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**URINARY TRACT INFECTION
IN CHILDREN**

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URINARY TRACT INFECTION IN CHILDREN

Учебно-методическое пособие



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Освещены вопросы этиологии, патогенеза, классификации, клинических проявлений
пиелонефрита, цистита у детей. Приведены современные рекомендации по диагностике, лечению,
профилактике рецидивирования инфекции мочевой системы.

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обучающихся на английском языке.

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INFECTION OF THE URINARY SYSTEM. DEFINITION

Infection of the urinary system (IUS) — a non-specific inflammation in the urinary system without a clear indication of the level of damage (urinary tract, bladder, kidney parenchyma).

Urinary tract infection (UTI) is an inflammatory process in the urinary tract (in the pelvis, ureter, bladder, urethra) without lesions of the renal parenchyma.

Pyelonephritis — when UTI involved the kidney (renal parenchyma). Pyelonephritis is associated with fever and systemic involvement.

Cystitis is an inflammatory process in the urinary bladder, usually fever is absent or low grade.

Up to 50 % of children with a UTI have a structural abnormality of their urinary tract. UTI is important because if the upper tracts are affected it may damage the growing kidney by forming a scar, predisposing to hypertension and, if bilateral chronic renal failure.

Frequency and structure. 3 % of girls and 1 % of boys have a symptomatic UTI before the age of 11 years, and 50 % of them have a recurrence within a year.

Frequency in Russian and Belarusian population — 12–4 ‰ (Russia, 1989, M. S. Ignatova), 26 ‰ (Ukraine, 1989, A. I. Hnatiuk), 14,8 ‰ (Belarus, 1987, I. N. Usov), Belarus — 19,8 ‰ (A. V. Sukalo, 2002).

In the structure of the IUS pyelonephritis is approximately 60–65 %. The ratio of girls : boys — 8–9 : 1.

FACTORS CONTRIBUTING TO THE DEVELOPMENT OF IUS IN CHILDREN

Factors associated with macroorganism:

1. Anatomical abnormalities of the urinary system and disturbance of the normal passage of urine.
2. Female. Inflammation of the external genitalia.
3. Immaturity of the immune defense, reducing antimicrobial immunity (neutrophil phagocytic activity, the level of secretory IgA, T-lymphocytes).
4. Factors leading to tubulointerstitial changes (crystals in the urine — oxalates, phosphates etc.).
5. Intestinal infections and disbiosis, constipation.

Factors associated with microorganism:

1. High “colonization” of potential uropathogenic microorganism (invasins, adhesins).
2. Resistance to antibacterial medications.
3. Products endotoxins.
4. Impedines (factors of persistence).
5. Metabolic features, L-shaped forms.
6. Atypical flora.

ETIOLOGY OF UTI

Gram-negative family of Enterobacteriaceae: E. coli, Klebsiella, Proteus. The most common cause of acute pyelonephritis is E. coli — 90 %, which has a large set of pathogenicity factors.

According to the microbiological monitoring at the 2nd Children's Hospital Minsk (National Center of Pediatric Nephrology and Renal Replacement therapy) — the main agents were — E. coli up to 80 % of cases, Proteus, Klebsiella, Pseudomonas.

PYELONEPHRITIS

Definition. Pyelonephritis (PN) — microbial-inflammatory kidney disease (two or one kidney) with preferential localization of pathological process in the tubulointerstitial tissue and pyelo-caliceal lesions.

CLASSIFICATION OF PN

PN classified as primary or secondary, acute or chronic.

Primary pyelonephritis — when using modern methods of examination fails to identify the causes of distinct contributing fixing microorganisms in the tubulointerstitial tissue.

Secondary pyelonephritis — microbial-inflammatory process formed on the background of the anomalies or malformations of the urinary system — CAKUT (congenital abnormalities of the urinary tract) — vesico-urethral reflux (VUR), obstructive uropathy, megaureter, posterior urethral valves etc.

Up to 50 % of children with UTI have a structural abnormality of their urinary tract — CAKUT.

UTI is important because if the upper tracts are affected, it may damage the growing kidney by forming scars, predisposing to arterial hypertension, if bilateral — to chronic kidney disease.

On activity PN. Acute PN classified according periods:

1. The period of active manifestations.
2. The period of regression of symptoms.
3. Complete clinical and laboratory remission.

Chronic PN: the gold standard investigation for the detection of renal cortical scarring is static renal scintigraphy with DMSA.

1. Relapse.
2. Partial clinical and laboratory remission.
3. Complete clinical and laboratory remission.

Assessment of renal function:

1. The functions of the kidneys preserved.
2. Impaired of the partial kidney function.
3. Chronic renal failure.

Pathogenesis. Upward path (80 %) of urinary tract infection and/or renal parenchyma — pyelonephritis is typical.

Fixation and colonization of uropathogens with damage of the tubules and interstitial kidney tissue, clinical and laboratory features of pyelonephritis.

Under the influence of appropriate treatment occurs sanitation tissue from microorganisms, restoration of function of the tubules and recovery. Possible the formation conditions (from the microorganism and/or bacterial uropathogens) for persistent infection and chronic microbial-inflammatory processes.

CLINICAL FEATURES OF UTI

Presentation of UTI varies with age:

In the newborn — symptoms are non-specific and include fever, poor feeding, vomiting and jaundice, septicemia may develop rapidly.

The classical symptoms of dysuria, frequency and loin pain become more common with increasing age.

Dysuria without a fever is often due to vulvitis in girls or balanitis in uncircumcised boys rather than a UTI.

Clinical features:

1. *Intoxication syndrome.* The temperature rise to febrile digits, paleness, weakness, drowsiness, fatigue, lack of appetite. In infants — refusal of feeding, fever, vomiting, diarrhea — a mask of intestinal infection or acute respiratory tract infection.

2. *Pain or abdominal syndrome.* In infants — the equivalent of pain could be cry, refusal of feeding, anxiety. In infants and preschool children the pain is localized around the umbilical area due to irradiation in the solar plexus. At school and adolescence pain is marked in the lumbar region.

3. *Urinary syndrome* — cloudy urine, proteinuria up 0.1 to 1–1.5 g/l, bacterial leucocyturia, decline in the relative density of urine, bacteriuria, casts.

4. *Dysuria syndrome* — rapid frequent (pollakiuria), painful (strangury) micturition, incontinence indicate the presence of lower urinary tract infections and urinogenic path of infections. Voiding of micturition in pyelonephritis is due to involvement in the pathological process of the bladder.

How to diagnose UTI:

1. *Total blood count* — leukocytosis with neutrophil shifts, increased ESR, could be anemia.

2. *Urinalysis* — leukocytes, protein, epithelium, casts.

3. *Biochemical analysis of blood* (urea, creatinine, electrolytes, increased C-reactive protein (CRP)).

4. *Urine culture flora* and sensitivity/resistance to antibiotics (E. coli in diagnostic titer more than 10^5).

5. Quantitative analysis of urine (Nechiporenko) — leucocyturia.

6. Biochemistry of urine: 24 hours urinary protein excretion, salts.

7. Immune system investigation.

Additional methods — investigation on chlamydia, mycoplasma (polymerase chain reaction — PCR), fungi, Mycobacterium tuberculosis (urine culture, methods of rapid diagnosis) when prolonged course of UTI and there is no effect on the “traditional” therapy, or positive family history.

ADDITIONAL METHODS FOR DIAGNOSTICS

Additional methods also include:

1. **Ultrasound:** helps to reveal structural renal disease, renal agenesis, vesico-urethral reflux (VUR), cysts etc. (figure 1).

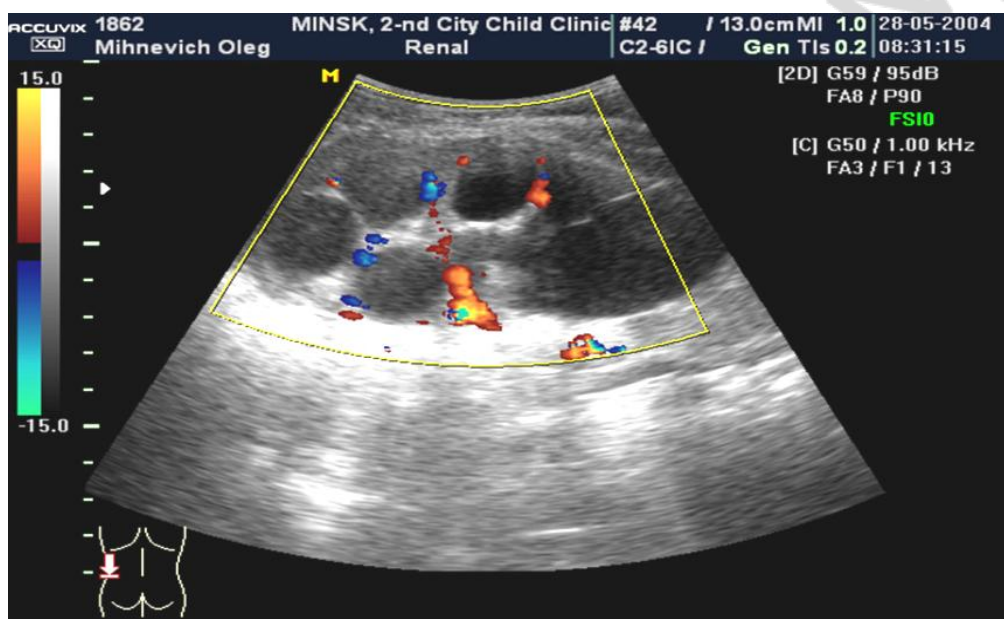


Figure 1. Hydronephrotic transformation of the left kidney. Severe dilatation of pelvis and calyces. Doppler: reduced renal blood flow

2. **Micturition urography.** Voiding (Micturition) cystourethrography (MCUG) — assessment of anatomic and functional state of the bladder, urethra, reveals reflux (reverse flow urine during micturition).

Gold standard for diagnostic of vesico-urethral reflux. VUR divided on primary (developmental anomaly of the vesico-urethral junction) or secondary (associated with bladder pathology) (figure 2–5).

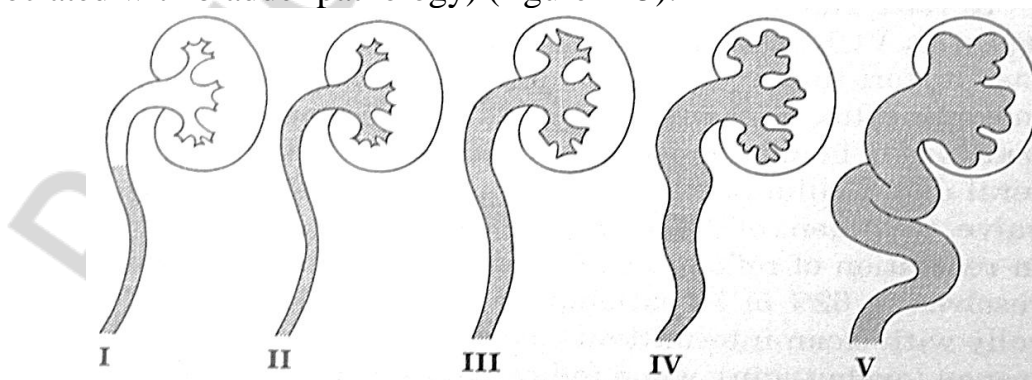


Figure 2. Five grades of vesico-urethral reflux

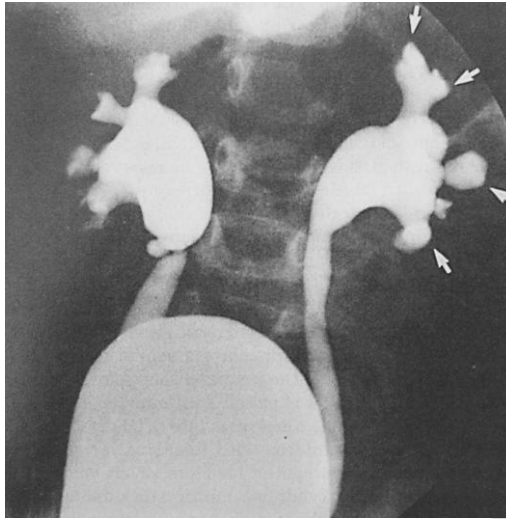


Figure 3. Bilateral vesico-urethral reflux, stage V. Bilateral severe dilatation of pelvis, calyces, ureters

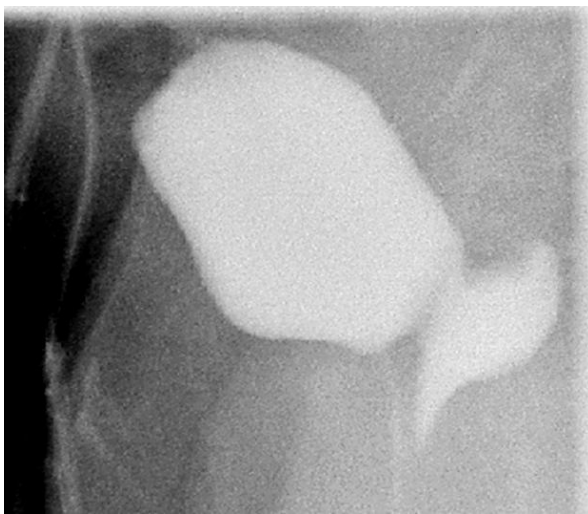


Figure 4. Micturition with reflux in the vagina

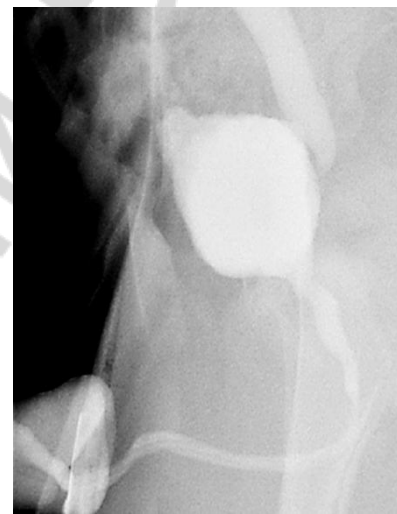


Figure 5. Micturition with reflux in the foreskin

Indications for MCUG — when hydronephrosis is bilateral, present in a solitary kidney or associated with ureteric dilatation.

3. Intravenous (IV) or Excretory urography reveals. Anatomical features of the structure of the kidneys, their status, mobility, shape, size, structure and condition of the renal pelvis system, ureters, and bladder (figure 6, 7).

Indications for IV urography:

- suspicion of malformation of the urinary tract;
- obstructive uropathy, identified by ultrasound and radionuclide study;
- renal colic;
- recurrent abdominal pain of unknown etiology;
- voiding dysfunction.

Contraindications to the IV Urography:

- inflammatory diseases of the kidney in acute phase;
- high level of creatinine and urea in the blood;

- low urinary relative density;
- allergic reaction to the X-ray solution.



Figure 6. Shoes-shoe kidney revealed by IV urography



Figure 7. Hydronephrotic transformation of the right kidney revealed by IV urography

4. Renal scintigraphy. Indications for static kidney scan Ts99/DMSA:

- Anomalies relationship, hypoplastic kidney, polycystic disease, destructive lesion of the parenchyma, volume formation.
- Detection of renal scarring tissue — the “gold standard” for the diagnostics of chronic pyelonephritis.

DMSA is taken up though not excreted by (predominately proximal) renal tubular cells (figure 8).

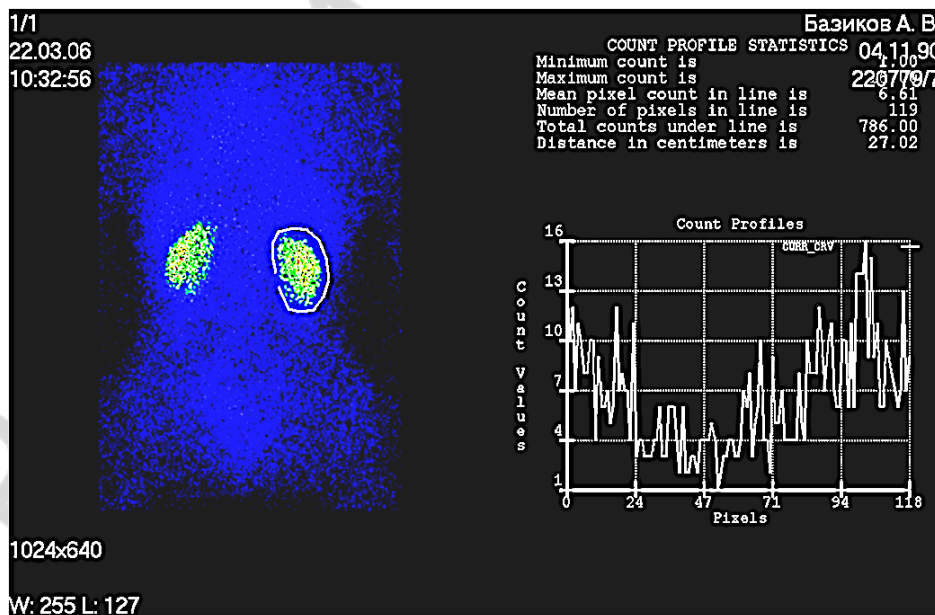


Figure 8. Normal uptake of Ts99

The image produced is that of functioning renal cortical mass and technique is the gold standard investigation for the detection of renal cortical scarring (figure 9). May also be helpful in identifying ectopic kidneys or confirming non-function. Information is also generated about differential renal function (the relative contribution of each kidney to total renal function).

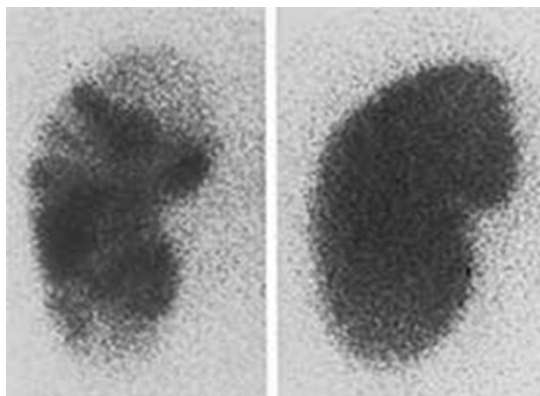


Figure 9. Renal scars of the left kidney revealed by scan

Many children diagnosed with renal scarring may in fact have congenitally dysplastic kidneys.

Dynamic renography (the DTPA or MAG3 scan) is used to detect the presence and site of urinary tract obstruction. Isotope is injected with furosemide.

1. Cystoscopy.
2. Computer scanning.
3. Magnetic resonance imaging.

Urologist/gynecologist — for diagnosis of penis (foreskin) or vulvitis (vaginitis) external genital infection.

Criteria for diagnosis of PN:

1. Symptoms of intoxication.
2. Inflammatory reaction of blood.
3. Proteinuria up to 1 g / l in combination with leukocyturia and bacteriuria.
4. Reduction of tubular functions.
5. Changes of pyelo-caliceal system with ultrasound and X-ray examinations.

CRP is usually used as a diagnostic marker — more than 20 units are typical for pyelonephritis.

CYSTITIS

Cystitis — inflammation of the mucous of the bladder, accompanied by a violation of its functions.

Classification:

1. On etiology: infectious, radioactive, medications, postoperative.
2. According to the cystoscopy changes: diffuse, focal.
3. Acute, chronic (cystoscopy).

Clinical picture: frequent, painful micturition, painful palpation of the bladder, no signs of intoxication.

Urinary Syndrome: white blood cells, desquamated epithelium; presence of bacteria.

Laboratory data: neutrophils in the urine; increased number of squamous cells; terminal hematuria; proteinuria small, less than 0.1 g / l).

THERAPY OF UTI

1. Regime (bed in acute PN, frequent emptying of the bladder, personal hygiene).

2. Diet (lacto-vegetarian).

3. High amount of liquids.

4. Infusion therapy if indicated (0.9 % sodium chloride, 5 % glucose).

5. Etiologic treatment (antibiotics).

6. Herbal medicine.

7. Physiotherapy.

8. Preventive/prophylaxis treatment if indicated.

Etiologic treatment: antibacterial medications. There are 3 groups of choice:

1. Protected penicillin (PP).

2. Cephalosporin II or III generation.

3. Aminoglycosides.

Among **Protected Penicillin's**:

1) amoxicillin + clavulanic acid (Augmentin, amoksiklav, flemoklav) — dosage 20–40 mg/kg/day;

2) ampicillin + sulbactam;

3) piperacillin + tazobactam (tazocin);

4) ticarcillin + clavulanic acid (Timentin).

Cephalosporin's generations II or III are highly active against *E. coli*.

Generation IV (Ceftaredim and cefepime) advisable to appoint during severe course of pyelonephritis and confirmed etiological role of *Pseudomonas aeruginosa*.

Prescription of 1st generation of cephalosporin is impractical because they have insufficient activity against gram-negative flora.

The presence of oral and parenteral forms of the antibiotics can be used for one group of sequential therapy (start intravenous or intramuscular for 3–5–7 days and continue orally for the total duration of 10–14 days).

The safest among **modern aminoglycosides** is netilmicin (netromycin). Amikacin is the drug of choice in the treatment of PN in children caused by *K. pneumoniae*, *Pseudomonas aer.*, *Enterobacter spp.*

Prescription in acute exacerbation of chronic PN Nitrofurans, Nitroxoline, Bisepolum, Nalidixic acid is impractical due to the fact that these drugs do not provide sanitation contribute to the renal parenchyma and chronic process.

Fluoroquinolones (ciprofloxacin, ofloxacin, etc.) in children is generally not used (before age 17–18 y.o.) (because of severe side effects on cartilages in experiment on young animals). An exception for fluoroquinolones severe course of the disease with the release of uropathogens multiresistant to other antibiotics.

Cystitis or pyelonephritis with not severe course — use oral forms.

In moderate and severe forms — sequential therapy — parenteral administration of AB drug (IV or Intra/muscular) for 5–7 days followed by oral administration of the same AB in the next 7–10 days, for example: Augmentin IV → Augmentin orally; cefuroxime IV → cefuroxime (Zinnat) orally; cefamandole IV → oral cefaclor; ceftriaxone IV → ceftibuten (cedeks) orally.

The duration of AB therapy for treatment of pyelonephritis is 10–14 days, for cystitis — 5–7 days.

Medications for treatment of cystitis:

1. Augmentin (amoxicillin + clavulanic acid) in tabs or suspension — 20–40 mg/kg/day.
2. Nitrofurantoin in capsules 0.025 g and 0.05 g — 5–7 mg/kg/day.
3. Nalidixic acid in tabs 0.25 g and 0.5 g — 30–60 mg/kg/day.
4. Co-trimoxazole in tabs 0.12 g or 0.48g, in suspension 240 mg / 5 ml — dosage 6 mg/kg/day of trimethoprim.
5. Monural (fosfomicin trometamol). Powder 3 grams, children 1–2 g 1 time/day.

PROPHYLAXIS (ANTI-RECURRENT) THERAPY

Indications and duration for prophylaxis therapy are presented in the table 1.

Table 1

Prophylaxis (anti-recurrent) therapy: indications and duration

Indications	Duration
1. Children under 2 years after acute PN	During 2 months before micturition cystography
2. Obstructive uropathy	Long-time, before surgical correction.
3. Vesico-urethral reflux	The duration of prophylaxis is long-term preservation of reflux
4. Relapsing UTI (3 or more relapses within a 1 year)	6 months – 1 year

Medications for prophylaxis (anti-recurrent) therapy. Use uroseptic medications in sub inhibitors doses (20 % of the therapeutic dose) overnight (table 2).

Table 2

Medication	Dosage
Nitrofurantoin	1–2 mg/kg / 1 time overnight
Co-trimoxazole	1–2 mg/kg of trimethoprim 1 time overnight
Nalidixic acid	5–10 mg/kg / 1 time overnight
Nitroxoline	3–5 mg/kg 1 time overnight

Additional therapy:

1. Immunomodulatory therapy.
2. Antioxidant agents (vitamins A, E, C).
3. Correction of intestinal microflora (normal daily stool).
4. Phytotherapy.
5. Physiotherapy during the period of clinical and laboratory remission.

LITERATURE

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