zofenopril) or levodopa.
- **Urobilinogen, bilirubin** - may be increased in urine in the case of intravascular hemolysis, polycythemia vera, liver disease.

They can be quickly determined by screening with the band or the quantity of urine in the morning.

- **Nitrites** - detection of nitrites in the urine indicates the presence of infection urination with gram negative bacteria;

e. The microscopic examination of the urinary sediment may reveal:

- **normal sediment**

<2 hematis / field

<5 leukocytes / field

<15 squamous cells

- **Adiss** (quantitative estimation of urine elements in time unit)

<2,000 haematics / min

<4,000 leukocytes / min

- **Stansfeld-Webb** (quantitative estimation of urine elements in volume unit) <3 hematomas / μ L, <10 leukocytes / μ L
- **Highlighting red blood cells > 3 red blood cells / field is pathological ; blood can come from any level of the urinary tract.**
 - In glomerular disorders (glomerulopathies) the red blood cells have the modified form (more than 30% of the red blood cells), while in other diseases they retain the biconcave disc shape.
 - Extraglomerular hematuria may be caused by polycystic kidneys, papillary necrosis, interstitial nephritis, infections, thrombosis of renal artery or vein, renal lithiasis, renal or urothelial tumors, prostate disorders, renal trauma, coagulopathy, overdosage of anticoagulants.
- Initial hematuria usually comes from lesions of the prostate or urethra
- Terminal hematuria originates in the bladder
- Total hematuria, the most common situation, originates from the renal or upper urinary tract.

The hematuria can be microscopic, when it does not produce changes in the color of the urine, or macroscopic (usually corresponds to more than 100 hematomas / field), when the urine is colored red. Any episode of hematuria should be investigated, anamnesis, clinical examination, urine examination and renal function examination followed by ultrasound, UIV, cystoscopy, MRI, CT, renal biopsy, other serological tests for systemic disorders.

- **Leukocytes > 5 / field (between 2 and 5 leukocytes / field is considered normal)** are found in urinary tract infections, tubulointerstitial nephropathies or by contamination. The presence of leukocytes in the urine determines the positivity of the flagella tests at 5-15 leukocytes / field.
 - if neutrophils predominate in the urine we think of a bacterial infection or contamination during harvest, the presence of eosinophils raises the suspicion of immune, allergic or drug interstitial nephritis.
 - Leukocytes can sometimes be detected as a sign of accompanying their neighborhood infections (acute appendicitis, inflammatory bowel disease).
- **Renal tubular epithelial cells** - arise from the scaling of the urothelium and may exist physiologically in the urine; if large, suggest tubulointerstitial nephritis, acute tubular necrosis or acute glomerulonephritis. Pavement and squamous epithelial cells originate from the lower urinary tract or from the genital tract, transitional epithelial cells (urothelium) originate from the upper urinary tract (basin, ureter, bladder, proximal urethra)
- **Fat cells, fatty bodies** - are epithelial cells that contain lipids and meet in nephrotic syndrome (cross of Malta)
- **Cylinders** - means kidney damage.

There are several types of cylinders: hyaline (non-specific, exists in normal urine and kidney disease), granular (non-specific, usually appear in kidney disease), waxy (signifies renal impairment), fatty cylinders that appear in nephrotic syndrome, cylinders hematics that appear in hematuria of glomerular origin, leukocyte cylinders found in tubulointerstitial nephropathies, epithelial cylinders that may occur in interstitial nephropathy, acute tubular necrosis, glomerulonephritis proliferative.

- **Bacterial flora** (requires identification of germs and sensitivity testing)
- **Crystals** (oxalates, scratches, struvite, cystine) - the presence is pathological in large amounts of crystals in the urine.

f. Uroculture - collected in sterile containers, from the first urine after the toilet of the urogenital region with soap and water urine is collected from the middle of the jet. Identification of pathogenic germs $\geq 10^5$ / ml is followed by antibiotic sensitivity testing. The result is correlated with clinical symptoms and other investigations. Asymptomatic bacteriuria does not require treatment, except in pregnant women and before urological interventions.

Evaluation of renal function and glomerular filtration (GFR) It is mandatory for any patient, being considered as a screening in the assessment of renal function, evaluation of disease progression, adjusting drug dosage and administration interval and establishing the need for dialysis or kidney transplant. The investigation of renal excretory function is performed periodically (annually) by any patient, and in the case of those exposed to the risk of renal disease (diabetes, HBP, infections, lithiasis, nephrotoxic medication) it is performed as often as necessary.

The values of urea (normal values = 10-50 mg / dl) and plasma creatinine (normal values = 0.6-1 mg / dl in women and 0.8-1.3 mg / dl in men) are determined.

Direct or indirect methods are used to determine GFR in medical practice. Serum creatinine is measured and formulas are used as computer applications, the most used being MDRD (Modification of Diet in Renal Disease) and CKD-EPI (Chronic Kidney Disease

Epidemiology).

Normal values are considered

95 ± 20 ml / min / 1.73 m^2 1a women,

125 ± 25 ml / min / 1.73 m^2 1a men.

According to GFR, the classification of the chronic kidney disease is performed in the 5 stages:

| stage | RFG (ml / min / 1.73 m^2) |
|--|--------------------------------------|
| G1 Normal / Increased | ≥ 90 |
| G2 Slightly low | 60-89 |
| G 3a Slightly to moderately low | 45-59 |
| G 3b Moderate-very low | 30-44 |
| G4 Very low | 15-29 |
| G5 Renal insufficiency | <15 |

The calculation of GFR is very important because the decrease of RFG <30 ml / min / 1.73 m^2 implies sending the patient for evaluation and monitoring by the nephrologist.

Physiologically GFR decreases by 1 ml / min / 1.73 m^2 every year after the age of 40 years.

There are factors that can alter the value of serum creatinine (age, muscle mass, cachexia, hepatic function, drugs), so that the determination of GFR more accurately evaluates renal function and should be performed on any patient.

Other determinations that are performed to complete the paraclinic picture of the patient with renal pathology are:

- **serum uric acid** (normal values: <5 mg / dl in women, <7 mg / dl in women) men) may be increased by consumption of excess purine rich foods, endogenous uric acid overproduction (haemolytic disease, multiple myeloma, myeloproliferative syndromes, psoriasis, rhabdomyolysis) or reduced renal excretion
 - **Serum and urinary ionogram** are performed on patients with impairment and electrolyte disorders can severely impair functioning heart or central nervous system
- Also, we must pay attention to the medication we are administering to the patient with chronic kidney disease, as it is often necessary to reduce the dose of drugs or to increase the interval of administration.
- acid-basic balance
 - hemolithogram - can highlight the anemia that is present in advanced kidney disease
 - glycemia profile (blood glucose, HbA1c)
 - lipid profile (cholesterol, LDL, HDL, triglycerides) - can show dyslipidemia as a cardiovascular risk factor in hypertensive patients, or it may help diagnose a nephrotic syndrome, when we find increased plasma and urinary lipids.

Paraclinically

1. Ultrasound is a non-invasive method commonly used and can evaluate: anatomical situation of the kidneys (ptosis, rotations), size of the kidneys (normal 9.5-11 cm), identification and measurement thickness of the cortex and spinal cord, highlighting of the urinary tract, presence of possible malformations. Measurement of kidney size is very important, because decreasing kidney size <9.5 cm is a sign of kidney disease, as well as a difference greater than 1.5 cm between kidneys.

The parenchymal index represents the distance between the sinus and the renal capsule and is normally > 14 cm, below this value being the expression of renal suffering. Also, in the presence of a ureteral obstruction hydronephrosis can be detected, the most frequent obstacle is the presence of a calculation located at different levels, and the ultrasound can identify calculations with high sensitivity and specificity. The ultrasound can also detect the presence of renal, urinary or bladder tumors, being the first-intention paraclinical examination in any situation, including in emergencies.

With Ultrasound Cysts, abscesses, intra- or extrarenal can be evaluated, their evolution over time, the perirenal space can be evaluated and the adrenal glands can also be evaluated.

Also, information can be obtained related to the prostate (size, structure, resonance on the urinary tract, measurement bladder residue), respectively information related to the genital female apparatus.

2. Simple renal radiography (empty abdominal) may be useful in urgency, because it provides information on kidney size, position and can identify radioopaque calculations.

3. Intravenous urography (IVU) is used only when detailed information on position, dimensions, kidney structure and function, localization of kidney stones for vision their extraction. It is indicated for the diagnosis of urothelial tumors and urinary tract abnormalities. It is not a routine examination and is not indicated in patients with nitrogen retention or a history of iodine allergy.

4. Computed tomography (TC) is performed when needed

accurate and thorough investigations of the renal apparatus, especially for the detection of tumor formations and their extension. Also, renal function can be assessed, guided biopsy points can be performed or information about the adrenal glands can be obtained (useful in detecting the cause of a secondary HBP).

It can be performed with or without a contrast substance, in the first case the tests of nitrogen retention are necessary, as well as the exclusion of patients with iodine allergy or renal dysfunction.

5. Radioisotopic investigations (scintigraphy) are used for thorough evaluation of renal function, urinary output, detection of obstructive lesions or renovascular disorders, especially when unilateral kidney damage is suspected. It is not a common method in practice because the other methods. Most of the time, the imagery offers the necessary information for diagnosis.

6. Nuclear magnetic resonance imaging (MRI) may identify some conditions with higher accuracy TC (tumor staging, renal cysts, loss of corticomedullary function), but is especially useful in renal vascular disorders. It can be used in patients with iodine allergy, but is contraindicated in patients with prostheses, staples or other implanted metal devices.

7. Renal vascular ultrasound by Doppler examination is indicated when we want to evaluate renal vascularization, the presence of arterial stenosis (including when suspected secondary HBP by renal artery stenosis), for suspected renal vein thrombosis.

8. Selective renal angiography is not performed routinely, but is the method of choice for highlighting stenosis or extrinsic compression of renal arteries, renal infarction. Similarly, renal venography is useful in confirming the suspicion of renal vein thrombosis if the ultrasound has not been conclusive.

9. Cystoscopy is performed in the case of hematuria for detecting source and cause of bleeding or other bladder disease.

Other explorations

Renal biopsy is performed (under ultrasound guidance or TC) in situations where the other methods could not establish the diagnosis with certainty or it is necessary to evaluate a condition in order to establish the therapy (CKD of non-specific etiology, primary nephrotic syndrome, systemic diseases with re kidney, renal amyloidosis, glomerulonephritis, suspected graft rejection). It is contraindicated in the case of single kidney, horseshoe kidney, hydronephrosis, terminal stages of nephropathy, renal tumors, hemorrhagic diathesis or uncontrollable HBP.

Immunological tests (ANCA dosage, anti MBG, C3, C4, rheumatoid factor, cryoglobulins and other antibodies) are required especially in the case of suspected glomerulonephritis in a systemic disease, in which antibodies and abnormalities of immunity occur. Detection of abnormal proteins in the urine examination, the existence of a systemic autoimmune disorder (spondylitis, rheumatoid arthritis) in the patient's history requires immunological tests. In the suspicion of glomerulonephritis, the patient will be referred to the nephrologist, respectively to the rheumatologist, in order to detect the cause in which renal changes occur.