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***Guidelines for conducting a practical lesson with 5th year students of the Faculty of Medicine on the topic:***

# DIFFERENTIAL DIAGNOSTICS OF BASIC PATHOLOGICAL SYNDROMES IN NEPHROLOGY

**(the duration of the lesson is 12 hours, the first lesson is 4 hours)**

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Guidelines for conducting a practical lesson with 5th year students of the Faculty of Medicine on the topic:
DIFFERENTIAL DIAGNOSIS OF MAIN PATHOLOGICAL SYNDROMES IN NEPHROLOGY.
PURPOSE OF THE LESSON: to increase the level (quality) of knowledge and skills of students in the differential diagnosis of the main pathological syndromes in the nephrology clinic, in particular urinary syndrome (proteinuria).
Students should be able to:
1. be able to identify the main syndromes in diseases of the urinary organs and the key points of the anamnesis, based on complaints, anamnesis and objective status, make a preliminary diagnosis of the presence of a kidney disease in a patient;
2. substantiate the need for additional research;
3. isolate the urinary syndrome; determine the nosological basis of the identified syndrome;
4. determine the scope of therapeutic care (pathogenetic, symptomatic treatment, treatment of complications).

MOTIVATION OF THE TOPIC RELEVANCE.

Identification of the leading syndrome or set of syndromes is an important part of the diagnosis of various diseases. At this stage, an attempt is made to link together a number of clinical, laboratory and data obtained using special research methods, which ultimately, on the one hand, allows, to a certain extent, to present the pathogenesis of the main manifestations of the disease in this patient, on the other hand, to outline the ways of differential diagnosis, i.e. determine the nosological basis of the identified syndrome.
This principle of diagnosis is also important because the clinical analysis of syndromes helps to assess the patient's condition as a whole and determine the amount of therapeutic assistance (pathogenetic, symptomatic treatment, treatment of complications). All this makes it possible to recognize the syndromic approach as an important way for the doctor to approach the establishment of the correct diagnosis and the choice of rational treatment.
In nephrological practice, a number of syndromes are distinguished:
• urinary;
• nephrotic;
• hypertonic;
• acute nephritic;
•acute renal failure;
• chronic renal failure;
• syndrome of tubular dysfunctions.
Some syndromes (for example, nephrotic, hypertensive) represent a detailed clinical picture of the disease, when patients, as a rule, have certain complaints and numerous manifestations of the disease. For the diagnosis of other syndromes, it is necessary to use special research methods.
In some cases, these syndromes may be the result of unilateral kidney damage, simulating a bilateral process, so you should always remember about asymmetric kidney damage. It should be borne in mind the frequent ephemerality of the syndrome, which may first occur at the onset of the disease, and then not recur (for example, nephrotic syndrome). Such an opportunity makes it necessary to study the patient's history with particular care, since the duration of the existence of one or another syndrome often determines the prognosis and treatment features.
Determining the level of students' preparation. Second level of knowledge:
control methods - written survey (20 min.). Students should know the main issues of etiology, pathogenesis, clinic and diagnosis of diseases of the kidneys and urinary tract, highlight the urinary syndrome, in particular proteinuria, determine the type of proteinuria. The main drugs used to treat kidney diseases, their mechanisms of action; students must be able to possess propaedeutic skills.

Report of students-curators in the chamber. When reporting a patient, students should pay attention to complaints, an anamnesis of the disease, and objective examination data. Students should pay special attention to the main syndromes in the supervised patient, to conduct differential diagnostics, i.e. to determine the nosological basis of the identified urinary syndrome - proteinuria.
For the nephrological diagnosis, the identification of proteinuria and hematuria is of great importance.
Proteinuria is an important and most common symptom of kidney damage, requiring a thorough examination of the patient. A urine test using test strips can detect proteinuria only if the protein excretion exceeds 0.3 g / l. if proteinuria is repeatedly detected using test strips, then the daily loss of protein in the urine is determined. Normally, protein excretion in the urine in adults does not exceed 150 mg / day, and in children under 10 years old - 100 mg / day. In the presence of severe leukocyturia and especially hematuria, a positive reaction to protein may be the result of the decay of formed elements during prolonged standing of urine; in this situation, pathological proteinuria is proteinuria exceeding 0.3 g / day. Sedimentary protein tests can give false positive results in the presence of iodine contrast agents, a large number of penicillin or cephalosporin analogues, sulfonamide metabolites in the urine. Proteinuria over 3 g/day leads to the development of nephrotic syndrome.

In the urine with kidney diseases, various plasma proteins are found - both low molecular weight (albumin, ceruloplasmin, transferrin, etc.) and high molecular weight (a2-macroglobulins, γ-globulins). Depending on the content of certain proteins in plasma and urine, selective and non-selective proteinuria is isolated (the term is conditional, it is more correct to speak of the selectivity of the isolation of protein fractions, the selectivity of their clearance).
• Selective proteinuria is called proteinuria, represented by proteins with a low molecular weight (no more than 65,000), mainly albumin.

• Non-selective proteinuria is characterized by increased clearance of medium and high molecular weight proteins (α2-macroglobulins, β-lipoproteins, γ-globulins predominate in urine proteins).

In addition to plasma proteins in the urine, proteins can be determined by

Chechen origin - Tamm-Horsfall mucoprotein, secreted by the epithelium of the convoluted tubules.

GLOMERULAR (GLOMERULAR) PROTEINURIA

In kidney pathology, proteinuria is most often associated with increased filtration of plasma proteins through glomerular capillaries - the so-called glomerular (glomerular) proteinuria. Filtration of plasma proteins through the capillary wall depends on the structural and functional state of the glomerular capillary wall, properties of protein molecules, pressure and blood flow velocity, which determine GFR.

The wall of the glomerular capillaries is made up of endothelial cells (with rounded holes between the cells), a three-layer basement membrane - a hydrated gel, as well as epithelial cells (podocytes) with a plexus of "pedunculated" processes. Due to such a complex structure, the glomerular capillary wall can "sift" plasma molecules from the capillaries into the space of the glomerular capsule, and this function of the "molecular sieve" largely depends on the pressure and current velocity in the capillaries. In pathological conditions, dimensions. "pores" can increase, deposits of immune complexes can cause local changes in the capillary wall, increasing its permeability for macromolecules.

In addition to mechanical obstacles (pore sizes), electrostatic factors are also important. BMC is negatively charged; the legs of podocytes also carry a negative charge. Under normal conditions, the negative charge of the glomerular filter repels anions - negatively charged molecules (including albumin molecules). The loss of negative charge contributes to the filtration of albumin. It is suggested that in the body of patients with minimal glomerular change disease and focal segmental glomerulosclerosis, certain substances are produced that change the charge of the BMC and podocyte pedicles. It is assumed that the fusion of the pedicle processes is the morphological equivalent of the loss of a negative charge.

Glomerular proteinuria is observed in most diseases of the kidneys - with glomerulonephritis, amyloidosis of the kidneys, diabetic glomerulosclerosis, thrombosis of the renal veins, as well as with hypertension, atherosclerotic nephrosclerosis, "stagnant" kidney.

tubular proteinuria

Tubular (tubular) proteinuria occurs less frequently. It is associated with the inability of the proximal tubules to reabsorb plasma low molecular weight proteins filtered in normal glomeruli. The amount of protein released rarely exceeds 2 g/day, the protein is albumin, as well as fractions with an even lower molecular weight (lysozyme, β-2-microglobulin, ribonuclease, free light chains of immunoglobulins), which are absent in healthy individuals and in glomerular (glomerular) proteinuria due to 100% reabsorption by the epithelium of the convoluted tubules . A characteristic feature of tubular (tubular) proteinuria is the predominance of β-2-microglobulin over albumin, as well as the absence of high-molecular proteins.

Tubular proteinuria is observed with damage to the kidney tubules and interstitium - with interstitial nephritis, pyelonephritis, potassium penic kidney, with acute tubular necrosis, chronic rejection of a kidney transplant, congenital tubulopathies (Fanconi's syndrome).

PROTEINURIA OVERFLOW

Overflow proteinuria develops with increased formation of plasma low molecular weight proteins (light chains of immunoglobulins, hemoglobin, myoglobin), which are filtered by normal glomeruli in an amount exceeding the ability of the tubules to reabsorb. This is the mechanism of proteinuria in multiple myeloma (Bence-Jones proteinuria; myoglobinuria. An example of such proteinuria is lysocymuria, described in patients with leukemia.

Differentiation of types of proteinuria can be carried out only by determining the protein fractions in the urine (biochemical and immunohistochemical methods).

In bright (non-systemic) and lupus glomerulonephritis, diabetic glomerulosclerosis, proteinuria is usually combined with erythrocyturia; purely proteinuric forms of rare. For amyloidosis of the kidneys, thrombosis of the renal veins, as well as for hypertension, isolated proteinuria (or proteinuria, combined with slight erythrocyteuria) is more characteristic. With hemorrhagic purpura of Schönlein-Genoch, polyarteritis nodosa, erythrocyturia is usually more pronounced than proteinuria.

In addition, proteinuria can be of extrarenal origin - be the result of cell breakdown in diseases of the urinary tract or genital organs, with prolonged standing urine (false proteinuria).

FUNCTIONAL PROTEINURIA

It should be borne in mind the possibility of the occurrence of functional proteinuria, the exact mechanisms of pathogenesis of which have not been established. These include orthostatic proteinuria, idiopathic transient proteinuria, strain proteinuria, and febrile proteinuria.

Orthostatic proteinuria

For her, the appearance of protein in the urine during prolonged standing or walking is typical, with a rapid disappearance in a horizontal position.

Characteristics of proteinuria: usually does not exceed 1 g / day, glomerular, non-selective, the mechanism of its occurrence is not clear. It is more often observed in adolescence, in half of the patients it disappears after 5-10 years.

The diagnosis of orthostatic proteinuria is made in the presence of the following criteria:

• age of the patient within 13-20 years;

• the isolated nature of proteinuria - the absence of other signs of kidney damage (other changes in urine, increased blood pressure, changes in the vessels of the fundus);

• exclusively orthostatic nature of proteinuria - in urine tests taken immediately after the patient was in a horizontal position (including in the morning before getting up from bed), there is no protein.

To confirm the diagnosis, it is necessary to conduct an orthostatic test. Urine is collected in the morning before getting out of bed, then after a 1-2-hour stay in a vertical position (walking, preferably with hyperlordosis, with a stick behind the back to straighten the spine). The test gives even more accurate results if the morning (night) portion of urine is poured out (since there may be residual urine in the bladder), and the first portion is collected after the subject has been in a horizontal position for 1-2 hours.

Idiopathic transient proteinuria

In adolescence, one can also observe idiopathic transient proteinuria, found in otherwise healthy individuals during a medical examination and absent from subsequent urine tests.

Tension proteinuria

Tension proteinuria, detected in 20% of healthy individuals (including athletes) after a sharp physical exertion with the

detection of protein in the first collected portion of urine, has a tubular (tubular) character.

It is believed that the mechanism of this proteinuria is associated with redistribution of blood flow and relative ischemia of the proximal and distal tubules.

Feverish proteinuria

Feverish proteinuria is observed in acute febrile conditions, especially in children and the elderly; it is predominantly glomerular in nature. The mechanisms of these types of proteinuria are poorly understood. The possible role of increased glomerular filtration along with transient damage to the glomerular filter by immune complexes is suggested.

CLINICALLY SIGNIFICANT PROTEINURIA

In the practice of a general practitioner, it is important to establish the very fact of proteinuria and the degree of its severity, since in the vast majority of cases proteinuria is one of the main signs of kidney damage.

High ("large", "massive") proteinuria

High proteinuria - the excretion of protein in the urine in an amount of more than 3 g / day, which often leads to the development of nephrotic syndrome. This type of proteinuria is observed in acute and chronic glomerulonephritis, kidney damage in systemic diseases (SLE, hemorrhagic vasculitis, etc.), in renal amyloidosis, subacute infective endocarditis. Severe proteinuria can also be observed in multiple myeloma and renal vein thrombosis, as well as diabetic nephropathy.

Moderate proteinuria

Moderate proteinuria - excretion of protein in the urine in an amount of 0.5 to 3 g / day; it is observed in all the diseases listed above, as well as in malignant arterial hypertension, periarteritis nodosa, hypertension, atherosclerosis of the renal vessels (ischemic kidney disease) and other diseases.

Microal6uminuria

Urinary excretion of albumin (microalbuminuria) appears earlier than other signs of renal disorders, which can be established by currently available methods, and reflects damage to the microvascular bed of the kidneys (and at the same time other vascular areas - heart, brain) . The diagnostic value of microalbuminuria is as follows. First, it is the earliest indicator of kidney damage in patients with type 1 and type II diabetes mellitus and in patients with hypertension; thus, it reveals the most severe prognostic group, which requires close monitoring with tight control of blood glucose and blood pressure. Secondly, the appearance of microalbuminuria predicts an unfavorable outcome of cardiovascular diseases (myocardial infarction, stroke), especially in patients with the so-called high-risk group - those with diabetes mellitus, obesity, arterial hypertension, or a family predisposition to vascular and Chechen diseases.

INFLUENCE OF PROTEINURIA ON KIDNEY TISSUE

In recent years, there is more and more data on the "toxic" effect of proteinuria. It has been established that plasma proteins passing through the glomerular membrane in nephropathies are not only a reliable marker of kidney damage, but also a factor that actively damages the structures of the kidney tissue, increases inflammation and induces fibrosis, primarily tubulointerstitial.

Attention to proteinuria as an important factor in the progression of parenchymal kidney diseases has especially grown after the establishment of a direct relationship between the amount of proteinuria and the risk of progression of renal failure, which is less dependent on the morphology of the renal process.

On the other hand, the degree of decrease in glomerular filtration (under the influence of a low-protein diet or angiotensin-converting enzyme (ACE) inhibitors) corresponded to the degree of simultaneous decrease in proteinuria.

In recent years, it has been proved that severe and prolonged proteinuria has a toxic effect on the epithelium of the tubules. Intense reabsorption of large amounts of filtered proteins by the epithelium of the proximal tubules leads to the activation of epithelial cells with the expression of genes for inflammatory and vasoactive substances.

Conducting classes in a thematic classroom. Analysis of the features of etiology, pathogenesis, clinic, diagnosis, treatment of a particular patient. Students should pay special attention to the main syndromes in the supervised patient, to conduct differential diagnostics, i.e. to determine the nosological basis of the identified urinary syndrome - proteinuria.

Indicate the main methods of non-drug exposure (changing lifestyle, nutrition, giving up bad habits, doing physiotherapy exercises). The main groups of drugs and their mechanisms of action, the main indications and contraindications for use and the rationale for choosing a particular drug from pharmacological groups.

The final part of the lesson: control of the acquired knowledge - solving situational problems without possible options for correct answers.

Summary.