MedicineToday 2015; 16(2): 12-18

PEER REVIEWED FEATURE
2 CPD POINTS

UTIs in children

Who to image, when to treat

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Urinary tract infections are common in childhood. Testing of correctly obtained urine specimens is the gold standard method of diagnosis. There is much debate about the use of imaging and antibiotic prophylaxis in affected children.

Key points

- **Appropriate urine collection is essential for the diagnosis of urinary tract infections (UTIs) in children.**
- **Prompt treatment of affected children minimises the risk of long-term damage after a UTI.**
- **All infants under 6 months of age and a select group over 6 months of age will require a renal ultrasound after their first UTI.**
- **Children should only undergo a micturating cystourethrogram after consultation with a paediatric nephrologist or paediatric urologist.**
- **Prophylactic antibiotics are beneficial to prevent further UTIs in some patients but they should not be prescribed routinely.**

Urinary tract infections (UTIs) are common and usually easily treated with no long-term consequences. For most children a UTI is a limited illness, but a small number will have anatomical abnormalities that predispose them to further UTIs, renal problems and/or urological problems. Identifying these 'at-risk' children for whom a UTI is a significant health risk has been the topic of debate for many years with periodic changes being made to the accepted investigation and management guidelines. This article reviews the current evidence for the diagnosis, acute management and investigation of children with UTIs, and also refers to the published guidelines of the National Institute for Health and Care Excellence (NICE) in the UK and the American Academy of Pediatrics (AAP).[1,2]

Some definitions of urinary conditions are provided in the Box because it is often helpful to differentiate pyelonephritis from cystitis or a lower UTI. These definitions are quite arbitrary but widely accepted and serve as a guide when deciding on follow up.

A retrospective Swedish study of 3553 children aged 7 years showed that 1.7% of boys and 8.4% of girls had had at least one confirmed UTI.[3] Other studies have confirmed the prevalence of UTIs in children less than 5 years of age to be between 3 and 8% with peaks in children aged 6 to 12 months and in uncircumcised boys less than 3 months old.[4,5] UTIs are uncommon in boys beyond infancy and if they occur should prompt further evaluation of the child.

CLINICAL PRESENTATION

The signs and symptoms of UTIs vary with the age of the child. Infants with UTIs will often present with nonspecific symptoms of fever, irritability, vomiting and poor feeding. Small babies will look very unwell as they often have concomitant bacteraemia.

Toddlers with UTIs also tend to have vague symptoms of general malaise, poor appetite and irritability with or without fever. Toddlers can show a reluctance to void with screaming episodes that coincide with them wetting their

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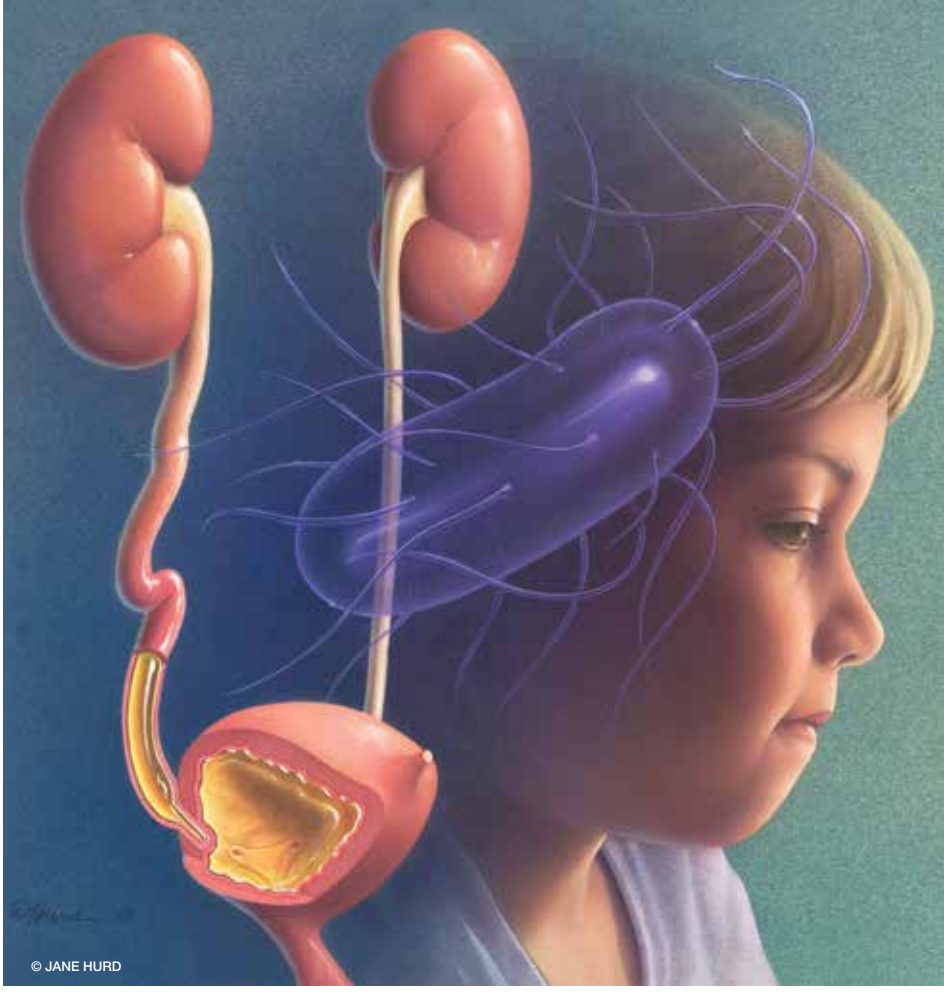

DEFINITIONS OF CLINICAL PRESENTATION OF BACTERIURIA

Significant bacteriuria
- More than 10^5 CFU/mL from a clean-catch specimen of urine; or more than 10^4 CFU/mL from a catheter specimen of urine; or more than 10^2 CFU/mL from a urine sample from a suprapubic aspirate.

Acute cystitis (lower UTI)
- Temperature below 38°C with significant bacteriuria and lower urinary tract symptoms such as dysuria, frequency, urgency and incontinence.

Acute pyelonephritis (upper UTI)
- Temperature above 38°C with significant bacteriuria, with or without abdominal or loin pain and symptoms of cystitis; or temperature below 38°C with significant bacteriuria and loin pain. Occasionally infants may have hypothermia rather than fever.

Atypical UTI
- Septicaemia, poor urine flow, abdominal or bladder mass, abnormal renal function, seriously ill, failure to respond to appropriate antibiotics within 48 hours or infection with an organism other than *Escherichia coli*.

Recurrent UTI
- At least two episodes of pyelonephritis; or one episode of pyelonephritis plus at least one episode of cystitis; or at least three episodes of cystitis.

Asymptomatic bacteriuria
- Repeated specimens with bacteriuria but no reported symptoms.

ABBREVIATIONS: CFU = colony-forming units; UTI = urinary tract infection.

nappies. Parents will often report an odd smell to the child's urine but this has been shown to be nonspecific in studies and is not a good discriminating feature for a UTI.[6] Older, verbal children are more likely to report dysuria, urinary frequency, wetting and lower abdominal or back pain. Children of any age may present with macroscopic haematuria but this is relatively uncommon and there is usually associated dysuria. Rigors are common in children with pyelonephritis but are nonspecific.

DIAGNOSIS OF UTIS

Even in very unwell children a urine specimen should be obtained before the initiation of antibiotics; this is the gold standard for the diagnosis of a UTI. Urine can be collected by suprapubic aspirate, with an in and out catheter, or using a clean-catch or midstream urine technique; however, bag specimens are not suitable. No growth from a bag specimen will confirm the absence of a UTI, but it is impossible to interpret accurately a positive growth because of the high risk of contamination. A study in which children who were not toilet trained had urine collections both by bag and by catheter found that 40% would have been misdiagnosed by bag collection.[7] In the primary care setting, a clean-catch or midstream urine specimen is the most appropriate, acknowledging the higher risk of contamination with these methods (up to 27%). The risk of contamination can be reduced by appropriate cleaning of the skin around the urethral opening followed by gentle retraction of either the labia in girls or the foreskin in uncircumcised boys.

Given the delay in obtaining urine culture results, several studies have assessed the use of rapid tests such as urine dipsticks and urine microscopy for the diagnosis of UTIs. An initial meta-analysis suggested that a negative urine dipstick test for leucocyte esterase and nitrite or a negative urine microscopy result for bacteria and pyuria excluded a UTI reasonably well.[8] A subsequent meta-analysis of 95 studies showed there was a specificity of 0.98 (95% confidence interval [CI], 0.96 to 0.99) for a UTI if the urine dipstick test was positive for both leucocyte esterase and nitrite.[9] Nitrite positivity alone is highly suggestive of a UTI; however, many children whose urine is nitrite negative may still have a UTI as they empty their bladders frequently and may be infected with a bacteria that does not break down nitrates to nitrites. A leucocyte esterase positive test alone is less predictive of a UTI. The most accurate predictor of a UTI is microscopy with Gram stain for bacteria but even this test misses 9% of infections.

It seems that the rapid tests are less helpful in children younger than 2 years of age.[10] Despite these flaws, urine dipstick testing and urine microscopy can certainly aid in the diagnosis of UTI and are recommended routinely. However, it is essential that a urine culture is also performed to confirm the diagnosis. There are different criteria for a positive culture based on the urine collection method. A growth of more than 10^5 colony-forming units per mL (CFU/mL) is commonly used as the definition of a UTI but with a catheter specimen this is decreased to 10^4 CFU/mL and with a specimen from a suprapubic aspirate 10^2 CFU/mL is significant.[5,11,12]

TREATMENT OF UTIS

Empiric antibiotic therapy should be initiated once a urine specimen has been obtained, because prompt treatment has been associated with a reduced risk of renal scarring.[13] The most common micro-organism causing UTIs is *Escherichia coli* followed by *Klebsiella*, *Proteus*, *Pseudomonas* and *Enterococcus* species.[14] There is emerging antibiotic resistance and more than 60% of micro-organisms associated with UTIs are resistant to ampicillin and about 30% are resistant to trimethoprim.[15,16] Infections with multiresistant extended-spectrum beta-lactamase (ESBL)-producing *E. coli* are increasingly being seen. Risk factors for infection with ESBL-producing *E. coli* include recent hospitalisation, previous use of third-generation cephalosporins or fluoroquinolones and UTI prophylaxis with cephalexin.[17,18]

Trimethoprim, amoxycillin or a cephalosporin is generally the suitable first-line treatment for a child with a UTI but the choice of initial antibiotic should take into account the local resistance patterns and any previous susceptibilities in a child with recurrent infection. The rise in antibiotic resistance also emphasises the need to follow up on culture results and micro-organism susceptibilities.

The duration of treatment remains debatable. In children with cystitis two to four days of antibiotics is as effective as a longer course, but several systematic reviews agree that a single dose of antibiotic is less effective than a 10-day course.[19,20] Most children with pyelonephritis can be treated with oral antibiotics for seven to 10 days, and it is recommended to choose an antibiotic with lower resistance rates such as a cephalosporin or amoxycillin and clavulanic acid. Children under 3 months of age, those assessed as being severely unwell and those not tolerating oral fluids will require urgent referral for consideration of hospital admission for intravenous therapy. If a child is already taking a prophylactic antibiotic then a different antibiotic should be used to treat a suspected UTI and not an increased dose of the same antibiotic.

Patients with asymptomatic bacteriuria do not require treatment and indeed recurrent courses of antibiotics for this condition may lead to alteration of the virulence of the bacteria, resulting in symptomatic bacteriuria.[21]

IMAGING FOLLOWING A UTI

Imaging of a child after a UTI is probably the area of most confusion and, despite the published guidelines, there is still no full consensus among paediatric nephrologists, urologists and paediatricians as to the appropriate investigations. The more recent guidelines from the AAP and NICE have tried to minimise the use of investigations while still identifying those children at risk of further renal problems.[2]

The age of the child, the nature of the infection and a first episode versus a recurrence are all taken into account when deciding on investigations to perform in children after a UTI.

Tables 1 and 2 outline the recommended investigations for children aged younger than 6 months and 6 months or older, respectively, and are adapted from the NICE guidelines.[1] Particular note should be made that only children younger than 6 months of age, those with atypical UTIs or those with recurrent UTIs should have a renal and bladder ultrasound scan performed routinely. For infants sick enough to be admitted to hospital this is usually performed during the acute admission, but for children treated in the community it can be carried out within six weeks of the infection if the child responds to appropriate treatment within 48 hours. Ultrasound will show abnormalities such as renal pelvis dilatation, hydronephrosis or cysts that may signify an underlying disease with a predisposition to UTI. Ultrasound is not a sensitive test for vesicoureteric reflux (VUR).

Although the AAP recommends a micturating cystourethrogram (MCUG) be performed in all children younger than 2 years of age with abnormal ultrasound findings after a first febrile UTI, this is not the practice in Australia. An MCUG would only be considered in infants aged less than 6 months of age with abnormal renal imaging. Most children older than 6 months will not need an MCUG and they should be referred to a paediatric specialist if an MCUG is thought to be necessary. There is a small risk of contracting a UTI during an MCUG and it is therefore recommended

TABLE 1. FOLLOW-UP INVESTIGATIONS IN A CHILD YOUNGER THAN 6 MONTHS

Type of UTI	Ultrasound during acute infection	Ultrasound within six weeks of infection	MCUG	DMSA scan four to six months after acute infection
Typical	Not essential	Yes	Consider if ultrasound is abnormal	Consider if ultrasound is abnormal
Atypical	Yes	No	Consider	Consider
Recurrent	Yes	No	Consider	Consider

Adapted from the NICE guidelines.[1]
ABBREVIATIONS: DMSA = dimercaptosuccinic acid; MCUG = micturating cystourethrogram; UTI = urinary tract infection.

TABLE 2. FOLLOW-UP INVESTIGATIONS IN A CHILD AGED 6 MONTHS OR OLDER

Type of UTI	Ultrasound during the acute infection	Ultrasound within six weeks of infection	DMSA scan four to six months after acute infection
Typical	Not essential	Not essential	No
Atypical	Yes*	N/A	Consider
Recurrent	Not essential	Yes	Consider

*If a micro-organism other than *Escherichia coli* is cultured but the child responds well to antibiotics the ultrasound could be performed within six weeks.
Adapted from the NICE guidelines.[1]
ABBREVIATIONS: DMSA = dimercaptosuccinic acid; N/A = not applicable; UTI = urinary tract infection.

that the infants receive a treatment dose of antibiotics the day before, the day of and the day after this procedure.

Ultrasound is not a sensitive test for renal scarring and a nuclear dimercaptosuccinic acid (DMSA) scan is therefore the investigation of choice if scarring is suspected. Only a small number of children with UTIs will require this investigation and it is generally only recommended for those with recurrent UTIs, when at least one infection has been febrile. There should be a period of at least four months between an acute UTI and the DMSA scan because if it is performed earlier it may pick up an area of resolving inflammation rather than a permanent scar. A DMSA scan carries a risk of significant radiation exposure and should only be performed if the result will alter the patient's treatment.

PREVENTION OF RECURRENT UTI

Up to one-third of children presenting with UTIs will have recurrent infections. Recurrence does not equate with the presence of VUR, although this is thought to increase the risk. In many children, the risk of recurrence can be reduced with simple conservative measures such as:

- an adequate fluid intake with regular voiding
- the prevention or treatment of constipation
- the management of dysfunctional voiding (e.g. difficulty emptying the bladder or urinary hesitancy, urgency and/or frequency)
- implementing the correct wiping technique.

Many preschool-aged girls in particular tend to drink minimal amounts of fluids and void only two to three times per day. These children should be set a minimum amount of fluid intake for the day and should be reminded to void about six times a day. The correct 'front to back' wiping technique should be described to girls and their mothers.

The role of prophylactic antibiotics is another topic of great debate. There have recently been two large randomised controlled trials (RCTs) and a meta-analysis that have shown a benefit of prophylaxis.[11,12,22] The first of the recent RCTs included children with and without VUR and showed a small benefit of about 6% in the prevention of further UTIs.[11] The second RCT, the Randomized Intervention for Children With Vesicoureteral Reflux (RIVUR) study, included only children with VUR and showed that prophylaxis reduced the risk of recurrent infection by 50%.[12] In both studies, there was an increase in the number of resistant micro-organisms in the antibiotic-treated arm.

The NICE guidelines were written before either of these two trials were published and do not recommend routine prophylaxis following a first UTI but do advise consideration of prophylaxis following recurrent UTIs. The AAP gathered data from the authors of six RCTs, before the RIVUR study, and performed a meta-analysis of the effect of prophylactic antibiotics in children less than 24 months

old.[2] They found no benefit of antibiotic use in children with or without VUR. Given the current evidence, parental preference will often dictate if prophylaxis is prescribed. In my personal practice, I have found a period of six to 12 months of prophylaxis can be useful in children with recurrent UTIs, along with the conservative measures of prevention being implemented at home.

Circumcision can be a very effective intervention in young boys. A meta-analysis showed that the benefits are significant in infant boys with a history of more than one UTI or in those with high-grade VUR and a previous UTI.[23]

Antireflux surgery is reserved for children with significant VUR who have recurrent UTIs despite prophylactic antibiotics. Often a cystoscopic injection of a polymer into the ureteric orifice is preferable to open surgery.

CONCLUSION

UTIs are common in childhood but most children have no significant underlying renal anomalies. Prompt diagnosis and treatment minimise any long-term damage to the kidneys. Far fewer children are now investigated radiologically than in the past and future studies will determine if these strategies are appropriate.

The effect of prophylactic antibiotics in preventing further infections is small but of benefit. Asymptomatic bacteriuria does not require antibiotic treatment and should not be investigated. MT

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

COMPETING INTERESTS: None.

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