Pitfalls in the investigation of children with urinary tract infection

J M Smellie, S P A Rigden

Abstract
The histories and imaging results are presented in 10 children in whom errors had been made in the interpretation of early investigations. Ultrasonography may not detect either vesicoureteric reflux (VUR) or renal scars or inflammation. The reduced nephrogram or renal swelling following a first attack of acute pyelonephritis may not be recognised without renal measurement on an intravenous urogram. Renal scarring may be diagnosed incorrectly on the basis of functional defects of isotope uptake on a technetium 99m-dimercapto-succinic acid study. In the absence of VUR, the micturating cystogram will not visualise the kidneys.

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Keywords: urinary tract infection, vesicoureteric reflux, renal scarring.

With the advent of new imaging methods for investigating the urinary tract after infection in children, paediatricians have increasingly tried to limit invasive procedures or those involving radiation in a condition in which the outcome in the majority is benign.

As yet no single non-invasive imaging technique is available to ascertain the cause of the infection and whether there is renal involvement or a risk of it, the main objectives of investigation.

We have become increasingly concerned by the referral to our specialist clinics of children with substantial renal damage in whom previous investigation has been undertaken without apparent awareness of the possible pitfalls of a limited approach. We therefore present the histories of some of these children seen at University College and Guy’s Hospitals and the Hospital for Sick Children, Great Ormond Street, to illustrate avoidable problems that can be encountered.

Commentary
The table lists 10 examples with related imaging in figs 1–9 illustrating a number of avoidable pitfalls surrounding the investigation of children with urinary tract infection (UTI) and the risks attending reliance on only one investigation. Nine of these children presented during 1989–91 but children with similar histories are still being referred.

All but one had a history of proved recurrence of UTI but only one child had a period of antibacterial prophylaxis before presentation.

ULTRASONOGRAPHY
Ultrasonography has the attraction of being a non-invasive technique, but alone is insufficient for identifying vesicoureteric reflux (VUR) or renal involvement.1 It detects renal cysts or obstruction to outflow by demonstrating dilatation of the renal pelvis or ureter or bladder enlargement (though the urethra is not visualised). It is thus particularly useful in infancy but, in general, obstruction is not a common finding on investigation of children with UTI.2

Ultrasonography is unreliable in diagnosing VUR, however, which is the most common abnormal finding in children with UTI. Dilatation of the ureter and renal pelvis associated with VUR may be intermittent and thus only seen when the bladder is full. A negative report will not therefore exclude even severe reflux as in patients 1, and on two occasions, 2 and 3. In these children, UTI recurred before either prophylaxis or a formal programme for VUR management was introduced; bilateral scarring was later demonstrated.

Marked asymmetry in renal size, due either to poor growth or scarring of one kidney or enlargement with a duplex kidney in the other, can be recognised as in the second scan in patient 6. However, ultrasonography is unreliable in detecting any but the larger scars (patient 2 and possibly 1, 3, 5, and 7) and because the technique is observer dependent, measurements of renal length and parenchymal thickness can be variable and inconsistent on follow up (patients 3, 4, 5, and 8). Patient 4 illustrates the problems that may arise in attempting the precise measurement of kidneys in infants and young children by ultrasonography. Exact measurements in a wriggling child can be difficult to obtain. There may be confusion between the kidney and the splenic or hepatic flexure of a loaded colon or a hepatic lobe (as probably occurred in this child with a single kidney).

Even in older children it was apparent that ultrasonography alone was inadequate. Patients 5–7 are of interest as they had presented aged 5 years and over. Two of them had normal ultrasonography reports at 8-5 and nearly 8 years. Either extensive late scarring developed, which is unusual, or scarring had not been detected earlier by ultrasound.
Brief clinical histories of children illustrating problems in diagnosis and investigation. Examples 1–9 have corresponding illustrations in figs 1–9

| No | Sex | Date of birth | Age on presentation (years) | History | Ultrasound examination | Outcome | Pupil | Notice
|----|-----|---------------|-----------------------------|---------|------------------------|---------|-------|-------|
| 1  | F   | 17/12/87      | 1-1                         | Recurrent UTI×5 from 6 weeks. No prophylaxis | Ultrasoundography at 6 months: NAD, MCU at 9 months: right and left severe VUR | At 1-1 years IVU and DMSA: bilateral renal scarring | Reliance on ultrasonography. Comment: no MCU or other investigation at 6 weeks | PUO=pyrexia of unknown origin; NAD=no abnormality detected; GFR=glomerular filtration rate.
| 2  | F   | 19/8/86       | 2-2                         | Recurrent UTI 5 months and 2-2 years | Ultrasoundography at 1-2 and 2-3 years: no dilatation or renal scarring | At 2-3–2-4 years IVU and DMSA: scarring. MCU: right and left VUR | Reliance on ultrasonography. Comment: no other investigation at 5 months. | IVU=mixed infection.
| 3  | F   | 2/8/84        | 5-5                         | Recurrent UTI at 3-1, 4-5, and 5-5 years. Episodes of lethargy and abdominal pain. Bedwetting started. Height on 90th centile. Unwell for 2 years after meningococcal meningitis at 7 months. No urine culture | Ultrasoundography at 3-1 and 4-5 years: normal reports | At 5-5 years plasma creatinine 192 μmol/l. Ultrasonography: both kidneys 8 cm, irregular left lower pole. DMSA: bilateral defects of isotope uptake – right 76%, left 24%. MCU: left VUR | Reliance on ultrasonography. Comment: no other investigation at 3-1 years. | IVU=mixed infection.
| 4  | F   | 21/6/83       | 6-0                         | Recurrent UTI from 6 months with fever and later day wetting | Ultrasoundography×6 between 2-5 and 4-0 years. (1) and (2) showed a pair of normal kidneys. (3) Left ureteric dilatation. (5) Only left kidney seen. No dilatation | At 2-5 years MCU: left VUR residual urine+ (no VUR at 3-5 and 5-0 years). At 2-7 years DMSA: defects in uptake of left kidney resolved by 6-0 years. No functioning right kidney. IVU: solitary left kidney, no scars | No investigation at 6 months. Solitary kidney and VUR overlooked on ultrasonography. | IVU=mixed infection.
| 5  | F   | 16/3/82       | 9-0                         | Recurrent UTI. At 6-5 years PUO after removal of normal appendix. At 7-8 years UTI, recurred until 9-0 years | Ultrasoundography at 7-8 years: two normal kidneys; thickened bladder wall | At 9-0 years DMSA: bilateral patchy changes. Small right kidney contributing 31% to total function | Reliance on ultrasonography alone at 7-8 years | IVU=mixed infection.
| 6  | F   | 21/8/85       | 5-5                         | Recurrent UTI from 3-8–4-3 years and from 5-3 years. Prophylaxis 1 year from 4-3 years | Ultrasoundography and plain abdominal film at 3-8 years: both normal | At 5-5 years DMSA: right kidney contributing 18% of total function. Ultrasoundography: 'dysplastic' right kidney. Indirect isotope MCU: no VUR | Reliance on ultrasonography and plain film. Comment: stone unlikely in girl aged 3-8 years | IVU=mixed infection.
| 7  | F   | 27/11/80      | 10-5                        | Intermittent dysuria and abdominal pain from 5-0 years. UTI 8-9 and 10-5 years | Ultrasoundography and plain abdominal film at 8-5 years: NAD | At 10-5 years DMSA: left irregular isotope uptake contributing 18% total function. MCU: no VUR. Ultrasoundography: disparity of size – left 7 cm, right 6 cm | At 5 and 6. Comment: recurrent UTI ever after aged 5-0 years needs investigation | Group B.
| 8  | F   | 7/5/88        | 1-3                         | At 6 weeks admitted with UTI while away on holiday. Discharged after treatment without follow up arrangements or prophylaxis. Recurrence of febrile UTI at 3 months–1 years | Ultrasoundography: kidneys NAD. Possible slight ureteric dilatation. IVU reported as normal at 6 weeks | At 1-3 years MCU: bilateral VUR. (Initial review of IVU: both kidneys enlarged left>right.) At 1-4 years DMSA: reduced left renal image and function (contributing 23% of total). At 1-5 years IVU: global scarring left kidney, normal right. | Initial IVU renal size not assessed (outlines clearly visible). No MCU. Comment: no prophylaxis. No follow up | IVU=mixed infection.
| 9  | M   | 11/3/81       | 9-0                         | At 5-0 years started day wetting. UTI diagnosed aged 8-3 years | DMSA at 9-0 years: large diffuse defect of isotope uptake left kidney (contributing 47% of total function). Scar diagnosed. MCU: bilateral VUR. Unequivocally normal. IVU: no cortical loss, duplex right kidney | At 11-0 years DMSA: normal function symmetrical | Diagnosis of renal scar based on single DMSA scan | IVU=mixed infection.
| 10 | M   | 22/6/77       | 9-0                         | Recurrent UTI at 2-0 years and 8-5 years. (No follow up between for social reasons.) Tiredness and feverish illnesses for several months | Ultrasoundography: kidney scars. IVU at 2-0 years: reported as normal. (On review both kidneys structurally normal but enlarged with relatively thick parenchyma.) | At 9-0 years MCU: bilateral severe VUR. IVU: small scarred poorly functioning kidneys. DMSA: right contributed 15% of total. | IVU=mixed infection. Replacement of normal kidney.

The addition of a plain abdominal film in patients 6 and 7 did not improve the sensitivity of imaging and was superfluous.3

INTRAVENOUS UROGRAPHY (IVU)
IVU provides the most comprehensive structural assessment of the renal tract but if it is carried out too soon after a first infection the renal swelling and reduced nephrogram that usually accompany infective renal involvement4 can be overlooked unless renal measurements are made (patients 8 and 10). In both of these boys the renal outlines were clearly visible on IVU and both the overall size and parenchymal thickness were visibly increased. Difficulty in visualising renal outlines on IVU in infancy have been given as a reason for avoiding this investigation in the first year of life,5 but this did not apply to patient 8 at the age of 6 weeks (fig 8). Neither of these boys aged 6 weeks and 2 years underwent cystography, although both were shown to have gross bilateral VUR when it was later carried out.

99m-TECHNETIUM DIMERCAPTOTRISANIC ACID (DMSA) STUDIES
The DMSA study provides an image of both kidneys and an estimate of the proportion contributed by each kidney to total renal function.
The renal image reflects renal vascular changes affecting the uptake of DMSA by the proximal renal tubules. After an acute urinary tract infection involving the kidney, there may be diffuse or patchy defects in isotope uptake or irregularity of the renal outline. These changes are presumed to provide a non-specific indication of the early inflammatory stage of the process that can lead to renal scarring. This is valuable in identifying those children needing energetic treatment, further investigation, and follow up. After treatment of a presumed first infection, these changes may resolve completely over a period of weeks or months. Alternatively they may persist. This may represent progression to scar formation, though the precise histopathological process involved has been explored only in the experimental animal or the acute inflammation may be superimposed on established scarring. There is thus a risk that the serious diagnosis of renal scarring can be made in a child who has only transient acute changes as seen in patients 4 and 9, condemning them to years of supervision. It is therefore important not to make a firm diagnosis of renal scarring without a follow up DMSA study demonstrating persistent change or a one film IVU of the renal areas after 6–12 months.

Scarred kidneys may be under diagnosed on the DMSA study when the renal images are reduced but have smooth outlines: duplex kidneys whether scarred or not are also confusing. A DMSA study alone gives no indication of lower tract structure or function or the presence or absence of reflux.

**Figure 1** (A) MCU at 9 months showing bilateral VUR. (B) DMSA study posterior view showing reduced function right kidney and left upper zone at 1–1 years. (C) IVU with bilateral scarring, generalised on right and left upper and mid zones. (D) Bilateral irregularities of isotope uptake on DMSA study at 2–5 years. (Ultrasoundography normal at 6 months.) Figure 1(A) is reproduced with permission from Smellie JM, Normand ICS. Urinary tract infection. In: Campbell AGM, McInnes N, eds. Forfar and Arnell’s Textbook of Paediatrics. 4th Ed. Edinburgh: Churchill Livingstone, 1992: 1031–1046.

**Figure 2** Bilateral VUR on MCU aged 2–4 years. (Ultrasoundography normal at 1–2 and 2–3 years.)

**Figure 3** DMSA study aged 5–5 years showing irregular defects in both kidneys: right 76% and left 24% of total function. (Ultrasoundography normal at 3–1 and 4–5 years.)
Conclusion

Our experience with these and other children suggest that it is unwise to rely on any single imaging technique in the investigation of childhood UTI. It confirms the findings of others that ultrasonography alone does not reliably demonstrate renal scars or VUR. Inflammatory renal enlargement may be overlooked on IVU if no assessment of renal size is made. A diagnosis of renal scarring should not be made on the basis of defects of isotope uptake on a DMSA scan unless changes persist on a follow-up DMSA study and their nature confirmed on limited IVU. Although a MCU allows the most comprehensive assessment of the lower urinary tract, it does not provide information about kidney structure and function.

Summary of pitfalls in the investigation of childhood UTI

<table>
<thead>
<tr>
<th>IMAGING METHODS</th>
<th>POTENTIAL PITFALLS</th>
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<tr>
<td>Ultrasonography</td>
<td>Observer dependent.</td>
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<tr>
<td></td>
<td>Unreliable in the diagnosis of VUR and renal scarring.</td>
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<td>Unreliable for serial renal measurement.</td>
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<td></td>
<td>urethra not visualised.</td>
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<tr>
<td>IVU</td>
<td>Immediately after a first acute infection, renal enlargement may be overlooked.</td>
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<tr>
<td>DMSA study</td>
<td>Renal scarring may be diagnosed when there is potentially reversible photon deficiency following acute UTI.</td>
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<tr>
<td>MCU</td>
<td>Duplex kidneys can cause confusion.</td>
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<td></td>
<td>No indication of lower tract function.</td>
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<td>In the older child in whom it may have resolved, the absence of VUR does not exclude the possibility of significant renal scarring.</td>
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<td>Isotope cystography does not demonstrate bladder defects, define the urethra, or assess ureteric calibre.</td>
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Figure 8  (A) IVU at 6 weeks showing structurally normal, large kidneys (+2 SD scores). (B) bilateral VUR on MCU aged 1-3 years. (C) DMSA study 1-4 years showing reduced left renal image. (D) IVU 1-5 years showing small scarred left kidney (-2 SD scores), normal right kidney. (Renal ultrasonography normal: enlarged kidneys on IVU overlooked at 6 weeks.)

Figure 9  (A) DMSA study aged 9-0 years showing diffuse and focal defects in the left upper pole diagnosed as scarring in boy with bilateral VUR; left 47%, right 53%. (B) IVU showing normal left and duplex right kidney with dilated right ureters. (C) DMSA study aged 11-0 years normal: left 46%, right 54%. (DMSA study: left upper pole scar diagnosed at 9 years: right kidney considered normal.)

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Commentary

These two papers illustrate several of the problems that remain unresolved in the management of childhood UTI. The authors have used their cases to illustrate the limitations of ultrasonography, which can only be regarded as a basic screening test. Ultrasonography is valuable in demonstrating the presence of two kidneys, excluding obstruction, demonstrating urinary tract dilatation and postmicturition voiding residue. These are all important factors that affect management. In addition, kidney length and volume can be measured relatively easily in the majority of children. Kidney size should be expressed in absolute values and in terms of SD scores or centiles using standard reference data.1 Kidneys can be enlarged during, and for a few weeks after, acute infection, so that comments on the report about the date of the last infection, whether or not the urine was sterile at the time of the examination, and the use of prophylaxis are helpful. The degree of dilatation of the collecting system seen on ultrasonography depends to some extent on the fullness of the bladder and how this relates to the normal for age. It has been suggested that in the presence of an overfilled bladder upper tract dilatation is seen not infrequently in children with 'normal urinary tracts'. The diameter of the collecting system and upper ureter should also be measured. In infants, the 97th centile is approximately 5 mm, and in older children it is 8 mm. At the end of the examination, the child should be sent to the toilet and the bladder rescanned to look for postmicturition residual urine. In order to put up all this information, it is essential to have a routine for ultrasound examination and reporting in children, which can permit a thorough and systematic evaluation of the complete urinary tract under optimum conditions. As with much of paediatric practice, this should start with a full explanation by the clinician, and instructions to come with a full bladder. Flexible arrangements within the radiology department, and
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