MEDICAL CARE FOR CHILDREN WITH ACUTE PYELONEPHRITIS

Learning guide for the 5th- and 6th-year students of level 3–4 accreditation higher medical education institutions, trainee physicians, pediatricians, general practitioners

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

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МЕДИЧНА ДОПОМОГА ДІТЯМ З ГОСТРИМ ПІЄЛОНЕФРИТОМ

Методичні вказівки для здобувачів вищої освіти 5–6-х курсів вищих медичних закладів освіти III–IV рівні акредитації за спеціальністю «Медицина», лікарів-інтернів, лікарів-педіатрів, лікарів загальної практики – сімейної медицини

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What is Pyelonephritis?

Pyelonephritis (PN) is a non-specific infectious-inflammatory disease of the kidneys, affecting one or both sides. It predominantly affects the renal pelvis-calyceal system, tubulointerstitial tissue, and often involves the glomerular apparatus. It is essential to note that the disease can be unilateral, unlike other kidney diseases (e.g., glomerulonephritis, analgesic nephropathy), which are typically bilateral. Pyelonephritis is mainly caused by a non-specific infectious agent. The inflammation starts in the renal pelvis-calyceal system (RPCS), gradually spreading to the interstitium and other kidney structures.

Epidemiological Features.

PN is a fairly common disease. In childhood, its frequency, according to various authors, ranges from 7 to 28 cases per 1000. Girls are at the highest risk of developing PN. Gender-wise, PN is most often seen in girls, while in boys and young men, non-obstructive PN is very rare.

Etiology.

In most cases, pyelonephritis is caused by a single uropathogen, but with frequent recurrences and against the background of defects in the development of the urinary system, microbial associations are found in up to 62 % of cases. Currently, gram-negative flora predominates among pathogens in children, while about 90 % is due to infection with Escherichia coli bacteria. Among other pathogens, Proteus mirabilis (in boys – about 30 %), Klebsiella spp. (Mostly in young children), Enterobacter spp. and Pseudomonas spp. – are detected in less than 2 % of cases. Nosocomial infections with strains of Klebsiella, Serratia and Pseudomonas spp. Gram-positive microorganisms are mainly represented by enterococci and staphylococci (5–7 %). In newborns, streptococci of groups A and B are a common cause. Recently, an increase in the detection of Staphylococcus saprophyticus has been noted, although its role remains controversial. Intrauterine viral infections are considered as a contributing factor to bacterial infection. The development of pyelonephritis can be caused by urogenital chlamydia, ureaplasmosis, mycoplasmosis, especially in children with nonspecific inflammatory diseases of the external genitalia. In children with immunodeficiency conditions (premature, with hypotrophy, intrauterine infection, developmental defects, children who have received immunosuppressive therapy for a long time), associations of bacteria with fungi are characteristic. Actinomyces species, Brucella spp., Mycobacterium tuberculosis are registered with the hematogenous route of infection.

Pathogenesis of pyelonephritis.

Conditions that lead to the development of pyelonephritis: pyelonephritis refers to diseases with a hereditary predisposition; dysembryogenesis in the kidney, immaturity of nephrons that create ischemic foci; the role of metabolic disorders (in primary and secondary tubulopathies with a change in urine pH and crystalluria, often as a result of enzymopathy) they create favorable conditions for the fixation of microorganisms in the kidney tissue; microbes

penetrate into the capillary network, from there into the interstitial tissue, where inflammatory foci appear.

Favorable conditions in young children: congenital anomalies of the genitourinary system, early transition to mixed or artificial feeding, frequent diseases of early age: intracranial birth trauma, dystrophy, rickets, atopic diathesis; diseases of other organs leading to urodynamic disorders and kidney hemodynamic disorders.

Leading risk factors for the development of pyelonephritis in children: children aged the first 2 years of life; anomalies of the development of the genitourinary system, urogenital area – organic disorders of the passage of urine; neurogenic dysfunction of the urinary bladder: rare or frequent urination, urinary incontinence – functional disorders of the urinary passage; violation of the composition of the urine itself (for example, diabetes, tubulopathy); constipation; worm infestations; inflammatory diseases of external genital organs (vulvovaginitis, balanitis, balanoposthitis); transurethral medical manipulations (bladder catheterization); masturbation, early sexual life; an important cold factor – muscle spasm and kidney hemodynamic disturbances occur.

Ways of infection. Ascending – the most frequent.Anatomical features determine the high frequency of infections of the urinary system and pyelonephritis in girls. The reservoir of uropathogenic bacteria is the rectum, perineum, and lower parts of the urinary tract. After the bacteria overcome the vesicoureteral barrier, their rapid reproduction occurs with the release of endotoxins. In response – activation of the local immunity of the macroorganism (macrophages, lymphocytes, endothelial cells) with the production of inflammatory cytokines (IL1, IL2, IL6, tumor necrosis factor), lysosomal enzymes, inflammatory mediators; activation of lipid peroxidation, which leads to damage of kidney tissue, primarily tubules. This view of the pathogenetic mechanism of pyelonephritis was called the block – cascade theory of the development of this disease. The hematogenous path of development of pyelonephritis occurs mainly in the development of septicemia in the newborn period and in the first months of life, especially in the presence of immune defects; this pathway also occurs during infection with Actinomyces species, Brucella spp., Mycobacterium tuberculosis. The lymphogenic pathway is less significant, possible in the presence of damaged urinary tract mucosa, not recognized by all nephrologists; there is a hypothesis about the lymphogenic migration of microorganisms from the intestine.

What is Acute Pyelonephritis (APN)?

Acute pyelonephritis (APN) is the first episode of bacterial-induced damage to the renal interstitium. APN can manifest as serous or purulent inflammation (apostematous, carbuncle, renal abscess, necrotizing papillitis).

Risk Factors for Pyelonephritis.

Risk factors include the following physiological and pathological processes:

- Refluxes at various levels (vesicoureteral, ureteropelvic);
- Bladder dysfunctions (e.g., “neurogenic bladder”);
- Conditions involving impaired urine flow (urolithiasis, tumors of the urinary tract, abdominal cavity, and pelvis compressing the urinary tract from outside, etc.);

- Nephroptosis, dystopia, and hypermobility of the kidneys;
- Kidney and urinary tract abnormalities (e.g., duplication);
- Diabetes mellitus;
- Metabolic disorders (e.g., oxalate-calcium, urate, phosphate crystalluria);
- Polycystic kidney disease;
- Instrumental procedures (e.g., various types of catheterizations);
- Medications (e.g., sulfonamides, cytostatics, etc.);
- Exposure to radiation or toxic chemicals.

What is a relapse, reinfection, and failed treatment? What is the Difference Between Relapse, Reinfection, and Treatment Failure?

A relapse of APN is documented when there are clinical-laboratory symptoms and the same pathogen is detected as at the onset of the disease. Reinfection is identified by the presence of PN signs and the detection of a different serotype or infectious agent during a bacteriological urine analysis.

- **Relapse**: Documented when there are clinical and laboratory symptoms, and the same pathogen, of the same strain, as at the onset of the disease is detected.
- **Reinfection**: Defined by the presence of pyelonephritis symptoms when another serotype or different infectious agent is identified during bacteriological analysis of the urine.

What are the epidemiological features of pyelonephritis?

Pyelonephritis is a relatively common disease. In childhood, its frequency, according to various authors, ranges from 7 to 28 cases per 1000. Girls are at the highest risk of developing pyelonephritis. Boys, however, are more frequently diagnosed with obstructive pyelonephritis.

Necessary actions:

1. Complaints: When admitting a patient, attention should be paid to the presence of hyperthermic syndrome, dysuria, weakness, abdominal or lower back pain, intoxication syndrome, cloudy and foul-smelling urine, and discharge from external genitalia.

2. Diagnosis:

Indications for hospitalization:

- To establish a diagnosis
- Pronounced dysuria
- Fever above 38.5 °C
- Severe abdominal or back pain
- Intoxication syndrome (nausea, vomiting, lethargy, convulsions)
- Impaired consciousness (excessive agitation or lethargy)
- Monitoring of renal function in stages II–V of chronic kidney disease (CKD)
- The need to administer radiopaque substances
- Referral from a military medical commission (MMC)

3. Collection of medical history:

- **At admission**: Careful attention should be given to determining the time of disease onset, symptoms at the start, and the course of the disease.
- **Medical history**: Therapies administered prior to hospitalization, clarification of whether it is a primary or secondary infection, the presence of congenital abnormalities in the urinary system, and prior surgeries.
- **Family history**: Kidney diseases in relatives, and any history of deaths due to kidney diseases.
- **Medication history**: Treatment received before hospitalization, allergic reactions to medications, and any surgeries performed.

4. Physical examination:

At the time of admission and daily thereafter, or when necessary, measurements of blood pressure (BP), heart rate (HR), body temperature, respiratory rate, body weight, and urine output should be taken. A full body examination should also be conducted, with special attention to the abdomen, and the genitalia.

5. Differential Diagnosis:

At the time of admission, it is essential to consider various diseases with similar symptoms, including urinary tract infections (UTI), cystitis, asymptomatic bacteriuria, vulvitis, vulvovaginitis, neurogenic bladder, and catheter-associated UTIs.

Clinical criteria:

- Abdominal or lower back pain
- Intoxication syndrome (fever, pale skin, periorbital cyanosis, nausea, vomiting)

Potential clinical manifestations:

- Sudden or gradual onset
- Recent infections or hypothermia (within 7–21 days)
- In infants, poor weight gain, skin mottling, anorexia, digestive disturbances, irritability, prolonged jaundice, seizures, signs of dehydration (decreased skin turgor, dry skin, tachycardia, thirst), and intestinal syndrome.

Investigation

- **Complete blood count**: Leukocytosis, a left shift in the leukocyte formula, increased ESR.
- **Urinalysis**: Leukocyturia (more than 10 leukocytes per field of view), pyuria; proteinuria and erythrocyturia (may be minimal or absent); cylindruria. The most important finding in urinalysis that confirms the diagnosis of PN and allows monitoring of treatment effectiveness is the presence of bacteriuria against the background of leukocyturia. Rarely, there may be pronounced clinical symptoms of APN without changes in the urine, as can happen in cases of complete obstruction of the ureter of the affected kidney.

• **Biochemical blood tests**: Elevated levels of C-reactive protein, increased levels of α_2- and γ-globulins, possible increased levels of urea and creatinine, decreased total protein concentration (in severe cases).

Paraclinical criteria:

• **Blood tests**: Increased ESR, neutrophilic leukocytosis, elevated C-reactive protein, and procalcitonin levels.

• **Urinary indicators**: Neutrophilic leukocyturia, microproteinuria, any number of colony-forming units (CFUs) of *Pseudomonas* directly from the bladder (via cystostomy or puncture), a positive nitrite test, and a positive leukocyte esterase test.

6. Consultations with other specialists:

• Upon hospitalization, specialist consultations should be conducted based on indications (ENT specialist, pediatric dentist, pediatric gynecologist, urologist, etc.).

7. Laboratory tests:

• **Blood tests**: Including clinical blood tests (increased ESR, leukocytosis with a shift to the left in the leukocyte formula), biochemical tests (elevated C-reactive protein levels, hypercreatinemia, and increased blood urea levels), and tests for antibacterial antibodies and bacteremia.

Urine tests: Using rapid diagnostic tests (leukocyte esterase for pyuria and nitrite tests), with specific changes such as hyposthenuria, microhematuria, and leukocytic casts. **What Instrumental Methods Are Used to Confirm the Diagnosis of PN?**

• **Kidney ultrasound**: The most important screening method for visualizing kidney pathology. Possible findings include an increase in the size of the affected kidney, thickening, and reduced echogenicity of the parenchyma due to edema and an increased cortico-medullary index.

• **Excretory urography**: It is not advisable, especially when obstruction of the urinary tract is suspected. In some cases, antegrade and retrograde contrast urography can be used to locate the stone. Spiral computed tomography can also be used for this purpose.

Instrumental methods:

• **Ultrasound (US)**: Of the kidneys and bladder, as well as excretory urography if needed (e.g., in cases of obstruction).

9. Additional examination methods:

Proteinogram (dysproteinemia); indicators of ALT, AST, bilirubin, determination of GFR; excretory urography; examination for urogenital infection; consulting specialists (dentist, ophthalmologist and others); radioisotope renoscintigraphy, computer tomography.

Treatment

Levels of Evidence and Classes of Recommendations

Classes of recommendations (the level of recommendation is related to the strength of the evidence on which it is based; it does not reflect the clinical importance of the recommendation):

- **Level A**: Evidence based on data from multiple randomized clinical trials or meta-analyses of systematic reviews.
- **Level B**: Evidence based on data from a single randomized clinical trial or multiple non-randomized studies.
- **Level C**: Consensus opinions of experts and/or a few retrospective studies or registries.
- **Level D**: Expert opinion.

Treatment should be initiated based on the diagnosis and the severity of the condition.

- **Antibiotic Therapy**:
  - **Level A recommendation**: Amoxicillin, co-amoxiclav, trimethoprim, and trimethoprim-sulfamethoxazole should not be used for empirical therapy.
  - Use evidence-based antibiotics with prolonged action, such as third-generation cephalosporins or aminoglycosides.
  - Severe UTIs: Parenteral therapy for 10–14 days, or until normothermia is achieved, with adequate hydration and third-generation cephalosporins.
  - Simple UTIs: Oral therapy for 5–7 days using third-generation cephalosporins.
  - For UTIs without a confirmed location: 7–10 days of therapy with nitrofurans (Furagin or Furamag) or third-generation cephalosporins.
- **Supportive Therapy**:
  - **Detoxification Therapy**: IV infusion of reosorbilact, saline, or 5–10 glucose solution for 3–5 days.
  - **Anti-inflammatory and antipyretic therapy**: Paracetamol or ibuprofen for 3-4 days.
  - **Spasmolytics**: As required.
- **Antibiotic dosing (level A recommendation):**
  - **Cefotaxime**: 75–100 mg/kg/day for 7–10 days.
  - **Ceftazidime**: 75–100 mg/kg/day.
  - **Ceftriaxone**: 75–100 mg/kg/day.
  - **Piperacillin/tazobactam**: 25–45 g, 3 times/day.

Rehabilitation:

Rehabilitation should be conducted for 3 months after achieving remission. This is typically carried out under local and national sanatorium conditions, with ongoing treatment (continuation of etiotropic therapy, physical therapy). Dispensary monitoring is maintained for 3 years after the active phase, with check-ups every 3 months. The main objective is to ensure the absence of recurrences of pyelonephritis.

Recommendations at Discharge:

Level A recommendations:

- After achieving remission, children should be monitored for 2 years if no recurrences occur.
- **Medical follow-up**: Conducted by district pediatricians and nephrologists.
- **Diet**: Continue Diet No. 5 with increased fluid intake.
- **Physical Activity**: Children should be exempt from physical exertion during the active disease phase, and contraindications for preventive vaccinations must be observed until remission is fully achieved.
- **Infection control**: Sanitation of chronic infection foci is essential.
- **Antibiotic therapy**: Administer antibiotics orally for up to 10 days, followed by the prescription of uroseptics (e.g., Biseptol at 5 mg/kg/day, Furamag at 5 mg/kg/day, or Fosfomycin depending on the child's weight) for 10 days. After this, continue in prophylactic doses for a month. If necessary, probiotics (e.g., Linex, Symbiter) may be prescribed for 10–14 days, as well as antifungal agents (e.g., Fluconazole at 3–6 mg/kg/day).
- **Vaccinations**: Can be resumed according to the schedule after one month of achieving remission.

Prevention:

Prevention measures should be taken for all children in the high-risk category, with the goal of preventing recurrences and disease progression.

Preventive care is carried out in the context of regular medical monitoring:

- **Regular blood tests**: Once every 3 months.
- **Urine tests**: Conducted every 14 days.
- **Urine culture tests**: Once a month.
- **Kidney US**: Once every 6–12 months.

For 3 to 12 months, a preventive course of uroseptics is administered, depending on the condition. If necessary, a vaccine regimen may also be considered (e.g., Uro-Vaxom, Urivac).

Requirements. Physical Activity.

During the period of pronounced clinical manifestations – bed rest for at least a week from the onset of the disease (or exacerbation). Activity can be gradually increased (room rest) as the pathological process subsides. Gradual inclusion of physical therapy exercises is advised. During remission, a general regimen is recommended according to age, with limitations on prolonged standing and avoidance of hypothermia. Under prophylactic therapy, outpatient monitoring is recommended. Physical and psychological overloads and hypothermia are contraindicated. Physical activity positively affects the overall health and functional state of the kidneys in individuals with chronic kidney disease. The success of exercise lies in cardiovascular training. Aim to follow these recommendations. Daily physical activity is better for your health than exercising 2–3 times per week.

Do not skip exercises on Sundays. The duration of physical activity should be at least 30 minutes per day if your condition allows. However, do not start with 30-minute sessions if you have not exercised before. Start with 3–5 minutes and increase by 1–2 minutes daily. The amount of physical activity depends on your condition. Walking is a standard form of exercise. Running is generally not recommended for people with chronic kidney disease. If your condition permits, the best activities for prolonging life are aerobic exercises: swimming, racket sports, and walking for more than 30 minutes a day. If you are unable to walk or are receiving dialysis, do arm and leg exercises, starting with 5–8 sessions lasting 4–6 minutes each, gradually increasing. Regularity is more important than the amount of exercise. Patients with chronic pyelonephritis, with sufficient kidney function and without significant hypertension (blood pressure not exceeding 170/100 mmHg), outside of exacerbations, can be recommended for sanatorium-resort treatment at balneological resorts using low-mineralization mineral water (Shayan, Truskavets, Karlovy Vary).

SELF-ASSESSMENT TESTS

1. Pseudomonas aeruginosa was isolated with a titer of 1 000 000 microbes per 1 ml from the urine of a 14-year-old boy with the exacerbation of secondary obstructive pyelonephritis. Which of the following antibiotics is the most advisable in this case?

A. Ciprofloxacin *C. Cefazolinum* *E. Chloramphenicol*
B. Ampicillin *D. Azithromycin*

2. A 9-year-old girl presents with fever up to 37.5°C, headache, inertness, weakness, loss of appetite, stomachache, and frequent painful urination. Provisional diagnosis of acute pyelonephritis is made. Clinical urine analysis shows specific gravity – 1018, no protein, leukocytes – 10–15 in the vision field. Which of the following investigation method can verify the diagnosis of urinary system infection?

A. Rehberg test (creatinine clearance test)
B. Bacteriological inoculation of urine
C. Zymnytsky test (measurement of daily diuresis)
D. Complete blood count
E. Clinical urine analyses, dynamic testing

3. A 13-year-oldgirl presents with fatigability, frequent headaches, cardialgia. Eight years ago she had a case of pyelonephritis. Urine analyses periodically revealed leukocyturia. The child has undergone no further treatment. On examination: her BP is 150/100 mm Hg. Ultrasound investigation reveales significant reduction of the right kidney. Which of the following process is leading in arterial hypertension pathogenesis in this case?

A. Disturbance of water-electrolytic balance
B. Disturbance of renal circulation
C. Hypersympathicotonia
D. Hyperactivity of renin-angiotensin system
E. Increased cortisol level

4. A 7-year-old boy has been an inpatient for 1.5 months. He had been brought to the hospital with complaints of edemas all over his body, low urine output, and headache. Clinical urinalysis shows proteins – 7.1 g/L, leukocytes – 1–2 in the vision field, erythrocytes – 3–4 in the vision field. During the course of treatment the edemas gradually dissipated, headache abated, diuresis normalized. Daily urine proteins are 3 g/L. Biochemical blood test shows total protein – 43.2 g/L, urea – 5.2 mmol/L, cholesterol – 9.2 mmol/L. Which of the following glomerulonephritis syndrome is the most likely to be present in the patient?

A. Mixed B. Nephritic C. Isolated urinary D. Hematuric E. Nephrotic

5. A 9-year-old girl presents with fever up to 38.5 °C, headache, inertness, weakness, loss of appetite, stomachache, and frequent painful urination. Provisional diagnosis of acute pyelonephritis is made. Clinical urine analysis shows specific gravity – 1016, no protein, leukocytes – 10–15 in the vision field. Which of the following investigation method can verify the diagnosis of urinary tract infection?

A. Zymnytsky test (density measurement of daily diuresis)
B. Rehberg test (creatinine clearance test)
C. Bacteriological inoculation of urine
D. Complete blood count
E. Clinical urine analyses, dynamic testing

6. During regular examination of a 2-yearold boy, he presents with enlarged left kidney, painless on palpation. The right kidney is undetectable on palpation. Excretory urography shows no contrast on the right. Cytoscopy detects hemiatrophy of the urinary bladder trigone, the right ureteral orifice is not detected. Which of the following pathology is it?

A. Dystopia of the right kidney
B. Agenesis of the right kidney
C. Hypoplasia of the right kidney
D. Agenesis of the right ureter
E. Ectopic right ureteral orifice

7. An 8-year-old girl with painful urination, frequent low-volume urination, and leukocyturia was diagnosed with acute cystitis. 10 days before the disease onset she was treated by the gynecologist for acute vulvitis. 5 days before she presented with mild catarrhal symptoms. Her mother ascribes the child's disease to her overexposure to cold. Specify the most likely infection route:

A. Descending B. Ascending C. Hematogenic D. Contact E. Lymphogenic

1 – A. **2** –B. **3** – D. **4** – E. **5** – C. **6** – D. **7** – B.

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Навчальне видання

МЕДИЧНА ДОПОМОГА ДІТЯМ З ГОСТРИМ ПІЄЛОНЕФРИТОМ

Методичні вказівки
для здобувачів вищої освіти 5–6-х курсів
вищих медичних закладів освіти III–IV рівнів акредитації
за спеціальністю «Медицина»,
лікарів-інтернів, лікарів-педіатрів,
лікарів загальної практики – сімейної медицини

Упорядники Іщенко Тетяна Борисівна
Гончарь Маргарита Олександрівна
Муратов Георгій Рафикович
Бойченко Альона Дмитрівна
Бужинська Надія Романівна

Відповідальна за випуск: Т. Б. Іщенко

Комп'ютерна верстка О.Ю. Лавриненко

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