

**DULY DIAGNOSIS OF URINARY INFECTIONS IN CHILDREN AND ANALYSIS OF
MODERN APPROACH TO THE THERAPY**

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✓ **Resume**

Thus, the need for early diagnosis and adequate antibacterial therapy of urinary system infections in children and adolescents is justified by the fact of the development of subsequent adverse disabling conditions (the development of arterial hypertension in young age, chronic renal failure, etc.). This article analyzes the current state of this problem in the studied industry.

Key words: urinary tract infection, children, diagnosis, treatment.

**АНАЛИЗ СОВРЕМЕННОГО ПОДХОДА К СВОЕВРЕМЕННОЙ ДИАГНОСТИКЕ И
ЛЕЧЕНИЮ ИНФЕКЦИЙ МОЧЕВЫВОДЯЩИХ ПУТЕЙ У ДЕТЕЙ**

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✓ **Резюме**

Необходимость ранней диагностики и адекватной антибактериальной терапии инфекции мочевой системы у детей и подростков, обосновывается фактом развития последующих неблагоприятных инвалидизирующих состояний (развитие артериальной гипертензии в молодом возрасте, хронической почечной недостаточности и др.) В данной статье анализируются современные состояния данной проблемы в исследуемой отрасли.

Ключевые слова: инфекция мочевыводящих путей, дети, диагностика, лечение.

**БОЛАЛАРДА СИЙДИК ЙЎЛЛАРИ ИНФЕКЦИЯЛАРИНИ ЎЗ ВАҚТИДА
ТАШХИСЛАШ ВА ДАВОЛАШГА БЎЛГАН ЗАМОНАВИЙ ЁНДОШУВИНИ ТАҲЛИЛИ**

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✓ **Резюме**

Болалар ва ўсмирларда сийдик йўллари инфекцияларини эрта ташхислаш ва адекват антибактериал терапиясини олиб бориш зарурати кейинчалик ноҳуш бўлган ногиронликка олиб келувчи ҳолатларнинг (эрта артериал гипертензия, сурункали буйрак етишмовчилиги ва бошқа касалликлар) ривожланиши билан асосланади. Ушбу таҳлилий илмий тадқиқот ўтказилган соҳадаги замонавий аҳоли таҳлили берилган.

Калит сўзлар: сийдик йўллари инфекциялари, болалар, ташхислаш, даволаш.

Relevance

Most of the patients suffering urinary infections (UI) are girls, but among newborn babies, that infection is 4 times more often diagnosed in boys [4]. Among the children, under seven about 7 - 9% of girls and 1.6-2% of boys at least once have bacteriologically confirmed diagnosis of UI.

According to location there are upper (pyelonephritis) and lower urinary (cystitis,

urethritis) infections. Children have pyelonephritis and cystitis more often. On the basis of the results of urinary bacteriological tests it can be concluded that the range of micro flora is effected by lots of factors such as age, gender, term of disease (debut or relapse), conditions of disease development (in hospital or out of it), anatomical obstruction, functional immaturity, resistance in a child's body and

social circumstances. Out of hospital, there is prevalence of *E. coli*, while clinical conditions the role of certain strains of *Proteus*, *Klebsiella* is significant.

In most cases UI is caused by a certain kind of micro organisms. Majority of nephrologists consider that viruses serve the basis for development of bacterial infection.

Fungous lesions in urinary duct, as a rule, can be observed in children with immune deficiency (preterm babies, children with congenital defects, fetal infection, and protein-energetic deficit). In most cases we can observe association of bacteria with fungi.

There are urinary, hem, and lymphatic ways of urinary infection transmission. Within newborn period the dominant way is hematogenic one. Later, particularly among girls, the first place is taken by urinogenic way. That happens due to shorter urethra in girls, compared to boys, and location of external urethral opening close to anus causing frequent contact with fecal masses. In urinogenic way of transmission important part is played by a phenomenon of bacterial adhesion, in other words certain micro organisms attach to mucous membrane of urinary ducts with the help of pili, resist opsonization and phagocytosis, release endotoxin and move against natural flow of urine. In children 40-60% of vesicoureteral reflux cases cause development of secondary pyelonephritis. At the time urine excretion the pressure in bladder rises and due to the reflux urine goes to calicies and pelvis of kidney [5].

Complete and regular emptying of bladder, high and low pH of urine, high urinary osmolarity, high concentration of antibodies in serum are considered to be the mechanisms of protection against reproduction of bacteria in urinary ways. Development of pyelonephritis is caused by multiple risk factors. In children, under 2 endogenic risk factors include development of urinary infection due to urinary bladder reflux. Later, the role of exogenic factors such as unfavorable ecologic conditions, irrational nutrition, chronic infections in the family, stress and other factors increases.

The risk of hematogenic transmission is higher in cases of sepsis and apostematous nephritis. Lymphogenic transmission is disputable. Inoculation of uropathogenic bacteria in the bladder does not always cause inflammation. In spite of being a good nutritious medium, urine in healthy children is considered to be sterile, except the distal part of urethra. Together with mechanical wash out of microbes with urine there are several factors protecting

mucous membrane of the bladder. Cellular layers of transient epithelium have mucopolysaccharide-glycosaminoglycan coating; it is hydrophilic and makes bacterial adhesion complicated, by these means preventing contact of bacteria with uroepithelium. Normally, in the bladder bacteria are eliminated within 15 minutes. When the amount of residual urine increases, local protection in the bladder diminishes significantly. It is known that, if urinary bladder is frequently emptied the concentration of bacteria decreases several times, and that is considered to be one of UI prevention ways. However in young children (4-5 years old) incomplete emptying of the bladder is physiological. Incomplete emptying of the bladder is often observed in cases of chronic constipation. Antimicrobial properties of urine are conditioned by its high osmolarity, low pH, high rate of urea and organic acids. These properties of urine are not expressed in infants and that increases the risk of UI infection in young children. When there are congenital defects such as fistula between the bladder and vagina or bladder and colon micro organisms penetrate the bladder. Normally, peristalsis in urinary ducts and their conjunction prevent bacteria from going to urinary ducts and elevation to calicies. Any disorders in urodynamics causing dilatation of urinary ways makes elevation of microorganisms easier. Microbial inflammation is mostly observed in renal cortex and papillae, which can be explained by low intensity of blood flow, low pH, high osmolarity and high concentrations of ammonia here. These factors provide favorable conditions for bacterial growth and suppress leukocytes hem taxis.

Clinical symptoms include frequent painful small amount urination (dysuria), epipubic pain, incomplete emptying of the bladder, urinary incontinence, subfebrile or normal body temperature. In common urine analysis we can see leukocyturia and bacteriuria.

Clinical symptoms of pyelonephritis include rise of body temperature above 38° C, stomachache and pain in spine, symptoms of intoxication (pallor, weakness, low appetite, headache, vomiting). In common urine analysis there is leukocyturia, bacteriuria, proteinuria (usually does not exceed 1g a day); in common blood analysis there is neutrophilic leukocytosis with shift to the left, ESR rise (above 20 mm/s), high CRP and procalcitonin.

In new-born and young children clinical presentation of UI is characterized by non-specific symptoms of intoxication such as fever,

pallor or marble-like skin, weakness, low appetite, vomiting, no weight gaining or weight loss, and diarrhea. In children under one anxiety and cry before, during and after urination, red face, small portions of urine, breaks in urination, and weakness can be equivalent of dysuria.

In elder children together with symptoms of intoxication, we can observe local symptoms such as stomachache and pain in spine, painful palpation and knocking of costovertebral angle, pain in epipubic area and dysuria.

In diagnosis of children with suspicion of UI the preference should be given to non-invasive methods with high sensitivity. The diagnosis of UI in young children (new-born and children under 2) causes certain difficulties. There are several reasons for that:

1. Manifestation of UI in young children is non-specific; UI can be underdiagnosed if based on body temperature measurement.

2. Problems in urine collection: in new-born and young children pure urine can be taken only by invasive way (transurethral catheterization of the bladder)

Symptoms of UI and significance of diagnostic methods.

A) Rise of body temperature. The basic reasons of rise of body temperature in 3-20% is pneumonia, bacteremia, meningitis and UI. Attention should be paid to children with body temperature 39°C and higher.

B) Isolation of microbe in urine. According to Kate Verrier-Jones (2007) the best method for children is collection of freely excreted urine. Bladder catheterization should be used only in cases when collection of urine with the help of non-invasive methods is impossible, but, anyway, it should be preceded by US to confirm there is some urine in the bladder. For isolation of microbe urine can be collected into clean dish during free urination after careful cleaning of the area. The diagnosis of UI is cancelled if there is no microbe in urine. The following bacteriuria parameters are significant:

1. There are 100 000 and more microbes in 1 ml of urine collected during free urination;

2. There are 10 000 and more microbes in 1ml of urine collected using catheter;

B) Clinical analysis of urine. Diagnosis of UI in children can be performed with the help of screening test for detection of leukocyte esterase and nitrites. Absence of esterase and nitrites serves the basis to say it is not UI [8].

Correct collection of urine and correct microscopy (calculation of leukocytes) can

provide 100% sensitivity and 97% specificity of the results. Results depend on the qualification of the specialists and the time of checking urine. Tests performed in three hours after collection of urine diminish the accuracy of the results by 35%.

Most pediatrician-nephrologists think it is enough to calculate the number of leukocytes in the field of vision and to perform common urine analysis for the detection of leukocyturia. Leukocyturia criteria: number of leukocytes in the field of vision in common urine analysis >5.

Instrumental methods of UI diagnosis include:

1. Ultra sound imaging (USI). It is considered to be non-invasive diagnostic method applied in children with UI. USI can be performed at any time convenient for a patient and doctor. It provides a possibility to detect urinary developmental abnormalities (hydronephrosis, dilatation of the distal part of urinary ducts and pelvis, hypertrophy of the bladder walls, urolithiasis). Besides that, USI can help to detect signs of acute renal inflammation and renal shrinking [15].

2. Cysturethrography is recommended for all children with UI under 2. Necessity of such an approach is conditioned by the high prevalence rate of renal reflux in children (prevalence of renal reflux among the children with UI under 1 is 50%). Shrinking of kidney is observed 4-6 times more often among the children with IV and V stages of reflux compared to those with I,II, and III stages. The earlier reflux is diagnosed the greater is the chance to choose correct therapy and to prevent relapses, which in its turn prevents development of reflux nephropathy and chronic renal failure [9, 17, 32].

- 3) Scintigraphy (renoscintigraphy – RSG). Static nephroscintigraphy with Technetium-99m-dimercaptosuccinic acid (DMSA) provides the possibility to detect complications of UI such as pyelonephritis and shrinking of kidneys [10]. Nowadays, RSG is considered to be the most accurate method for detection of kidney shrinking in children. Sensitivity of RSG is 84%, and its specificity is 92%.

Static RSG is limited by detection of parenchymal defects, while dynamic one helps to clarify possibility of renal duct obstruction.

- 4) Excretory urography. For a long period of time excretory urography was considered to be the only method for detection of urinary tract abnormalities, though USI is safe, non-invasive, and economically more preferable. That is why

indications for excretory urography were limited.

5) Cystoscopy. Cystoscopy is not the basic method of instrumental diagnostics of UI in children, as it demands a qualified specialist and high quality equipment.

In children suffering UI it is important to start antimicrobial therapy as soon as possible. Delay of adequate antimicrobial therapy in children can lead to severe complications including damage of renal parenchyma (with formation of shrinking areas) and development of urosepsis. Results of static scintigraphy performed in 120 hours after the initiation of the therapy showed (Hiraoka M. et al., 2003), that start of recommended antimicrobial therapy within initial 24 hours in children with the rise of body temperature and suspicion of UI provides complete elimination of focal defects in renal parenchyma. Late initiation of the therapy (2-5th days) results in development of parenchymal defects in 30-40% cases.

Choice of the therapy of UI for children is based on the knowledge of dominant uropathogens in that age, supposed antibacterial sensitivity of micro flora and clinical health status. Empiric choice of protected penicillin, cephalosporins III generation, parenteral or per os aminoglycosides has proven its efficiency [3, 5]. According to Allen U.D. et al. (1999), sensitivity of *E. coli* to aminoglycosides can reach 98%. The main problem in the choice of antimicrobial therapy for UI is development of urinary micro flora resistance. Resistance mostly develops in cases of abnormalities of urinary tract, long-term application of antibiotics or violation of doses and terms. That is why while changing antibacterial therapy it is important to take into account confirmed sensitivity of urinary micro flora to antimicrobial agent.

Parenteral (intra venous or intra muscular) injection of antimicrobial agent is indicated when there is high body temperature, intoxication, and no possibility of per os therapy. parenteral method is recommended to reach optimal antimicrobial concentration in blood, elimination of acute infection, prevention of urosepsis and renal lesions. In children with UI it is recommended to inject a day dose of aminoglycosides and ceftriaxone intravenously once a day, while intramuscular injections should be performed in compliance with standard recommendations. When clinical status of a patient improves (usually in 24-48 hours after start of the therapy) and there is no vomiting the injection of the agent can be

changed to per os administration.

In plenty of randomized studies it was confirmed that duration of antimicrobial therapy in children with UI varies from 1 day (cystitis) to 14 days [8, 13]. Optimal total duration of UI therapy is 10-14 days.

Assessment of the efficacy of antibacterial therapy

- Improvement in clinical symptoms in 24-48 hour after the initiation of the therapy.
- Eradication of micro flora (in case of correct therapy urine becomes sterile in 24-48 hours).
- Decrease or elimination of leukocyturia in 2-3 days after start of the therapy.

Absence of remission at the 14th day of the therapy can be observed in children with abnormalities of urinary system. Expediency to continue antibacterial therapy is decided after repeated check-up of the child including urine test, definition of microbial sensitivity to antimicrobial agents, and microscopic tests of urine.

The patient required urologist's consultation.

Obligatory tests performed during the term of antibacterial therapy:

1. Urine microscopic tests are performed at the 2-3 days of the therapy. Absence of clinical status improvement within initial 48 hours of the therapy is indication for definition of bacteriuria stage and sensitivity of urinary micro flora to antimicrobial agent.

2. After the end of antibacterial therapy microscopic urine tests are performed. It is recommended to perform common blood analysis.

Antibacterial agents recommended for the therapy of cystitis in children.

For the therapy of cystitis antibiotics with high degree of urinary excretion are chosen. Drugs of choice for peroral administration are protected penicilins, cephalosporins II and III generation, and furazidine.

Antibiotics recommended for the therapy of pyelonephritis in children.

Results of meta-analysis of randomized studies performed in various countries show that peroral antibiotic administration can be recommended for the therapy of pyelonephritis without complications in children. It was proven that remission and its duration do not depend on the type of antibiotic administration. When there is necessity in parenteral injection of antibiotic it is injected intravenously or intramuscular not more than 2-3 days. After that child starts

administering the agent per os. Cephalosporins are very efficient in children with pyelonephritis without complications. Per oral administration of cephalosporins III generation has bactericidal effect on gram positive and gram negative micro flora; and that makes it convenient for application in children.

Preventive therapy against recurrent pyelonephritis is performed in out-patient polyclinic conditions and it is based on long-term administration of small doses of antibacterial agents. Administration of antimicrobial agents in sub-inhibitory doses (20% of therapeutic dose) is considered to be the most effective method [16]. Agents recommended in sub-inhibitory doses have following advantages: low concentrations preserve ability to prevent bacterial adhesion; do not affect intestinal micro flora; recommended once a day (in the evening); keep constant concentration in the bladder at night; have good tolerance rates in patients; reliably diminish frequency of relapses. In pediatric practice

for prevention of relapses therapeutic agents recommended in most cases are nitrooline, 5-NOK, furamag, protected penicillin. The terms of anti-recurrent therapy of acute pyelonephritis is 3-6 months and chronic pyelonephritis from 6 months to a year.

During remission in out-patient-polyclinic conditions at the same time with anti-recurrent therapy it is recommended to prescribe a therapy for improvement of urine passage, decrease of inflammation, improvement of blood circulation in kidneys, and phytotherapy.

It is recommended to drink certain tinctures and decoctions made of herbs (corn silk, rose hip, dandelion, sage, St.John's wort, etc) for 10 days every month.

Physiotherapeutic methods (UHF, ultra sound, ozokerite, paraffin applications, electrophoresis of 1% furadonin solution on the area of kidneys, therapeutic baths, and mineral water) are applied when the activity of the process diminishes during clinical-laboratory remission to prevent relapses.

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