MINISTRY OF HEALTH OF UKRAINE

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Departments of Pediatrics №2

CONFIRMED by

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METHODOLOGICAL RECOMMENDATIONS ON PRACTICAL CLASSES FOR STUDENTS

International Medical Faculty, course 6

Educational discipline "**PEDIATRICS**"

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1. **Topic** №23

Differential diagnosis of hereditary diseases of the urinary system in children. Leading clinical symptoms and syndromes in dysmetabolic nephropathies and hereditary tubulopathies (phosphate-diabetes, Debré-de-Tony-Fanconi syndrome, renal diabetes insipidus, renal tubular acidosis) in children. Clinical variants of the course in dysmetabolic nephropathies and hereditary tubulopathies. Differential diagnosis of hereditary diseases of the urinary system in children. Data of laboratory and instrumental studies in dysmetabolic nephropathies and hereditary tubulopathies. Differential diagnosis of dysmetabolic nephropathies and hereditary tubulopathies in children. Differential diagnosis of hereditary diseases of the urinary system in children. Management tactics for dysmetabolic nephropathies and hereditary tubulopathies in children. Principles of treatment of chronic renal failure in children.

2. **Relevance of the topic.**

In recent years, interest in the problem of damage to the interstitial tissue and kidney tubules as a result of infectious, metabolic, immune, toxic and other processes has increased significantly. Often, the disease is not recognized in a timely manner, often proceeds under the guise of other kidney diseases. One of the urgent problems of modern nephrology is the problem of urolithiasis and dysmetabolic nephropathy (DN) in children. Treatment of metabolic nephropathies as a polyetiological disease should be complex: it is necessary to influence both the causative factor and the mechanisms that promote lithogenesis.

In the literature, there are only a few epidemiological studies that provide data on the frequency of tubulointerstitial nephritis. According to puncture biopsy, tubulointerstitial nephritis accounts for 5-7% of all cases of kidney pathology in children and occurs in 2% of children with acute renal failure. Tubulointerstitial nephritis (TIN) is observed in about 14% of children with nephropathology who are registered at the dispensary. The urgency of the problem is also due to the tendency to a recurrent course and the lack of effectiveness of modern methods of therapy.

3. Objectives of the lesson:

3.1. General goals:

- to get acquainted with the modern definitions of the concepts of DN, TIN, etiology, clinical signs, be able to diagnose children, draw up a plan of therapeutic and preventive measures.

3.*2. Educational goals:*

- to get acquainted with the contribution of domestic and foreign scientists in determining the problems of DN, TIN, which contribute to the development of diseases, to determine the need for prevention of DN, TIN in children.

3.3. Specific objectives:

- to know:

Dismetabolic nephropathy.

1. Dysmetabolic nephropathies - definition, classification.
2. Prevalence and incidence of dismetabolic nephropathy in children in Ukraine.
3. Risk factors for the development of dismetabolic nephropathy in children.
4. General clinical picture of dismetabolic nephropathy in children.
5. Characteristics of the oxalate type of nephropathy in children.
6. Characteristics of the phosphate type of nephropathy in children.
7. Characteristics of urate type nephropathy in children.
8. The program of examination with dismetabolic nephropathy.
9. Components of complex treatment. Dietotherapy for various variants of dysmetabolic nephropathies.
10. Prevention and sanatorium treatment of dismetabolic nephropathies.

Tubulointerstitial nephritis.

1. Tubulointerstitial nephritis - definition, classification.
2. Factors and risk groups of tubulointerstitial nephritis.
3. Screening of the tubulointerstitial nephritis.
4. Pathogenetic mechanisms of development of acute and chronic tubulointerstitial nephritis in children.
5. Features of the clinical picture of acute and chronic tubulointerstitial nephritis.
6. Diagnostic criteria of the tubulointerstitial nephritis (algorithm for diagnosis of acute and chronic TIN) in children.
7. Instrumental methods of research of the tubulointerstitial nephritis: features of the ultrasound, CT, nephrobiopsy of acute and chronic tubulointerstitial nephritis in children.
8. General principles of therapy of tubulointerstitial nephritis. Criteria for the effectiveness of treatment of tubulointerstitial nephritis.
9. Physiotherapy, phytotherapy in the treatment of tubulointerstitial nephritis. Rehabilitation measures of tubulointerstitial nephritis.
10. Prevention. Forecast. Dispensary observation.

3.4. Based on theoretical knowledge on the topic:

- to master the methods / to be able /:

1. Collect anamnesis.
2. Identify the risk factors for chronic kidney disease.
3. Conduct a clinical examination of the nephrologic patient.
4. Select the most informative methods of examination to determine the diagnosis and conduct differential diagnosis.
5. Interpret the results of laboratory tests, ultrasound and x-ray examination.
6. Establish a diagnosis according to the classification.
7. Develop a therapy plan for the child with chronic kidney disease.

4. Materials of pre-classroom independent training (interdisciplinary integration).

№	Discipline	To Know	Be able to
1.	Previous disciplines		
	1. Anatomy	Anatomical structure of the kidneys and urinary tract	Identify peculiarities in children.
	2. Normal physiology	Functional state of kidneys and urinary tract in children.	Identify peculiarities in children.
	3. Pathological anatomy and pathological physiology	Diseases of the kidneys and urinary tract: microbial-inflammatory, immuno-pathological, metabolic. Congenital malformations of the UT	Correctly assess the nature of the process
	4. Biochemistry	The components of the biochemical analysis of blood, which reflect the function of the kidneys and UT	Correctly assess the nature of the process
	5. Propedeutics of childhood diseases	Anatomical - physiological features of the kidneys and UT in children of all ages. Semiotics of violations. Survey methodology.	Conduct a clinical examination of a child with UT disease
2.	The following disciplines		

	1. Pediatrics	Methods of diagnostics and differential diagnostics of diseases of kidneys and UT in children.	Perform a differential diagnosis with other nosoforms with a similar clinical and laboratory pattern.
3.	Intra-object integration		
	1. Dismetabolic nephropathy 2. Interstitial nephritis 3. Chronic kidney disease	Methods of diagnostics and differential diagnostics.	Conduct a clinical examination of the patient. Evaluate the results of paraclinical tests.

5. Content of the topic.

Dysmetabolic nephropathy is a group of diseases characterized by an interstitial process in the kidneys due to a metabolic disorder. The appearance of salts in the urinary sediment can be transient (with monotonous nutrition or temporary disturbances of the enzyme systems of the body) or permanent (for chronic diseases, genetically determined metabolic disorders, low quality of drinking water). The factors contributing to the formation of crystals include a high concentration of stone-burning salts in the urine, inadequate water regime, liquid urination, prolonged use of medicines, the presence of a urinary tract infection, digestive disorders, etc. Prolonged crystalluria, regardless of its cause, leads to the deposition of crystals in the kidney Tissue with the development of the interstitial process or salts in the renal cavity system with the formation of concrements, a complication in the form of microbesophageal diseases of the kidneys and urinary tract Their ways, violation of urodynamics.

Epidemiology. Crystalluria and urolithiasis (UL) occupy one of the leading places in the structure of urological and nephrologic diseases in terms of prevalence, the frequency of seeking medical help and hospitalization in a hospital. Thus, 8-15% of the population of Europe and North America suffer from urolithiasis. In the CIS countries, from urolithiasis, according to some authors, 3 to 6% of the population suffers. The greatest prevalence is noted among residents of Central Asia, the North Caucasus, Belarus, Kazakhstan, Altai. The incidence of UL in Russia is 500-550 cases per 100 thousand. Population. In general, in children and adults, the UL is more likely to be among the males. The prevalence of the disease among the child population is much lower than that of adults, and is 19-20 cases per 100 thousand. Population, while in adolescents - 80-82 cases (an average of 40.6 - according to 2006 and 109.31 - according to Data of 2010), in adults - 450-460 cases per 100 thousand population. According to the annual reports of the Department of Nephrology of Kyiv City Children's Clinical Hospital No. 1, the number of children hospitalized for dysmetabolic nephropathy increased from 4.58% in 2006. Up to 9.65% in 2011 In addition, 34% of children hospitalized in the nephrology department are concomitant with dismetabolic nephropathy or crystalluria. According to Russian colleagues, the incidence of dysmetabolic nephropathy in recent years varies between 11-13%, which is also significantly higher than in the 2000s, when they were 9.6-7.9% in the total structure of kidney diseases.

Classification of Crystalluria, ICD-10

E 79. Disorders of purine and pyrimidine metabolism.
E 79.0 Hyperuricaemia without signs of inflammatory arthritis and tophaceous disease.
E 79.1 Lesch-Nyhan syndrome.
E 79.8 Other disorders of purine and pyrimidine metabolism.
E 79.9 Disorder of purine and pyrimidine metabolism, unspecified.
E 83. Disorders of mineral metabolism.
E 83.4 Disorders of magnesium metabolism.
E 83.5 Disorders of calcium metabolism.
E 83.8 Other disorders of mineral metabolism.
E 83.9 Disorder of mineral metabolism, unspecified

Kidney damage in case of disturbance of uric acid metabolism: hyperuricemia (primary and secondary); Hyperuricosuria; gout; Xanthuria; Lesch-Nyhan syndrome.
Renal impairment in case of violation of glyoxyl acid exchange: primary hyperoxaluria (types I and II); Oxalate nephropathy; Secondary hyperoxuria; Phosphaturia; Hypercalciuria; Cystinuria.

Etiology

The causes of hyperuricosuria / hyperuricemia are: peculiarities of nutrition (prevalence of products containing purines - meat, sausage, offal, canned food, caviar, chocolate), neuro-arthritic anomaly of the constitution with recurrent acetoneemic syndrome, gout from close relatives, hereditary diseases that are based on a violation of the synthesis of uric acid - xanthuria, Lesh-Nichan's disease, prolonged use of medications (diuretics, cytostatics, antihypertensive drugs, non-steroidal anti-inflammatory drugs), lymphoproliferum ratyvni disease.

Hyperoxaluria develops: in genetically determined diseases - primary hyperoxuria, oxalate nephropathy; Secondary - in the use of a large number of green, citrus, wild rose; In frequently sick children, children with chronic diseases of the gastrointestinal tract, with urinary tract infections, prolonged use of glucocorticoids, anticonvulsants, deficiency of vitamin B6.

An increase in the excretion of phosphates (tripelphosphates or amorphous phosphates) and calcium occurs when vitamin D is deficient in rickets, tubulopathies (hereditary diseases accompanied by disturbances of phosphoriccalcium metabolism), juvenile osteoporosis, prevalence of dairy products in the child's diet, and often sick children.

Diagnostics

The criteria for establishing a diagnosis are: documented metabolic disturbances from excessive salts in the urine, the detection of epo-positive inclusions in bowls of the kidneys according to ultrasound and the presence of urinary syndrome.

A survey of patients with dismetabolic nephropathy include: medical history (including family) of urine (general, analysis of Nechyporenko, bacteriological examination of urine analysis of Zimnitskiy, daily proteinuria), transport of salts, blood count, biochemical blood tests, ultrasound kidney and bladder, if necessary - an X-ray examination (Plain radiography of the abdomen, excretory urography). "Colorful" urinary syndrome in a patient with dismetabolic nephropathy is characterized by the presence of salts (urates, phosphates, oxalates), and leukocyturia, erythrocyturia, proteinuria; can be accompanied by discoloration of urine, increasing its relative integrity. Analysis of salt transport involves determining the pH of urine excretion of uric acid, oxalate, calcium and phosphorus in the urine, uric acid, phosphorus and calcium in serum. When ultrasound, salt looks like epositive formations.

Clinic, possible complications

Clinical manifestations of dysmetabolic nephropathy are most often: dysuric phenomena, pain syndrome, change in the color of urine - bronze-red (with urate), milkyrass (with phosphaturia), white-yellow (with oxaluria); Hematuria, dyspeptic disorders.

Possible complications: joining inflammation (cystitis, pyelonephritis), bleeding, increased blood pressure (especially in adolescents and adults), CKD, acute renal failure, formation of interstitial process in the kidneys, chronic renal failure.

Treatment

Treatment should be comprehensive and aimed at the implementation of the following rules:

- Healthy lifestyle.
- Nutrition and drinking regimen.
- Diet.
- Specific therapy.

Increasing fluid intake, thereby reducing the concentration of solutes in the urine.In addition, the targeted volume increase nocturnal urination due to fluid intake before bedtime.In this case it is best to drink mineral or just pure water.Reduced salt load on the kidneys as a result of the appointment of diet. When oxalate nephropathy kidney in children excluded meat broth, sorrel, carrots, cocoa, chocolate, cranberries, beets.It is recommended to use a potato, cabbage, dried apricots, prunes, pears.Assign reception of mineral waters (Slavyanovskaya, Smirnoff).Assign vitamins A, E, B6, magnesium preparations. If urate nephropathy preferred dairy and vegetable diet.Limited consumption of meat products, beans, nuts, cocoa.The important point is sufficient fluid intake (up to two liters per day).Mineral water should be drunk slightly alkaline.Preferably drink teas horsetail, dill, knotweed, birch buds.Good help from the broth of oats.Under the strict supervision of prescribed allopurinol and nicotinamide, Phytolysinum. When renal phosphate nephropathy in children prescribed mineral water Narzan, DzauSoir.From preparations: tsistinal, vitamin C, methionine.Limit the consumption of cheese, biscuits, chocolate, caviar. Cystine nephropathy treated with diet, including the limitation or exclusion from the diet of fish, eggs, meat, cheese.Mineral water is desirable to consume alkaline.It is important to consume at least two liters of fluid.It is useful to drink a lot before bedtime. Long penicillamine treatment is carried out, as well as its less toxic analogue kuprenilom.Assign vitamins A, E. In addition, when cystinosis successfully used kidney transplantation, which should be carried out at a young age, preferably before 18-19 years.However, there is a risk of the transplanted kidney as well. Prognosis of kidney nephropathy in children is usually favorable in compliance with all standards of treatment and prevention of exacerbations of the disease. Preventive measures are directed generally to maintain and respect a strict diet, routine checkups and laboratory and instrumental methods of investigation of kidney function, conducting urine tests. Carry out the spa treatment and rehabilitation of children. It is advisable to visit the mineral springs resorts in Morshyn, Truskavets, etc.

Prevention and sanatorium treatment

Analysis of the incidence of diseases of the urinary system led to the conclusion about the need for convergence of Urology and Nephrology in solving common problems to further improve specialized care for children. This applies in the first place not only to congenital malformations of the urinary system, but also to the metabolic pathology of the kidneys. A joint analysis of the situation allowed us to work out a position on the prevention of dysmetabolic nephropathy. For the prevention of crystalluria recommended clinical supervision for children from families who have a genetic predisposition to urolithiasis, sickly children with chronic diseases of the gastrointestinal tract, children who for a long time (months, years) receiving any medication (corticosteroids, cytostatics, non-steroidal anti-inflammatory drugs, diuretics, anticonvulsants, antihypertensives and others). Periodically monitor urinalysis, if necessary - to conduct more in-depth examination - ultrasound of the kidneys, the analysis of transport and other salts. In order to prevent dismetabolic nephropathy should take plenty of fluids: in the cold season - 40 ml / kg body weight per day in the summer - 60 ml / kg / day (in the absence of hypertension). Children with dismetabolic nephropathy should be at the dispensary in the children's nephrologist, control urinalysis 1 per month (if UTI 1 every 2 weeks), the analysis of transport salts and ultrasound of the kidneys - 1 in every 6 months, in-depth survey in Conditions of the hospital to pass once a year. Obligatory is the control of renal function with the determination of the velocity of glomerular filtration. Given the concept of chronic kidney disease, the urological approach to patient data is not sufficient. The nephrology component is essential for the prevention of metabolic nephropathy in order to prevent the development of complications.

Interstitial nephritis (IN) - abacterial nonspecific inflammation of the intermediate tissue with lesion of the tubules, blood vessels and lymphatic vessels of the kidney stroma. May be manifested in any age period, including newborns. Acute interstitial nephritis has a duration of up to 3 months, chronic - more than 3 months (chronic illness).

Risk factors for IN in children: burdened history, hyperchristalluria, kidney dysplasia, allergic diathesis, infectious and drug intoxication.
Causes of the disease:
1. Application of drugs: antibiotics (penicillin, ampicillin, methicillin, carbenicillin, gentamicin, cephalosporins), sulfanilamides, nonsteroidal anti-inflammatory drugs (indometacin, brufen), barbiturates, analgesics (analgin, amidopyrin).
2. Introduction of serums, vaccines.
3. Impact of chemicals.
4. Intoxication with salts of heavy metals, especially lead, cadmium.

It's not so much the dose of the drug, how much the duration of its intake and increased its sensitivity.

Induction of infants in children can develop on the background of kidney diestrogenesis, urinary tract abnormalities, disorders of oxalate and uranium metabolism.
Distinguish between acute (AIN) and chronic (CIN) interstitial nephritis.

Acute interstitial nephritis - is an immune tubulo-interstitial non-destructive abacteric inflammation. Most authors see it as the most severe renal response in the chain of general reactions of the body to the administration of drugs. It has been established that the kidney possessing active enzyme systems, like the liver, can activate the metabolism of drugs and other chemicals, sometimes to the detriment of oneself. AIN can be observed with such infections as hepatitis, leptospirosis, infectious mononucleosis, as well as shock, burns.

PATHOGENESIS.

The first mechanism - interstitial tissue damage and renal tubules is due to the deposition of antibodies to the basement membrane tubules. These antibodies are formed on a glycoprotein which has a molecular weight of 48 kDa and is found in basal membrane proximal tubules and on a glycoprotein, called protein Tamm Horsfall, which has a molecular weight of 80 kDa and is synthesized by epithelial cells of the ascending loop of Henle. Antibodies to these antigens basement membrane tubules formed by: a) damage to the basement membrane (such as microorganisms) and release antigens that enter the circulatory channel and are formed autoantibodies b) tubular basement membrane can acquire new antigenicity by the addition of various chemical compounds such drugs, and c) due to the presence of microorganisms cross-reactive areas antigens and basal membrane tubules. Thus resulting antibodies are deposited along the basement membrane tubules as linear deposits inducing complement activation and cellular infiltration. This mechanism of tubulo-interstitial nephritis characteristic feature is the presence of linear deposits along the tubular basement membrane.

The second mechanism - the disease caused by the deposition of immune complexes containing renal endogenous or exogenous antigens, which are formed in line with circulatory or formed in situ. Immune complexes deposited along the basement membrane tubules and sometimes in the wall peritubular capillaries or interstitial tissue in the form of granular deposits of IgG and NW (rarely IgM and IgA). This leads to local cell infiltration, mainly - mononuclear cells, damage to the tubules, thickened and / or splitting of the basement membrane, interstitial fibrosis.

The third mechanism - tubulo-interstitial nephritis is the result of cell-mediated delayed type hypersensitivity reactions. The basis of the tubules and interstitial lesions in this mechanism tubule-interstitial nephritis is kidney tissue infiltration of activated T lymphocytes that have receptors for interleukin-2, S08 are positive and have cytotoxic activity.

The fourth mechanism - the formation of pathological process may be due to IgE-mediated immediate hypersensitivity reactions. This has been a significant increase in the level of IgE in the blood and in the presence of plasma cells located in the interstices. In support of allergic inflammation component testify frequently observed in patients with polymorphic skin rash, eosinophilia, presence of eosinophils in the inflammatory infiltrates and interstitial tissue of urinary excretion.

These immune mechanisms provide primary cell injury, inflammation causes swelling of the kidney interstitial tissue that causes mechanical compression of blood vessels and tubules of the nephron. The result is a reduction in renal hemodynamics, increased intratubular pressure drop in glomerular filtration rate, which ultimately leads to increased concentrations of serum creatinine and other nitrogenous products. In cases of severe ischemia papillary zone renal papillary necrosis may develop with massive hematuria. Edema and interstitial tubular lesions lead to a decrease reabsorption of water and protein, causing polyuria and hypostenuria, despite the decrease in glomerular filtrate. Prolonged compression peritubular underlying capillaries of tubular acidosis, disturbances in the electrolyte, providing a cluster of tubular crystals of calcium oxalate and others.

Clinic and diagnosis.

Acute TIN is characterized by a distinct beginning and is generally cyclic flow develops due to an allergic or toxic-allergic reaction to proteins, drugs (aminoglycosides, diuretics, corticosteroids, vitamin D and others.), Viral (in 34% of children, cytomegalovirus, herpes, chlamydia, pneumocysts, Mycoplasma, Toxoplasma) and other agents. Getting the disease may be accompanied by abdominal pain, nausea, anorexia, sometimes vomiting, fever. There is weakness, fatigue. Often (as opposed to pyelonephritis) appear widespread exanthema, eosinophilia. Number of urine per day decreases urine color varies from pink to dark cherry, and in the later stages of the disease becomes urine color "meat slops". Serum creatinine is an increase, decrease glomerular filtration. Urine protein appears, microhematuria, cylindruria, low density determined by urine glycosuria. Urine is sterile. The feature bladder syndrome are lymphomas and monocytic nature leukocyturia.

In 9% of children TIN flows by type of acute renal failure. Chronic TIN (including as a manifestation of toxic reactions to xenobiotics, particularly on heavy metals, pesticides, asbestos) is characterized by a long latent period often to detect bladder syndrome.

Tubulo-interstitial nephritis thus at first has a bright manifestation. Often appearing red blood cells in the urine with possible small amounts of protein and even / on and leukocytes. Gradually the disease progresses, almost imperceptibly decreasing function tubulointerstitium then glomeruli. Undulating progressive course tubulo-interstitial nephritis rarer: in renal dysfunction, dismetabolic disorders hypoimmune states.

During exacerbation of chronic TIN are signs of intoxication, changes in blood pressure, abdominal pain, allergic reactions and sometimes disurical symptoms. Frequent and pronounced "sensitive" pain, disurical syndromes. Maybe "accidental" in a latent disease on the background of an imaginary full welfare detect signs of kidney as polyuria, hypostenuria, and subsequently reabsorption (proteinuria, glycosuria, phosphaturia), acid-ability (decrease urinary ammonia secretion titrated acids) tubular apparatus of kidneys.

Laboratory studies:

• KLA: anemia is found only in the steady deterioration of kidney function, sometimes with Tina syndrome, eosinophilia can be observed in the drug etiology TIN;

• ZAC: point decrease relative density of urine, its alkaline Chance eritrotsiturii "sterile" (without bacteriuria) leukocyturia, proteinuria less than 3 g / day or calcium oxalate, crystalluria;

• Biochemical analysis of blood: increase of plasma creatinine often moderate (up to 3 mg / dL), the urate TIN - hyperuricemia;

• Test Zimnitskiy: decrease the relative density of urine, the prevalence of nocturnal urine output over the day.

Instrumental research:

• ultrasound of the kidneys, swelling, increase in size - in the acute phase, reduction in size, roughness of contours, cysts, calcifications - characteristic of chronic TIN, the oxalate nephropathy exhibit linear plot seal in pyelocaliceal system;

• Kidney CT: is not considered mandatory by the study, but the superior reliability of ultrasound in identifying and describing the thickness of the cortical layer of kidneys, shape and size of cysts, calcifications;

• nephrobiopsy not reflected in benign, a typical course. In some cases, examination is necessary - if necessary exception glomerulonephritis, amyloidosis and other glomerular lesions rapidly progressive deterioration of renal function.

Additional laboratory and instrumental investigations

• Bacteriological urine culture and sensitivity of the pathogen to antibiotics (for suspected bacterial TIN);
• concentration of urate, phosphate, oxalate in the blood and urine;
• biochemical urine (increased concentration of sodium and ammonium);
• immunological tests (increased levels of IgE, reducing complement levels, increased secretion of secretory IgA);
• radioisotope studies of kidneys;
• kidney biopsy.

GENERAL PRINCIPLES OF TREATMENT

`Polyetiologic TIN requires a differentiated approach to treatment is to identify the causes and termination triggers, excretion of the drug that caused the disease. Treatment should be conducted in a specialized hospital.

Treatment TIN children:

• the impact of the termination of the etiological factors (chemical, physical, infectious, autoimmune, toxic-allergic and others). Interstitium of kidney tissue;
• organization of general and motor modes to reduce the burden on functional renal tissue;
• rational, sparing diet, which aims to reduce the metabolic burden on renal tissue;
• abacterial elimination of inflammation in the kidney tissue;
• elimination of metabolic disorders;
• Prevention interstitium sclerosis;
• Recovery of renal function.

Pronounced syndrome of endogenous intoxication shows infusion therapy acute TIN. The composition and volume of infusion therapy depends on the severity of the patient's hemostasis parameters and degree of renal function. High activity TIN process leads to an immediate cessation of treatment, the use of corticosteroids to reduce inflammation and prevent sclerosis. Prednisolone administered at a dose of 1-2 mg / kg per day for 14 days followed by a gradual drug and its complete abolition.

With the development postviral TIN antivirals, the following:

- Herpetic infections (acyclovir 5 mg / kg / knocks in 5 receptions for 10 days);
- CMV infection (ganciclovir 250-500 mg 2 times daily for 10 days);
- EBV infection and others. - Interferon (viferon, Henferon, Laferobion 150,000 Units. Children up to 3 years and 500 000 units. Patients preschool and school age, 1 candle 2 times a day, 7 days, then 2-3 times a week for 4 weeks).

In patients TIN metabolic origin leading role diet. In uraturia excluded from the diet foods rich in purine, chicken, beef, liver, jellies; legumes (peas, beans); mackerel, sprats, sardines. In identifying oxalate - a food rich in oxalic and ascorbic acid: spinach, sorrel, rhubarb, beets, tomatoes, cocoa, chocolate, currant, wild rose. Shown cabbage -potato diet appointed for 3 weeks with 3 breaks. It should be noted that the combined crystalluria, patients should receive table №5.

Requires sufficient drinking regime and the regime forced urination to remove products of metabolism and reduce crystallization. To increase diuresis increase fluid intake to 30-50% of the age norm. Recommended decoction of dried fruit, oats, juice drinks, mineral water of weak mineralization. In order to prevent stone formation and dissolution of urate salts urine intake of mineral water "Borjomi", while phosphaturia for this purpose urine juice. In oxalaturia for the Prevention of stone required copious drinking regime used mineral water Donat Mg.

With the development of TIN due to violation of purine metabolism, in addition to diet, using funds inhibit the synthesis of uric acid (potassium orotate 20 mg / kg / day in 2 divided doses before meals for I Miss., Repeating courses quarterly diodoron, orotsid, oraturik).

If oxalate crystalluria shown appointment of membrane stabilizers, vitamin B6 at a dose of 1-3 mg / kg / day in the morning combined with vitamin. A and E of magnesium (magnesium oxide) in a dose of 50-150 mg / day, once within 3 weeks of courses 3-4 times a year.
In phosphate crystalluria use almagel (fosfaluhel) courses for 10 days in a month. Also used Fytolyzyn (paste) 1 tsp in ½ cup warm water 3 times a day.
To improve microcirculation Antiplatelet agents dipyridamole administered 2.3 mg / kg / day in 3 divided doses, pentoxifylline 5.10 mg / kg / day in 3 divided doses. Positive dynamics is observed in renal blood flow using Aktovegin 20 mg / kg per day for 4 weeks.
Membrane stabilizers shown in a period of recovery, especially in patients with metabolic disorders. Ingestion within 1 month. Repeated administered every 3 months. during the year:
- Vitamin A 3.44% solution, 1 drop / 1 year of life / 1 per day after meals for 2 weeks;
- Vitamin E 5%, 10% solution of 1.2 mg / kg 1 per day;
- Magnesium + B6 (Mahnefar) 1 / 2-1 Table. 2 times a day;
- Pyridoxine 1-3 mg / kg / day in the morning;
- Essentiale 1 capsule 2 times a day;
- 15% Dimefosfon 0.2 ml / kg 3 times a day;
- 2% pp Xydifone 5.10 mg / kg / day for 30 minutes. to food, the appointment must be combined with ksidifina in vitamins E.
Patients with chronic TIN without exacerbation shown prescriptions, normalize cell energy metabolism:
- L-carnitine (Elkar 10%)) children 1 to 3 years, 5 drops, 8 drops of 4-10 years, over 10 years - 10-15 drops 1 time a day for 4 weeks;
- Water-soluble coenzyme Q10 (Qudesan) children from 1-5 years 5 drops of 5-10 years 8 drops over 10 years - 10-15 drops 1 time a day for 4 weeks.

In the recovery period, patients with TIN dismetabolic character prescribe mineral alkaline water low and medium mineralization.

As nephroprotecor to reduce the degree of proteinuria using ACE inhibitors (enalapril) at a dose of 0.1 mg / kg in one go in the morning process 4-6 weeks. Also recommend the use of enalapril 3 or more months.

At the stage of recovery and remission herbal medicine, aimed at improving the urodynamics, restoration tubular function. Apply "Canephron": infants administered 10 drops in the preschool years - 15 drops, school age 25 drops 3 times or 1 tablet 3 times daily for 10 days every month. Shown as mother and stepmother, herd, mint , cranberry and strawberry leaf, kidney tea for 2-3 weeks every month.

Physiotherapy treatment: balneotherapy (coniferous, pearl baths), mineral water courses, magnet, hyperbarium oxygen therapy, therapeutic exercise.

Removal from the register after acute TIN stable after 3 years of clinical and laboratory remission.
In conclusion, it should be emphasized that the TIN is an important issue as the medical, social and scientific nature. Continuing his search for optimal methods of diagnosis, treatment and prevention. Remains unclear as the possibility of therapeutic intervention in disease progression.

6. Materials of methodological support of the lesson.

6.1 Tests.

1. In cases of diagnosing oxalate dysmetabolic nephropathy in a child, foods containing:
A. Ascorbic acid
V. Purins
C. Tryptophan
D. Methionine
E. Triglycerides

2. What are the main nutritional components of a child with phosphate dysmetabolic nephropathy?

A. Dairy products and foods rich in potassium
B. Cabbage - potato products
C. Fermented milk products and pickled vegetables
D. Restriction of dairy products and alkaline valences
E. Foods high in coarse fiber and potassium

3. What morphological signs are not typical for chronic interstitial nephritis?
A. Proliferation of mesangial and endothelial cells of the glomerulus, thickening of the glomerular basement membrane
B. Lymphohistocytic infiltration of the interstitium with the presence of eosinophils, polymorphonuclear leukocytes
C. Thickening of tubular basement membranes
D. Sclerosis of the interstitium
E. Dystrophy and atrophy of tubular epithelium

4. What morphological signs are not typical for acute interstitial nephritis?
A. Interstitial edema
B. Proliferation of mesangial and endothelial cells of the glomerulus
C. Lymphocytic infiltration of the interstitium with the presence of rare eosinophils, polymorphonuclear leukocytes
D. Dystrophy and necrosis of tubular epithelium
E. Unchanged glomerular basement membranes

5. What structures of the kidney are predominantly involved in the pathological process in interstitial nephritis?
A. Nerves
B. Vessels
C. Glomerulus
D. Tubules, stroma
E. Ureter

Answers: 1 -A; 2 - D; 3 - A; 4 - B; 5 -D.

6.2. List of recommended reading:

- basic:

1. Kliegman, R.M., St Geme, J.W., Blum, N.J., Shah, S.S., Tasker, R.C., Willson, K.M., & Behrman, R.E. (Eds.). (2019). Nelson Textbook of Pediatrics (21st ed.). 4264 p.
2. Ghai ”Essential pediatrics ” 9th Edition. 2019. 814 p.
3. Roy, S., Awogbemi, T. & Holt, R.C.L. Acute tubulointerstitial nephritis in children– a retrospective case series in a UK tertiary paediatric centre. *BMC Nephrol* 21, 17 (2020). https://doi.org/10.1186/s12882-020-1681-7.
4. Dysmetabolic Nephropathy In The Practice Of A Pediatrician. *The American Journal of Medical Sciences and Pharmaceutical Research*, *2*(11), 78-85. https://doi.org/10.37547/TAJMSPR/Volume02Issue11-14.

- *additional:*

1. Yurieva E.A., Dlin V.V., Vozdvizhenskaya E.S., Sukhorukov V.S., Semyachkina A.N., Kharabadze M.N. Dysmetabolic nephropathy in children with hereditary connective tissue dysplasia. *Rossiyskiy Vestnik Perinatologii i Pediatrii (Russian Bulletin of Perinatology and Pediatrics)*. 2020;65(1):71-76. (In Russ.) https://doi.org/10.21508/1027-4065-2020-65-1-71-76.
2. Takahashi N, Saeki T, Komatsuda A, et al. Tubulointerstitial Nephritis with IgM-Positive Plasma Cells. J Am Soc Nephrol 2017; 28:3688.

3. Muriithi AK, Leung N, Valeri AM, et al. Clinical characteristics, causes and outcomes of acute interstitial nephritis in the elderly. Kidney Int 2015; 87:458.
4. Joyce E, Glasner P, Ranganathan S, et al. Tubulointerstitial nephritis: diagnosis, treatment, and monitoring. Pediatr Nephrol 2017;32:577–87. doi:10.1007/s00467-016-3394-5pmid:http://www.ncbi.nlm.nih.gov/pubmed/27155873.
5. Joyce E, Glasner P, Ranganathan S et al. Tubulointerstitial nephritis: Diagnosis, treatment and monitoring. Pediatr. Nephrol. 2017; 32: 577-87.

6.3. Indicative map for independent work with literature.

№	Main Task	Directions	Answers
1	**2**	**3**	**4**
1.	Read the literature and the objectives of the lesson	Formulate definition of TIN, DN in children	Formulate the concept of multifactorial disease and its functional character.
2.	Epidemiology	Know the prevalence of TIN, DN among children. List the risk factors for TIN, DN in children.	Risk factors for IN in children: burdened history, hyperchristaluria, kidney dysplasia, allergic diathesis, infectious and drug intoxication.
3.	Etiology	List the main factors of development of dysmetabolic nephropathy	The causes of hyperuricosuria / hyperuricemia are: eating habits, neuro-arthritic anomaly of the constitution with recurrent acetone syndrome, gout in close relatives, hereditary diseases based on disorders of uric acid synthesis, xanthinuria, Lesch-Nichena disease, long-term use of medicines, lymphoproliferative diseases. Hyperoxaluria develops: with genetically determined diseases, secondary - with the use of a large amount of greenery, citrus, dogrose in children with chronic diseases of the gastrointestinal tract, with infections of the urinary tract, prolonged use of glucocorticoids, anticonvulsants, vitamin B6 deficiency. Increase in the excretion of phosphates and calcium occurs with vitamin D deficiency rickets, tubulopathies, juvenile osteoporosis, the predominance of dairy products in the baby's diet, and often ill children.
2.	Pathogenesis	Know modern ideas about the pathogenesis of TIN, DN	The basis of pathogenesis is specific and nonspecific mechanisms.
5.	Classification	Know the classification of TIN, DN in children.	Be able to diagnose

6.	Clinic	Indicate the main symptoms and their characteristics in the TIN, DN.	General signs are clinical signs, functional disorders
7.	Diagnosis	Identify the main methods of clinical and paraclinical examination in the TIN, DN.	To assess the results of laboratory and functional methods of investigation.
8.	Differential diagnosis	List diseases with similar clinical and laboratory manifestations.	Glomerulonephritis, hereditary nephritis, inflammatory diseases of the lower and upper urinary tract.
9.	Treatment, prevention	dentify the main areas of treatment, prevention and prophylaxis in children with chronic renal insufficiency	Pay attention to the complexity of diagnosis of the urinary system.

7. Materials for self-control on the quality of training.

A. Questions.

1. Definition of TIN, DN.
2. The prevalence and incidence of dysmetabolic nephropathy, tubulointestinal nephritis in children's populations, risk factors for the disease.
3. Pathogenesis of TIN, DN.
4. Classification of TIN, DN.
5. Clinical picture of TIN, DN depending on the form.
6. Diagnosis of TIN, DN.
7. Programs of treatment of TIN, DN.
8. Rehabilitation measures for children with this pathology.

B. Tests.

1. The girl is 4 years, suffers from allergic dermatitis, occasionally worried about abdominal pain. The abdomen is soft, painless when palpated. The liver is 2 cm below the edge of the costal arch. Stool and urination normal. The general analysis of urine is cloudy, urine pH 7.0, protein 0.05 g / l, red blood cells are changed, and−30-40, leukocytes−6-8, salt-oxalate is increased in quantity. Daily proteinuria is 0.03. Establish a preliminary diagnosis.

A. Allergic Nephropathy
B. Pyelonephritis
C. Dysmetabolic nephropathy
D. Glomerulonephritis
E. Hemorrhagic cystitis

2. At the child of 2 years, received biseptol against a background of ARVI, proceeded with a hyperthermic syndrome, the diuresis was reduced to 100 ml per day. At inspection sharp flaccidity, pallor. Edema of the eyelids, shins. BP - 120/80 mm Hg. Urea of blood - 38 mmol / l, creatinine of blood - 0.2 mmol / l. A sample with lasix did not lead to the appearance of an adequate diuresis. Acute renal failure was diagnosed. Indicate the reason for the development of this condition:

A. Acute disturbance of renal hemodynamics
B. Intravascular blockage of renal blood flow
C. Tubulo-interstitial kidney lesions

D. Dehydration
E. A sharp decrease in colloid-oncotic blood pressure

3. A 7-years girl's mother complains of recurrent abdominal pain and a rash, excessive sweating, a decrease in the amount of urine and a saturated character. There is nocturia. BP - 90/60 mm Hg. Total urine analysis: relative density of urine - 1028, protein - 0.04 g / l, leukocytes - 9-10, erythrocytes - changed 6-8, Cylinders - not detected. Salts - oxalates. Establish a preliminary diagnosis:
A. Acute glomerulonephritis with nephritic syndrome
B. Acute renal failure
C. Dysmetabolic nephropathies
D. Tubulopathy
E. Urinary tract infection

4. A girl, 13 years, complains of recurrent abdominal pain, excessive sweating, a decrease in the amount of urine and her saturated character. Nocturia was found. Blood pressure 110/75 mm Hg. In the general analysis of urine: specific gravity - 1028, protein - 0,003 g / l, Le - 4-5, er. - 1-2, salt - oxalate, a significant amount. Your preliminary diagnosis.

A. Dismetabolic nephropathy.
B. Acute glomerulonephritis with nephritic syndrome.
C. Urinary tract infection.
D. Tubulopathy.
E. Acute renal failure.

5. A boy receives ampicillin 5 years for ARVI. On the 5th day of treatment, the symptoms of intoxication appeared, the pastosity of the face appeared, the pain in the joints. Blood pressure 140/90 mm Hg, 2100 ml of urine (a liquid of 2000 ml). In the blood test: creatinine 0.22 mmol / l, urea 11.8 mmol / l, potassium 3.8 mmol / l, sodium 125 mmol / l. In the analysis of urine proteinuria 0.99 g / l, erythrocyturia, leukocyturia. Relative density of urine during the day ranges from 1002 to 1010. Urine incontinence did not give rise to sterility. What is the most likely diagnosis?
A. Acute pyelonephritis
B. Acute interstitial nephritis
C. Acute glomerulonephritis with nephritic syndrome
D. Acute glomerulonephritis with nephrotic syndrome
E. Dismetabolic nephropathy

Answers: 1 - C, 2 -C, 3 -C, 4 - A, 5 -B.

B. Tasks for self-control with answers.
1. Patient, 15 years, diagnosed with acute bronchitis, received NSAID therapy, symptomatic treatment. However, the patient's condition continued to deteriorate and after 5 days pneumonia was diagnosed and antibacterial drugs (cephalosporins, aminoglycosides) were added to the treatment. After a few days, the patient's condition improved, her body temperature returned to normal. After 12 days from the start of antibiotic therapy, fever, skin rashes, lethargy, headache, "aches" in the joints, pasty eyelids and face, pain in the lumbar region reappeared. On examination in a hospital: a serious condition, body temperature 380C, pasty eyelids and face, rash. The tapping symptom is positive on both sides. The daily urine output is 2800 ml. In the general analysis of blood: mild anemia, leukocytosis, neutrophilia, eosinophilia, accelerated ESR (hereinafter - ESR). In the general analysis of urine: relative density 1005, protein 1.3 g / l, glucose 1+, erythrocytes up to 100 in the field of view, leukocytes 25-30 in the field of view, cylinders - hyaline, granular, erythrocytic, moderate amount of mucus, no bacteria. In a biochemical blood test: urea - 11.5 mmol / L, creatinine - 145 μmol / L, total bilirubin - 58 mmol / L, alanine aminotransferase (hereinafter - ALT) - 51 U / L,

aspartate aminotransferase (hereinafter - AST) - 69 units / l, sodium - 127 mmol / l, potassium - 4.5 mmol / l.
1. What is the most likely diagnosis?
2. What is the cause of the condition that has arisen?
3. How can you characterize the functional state of the patient's kidneys?
4. What is the most optimal doctor's tactics in this case?

Sample answer:
1. Acute tubulointerstitial nephritis.
2. Medicines.
3. Acute renal failure, renal.
4. The difference between antibiotic therapy, NSAIDs. Appointment of prednisolone, hemodialysis.

2. A 12-years girl complains of pain in the abdomen and lower back, frequent painful urination. A history of atopic dermatitis, recurrent pain and swelling of the joints, recurrent urinary syndrome with leukocyturia and hematuria. On examination, the child's condition is moderate. Correct physique, physical development corresponds to age. The skin is somewhat pale, periorbital "shadows" and eyelid pathosis. There are no physical changes on the part of the respiratory system and the cardiovascular system. Blood pressure is 120/80 mm Hg. Art. The abdomen is soft, moderately painful in the area of the bladder projection. The urine is yellow, cloudy. Daily urine output - 1500 ml. Complete blood count: hemoglobin - 110 g / l, erythrocytes - 3.4 T / l, color indicator - 0.97; leukocytes - 10.2 g / l; leukocyte formula: eosinophils - 8%; basophils - 1%; paliconuclear neutrophilic granulocytes - 5%; segmented neutrophilic granulocytes - 56 %; lymphocytes - 25%; monocytes - 5%; ESR - 15 mm / hour. General urine analysis: color - yellow; cloudy urine; relative density - 1025; protein - 0.066 g / l; sediment microscopy - in the field of view: leukocytes - 20-25; fresh erythrocytes - 3-5; leached erythrocytes - 20-25; salts - crystals of calcium oxalate in large quantities. Urine analysis according to Nechiporenko: leukocytes - 12,000 in 1 ml erythrocytes - 15,000 in 1 ml. Urine analysis according to Zimnitsky: daily diuresis - 1500 ml, daily diuresis - 1000 ml, night diuresis - 500 ml; fluctuations in the relative density of urine from 1008 to 1025. Biochemical blood tests: blood serum urea - 7.5 mmol / l; creatinine - 0.085 mmol / l; total calcium - 2.2 mmol / l; sodium - 135 mmol / l; potassium - 4.5 mmol / l; phosphorus - 1.5 mmol / l. Excretion of oxalates in the urine - 3000 mg per day. Culture of urine from a medium portion - $1O^3$ CFU in 1 ml.

1. Formulate the diagnosis.
2. What is the most informative diagnostic method for confirming the diagnosis?
Sample answer:
1. Oxalate nephropathy
2. Daily urinary excretion of oxalates

8. Materials for classroom self-study.
8.1. The list of educational practical tasks that must be completed during practical exercises.
1. Collect history, highlight the points that indicate the nature of the TIN and DN.
2. Identify the most informative features of the disease during objective and laboratory and instrumental examination of the patient.
3. Clinical diagnosis in modern classification.

9. Instructional materials for mastering professional skills.
9.1. Methodology for performing work, stages of implementation
1 .Evaluate the data and medical history of the disease, seen risk factors that play a role in causing the disease.
2. Conduct the clinical examination of the patient.

3. Make a plan to further investigation.
4. Evaluate the results of laboratory and instrumental examination of the patient.
5. Formulate a clinical diagnosis according to the classification

10. Materials for self-control of mastering knowledge, abilities, skills.

10.1 Tests.

1. A patient with acute respiratory infection on the third day of illness developed: back pain, nausea, dysuria, oliguria. In the urine - hematuria. In the blood: creatinine 0.18 mmol / l, potassium - 6.4 mmol / l. In urine - the specific gravity is 1002, erythrocytes (leached) - 100-200 in the field of view. What is the diagnosis?
A. Tubulointerstitial nephritis
B. Acute glomerulonephritis
C. Acute renal failure
D. Acute cystitis
E. Acute renal colic

2. A patient with angina, 16 years old, was prescribed injections of cefazolin and biseptol. 3 days after the start of treatment, the condition worsened, there were unpleasant sensations in the lower back, dizziness, nausea. BP - 140/80 mm Hg. Blood test: er. - 3.12 * 10^{12} / l, Hb - 120 g / l, Lake. - 10 * 10^{9} / l, ESR - 28 mm / hour. Urine analysis: rel. density (density) - 1.010, protein - 0.99 g / l. Zimnitsky test: the daily amount of urine is 3.2 liters, fluctuations in rel. density - 1.007-1.010. The blood creatinine level is 0.380 mmol / l. What is your diagnosis?
A. Acute interstitial nephritis
B. Acute glomerulonephritis, anephrotic variant
C. Chronic glomerulonephritis, anphrotic variant
D. Rapidly progressive glomerulonephritis
E. Acute pyelonephritis

3. What symptom is typical for tubulointerstitial nephritis?
A. Bacteriuria
B. Hypoisostenuria
C. Hypertension
D. Dysuria
E. Nikturia

4. In what disease is the nephrotic syndrome is absent:
A. Diabetic glomerulosclerosis
B. Amyloidosis of the kidneys
C. Acute glomerulonephritis
D. Tubulo-interstitial nephritis
E. Chronic glomerulonephritis

5. The reasons for the increase in the level of oxalic acid in the body:
A. Excessive consumption of foods containing glycine and oxalic acid
B. Increased intake of amino acids (glycine, proline), carbohydrates, ascorbic acid into the body
C. Functional impairment
D. lining of the tubular apparatus of the kidneys
E. Peptic ulcer and duodenal ulcer
F. All of the above

Answers: 1 -A, 2 -A, 3 -B, 4 -D, 5 -E.