

# BMJ Best Practice

## Urinary tract infections in children

Straight to the point of care



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## Summary

Urinary tract infections (UTIs) are common in children. Symptoms and signs may be nonspecific, particularly in neonates and infants. Older children may have dysuria, urgency, or frequency with a lower urinary tract infection, or fever, loin or back pain, and vomiting with upper UTI (pyelonephritis).

An appropriately obtained urine specimen can confirm the diagnosis and pathogen; urine culture and antimicrobial susceptibility testing will define the appropriate antibiotic for treatment.

Anatomic and functional abnormalities of the urinary tract and bowel may predispose children to recurrent UTIs. Further evaluation of children with recurrent UTIs is required to identify any treatable underlying cause. Recurrent UTIs may lead to renal scarring and renal insufficiency.

## Definition

Pediatric urinary tract infection (UTI) is an illness caused by infection of the lower urinary tract (cystitis), the upper urinary tract (pyelonephritis), or both. The presence of pyuria and symptoms distinguishes UTI from asymptomatic bacteriuria.[1]

Asymptomatic bacteriuria is the presence of bacteria in urine obtained in asymptomatic children on routine screening or incidentally during other investigations. The prevalence of asymptomatic bacteriuria is 0.37% in boys and 0.47% in girls, with highest rates in uncircumcised boys younger than 1 year old and girls older than 2 years of age.[2] Asymptomatic bacteriuria does not require treatment.[3]

Uncomplicated UTI occurs in a child who has a structurally and functionally normal urinary tract, normal renal function, and a competent immune system. Complicated UTI occurs in a child who has a structural or functional abnormality of the urinary tract.[1]

## Epidemiology

UTI is one of most common childhood bacterial infections, affecting approximately 8% of children <19 years with urinary symptoms and/or fever.[7] [8] Nearly 50,000 children were admitted to hospital with UTI each year between 2000 and 2006 in the US, accounting for 1.8% of pediatric hospitalizations.[9]

Infant boys <3 months of age and infant girls <1 year old show the highest prevalence rates.[10] Prevalence also increases between ages 2 and 4 years, during toilet training.[11]

The overall prevalence of UTI in children <2 years of age with an undifferentiated febrile illness is approximately 5%.[12]

UTI is more common in boys than in girls during the first year of life. After 12 months of age the prevalence of UTI is higher in girls than in boys.[13]

## Etiology

The majority of bacterial pathogens implicated in UTIs in children are gram-negative.

*Escherichia coli* is the most common cause, accounting for 85% to 90% of pediatric UTIs.[7]

Other potential bacterial pathogens include:[13][14] [15] [16] [17]

- *Proteus mirabilis* in uncircumcised males
- *Staphylococcus saprophyticus* in female adolescents
- *Pseudomonas* species in congenital anomalies of the kidneys and urinary tract
- *Serratia marcescens*, *Citrobacter* species, and *Staphylococcus epidermidis*, which may cause infections in patients with malformation or dysfunction of the urinary tract
- *Klebsiella aerogenes* and *Enterococcus* species.

*Candida* species may cause UTI in immunocompromised children, those with complex congenital anomalies of the kidneys and the urinary tract, postoperatively, and those with stents and urinary catheters for prolonged periods of time.

*Schistosoma haematobium* infection may affect children in endemic regions.

UTIs can be classified as uncomplicated or complicated. The etiology of complicated UTI may be due to a structural abnormality or a functional abnormality.[1]

- Structural abnormality is mostly due to the presence of posterior urethral valves, strictures, or stones.
- Functional abnormality most commonly results from lower urinary tract dysfunction of neurogenic (e.g., spina bifida) or non-neurogenic (e.g., voiding dysfunction) origin, as well as dilating vesicoureteral reflux (VUR).

## Pathophysiology

Colonization of periurethral mucosa with genitourinary bacteria is hypothesized to precede UTI. Ascending infection into the bladder is the mechanism for most episodes of cystitis. Shorter urethral length in girls predisposes to ascending infection.

Vesicoureteral reflux facilitates infection of the ureters and kidneys. In the absence of vesicoureteral reflux, uropathogenic *Escherichia coli* are able to inhibit ureteric peristalsis, facilitating infection of the upper urinary tract.[18] Bacterial infection is more likely if abnormalities in bladder emptying exist (e.g., bladder and bowel dysfunction, chronic constipation, vesicoureteral reflux), because elimination of bacteria from the bladder after micturition is incomplete.[19]

Constipation also facilitates development of UTI by increasing the number of uropathogenic organisms in the gastrointestinal tract.[19]

*E coli* isolates from UTI more commonly express virulence factors. Adhesins such as the type 1 pilus and P fimbriae may mediate attachment to uroepithelial receptors, and aerobactin may enhance bacterial growth through iron acquisition.[20] [21] [22]

## Classification

### Classification according to site of infection[1] [4] [5]

Lower UTI (cystitis)

- Lower tract symptoms only, including frequency, urgency, dysuria, hematuria, malodorous urine, enuresis, and suprapubic pain.

Upper UTI (pyelonephritis)

- Abrupt onset with systemic signs and symptoms, including fever ( $\geq 100.4^{\circ}\text{F}$  [ $\geq 38^{\circ}\text{C}$ ]), chills, flank pain, and costovertebral angle tenderness.

### Classification according to severity of infection[1]

Non-severe UTI

- Mostly lower UTIs.
- Child has mild pyrexia at most, is able to take fluids and oral medication, and is only slightly or not dehydrated.

Severe UTI

- Mostly upper UTIs.
- Child has a high fever ( $>102.2^{\circ}\text{F}$  [ $>39^{\circ}\text{C}$ ]), feels unwell, is persistently vomiting, and is moderately to severely dehydrated.

### Classification according to complicating factors[1]

Uncomplicated UTI

- UTI in a child who has a structurally and functionally normal urinary tract, normal renal function, and a competent immune system.

Complicated UTI

- UTI in a child who has a structural or functional abnormality of the urinary tract.

## Classification according to episode of infection[1] [4]

### First UTI

- May be indicative of anatomic anomalies and so anatomic evaluation is warranted.

### Recurrent UTI

- May be due to unresolved infection or persistent infection.
  - Unresolved infection: initial treatment is inadequate for elimination of bacteria in the urinary tract.
  - Persistent infection: caused by re-emergence of bacteria in the urinary tract due to a site of persistent infection that cannot be eradicated (e.g., infected stones or fistulas).
- Same pathogen is implicated in each recurrent infection.
- In the UK, the National Institute for Health and Care Excellence (NICE) classifies recurrent UTIs as follows:
  - $\geq 2$  episodes of acute upper UTI, or
  - 1 episode of acute upper UTI plus  $\geq 1$  episode of lower UTI, or
  - $\geq 3$  episodes of lower UTI.

### Breakthrough UTI

- May be seen in patients undergoing antibiotic prophylaxis.
- Usually the result of resistant strains of the infecting pathogen.
- May also be due to a parent or guardian's noncompliance with their child's treatment, and/or severe urogenital anomalies.

### Reinfection

- Unlike recurrent UTI, reinfection involves different types of pathogens or different serotypes of the same pathogen.

## Classification according to clinical presentation[1] [4]

### Atypical UTI

- Child is seriously ill, with signs and symptoms including:
  - Poor urine flow
  - Abdominal or bladder mass
  - Raised creatinine
  - Septicemia
  - Failure to respond to treatment with 48 hours
  - Infection with non- *Escherichia coli* organisms.

### Asymptomatic UTI

- Child has leukocyturia without any other symptoms.

### Symptomatic UTI

- Child may have irritative voiding symptoms and suprapubic pain (cystitis) or fever and malaise (pyelonephritis).



## Case history

### Case history #1

A 19-month-old girl presents with a 24-hour history of fever to 104°F (40°C) and vomiting. She is mildly dehydrated (slightly dry mucous membranes but normal capillary refill) and has no localized findings on exam.

### Case history #2

A 3-week-old uncircumcised boy presents with fever to 101.3°F (38.5°C) and poor feeding. He is fussy, with poor capillary refill. His abdomen is distended and diffusely tender.

### Other presentations

An uncommon presentation of UTI in young infants may be with late-onset jaundice or failure to thrive.<sup>[6]</sup> Toddlers rarely present with urinary symptoms; nonspecific symptoms are much more common.

# Approach

Children presenting with fever of unknown origin or urinary symptoms should be promptly evaluated for a diagnosis of UTI.[39] The general diagnostic approach to pediatric UTIs is differentiated by:

- Patient age
- Severity of illness
- History of underlying urogenital abnormalities.

Infection may involve the upper or lower urinary tract; be complicated or uncomplicated; severe or nonsevere; recurrent, breakthrough, or a reinfection; atypical, asymptomatic, or symptomatic. See Classification for more information.

Neonates and infants ages  $\leq 2$  months are at high risk for serious bacterial infection and sepsis.[1] [40] Symptoms are nonspecific in this age group, making it difficult to distinguish UTI from other causes of serious bacterial infection at initial evaluation.[41] These children should be admitted to hospital for evaluation and most should receive empiric parenteral antibiotic therapy. See Sepsis in children for more information.

Children ages  $>2$  months may first have urinalysis via dipstick testing, microscopy, or, if available, flow cytometry.[1]

Diagnosis and treatment are often concurrent processes. Empiric therapy may be commenced before diagnostic assessment is completed if there is a high risk of serious illness. Further investigation may depend on response to initial therapy.

## History

The history may reveal risk factors that are strongly associated with UTI, such as age  $<1$  year, female sex or uncircumcised infant boy, previous history of UTI, bladder bowel dysfunction, vesicoureteral reflux (VUR), and instrumentation of the urinary tract.[5]

Neonates often present with very nonspecific symptoms such as an undifferentiated febrile illness, irritability, vomiting, or poor feeding.[7] A generally ill appearance, mottling, unstable vital signs, decreased activity, and poor oral intake indicate that they may have sepsis. Less commonly, neonates with a urinary tract infection can present with late-onset jaundice or faltering growth.

In infants and toddlers the presentation is also likely to be nonspecific, including fever, diarrhea, or vomiting with dehydration, or faltering growth. Urinary symptoms in this age group include abdominal/flank pain, foul-smelling urine, and new-onset urinary incontinence.[7] Even with serious bacterial infection, signs and symptoms may be subtle.

In older (verbal) children and adolescents, symptoms and signs may be more specific to the urinary system, and include dysuria, foul-smelling urine, urgency, frequency, new-onset urinary incontinence, or gross hematuria.[7] Systemic symptoms such as fever, abdominal or flank pain, and vomiting are highly suggestive of pyelonephritis.

Enquire about sexual activity in adolescents. Sexual intercourse increases the risk of UTI in females. Symptoms of urethritis caused by sexually transmitted infections may mimic UTI in both sexes.



## Physical exam

The physical exam is useful to detect signs of urinary tract infection and exclude other possible causes for the patient's symptoms.

A full physical exam is indicated in infants and febrile patients.

In older patients, the abdomen and genitalia should be examined, and the costovertebral angles should be palpated. Palpable bladder or abdominal mass, poor urinary flow, poor growth, and elevated blood pressure may be seen with obstructive uropathy or chronic kidney disease and should prompt the clinician to consider abnormalities of the urinary tract.

Vaginal irritation or discharge may be seen with vaginitis (including irritant vaginitis) and may identify the reproductive tract, rather than the urinary tract, as the source of symptoms, particularly in infants and toddlers. Labial adhesions in girls and severe phimosis in boys can predispose recurrent UTIs.

## Initial investigations

### Urinalysis

Initial test in symptomatic children  $\geq 2$  months.

The urine sample should be collected as soon as possible, ideally at the consultation. If this is not possible, a sample should be collected and returned within 24 hours.<sup>[4]</sup> Urine samples should be taken before any antibiotic treatment is initiated, unless there is high risk of serious illness.<sup>[4]</sup>

The urine sample is analyzed either by urine dipstick, microscopy, or, if available, flow cytometry.<sup>[1]</sup>

Urine is examined for evidence of pyuria (positive leukocyte esterase/presence of white blood cells on microscopy) and/or bacteriuria (positive nitrites/bacteria visible after Gram stain).

Possible dipstick results are as follows.

- Positive for leukocyte esterase and nitrite: positive likelihood ratio (LR+) 28.2.<sup>[42]</sup> This test is best at ruling in disease, with the best yield in children  $>2$  years of age.<sup>[43]</sup>
- Positive for either leukocyte esterase or nitrite: sensitivity 92%, negative likelihood ratio (LR-) 0.2.<sup>[42]</sup> <sup>[44]</sup> This test is best at ruling out disease.
  - Positive nitrite alone: sensitivity 58%, specificity 99%, LR+ 15.9, LR- 0.51.<sup>[42]</sup> <sup>[44]</sup> This test has a high positive predictive value. In children of all ages, nitrites are highly specific for UTI.<sup>[45]</sup> Nitrites are formed by conversion of urinary nitrates to nitrites by gram-negative bacteria. In children ages  $<2$  years, the sensitivity of nitrites is particularly low (23%).<sup>[45]</sup> Formation of nitrites by bacteria requires urine to be held in the bladder for 4 to 6 hours, and young children usually void more frequently than this.<sup>[46]</sup> Nitrites will not be present in infections with enterococcal or staphylococcal species. Therefore, the absence of nitrites does not exclude UTI.
  - Positive leukocyte esterase alone: sensitivity 84%, specificity 77%, LR+ 5.5, LR- 0.26.<sup>[42]</sup> <sup>[44]</sup>
- Negative for leukocyte esterase and nitrite: an alternative cause for the patient's symptoms should be sought. However, false negatives may occur if the patient has been exposed to antibiotics; in this instance a sample should be sent for culture.

Possible microscopy results are as follows.

- Pyuria (the presence of white blood cells [WBCs]): sensitivity 78%, specificity 87%; LR- 0.27.[42] [44] Significant pyuria is  $\geq 10$  WBCs/mm<sup>3</sup> on an enhanced urinalysis or  $\geq 5$  WBCs per high-power field on a centrifuged specimen of urine. The optimal cut point for diagnosing pyuria varies according to urine concentration in children ages <24 months, from 3 WBCs per high-power field in dilute urine to 8 WBCs per high-power field in concentrated urine.[47] Other inflammatory conditions, or the presence of renal stones, may cause pyuria in the absence of UTI.[13]
- Bacteriuria: sensitivity 88%, specificity 93%, LR+ 14.7, LR- 0.19.[42] [44] Presence of any bacteria on microscopy indicates bacteriuria. Morphology and gram-staining characteristics may aid early identification of the causative organism.

Flow cytometry is performed on uncentrifuged specimens and provides counts of WBCs and bacteria in the urine.[1] Studies suggest that this technique may have a greater sensitivity and specificity in children than dipstick testing or microscopy; however, it is not yet widely available.[48] [49]

A positive nitrite (bacteriuria) or leukocyte esterase (pyuria) result should be followed by a urine culture.[1] [4] The American Society of Microbiology and the Infectious Diseases Society of America do not recommend ordering urine cultures unless patients have clinical signs of UTI because routine culture of asymptomatic individuals may detect asymptomatic bacteriuria.[50] [51]

However, the UK National Institute for Health and Care Excellence (NICE) recommends urine culture in the following scenarios:[4]

- The child is <3 months old
- There is suspicion of upper UTI
- There is an intermediate to high risk of serious illness
- The child has a positive result for leukocyte esterase or nitrite
- The UTI is recurrent
- The UTI does not respond to treatment within 24-48 hours
- The child has signs and symptoms, but the dipstick test results are negative.

#### Urine culture

Samples for culture should be obtained by clean-catch, suprapubic aspiration, or catheterization. Do not perform a bagged urine specimen for urine culture because there is a high false-positive rate.[1] [52] However, bag urine specimens can be used for urinalysis. If urinalysis is negative, a UTI is unlikely. If positive, an appropriate specimen should be obtained for culture.[1] The following concentrations generally indicate a positive result:[1] [40]

- Suprapubic aspirate: any growth
- Clean-catch midstream:  $>1000$ - $10,000$  cfu/mL
- Catheterization:  $>10,000$  cfu/mL.

A value of  $\geq 100,000$  cfu/mL constitutes severe infection.[1]

Preliminary results are usually available after 24 to 48 hours.

## Imaging

Imaging is performed to identify structural or functional abnormalities that predispose to recurrent infection, and to detect any complications of infection.

There is divergent clinical opinion as to whether to perform imaging in all children after the first UTI or only in those who are considered to be at highest risk of scarring and underlying abnormalities following UTI. Guideline recommendations differ between world regions.

### Ultrasound

Ultrasound is readily available and noninvasive. It can identify anatomic abnormalities such as hydronephrosis, duplex renal system, ureterocele, and hydroureter, but has a low sensitivity for detecting vesicoureteral reflux or renal scarring.[11] Ultrasound may also identify bladder wall trabeculation, increased bladder wall thickness (suggestive of voiding dysfunction or neurogenic bladder), pre- and post-void residual bladder volumes, and rectal diameter (increased in chronic constipation). Ultrasound may be performed to look for evidence of a renal or perinephric abscess when the urinalysis and culture are negative, but abdominal pain and fever persist.

The American College of Radiology (ACR) and the American Academy of Pediatrics (AAP) recommend that all infants under 2 months of age should have a renal ultrasound following their first UTI.[5] [11]

The AAP and the Canadian Paediatric Society also recommend a renal and bladder ultrasound (RBUS) after the first confirmed febrile UTI for children between 2 and 24 months, and 2 and 36 months of age, respectively.[5] [40]

European Association of Urology (EAU) guidelines recommend renal and bladder ultrasound within 24 hours in infants with febrile UTI to exclude obstruction of the upper and lower urinary tract.[1]

In the UK, NICE recommends ultrasound for infants and children with atypical UTI to identify any structural abnormalities. Infants younger than 6 months with first-time UTI who respond well to treatment should have a non-urgent ultrasound within 6 weeks of diagnosis. Ultrasound is also indicated in those ages 6 months to <3 years in the presence of recurrent UTIs.[4]

### Voiding cystourethrogram (VCUG)

VCUG detects vesicoureteral reflux.[11] VCUG allows evaluation of bladder anatomy (to exclude ureterocele, polyps, and diverticulae) and post-void residual volume. Contrast medium is instilled into the bladder and fluoroscopic images are taken during filling and micturition. A film during voiding permits visualization of the urethra and is essential in male children to exclude posterior urethral valves.[53]

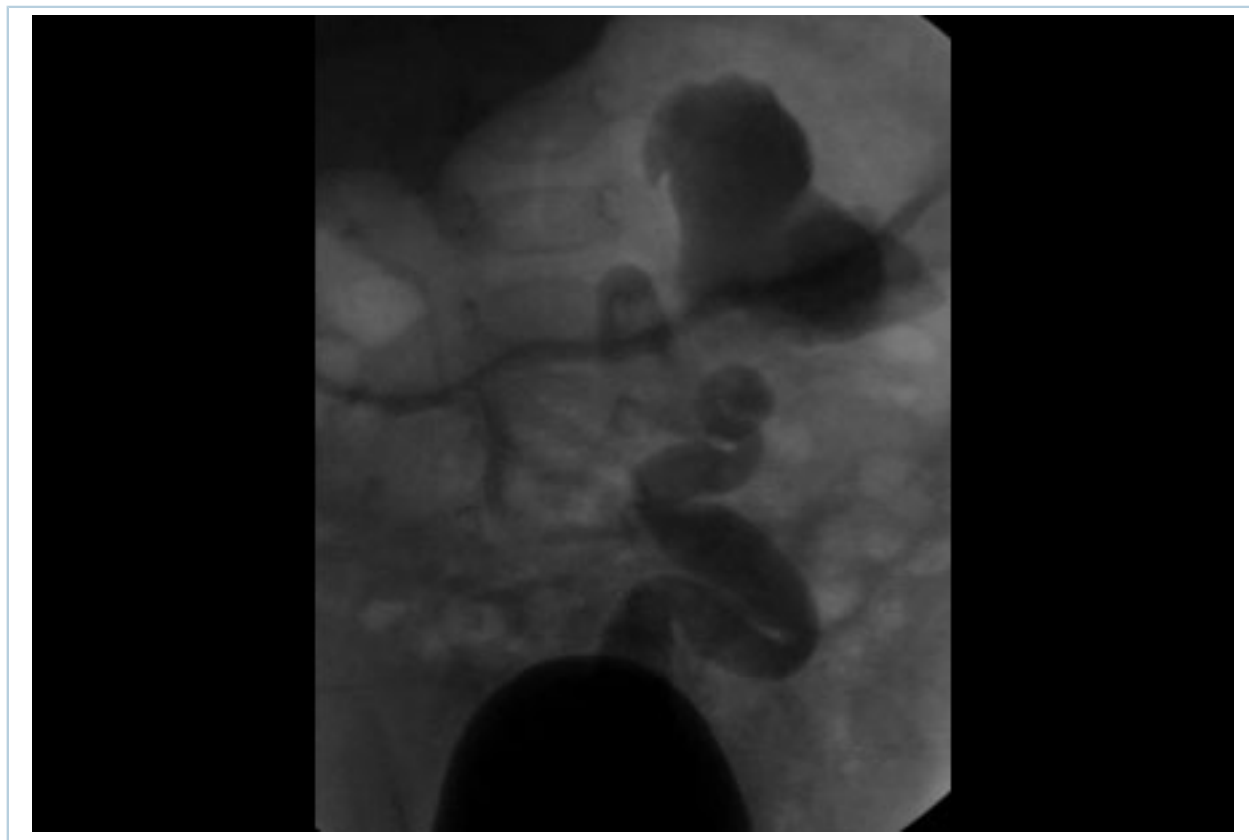
The AAP recommends that a VCUG is considered in children with abnormal RBUS, atypical causative pathogen, complex clinical course, or known renal scarring.[5] VCUG may also be considered in patients with a family history of VUR or congenital anomalies of kidneys and the urinary tract after first febrile UTI.[5]

Similarly, the EAU advises that VCUG should only be used if there is a suggestion of high-grade VUR, for example, febrile UTI, abnormal renal ultrasound, and/or non- *Escherichia coli* infection.[1]

NICE recommends VCUG in infants younger than 6 months if they have an abnormal ultrasound, atypical UTI, or recurrent UTI.[4]

A systematic review comparing detection rates of VUR on VCUG found no significant difference between early testing (<8 days after initiation of antibiotics) compared with later testing (≥8 days after initiation of antibiotics).[54]

Neither ultrasound nor renal cortical scintigraphy is sufficiently accurate at detecting VUR to recommend its use for this purpose.<sup>[55]</sup>



*Fluoroscopic image showing high-grade vesicoureteral reflux*

*From the collection of Dr Mary Anne Jackson*

### Renal cortical scintigraphy

Renal cortical scintigraphy uses Tc-99m dimercaptosuccinic acid (DMSA) to detect renal scarring and pyelonephritis.<sup>[11]</sup> It is recommended in children with recurrent or atypical UTI by both UK and US guidelines, 4-6 months following the acute infection.<sup>[4] [11]</sup>

## Further investigations

Serum creatinine, cystatin c, blood urea nitrogen and electrolytes, blood pressure measurements, and urine screening for proteinuria should be performed in patients who are hospitalized with complicated UTI.<sup>[1]</sup>

Inflammatory markers (C-reactive protein and procalcitonin) are not recommended routinely. Do not perform procalcitonin testing without an established, evidence-based protocol.<sup>[56]</sup> Due to heterogeneity between studies, a Cochrane review concluded that there was no compelling evidence to use procalcitonin, C-reactive protein, and erythrocyte sedimentation rate tests in clinical practice.<sup>[57]</sup> Clinicians may request inflammatory markers and complete blood count to guide decisions about performing lumbar puncture and starting empiric antibiotic therapy in well-appearing infants  $\leq 2$  months old.<sup>[58]</sup>

Immunosuppressed patients are susceptible to candidal UTIs. Urine culture for fungus should be specifically requested; this requires different laboratory techniques compared with standard bacterial culture.[59]

Nucleic acid amplification testing for chlamydial infection and gonorrhea is recommended in sexually active adolescents. See Genital tract chlamydia infection and Gonorrhea infection for more information.

Possible infection with schistosomiasis should also be considered, especially with a recent or past history of travel to a tropical country. See Schistosomiasis for more information.

## History and exam

### Key diagnostic factors

#### fever $>102.2^{\circ}\text{F}$ ( $>39^{\circ}\text{C}$ ) (common)

- Higher fever and fever duration  $>24$  hours increase the likelihood of UTI in infants.[39] [60]
- Absence of high fever does not preclude the presence of UTI.[61]
- The overall prevalence of UTI in children  $<2$  years of age with an undifferentiated febrile illness is approximately 5%.[12]

#### irritability (neonates and infants) (common)

- Signs and symptoms in infants with serious bacterial infection may be subtle.

#### poor feeding (neonates and infants) (common)

- Neonates with UTI often present with very nonspecific symptoms.

#### suprapubic tenderness (common)

- In infant girls, may be the only helpful sign for making the diagnosis of UTI (positive likelihood ratio 4.4).[39]

#### costovertebral angle tenderness (uncommon)

- May be seen with pyelonephritis and renal capsular stretch.

### Other diagnostic factors

#### foul-smelling urine (infants, older children, and adolescents) (common)

- May be secondary to increased urine urea concentration.
- In previous studies, it has not been shown to have increased predictive value.[39]

#### dysuria (preschool age, older children, and adolescents) (common)

- Increases the likelihood of a UTI (positive likelihood ratio range 2.2 to 2.8) in patients able to verbalize.[39]

#### urinary frequency (older children and adolescents) (common)

- Older children and adolescents are more likely to have symptoms that are more specific to the urinary system.

**abdominal/flank pain (infants, older children, and adolescents) (common)**

- Increases the likelihood of a UTI (positive likelihood ratio 6.3) in patients able to verbalize.[39]

**vomiting (uncommon)**

- May occur in all ages and can result in dehydration.
- Toddlers may also have diarrhea.
- In older children, systemic symptoms such as fever, abdominal or flank pain, and vomiting are highly suggestive of pyelonephritis.

**ill appearance (neonates) (uncommon)**

- Neonates may appear mottled, or have vital sign instability, decreased activity, and poor oral intake.
- Signs and symptoms in infants with serious bacterial infection may be subtle.

**gross hematuria (older children and adolescents) (uncommon)**

- Older children and adolescents are more likely to have symptoms that are more specific to the urinary system.

**new-onset urinary incontinence (toddlers, older children, and adolescents) (uncommon)**

- Increases the likelihood of a UTI (positive likelihood ratio 4.6) in patients able to verbalize.[39]

## Risk factors

**Strong****age <1 year**

- Infant boys <3 months of age and infant girls <1 year show the highest prevalence rates.[10]

**female sex**

- UTI is more common in girls than in boys after 12 months of age.[13]
- The most likely etiology is shorter urethral length for ascension of periurethral bacteria.

**uncircumcised boys in the first year of life**

- Have a >8-fold higher incidence than circumcised boys.[23]
- Presence of the foreskin allows for easier bacterial colonization of the periurethral region.

**previous UTI**

- Approximately 78% of girls and 71% of boys presenting with UTI within the first year of life experienced recurrence. After their first year of life, 45% of girls and 39% of boys developed further infections.[24]
- Previous UTI is one of the most useful historical factors for diagnosis of UTI in infants.

**bladder and bowel dysfunction**

- Children with bladder and bowel dysfunction (BBD) have a twofold increased risk of recurrent UTI.[25] BBD is associated with an increased risk of renal scarring following a febrile UTI.[26] BBD increases the risk of breakthrough febrile UTI in children with vesicoureteral reflux.[27]



- BBD is very common and likely underdiagnosed.[19] It is estimated that BBD represents approximately 40% of pediatric urology visits.[28]
- BBD is a functional condition that describes a constellation of lower urinary tract symptoms associated with functional constipation and/or encopresis. Children with BBD have no recognizable neurologic or anatomic abnormality.[19] The increased fecal load affects bladder dynamics by both direct mechanical compression and by changing neural stimuli on the bladder and pelvic floor muscles.[28] Symptoms include urinary storage symptoms (incontinence, increased or decreased voiding frequency, urgency, nocturia); urinary voiding symptoms (hesitancy, straining, weak stream, intermittent micturition, dysuria); holding maneuvers to postpone micturition (e.g., standing on tiptoe, forcefully crossing legs, pushing on the genitals or abdomen); a feeling of incomplete bladder emptying; pain in the bladder, urethra, or genitals; fecal incontinence and constipation.[19] [29]

### vesicoureteral reflux

- Approximately 25% of children with first-time UTI have vesicoureteral reflux (VUR).[30] VUR has been detected in 41.7% of neonates admitted to hospital with a UTI.[31]

### sexual activity

- In adolescent girls there is an increased relative risk in response to increased frequency of sexual intercourse.[32] Symptoms of urethritis caused by sexually transmitted infections may mimic UTI in both sexes.
- Sexual abuse can cause urinary symptoms in girls, but infection is uncommon.[33]

### no history of breastfeeding

- Breastfeeding has a protective effect, which is more pronounced in infant girls.
- This depends on the duration of breastfeeding, and the effect appears to persist even after weaning.[34]

### anatomic abnormalities or previous surgery to the urinary tract

- Obstructive anomalies have been found in up to 4% of children with first-time UTI.[35]
- Obstructive anomalies include ureteropelvic junction (UPJ) obstruction, obstructive megaureter, posterior urethral valves, and ureterocele. Other anatomic abnormalities that predispose to UTI include urachal remnant, nephrolithiasis, and duplicated collecting system.[7]
- May have atypical (non- *Escherichia coli*) bacteria as the cause of their UTI.

### Weak

### immunosuppression

- Patients are susceptible to candidal UTIs in addition to bacterial UTIs.

### protein-energy malnutrition

- Malnourished children have a twofold increased risk of UTI compared with healthy children. One meta-analysis reported a pooled prevalence of UTI of 17% in malnourished children.[36]

## Tests

### 1st test to order

Test	Result
<b>urine dipstick</b> <ul style="list-style-type: none"> <li>Urinalysis should be performed within 60 minutes of obtaining specimen. First morning voids may be best for yielding a positive nitrite test. A positive nitrite (bacteriuria) or leukocyte esterase (pyuria) result should be followed by a urine culture.[1] [4]</li> </ul>	<b>positive leukocyte esterase and/or positive nitrite</b>
<b>urine microscopy</b> <ul style="list-style-type: none"> <li>The optimal cut point for diagnosing pyuria varies according to urine concentration in children ages &lt;24 months, from 3 white blood cells (WBCs) per high-power field in dilute urine to 8 WBCs per high-power field in concentrated urine.[47]</li> <li>Other inflammatory conditions, or the presence of renal stones, may cause pyuria in the absence of UTI.[13]</li> <li>Presence of any bacteria on microscopy indicates bacteriuria. Morphology and gram-staining characteristics may aid early identification of the causative organism.</li> </ul>	<b>&gt;5 WBC/high-power field or any bacteria</b>
<b>urine culture</b> <ul style="list-style-type: none"> <li>This is the diagnostic standard test following positive urinalysis.[1] [4]</li> <li>The American Society of Microbiology and the Infectious Diseases Society of America do not recommend ordering urine cultures unless patients have clinical signs of UTI because routine culture of asymptomatic individuals may detect asymptomatic bacteriuria.[50] [51] However, the UK National Institute for Health and Care Excellence (NICE) recommends urine culture in the following scenarios:[4] <ul style="list-style-type: none"> <li>The child is &lt;3 months old</li> <li>There is suspicion of upper UTI</li> <li>There is an intermediate to high risk of serious illness</li> <li>The child has a positive result for leukocyte esterase or nitrite</li> <li>The UTI is recurrent</li> <li>The UTI does not respond to treatment within 24-48 hours</li> <li>The child has signs and symptoms, but the dipstick test results are negative.</li> </ul> </li> <li>A value of <math>\geq 100,000</math> cfu/mL constitutes severe infection.[1]</li> <li>Samples for culture should be obtained by clean-catch, suprapubic aspiration, or catheterization. Do not perform a bagged urine specimen for urine culture because there is a high false-positive rate.[1] [52]</li> </ul>	<b>suprapubic aspirate: any growth; clean-catch midstream: &gt;1000-10,000 cfu/mL; catheter: &gt;10,000 cfu/mL</b>

## Other tests to consider

Test	Result
<b>urine flow cytometry</b> <ul style="list-style-type: none"> <li>Alternative test to dipstick testing or microscopy.</li> <li>Performed on uncentrifuged urine specimens and provides counts of WBCs and bacteria in the urine.[1]</li> <li>Studies suggest that this technique may have a greater sensitivity and specificity in children than dipstick testing or microscopy; however, it is not yet widely available.[48] [49]</li> </ul>	<b>presence of leukocytes and bacteria</b>
<b>blood culture</b> <ul style="list-style-type: none"> <li>All febrile/systemically unstable neonates (<math>\leq 28</math> days of age) and febrile/systemically unstable infants (1-24 months) should have blood cultures taken on presentation.[58] Follow-up blood cultures should be performed for any patient who is still febrile 24 hours after initiation of therapy.</li> </ul>	<b>positive for infecting organism</b>
<b>complete blood count</b> <ul style="list-style-type: none"> <li>Absolute neutrophil count may be used to guide decisions about performing lumbar puncture and starting empiric antibiotic therapy in well-appearing term infants <math>\leq 2</math> months old.[58]</li> </ul>	<b>elevated absolute neutrophil count</b>
<b>inflammatory markers</b> <ul style="list-style-type: none"> <li>Inflammatory markers may be used to guide decisions about performing lumbar puncture and starting empiric antibiotic therapy in well-appearing term infants <math>\leq 2</math> months old.[58]</li> <li>Do not perform procalcitonin testing without an established, evidence-based protocol.[56]</li> </ul>	<b>elevated C-reactive protein or procalcitonin</b>
<b>fungus urine culture</b> <ul style="list-style-type: none"> <li>Consider in immunosuppressed patients.</li> <li>Urine culture for fungus should be specifically requested; this requires different laboratory techniques compared with standard bacterial culture.[59]</li> </ul>	<b>positive for candida</b>
<b>serum creatinine, BUN and electrolytes</b> <ul style="list-style-type: none"> <li>In patients hospitalized with complicated UTI, serum creatinine, cystatin c, BUN and electrolytes, blood pressure measurements, and urine screening for proteinuria should be pursued.</li> </ul>	<b>normal or elevated creatinine, cystatin c, and urea</b>
<b>renal and/or bladder ultrasound</b> <ul style="list-style-type: none"> <li>Initially performed to look for any anatomic abnormalities of the urinary tract.</li> <li>Also may be performed to look for evidence of a renal or perinephric abscess when the urinalysis and culture are negative but abdominal pain and fever persist.</li> <li>The American College of Radiology (ACR) and the American Academy of Pediatrics (AAP) recommend that all infants under 2 months of age should have a renal ultrasound following their first UTI.[5] [11]</li> <li>The AAP and the Canadian Paediatric Society also recommend a renal and bladder ultrasound (RBUS) after the first confirmed febrile UTI for children between 2 and 24 months, and 2 and 36 months of age, respectively.[5] [40] European Association of Urology guidelines recommend renal and bladder ultrasound within 24 hours in infants</li> </ul>	<b>abnormalities may be present such as dilation of the renal pelvis or ureters, distention of thick-walled bladder, renal stones, ureterocele, bladder wall trabeculation, high post-void residual volume, enlarged rectal diameter; renal abscess: area of radiolucency to the renal parenchyma with local hypoperfusion on color Doppler; perinephric abscess: hypoechoic fluid</b>

Test	Result
<p>with febrile UTI to exclude obstruction of the upper and lower urinary tract.[1]</p> <ul style="list-style-type: none"> <li>In the UK, the National Institute for Health and Care Excellence recommends ultrasound for infants and children with atypical UTI to identify any structural abnormalities. Infants younger than 6 months with first-time UTI who respond well to treatment should have a nonurgent ultrasound within 6 weeks of diagnosis. Ultrasound is also indicated in those ages 6 months to &lt;3 years in the presence of recurrent UTIs.[4]</li> </ul>	
<p><b>dimercaptosuccinic acid (DMSA) scan</b></p> <ul style="list-style-type: none"> <li>Detects renal scarring and pyelonephritis.</li> <li>Recommended in children with recurrent or atypical UTI by both UK and US guidelines, 4 to 6 months following the acute infection.[4] [11]</li> <li>May be difficult to distinguish acute changes of pyelonephritis from old renal scarring.</li> </ul>	<p><b>pyelonephritis or renal scarring: focal or diffuse areas of decreased uptake</b></p>
<p><b>voiding cystourethrogram (VCUG)</b></p> <ul style="list-style-type: none"> <li>Performed to evaluate for the presence and degree of vesicoureteral reflux (VUR). Also permits evaluation of bladder anatomy and post-void residual volume.</li> <li>A film during voiding permits visualization of the urethra and is essential in male children to exclude posterior urethral valves.[53]</li> <li>The American Academy of Pediatrics recommends that a VCUG is considered in children with abnormal RBUS, atypical causative pathogen, complex clinical course, or known renal scarring.[5] VCUG may also be considered in patients with a family history of VUR or congenital anomalies of kidneys and the urinary tract after first febrile UTI.[5]</li> <li>Similarly, the European Association of Urology advises that VCUG should only be used if there is a suggestion of high-grade VUR, for example, febrile UTI, abnormal renal ultrasound, and/or non-<i>Escherichia coli</i> infection.[1]</li> <li>The UK National Institute for Health and Care Excellence recommends VCUG in infants younger than 6 months if they have an abnormal ultrasound, atypical UTI, or recurrent UTI.[4]</li> </ul>	<p><b>if vesicoureteral reflux is present: contrast seen ascending out of the bladder into the upper urinary tract; if posterior urethral valves present: dilation and elongation of the posterior urethra; may reveal ureterocele, bladder polyp or diverticulae, or post-void residual volume</b></p>

## Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
<b>Appendicitis</b>	<ul style="list-style-type: none"> <li>Focal right lower quadrant pain, guarding.</li> </ul>	<ul style="list-style-type: none"> <li>Ultrasound or CT scan abdomen may show enlarged appendix.</li> </ul>
<b>Gastroenteritis</b>	<ul style="list-style-type: none"> <li>Diarrhea present.</li> </ul>	<ul style="list-style-type: none"> <li>Rotavirus detection in stool may be positive.</li> </ul>
<b>Kawasaki disease</b>	<ul style="list-style-type: none"> <li>Rash, mucositis, extremity swelling, cervical lymph node swelling, conjunctivitis.</li> <li>No signs may be present in those &lt;6 months of age.</li> </ul>	<ul style="list-style-type: none"> <li>Sterile pyuria, transaminase elevation, coronary ectasia, or aneurysms on echocardiogram (late).<sup>[62]</sup></li> </ul>
<b>Vulvovaginitis or vaginal foreign body</b>	<ul style="list-style-type: none"> <li>History of sexual activity/abuse, use of bubble baths, poor hygiene. Dysuria may be associated with vaginal discharge. Vulval appears erythematous on examination.</li> </ul>	<ul style="list-style-type: none"> <li>May be diagnosed clinically based on history, examination, and sterile urine culture. Group A <i>Streptococcus</i> isolated on vaginal culture.</li> <li>Pinworm prep may be positive.</li> </ul>
<b>Sexually transmitted infection</b>	<ul style="list-style-type: none"> <li>History of sexual activity, urethral discharge, frequency, urgency, dysuria.</li> </ul>	<ul style="list-style-type: none"> <li>Chlamydia infection or gonococcus identified on nucleic acid amplification test.</li> </ul>
<b>Nephrolithiasis</b>	<ul style="list-style-type: none"> <li>Colicky pain, family history of urolithiasis, passing of particulate matter in urine.</li> </ul>	<ul style="list-style-type: none"> <li>Urine calcium-creatinine, crystals on microscopic exam.</li> <li>Calculus may be visible on ultrasound.</li> </ul>
<b>Bladder and bowel dysfunction</b>	<ul style="list-style-type: none"> <li>Urinary storage symptoms (incontinence, increased or decreased voiding frequency, urgency, nocturia); urinary voiding symptoms (hesitancy, straining, weak stream, intermittent micturition, dysuria); holding maneuvers to postpone micturition (e.g., forcefully crossing legs, pushing on the genitals or abdomen); a feeling of incomplete bladder emptying; pain in the bladder, urethra, or genitals; fecal incontinence and constipation.</li> </ul>	<ul style="list-style-type: none"> <li>Abnormal urodynamic testing and negative urine cultures.</li> <li>Imaging may show ureterocele, stones, trabeculation, high post-void residual volume, or enlarged rectal diameter.</li> </ul>

Condition	Differentiating signs / symptoms	Differentiating tests
<b>Sepsis with no urinary tract source</b>	<ul style="list-style-type: none"> <li>• Hemodynamic instability.</li> <li>• In infants, symptoms are often nonspecific and may include vomiting, irritability, poor feeding, and jaundice.</li> </ul>	<ul style="list-style-type: none"> <li>• Positive blood and cerebrospinal fluid cultures.</li> </ul>
<b>Urethritis</b>	<ul style="list-style-type: none"> <li>• Urethral discharge, pelvic pain.</li> </ul>	<ul style="list-style-type: none"> <li>• Urine positive polymerase chain reaction results for gonorrhea, chlamydia, or candida.</li> </ul>
<b>Hemorrhagic (viral) cystitis</b>	<ul style="list-style-type: none"> <li>• Hematuria more likely.</li> </ul>	<ul style="list-style-type: none"> <li>• Negative urine culture.</li> </ul>
<b>Interstitial cystitis</b>	<ul style="list-style-type: none"> <li>• Specific symptoms of urinary frequency, urgency, bladder pain with relief on voiding.</li> </ul>	<ul style="list-style-type: none"> <li>• Negative urine culture, hypervascular bladder mucosa, and linear scarring on cystoscopy.<sup>[63]</sup></li> <li>• Some children have persistently positive urine cultures due to bacterial colonization of the bladder.</li> </ul>
<b>Glomerulonephritis</b>	<ul style="list-style-type: none"> <li>• Swelling of hands or feet; gross hematuria; hypertension.</li> </ul>	<ul style="list-style-type: none"> <li>• Significant proteinuria; red cell casts on urinalysis or urine microscopy.</li> </ul>
<b>Meningitis</b>	<ul style="list-style-type: none"> <li>• Photophobia, rash, neck stiffness.</li> <li>• In infants, symptoms are often nonspecific and may include vomiting, irritability, and poor feeding.</li> </ul>	<ul style="list-style-type: none"> <li>• Infants &lt;6 weeks of age may have associated meningitis when <i>Escherichia coli</i> is the UTI pathogen.</li> </ul>
<b>Wilms tumor</b>	<ul style="list-style-type: none"> <li>• Pain, hematuria, no urinary symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>• Ultrasound shows an abdominal mass.</li> <li>• This is the most common form of renal malignancy in childhood.</li> </ul>
<b>Schistosomiasis</b>	<ul style="list-style-type: none"> <li>• Can cause urinary symptoms, including gross hematuria or dysuria.</li> <li>• History of travel to tropical countries, even going several years back, as the child may have been asymptomatic for a prolonged period of time.</li> <li>• The prevalence of infection among school-aged children can be as high as 90%, even in urban areas.<sup>[64]</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Circulating cathodic antigen urine reagent strip: a rapid enzyme-linked immunosorbent assay test that detects adult worm gut-associated glycoproteins and eggs, with a sensitivity of 88.2% (for glycoproteins) and 95.8% (for eggs). Specificity is 100%. Detects <i>Schistosoma mansoni</i> and <i>Schistosoma haematobium</i>. It is used as a diagnostic and monitoring tool to</li> </ul>



Condition	Differentiating signs / symptoms	Differentiating tests
		assess the success of treatment. <a href="#">[65]</a>

## Screening

### Screening for vesicoureteral reflux (VUR)

The American Urological Association recommends screening for VUR in:[\[37\]](#)

- Neonates with prenatally detected hydronephrosis (Society for Fetal Urology [SFU] grade 3 or 4)
- Siblings of children with VUR, if the untested sibling has renal cortical abnormalities or renal size asymmetry on ultrasound, or a history of UTI.

Screening voiding cystourethrogram may be considered in neonates with prenatal hydronephrosis of SFU grade 1 or 2.[\[37\]](#)

## Approach

The decision to start empiric antibiotic therapy is informed by the child's likelihood of having a urinary tract infection and their overall clinical condition. Infection may involve the upper or lower urinary tract; be complicated or uncomplicated; severe or non-severe; recurrent, breakthrough, or a reinfection; atypical, asymptomatic, or symptomatic. See Classification for more information.

Diagnosis and treatment are often concurrent processes. Empiric therapy may be commenced before diagnostic assessment is completed if there is a high risk of serious illness.

Children who are systemically unwell (toxic-looking, hemodynamically unstable, immunocompromised, unable to tolerate oral medication, or not responding to oral medication), and most children ages  $\leq 2$  months, should receive urgent empiric parenteral treatment.<sup>[58] [67]</sup>

Treat children with febrile UTIs as soon as possible (within 48-72 hours) to avoid subsequent renal scarring.<sup>[1] [26]</sup>

Children who have a positive urinalysis but are not systemically unwell may be monitored closely until urine culture results are available.<sup>[1] [4]</sup>

The goal of treatment is the eradication of bacteria. Choice of antimicrobial agents and route of administration (oral versus parenteral) should be based on:

- Severity of illness
- Patient factors (e.g., age, underlying renal disease, immunocompromised, recent antibiotic exposure)
- Most likely pathogen: target initial therapy at *Escherichia coli* and other Enterobacterales, including *Klebsiella* and *Enterobacter* species
- Local antimicrobial resistance patterns: antimicrobial resistance among uropathogens is a significant concern: more than 40% of *E coli* isolates from children with UTIs are resistant to ampicillin, and >20% are resistant to trimethoprim/sulfamethoxazole, which limits their use as initial therapy.<sup>[68]</sup> Consult local guidelines and formularies.

Adjust therapy to the nearest spectrum antibiotic following complete identification of the pathogen and susceptibility data.

Cure rates with antibiotics exceed 95%.<sup>[69]</sup>

Renal function and aminoglycoside blood levels should be monitored in patients treated with aminoglycosides (e.g., gentamicin) for >48 hours.<sup>[40]</sup>

## Uncomplicated UTI

An uncomplicated UTI is one that occurs in a patient who has a structurally and functionally normal urinary tract, normal renal function, and a competent immune system. Uncomplicated UTIs generally involve the lower urinary tract (cystitis) rather than the upper urinary tract.<sup>[1]</sup>

Children may have mild pyrexia and mild dehydration, but do not have vomiting or any signs of sepsis, dehydration, or hemodynamic instability.

Choice of empiric therapy is guided by local antimicrobial resistance patterns. Therapy should be reviewed when the organism and its antimicrobial sensitivities are confirmed by culture, and changed to a narrower-spectrum agent if appropriate.

Oral therapy is usually appropriate for children with uncomplicated UTI. Options include a second- or third-generation cephalosporin (e.g., cefixime), amoxicillin/clavulanate, trimethoprim, trimethoprim/sulfamethoxazole, or nitrofurantoin.[1] [5][70] [71] Cephalexin or amoxicillin may be used second-line if culture results confirm susceptibility.[70] Trimethoprim/sulfamethoxazole is active against multiple antibiotic-resistant bacteria, including extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales such as *E coli* and AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species.[71] Nitrofurantoin is active against cystitis caused by ESBL-producing Enterobacterales and AmpC-beta-lactamase-producing Enterobacterales.[71]

Treatment for penicillin-allergic patients depends on the age of the patient, history of drug allergy, and severity of illness. Consult a specialist for guidance on antibiotic selection in these patients. Allergy to penicillin is generally not a concern in neonates and young infants because they have not been challenged with penicillin before.

Typical treatment course is 7-14 days.[1] The American Academy of Pediatrics (AAP) recommends that oral antibiotic therapy for 7 to 10 days is adequate for uncomplicated febrile UTI that responds well to treatment.[5] One systematic review found that a 2- to 4-day course of antibiotics was as effective as a 7- to 14-day course at eradicating lower UTI in children.[72] A 3- to 5-day course may be considered.[1]

## Complicated UTI

A complicated UTI is one that occurs in a child who has a structural or functional abnormality of the urinary tract. Complicated UTIs generally involve the upper urinary tract (pyelonephritis) rather than the lower urinary tract.[1]

Children  $\leq 2$  months

Neonates and infants ages  $\leq 2$  months are at high risk for serious bacterial infection and sepsis.[1] [40]

Symptoms are nonspecific in this age group, making it difficult to distinguish UTI from other causes of serious bacterial infection at initial evaluation.[41] [58] These children should be admitted to hospital for evaluation and most should receive empiric parenteral antibiotic therapy. See Sepsis in children for more information.

Oral antibiotics may be appropriate for well-appearing, febrile, term infants ages 29-60 days who have positive urinalysis result and normal inflammatory markers.[58]

Choice of empiric therapy is guided by past infections and associated antibiotic susceptibility data from the past 6 months, antibiotic exposures within the past 30 days, and local antimicrobial resistance patterns.[71] Suitable regimens include ampicillin plus gentamicin or ampicillin plus a third-generation cephalosporin (e.g., cefotaxime, cefepime, ceftriaxone).[67] [73] The UK National Institute for Health and Care Excellence (NICE) recommends a third-generation cephalosporin plus an antibiotic active against listeria (e.g., ampicillin) for infants ages  $<3$  months admitted to hospital with fever.[74] Gentamicin is active against multiple antibiotic-resistant bacteria, including ESBL-producing Enterobacterales such as *E coli*, AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species, and *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR).[71] Cefepime is active against AmpC-beta-lactamase-producing Enterobacterales.[71]

Adjust therapy to the nearest spectrum antibiotic treatment following complete identification of the pathogen and determination of susceptibility data. Treatment is usually given for 7-14 days.[40]

Children  $>2$  months with no structural renal disease

The choice between oral and intravenous therapy depends on patient age, suspicion of sepsis, illness severity, hydration status, tolerance for oral medication, and whether there are complications of infection.[1] NICE recommends intravenous antibiotics for children with pyelonephritis who are vomiting, unable to take oral antibiotics, or severely unwell.[75]

Choice of empiric therapy is guided by past infections and associated antibiotic susceptibility data from the past 6 months, antibiotic exposures within the past 30 days, and local antimicrobial resistance patterns.[71] Therapy should be reviewed when the organism and its antimicrobial sensitivities are confirmed by culture, and changed to a narrower-spectrum agent if appropriate.

Examples of suitable oral antibiotics include cephalexin, cefixime, and amoxicillin/clavulanate (if cultures confirm sensitivity).[1] [75] Cefuroxime, ceftriaxone, gentamicin (with or without ampicillin), amikacin, or tobramycin may be used if intravenous treatment is required.[1] [75] Ampicillin is added to cover Enterococci.[67] Amikacin is active against ESBL-producing Enterobacterales such as *E coli* .[71] Similarly to gentamicin, tobramycin is active against multiple antibiotic-resistant bacteria, including ESBL-producing Enterobacterales, AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species, and *Pseudomonas aeruginosa* with DTR.[71]

Treatment course is 7-14 days.[1] Switching from parenteral to oral antibiotic treatment in a stepwise manner for hospitalized patients should be considered whenever possible.[71] One systematic review reported no significant difference in microbiologic eradication, renal scarring, clinical cure, reinfection, persistence of acute pyelonephritis, or reinfection in children who were switched to oral antibiotics after 5-10 days, compared with children who received intravenous antibiotics for 14 days.[76]

Children >2 months with structural renal disease

Choice of empiric therapy is guided by past infections and associated antibiotic susceptibility data from the past 6 months, antibiotic exposures within the past 30 days, and local antimicrobial resistance patterns.[71]

Cephalexin or amoxicillin/clavulanate may be used as first-line oral antibiotics (if culture results are available and bacteria are susceptible).[75]

In patients with an underlying renal disorder who require broader gram-negative and *Pseudomonas* coverage and who are systemically stable at presentation, consider a fluoroquinolone such as oral ciprofloxacin.[77] [78] Ciprofloxacin is active against ESBL-producing Enterobacterales such as *E coli* and AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species.[71]

Systemic fluoroquinolone antibiotics, such as ciprofloxacin, may cause serious, disabling, and potentially long-lasting or irreversible adverse events. This includes, but is not limited to: tendinopathy/tendon rupture; peripheral neuropathy; arthropathy/arthritis; aortic aneurysm and dissection; heart valve regurgitation; dysglycemia; and central nervous system effects including seizures, depression, psychosis, and suicidal thoughts and behavior.[79]

- Prescribing restrictions apply to the use of fluoroquinolones, and these restrictions may vary between countries. In general, fluoroquinolones should be restricted for use in serious, life-threatening bacterial infections only. Some regulatory agencies may also recommend that they must only be used in situations where other antibiotics, that are commonly recommended for the infection, are inappropriate (e.g., resistance, contraindications, treatment failure, unavailability)

- Consult your local guidelines and drug formulary for more information on suitability, contraindications, and precautions.

Consider second-line parenteral ampicillin plus gentamicin for patients with preexisting structural renal disease and normal renal function. Alternative options include cefotaxime or ceftriaxone.[1] Both oral and intravenous formulations of cephalosporins have been demonstrated to be effective.[80]

### Special patient populations

Consult a specialist for guidance on antibiotic selection in patients with penicillin allergy and those who are immunosuppressed, have renal impairment, or do not respond adequately to initial treatment. Therapy is individualized depending on patient factors, severity of illness, likely causative organisms, and local antimicrobial susceptibility patterns.

Allergy to penicillin is generally not a concern in neonates and young infants because they have not been challenged with penicillin before.

Nitrofurantoin should be avoided in children with renal impairment.

Antifungal therapy may be required in immunosuppressed patients.

### Supportive care

Some patients may require supportive care with intravenous fluids and/or an antipyretic (e.g., acetaminophen).

### Lack of response to initial treatment

Lack of response to initial therapy may indicate that the organism is not susceptible to the antimicrobial agent used, or indicate the development of pyonephrosis, renal abscess, or obstructed urine drainage. Culture results should be reviewed and urgent ultrasound performed.

## Recurrent UTI

A recurrent UTI is defined as:[4]

- $\geq 2$  episodes of acute pyelonephritis, or
- 1 episode of acute pyelonephritis plus  $\geq 1$  episode of cystitis, or
- $\geq 3$  episodes of cystitis.

Recurrent UTIs may be due to unresolved infection (initial treatment is inadequate for elimination of bacteria in the urinary tract) or persistent infection (caused by re-emergence of bacteria in the urinary tract due to a site of persistent infection that cannot be eradicated [e.g., infected stones or fistulas]). The same pathogen is implicated in each recurrent infection.[1]

The American Urological Association recommends antibiotic prophylaxis for children ages  $<1$  year with vesicoureteral reflux (VUR) and a history of febrile UTI, or grade 3 to 5 VUR identified through screening. Antibiotic prophylaxis may be considered for children with grade 1 to 2 VUR identified through screening without a history of febrile UTI.[37] The use of antibiotic prophylaxis for children ages  $\geq 1$  year with VUR is determined on a case-by-case basis. Clinical context, including the presence of bladder bowel dysfunction (BBD), patient age, VUR grade, the presence of scarring, and parental preferences, should be taken into account. Prophylaxis is recommended for children with both VUR and BBD.[37] BBD increases the risk of recurrent UTI twofold, and increases the risk of breakthrough UTI in children who also have vesicoureteral reflux.[25] [27]

A short course of prophylactic antibiotics may be considered for toilet-trained children with BBD and recurrent UTIs, while optimizing bladder and bowel management.[19] Children and caregivers should be educated about adequate hydration and ready access to toilets, to prevent delayed voiding.[4] Constipation should be treated to prevent further infections. Maintenance therapy may be required for months or years. See Constipation in children for more information.

Antibiotic prophylaxis may also be considered in children with a significant urologic anomaly.[37] [38]

Prophylactic antibiotics have not been conclusively shown to reduce the risk of recurrent infection or renal scarring in children with or without VUR.[81] [82] [83] [84]

Suitable choices for prophylaxis include a first- or second-generation cephalosporin, trimethoprim, trimethoprim/sulfamethoxazole, or nitrofurantoin.[1] [85] Nitrofurantoin and trimethoprim are preferred where available.[1]

Where possible, choice of prophylactic antibiotic should be guided by recent culture and sensitivity results. Rotating the prophylactic antibiotic used may increase the risk of antibiotic resistance. One meta-analysis calculated that one multidrug-resistant infection occurs for every 21 patients with VUR treated with antibiotic prophylaxis.[86] If a child develops acute UTI while taking prophylaxis, a different antibiotic should be used to treat the acute infection.[85]

The risk of resistance increases with the duration of antibiotic therapy. A course of prophylactic antibiotics usually lasts 3-6 months, after which it should be reassessed.[37] [38]

Surgical management of high-grade VUR has also generally been recommended for children with recurrent UTI, but the added benefit of surgical or endoscopic correction of VUR over antibiotic treatment alone is unclear.[84] [87] Refer patients with grade 4/5 VUR or a significant urologic anomaly to a urologist.[38]

## Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Initial ( summary )	
vesicoureteral reflux: no history of febrile UTIs	
1st	consider prophylactic antibiotics



Acute ( summary )		
age ≤2 months		
	1st	parenteral or oral antibiotics
	adjunct	supportive care
	adjunct	antifungal therapy
age >2 months		
■ uncomplicated UTI	1st	oral antibiotics
■ complicated UTI: no structural renal disease	1st	oral or intravenous antibiotics
	adjunct	supportive care
	adjunct	antifungal therapy
■ complicated UTI: structural renal disease	1st	oral or intravenous antibiotics
	adjunct	supportive care
	adjunct	antifungal therapy
Ongoing ( summary )		
recurrent UTIs		
	1st	consider prophylactic antibiotics
	adjunct	optimize bladder and bowel function
	adjunct	urology referral

# Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

## Initial

vesicoureteral reflux: no history of febrile UTIs

**1st consider prophylactic antibiotics**

### Primary options

» [nitrofurantoin](#): 1 mg/kg orally once daily at bedtime

**OR**

» [trimethoprim](#): 2 mg/kg orally once daily at bedtime

### Secondary options

» [cephalexin](#): 10-15 mg/kg orally once daily at bedtime

**OR**

» [sulfamethoxazole/trimethoprim](#): children  $\geq 2$  months of age: 1-2 mg/kg orally once daily at bedtime

Dose refers to trimethoprim component.

» The American Urological Association recommends antibiotic prophylaxis for children ages <1 year with grade 3 to 5 vesicoureteral reflux (VUR) identified through screening, without a history of febrile UTI. Antibiotic prophylaxis may be considered for children with grade 1 to 2 VUR identified through screening without a history of febrile UTI.[37]

» Suitable choices for prophylaxis include a first- or second-generation cephalosporin, trimethoprim, trimethoprim/sulfamethoxazole, or nitrofurantoin.[1] [85] Nitrofurantoin and trimethoprim are preferred where available.[1]

» Trimethoprim/sulfamethoxazole is active against multiple antibiotic-resistant bacteria, including extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales such as *Escherichia coli* and AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species.[71] Nitrofurantoin is active against cystitis caused by ESBL-producing

## Initial

Enterobacterales and AmpC-beta-lactamase-producing Enterobacterales.[71]

» Where possible, choice of prophylactic antibiotic should be guided by recent culture and sensitivity results. Rotating the prophylactic antibiotic used may increase the risk of antibiotic resistance. If a child develops acute UTI while taking prophylaxis, a different antibiotic should be used to treat the acute infection.[85]

» The risk of resistance increases with the duration of antibiotic therapy. A course of prophylactic antibiotics usually lasts 3 to 6 months, after which it should be reassessed.[37]  
[38]

## Acute

age  $\leq 2$  months

## 1st parenteral or oral antibiotics

## Primary options

» **ampicillin**: neonates: consult specialist for guidance on dose; infants: 50-200 mg/kg/day intravenously given in divided doses every 6 hours, maximum 8 g/day

## --AND--

» **gentamicin**: neonates: consult specialist for guidance on dose; infants: 5 to 7.5 mg/kg intravenously every 24 hours

Adjust dose according to serum gentamicin level. Monitor renal function during treatment.

## -or-

» **cefotaxime**: neonates: consult specialist for guidance on dose; infants: 150-180 mg/kg/day intravenously given in divided doses every 8 hours, maximum 8 g/day

## -or-

» **ceftriaxone**: neonates: consult specialist for guidance on dose; infants: 50-75 mg/kg/day intravenously given in divided doses every 12-24 hours

## -or-

» **cefepime**: neonates: consult specialist for guidance on dose; infants: 100 mg/kg/day intravenously given in divided doses every 12 hours, maximum 4 g/day

## OR

» **amoxicillin/clavulanate**: neonates: consult specialist for guidance on dose; infants: 30 mg/kg/day orally given in 2 divided doses  
Dose refers to amoxicillin component.

» Neonates and infants ages  $\leq 2$  months are at high risk for serious bacterial infection and sepsis.<sup>[1] [40]</sup> Symptoms are nonspecific in this age group, making it difficult to distinguish UTI from other causes of serious bacterial infection at initial evaluation.<sup>[41] [58]</sup> These patients should be admitted to hospital for evaluation and most should receive empiric parenteral antibiotic therapy. See Sepsis in children for more information.

» Oral antibiotics may be appropriate for well-appearing, febrile, term infants ages 29 to 60 days who have positive urinalysis result and normal inflammatory markers.<sup>[58]</sup>

## Acute

» Choice of empiric therapy is guided by past infections and associated antibiotic susceptibility data from the past 6 months, antibiotic exposures within the past 30 days, and local antimicrobial resistance patterns.[71] Suitable regimens include ampicillin plus gentamicin, or ampicillin plus a third-generation cephalosporin (e.g., cefotaxime, cefepime, ceftriaxone).[67] [73] The UK National Institute for Health and Care Excellence (NICE) recommends a third-generation cephalosporin plus an antibiotic active against listeria (e.g., ampicillin) for infants ages <3 months admitted to hospital with fever.[74]

» Gentamicin is active against multiple antibiotic-resistant bacteria, including extended-spectrum beta-lactamase-producing Enterobacterales such as *Escherichia coli*, AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species, and *Pseudomonas aeruginosa* with difficult-to-treat resistance.[71] Cefepime is active against AmpC-beta-lactamase-producing Enterobacterales.[71]

» Adjust therapy to the nearest spectrum antibiotic treatment following complete identification of the pathogen and determination of susceptibility data.

» Consult a specialist for guidance on antibiotic selection in patients with penicillin allergy and those who are immunosuppressed, have renal impairment, or do not respond adequately to initial treatment. Treatment for penicillin-allergic patients depends on the age of the patient, history of drug allergy, and severity of illness. However, allergy to penicillin is generally not a concern in neonates and young infants because they have not been challenged with penicillin before.

» Lack of response to initial therapy may indicate that the organism is not susceptible to the antimicrobial agent used, or indicate the development of pyonephrosis, renal abscess, or obstructed urine drainage. Culture results should be reviewed and urgent ultrasound performed.

» Treatment is usually given for 7 to 14 days.[40]

### adjunct supportive care

Treatment recommended for SOME patients in selected patient group

#### Primary options

## Acute

» **acetaminophen**: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day

» Some patients may require supportive care with intravenous fluids and/or an antipyretic (e.g., acetaminophen).

## adjunct

## antifungal therapy

Treatment recommended for SOME patients in selected patient group

» May be required in immunosuppressed patients. Consult local guidelines for choice of antifungal regimen.

## age &gt;2 months

## ■ uncomplicated UTI

## 1st

## oral antibiotics

## Primary options

» **cefixime**: 8 mg/kg/day orally given in 1-2 divided doses

## OR

» **amoxicillin/clavulanate**: 20-40 mg/kg/day orally given in 3 divided doses; 25-45 mg/kg/day orally given in 2 divided doses  
Dose refers to amoxicillin component.

## OR

» **trimethoprim**: 4-6 mg/kg/day orally given in 2 divided doses

## OR

» **sulfamethoxazole/trimethoprim**: 6-12 mg/kg/day orally given in 2 divided doses  
Dose refers to trimethoprim component.

## OR

» **nitrofurantoin**: 5-7 mg/kg/day orally given in 4 divided doses

## Secondary options

» **cephalexin**: 25-50 mg/kg/day orally given in 2-4 divided doses, maximum 500 mg/dose

## OR



## Acute

» **amoxicillin**: 20-40 mg/kg/day orally given in 3 divided doses; 25-45 mg/kg/day orally given in 2 divided doses

» An uncomplicated UTI is one that occurs in a child who has a structurally and functionally normal urinary tract, normal renal function, and a competent immune system. Uncomplicated UTIs generally involve the lower urinary tract (cystitis) rather than the upper urinary tract.[1]

» Children with uncomplicated UTI may have mild pyrexia and mild dehydration, but do not have vomiting or any signs of sepsis, dehydration, or hemodynamic instability.

» The decision to start empiric antibiotic therapy is informed by the child's likelihood of having a UTI and their overall clinical condition. Children who have a positive urinalysis but are not systemically unwell may be monitored closely until urine culture results are available.[1] [4]

» Treat febrile UTIs as soon as possible (within 48-72 hours) to avoid subsequent renal scarring.[1] [26]

» Choice of empiric therapy is guided by local antimicrobial resistance patterns. Therapy should be reviewed when the organism and its antimicrobial sensitivities are confirmed by culture, and changed to a narrower-spectrum agent if appropriate. Cure rates with antibiotics exceed 95%.[69]

» Oral therapy is usually appropriate for children with uncomplicated lower UTI. Options include a second- or third-generation cephalosporin (e.g., cefixime), amoxicillin/clavulanate, trimethoprim, trimethoprim/sulfamethoxazole, or nitrofurantoin.[1] [70] [71] Cephalexin or amoxicillin may be used second-line if culture results confirm susceptibility.[88]

» Trimethoprim/sulfamethoxazole is active against multiple antibiotic-resistant bacteria, including extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales such as *Escherichia coli* and AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species.[71] Nitrofurantoin is active against cystitis caused by ESBL-producing Enterobacterales and AmpC-beta-lactamase-producing Enterobacterales.[71]

» Treatment for penicillin-allergic patients depends on the age of the patient, history of drug allergy, and severity of illness. Consult a

## Acute

- **complicated UTI: no structural renal disease**

1st

specialist for guidance on antibiotic selection in these patients. Allergy to penicillin is generally not a concern in neonates and young infants because they have not been challenged with penicillin before.

» Typical treatment course is 7-14 days.[1] One systematic review found that a 2- to 4-day course of antibiotics was as effective as a 7- to 14-day course at eradicating lower urinary tract infection in children.[72] A 3- to 5-day course may be considered.[1]

**oral or intravenous antibiotics****Primary options**

» **cephalexin**: 50-100 mg/kg/day orally given in 3-4 divided doses, maximum 1000 mg/dose

**OR**

» **cefixime**: 8 mg/kg/day orally given in 1-2 divided doses

**OR**

» **amoxicillin/clavulanate**: 20-40 mg/kg/day orally given in 3 divided doses; 25-45 mg/kg/day orally given in 2 divided doses  
Dose refers to amoxicillin component.

**OR**

» **cefuroxime sodium**: 50-100 mg/kg/day intravenously given in divided doses every 6-8 hours, maximum 9 g/day

**OR**

» **ceftriaxone**: 50-75 mg/kg/day intravenously given in divided doses every 12-24 hours

**OR**

» **gentamicin**: 5 to 7.5 mg/kg intravenously every 24 hours  
Adjust dose according to serum gentamicin level. Monitor renal function during treatment.

**OR**

## Acute

» **ampicillin**: 50-200 mg/kg/day intravenously given in divided doses every 6 hours, maximum 8 g/day

**-and-**

» **gentamicin**: 5 to 7.5 mg/kg intravenously every 24 hours

Adjust dose according to serum gentamicin level. Monitor renal function during treatment.

**OR**

» **amikacin**: 15 to 22.5 mg/kg intravenously every 24 hours

Adjust dose according to serum amikacin level. Monitor renal function during treatment.

**OR**

» **tobramycin**: 2 to 2.5 mg/kg intravenously every 8 hours

Adjust dose according to serum tobramycin level. Monitor renal function during treatment.

» A complicated UTI is one that occurs in a child who has a structural or functional abnormality of the urinary tract. Complicated UTIs generally involve the upper urinary tract (pyelonephritis) rather than the lower urinary tract.[1]

» The choice between oral and intravenous therapy depends on patient age, suspicion of sepsis, illness severity, hydration status, tolerance for oral medication, and whether there are complications of infection.[1] The National Institute for Health and Care Excellence in the UK recommends intravenous antibiotics for children with pyelonephritis who are vomiting, unable to take oral antibiotics, or severely unwell.[75]

» Choice of empiric therapy is guided by past infections and associated antibiotic susceptibility data from the past 6 months, antibiotic exposures within the past 30 days, and local antimicrobial resistance patterns.[71] Therapy should be reviewed when the organism and its antimicrobial sensitivities are confirmed by culture, and changed to a narrower-spectrum agent if appropriate.

» Examples of suitable oral antibiotics include cephalexin, cefixime, and amoxicillin/clavulanate (if cultures confirm sensitivity).[1] [75] Cefuroxime, ceftriaxone, gentamicin (with or without ampicillin), amikacin, or tobramycin may

## Acute

be used if intravenous treatment is required.[1]  
[75]

» Ampicillin is added to cover Enterococci.[67]  
Amikacin is active against extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales such as *Escherichia coli* .[71]  
Tobramycin is active against multiple antibiotic-resistant bacteria, including ESBL-producing Enterobacterales, AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species, and *Pseudomonas aeruginosa* with difficult-to-treat resistance.[71]

» Treatment course is 7-14 days.[89] Switching from parenteral to oral antibiotic treatment in a stepwise manner for hospitalized patients should be considered whenever possible.[71]  
One systematic review reported no significant difference in microbiologic eradication, renal scarring, clinical cure, reinfection, persistence of acute pyelonephritis, or reinfection in children who were switched to oral antibiotics after 5-10 days, compared with children who received intravenous antibiotics for 14 days.[76]

» Consult a specialist for guidance on antibiotic selection in patients with penicillin allergy and those who are immunosuppressed, have renal impairment, or do not respond adequately to initial treatment. Treatment for penicillin-allergic patients depends on the age of the patient, history of drug allergy, and severity of illness.

» Nitrofurantoin should be avoided in children with renal impairment. Lack of response to initial therapy may indicate that the organism is not susceptible to the antimicrobial agent used, or indicate the development of pyonephrosis, renal abscess, or obstructed urine drainage. Culture results should be reviewed and urgent ultrasound performed.

#### adjunct supportive care

Treatment recommended for SOME patients in selected patient group

#### Primary options

» **acetaminophen**: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day

» Some patients may require supportive care with intravenous fluids and/or an antipyretic (e.g., acetaminophen).

#### adjunct antifungal therapy

## Acute

■ **complicated UTI:  
structural renal disease**

1st

Treatment recommended for SOME patients in selected patient group

» May be required in immunosuppressed patients. Consult local guidelines for choice of antifungal regimen.

**oral or intravenous antibiotics**

**Primary options**

» **cephalexin**: 50-100 mg/kg/day orally given in 3-4 divided doses, maximum 1000 mg/dose

**OR**

» **amoxicillin/clavulanate**: 20-40 mg/kg/day orally given in 3 divided doses; 25-45 mg/kg/day orally given in 2 divided doses  
Dose refers to amoxicillin component.

**OR**

» **ciprofloxacin**: 20-40 mg/kg/day orally given in 2 divided doses

**Secondary options**

» **ampicillin**: 50-200 mg/kg/day intravenously given in divided doses every 6 hours, maximum 8 g/day

**-and-**

» **gentamicin**: 5 to 7.5 mg/kg intravenously every 24 hours  
Adjust dose according to serum gentamicin level. Monitor renal function during treatment.

**OR**

» **cefotaxime**: 150-180 mg/kg/day intravenously given in divided doses every 8 hours, maximum 8 g/day

**OR**

» **ceftriaxone**: 50-75 mg/kg/day intravenously given in divided doses every 12-24 hours

» A complicated UTI is one that occurs in a child who has a structural or functional abnormality of the urinary tract. Complicated UTIs generally involve the upper urinary tract (pyelonephritis) rather than the lower urinary tract.<sup>[1]</sup>

» Choice of empiric therapy is guided by past infections and associated antibiotic

## Acute

susceptibility data from the past 6 months, antibiotic exposures within the past 30 days, and local antimicrobial resistance patterns.[71]

» Cephalixin or amoxicillin/clavulanate may be used as first-line oral antibiotics (if culture results are available and bacteria are susceptible).[75]

» In patients with an underlying renal disorder who require broader gram-negative and *Pseudomonas* coverage and who are systemically stable at presentation, consider a fluoroquinolone such as oral ciprofloxacin.[77] [78]

» Ciprofloxacin is active against extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales such as *Escherichia coli* and AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species.[71]

» Systemic fluoroquinolone antibiotics, such as ciprofloxacin, may cause serious, disabling, and potentially long-lasting or irreversible adverse events. This includes, but is not limited to: tendinopathy/tendon rupture; peripheral neuropathy; arthropathy/arthritis; aortic aneurysm and dissection; heart valve regurgitation; dysglycemia; and central nervous system effects including seizures, depression, psychosis, and suicidal thoughts and behavior.[79] Prescribing restrictions apply to the use of fluoroquinolones, and these restrictions may vary between countries. In general, fluoroquinolones should be restricted for use in serious, life-threatening bacterial infections only. Some regulatory agencies may also recommend that they must only be used in situations where other antibiotics, that are commonly recommended for the infection, are inappropriate (e.g., resistance, contraindications, treatment failure, unavailability). Consult your local guidelines and drug formulary for more information on suitability, contraindications, and precautions.

» Consider second-line parenteral ampicillin plus gentamicin for patients with preexisting structural renal disease and normal renal function. Alternative options include cefotaxime and ceftriaxone.[1] Both oral and intravenous formulations of cephalosporins have been demonstrated to be effective.[80]

» Gentamicin is active against multiple antibiotic-resistant bacteria, including ESBL-producing Enterobacterales, AmpC-beta-lactamase-

## Acute

producing Enterobacterales, and *Pseudomonas aeruginosa* with difficult-to-treat resistance.[71]

» Consult a specialist for guidance on antibiotic selection in patients with penicillin allergy and those who are immunosuppressed, have renal impairment, or fail to respond adequately to initial treatment. Treatment for penicillin-allergic patients depends on the age of the patient, history of drug allergy, and severity of illness.

» Nitrofurantoin should be avoided in children with renal impairment. Lack of response to initial therapy may indicate that the organism is not susceptible to the antimicrobial agent used, or indicate the development of pyonephrosis, renal abscess, or obstructed urine drainage. Culture results should be reviewed and urgent ultrasound performed.

#### adjunct **supportive care**

Treatment recommended for SOME patients in selected patient group

##### Primary options

» **acetaminophen**: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day

» Some patients may require supportive care with intravenous fluids and/or an antipyretic (e.g., acetaminophen).

#### adjunct **antifungal therapy**

Treatment recommended for SOME patients in selected patient group

» May be required in immunosuppressed patients. Consult local guidelines for choice of antifungal regimen.



## Ongoing

## recurrent UTIs

## 1st consider prophylactic antibiotics

## Primary options

» **nitrofurantoin**: 1 mg/kg orally once daily at bedtime

## OR

» **trimethoprim**: 2 mg/kg orally once daily at bedtime

## Secondary options

» **cephalexin**: 10-15 mg/kg orally once daily at bedtime

## OR

» **sulfamethoxazole/trimethoprim**: children  $\geq 2$  months of age: 1-2 mg/kg orally once daily at bedtime

Dose refers to trimethoprim component.

» A recurrent UTI is defined by the UK National Institute for Health and Care Excellence as:  $\geq 2$  episodes of acute pyelonephritis, or 1 episode of acute pyelonephritis plus at least one episode of cystitis, or  $\geq 3$  episodes of cystitis.[4]

» Recurrent UTIs may be due to unresolved infection (initial treatment is inadequate for elimination of bacteria in the urinary tract) or persistent infection (caused by re-emergence of bacteria in the urinary tract due to a site of persistent infection that cannot be eradicated [e.g., infected stones or fistulas]). The same pathogen is implicated in each recurrent infection.[1]

» The American Urological Association recommends antibiotic prophylaxis for children ages  $<1$  year with vesicoureteral reflux (VUR) and a history of febrile UTI. The use of antibiotic prophylaxis for children ages  $\geq 1$  year with VUR is determined on a case-by-case basis. Clinical context, including the presence of bladder bowel dysfunction (BBD), patient age, VUR grade, the presence of scarring, and parental preferences, should be taken into account. Prophylaxis is recommended for children with both VUR and BBD.[37]

» A course of prophylactic antibiotics may be considered for toilet-trained children with BBD

## Ongoing

and recurrent UTIs, while optimizing bladder and bowel management.[19]

» Prophylaxis may also be considered in children with a major urologic anomaly.[38]

» Prophylactic antibiotics have not been conclusively shown to reduce the risk of recurrent infection or renal scarring in children with or without VUR.[81] [82] [83] [84]

» Suitable choices for prophylaxis include a first- or second-generation cephalosporin (e.g., cephalexin), trimethoprim, sulfamethoxazole, trimethoprim/sulfamethoxazole, or nitrofurantoin.[1] [85] Nitrofurantoin and trimethoprim are preferred where available.[1]

» Trimethoprim/sulfamethoxazole is active against multiple antibiotic-resistant bacteria, including extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales such as *Escherichia coli* and AmpC-beta-lactamase-producing Enterobacterales such as *Klebsiella* species.[71] Nitrofurantoin is active against cystitis caused by ESBL-producing Enterobacterales and AmpC-beta-lactamase-producing Enterobacterales.[71]

» Where possible, choice of prophylactic antibiotic should be guided by recent culture and sensitivity results. Rotating the prophylactic antibiotic used may increase the risk of antibiotic resistance. One meta-analysis calculated that one multidrug-resistant infection occurs for every 21 patients with VUR treated with antibiotic prophylaxis.[86] If a child develops acute UTI while taking prophylaxis, a different antibiotic should be used to treat the acute infection.[85]

» The risk of resistance increases with the duration of antibiotic therapy. A course of prophylactic antibiotics usually lasts 3 to 6 months, after which it should be reassessed.[37] [38]

#### adjunct optimize bladder and bowel function

Treatment recommended for SOME patients in selected patient group

» Any bladder or bowel dysfunction associated with recurrent UTIs must be addressed. Bladder bowel dysfunction increases the risk of recurrent UTI twofold, and increases the risk of breakthrough UTI in children who also have vesicoureteral reflux.[25] [27] Children and caregivers should be educated about adequate hydration and ready access to toilets,

## Ongoing

to prevent delayed voiding.[4] Constipation should be treated to prevent further infections. Fecal disimpaction with laxatives and enemas is followed by maintenance therapy with stool softeners such as polyethylene glycol.[19] Maintenance therapy may be required for months or years.

### **adjunct urology referral**

Treatment recommended for SOME patients in selected patient group

» Surgical management of high-grade vesicoureteral reflux (VUR) has also generally been recommended for children with recurrent UTI, but the added benefit of surgical or endoscopic correction of VUR over antibiotic treatment alone is unclear.[84] [87] Refer patients with grade IV/V VUR or a significant urologic anomaly to a urologist.[38]

## Emerging

### Ceftolozane/tazobactam

Ceftolozane/tazobactam, a fifth-generation cephalosporin in combination with a beta-lactamase inhibitor, is approved in the US and Europe for the treatment of complicated UTIs (including pyelonephritis) in children. Clinical trial results published in the prescribing information for ceftolozane/tazobactam indicate that the safety profile of the antibiotic in children is similar to that observed in adults, with thrombocytosis and diarrhea representing the most common adverse effects. Further data are needed to determine the role of ceftolozane/tazobactam in the treatment algorithm for UTI in children.

### MV140

Recent studies have shown that MV140, a preparation of whole-cell inactivated bacteria, can decrease UTI incidence and prevent recurrence for up to 1 year in women, when compared with placebo.[90] [91] The preparation consists of equal percentages of selected strains of four bacterial species (V121 *Escherichia coli*, V113 *Klebsiella pneumoniae*, V125 *Enterococcus faecalis*, and V127 *Proteus vulgaris*), and is administered sublingually. Further studies are required and ongoing; however, results have been promising in global literature.[92]

## Primary prevention

The American Urological Association recommends antibiotic prophylaxis for children <1 year old with grade 3 to 5 vesicoureteral reflux (VUR) identified through screening, but no history of febrile UTI. Antibiotic prophylaxis may be considered for children with grade 1 to 2 VUR identified through screening, without a history of febrile UTI.[37]

Some experts recommend targeted antibiotic prophylaxis in patients with other anatomic urinary abnormalities.[38]

## Secondary prevention

After a first UTI, it is recommended that patients' families and clinicians maintain a high index of suspicion for recurrent UTI.[4]

For children with bladder and bowel dysfunction (BBD), timed voiding every 2 hours during the day is helpful. Constipation is the main cause of voiding symptoms in children with BBD. Fecal disimpaction with enemas and laxatives should be followed by maintenance therapy with stool softeners such as polyethylene glycol to achieve soft, painless bowel movements.[19] Therapy may be required for months or years.

A placebo-controlled randomized study analyzing the utility of cranberry products in preventing recurrent UTIs in children showed that, while it did not significantly reduce the number of children who experienced a recurrence of UTI, it was effective in reducing the actual number of recurrences and related antimicrobial use.[98] However, the compliance rate with chronic consumption of cranberry products was unsatisfactory. One meta-analysis demonstrated that probiotics are not effective in the secondary prevention of UTIs.[99]

The American Urological Association recommends antibiotic prophylaxis for children ages <1 year with vesicoureteral reflux (VUR) and a history of febrile UTI.[37] The use of antibiotic prophylaxis for children ages ≥1 year with VUR is determined on a case-by-case basis. Clinical context, including the presence of BBD, patient age, VUR grade, the presence of scarring, and parental preferences, should be taken into account. Prophylaxis is recommended for children with both VUR and BBD.[37] A short course of prophylactic antibiotics may be considered for toilet-trained children with BBD and recurrent UTIs, while optimizing bladder and bowel management.[19] Prophylaxis may also be considered in children with a major urologic anomaly.[37] [38]

## Patient discussions

For children with bladder bowel dysfunction (BBD), timed voiding every 2 hours during the day is helpful. Constipation is the main cause of voiding symptoms in children with BBD. Fecal disimpaction with enemas and laxatives should be followed by maintenance therapy with stool softeners such as polyethylene glycol to achieve soft, painless bowel movements.<sup>[19]</sup> Therapy may be required for months or years.

## Monitoring

### Monitoring

Routine follow-up is not required for patients with episodes of uncomplicated UTI who receive antimicrobial treatment and experience resolution of symptoms.

Renal scintigraphy (dimercaptosuccinic acid [DMSA] scan) to detect renal scarring should be arranged 4 to 6 months following acute infection for children with recurrent or atypical/complicated UTI.<sup>[4]</sup> <sup>[11]</sup>

Periodic renal function monitoring, blood pressure, height, weight, and testing for proteinuria should be performed in patients with renal parenchymal defects.<sup>[4]</sup>

## Complications

Complications	Timeframe	Likelihood
<b>antibiotic drug rash</b>	<b>short term</b>	<b>medium</b>
<p>Therapy should be stopped if rash is urticarial.</p> <p>Initiation of a different class of antibiotics, based on susceptibility testing, should be considered.</p>		
<b>renal abscess</b>	<b>short term</b>	<b>low</b>
<p>Risk factors for renal abscess include underlying urinary tract abnormalities, primary infection elsewhere with bacteremia, preceding urinary tract surgery, immunodeficiency, trauma to the kidney, and diabetes mellitus.</p> <p>In patients presenting with renal abscess, percutaneous aspiration of the abscess, performed by an interventional radiologist, is useful to identify the pathogen and guide therapy.</p> <p>A pediatric infectious disease specialist and pediatric nephrologists should be consulted in cases where open surgical drainage is being considered.</p> <p>Follow-up can consist of serial ultrasounds and monitoring of inflammatory markers (C-reactive protein).</p>		
<b>phlegmon (lobar nephronia)</b>	<b>short term</b>	<b>low</b>
<p>In most children with lobar nephronia, prolonged parenteral antimicrobial therapy is usually curative.</p>		
<b>sepsis</b>	<b>short term</b>	<b>low</b>
<p>Sepsis is more common in neonates, premature infants, and infants with urinary symptoms.</p>		
<b>antibiotic-related colitis</b>	<b>short term</b>	<b>low</b>
<p>Stool should be tested for <i>Clostridium difficile</i>. If the result is positive, vancomycin, fidaxomicin, or metronidazole is added.</p> <p>Causative antibiotic is stopped if possible.</p>		
<b>renal scarring</b>	<b>long term</b>	<b>low</b>
<p>Scarring occurs secondary to renal parenchymal involvement (pyelonephritis).</p> <p>It has increased risk of occurrence with delay in treatment, increased number of episodes of pyelonephritis, and with acute lobar nephronia.[96] Children with high-grade vesicoureteral reflux commonly have associated renal dysplasia, which is indistinguishable from renal scars on the baseline dimercaptosuccinic acid (DMSA) scan. However, progression or new scarring on repeat DMSA scan suggests acquired renal scarring.</p>		
<b>chronic kidney disease</b>	<b>long term</b>	<b>low</b>
<p>Increased areas of renal scarring from pyelonephritis may lead to decreased amounts of functional renal tissue and the development of renal insufficiency with time.</p>		



Complications	Timeframe	Likelihood
A childhood history of clinically evident kidney disease was associated with a significantly increased risk (hazard ratio 4.19) of end-stage renal disease, even if renal function was apparently normal in adolescence. This suggests that kidney injury or structural abnormality in childhood has long-term sequelae.[97]		

## Prognosis

Following a first urinary tract infection, 15% of patients develop renal scarring detectable with renal scintigraphy.[30] Vesicoureteral reflux increases the risk of renal scarring, especially at higher grades.[83] [93] The risk of scarring is reduced by prompt administration of antibiotics to febrile children with UTI.[26] Nevertheless, most children with UTI do not have any long-term sequelae.[94]

Recurrent upper UTI can lead to renal scarring and renal impairment.[95] Children who are immunocompromised or who have structural or functional renal abnormalities are at an increased risk of recurrent infection.[83]

# Diagnostic guidelines

## International

**Evaluation and management of well-appearing febrile infants 8 to 60 days old** (<https://pediatrics.aappublications.org/content/148/2/e2021052228>) [58]

**Published by:** American Academy of Pediatrics

**Last published:** 2021

**Appropriateness criteria: urinary tract infection - child** (<https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria>) [11]

**Published by:** American College of Radiology

**Last published:** 2023

**Urinary tract infection in infants and children: diagnosis and management** (<https://cps.ca/en/documents>) [40]

**Published by:** Canadian Paediatric Society

**Last published:** 2014 (re-affirmed 2020)

**Paediatric urology: urinary tract infections in children** (<https://uroweb.org/guidelines>) [1]

**Published by:** European Association of Urology

**Last published:** 2024

**Updated Italian recommendations for the diagnosis, treatment and follow-up of the first febrile urinary tract infection in young children** (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7004047>) [66]

**Published by:** Italian Society of Pediatric Nephrology

**Last published:** 2020

**Urinary tract infection in under 16s: diagnosis and management** (<https://www.nice.org.uk/guidance/ng224>) [4]

**Published by:** UK National Institute for Health and Care Excellence

**Last published:** 2022

# Treatment guidelines

## International

**Evaluation and management of well-appearing febrile infants 8 to 60 days old** (<https://pediatrics.aappublications.org/content/148/2/e2021052228>) [58]

**Published by:** American Academy of Pediatrics

**Last published:** 2021

**Management and screening of primary vesicoureteral reflux in children** (<https://www.auanet.org/guidelines-and-quality/guidelines>) [37]

**Published by:** American Urological Association

**Last published:** 2017

**Urinary tract infections in infants and children: diagnosis and management** (<https://cps.ca/en/documents>) [40]

**Published by:** Canadian Paediatric Society

**Last published:** 2014 (re-affirmed 2020)

**Guidelines on paediatric urology: urinary tract infections in children** (<https://uroweb.org/guidelines>) [1]

**Published by:** European Association of Urology

**Last published:** 2024

**Updated Italian recommendations for the diagnosis, treatment and follow-up of the first febrile urinary tract infection in young children** (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7004047>) [66]

**Published by:** Italian Society of Pediatric Nephrology

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**Urinary tract infection in under 16s: diagnosis and management** (<https://www.nice.org.uk/guidance/ng224>) [4]

**Published by:** UK National Institute for Health and Care Excellence

**Last published:** 2022

## Key articles

- European Association of Urology. Guidelines on paediatric urology. 2024 [internet publication]. [Full text \(https://uroweb.org/guidelines/paediatric-urology/chapter/introduction\)](https://uroweb.org/guidelines/paediatric-urology/chapter/introduction)
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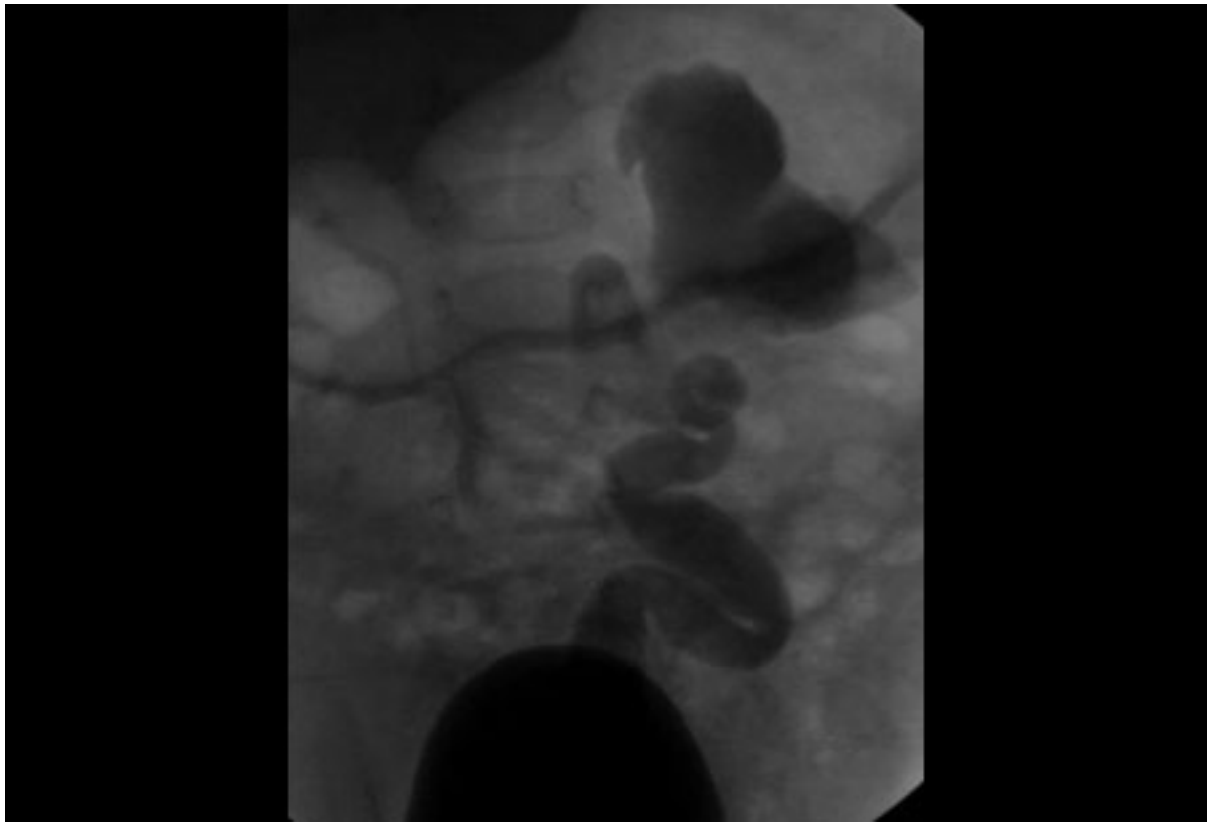
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## Images



*Figure 1: Fluoroscopic image showing high-grade vesicoureteral reflux*

*From the collection of Dr Mary Anne Jackson*



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### Figure 1 – BMJ Best Practice Numeral Style

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