

## Causes and Management of Recurrent Urinary Tract Infection (UTI) in Children

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### Abstract

Urinary tract infection (UTI) is one of the most common bacterial infections of childhood. We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases the medical subject headings (MeSH). Papers discussing the causes and management of recurrent UTI in children were screened for relevant information. There were no limits on date, language, age of participants or publication type. About 91% to 96% of UTI in children have been caused by the retrograde bacterial ascent through the urethra to reach the bladder or the upper urinary tract. The most common organism causing UTI in children is *Escherichia coli*, which is responsible for 80 to 90% of all cases. Less frequent cases can be caused by viral and even fungal infectious organisms. General instructions given to children with UTI include voiding frequently, in a proper position and with complete emptying of the bladder. Once the diagnosis is confirmed, prompt antibiotic therapy should be initiated without waiting for the culture results. Moreover, the limited use of imaging studies may be indicated to follow up.

**Keywords:** UTI; Children; Etiology; Treatment; Antibiotic

### Introduction

Urinary tract infection (UTI) is defined as a bacterial infectious process affecting any part of the urinary tract, most commonly the bladder and the urethra [1]. Symptoms include urinary urgency and frequency, burning sensation during urination, lower abdominal discomfort, and cloudy urine [1]. It is further divided into lower (cystitis) and upper (pyelonephritis) UTI [2]. Cystitis is less common than pyelonephritis in children below 2 years of age [3], whereas in adults' cystitis is much more common than pyelonephritis [4]. UTI is

a common disease in children. At the age of 8 years, 7 - 8% of all girls and 2% of all boys have experienced at least one episode of UTI [5]. Around 7.0% of children below 2 years of age presenting with fever are reported to have a UTI [6]. In the US it is reported that girls, infants < 1 year of age, white children and uncircumcised children are at greatest risk of having UTI [6].

The primary and sometimes only symptom of UTI in children younger than 2 years of age is fever [7]. In a study conducted from 1976 through 1981, 63 out of 100 children aged 5 days to 8 months with clinical signs and features of UTI, were brought to medical attention because of fever [8]. For neonates, some of the recorded numbers for fever as the main symptom have been 32/80 (40%) [9] and 11/64 (17%) [10]. In other instances, vomiting (16/43), jaundice (16/43) and failure to thrive (13/43) were more prominent features than fever (9/43), with poor feeding and loose stools/diarrhea being more seldom [10,11].

In a meta-analysis of studies including children with UTI [12] a history of previous UTI (Likelihood ratio (LR) 2.3 - 2.9) and fever > 40°C (LR 3.2 - 3.3) were the two most helpful signs in identifying UTI in children below 2 years of age. Older children present also with fever, symptoms of the lower urinary tract and abdominal pain. Flank pain, chills, and fever are suggestive of pyelonephritis [13]. Abdominal pain (LR 6.3), back pain (LR 3.6), frequency and/or dysuria (LR 2.2 - 2.8) and new-onset urinary incontinence (LR 4.6) were the most useful signs in predicting UTIs in verbal children [12]. In the case of acute cystitis, children typically present with the absence of fever and symptoms from the lower urinary tract, which includes dysuria, frequency, urge, new-onset urinary incontinence, suprapubic/abdominal pain and/or hematuria [14].

Treatment of the UTI should not be initiated before adequate urine samples have been obtained [15]. Treatment is to be adjusted depending on culture and susceptibility tests [15]. If the patient becomes clinically stable, the medicine can be given orally; mainly based on an appropriate antibiotic course [15]. In this study, we provide an overview of the etiology and management of children with UTI.

### Methods

We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases on 15 December 2019 using the medical subject headings (MeSH). Papers discussing the causes and management of recurrent UTI in children were screened for relevant information. There were no limits on date, language, age of participants or publication type.

### Etiology

About 91% to 96% of UTI in children have been caused by the retrograde bacterial ascent through the urethra to reach the bladder or the upper urinary tract [14,16]. The most common organism causing UTI in children is *Escherichia coli*, which is responsible for 80 to 90% of all cases [17-19]. Other organisms include *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Citrobacter*, *Pseudomonas aeruginosa*, *Enterococcus* spp., and *Serratia* spp. [20,21]. In males, *Proteus mirabilis* is more common compared to females [22], while *Streptococcus agalactiae* is more in younger ages especially newborn infants [23]. Furthermore, in older females (adolescents) who are sexually active; *Staphylococcus saprophyticus* is more common causing about 15% of UTI cases [14,24].

In the case of children having urinary tract anomalies; the most common causative organisms included *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Streptococcus viridians*, and *Streptococcus agalactiae* [14,25]. Moreover, *Mycobacterium tuberculosis* and *Streptococcus pneumonia* are rare causative organisms for UTI [14,26,27].

Noteworthy, some viral organisms may also cause UTI; including adenoviruses, enteroviruses, echoviruses, and coxsackieviruses [14,18]. These viral infections are usually limited to the lower urinary tract [14,18]. In specific, adenoviruses are known to be associated with hemorrhagic cystitis in children [28]. Nevertheless, fungal infections rarely cause UTI and would be mainly limited to children with urinary tract anomalies, those using an indwelling urinary catheter, immuno-compromised children, and those using a broad-spectrum antibiotic for a long-term [6,14,28].

## Management

### General

The children with UTI should be instructed to void frequently (every 1.5 to 2 hours) and avoid holding urine for any reason [14]. Moreover, voiding should be done in an optimal posture along with the complete emptying of the bladder [14]. Any co-morbid condition, like constipation and dysfunctional voiding, should be also treated [14]. Although most of the children would be managed appropriately at home, a small percentage may require hospitalization and intravenous therapy [29].

### Antibiotic therapy

For symptomatic UTI, a rapid antibiotic therapy is indicated after confirmation with positive urinalysis and adjuvant clinical features, while the culture results are only used for the proper eradication of the infection [6,30-32]. In contrast, asymptomatic bacteriuria does not require treatment [28,33]. The choice of antibiotic should take into consideration the patient’s response, sensitivity testing, and antibiotic resistance data [14]. Some of the commonly used antibiotics in children’s’ UTI are listed in table 1 [3]. There is no documented advantage of oral antibiotics compared to the parenteral ones in terms of efficacy [34,35]. Indication of parental antibiotic therapy; includes infants ≤ 2 months or any child who is immunocompromised, unstable, toxic-looking, and those not tolerating or not responding to oral treatment [6,14].

Antibiotic	Dosing	Common adverse effects
Amoxicillin/clavulanate (Augmentin)	25 to 45 mg per kg per day, divided every 12 hours	Diarrhea, nausea/vomiting, rash
Cefixime (Suprax)	8 mg per kg every 24 hours or divided every 12 hours	Abdominal pain, diarrhea, flatulence, rash
Cefpodoxime	10 mg per kg per day, divided every 12 hours	Abdominal pain, diarrhea, nausea, rash
Cefprozil (Cefzil)	30 mg per kg per day, divided every 12 hours	Abdominal pain, diarrhea, elevated results on liver function tests, nausea
Cephalexin (Keflex)	25 to 50 mg per kg per day, divided every 6 to 12 hours	Diarrhea, headache, nausea/vomiting, rash
Trimethoprim/sulfamethoxazole (Bactrim, Septra)	8 to 10 mg per kg per day, divided every 12 hours	Diarrhea, nausea/vomiting, photosensitivity, rash

**Table 1:** Antibiotics commonly used to treat urinary tract infections in children [3].

The best duration for optimal UTI treatment is controversial [14,32]. According to a systematic review and meta-analysis of randomized controlled trials, no significant difference found in children treated for 2 - 4 days when compared to those treated for 7 - 14 days [36]. However, there is evidence that antibiotic treatment for 10 days is more likely to eradicate the infection and treatment for less than three days is not recommended [34,35,37]. It is that lower (afebrile) UTI should be treated for five to seven days [14].

### Imaging

The historical guidelines were suggesting and aggressive imaging follow up; however, newer guidelines are suggesting less or no imaging studies (Table 2) [29,38].

<b>National Institute for Health and Clinical Excellence (NICE) UK [39]</b>	
<b>Age 0 - 6 months</b>	
Uncomplicated first UTI	Outpatient ultrasound.
Atypical UTI	Inpatient ultrasound, outpatient DMSA scan and VCUG.
Recurrent UTI	Inpatient ultrasound, outpatient DMSA scan and VCUG.
<b>Age 6 months - 3 years</b>	
Uncomplicated first UTI	No imaging.
Atypical UTI	Inpatient ultrasound, outpatient DMSA scan.
Recurrent UTI	Outpatient ultrasound, outpatient DMSA scan.
<b>Age &gt; 3 years</b>	
Uncomplicated first UTI	No imaging.
Atypical UTI	Inpatient ultrasound.
Recurrent UTI	Outpatient ultrasound, outpatient DMSA scan.
<b>American Academy of Pediatrics (AAP) [40]</b>	
<b>Age 0 - 24 months</b>	
Any febrile UTI	Ultrasound.
Complex or atypical circumstances	VCUG.
Recurrent UTI	Further evaluation.
<b>Canadian Pediatric Society (CPS) [21]</b>	
Any febrile UTI aged < 2 years	Ultrasound.
<b>European Association of Urology/European Society for Pediatric Urology [32]</b>	
Any febrile UTI	Ultrasound.
Suspicion of VUR and/or pyelonephritis	VCUG and/or DMSA scan.
<b>Spanish Association of Pediatrics [41]</b>	
UTI that requires admission, is recurrent or with suspected complications	Inpatient ultrasound.
First UTI if aged <6 months	Outpatient ultrasound.
Recurrent or atypical UTI	Outpatient ultrasound, and VCUG or contrast-enhanced bladder ultrasound especially if aged <6 months, and DMSA scan especially if aged <3 years.

**Table 2:** Summary of imaging recommendations from selected international guidelines for young children with UTI [29,38].  
 DMSA: Dimercaptosuccinic Acid; UTI: Urinary Tract Infection; VCUG: Voiding Cystourethrogram; VUR: Vesicoureteric Reflux.

**Conclusion**

Once the diagnosis is confirmed, prompt antibiotic therapy should be initiated without waiting for the culture results. Moreover, the limited use of imaging studies may be indicated to follow up.

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### Conflicts of Interest

No conflicts related to this work.

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