Investigation of urinary tract infection

Urinary tract infection (UTI) is common in infants and children, with a female preponderance except during early infancy. In an early report from University College Hospital, London, Smellie et al described 200 consecutively diagnosed children with UTI, of whom 188 were investigated by excretory urography or micturating (voiding) cystourethrography, or both.1 Abnormalities were found in 50% and in 35% of those investigated after their first infection (47% of boys and 28% of girls). In particular, chronic atrophic pyelonephritis (also known as reflux nephropathy) was detected in 13% of the total; nearly all of these were children with bacteriologically proven or clinically suspected multiple infections. Vesicoureteric reflux was present in 30% of investigated subjects but in 85% of those with pyelonephritis.

Numerous subsequent studies have yielded results in broad agreement with these, the proportion of investigated children showing some radiological abnormality ranging from 25 to 55% and the proportion with reflux from 8 to 52%.2-8 In at least some of these reports a significant proportion of patients had severe (grade III or IV) reflux in the presence of a normal urogram, suggesting that excretory urography alone is not adequate to exclude serious and potentially damaging reflux.2 6-9 Since reflux is known to be causally associated with pyelonephritis, which itself is responsible for roughly 20% of the end stage renal failure occurring in European patients below 40 years of age,10 the early identification of patients with reflux might offer the prospect of preventing some cases of renal failure by appropriate intervention before severe damage has occurred. In addition, some children with UTI have surgically correctable abnormalities of the urinary tract other than reflux, such as obstructive lesions or urolithiasis.

On the basis of arguments such as these, many paediatricians, radiologists, and urologists teach that all children in whom urinary tract infection has been diagnosed should be studied by urography and micturating cystourethrography, the former investigation being necessary to obtain a reliable image of the renal parenchyma, collecting systems, and lower urinary tract and the latter to identify or exclude reflux;3 7 9 this view seems to be particularly widely held in North America. A few advocate cystoscopy in most or all children,2 8 but this is certainly a minority opinion. Some experts in the United Kingdom recommend a slightly less invasive approach, in which all children are investigated by urography (or, in appropriately equipped centres, abdominal ultrasonography supplemented when necessary by a renal radionuclide scan), micturating cystourethrography being reserved for children under 5 and patients in whom the urogram is abnormal or who suffer from frequent infections.11 12

When experts disagree, how is the non-specialist to decide how to investigate the rather small number of children presenting to him with urinary infection (two a year for the average general practitioner13)? To answer this question, it is necessary to understand the capabilities and, perhaps more importantly, the limitations of the various techniques available for imaging the urinary tract, so that the most appropriate test or combination of tests can be selected to suit the needs of each particular case.

Excretory urography

Urography is a powerful diagnostic tool that is capable of providing useful information about the entire urinary tract except the urethra. The early (nephrogram) phase shows the renal outlines accurately, particularly when enhanced by tomography, and the slightly later pyelogram phase delineates the pelvicalyceal (collecting) systems. The coarse, irregular scarring of pyelonephritis is readily recognisable, as is the clubbed calyx and overlying cortical thinning of the more localised lesion. Radio-opaque stones will be seen on the control (‘scout’) film taken before contrast is injected and radiolucent ones show as filling defects. Obstructive lesions such as obstruction of the pelviureteric junction are well shown. In the non-obstructed system renal function can be roughly inferred from the amount of opacified tissue seen on the nephrogram, in the absence of diffuse parenchymal disease such as glomerulonephritis. A reasonably good view of the ureters and bladder (full and empty) can normally be obtained.

Advantages of the method include familiarity, universal availability, and relative ease of interpretation. No other technique approaches it for showing the fine detail of the pelvicalyceal systems. It probably gives a better overall view of the renal tract than any other single test. Disadvantages include the risk of allergic reactions to contrast
material, which although usually minor can be serious, the discomfort of the injection in small children, the entailed irradiation of the gonads, especially in girls, and the dependence of the image quality on good renal function. Satisfactory pictures are difficult to obtain in infants and especially the newborn. Small renal scars may be missed if located on the anterior or posterior aspect of the kidney.

**Micturating (voiding) cystourethrography**

Micturating cystourethrography is the definitive method of showing reflux. It also gives a higher definition view of the bladder than excretory urography, and in the lateral projection, during voiding, the urethra is outlined in its full length. Its major disadvantage is the need for bladder catheterisation, which is at best uncomfortable and at worst painful and frightening for small children. Infection may be introduced, and urethral strictures occasionally occur. Nine serious complications of micturating cystourethrography, including two fatalities, were described in a series of 14 children reported by McAlister. As with excretory urography, some gonadal irradiation is inevitable, especially in girls. It is by far the most unpopular procedure with patients and their parents of those considered here.

**Ultrasonography**

Given up to date equipment and an experienced operator, real time ultrasonography is capable of providing a great deal of information about the anatomy of the renal tract. The shape, size, and position of the kidneys can be determined with considerable accuracy; the degree of 'echogenicity' of the renal substance and the sharpness of corticomedullary differentiation provide a clue to the presence of diffuse parenchymal disease or damage. Hydronephrosis, hydrourerter, and ureteroceles are reliably detected, as are bladder dilatation, trabeculation, and other relatively gross abnormalities of the lower urinary tract. Intermittent dilatation of the retrovesical ureter sometimes provides a clue to the presence of reflux, although normal ultrasonography certainly does not exclude it. Nor does it exclude focal scarring of the kidneys due to pyelonephritis, and of course it provides no information at all about renal function. More than any other test mentioned in this annotation, it is 'driver dependent'; at the time of writing, relatively few ultrasonographers have the skill, the experience, or perhaps even the aptitude to obtain the maximum available information from renal ultrasonography, while the pictures themselves are difficult for the clinician to evaluate.

**99mTc dimercaptosuccinic acid (DMSA) scan**

DMSA is selectively taken up by renal tubular epithelial cells; the emitted γ radiation can be used to form an 'autoradiograph' of the kidneys, which shows the renal outlines fairly well, though lacking the definition of urography.

Focal scars show as 'holes' in the image and will be seen even if they are on the anterior or posterior aspect of the kidney, where they are likely to be missed by urography. By counting the radioactivity over the two kidneys, differential renal function can be estimated. The radiation dose is less than urography; reactions to the radionuclide are not seen. The technique gives good results in neonates.

**99mTc diethyleneetriamine penta-acetic acid (DTPA) scan**

DTPA is handled by the kidney in the same manner as inulin and radiocontrast media such as sodium iotobamate (Conray)—that is, it is filtered at the glomerulus and neither secreted nor reabsorbed by the tubule. When labelled it therefore provides a 'radionuclide urogram' with the same phases as an excretory urogram: nephrogram followed by pyelogram with subsequent visualisation of ureters and bladder. Image definition is considerably inferior to that obtainable by urography, and the technique should not be considered a substitute for it; by measuring the transit time of radioactivity from kidneys to bladder after an injection of furosemide, however, obstructive lesions such as obstruction of the pelviureteric junction can be detected. In a further refinement a secondary rise in activity over one or both kidneys coinciding either with bladder emptying or with a fall in bladder activity without emptying may indicate the presence of reflux.

**Purpose of imaging studies**

Before submitting a patient to a series of imaging studies of the urinary tract, it is desirable to define as precisely as possible the questions being asked. These will vary according to the age of the patient and the clinical circumstances of the case. They may include any or all of the following:

(i) Is there any structural abnormality of the urinary tract—for example, obstruction, stone, neuropathic bladder—predisposing to infection?

(ii) Are the kidneys scarred as a result of the infection(s)?

(iii) Is reflux present and, if so, in what degree of severity?

Questions (i) and (ii) can be answered with a high degree of reliability either by excretory urography;
or by a combination of plain abdominal x-ray, ultrasonography, and DMSA scan. Question (iii) can only be definitively answered by micturating cystouretrography, and it is here that controversy is centred: how important is it to detect every case of reflux after the first infection? Put another way: is it possible to identify subgroups of children in whom the risk of progressive renal damage after their first UTI is so low that cystouretrography can safely be omitted? I believe that with a proper understanding of the epidemiology of chronic atrophic pyelonephritis, it can.

It is difficult to know the exact incidence of UTI in childhood, but a reasonable approximation may be made from a carefully conducted, prospective study published by Dickinson in 1979. He found that 3-1/1000 girls and 1-7/1000 boys, aged 0-14, presented annually with a first, symptomatic UTI; this corresponds to about 780 and 430 per million total population, respectively. (An incidental, but very important, observation made in the same study was that only 18% of children with dysuria and frequency proved to have infected urine, a figure that agrees well with the 24% reported earlier by Williams; this underlines the importance of properly establishing the diagnosis at the first presentation, the single most effective way of avoiding unnecessary investigations.) The incidence of end stage renal failure due to pyelonephritis in Europeans aged <40 is in the region of 4-5 per million. Combining these figures, the crude risk of renal failure due to pyelonephritis in children presenting with a first, symptomatic UTI is not greater than 1% for boys and 0.5% for girls. This must be an overestimate of the true risk as it assumes that detection and investigation of childhood UTI would have identified all those who would later develop renal failure, which is not the case; many adult patients with end stage pyelonephritis have no history of symptomatic UTI in childhood. Furthermore, identification of those with reflux with or without pyelonephritis in childhood would not necessarily lead to prevention of renal failure in all cases. It is therefore likely that the probability that any individual child with a first UTI is at risk from potentially preventable renal failure is of the order of one in several hundred.

The bulk of the published evidence suggests that scarring is present at the first investigation in most of those children in whom renal damage develops. A recent study has shown unequivocally that new scars can develop in both previously undamaged and damaged kidneys; as pointed out by Sherwood and Whitaker, however, this is a rare event. In the study of Smellie et al new scars were seen in 74 children. In 56 of these, however, 'repeated symptomatic recurrences of infection were recorded'. These cases were assembled from 23 centres over a span of 22 years. Therefore, new scars were seen in only one asymptomatic patient per centre every 28 years—hardly a common event.

Suggested scheme of investigation

The following proposed guidelines are similar to, but not identical with, those recently put forward by Whitaker and Sherwood. Three age bands can be identified.

1. Infants <1 year of age. All cases should be investigated by micturating cystouretrography, ultrasonography, and DMSA scan. If apparatus for or expertise in the last two are not locally available, excretory urography (intravenous urogram) can be substituted, but visualisation of the kidneys and ureters is often unsatisfactory.

2. Children aged 1–7 years. All children should be studied by either excretory urography or the combination of plain abdominal film, ultrasonography, and DMSA scan.

3. Children aged 7 years and over. A plain film and ultrasonography are sufficient.

If excretory urography is selected as the initial investigation a strong case can be made for delaying the study for six weeks after the infection has been diagnosed and treated. This is because the characteristic radiological appearances of pyelonephritis are due to contraction of the scar tissue, which replaces the damaged parenchyma, a process that takes time; urography performed immediately after the infection may give a false negative result. In this case a small prophylactic dose of a suitable antimicrobial agent should be continued after the infection has been eradicated until the result of the urogram is known.

A micturating cystouretrogram should be performed in children of 1 year and over if: (i) the infection recurs; (ii) the studies recommended above are abnormal; (iii) the clinical features of the first infection were suggestive of acute pyelonephritis; or (iv) there is a known family history of chronic atrophic pyelonephritis. If this scheme is followed, and provided that the recommended imaging studies are performed and interpreted by staff skilled in the investigation of children, most of those presenting with a first UTI after their first birthday can be spared a micturating cystouretrogram without great risk of missing important reflux.

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