

Management of urinary tract infections in children

Natalie Schellack,¹ Cahlia Naested,² Nicolene van der Sandt,³ Neelaveni Padayachee⁴

¹ Associate Professor, School of Pharmacy, Faculty of Health Care Sciences, Sefako Makgatho Health Sciences University

² Pharmacist at Netcare Greenacres Hospital

³ Community Service Pharmacist, Madibeng Sub-District Pharmacy, Department of Health, North-West Province

⁴ Pharmacy and Pharmacology, University of Witwatersrand

Correspondence to: Natalie Schellack, e-mail: natalie.schellack@smu.ac.za

Keywords: urinary tract infection (UTI), paediatrics, antibiotics, sepsis, cystitis, pyelonephritis

Abstract

Urinary tract infections (UTIs) are a common occurrence in paediatrics. UTIs present in children as fever, anorexia, vomiting, lethargy and dysuria. Approximately 80% of the time, *Escherichia coli* is the causative bacteria in paediatrics, however, fungal UTI caused by *Candida* species can occur in premature infants. With an estimated 150 million UTIs occurring worldwide annually, this paper aims to establish the ideal management of urinary tract infections in paediatrics. Clinical signs and symptoms of UTI in paediatrics are dependent on age of the child. Neonates (0–27 days old) present with sepsis, vomiting, fever, and prolonged jaundice, while school aged children present with symptoms similar to adults such as dysuria and urgency. Diagnosis of a UTI can be done by using a urine dipstick or using the midstream clean catch method in toilet trained children, and using the transurethral catheterisation or suprapubic aspiration method for infants and young children. In the wake of antibiotic resistance, choosing the best anti-microbial agent for treatment is imperative. Whilst asymptomatic bacteriuria does not require antibiotic treatment, amoxicillin and clavulanic acid combination, cephalixin, cefixime and cefpodoxime are the preferred oral antibiotics, provided there are no known allergies. Ceftriaxone, ampicillin, cefotaxime and gentamycin are the recommended parenteral antibiotics, provided age, allergic status and renal function are considered prior to use. Careful consideration needs to be given before using prophylaxis in UTIs and should be reserved for extreme cases.

© Medpharm

S Afr Pharm J 2018;85(6):54-58

Introduction

Urinary tract infection (UTI) is defined as a significant growth of bacteria in the urine, together with fever, lethargy, dysuria, pain, anorexia, vomiting and possible kidney scarring.^{1,2,3} UTIs are usually caused by gram-negative aerobic bacilli; approximately 80% are caused by *Escherichia coli*.^{2,4} Other causative enterobacteria include *Enterobacter*, *Citrobacter*, *Proteas*, *Providencia*, *Morganella* and *Serratia*.⁴ *Proteus* is common in boys and in children with renal stones.⁵ Coagulase-negative Staphylococci have also been isolated.⁵ Premature infants can also develop a fungal UTI, usually caused by *Candida* species.⁴

Classification of UTIs

Urinary tract infections may be classified as follows:

- Asymptomatic bacteriuria: is the absence of clinical signs and symptoms with the presence of bacteriuria.
- Cystitis: localised to the urethra and bladder. Dysuria, frequency, urgency, cloudy urine and lower abdominal discomfort are diagnostic symptoms, while pyuria and haematuria can also occur. This condition is common in girls over two years of age.
- Acute pyelonephritis (AP): presents systemically as high fever, malaise, vomiting, abdominal and loin pain and tenderness,

poor feeding and irritability in infants.⁶ AP is a serious bacterial illness and has a high risk of sepsis and meningitis in young children.⁷

- Uncomplicated UTI: infection is limited to the lower urinary tract and there are no associated urological anomalies. Symptoms include dysuria, frequency, urgency, cloudy urine and abdominal discomfort. Urine dipstick tests are positive for leukocyte esterase, nitrites and haematuria.^{8,9}
- Complicated UTI: an infection of the urinary tract involving the renal parenchyma (AP) or which is associated with underlying congenital anomalies of the kidneys or the urinary tract. It may result in significant short-term morbidity, including septic shock and acute renal failure, especially in infants.^{8,9}

UTIs can be a significant source of morbidity in paediatrics and is a common cause of acute illness.^{1,10} Congenital genitourinary conditions, immature host defences, female gender, lack of circumcision in boys, and a prior history of UTI, are all risk factors for UTIs in paediatrics.¹¹ According to Alper, 7% of girls and 2% of boys will have a UTI that is culture-confirmed and symptomatic by the age of six.⁵

In both sexes, in the first year of life, febrile UTIs show the highest incidence whilst non-febrile UTIs occur predominately in girls older

than three years of age.¹² Diagnosing UTI in paediatrics can be a challenge because the clinical presentation may be nonspecific in infants. Invasive methods like urethral catheterization are needed to obtain a reliable urine culture, and for this reason there may be a delay in diagnosis and treatment.¹³ Boys under the age of one have a higher incidence of UTI; however, UTI prevalence increases in girls after the age of one. Renal scarring is thought to develop after a single UTI in approximately 15–41% of children and chronic kidney disease, proteinuria, hypertension, and complications during pregnancy (if applicable) some few of the long-term problems.¹

More than 6 billion dollars in direct healthcare costs are incurred by an estimated 150 million cases of UTI that occur annually worldwide.¹⁴ With pyelonephritis, younger age, male gender, higher comorbidity status, and concurrent hydronephrosis, stones or sepsis being the strongest predictors for inpatient admission, early signs and symptoms of UTIs in paediatrics need to be identified and treated aggressively to potentially reduce direct healthcare costs.¹¹

The ages of paediatric patients were categorised according to the paediatric terminology defined by the National Institute of Child Health and Human Development (NICHD) (2015), developed by Eunice Kennedy Shriver in the USA (Table 1).

Table 1: The 2015 classification of paediatric patients according to the National Institute of Child Health and Human Development

Classification	Months/Years
Neonates	0–27 days
Infants	Birth to 12 months
Toddlers	13 months to 2 years
Early childhood	2–5 years
Middle childhood	6–11 years
Early adolescence	12–18 years
Late adolescence	19–21 years

Pathogenesis

UTIs typically develop when uropathogens that have colonized the periurethral area ascend via the urethra to the bladder. The pathogens can then spread from the bladder to the kidneys (pyelonephritis) or to the blood stream (bacteraemia). Pathogens can also infect the urinary tract through the direct spread via the faecal-perineal-urethral route.¹⁵

Clinical signs

Clinical signs and symptoms depend on the age of the child.

Diagnosis

A urine dipstick test can be done for screening purposes, and if the dipstick test reveals the presence of leucocytes or nitrites, a clean urine sample should be obtained and sent for microscopy, culture and sensitivity testing.^{8,9,16}

For infants and young children the urine sample should be obtained by transurethral catheterisation or suprapubic aspiration. For older, toilet-trained children, the urine sample can be obtained using the mid-stream clean catch method.^{4,8}

Criteria for the diagnosis of a UTI:^{8,9}

Any culture from the suprapubic urine sample

- A culture of >100 colonies/ml urine of a single organism from a catheter specimen
- A pure culture of >100 colonies/ml in a midstream clean catch sample
- A consistent culture of a pure growth even with low counts.

A renal ultrasound is recommended for all children who have their first culture-confirmed UTI to assess for structural and functional abnormalities of the urinary tract. Abnormalities include vesicoureteric reflux, posterior urethral valves, ectopic ureters, polycystic kidneys and renal dysplasia. Should the ultrasound reveal an abnormality, a micturating cystourethrogram (MCUG) should be done.^{4,8,9}

Treatment

Treatment should be tailored to the clinical severity, paediatric age, urosepsis suspicion, non-compliance (refusal of fluids, food and/or oral medication) and hydration status (in the case of severe vomiting or diarrhoea). Those with a high risk of serious illness should immediately be referred to a paediatric specialist for optimal care. Also, refer to Figure 1.^{15,17-19}

Antibiotics are used in the acute management of UTIs, as well as for the prevention of recurrent UTIs. It is important to note that nephrotoxic agents should be avoided where possible. Analgesics may be used to ease voiding symptoms.^{15,17-19}

Table 2: Clinical signs and symptoms of UTI

	Neonates	Infants and young children	School-aged children
Signs and symptoms	Prolonged jaundice Sepsis Failure to thrive Vomiting Fever Renal failure	Persistent fever Dysuria Failure to thrive Strong smelling urine Haematuria Abdominal or flank pain New-onset urinary incontinence	Symptoms similar to adults that present with UTI, including: Dysuria Frequency Urgency

16,8,9,4

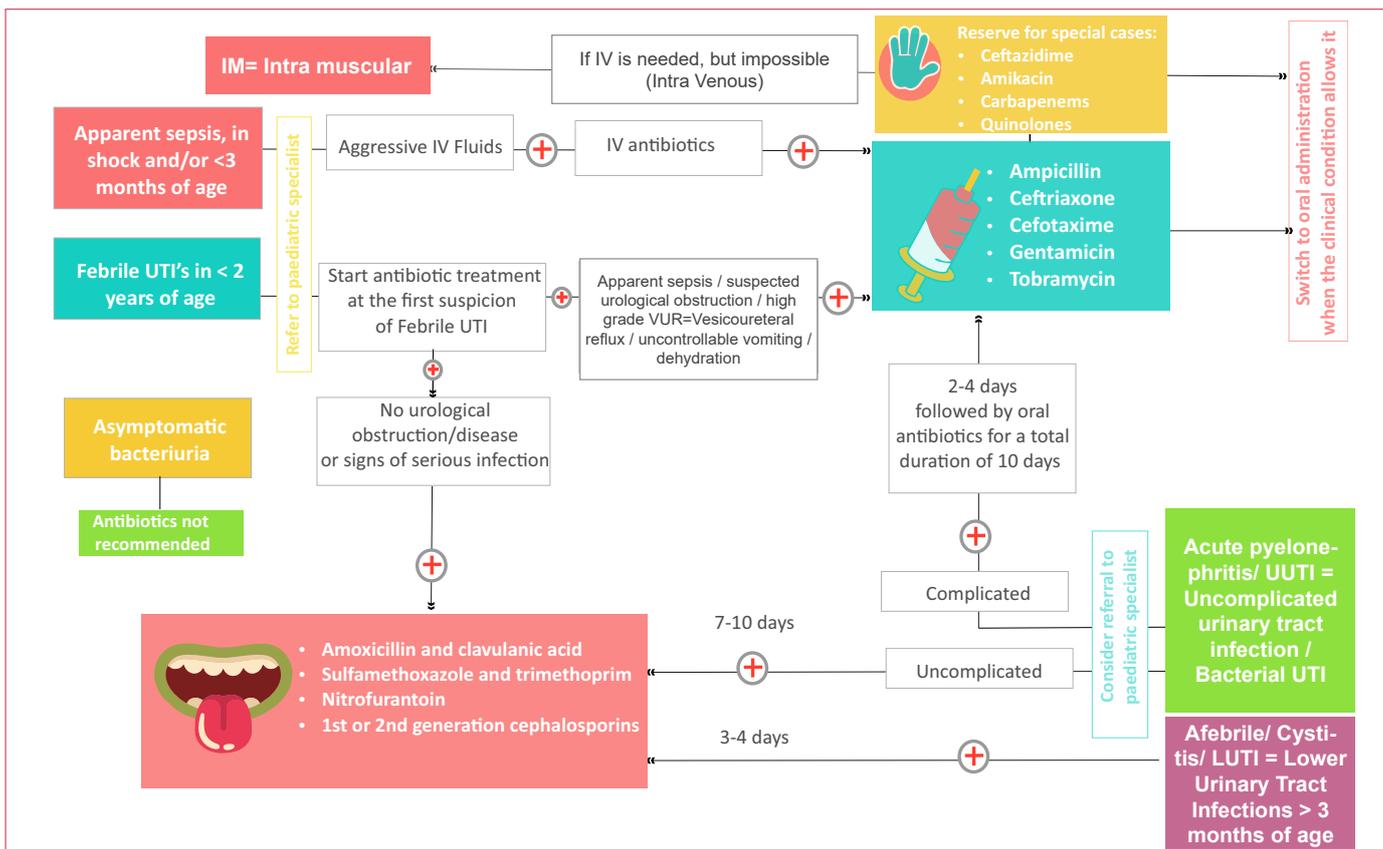


Figure 1: Suggested approach to the management of paediatric UTIs^{15,17-19}

Recommended oral antibiotics typically includes sulfamethoxazole and trimethoprim, amoxicillin/clavulanate, first and second generation cephalosporins and nitrofurantoin (Table 3). Parental agents used in the treatment of paediatric UTIs include ceftriaxone, cefotaxime, ampicillin, gentamicin and tobramycin (Table 4). A list of principles to ensure appropriate antibiotic use and an algorithm providing guidance for paediatric UTI treatment per UTI classification can be seen in Table 3.

Analgesics

Paracetamol can be used to provide relief from voiding symptoms.^{9,15,20} The recommended dose of paracetamol is 15 mg/kg 6 hourly. Both the World Health Organization and the National Department of Health recommend against the use of Non-Steroidal Anti-inflammatories (NSAIDs) as an analgesic for children with UTIs.^{9,20}

Antibiotic prophylaxis

In paediatrics with a single prior UTI, the use of antibiotic prophylaxis is not routinely recommended. In asymptomatic bacteriuria, antibiotic prophylaxis should not be used. Paediatric patients with recurrent UTIs should be thoroughly assessed to rule out any urinary tract abnormalities, where prophylactic antibiotics may be used, based on an individual evaluation. When prescribing prophylactic antibiotics, it is important to consider the ever increasing AMR (antimicrobial resistance) patterns. Local

Table 3: Principles of appropriate antibiotic use in paediatric UTI care

Principles for appropriate antibiotic use in paediatric UTI care
Only initiate an antibiotic once a urinalysis has been performed and a urine specimen for culture was obtained.
With the alarming increase in AMR , due care should be taken when choosing an agent.
Local antimicrobial susceptibility patterns should be used when deciding on empiric treatment and should cover the most common uropathogens (<i>Escherichia coli</i> , <i>Enterococcus</i> , <i>Proteus</i> , and <i>Klebsiella</i> species).
Reassess antibiotic 48 hours after initiation and modify according to susceptibility results.
Complicated or uncomplicated UTIs should be treated for 7-10 days .
However, short-courses of therapy may be used in adolescent girls with non-toxic UTIs.
If during the use of prophylactic medication a paediatric develops an infection: do not increase dose of current antibiotic, switch to a different agent.
Antibiotic treatment in the case of asymptomatic bacteriuria is not recommended.

^{16,17,18}

microorganism susceptibility should be taken into consideration when choosing an agent, and preferably a narrow-spectrum antibiotic should be used. Table 6 shows age-based prophylactic antibiotic recommendations.^{15,17-19} Tables 4 and 5 provides an overview of antibiotics used in the treatment of paediatric UTI.

Table 4: Oral antibiotics used in paediatric UTI care

Oral antibiotics	Dosing	Notes
Amoxicillin and clavulanic acid	20–40 mg/kg divided q8h Uncomplicated UTI: 30 mg/kg/dose 8h po Complicated UTI: 25mg/kg/dose 8H IV =intra venous ^{8,9}	Alternative if allergic/intolerant to macrolides
Amoxicillin	Not recommended due to high <i>E.coli</i> resistance	
Sulfamethoxazole and trimethoprim	30–60 mg/kg SMZ, 6–12 mg/kg TMP divided q12	Not recommended as an option by South African guidelines ^{4,8,9}
Cephalexin	50–100 mg/kg/day divided q6h	
Cefixime	8 mg/kg/day	
Cefpodoxime	10 mg/kg/day divided q12h	Use in mixed aerobic-anaerobic UTIs
Ciprofloxacin	Not recommended as a first choice in paediatrics Can be used to treat MDR infections when there is no other safe and effective alternative. Limit to treat UTIs caused by <i>Pseudomonas aeruginosa</i> or other MDR gram-negative bacteria. ¹³	

SMZ= sulfamethoxazole, TMP= trimethoprim, q= every ^{15,17-19}

Table 5: Parenteral antibiotics used in paediatric UTI care

IV antibiotic	Dosing	Notes
Ceftriaxone	50–75 mg/kg/day IV/IM single dose or divided q12h	Contra-indicated in < 6 weeks of age; bilirubin may be displaced from albumin
Ampicillin	100 mg/kg/day IV/IM divided q8h	< 2 weeks of age used in combo with gentamicin Used in paediatrics allergic to cephalosporins Initial therapy where either gram-positive cocci or no organism is found in urinary sediment
Cefotaxime	150 mg/kg/day IV/IM divided q6-8h	Safe in < 6 weeks of age Aged 2–8 weeks: Used in combo with ampicillin Use in neonates and jaundiced paediatrics
Gentamicin	< 7 days: 3.5–5 mg/kg/dose IV q24h < 5 years: 2.5 mg/kg/dose IV q8h or single daily dosing with normal renal function of 5–7.5 mg/kg/dose IV q24h ≥ 5 y: 2–2.5 mg/kg/dose IV q8h or single daily dosing with normal renal function; 5–7.5 mg/kg/dose IV q24h	Monitor blood levels and kidney function if therapy extends > 48 hours Empirical therapy should not be used for > 3 days. If empirical therapy is still required, consider changing to ceftriaxone

IV= Intravascular, IM= Intramuscular, q= every^{15,17-19}

Table 6: Prophylactic antibiotic recommendations

Age	Antibiotic	Dosage
< 2 months of age*	Amoxicillin** 1st/2nd generation Cephalosporin***	A 1/3 or 1/4 of normal recommended dose
< 8 weeks of age		
If nitrofurantoin/ TMP/ SMZ-TMP cannot be used		
> 2 months	SMZ-TMP	5–10 mg/kg/day SMZ, 1–2 mg/kg/day TMP
> 2–3 years of age	Nitrofurantoin	1–2 mg/kg/day

*Nitrofurantoin should not be used.

**Amoxicillin is typically not recommended because of the high incidence of resistant *E. coli*.

***Reduce dosages of 1st generation cephalosporin (e.g. cephalexin at 10 mg/kg), until patient reaches 6 weeks of age.

SMZ= sulfamethoxazole^{15,17-19}

Non-pharmacological interventions^{18,20}

The following interventions may be applied:

- Addressing dysfunctional elimination syndromes and constipation
- Improving bowel habits
- Encouraging adequate hydration
- Not delaying voiding
- Improving general hygiene

Preventative measures

The use of vitamin C, cranberry juice, vaccines with uropathogenic strains and/or probiotics is not recommended due to a lack of scientific evidence.²¹

Referral

Referral should be considered in the following circumstances^{8,9}:

- Poor response, despite adequate treatment (persistent positive culture or fever)

- Recurrent UTIs
- Suspected obstruction or abnormal imaging
- Abnormal renal function

Conclusion

UTI is an uncomfortable and unpleasant condition, which requires immediate attention in paediatrics. Adequate urine tests are necessary to isolate the bacteria, thus narrowing the choice of antibiotic. Appropriate antibiotic and supportive treatment must be considered to ensure a quick recovery and to prevent complications like renal scarring in young children. With antibiotic resistance taking centre stage globally, using the most appropriate antibiotic is essential to obtain the best results without compromising the patients' wellbeing. Prior to choosing an antibiotic, the allergic status, age and renal function must be established. Supportive treatment like paracetamol together with non-pharmacological advice, such as good hygiene and adequate hydration, can reduce the discomfort for the patient.

References

- Ramlakhan S, Singh V, Stone J, Ramtahal A. Clinical Options for the Treatment of Urinary Tract Infections in Children. *Clinical Medicine Insights. Pediatrics*. 2014; 8:31-7. Available from: <http://doi.org/10.4137/CMPed.S8100>
- Noorbakhsh S, Zarabi V. UTI in Children, *Urinary Tract Infections*, Tenke P, ed. ISBN: 978-953-307-757-4, InTech; 2011. Available from: <http://www.intechopen.com/books/urinary-tractinfections/uti-in-children>
- Keren R, Shaikh N, Pohl H, Gravens-Mueller L, Ivanova A, Zaoutis L, et al. Risk factors for recurrent urinary tract infection and renal scarring. *Pediatrics*. 2015;peds-2015.
- Ampath Infectious Diseases Peer Group. Treatment of urinary tract infections, in *Guidelines to antimicrobial therapy and the laboratory diagnosis of infectious diseases*. 5th ed. AmpathTrust; 2017;438.
- Alper BS, Curry SH. Urinary Tract Infection in Children. *Am Fam Physician*. 2005;15-72(12):2483-8.
- Strohmeier Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. *The Cochrane Library*. 2014.
- Morello W, La Scola C, Alberici I, Montini G. Acute pyelonephritis in children. *Pediatr Nephrol*. 2016;31(8):1253-65.
- Murray J. *Urinary Tract Infections*. Paarl Hospital Paediatric Guideline. EMGuidance application. 2015 [accessed 4 Nov 2017].
- National Department of Health. *Standard treatment guidelines and essential medicines list for South Africa, Hospital level paediatrics*, 2013. National Department of Health, Pretoria, South Africa; 2013.
- Robinson JL, Finlay JC, Lang ME, Bortolussi R. Urinary Tract Infections in Infants and Children: Diagnosis and Management. *Paediatr Child Health*. 2014;19(6):315-9.
- Sood A, Penna F, Eleswarapu S, Pucheril D, Weaver J, Wagner JC, et al. Incidence, admission rates, and economic burden of pediatric emergency department visits for urinary tract infection: Data from the nationwide emergency department sample, 2006 to 2011. *J Pediatr Urol*. 2015;11(5):246-e1.
- Montini G, Tullus K, Hewitt I. Febrile Urinary Tract Infections in Children. *N Engl J Med*. 2011;365:239-50.
- Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *American Academy of Pediatrics*. 2011;595-610.
- Hanna-Wakim RH, Ghanem ST, El Helou MW, et al. Epidemiology and characteristics of urinary tract infections in children and adolescents. *Front Cell Infect Microbiol*. 2015;5(45).
- Fisher D. Pediatric urinary tract infections. 2017 [accessed on 4 November 2017]. Available from: <https://emedicine.medscape.com/article/969643-overview#a4>
- White B. Diagnosis and treatment of urinary tract infections in children. *Am Fam Physician*. 2011;83(4):409-15.
- Cdc.gov. Pediatric Treatment Recommendations | Community | Antibiotic Use | CDC [online]. 2017 [accessed on 3 Nov 2017]. Available from: <https://www.cdc.gov/antibiotic-use/community/for-hcp/outpatient-hcp/pediatric-treatment-rec.html>
- Nice.org.uk. Urinary tract infection in under 16s: diagnosis and management | Guidance and guidelines | NICE [online]. 2007 [accessed on 3 Nov 2017]. Available from: <https://www.nice.org.uk/guidance/cg54/chapter/Recommendations#acute-management>
- Tekgül S, Dogan H, Kočvara R, Nijman J, Radmayr C, Stein R. *Paediatric Urology* | Uroweb [online]. 2017 [accessed on 3 Nov 2017]. Available from: <http://uroweb.org/guideline/paediatric-urology/?type=pocket-guidelines>
- World Health Organization. *Pocket book of hospital care for children: Guidelines for the management of common childhood illnesses*, 2nd edition. World Health Organization; 2013.
- SNS. *Clinical Practice Guideline for Urinary Tract Infection in Children*. SNS Ministry of Science and Research [ebook]. 2011 [accessed 3 Nov 2017];123-60. Available from: http://www.guiasalud.es/GPC/GPC_483_ITU_poblacion_pediatica_IC3_ing.pdf