MINISTRY OF HEALTH OF UKRAINE

ODESA NATIONAL MEDICAL UNIVERSITY

Departments of Pediatrics №2

CONFIRMED by

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	OGICAL RECOMMENDATIONS CAL CLASSES FOR STUDENTS
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1. Topic №22

Differential diagnosis of infectious and inflammatory diseases of the urinary system in children. Leading clinical symptoms and syndromes in urinary system infection in children. Clinical variants of the course of infection of the urinary system. Management tactics for urinary system infection in children. Emergency care for acute urinary retention in children. Medical supervision.

2. Relevance of the topic.

Infections of the urinary system (IUS) is the most common infection in children under 2 years of age and occupies second to third place among all childhood infections, second to the disease of the respiratory tract and intestinal infections. According to the statistical reports of the Ministry of Health of Ukraine, the prevalence of kidney and urinary system diseases in children has increased in Ukraine in the last 5 years, namely: from 40 to 56/1000 children. In the first year of life, boys are more likely to suffer from IUS (3.7% versus 2% for girls), then the opposite is observed. However, in boys under 3 years, IUS are the most frequent cause of fever and often develop against the background of abnormalities of the development of the organs of the urinary system. Progression of IUS with the development of sclerosis, and in the antenatal period, even in the absence of infection on the background of dysplasia and reflux, leads to the development of arterial hypertension and the need for nirkovozamosnoi therapy.

3. Objectives of the lesson:

3.1. General goals:

- to get acquainted with modern ideas about etiopathogenesis, classification, clinical course, basic and additional methods of examination children with IUS, as well as key areas of therapy.

3.2. Educational goals:

- to get acquainted with the work of the leading pediatric nephrologists in studying the features of the etiopathogenesis of IUS. Get an idea about the modern definition of the IUS. Identify risk factors for IUS development. To study the etiological spectrum of IUS in children of different ages. Know the requirements for antibacterial drugs in pediatric nephrology.

3.3. Specific goals:

- know:

- 1. Prevalence and incidence of urinary tract infections in children in Ukraine and CIS countries.
- 2. Definitions of infection of the urinary system, pyelonephritis, cystitis.
- 3. Risk factors for developing of urinary tract infection.
- 4. Modern classification of pyelonephritis in children.
- 5. Clinical characteristics of infection of the urinary system (pyelonephritis, cystitis).
- 6. Age features of urinary tract infections.
- 7. Hematologic signs of the disease, manifestations of urinary syndrome, US-signs of the urinary system.
- 8. Signs of a of significant bacteriuria.
- 9. Components of complex treatment.
- 10. Prevention of diseases of the urinary system in children.

3.4. On the basis of theoretical knowledge on the topic:

- to master the techniques / be able to /:
 - 1. Collect anamnesis.
 - 2. To find out the risk factors for the development of infections of the urinary system.
 - 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. Carry out differential diagnosis of the most common diseases of the urinary system.
- 7. Establish a diagnosis according to the classification.
- 8. Draw up a therapy plan for the child with infections of the urinary system.

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

No	Discipline	To know	To be able
1.	Previous disciplines		
	1. Anatomy	Anatomical structure of the	Identify peculiarities in
		kidneys and urinary tract	children.
	1. Normal physiology	Functional state of kidneys and	Identify peculiarities in
		urinary tract in children.	children.
	2. Pathological	Diseases of the kidneys and	Correctly assess the nature
	physiology	urinary tract: microbial-	of the process
		inflammatory, immune-	
		pathological, metabolic.	
	4 B: 1 : .	Congenital malformations of US.	
	4. Biochemistry	Components of the biochemical	Correctly evaluate the
		blood test, which reflect the	results of the study.
	5 Duanadaystics of shildhood	function of the kidneys and US	Conduct a clinical
	5. Propedeutics of childhood diseases	Anatomical - physiological features of the kidneys and US in	Conduct a clinical examination of a child with
	diseases	children of all ages.	a disease of the US.
		Semiotics of violations. Survey	a disease of the OS.
		Methodology.	
2.	Next disciplines	Wethodology.	
	1. Pediatrics	Methods of diagnostics and	Carry out a differential
		differential diagnostics of	diagnosis with other
		diseases of kidneys and US in	nosoforms with a similar
		children.	clinical and laboratory
			picture.
3.	Interdisciplinary integration		
	1. Pyelonephritis	Methods of diagnostics and	Conduct a clinical
	2. Interstitial nephritis	differential diagnostics.	examination of the patient.
	3. Cystitis		Evaluate the results of
			paraclinical tests.

5. Contents of the topic.

<u>Infections of the urinary system (IUS)</u> - microbial injury to the organs of the urinary tract without clarifying the topical level of lesion. Pyelonephritis (PN) is a nonspecific microbial inflammation of the kidney with a predominant focal damage to the tubulointerstitial tissue, calyx and pelvis.

Cystitis is a nonspecific microbial inflammation of the mucous membrane of the bladder.

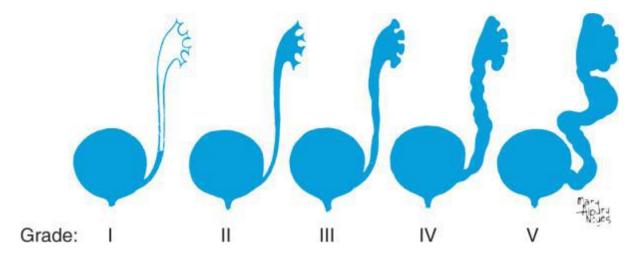
According to the decision of the 2nd congress of nephrologists of Ukraine, 2005, the UTS are classified as follows.

CLASSIFICATION OF PYELONEPHRITIS

Forms of pyel	onephritis	Activity of diseases	Function of kidney
Primary no-obstructive	Acute	Active stage	Without functional renal disorders
Secondary no-obstructive obstructive	Chronic a) manifest b) latent	Partially clinic.& labor. remission	With functional renal disorders
		Total clinical remission	Chronic renal insufficiency

1. Differential diagnosis of UTI

It includes urethritis, vaginitis, trauma, hyper-calciuria (dysuria), detrusor/sphincter dysfunction, neurogenic urinary bladder, different anatomical abnormalities.



(Table 2)

TYPE	CAUSE
Primary	Congenital incompetence of the valvular
	mechanism of the vesicoureteral junction
Primary associated with other malformations of	Ureteral duplication
the ureterovesical junction	Ureterocele with duplication
	Ureteral ectopia
	Paraureteral diverticula
Secondary to increased intravesical pressure	Neuropathic bladder
	Non-neuropathic bladder dysfunction
	Bladder outlet obstruction

Secondary to inflammatory processes	Severe bacterial cystitis
	Foreign bodies
	Vesical calculi
	Clinical cystitis
Secondary to surgical procedures involving	Surgery
the ureterovesical junction	

2. Congenital anomalies of urinary tract

Renal agenesis - unilateral renal agenesis incidence of 1 in 450 to 1,000 births. In true agenesis, the ureter and the ipsilateral bladder hemitrigone are absent. The contralateral kidney undergoes compensatory hypertrophy, to some degree prenatally but primarily after birth. Approximately 15% of these children have contralateral vesicoureteral reflux.

Aplasia - nonfunctioning tissue and normal or abnormal ureter. If there is a normal contralateral kidney, renal function should remain normal over time.

Bilateral renal agenesis - incompatible with extrauterine life and is termed Potter syndrome. Death occurs shortly after birth from pulmonary hypoplasia. The newborn has a characteristic facial appearance, termed Potter face.

Familial renal adysplasia describes disease in which renal agenesis, renal dysplasia, multicystic kidney (dysplasia), or a combination, occurs in a single family. This disorder has an autosomal dominant inheritance pattern with a penetrance of 50–90% and variable expression. Renal dysgenesis refers to maldevelopment of the kidney that affects its size, shape, or structure. The 3 principal types of dysgenesis are:

- Dysplastic
- Hypoplastic
- Cystic.

A multicystic kidney: a congenital condition in which the kidney is replaced by cysts and does not function, and may result from ureteral atresia. Renal size is highly variable. The incidence is approximately 1 in 2,000. An inherited disorder that may be autosomal recessive or autosomal dominant and affects both kidneys Multicystic kidney usually is unilateral and is not inherited. Bilateral multicystic kidneys are incompatible with life. Multicystic dysplastic kidney is the most common cause of an abdominal mass in the newborn. In most cases it is discovered incidentally during prenatal sonography. Contralateral hydronephrosis is present in 5–10% of patients.

Renal hypoplasia: a small nondysplastic kidney that has fewer than the normal number of calyces and nephrons. If the condition is unilateral, the diagnosis usually is made incidentally. Bilateral hypoplasia usually presents with the manifestations of chronic renal failure and is a leading cause of end-stage renal disease during the first decade of life. A history of polyuria and polydipsia is common. Urinalysis results may be normal.

The Ask-Upmark kidney, also termed segmental hypoplasia. Small kidneys, usually weighing not more than 35 g, with one or more deep grooves on the lateral convexity, underneath which the parenchyma consists of tubules resembling those in the thyroid gland. It is unclear whether the lesion is congenital or acquired. Most patients are 10 yr or older at diagnosis and have severe hypertension. Nephrectomy usually controls the hypertension.

3. Urinary tract infection

Etiology.

Escherichia coli is the most common cause of bacterial UTI.

Other organisms: Klebsiella spp, Enterococcus, Staphylococcus saprophyticus, Proteus mirabilis; Pseudomonas, Streptococcus, Candida albicans (usually associated with complicated UTIs or chronic antibiotic treatment).

Risk factors in all children include:

- Indwelling catheters
- Urologic tract anomalies

- Neurogenic bladders
- Risk factors specific to girls include:
- Chemical irritants
- Sexual activity
- Sexual abuse
- Constipation
- Pinworms
- Risk factors specific to boys include:
- Phymosis

Uncircumcised boys have an incidence of infection 10 times that of circumcised boys. Epidemiology.

- Bacteriuria is present in 1%–2% of prepubertal children.
- In the first year of life, the risk of infection is equal among boys and girls
- The risk in girls is considerably higher in toddlers and older children.
- The incidence of UTI is 3.0% in febrile infants younger than 12 mo of age without an obvious cause for fever
- Vesicoureteral reflux is present in 18% 50% of children with UTI.

Symptoms.

- In infants, vomiting, poor feeding, and irritability.
- Older children develop dysuria, urgency, frequency, incontinence, hesitancy, and retention; fever, chills, back pain are symptoms that suggest an upper tract infection (pyelonephritis). Signs.
- Fever
- Jaundice (may be seen in neonates).
- Suprapubic or costovertebral angle tenderness
- Abdominal or flank mass: suggestive of obstructive uropathy.
- Sacral dimple, hairy patch over the sacrum, abnormal gluteal cleft, decreased rectal tone, lipoma: suggest spinal cord anomalies.
- Labial adhesion, trauma, and irritation: may increase the risk of infection. Investigations.
- Urine culture: considered positive if any organisms are present on a suprapubic collection; > 104 colony forming units (CFU)/mL of a urinary pathogen from a catheterized specimen; > 105 CFU/mL of a urinary pathogen from a clean catch.
- Urinalysis with dipstick: demonstrating positive leukocyte esterase and nitrite test with microscopic examination demonstrating more than five leukocytes per hpf, bacteria is highly suggestive of a urinary tract infection (UTI); this is not reliable in infants in whom the urine is dilute; 10% may have a negative urinalysis result despite a positive culture.
- Radiographic imaging: indicated in every boy with an infection and girls with pyelonephritis; girls with recurrent lower tract infections or those who are younger than 5 years of age with their first infection should be studied as well.
- Renal and bladder ultrasound: a noninvasive aid to look for hydroureteronephrosis, duplex kidneys, and ureteroceles, which may be a sign of obstruction.
- Voiding cystourethrography: might demonstrate vesicoureteral reflux and is especially important in the male to exclude posterior urethral valves.
- 99m Tc-DMSA scan: controversial; it is an excellent study to identify pyelonephritis as the cause of fever when the source is not known; it is the most sensitive study to determine the presence of scars; however, it may not ultimately change the course of treatment. Complications.
- Septicemia: more likely to be present in neonates or in children with abnormal urinary tracts.

- Renal scarring: can develop years after infections that occurred in infancy or early childhood; it is associated with hypertension, toxemia, and the risk of chronic renal failure leading to end-stage renal disease.
 - Staghorn calculi: can form in the presence of repeated infections.

Urinary tract obstruction may be functional and organic (Table 3).

Functional obstruction	Organic obstruction
Neurogenic disorders of urination	Anomalies of the urinary system (Froline's syndrome, hydronephrosis, ureterohydronephrosis, megaureter)
Bladder-ureter reflux	Intramuscular obstruction (contracture of the bladder neck, valves, diverticulum, stenosis urinary tract)
Congenital neuromuscular defects of the bowel-ureteric compound, ureters, bladder	Injuries Compression by tumors, concretions

Criteria for activity of pyelonephritis (Table 5)

Activity degree

		Activity		
	I,	II	III	
t	N or subfebrile	≤ 38.5	> 38.5	
intoxication	-	slightly expressed	expressed	
Leucocytes	< 10	11-14	≥ 15	
ESR	< 15	16-24	≥ 25	
C-reactive protein	-/+	++	+++/++++	

Diagnostic criteria (Table 6)

Nosology	Clinical Symptoms	Laboratory Data
Acute cystitis	Dysuria, frequent painful urination in the absence of such manifestations during the last month	 Leukocyturia> 10/ cub. mm Colon-forming units> 10 ³/ml
Acute uncomplicated pyelonephritis	Fever, abdominal and lower back pain in the absence of other diagnoses and developmental defects	 Leukocyturia > 10/cub.mm Colon-forming units > 10 4/ml

Complications of urinary tract infections	Various combinations of the above- mentioned symptoms in the presence	Leukocyturia > 10/cub.mm	
tract infections	of risk factors	- Colon-forming units > 10 ⁴⁻⁵ /ml	
Asymptomatic bacteriuria	There are no clinical symptoms	- Colon-forming units >	
		$10^{5}/\text{ml}$ in 2	
		cultures taken with an	
		interval of 24 hours	
Recurrent IUS (antibiotic	At least 3 episodes of uncomplicated	Leukocyturia >	
prophylaxis)	IUT, confirmed by crops during the	10/cub.mm	
	last 12 months. Only for girls who do	Colon-forming units >	
	not have structural or functional	10 ⁴ /ml	
	disorders		

BASIC CLINICO – LABORATORY SYNDROMS

- Dysuric syndrom
- Painful syndrom
- General intoxication
- Uric syndrom

Treatments

Increased water intake offers several benefits; it dilutes urine, increases voiding frequency, and reduces constipation. Stool softeners should be considered if the latter problem persists. Irritants, particularly soap, should be avoided near the perineum in prepubertal girls.

Sexually active women may benefit from postcoital voiding.

Pharmacologic treatment.

Complicated febrile urinary tract infections.

Complicated infections are defined as those seen in infants younger than 6 months of age and any child who is clinically ill, persistently vomiting, moderately dehydrated, or poorly compliant; these cases warrant intravenous antibiotics and hospitalization.

Standard dosage.

Ampicillin, 50–100 mg/kg/d in four divided doses.

Gentamicin, 2–2.5 mg/kg/dose every 8 h.

Ceftriaxone, 75 mg/kg/dose every 12 h (does not cover Enterococcus, which is more

frequently encountered in children with recurrent infection and should be avoided in neonates). Special points. An oral agent can be used after the child improves clinically (>24 h afebrile) pending the results of the culture and sensitivities; total treatment should last 14 d or longer if there is a renal abscess or an abnormal urinary tract.

Uncomplicated febrile urinary tract infections.

These children do not appear clinically ill, can take oral antibiotics, and are only mildly dehydrated (if at all) and compliant. Treatment can start with one dose of a parenteral agent (ceftriaxone, 75 mg/kg; gentamicin, 2.5 mg/kg) followed by oral therapy or with oral therapy alone.

Good follow-up is essential to ensure the child has responded appropriately, with treatment lasting 10–14 d.

Standard dosage.

Cotrimoxazole, 6–12 mg/kg/d trimethoprim divided twice daily.

Amoxicillin, 20– 40 mg/kg/d divided 3 times daily (many strains of E. coli are resistant to amoxicillin).

Cephalexin, 25–50 mg/kg/d divided 4 times daily.

Cefprozil, 15–30 mg/kg/d divided 2 times daily.

Afebrile urinary tract infections (acute cystitis).

Oral therapy with the agents listed above for a total of 5–7 d assuming clinical improvement is seen; in addition, nitrofurantoin 5–7 mg/kg/d divided 4 times daily can be considered; the liquid form of nitrofurantoin is not well tolerated.

Covert (asymptomatic) bacteriuria.

The treatment of this subgroup is controversial even in the presence of reflux; treatment may lead to the emergence of resistant organisms.

Prophylaxis.

Standard dosage.

Cotrimoxazole: 1–2 mg/kg trimethoprim daily.

Nitrofurantoin, 1–2 mg/kg/d.

Both of the above medications should be avoided in infants younger than 6 months of age.

Amoxicillin (10 mg/kg/d) or cephalexin (10 mg/kg/d) can be used instead.

Other treatments.

Infection in the presence of obstruction requires effective drainage of the urinary tract (e.g., nephrostomy, bladder catheterization) in addition to antibiotic therapy. Surgical correction of vesicoureteral reflux in indicated when the reflux is massive, when breakthrough infections develop, or when poor compliance is suspected.

Prognosis.

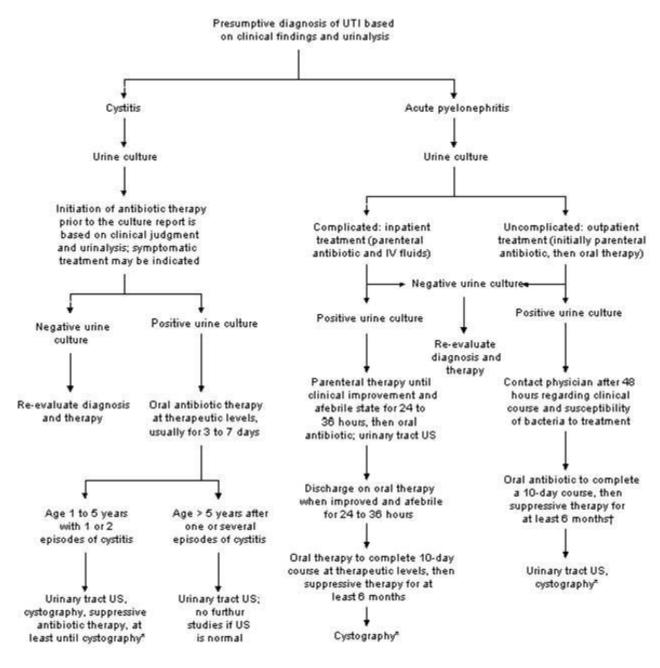
Rick for renal damage includes infant and young children with febrile infections in whom treatment is delayed.

Children with massive vesicoureteral reflux, and those with anatomic or neuropathic urinary tract obstruction.

Follow-up and management

Follow-up cultures should be obtained in children with febrile UTIs to assure an appropriate response. Infants and young children with documented vesicoureteral reflux should remain on antibiotic prophylaxis until the reflux resolves.

Some children with recurrent infections benefit from a short course of prophylactic therapy even when reflux is not present.



Differential diagnosis of pyelonephritis.

Symptom	PN	Cystitis	IUT	Acute GN
Communication	ARVI, bronchitis,	ARVI,	ARVI,	2-3 weeks after
with the disease	pneumonia	Overcooling	pneumonia	streptococcal
				infection
Symptoms of	+	- Or insignificant	-	+
intoxication				
Body temperature	>38	N or not high	-	-
Dysuria	1	+	<u>±</u>	-
Pain syndrome	+	in the abdomen	-	Rarely
Leukocytosis	+	Rarely	-	<u>±</u>
ESR	Up to 30 mm / h	-	-	More than 30
				mm / h
Bacteriuria	+	+	+	-
Осмолярність сечі	Lowered	N	N	N

Thermoassimetry	+	-	-	-
of the lower back				

Differential treatment of intestinal and decaying nephritis

Sign	Hereditary Nephritis	Interstitial Nephritis	
Kidney disease in family	+	Rarely	
members			
Loss of hearing in proband in	Often	_	
the family			
Anomalies of sight	In 20%	-	
The most common clinical	Stigma diesembriogenesis	Abdominal pain, dysuria,	
signs		intoxication, decrease	
		(increase) of blood pressure	
Pyeloectasiya, defects of	Often	Rarely	
kidney development			
Relative density of urine	Normal for a long time	Reduced	
Hematuria	More often micro hematuria	Expressed	
Leukocyturia	Rarely	Often, abacterial	
Increase in kidney area	-	+	
(ultrasound)			
Morphobioptic data	Focal-segmental glomerulitis	Infiltration of interstitial	
		lymphocytes and plasma cells,	
		tubular atrophy, fibrosis,	
		scarring in interstitium	

Differential diagnosis of pyelonephritis and interstitial nephritis.

Sign	Primary PN	Interstitial nephritis:			
		Urinary tract abnormalities	Hyperoxaluria	Dysplasia of kidneys	Viral infections
Age in case of disease	3-6	1-3	1-5	2-9	2-7
The presence of nephropathy in the family	-	±	+	±	±
Physical development	N	N	Increased	Reduced	Frequently lowered
The presence of stigmas	-	+	+	+	-
Detection of the disease	Acute	accidentally	Often by accident	accidentally	In connection with ARVI
The most frequent clinical sign	t°, back pain	Abdominal pain, dysuria	Dysuria, manifestations of allergy	Intoxication syndrome	Toxicology, dysuria
Bacteriuria	+	±	-	-	-
Hematuria	-	±	+	+	+
Abdominal syndrome	+	+	+	±	-

Differential diagnosis of tubulointerstitial nephritis and chronic glomerulonephritis.

Differential diagnosis of taodiointerstitial nephritis and emonie giomeratonephritis.			
Sign	Glomerulonephritis, hematuric	Interstitial nephritis	
	form		
Causes of development	Acute and chronic	Metabolic disorders, drugs,	
	streptococcal infection	viral infection, dysplasia of the	
		kidneys, vascular, physical,	
		allergic factors	
Edema	+	-	
Hypertension	Joins in the late stages	Joins early	
Lumbar pain	-	+	
Rising temperatures	-	+	
Anorexia, vomiting	-	+	
Macrohematuria	When exacerbating the	It is possible	
	process		
Proteinuria	+	Not high	
Glucosuria	-	It is possible	

6. Materials of methodological support of the lesson.

6.1 Tests

- 1. A 4.5-year child was admitted to the hospital with complaints of poor appetite, weakness, vomiting and abdominal pain, not associated with eating, temperature 37.5°C. 2 weeks before that, he had an acute respiratory viral infection, during which traces of protein, leukocyturia (up to 40), microhematuria were detected in the urine. Objectively: the skin and mucous membranes are clean. The abdomen is soft, moderately painful. The liver and spleen are not enlarged. Pasternatsky's symptom is positive. What is the most likely diagnosis?
- A. Acute primary pyelonephritis
- B. Acute appendicitis
- C. Acetonemic syndrome
- D. Functional disorders of the gallbladder
- E. Helminthic invasion
- 2. A 5-year child has acute abdominal pain, fever up to $40\,^{\circ}$ C, nausea, without signs of a respiratory infection. From the anamnesis it is known that the child has already had these symptoms before. The child urinates 2-3 times, the urine is cloudy with an unpleasant odor. What is the most likely diagnosis for a child?
- A. Obstructive pyelonephritis
- B. Glomerulonephritis
- C. Cystitis
- D. Dysmetabolic nephropathy
- E. Hereditary nephritis
- 3. A 10-year child has attacks of fever up to 38.5°C, deterioration of health and appetite, there are periorbital shadows, moderate pain in the right lumbar region. In the hemogram: Le 14x10 ^ 9 / 1, stab 12% segment. 72%, ESR 35 mm / h. Urine analysis yellow, cloudy, in the remainder fibrin flakes, Le 50-70 in the field of view, active leukocytes were found, a lot of bacteria. Bacteriuria more than 10 ^ 5 in 1 ml of urine. Ultrasound of the kidneys increased echogenicity of the calyx-pelvic system on the right, edema of the interstitium. Make a preliminary diagnosis.
- A. Acute pyelonephritis
- B. Dystopia of the right kidney
- C. Acute cystitis
- D. Dysmetabolic nephropathy

E. Dysplasia of the right kidney

- 4. What microorganisms most often causes pyelonephritis?
- A. Proteus
- B. Klebsiella
- C. Streptococcus
- D. Escherichia coli
- E. Staphylococcus aureus
- 5. A 9-year girl complains of fever up to 37.5°C, headache, lethargy, weakness, decreased appetite, abdominal pain, frequent and painful urination. Acute pyelonephritis was suspected. In the clinical analysis of urine the specific gravity is 1018, there is no protein, leukocytes are 10-15 in the field of view. Which test method will reliably help confirm the diagnosis of urinary tract infection?
- A. Bacteriological urine culture
- B. Rehberg's test
- C. Zimnitsky test
- D. Complete blood count
- E. Conducting clinical analyzes of urine in dynamics

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

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. National Institute for Health and Clinical Excellence (NICE). Urinary tract infection in children (CG54). Available at: http://www.nice.org.uk/CG054. Last accessed: 30 November 2019.
- 4. Subcommittee on Urinary Tract Infection. Reaffirmation of AAP Clinical Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age. Pediatrics 2016;138(6). pii: e20163026.
- additional:
- 1. Selekman RE, Shapiro DJ, Boscardin J, Williams G, Craig JC, Brandström P, et al. Uropathogen resistance and antibiotic prophylaxis: a meta-analysis. Pediatrics. 2018:142.
- 2. Millner R, Becknell B. Urinary tract infections. Pediatr Clin North Am. 2019;66:1-13.
- 3. Shaikh N, Martin JM, Hoberman A, Skae M, Milkovich L, Nowalk A, et al. Host and bacterial markers that differ in children with cystitis and pyelonephritis. J Pediatr. 2019;209:146-53.
- 4. Uwaezuoke SN et al. The prevalence and risk of urinary tract infection in malnourished children: a systematic review and meta-analysis. BMC Pediatr. 2019; 19:261.
- 5. American College of Radiology. ACR Appropriateness Criteria: urinary tract infection-child. Available at: https://acsearch.acr.org/docs/69444/Narrative/. Last accessed: 30 November 2019.

6.3. Indicative map for independent work with literature.

No	Main Task	Directions	Answers
1	2	3	4
1.	To get acquainted with the	Formulate Definition of	Formulate the concept of
	purpose and tasks of the	IUT in Children	multifactorial disease and its
	class		functional character.

2.	Epidemiology	Know the prevalence of IUS among children. List the risk factors for IUT in children.	According to statistical reports of the Ministry of Health of Ukraine, the prevalence of kidney and urinary disorders in children in Ukraine has increased in the last 5 years, namely: from 40 to 56/1000 children. In the first year of life, boys suffer more often in the IUS (3.7% vs. 2% in girls), then the opposite is observed.
3.	Etiology	List the main etiological agents in the IUS	Among uropathogenic microorganisms, which play a role in the development of IUS, the first place belongs to the gram-negative flora of the Enterobacteriaceae family (up to 80%), and E. coli (80-90%) predominates in the microbial spectrum. The gram-positive flora is represented by Staphylococcus spp., Enterococcus spp. Also, a specific place in the etiology of IC is occupied by intracellular pathogens (Chlamidia, Ureaplasma, Mycoplasma), viruses (adenoviruses, enteroviruses, herpes virus viruses), mushrooms.
4.	Pathogenesis	Determine the pathways for infectious pathogens in the IUS. To characterize the main pathogenetic mechanisms in children with pyelonephritis.	Among the abilities of microorganisms, a special place belongs to the phenomenon of uropathogeny Uropathogenicity - the potential ability of microorganisms to cause the development of pathological process when penetrated into the organs of the urinary system. An important common feature of the activators of the IUS is their adhesive ability to uroepithelium, which provides reliable fixation of bacteria in the urinary system and prevents their hydrodynamic elimination.
5.	Classification	Know the classification of pyelonephritis in children	Be able to diagnose.
6.	Clinic	Indicate the main symptoms and their characteristics in the IUS.	General signs are clinical signs, functional disorders.

7.	Diagnosis	Identify the main methods	To assess the results of laboratory
		of clinical and paraclinical	and functional methods of
		examination in the IUS	investigation.
8.	Differential diagnosis	List diseases with similar	Interstitial nephritis,
		clinical and laboratory	glomerulonephritis
		manifestations.	
9.	Treatment, prophylaxis	Determine the main areas	Pay attention to the complexity of
		of treatment, prevention	diagnosis of the urinary system.
		and medical examination	
		in children with US.	

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

A. Questions.

- 1. The main anatomical and physiological features of the urinary system in children.
- 2. Basic provisions on infections of the urinary system in children.
- 3. Causes of development, the main clinical manifestations of cystitis in children.
- 4. Definition, etiology, pathogenesis, classification and clinic of pyelonephritis in children.
 - 5. Method of objective examination of a patient with urinary system infection.
- 6. Basic laboratory and instrumental methods of examination of a patient with urinary system infection.
 - 7. Basic principles of differential diagnosis of cystitis, pyelonephritis in children.
- 8. Methods of treatment of infections of the urinary system (cystitis, pyelonephritis) in children.
 - 9. Differential diagnosis of urinary tract infections.
 - 10. Prevention and prognosis of pyelonephritis in children.

B. Tests

- 1. A child of 13 years complains of pain in the suprapubic region, frequent urination with small portions of urine. Fever 37.7 °C. In the analysis of swine-proteinuria-0.033 g / l, red blood cells are fresh, completely in the preparation, salt-oxalate is insignificant. What is the most likely diagnosis?
- A. Dismetabolic Nephropathy
- B. Acute cystitis
- C. Acute glomerulonephritis
- D. Acute pyelonephritis
- E. Urolithiasis
- 2. A 6-years girl became acutely ill: temperature increase to 39° C, vomiting, abdominal pain, cloudy urine. Urination in small portions. BP 100/60 mm Hg art. General analysis of urine rel. density 1006, protein 0.58 g / l, leukocytes entirely, erythrocytes 20-25. Blood test: ESR 30 mm / hour. Make a preliminary diagnosis
- A. Acute pyelonephritis
- B. Acute cystitis
- C. Acute glomerulonephritis
- D. tubulointerstitial nephritis
- E. Dismetabolic nephropathy
- 3. Within 2 years in a 4-year-old child there are relapses of the disease, accompanied by an increase in body temperature, lethargy, abdominal pain, increased urination. Urine test specific gravity 1010, protein 0.12 g / l, leukocytes 1-2, red blood cells 4-5, Cylinders not detected. Salts oxalates. Presumed chronic pyelonephritis. What kind of examination is needed to clarify the cause of the disease:

- A. Mictorial cystography
- B. Daily excretion of salts
- C. Immunogram
- D. General urine test
- E. Blood culture for sterility
- 4. At the child of 7 years the expressed signs of an inflammation, a dysuria, a pollakiuria, nocturia; Leukocytosis with a left shift; Significant leukocyturia with active leukocytes, small proteinuria, bacteriuria, leukocyte cylinders this clinic:
- A. Acute pyelonephritis
- B. Acute glomerulonephritis
- C. Acute cystitis
- D. Amyloidosis of the kidneys
- E. chronic renal failure
- 5. A 8-years girl turned to the district pediatrician for a pain and burning sensation when urinating, aching pain over the pubis, more often a train to urinate. A month ago I was treated for enterobiasis. Objectively: the condition is not broken, the skin is clean, there is no swelling, with a deep palpation a moderate soreness over the pubis. When tapping in the projection of the kidneys, soreness was not observed. Urination is frequent, urine cloudy. Which of the diagnoses is most likely?
- A. Acute vulvovaginitis
- B. Tuberculosis of the kidneys
- C. Acute glomerulonephritis
- D. Acute pyelonephritis
- E. Acute cystitis
- 6. The child has 8 months of body temperature 39.2 °C, lethargy, pallor, refusal to eat, one-time vomiting, frequent urination. At physical examination of a pathology it is not revealed. The urine is turbid. What additional research will help to establish the diagnosis?
- A. Blood test for sugar
- B. General blood test
- C. General analysis of urine
- D. Urine analysis for sugar from the daily amount
- E. Coprocyclotogram
- 7. A sick child complains of pain in the abdomen for 8 years, headache, fever, painful urination. Objectively: the skin is pale, hot, t body 39 $^{\circ}$ C, bruises under the eyes. In the blood leukocytosis 14 T / L, ESR-34mm / h. In urine: protein-0.066 g / l, leukocytes densely cover the field of view. Eure fresh 5-10 in the field of view, bacteria a lot. What is the likely diagnosis of the patient?
- A. Cystitis
- B. Acute pyelonephritis
- C. Acute glomerulonephritis
- D. Polycystic kidney disease
- E. Dismetabolic nephropathy
- 8. The girl has 9 years of minor general inflammatory syndrome, the dysuria with pronounced cutting pain and premature termination of urination moderate leukocyturia, fresh red blood cells, small proteinuria, bacteriuria (25-100) small leukocytosis is the clinic:
- A. Acute pyelonephritis
- B. Acute glomerulonephritis
- C. Acute cystitis
- D. Amyloidosis of the kidneys

E. chronic renal failure

- 9. At the child of 6 years at registration in school have found out changes in urine: insignificant proteinuria, leukocyturia, bacteriuria. What kind of illness can you think of?
- A. Pyelonephritis.
- B. Chronic renal failure.
- C. Acute myocarditis.
- D. Rheumatism.
- E. Acute glomerulonephritis.
- 10. At the child of 6 years at registration in school have found out changes in urine: insignificant proteinuria, leukocyturia, bacteriuria. What examinations do you need?
- A. Clearance of endogenous creatinine.
- B. Urinalysis by Nechiporenko, Zimnitsky, urine culture on flora, renal ultrasound, biochemical blood test (protein, urea, creatinine).
- C. Urinalysis by Nechiporenko, Zimnitsky.
- D. Biochemical analysis of blood (protein, urea, creatinine), ultrasound of the kidneys.
- E. Intravenous urography.

Answers: 1 -B, 2 -A, 3 -A, 4 -A, 5 -E, 6 -C, 7 -A, 8 -C, 9 -A, 10 -B.

B. Tasks for self-control with answers.

№1. At the girl of 6 years after a supercooling the temperature to 39 °C has raised, there was a pain in a loin on the left, fastened (up to 8 times a day) and morbid urination. From the anamnesis zhittyavidomo that the child was born on time, with a mass of 2800, an assessment on the Apgar scale of 5 points, in childbirth twice encircling the umbilical cord around the neck 2 times. Pregnancy preceded with gestosis I and II half. Heredity is weighed down: the mother has cystitis, her father has urolithiasis. Postponed diseases: ARVI from 3 years to 4-5 times a year, cystitis in 3 years. Objective data for admission to the hospital: heart rate - 100 in 1 min., BP - 90/45 mm. State of moderate severity, temperature 39,0 °C, skin pale, there is no swelling. The tongue is coated with a white bloom. Heart sounds of satisfactory sonority. At palpation - mild, painful over the bosom, in the left ileal region. Pasternatsky sing positive left. The kidneys are not palpable. Results of the laboratory examination: Hb - 128 g / l, Er - 4,5x10¹² / l, ESR - 24 mm / h, Le - 12,8 x10⁹ / l, S - 6%, Seg - 66%, L - 22%, M - 6%, E - 0. The general analysis of urine: volume - 115ml, specific gravity - 1016, color - yellow, cloudy, reaction - neutral, protein - no, leukocytes - everywhere in the field of vision., Erythrocytes 1-2.

Question:

- A). Establish a preliminary diagnosis and conduct differential diagnosis of diseases characterized by urinary syndrome.
 - B). Make a plan for further investigation.

The standard of the answer:

- A). Acute pyelonephritis, activity of 2 degrees, without disturbance of kidney function. Differential diagnosis: cystitis, interstitial nephritis, glomerulonephritis.
- B). Laboratory studies: biochemical blood test with definition of creatinine and urea, general urine analysis, Nechiporenko and Zimnitsky test, bacteriological examination of urine, swab from the vagina; Analysis of daily excretion of salts; Studies on enterobiasis and dysbiosis; Instrumental studies: ultrasound of the urinary system, X-ray examination (after the elimination of the inflammatory process).

 \mathbb{N}_{2} 2. The girl of 11 years during a year there are pains in a tummy, not connected with reception and character of nutrition, sometimes disturb pains in a loin. Appetite is lowered, the child notes fatigue at the end of the day, sleep restless. At outpatient examination in the analysis of urine protein - 0,33%, specific gravity - 1014, leukocytes to 20-25, Epithelial cells in a small amount, erythrocytes 0-2, Salts - oxalates in insignificant Quantity. Objective data at admission: heart rate - 92 per minute, blood pressure - 100/70 mm Hg. The patient's condition is moderate, the girl is pale, periorbital cyanosis; Edema is not present. The symptom of percussion (Pasternatsky) in the projection of the kidneys is a positive thing. Palpation of the abdomen is painless. The kidneys are not palpable. The results of the survey are as follows: Er $4.1 \times 10^{12} / 1$, Hb - 120 g / 1, Le - $9.4 \times 10^{9} / 1$, e - 2%, s - 4%, seg - 50%, L - 38%, M - 6%, ESR - 17 mm / h. Urinalysis data - specific gravity 1015, protein 0.066%, Leukocytes in large numbers, erythrocytes up to 2 in sp. The degree of bacteriuria is 100,000 in 1 ml of urine, a proteic stick is allocated. Analysis of urine according to Zimnitsky - fluctuations in specific gravity - 1010-1021, daily diuresis - 1200 ml, diuresis daily - 700 ml, no one diuresis - 500 ml. Biochemical blood test - total protein - 62 g/l, urea - 6 mmol/l, creatinine - 0.07 mmol/l, cholesterol - 4.5 mmol / l. Glomerular filtration - 60 ml per minute. Data of ultrasound of the kidneys and bladder: bilateral vesicoureteral reflux.

Question:

- A). Establish the diagnosis. Assess the kidney function.
- B) .To test which is necessary to clarify the diagnosis and characterize the degree of vesicoureteral reflux (VUR).

The standard of the answer:

- A). Chronic obstructive pyelonephritis, recurrent course, decreased renal filtration function. VUR 2 d.
- B). VUR degree according to the X-ray contrast study data (mikstatsionnaya cystography) 1 degree throwing contrast agent only in the ureter 2 degree contrast in the ureter, bowl and calyxes, without their expansion, fornicks normal 3 degree easy or moderate ureter dilatation and pelvis, no or easy smoothness of the fornicative 4 degree moderate enlargement and / or tortuosity of the ureter, moderate widening of the pelvis and calyces, violation of the structure of the fornix 5 degree marked enlargement and / or tortuosity of the ureter, and cups, most cups and indistinctly
- № 3. Girl 9 years old, entered the department for back pain, increased frequency of urination. A child from I pregnancy, which was taking place with a toxicosis of the first half. Childbirth on the 38th week. Weight at birth is 3000 g, length is 52 cm. In the anamnesis frequent ARVI (more than 6 times a year). This disease was preceded by hypothermia. The next day there was a headache, adynamia, pain in the tummy and lower back on the left, the temperature rose to 39 ° C. There were no catarrhal phenomena. During the next 4 days, she continued to fever, there was a pollakiuria, urine was turbid with a peculiar smell. When entering the hospital a moderate state, body temperature 38 $^{\circ}$ C, the skin curves are pale, edema is not observed. The symptom of a tapping (Pasternatsky) is positive on both sides, more to the left. When palpation of the left kidney soreness. Total blood test: Hb - 120 g / l, Er - 4.5×10^{12} / l, Le - 10.5×10^{9} / l, s - 10%, seg - 60%, l - 22%, m - 8%, ESR - 28 mm / hour. The general analysis of urine: the reaction is neutral, the protein is 0.09% o, the leukocytes are all fields of vision, the red blood cells are 1 in p / z, the salts are oxalates, the bacteria are +++. Biochemical blood test: total protein - 72.0 g / l, CRP - +++, seromucoid - 0.3, urea - 4.3 mmol / l. Urine culture: 10000 microbial bodies / ml of E. coli were isolated. Kidney ultrasound: the kidneys are located correctly; the left one is 107x42x13 mm, the right one - 94x37x13 mm. The echo from the prefabricated system is changed from both sides, more to the left, expanded. Suspicion of doubling left kidney.

Ouestion:

A). Formulate and justify a preliminary diagnosis.

B). Describe the criteria for the activity of pyelonephritis.

The standard of the answer:

- A). Secondary obstructive pyelonephritis against the background of a congenital anomaly of the development of the urinary system.
- B). Criteria for activity of PN I activity: temperature <37.5 ° C, low intoxication, leukocytosis <10x109, ESR <15 mm / h, CRP / + II activity: temperature <38.5 ° C, moderate intoxication, leukocytosis < (11-14) x109, ESR < (16-24) mm / h, CRP ++ III degree of activity: temperature> 38.5 °C, significant intoxication, leukocytosis> 15x109, ESR> 25 mm / h, CRP- / +.
- №4. The girl 4 years after hypothermia makes complaints about pains in the suprapubic region, frequent painful urination in small portions. Dietina from the 2nd pregnancy, which was without pathology. Childbirth on time. The birth weight was 3300 g, and the length was 50 cm. The period of newborns was uneventful. In the history of ARVI 1 2 times a year, signs of atopic dermatitis. When entering the department temperature of 36.7 ° C, the state is satisfactory. There are no catarrhal phenomena. Soreness in palpation of the bladder. The symptom of a tapping (Pasternatsky) in the projection of the kidneys is negative. Urine turbid, with a specific odor, the volume of single portions is 10 20 ml. The general analysis of the blood: Hb 140 g / l, Er 4,5x10¹² / l, Le- 8,5x10⁹ / l, ESR 5 mm / hour. The general analysis of urine: reaction alkaline, protein 0,033 ‰, leukocytes completely all fields of vision, erythrocytes unchanged 15-25 in p / z, mucus +, bacteria ++. Urine culture: an intestinal stick was sown in the amount of 1000 microbial bodies / ml. Ultrasound of the urinary system: the kidneys are located correctly, the left 95x41x11 mm, the right 94x42x12 mm. The bowel-and-pelvic system of both kidneys is not expanded, cortico-medullary differentiation is preserved; Wall of the bladder 3.5mm, layered, volume of residual urine 110ml.

Question:

- A). Preliminary diagnosis.
- B). Make a plan for the treatment of the child.

Standards of answers:

- A). Acute cystitis
- B). Antibacterial therapy (cephalosporins II or protected penicillins or phosphomycin trometamol), uroseptics (furamag), vegetable uroantiseptics (kanefron), spasmolytics (drotaverin, papaverine), physiotherapy (variants: overtone frequency currents, Zinc-electrophoresis, peloid-therapy).
- №5. A 15-year-old girl is hospitalized for chronic relapsing pyelonephritis. When you receive a complaint about painful urination, the pain in the abdomen and lower back is greater on the left. The signs of the disease appeared the next day after unprotected sex. At inspection: the state of health is not broken, dermal crooked pale, there is no swelling, the temperature is 37,0 ° C. The symptom of a tapping in the projection of the kidneys is positive on the left. The general analysis of the blood: Hb 120 g / l, Er 4,0x10¹² / l, Le 10,5x10⁹ / l, ESR 17 mm / h. In the general analysis of urine, the volume is 100 ml, the specific gravity is 1015, the protein is 0.33 ‰, the leukocytes are 10-15, the erythrocytes are 15-20. With ultrasound of the kidneys: the kidneys are located correctly, the left one is 102x40x13 mm, the right is 103x37x13 mm, the cortico-medullary differentiation is preserved, the bowl on the left is 15 mm, the case is 10 mm. According to the PCR analysis in the urine is determined by Mycoplasma genitalis. Examined by a gynecologist a diagnosis of vulvovaginitis.
 - question:
 - A). Preliminary the diagnosis.
- B). What clinical and laboratory indicators characterize the mycoplasmal etiology of the process, and which antibacterial drugs are active against Mycoplasma.

The standard of the answer:

- A). Chronic pyelonephritis, recurrent course, without disturbance of renal function. Vulvovaginitis.
- B). Characteristic features of mycoplasma pyelonephritis: chronic recurrent course, low severity of clinical manifestations, disorders of urination, concomitant pathology of the genital tract, urinary syndrome with microhematuria, microproteinuria and leukocyturia, usually the absence of bacteria. Concerning mycoplasma, the active antibacterial preparations of the macrolide group: azithromycin (Azimed), clarithromycin (klatsid), spiramycin (rovamycin), roxithromycin (LEK), josamycin (vilprafen).

8. Classroom materials for self-study.

- 8.1. List of educational practical tasks that must be completed during the practical exercises.
 - 1. Collect history, highlight the points that indicate the nature of the inflammatory disease.
 - 2. Identify the most informative features of the disease during objective and laboratory and instrumental examination of the patient.
 - 3. Prescribe treatment.

9. Instructional materials for learning 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. The girl, 9, She is ill for 3 years. Thrice was treated permanently. On examination, the pallor of the skin and mucous membranes was found, the pastosity of the face, with Pasternatsky positive on the left. In the biochemical analysis of blood: total protein 70.3 g / l, cholesterol 5.92 mmol / l, urea 6 mmol / l; in the analysis of urine: specific gravity 1.006, protein 0.33 g / l, white blood cells per ½ field of view, erythrocytes 8-10. When urine was sown, E. Coli was found to be 150000. In the sample according to Zimnitsky, the specific gravity fluctuated from 1.002 to 1.006. What disease is diagnosed in a child?
- A. Pyelonephritis
- B. Cystitis
- C. Acute myocarditis
- D. Rheumatism
- E. Acute glomerulonephritis
- 2. A 5-year-old boy is on inpatient treatment for acute pyelonephritis. After the course of treatment, the boy's condition returned to normal. In the general analysis of urine: the relative density is 1012, the reaction is acidic, the transparency is slightly turbid, the protein and sugar are absent. When microscopic sediment epithelial cells, leukocytes 2-4, erythrocytes 1-2, hyaline cylinders 0-1, mucus a little. What research should be done?
 - A. bacteriological culture of urine in flora
 - B. Analysis of urine according to Zimnitsky
 - C. Urinalysis by Nechiporenko
 - D. Urine analysis for 24-hour urinary acid excretion.

- E. Obstetric radiography of the abdominal cavity.
- 3. A child of 13 years is under clinical supervision in connection with chronic pyelonephritis. What tests should be performed to assess the functional state of the kidneys in the first place?
- A. Urinalysis clinical
- B. Urinalysis by Nechiporenko
- C. Urinalysis
- D. Rheberg test
- E. Acid Phase Indicators
- 4. The child has 1.5 years after the acute respiratory viral infection, dysuria (frequent and false urination), the temperature fluctuates from normal to 37.8 °C during the day. The skin is pale, there are no catarrhal phenomena, refuses to eat. Auscultatory in the lungs without deviations from the norm. Heart sounds are rhythmical, muffled. The abdomen is soft, painless. Parenchymal organs are not enlarged. When examined, stigmata are observed. In the outpatient analysis of urine leukocyturia up to ½ of the field of view. What diagnostic methods should be envisaged in this situation in the first place?
- A.Mictional cystography
- B. Chest X-ray
- C. ECG
- D. Analysis of urine according to Zimnitsky
- E. Renascintigraphy
- 5. The child is 7 years old. Complains of frequent urination, abdominal pain, nausea, vomiting, fever up to 38.3 0 C. It hurts 4 days. At an objective inspection the paleness of a skin, a BP 100/50 mm Hg is revealed. The heart rhythmic activity, tachycardia 100 in 1 min. Positive symptom Pasternatsky on the right. Urinalysis: specific gravity 1018, protein 0.098 g / l, leukocytes up to ½ of the field of view, red blood cells 1-3 in the field of view, many bacteria. Blood analysis: erythrocytes 3.8 * 10¹² / l, hemoglobin 120 g / l, leukocytes 18 * 10⁹ / l, s-12%, seg.-47%, lymph-35%, mon.-6 %, ESR-26 mm / hour. Make a preliminary diagnosis.
- A. Acute glomerulonephritis
- B. Acute pyelocystitis
- C. Acute pneumonia
- D. ARVI
- E. Dismetabolic nephropathy.

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