RATIONAL IMAGING

Investigating urinary tract infections in children

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This series provides an update on the best use of different imaging methods for common or important clinical presentations. The series advisers are Fergus Gleeson, consultant radiologist, Churchill Hospital, Oxford, and Kamini Patel, consultant radiologist, Homerton University Hospital, London. To suggest a topic for this series, please email us at practice@bmj.com

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- Inhaled corticosteroids for chronic obstructive pulmonary disease (*BMJ* 2012;345:e6843)
- Newer insulins in type 2 diabetes (*BMJ* 2012;345:e4611)

Urinary tract infection is common in childhood, and most children recover without complications. Use of imaging to check for abnormalities or complications therefore needs to be targeted carefully. This article summarises current guidance on clinically and cost effective use of imaging for urinary tract infection in childhood

A 5 month old boy presented to his local accident and emergency department with irritability, fever, poor urine output, and foul smelling nappies when they were wet. His mother had had an uncomplicated pregnancy with no abnormalities detected on antenatal ultrasonography. On clinical examination the child looked unwell, with signs of sepsis, including a temperature of 39.8°C and raised C reactive protein and white cell count. A urinary tract infection was confirmed by clean catch mid-stream urine sample. His urine analysis was positive for blood and leucocytes, and *Klebsiella* was grown in the culture sample. His urine infection was considered atypical because of his septicaemia and infection with a non-*Escherichia coli* organism (see box 1). He was admitted to the paediatric ward for treatment and further investigation.

Box 1 | Features of atypical urine infection (from NICE guideline[2])

- Failure to respond after 48 hours of appropriate antibiotic treatment
- Poor urine flow
- Bladder or abdominal mass
- Infection with non-*E coli* organisms
- Septicaemia
- Raised serum creatinine concentration

Box 2 | Definitions of recurrent urinary tract infection (from NICE guideline[2])

- ≥1 episode of upper urinary tract infection or acute pyelonephritis* *plus* ≥1 episode of lower urinary tract infection or cystitis, *or*
- ≥2 episodes of upper urinary tract infection or acute pyelonephritis,* *or*
- ≥3 episodes of lower urinary tract infection or cystitis

*NICE guidelines define pyelonephritis or upper tract infection as a urinary tract infection with a temperature of ≥38°C

What are the next investigations?

Urinary tract infection affects at least 3.6% of boys and 11% of girls in childhood.[1] The role of imaging in children with confirmed urinary tract infection is to identify underlying abnormalities that may predispose to further urinary tract infection (such as obstruction or vesicoureteric reflux), to identify complications of infection (such as renal scarring), and to identify and treat those at risk of long term complications from renal scarring (such as hypertension and end stage renal disease). The lack of long term follow-up studies means the lifetime risk of complications from urinary tract infection cannot be reliably calculated, and so the balance of benefits versus costs of further investigations remains debateable.[2 3] The current guidelines from the National Institute for Health and Clinical Excellence (NICE)—which were developed from systematic reviews of the evidence and consideration of cost effectiveness—recommend early imaging should be targeted to children with atypical infection (box 1), in whom it will be clinically useful and cost effective. Delayed imaging is recommended for those that do not meet these criteria.[2]

LEARNING POINTS

The role of imaging is to identify underlying abnormalities that may predispose to urinary tract infection (such as obstruction or vesicoureteric reflux) and possible complications from urinary tract infection (such as renal scarring)

Early imaging should be targeted towards patients most at risk of structural abnormalities or complications, including all children with recurrent urinary tract infection, those aged <3 years with atypical infection, and babies <6 months old with urinary tract infection

This subset includes all children with recurrent infection and children aged <3 years with atypical urinary tract infection

Consider further imaging for babies <6 months old who do not have atypical or recurrent infection but who have an abnormal ultrasound result

Micturating cystography is the gold standard test for detecting vesicoureteric reflux, as the dimercaptosuccinic acid (DMSA) scan is for detecting renal scarring, and each is indicated for specific subgroups

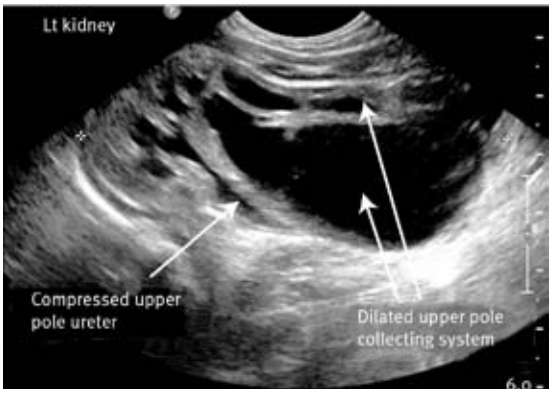

Fig 1 | Ultrasound image of a 2 month old boy which shows a longitudinal view of a duplex left kidney with marked dilation of the lower pole moiety collecting system which compresses and distorts the upper pole moiety collecting system

Ultrasonography

The first line test in children undergoing investigation for urinary tract infection is ultrasound scanning, the timing of which depends on the child's age and presentation. The table outline the imaging schedule recommended in the NICE guidelines.[2] NICE recommends ultrasound scanning at the time of acute infection for all children under 3 years old with atypical infection (box 1) and babies under 6 months with recurrent infection (box 2). Non-urgent ultrasound (within six weeks) is indicated for children over 6 months old with recurrent infection and babies less than 6 months with "typical" infection.

Ultrasonography is a non-invasive test that does not use ionising radiation. It is easy to perform and widely available, although its accuracy is dependent on the operator. It can accurately assess renal size and outline, and identify most congenital abnormalities, renal calculi, and hydronephrosis or hydroureter, indicating the presence of obstruction or severe reflux (see examples in figs 1 and 2). Ultrasound scanning can also be used to assess for bladder emptying in older children, but this is not routinely performed in infants.

However, it is less effective in detecting mild or moderate vesicoureteric reflux in children with urinary tract infections. Progressive scarring is seen in children with high grade reflux and recurrent urine infections. These long term complications are likely to be greater in those with bilateral and more severe defects, although this is yet to be confirmed by a large cohort study investigating long term outcomes of renal scarring and renal function of children who have had urine infection.[2] A prospective cohort study concluded the sensitivity and specificity of ultrasonography reporting vesicoureteric reflux to be 40% and 76% respectively, with a positive predictive value of only 32%.[4] Further imaging is therefore required to look for vesicoureteric reflux in a select group of patients. This subset includes all children with recurrent infection and children aged less than 3 years who have atypical or recurrent urinary tract infection (boxes 1 and 2). Babies less than 6 months old who do not have atypical or recurrent infection, but who have an abnormal ultrasound result should also be considered for further imaging (table).[2]

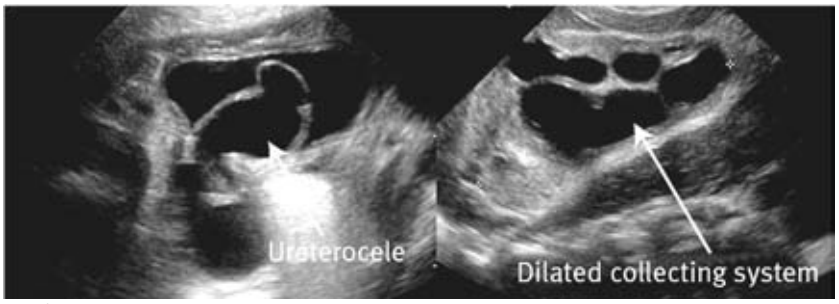

Fig 2 | Ultrasound image of a 3 month girl showing a transverse view of a large ureterocele within the bladder (left) and a longitudinal view of the right kidney in the same patient showing an obstructed, dilated collecting system associated with the ureterocele (right).

Recommended imaging schedule for children with urinary tract infection (from NICE guideline[2])

Child age and tests	Type of infection: Responds well to treatment within 48 hours	Type of infection: Atypical infection	Type of infection: Recurrent infection
Children <6 months old			
Ultrasound scan during acute infection	No	Yes	Yes
Ultrasound scan within 6 weeks of infection	Yes	No	No
DMSA scan 4–6 months after acute infection	No	Yes	Yes
Micturating cystograms	Consider if ultrasound scan abnormal	Yes	Yes
Children 6 months–3 years old			
Ultrasound scan during acute infection	No	Yes	No
Ultrasound scan within 6 weeks of infection	No	No	Yes
DMSA scan 4–6 months after acute infection	No	Yes	Yes
Micturating cystograms	No	Not routine, consider if dilatation on ultrasound, poor urine flow, non-*E coli* infection, or family history of vesicoureteric reflux	
Children >3 years old			
Ultrasound scan during acute infection	No	Yes	No
Ultrasound scan within 6 weeks of infection	No	No	Yes
DMSA scan 4–6 months after acute infection	No	Yes	Yes
Micturating cystograms	No	No	No

DMSA= dimercaptosuccinic acid.

Investigating vesicoureteric reflux: micturating cystourethrography and cystosonography

Historically, imaging after urinary tract infection has focused on detecting vesicoureteric reflux because of its association with renal scarring. Between 25% and 40% of children with confirmed infection will have vesicoureteric reflux detected on follow-up imaging, slightly more common in boys than girls.[5] Micturating cystography is considered the gold standard investigation for reflux and is the only imaging technique that provides information about the urethra. It should be performed by a skilled radiologist with experience in acquiring and interpreting the images. The disadvantage of micturating cystography is its invasiveness, requiring catheterisation, which is associated with complications such as infection and urethral trauma. This test also uses ionising radiation and carries a dose of approximately 1 mSv, equivalent to about four months of background radiation.[2]

NICE recommends that micturating cystourethrography is indicated in all babies less than 6 months old with atypical or recurrent infection, and it should be considered in those with typical infection but an abnormal follow-up ultrasound scan.[2] It is not routinely performed in children aged between 6 months and 3 years, but should be considered if there is dilatation of the collecting system on ultrasonography, poor urine flow at the time of infection, a family history of vesicoureteric reflux, or there is a non-*E coli* infection. Micturating cystourethro-graphy is not recommended for children aged over 3 years (table).[2]

A systematic review of 14 studies advocates the use of contrast enhanced cystosonography to look for reflux, quoting high sensitivities (56.8–96.3%) and specificities (80–100%).[6] It also has the benefit of not using ionising radiation, and is similar in price to micturating cystography. However, its use is not yet widespread, it still requires catheterisation, and there are no recognised standard international grading systems for reflux as there are for micturating cystograms (fig 3). The contrast used for cystosonography is not licensed for use in children; centres that perform this test do so with parental consent to use the contrast 'off-licence'.

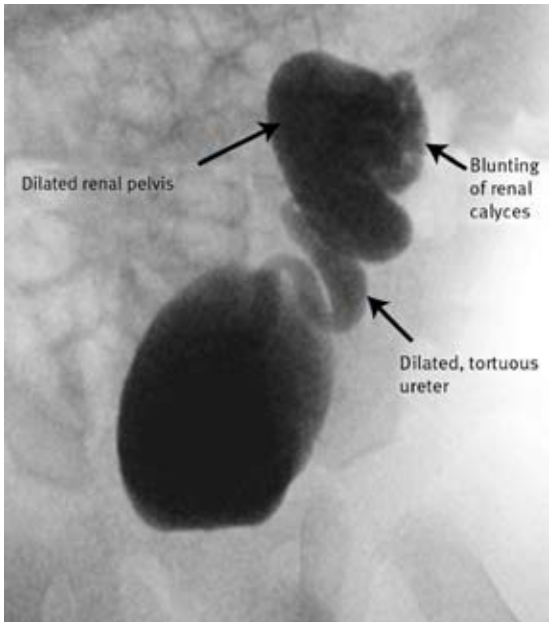

Fig 3 | Micturating cystogram of the same case shown in fig 1, confirming grade 5 reflux into the lower pole moiety collecting system of the duplex left kidney. There is a tortuous ureter with dilation of the renal pelvis and blunting of the renal calyces.

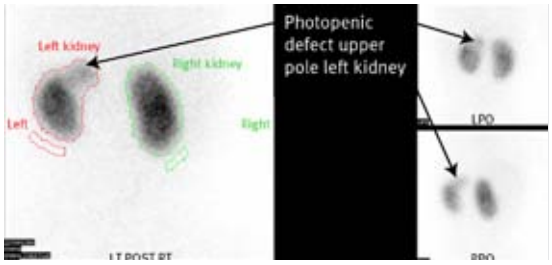

Fig 4 | DMSA scintigraphy of a 6 month old boy showing a photopenic defect in the upper pole of the left kidney consistent with renal scarring

Identifying renal parenchymal defects (scarring): DMSA (dimercaptosuccinic acid) scan

A DMSA scan is recommended in children younger than 3 years with atypical or recurrent urinary tract infections (table). The aim is to detect renal parenchymal defects or scarring, which occur in about 5% of children as a result of infection.[2] DMSA scintigraphy is able to look at renal function using a radiopharmaceutical such as technetium-99m. After intravenous injection, the isotope is concentrated in the proximal renal tubules, and its distribution correlates with functioning renal tissue (fig 4). Despite being an invasive test and carrying a radiation dose equivalent to four months' background radiation for a toddler, DMSA scans are considered the gold standard for detecting renal parenchymal defects.[2] The timing of a DMSA scan is important, and the optimal time is still a matter of debate because of lack of evidence. The problem is that renal parenchymal defects identified as photopenic areas cannot be distinguished from those caused by the acute infection, which will eventually resolve. The recent NICE guidance recommends DMSA scans should be performed between four and six months after urinary tract infection,[2] but some studies have shown improvement in renal parenchymal defects up to 12 months after infection.[6]

Is there a role for magnetic resonance urography?

Magnetic resonance imaging is a popular choice in paediatric patients because it does not use ionising radiation and so does not convey a radiation risk to the patient. Magnetic resonance urography is able to provide detailed anatomical information. It is more invasive and time consuming than ultrasound because of the need for intravenous contrast medium. However, this enables it to provide functional information that ultrasonography cannot—such as renal transit time, differential renal function, and estimated glomerular filtration rate. Several comparison studies have shown magnetic resonance imaging to have similar sensitivity and specificity (81–100% and 78–91% respectively) to DMSA scintigraphy.[7] Its disadvantage is the need for sedation and intravenous contrast that can be given only to patients with normal renal function. Experience of magnetic resonance uro-graphy in children is limited, and further evidence is needed before conclusions about its clinical benefit over existing tests and cost effectiveness can be made.

Outcome

Our patient was treated with a 10 day course of cefotaxime. An ultrasound scan performed the day after admission showed no structural defects of the renal tract and no hydronephrosis. Four months after discharge, micturating cystourethrography diagnosed grade 4 vesicoureteric reflux. At six months, a DMSA scan showed no evidence of renal scarring. He has not had any further episodes of urine infection.

AD developed the concept for the article and wrote the first draft. AD and MI sourced the images. MI revised the radiology content of the first draft and final article. BO drafted the hypothetical case and outcome and revised the article for clinical content. All authors approved the final draft for intellectual content and each contributed to the revisions relevant to area of expertise. All authors approved the final version for publication. AD is guarantor for the article.

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1 Mori R, Lakhanpaul M, Verrier-Jones K. Diagnosis and management of urinary tract infection in children: summary of NICE guidance. *BMJ* 2007;335:395.
2 National Institute for Health and Clinical Excellence. *Urinary tract infection in children: diagnosis, treatment, and long term management.* Clinical guideline 54. NICE, 2007.
3 Lim R. Vesicoureteral reflux and urinary tract infection: Evolving practices and current controversies in paediatric imaging. *Am J Roentgen* 2009;192:1197-208.
4 Mahant S, Friedman J, MacArthur C. Renal ultrasound findings and vesicoureteral reflux in children hospitalised with urinary tract infection. *Arch Dis Child* 2002;86:419-20.
5 Cleper R, Krause I, Eisenstein B, Davidovitis M. Prevalence of vesicoureteric reflux in neonatal urinary tract infection. *Clin Paediatr (Phila)* 2004;43:619-25.
6 Whiting P, Westwood M, Bojke L, Palmer S, Richardson G, Cooper J, et al. Clinical and cost-effectiveness of tests for the diagnosis and evaluation of urinary tract infection (UTI) in children: a systematic review and economic model. *Health Technol Assess* 2006;10:1-154.
7 Rosenburg AR, Rossleigh MA, Brydon MP, Bass SJ, Leighton DM, Farnsworth RH. Evaluation of acute urinary tract infection in children: a prospective study. *J Urol* 1992;148:1746-9.

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