Investigating and managing the child with recurrent UTIs

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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Urinary tract infections (UTIs) are among the most common bacterial infections in children. While UTIs may cause significant short term morbidity, most children recover completely and have no long term clinically important sequelae, even when imaging studies demonstrate underlying urinary tract pathology such as vesicoureteric reflux.

Epidemiology of UTIs

By the age of 7 years, 7.8% of girls and 1.6% of boys have had at least one UTI verified on urine culture.[1] The incidence of first time UTI is highest in the first year of life: of children who get UTI, 75% of boys and 50% of girls have their first infection when aged under 1 year.[2]

The recurrence rate of symptomatic UTI is 12 to 15% for boys and girls.[3] The risk for recurrence is greatest in the first year after the initial UTI and declines in subsequent years.[4]

Pyelonephritis is the dominant infection in young children, while acute cystitis is more common in older patients.[5]

The prevalence of asymptomatic bacteriuria in schoolgirls is around 1.8%.[6] Elimination of the bacteriuria with antibiotics is followed by recurrent UTIs in 80% of patients.[7]

Factors predisposing to recurrent symptomatic UTIs

Age

UTIs are more likely to recur when the child is below 6 months of age at the first infection.[2]

Ureteric reflux

Recurrence of UTI is more common if the child has vesicoureteric reflux associated with pelvicalyceal and ureteric dilatation (grades 3 to 5 of vesicoureteric reflux).[2] The presence of lower grades of vesicoureteric reflux is not associated with recurrence.[2]

Renal damage

Recurrence is more likely if the child has severe renal damage evident at the first infection.[2] In addition, pyelonephritis is the predominant type of UTI in patients with renal damage.[5]

Bladder dysfunction

Commonly, children with recurrent UTI suffer from urgency and urge incontinence between infections. Urodynamic studies of children with recurrent UTI and the urge syndrome have demonstrated three patterns of bladder dysfunction.[8]

IN SUMMARY

- **A positive urine culture is required to diagnose urinary tract infections (UTIs).**
- **If the child has no significant fever with UTIs and the initial ultrasound was normal, no further investigation is required.**
- **In recurrent febrile UTIs, DMSA scans looking for chronic scarring should be performed six to 12 months after the last infection.**
- **Incomplete bladder emptying could contribute to recurrent UTI.**
- **The risk for recurrence is greatest in the first year after the initial UTI and declines in subsequent years.**

In the first type, the child suffers extreme urgency during bladder filling (due to uninhibited detrusor muscle contractions) and forcefully contracts all pelvic floor muscles to prevent wetting. With pelvic floor contraction, the intravesical pressure may rise markedly during bladder filling. However, when the bladder is full, the child voids completely with normal bladder pressure.

In the second type, the child's urine flow is intermittent, with bursts of pelvic floor muscle contraction occurring simultaneously with detrusor contraction. Bladder pressure rises during voiding, and voiding may be incomplete.

In the third type, the child acquires the habit of voiding with abdominal pressure using the Valsalva manoeuvre. These children develop increased bladder volumes and incomplete bladder emptying. Although UTIs are often associated with bladder dysfunction, the exact relationship is hard to define. In some cases, symptoms of bladder dysfunction develop after the first UTI, while in other cases the UTIs appear in children with pre-existing bladder dysfunction.

Investigating the child with recurrent UTIs

The flowchart on page 54 provides an algorithm for investigating and managing a child with recurrent UTIs. It is still recommended that all children be investigated with at least a renal and bladder ultrasound after the first documented UTI (Figure 1). The extent of investigation after the initial UTI remains controversial and is addressed in more detail in the final section headed 'UTIs and imaging studies'. In the discussion below, it has been assumed that major urinary tract pathology other than vesicoureteric reflux has been excluded and that the child has no serious neurological abnormality such as spina bifida.

Has the infection been confirmed by urine culture?

Since up to 80% of children who present with lower urinary tract symptoms do not have a UTI, a positive urine culture is required to diagnose UTI.[9] In children the presence or absence of nitrites and leucocytes on dipstick are not sufficiently sensitive or specific to diagnose or exclude UTI.[1]

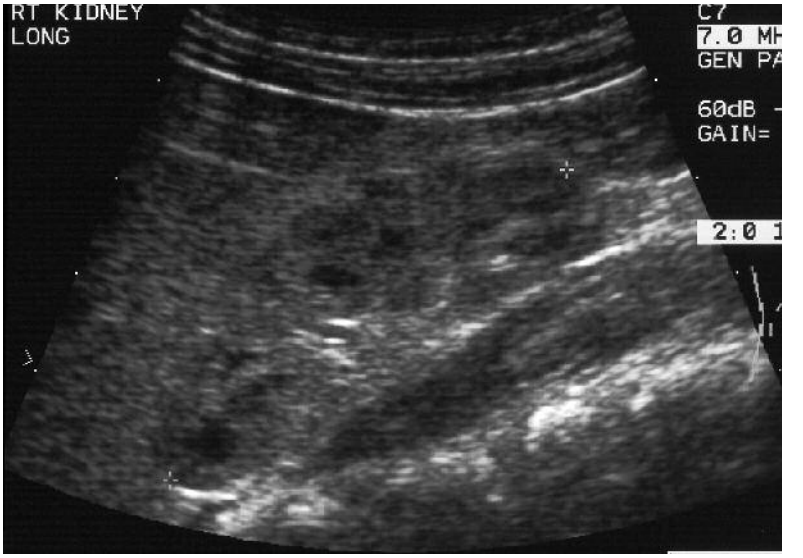


Figure 1. Normal renal ultrasound. Sagittal view of right kidney. Note the fetal lobulation, which is a normal finding in babies.

Does the child have symptoms of UTI?

Antibiotic treatment of children with asymptomatic bacteriuria should be avoided. Unlike pregnant women, untreated girls with asymptomatic bacteriuria are not at a higher risk of acute pyelonephritis than treated girls.[6] In addition, there is no impairment of renal growth or deterioration in glomerular filtration rate in untreated girls, even if renal scarring is present.[6,7] Asymptomatic bacteriuria commonly recurs after antibiotic treatment; in 15% of girls without and 30% of those with renal scarring, it recurs as acute pyelonephritis.[7]

Does the child have bladder dysfunction?

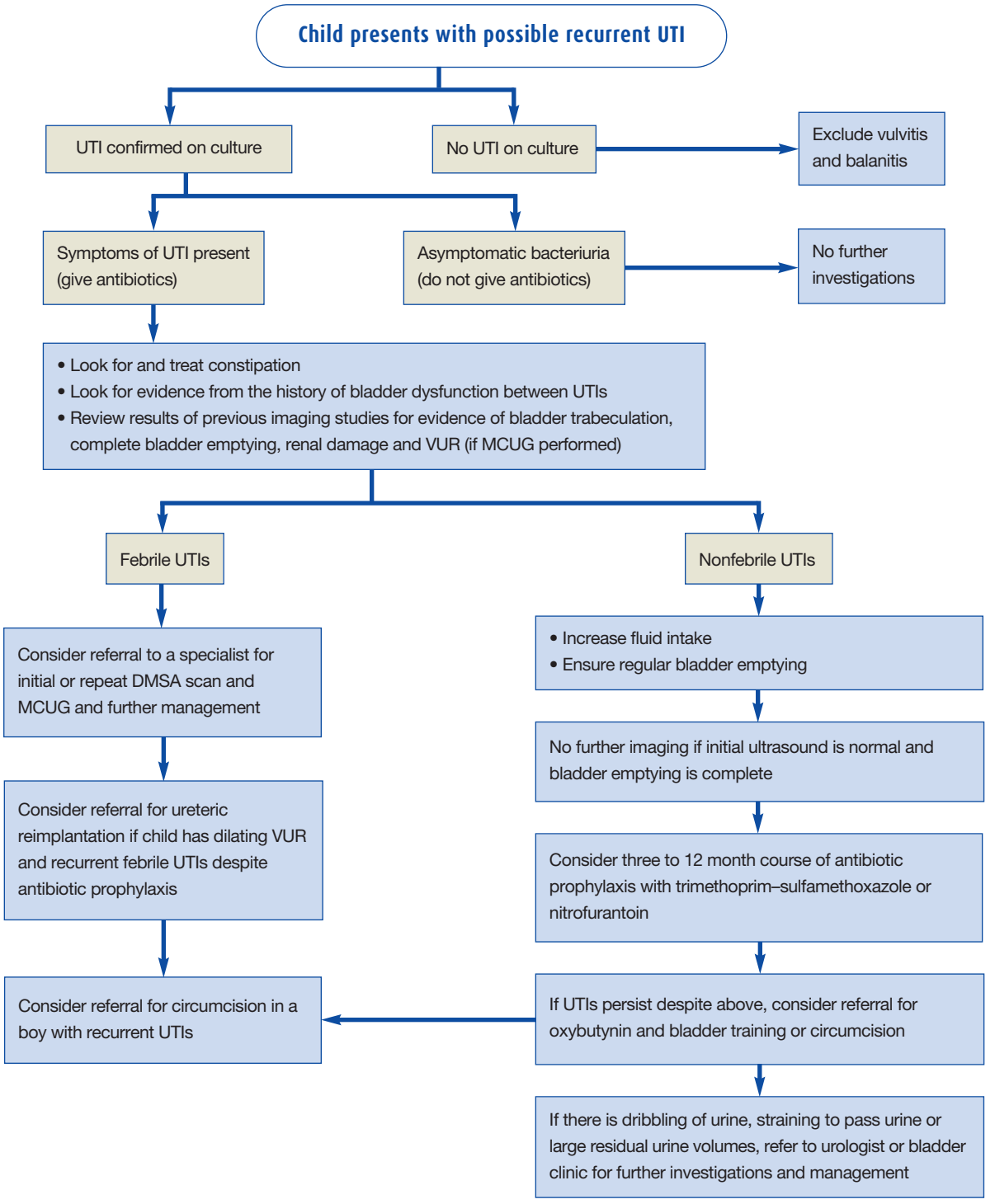
The child and his or her family need to be questioned specifically about symptoms of wetting with or without urgency, and urge incontinence associated with attempts to prevent wetting, such as squatting, crossing the legs or holding the penis. The family may not consider them relevant to UTIs, and the child may be unwilling to discuss them because of embarrassment. It is particularly important to establish that urine flow is continuous and that the child does not strain to empty the bladder.

Does the child have constipation with or without faecal soiling?

Constipation with faecal overflow is commonly associated with bladder dysfunction and recurrent UTI. Often the family will be unaware of

continued

The investigation of children with recurrent UTIs



DMSA=^{99m}Tc-dimercaptosuccinic acid. MCUG=micturating cystourethrogram. VUR=vesicoureteric reflux.

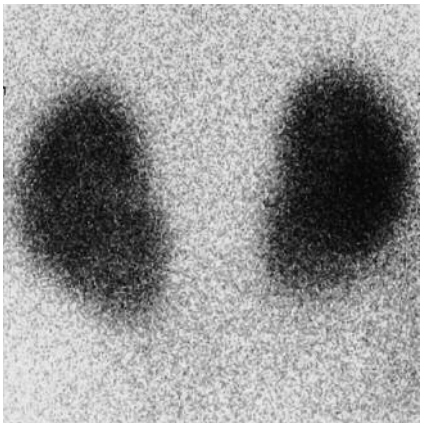


Figure 2. DMSA scan. This is a normal DSMA scan showing an even distribution of uptake of the tracer.

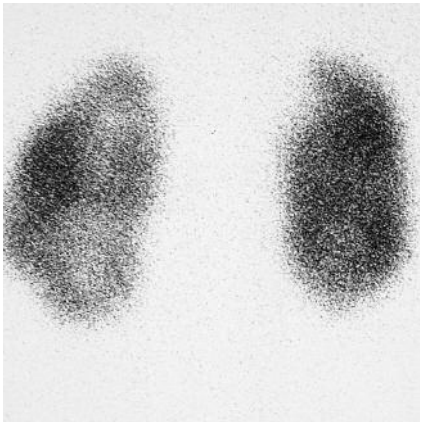


Figure 3. DMSA scan. Both kidneys are abnormal, with irregular distribution of tracer and focal areas of reduced uptake consistent with either acute pyelonephritis or permanent scarring.

constipation, so the child must be asked specifically whether he or she passes hard, pebble-like stools infrequently.

Is the child normal on physical examination?

Physical examination should include an examination of the abdomen, genitalia and back. The back should be inspected for evidence of dimples, hairy patches, short sacrum and spinal defects. In children with bladder dysfunction, lower limb neurological examination should be carried out, together with assessment of perianal sensation and anal tone.

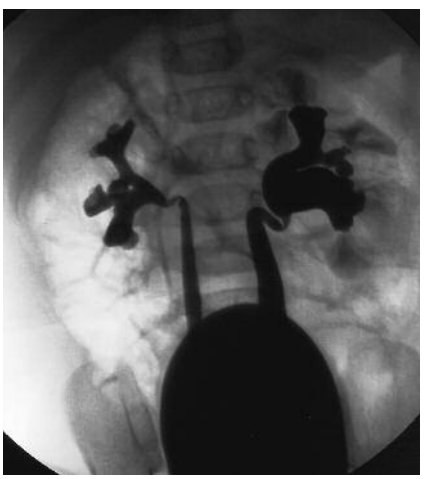


Figure 4. Micturating cystourethrogram. Vesicoureteric reflux is shown to both kidneys (grade 3 on the right, and grade 4 on the left). There is also evidence of intrarenal reflux in the upper, mid and lower poles on the left side.

Does the child empty the bladder adequately?

Ultrasound examination of the bladder should include measurement of the residual urine volume. Some 50% of children with acute cystitis have high residual volumes, suggesting that incomplete bladder emptying could contribute to recurrent UTI.[10] Children aged below 1 year have 5 to 10 mL of residual urine. In school-age children, the residual urine volume is generally below 5 mL and should not exceed 10% of the child's maximum urine storage capacity.

Does the child have fever with UTIs?

If the child has no significant fever with UTIs and the initial ultrasound was normal, no further investigation is required. A child with recurrent febrile UTIs may require a DMSA scan to assess the development and progression of chronic renal damage (Figures 2 and 3). DMSA scans looking for chronic scarring should be performed six to 12 months after the last infection because acute changes may take up to a year to resolve.

A repeat micturating cystourethrogram is rarely required if the bladder is normal on ultrasound. If the recurrent febrile UTIs are not being prevented with antibiotics and bladder training (if needed), a micturating cystourethrogram may be indicated to look for bladder trabeculation and for the development or worsening of vesicoureteric reflux (Figure 4). These can occur in a child with bladder dysfunction and contraction of the external sphincter during voiding.

Management of recurrent UTIs

Fluids, voiding and treatment of constipation

Many children with UTI void infrequently and have poor fluid intakes, especially at school. It is important to get them to drink at least 250 mL before school, at recess and lunch as well as plenty of fluid later in the day. They should also void at recess and lunch. Children should be encouraged to sit on the toilet with the legs apart and to contract the abdominal muscles at the end of micturition to facilitate complete bladder emptying. Constipation should be treated.

Antibiotic prophylaxis

Some children get into a cycle of infections and bladder dysfunction with urgency, urge incontinence, interrupted voiding and incomplete bladder emptying. Antibiotic prophylaxis may interrupt the cycle of infections and allow bladder inflammation to resolve. This can assist in the child's ability to overcome urgency and urge incontinence. Trimethoprim–sulfamethoxazole (1 to 2 mg/kg trimethoprim once at night) or nitrofurantoin (Furadantin Suspension, Macrodantin, Ralodantin; 1 to 2 mg/kg once at night) are the most useful antibiotics. Broad spectrum antibiotics should be avoided.

Circumcision

There is an increased prevalence of UTIs in uncircumcised boys.[11] While there is no controlled clinical trial of the efficacy of circumcision in preventing recurrent UTIs, this increased prevalence suggests that circumcision may have a role in preventing further infections. It should be considered in young children with recurrent UTI.

Bladder training

Data suggest that treatment of bladder dysfunction with anticholinergic agents and bladder training may decrease the rate of recurrent UTI and enhance the resolution of vesicoureteric reflux.[8,12] Children with the urge syndrome benefit from bladder training. The child with uninhibited detrusor muscle contractions needs to learn how to suppress the urge to void by central inhibition. Children in whom pelvic floor muscle contraction occurs simultaneously with detrusor contraction need to learn how to void with a completely relaxed pelvic floor.

Uroflow studies can examine the pattern of bladder emptying, and referral for these studies together with measurements of post-void residual volumes should be considered if bladder emptying problems are suspected. In children undergoing bladder training, uroflow studies can also be used to show them improvement in their bladder function.

Anticholinergic agents

The anticholinergic agent oxybutynin (Ditropan) may be a useful adjunct to bladder training if bladder emptying is complete. Oxybutynin administration should be timed to give the maximum effect. For example, a child who wets in the afternoon should receive 2.5 to 5 mg of oxybutynin at lunchtime, while one who wets predominantly in the afternoon and evening should receive 2.5 to 5 mg both at lunchtime and after school. Oxybutynin is unlikely to be effective unless the dose administered is sufficient to cause mouth dryness.

Specialist referral

The child with recurrent UTIs should be referred for further management if he or she is having febrile UTIs. Most children with recurrent UTIs remain afebrile. They should be referred if history and/or physical examination suggest intermittent urine flow and incomplete bladder emptying. Also, children should be referred if increasing the fluid intake, instituting regular and complete bladder emptying, and correcting constipation with or without antibiotics have not been successful in preventing further UTIs.

UTIs and imaging studies

The extent of investigations in UTI has become increasingly controversial in the light of information obtained from renal cortical imaging with DMSA (^{99m}Tc-dimercaptosuccinic acid).

Until the advent of the DMSA scan, events leading to pyelonephritis and subsequent renal scarring seemed reasonably clearcut. It was considered that vesicoureteric reflux carried infected urine to the renal pelvis, where intrarenal reflux into compound renal papillae allowed refluxed urine to enter and damage the renal parenchyma. Since vesicoureteric reflux was considered the most important risk factor for renal damage, it was recommended that all children with their first UTI should be investigated with a micturating cystourethrogram and be placed on long term antibiotic prophylaxis to prevent further UTI if vesicoureteric reflux was detected. Children without reflux did not generally receive prophylaxis.

The DMSA scan is the most sensitive examination available for identifying renal cortical defects due to acute pyelonephritis or to chronic renal scarring. While dilating vesicoureteric reflux (grades 3 to 5) remains an important risk factor for acute and chronic renal damage, several studies have demonstrated that fewer than 50% of children with cortical defects on DMSA scan due to acute pyelonephritis have vesicoureteric reflux, whereas up to 40% of children with reflux have normal DMSA scans.[13] In addition, children with acute pyelonephritis without vesicoureteric reflux may develop new renal cortical defects with further episodes of acute pyelonephritis.[13] While these defects resolve in about 60% of patients, some of these children develop permanent renal scarring.[13] Thus, the emphasis of investigation is moving from detecting vesicoureteric reflux in all children with UTI to identifying children who have acute pyelonephritis and investigating those children more extensively.

After the first few months of life, fever exceeding 38.5°C is a sensitive, though not specific, indicator of the likelihood of acute parenchymal defects on DMSA scan. Acute defects on DMSA scans are found in 40 to 80% of children with UTI and a fever of 38.5°C or more.[1,13,14] Other factors predictive of acute renal damage are pyuria and elevated C-reactive protein concentration.[1,14] Most acute renal cortical defects resolve completely within a year of the acute infection.[2] C-reactive protein greater than 20 mg/L and fever over 38.5°C at the index infection are sensitive but not specific predictors of chronic renal scarring.[15]

Most authors continue to recommend that children with febrile or non-febrile UTI who are aged below 1 year should be investigated with an ultrasound, micturating cystourethrogram and DMSA. Controversy remains as to whether the DMSA should be performed soon after acute infection to detect parenchymal defects that may subsequently resolve or whether DMSA should be delayed till six to 12 months after the infection to detect chronic scarring only. Children aged above 1 year who are significantly febrile at their first UTI should be investigated intensively. However, it remains unclear whether all children require ultrasound, micturating cystourethrogram and DMSA scans after their first febrile UTI and whether the cystourethrogram should be limited to children aged under 4 to 5 years, as currently recommended. In contrast, children aged more than 1 year who have normal renal ultrasounds and no fever at presentation are at a low risk of renal parenchymal injury; thus, DMSA scan and a cystourethrogram can be avoided in those children.[15,16]

Currently, antibiotic prophylaxis is recommended following the first UTI in young children with vesicoureteric reflux, though there are no data from randomised controlled trials to support this practice.[17] A randomised, double-blind placebo-controlled trial, funded by the NHMRC, is being undertaken at The Children's Hospital at Westmead, Sydney, to determine the benefits and harms of using antibiotic prophylaxis to prevent further UTI in children with or without vesicoureteric reflux. It is hoped that the results of this trial will help to clarify which children benefit from antibiotic treatment. This information will help to determine renal imaging protocols in the future.

Conclusion

Recurrent symptomatic UTIs are common in children. Boys rarely develop recurrent UTI after the first year of life. Dilating vesicoureteric reflux and renal damage are important risk factors for recurrent UTI, especially acute pyelonephritis. However, further imaging studies are rarely required in most children with recurrent UTI. Identification and treatment of bladder and bowel dysfunction are often the most important factors in the management of recurrent UTIs in children. MT

A list of references is available on request to the editorial office.

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