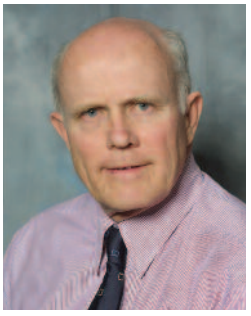
Urinary tract infections
investigation in children

In this series we present authoritative advice on the investigation of a common clinical problem, specially commissioned for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.



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Urinary tract infection (UTI) occurs in approximately 10% of children aged less than 15 years, and an underlying structural renal abnormality such as vesicoureteric reflux is found in 30 to 35% of these patients. Infection of the urinary tract and an abnormal antenatal ultrasound is a common presentation of a structural renal abnormality. Many children with a UTI and a severe renal abnormality have a pre-existing dysplasia/hypoplasia of the kidneys from birth.

Although about 7% of patients commencing dialysis each year in Australia have a congenital renal abnormality, only 1 in 20,000 children presenting with a UTI will develop end-stage renal failure.

Symptoms of UTI

The typical and atypical presenting symptoms of UTI are listed in Table 1. It is rare to see infection of the urinary tract in a child with nocturnal enuresis, but it should be suspected in a child with diurnal enuresis. A careful history is required in girls with detrusor instability because, although recurrent UTIs are common in these patients, a history of urgency and wetting persisting after eradication of infection usually indicates UTI is not the only problem. Asymptomatic bacteriuria occurs in about 1% of schoolgirls.

Collection of urine

Major problems often arise in the diagnosis of UTI because of unsatisfactory urine collection. About 30% of children who have symptoms suggestive of a UTI have a negative result on a well collected urine. Appropriate methods of collection for children of different ages are given in Table 2.

In general practice, urine collection in a bag is the most convenient method for children under the age of 2 years. However, false positive results are often seen with this method. The perineal area should be washed with soap and water before applying the bag, and if the child has not passed urine within 60 to 90 minutes, the bag should, ideally, be changed. Home collection by parents is not appropriate because of contamination problems, even if they are given the appropriate equipment. If the child is acutely ill or contamination on bag collection is suspected, suprapubic aspiration or transurethral catheterisation should be performed, preferably in a hospital casualty department. Suprapubic

IN SUMMARY

- **Suspect urinary tract infection in a young child with unexplained fever.**
- **Bag urines should be collected by health professionals and not parents.**
- **Dipstick tests should be regarded as screening tests and not diagnostic of UTI.**
- **About 30% of children with UTIs have an underlying structural renal abnormality.**
- **Ultrasound is the initial investigation in all children with proven urinary infection.**
- **Consider detrusor instability in the girl who continues to be wet after eradication of infection.**

aspiration is a safe and effective way of collecting urine, especially in neonates, in whom the bladder tends to be an abdominal organ. A 23-gauge needle attached to a syringe is inserted vertically just above the symphysis pubis; care should be taken to not insert the needle too deeply or contamination from bowel flora may occur. A time interval of 60 minutes after the last void should ensure adequate urine is in the bladder.

A clean catch specimen is often collected in children between 2 and 3 years old who are not toilet trained. The perineal area is washed and the sterile container is inserted between the legs as soon as micturition occurs.

Midstream collection is recommended for toilet trained children, although in girls it is often not adequately performed because the labia are not separated, which leads to pyuria from vaginal secretion. Catheter specimens are normally reserved for children with a neurogenic bladder, such as those with spina bifida.

Table 1. Symptoms of urinary tract infection in children

Typical symptoms
Frequency, dysuria
Abdominal pain
Enuresis
Atypical symptoms
Recurrent fevers
Neonatal jaundice
Failure to thrive

Diagnosis

Dipstick testing is often used in screening for urinary infection. If leucocyte esterase and nitrite are negative, there is a 98% probability that infection is absent. If these tests are positive, then the positive predictor value is less than 50%.[1] In most instances, therefore, urine culture is only necessary with a positive dipstick test. Urine samples should be sent to the laboratory for microscopy, culture and sensitivity testing as soon as possible, although they may, if necessary, be stored at 4ºC for up to 24 hours without significant alteration in the bacterial count.

Accurate diagnosis of a UTI can be made on microscopy of a fresh unspun specimen. The presence of bacteria can give up to a 95% positive predictive result and the absence of bacteria almost a 100% negative result. In a freshly voided specimen, the presence of 1 x 10^5 organisms of a single species per millilitre is considered significant (80 to 85% likelihood of infection). If two consecutive samples reveal 1 x 10^5 organisms/mL, the likelihood of infection increases to 95%. With a suprapubic tap or catheter specimen, the presence of any bacteria is significant. Pyuria assists in the confirmation of a UTI, but the absence of leucocytes does not exclude it and leucocytes can also be seen in uninfected urine.

Table 2. Urine collection in children

Method	Appropriate situations
Bag	Children aged < 2 years
Clean catch	Children aged 2 to 3 years
Midstream	Toilet trained children
Catheter	Children with a neurogenic bladder
Suprapubic aspiration	Acutely ill children aged < 1 year

Causative organisms

Escherichia coli is the most common cause of a UTI, followed by *Klebsiella, Proteus, Pseudomonas* and *Streptococcus faecalis*. Most UTIs arise from ascending infection from the perineal area. Bloodborne infection can occur in neonates and some older children with skin infections, *Staphylococcus* then being the organism responsible.

Antibiotic treatment

If a UTI is suspected, broad spectrum antibiotic therapy should be commenced before culture and sensitivity results are available as animal experiments have shown that renal scarring is reduced when antibiotics are introduced immediately. Suitable oral antibiotic therapies include sulfamethoxazole–trimethoprim, trimethoprim (Alprim, Triprim), amoxycillin–clavulanic acid (Augmentin, Clamoxyl, Curam), nitrofurantoin (Furadantin Suspension, Macrodantin, Ralodantin) and cephalexin. In the sick child with vomiting, admission to hospital for intravenous antibiotics will be necessary; initial therapy may include a combination of an aminoglycoside and amoxycillin or a cephalosporin. Once the identity of the organism and its *in vitro* antibiotic sensitivities are known, treatment with appropriate antibiotics can be commenced.

Although there are no definite guidelines concerning the duration of treatment, five to seven days is often sufficient in uncomplicated UTI. Poor compliance may occur when the child becomes asymptomatic, and a repeat urine culture is recommended at the end of a course of therapy. If severe pyelonephritis (abdominal pain, temperature above 38ºC) is suspected clinically, therapy should continue for seven to 10 days. Some authors recommend longer courses as this may reduce the reinfection rate.

After eradication of the infection, prophylactic antibiotic therapy is recommended in children under 2 years of age until radiological investigations are completed.

Radiological investigation

Radiological investigation is recommended in all children with a first UTI (see the flowchart on page 72). However, a micturating cystogram should not be performed until after the infection has been eradicated. Without radiological investigations there is no way to differentiate an upper from a lower urinary infection. Radiological tests are, therefore, indicated with lower tract symptoms (i.e. frequency and dysuria).The common radiological investigations are:

- ultrasound – to detect structural abnormalities
- micturating cystogram – to detect structural abnormalities and reflux
- DMSA (Tc 99m-dimercaptosuccinic acid) renal scan – to detect renal scarring
- MAG_3 (Tc 99m-mercaptoacetyltriglycine) renography – to identify obstruction.

Children under 2 years of age

Initial investigations in children under the age of 2 years should include an ultrasound and a radiographic micturating cystogram. All clinically important abnormalities in the urinary system should be detected with this combination (Figure 1). When a micturating cystogram is performed, it is important that the bladder be filled and emptied adequately or ureteric reflux, the most common structural abnormality, may be missed. In boys, the urethra should be visualised in a micturating film so that urethral valves are not missed (Figure 2).

Further radiological investigation will be determined by the abnormality suspected. With ureteric reflux, a normal ultrasound does not exclude renal scarring and a DMSA scan is a more accurate investigation (Figure 3). If the ultrasound suggests a scar or the micturating cystogram shows greater than grade 2 reflux, a DMSA scan is indicated about 10 to 12 weeks after the infection has cleared. (Vesicoureteric reflux is graded radiologically on a scale of 1 to 5, according to the degree of dilatation of the ureter and renal pelvis.) A DMSA scan performed shortly after a UTI may show renal tubule uptake defects that do not necessarily represent permanent scarring and may gradually resolve. If the ultrasound suggests an obstructive uropathy (pelviureteric, vesicoureteric or a ureterocele) then MAG_3 renography is the next investigation of choice. The severity of obstruction and differential renal function is measured by the urinary excretion time of the isotope after frusemide; a half clearance time ($T_{1/2}$) of greater than 20 minutes indicates significant obstruction.

Figure 1 (above left). Micturating cystogram showing bilateral grade 4 reflux.
Figure 2 (above). Micturating cystogram showing posterior urethral valve (dilated proximal urethra) and bilateral gross reflux in a baby boy.
Figure 3 (left). DMSA renal scan showing scarring to both kidneys.

Table 3. Radiological investigations for suspected UTI

Children aged < 2 years

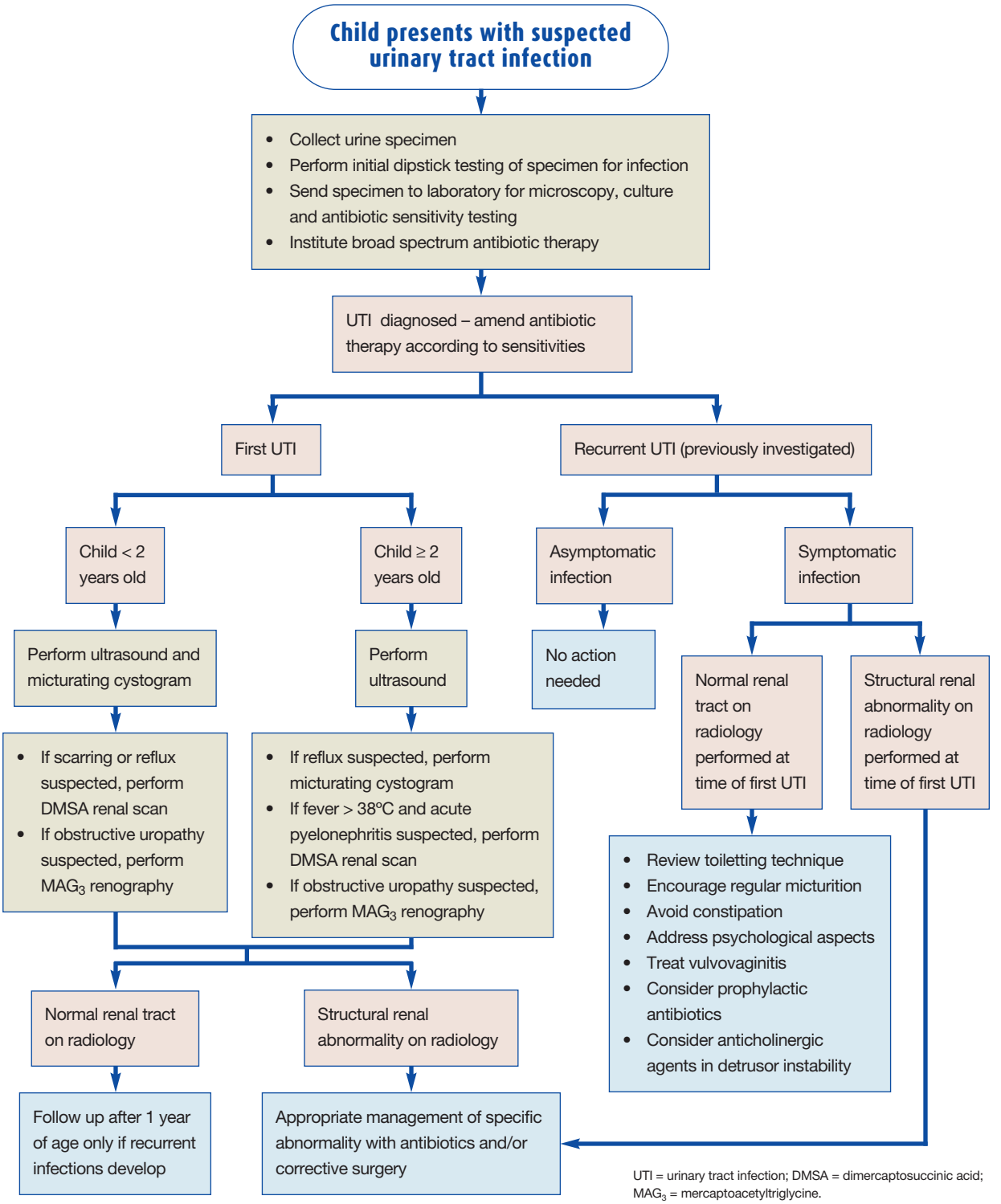
Ultrasound and micturating cystogram – initial investigation
DMSA scan – if greater than grade 2 ureteric reflux or scarring on ultrasound
MAG_3 renography – if dilatation on ultrasound suggests obstructive uropathy

Children aged 2 years and over

Ultrasound – initial investigation
DMSA scan – if recurrent UTI or fever > 38°C
Micturating cystogram – if scarring on ultrasound or perfusion defects on DMSA
MAG_3 renography – if dilatation on ultrasound suggests obstructive uropathy

continued

Investigating urinary tract infections in children



UTI = urinary tract infection; DMSA = dimercaptosuccinic acid; MAG_3 = mercaptoacetyltriglycine.

Intravenous pyelography is now rarely performed but assists in the diagnosis of a ureteroceles and duplex collecting systems.

Children 2 years and older

An ultrasound is the recommended investigation in children over the age of 2 years with a first UTI and should detect any significant structural abnormality or calculus and show evidence of significant reflux nephropathy. Micturating cystography, an uncomfortable and potentially distressing invasive procedure, is not well tolerated in this age group and is often not necessary. Most cases of renal scarring associated with reflux and infection occur in children in the first two to three years of life.

In the older child with a fever above 38ºC (suggesting acute pyelonephritis) or a girl with recurrent urinary infections, a DMSA renal scan is better tolerated than a micturating cystogram, although the latter is indicated if a defect is present on ultrasound. If the DMSA scan shows no scarring and reflux is present, it is most unlikely that scarring will occur with further infections.

If the ultrasound suggests an obstructive uropathy, then MAG_3 renography is the next investigation of choice.

Alternative regimens and other investigations

Some authors recommend a DMSA renal scan and ultrasound in all children and the addition of a micturating cystogram in children under 1 year of age, and in the older child if reflux is suspected. This regimen does not appear to be as cost effective as that described above.[2,3]

Radionuclide cystography has the advantage over radiographic micturating cystography of a lower radiation dose, but does not provide the detail of the latter procedure, particularly for grading of reflux. It is, however, often used for the follow up of ureteric reflux.

Recurrent UTI with normal renal tract

If radiological investigations are normal, follow up after the first 12 months of life is not necessary unless the child develops further symptomatic infection of the urinary tract. This is much more common in girls than boys, and in practice, it is unusual to see boys over 1 year of age with recurrent UTIs. Antibiotic therapy and investigation are not indicated in the 1% of schoolgirls who have asymptomatic bacteriuria.

General advice to girls with recurrent UTIs (and their parents) should include treatment of recurrent vulvovaginitis with an antiseptic solution, correct toileting technique, avoidance of constipation and regular micturition. A few young girls with recurrent symptomatic cystitis will require prophylactic antibiotics such as trimethoprim–sulfamethoxazole, trimethoprim or nitrofurantoin for six to 12 months. The frequency of infection decreases with age.

Functional abnormalities of micturition, such as detrusor instability, may cause diurnal enuresis with predisposition to infection of the lower urinary tract. This group of children (usually girls) requires attentive management. Self-esteem is usually low and patients may be teased at school by other students or at home by siblings. A careful bowel history is important so that constipation or encopresis is not missed. Family disharmony may aggravate the problem.

Eradication of infection has little immediate effect on the frequency of enuresis. Improvement over six to 12 months usually occurs with psychological support of both the child and parents, a relaxed micturition schedule for both school and home, and prophylactic antibiotics. Advice about toilet training by an occupational therapist may also be of benefit. A trial of anticholinergic medication (oxybutynin [Ditropan]) may be required in some cases.

Urodynamic studies are limited to children whose radiological investigations suggest a neurogenic bladder (cone shaped with a significant residual), or older children (8 to 9 years old) who do not respond to the above regimen.

Vesicoureteric reflux

Ureteric reflux is the most common underlying structural renal abnormality, and risk factors for recurrent UTI include age less than 6 months at the initial infection and grades 3 to 5 reflux.[4] Renal scarring is more likely to be associated with the higher grades of reflux (grades 3 to 5). Detailed management of ureteric reflux is not within the scope of this paper.[5]

The age at diagnosis and the degree of reflux will influence the decision for early ureteric reimplantation. Most cases with reflux greater than grade 2 are initially managed with a prophylactic antibiotics such as trimethoprim–sulfamethoxazole, trimethoprim or nitrofurantoin, in a single dose at night. It is not necessary to test the urine for break through infection unless there are symptoms suggestive of an infection. Endoscopic correction of primary vesicoureteric reflux by subureteric injection of polytetrafluoroethylene is performed in some centres.

Circumcised males have a lower incidence of UTI and, although there are no published control trials, some boys with recurrent UTIs are circumcised in an attempt to reduce infection.[6]

Progression to chronic renal failure

Chronic renal insufficiency becomes established when severe bilateral renal scarring occurs, and there will be slow progression towards end stage renal failure. The remaining glomeruli are exposed to a high solute load and this may contribute to an increase in glomerular hydrostatic pressure with resulting damage to the glomerular basement membrane and an increase in the mesangial matrix. There is release of growth and

inflammatory factors, including transforming growth factor β, insulin growth factor, vascular endothelial growth factor and nitric oxide, with the end result being glomerular sclerosis, tubular atrophy and interstitial fibrosis.[7] The presence of proteinuria greater than 0.4g/day is a bad prognostic sign.

Efforts to halt this progression with better control of infections and ureteric reimplantation have been unsuccessful. Treatment with angiotensin converting enzyme inhibitors and adequate blood pressure control may result in partial slowing of renal failure.

Screening for UTIs and structural abnormalities

The major problem with screening for UTIs is that infections of the urinary tract are intermittent. Screening for UTI in children has been shown in studies performed in Sweden and Canada to be cost-ineffective.[8,9]

Structural renal abnormalities that may predispose to UTI are often detected on antenatal ultrasound performed for obstetric reasons. Obstructive uropathies, such as pelviureteric obstruction, a ureterocele and urethral valves, are often detected in this way. This early detection allows corrective surgery to be performed in the neonatal period. As yet, there are no controlled trials to show that antenatal procedures such as vesicoamniotic shunting improves renal prognosis.

Between 15 and 20% of children with vesicoureteric reflux will have a family history of the condition. A normal antenatal or postnatal ultrasound does not exclude ureteric reflux, and many authors recommend a micturating cystogram in newborns with a family history of reflux, with commencement of a prophylactic antibiotic if reflux is present. However, an Australian randomised study using placebo and trimethoprim in 46 babies from birth did not show any change in renal scarring over a three-year period.[10]

Conclusion

A diagnosis of UTI should not be overlooked in children presenting with atypical symptoms of the infection, such as prolonged neonatal jaundice, fevers and poor weight gain. Depending on the child's age, careful consideration should be given to the method of urine collection and the interpretation of its analysis. After eradication of infection, appropriate radiological investigation commencing with ultrasound is indicated in all children with a first infection.

Early detection of a structural renal abnormality after a urinary infection or by antenatal ultrasound allows surgical intervention or prophylactic antibiotic therapy to preserve renal parenchyma. With this management, the number of cases of UTI and the rate of progression to end stage renal failure should both be decreased. MT

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Further reading

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