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Imaging in Urinary Tract Infections: Current Strategies and New Trends

Lorenzo Biassoni, MD, and Samantha Chippington, FRCR

The aim of imaging in a child with urinary tract infection (UTI) is to detect abnormalities that require appropriate treatment or findings that can be acted on to prevent development of complications (hypertension, chronic renal failure or pregnancy-related complications). Imaging protocols in pediatric urinary tract infections are evolving. From strategies based on extensive investigations in all children younger than 7 years of age, we are slowly moving to imaging strategies focused on children at risk of developing renal damage and possibly long-term complications. The article provides an overview on urinary tract infections, their complications and the use of imaging in their management. The different imaging strategies in children with UTIs (including the recommendation of excluding from imaging certain groups of patients) still needs full evaluation. It is interesting to note, however, a slow move from wide use of cystography in all children with UTI, which has been standard practice for many years but was probably not based on solid scientific evidence, toward a more focused use of cystograms in specific groups of children.
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Imaging in urinary tract infections (UTIs) is still controversial, with several different imaging strategies being adopted. Many centers make use of protocols based on historical practice rather than on strong scientific evidence. In some institutions, protocols based on the recommendations of official guidelines published several years ago[1,2] are still in use.

A few years after the publication of the existing guidelines, doubts were raised as to whether the recommendations of these guidelines were based on firm evidence.[3] Also, referring clinicians have increasingly become aware that too many imaging tests are requested unnecessarily and that imaging does not influence patient's management in the vast majority of cases. Therefore, many pediatricians are beginning to question the need to refer every child with UTI for imaging. Imaging should be targeted at the child at risk of developing permanent renal damage. Its aim should be to demonstrate anatomical or functional abnormalities that predispose the urinary tract to new or progressive renal damage.

Department of Radiology, Great Ormond Street Hospital for Children and Institute of Child Health, University College London, London, United Kingdom.

Address reprint requests to Lorenzo Biassoni, MD, Department of Radiology, Great Ormond Street Hospital for Children and Institute of Child Health, University College London, Great Ormond Street, London WC1N 3JH, UK. E-mail: BiassL@gosh.nhs.uk

In an attempt to incorporate results of many studies published in the last 15 years in children with UTI into an official document, the National Institute for Health and Clinical Excellence of the United Kingdom (NICE) published a new set of guidelines, available online at www.nice.org.uk. Many pediatricians have welcomed the draft document because it recommends a significant reduction in the number of imaging tests in the management of pediatric UTI. However, it is likely that the NICE guidelines will stimulate controversy among pediatric radiologists and nuclear medicine physicians because of the very limited imaging strategy they advocate in some specific clinical settings.

Data on the effectiveness of antibiotic prophylaxis and of surgical intervention for vesico-ureteric reflux in children with UTI await confirmation by properly designed randomized controlled studies. It is hoped that the results of these studies will shed further light on the role of imaging in the follow-up of children with a history of UTI.

The different imaging strategies in children with UTI in use are based on different assumptions and a full evaluation of them is still awaited. Overall, it seems justified to reduce the number of imaging investigations. In particular, there is a trend to slowly move away from the traditional strategy, based on the detection of reflux in all children with UTI as the major risk factor for renal damage and recurrent UTI, in favor of a more focused use of cystography in selected patients. Some children, for example, those older than 6 months with

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cystitis-like symptoms, probably do not need any form of imaging at all.

Epidemiology

UTIs are caused by invasion of the urinary tract (bladder and/or kidneys) with bacteria. Bacteria trigger an inflammatory response (with an inflammatory infiltrate) and symptoms. Both the bacteria and the response elicited by them can cause renal damage. A significant bacteriuria has to be present to diagnose a UTI, with at least 10^5 micro-organisms per milliliter of urine.

Approximately 1% of boys and 3% of girls have a UTI in their first decade of life. A total of 5% of children from 2 months to 2 years of age with an unexplained fever will have a UTI. UTI is more common in boys between 0 and 6 months of age and in girls is more common in those older than 6 months of age. Girls are more likely to develop a UTI and have an increased incidence of recurrent UTI when compared with boys. Congenital renal damage in the form of renal dysplasia is more common in boys than in girls. Acquired renal damage in the form of renal scarring is more common in girls (probably due to the higher incidence of UTI and of recurrent UTI).

Escherichia coli is responsible for approximately 80% of UTIs. Different types of Gram-negative micro-organisms exist, with different degrees of virulence. A more virulent type of *E. coli* shows *fimbriae*. More than 90% of children with acute pyelonephritis have a fimbriated *E. coli* in their urine, with only 19% of children with cystitis having this more virulent subtype of *E. coli*. Other micro-organisms responsible for the remaining 20% of UTI are *Proteus*, *Enterococcus*, *Pseudomonas*, *Klebsiella*, *Staphylococcus aureus*, and *Staphylococcus epidermis*. An atypical micro-organism often results in greater clinical concern because of the more virulent nature of the infection and the greater risk of renal damage.

Renal scarring associated with UTI varies according to the features of the UTI itself: in a relatively recent report only 1% of children with a UTI not requiring hospitalization had renal scarring, whereas 22% of hospitalized children with UTI had renal scarring.[4] Recurrent acute pyelonephritis is associated with a higher risk of renal damage.[5]

Diagnosis of a UTI

The diagnosis of UTI can be challenging. Clinical symptoms are very often nonspecific, especially in infants; urinalysis may be indeterminate, and the result of urine culture may take several days to become available. A child with a UTI can present in different ways. The majority of children with a UTI have no significant systemic symptoms (cystitis-like symptoms are more common, particularly in girls). Localizing urinary tract symptoms in infants is exceptionally difficult. A child with acute pyelonephritis usually is systemically unwell, with a fever >38°C and one of the following symptoms: loin or abdominal pain/tenderness, vomiting, irritability, poor feeding, chills, and rigors. Only a few children present with symptoms suggestive of acute septicemia: signs of dehydration, reduced activity/responsiveness, and ill appearance.

It may be difficult to obtain a clean catch of urine for urinalysis, microscopy, and urine culture, especially in very young children. If a clean catch cannot be obtained, a urine sample in a pad or a bag is the second best option in a primary care setting, although it is often far from ideal as contamination because inappropriate handling of the sample can occur. In a hospital setting, supra-pubic aspiration, performed by a skilled operator, is a satisfactory alternative to a clean catch. The first test on a urine sample is a dipstick test with leukocyte esterase and nitrite analysis. If the sample is positive for both tests the diagnosis of UTI is made and the child is treated with antibiotics. If the sample is negative for both leukocyte esterase and nitrite analysis, UTI is excluded. In case one test is positive and the other is negative, further evaluation with microscopy (or flow cytometry) to assess the presence of a sufficient number of white cells and bacteria in the urine is necessary. Urine culture may be required to confirm the diagnosis of a UTI or to test the sensitivity of the micro-organism to different antibiotics (especially in case of resistance to the first line antibiotics). It normally takes 2 to 3 days for the result of the urine culture to become available. Therefore, it is possible that the child can either fail to receive appropriate treatment or receive unnecessary treatment and investigations.

The best imaging technique to diagnose an acute pyelonephritis is a DMSA scan performed during the acute infection. Ultrasound has a lower sensitivity for focal nephronia, even with power Doppler. A CRP greater than 20 mg/mL is highly sensitive for acute inflammatory renal involvement but has a very low specificity. The evaluation of serum procalcitonin appears much more specific for parenchymal involvement,[6] retaining the same sensitivity; the preliminary results of this test are encouraging but have to be confirmed.

Recurrent UTI

Recurrent UTI is defined by cystitis that occurs 3 or more times or a minimum of 2 episodes of acute pyelonephritis. A recurrent acute pyelonephritis normally causes clinical concern as it can be associated with conditions such as bladder dysfunction, vesico-ureteric reflux and congenital anatomical abnormalities, which predispose to re-infection and possible subsequent renal damage. It has been shown that the risk of renal scars is much higher after recurrent acute pyelonephritis compared with a single episode. In the experience of Jodal and coworkers[5] 4 repeated episodes of acute pyelonephritis caused renal damage in 58% of patients, compared with 9% in patients with a single episode.

Aim of Management of a Child With UTI

The aim of management in the child with a UTI is prompt diagnosis, rapid treatment, and the detection of any underlying cause that may predispose the child to repeated infec-

tion with the consequent risk of renal damage and the possibility of long-term renal insufficiency. Imaging can aid the clinician in the localization of infection, help demonstrate any anatomical or functional abnormality, and help to assess renal damage and scarring.

The Existing Guidelines on Imaging UTI in Children

In the mid 1970s some studies reported a number of significant complications following UTI.[7] The complications documented were hypertension, chronic renal failure, and serious events during pregnancy (preeclampsia, hypertension, acute pyelonephritis). As a consequence, action was taken in the form of guidelines on the management of children with UTI.

In the United Kingdom, the Royal College of Physicians (RCP) published a set of guidelines on UTI in children in 1991.[1] As regards imaging, the document recommended that every child with a first UTI between 0 and 7 years of age should have an ultrasound and a DMSA scan. Children in the first year of life should also have a micturating cysto-urography (MCUG). A few years later, the American Academy of Pediatrics issued guidelines on the management of UTI in children[2]: the guidelines focused more specifically on children with a febrile UTI and recommended that in the age group from 2 months to 2 years an ultrasound and a MCUG should be performed.

The RCP guidelines were based on the assumption that vesico-ureteric reflux has a detrimental effect on the kidney and that children with reflux should be considered at risk of developing renal damage. Therefore, these children should be identified with a cystogram and put on antibiotic prophylaxis until the reflux had resolved. Another assumption was that a scarred kidney is a risk factor for hypertension, chronic renal failure and, in girls, complications in pregnancy.

After the publication of the RCP guidelines, an enormous burden was put on radiology departments and children with UTI and their families. A huge number of ultrasounds, cystograms, and DMSA were performed on children with a first diagnosis of UTI. A child with a history of UTI was considered as having chronic pathology, which required long-term medications and follow-up.

Pediatricians and radiologists were assiduous in following the guidelines; an audit of the imaging strategy suggested by the guidelines was therefore possible. It resulted in the finding that the vast majority of ultrasounds and DMSAs performed in children with a first diagnosed UTI in a primary care context were normal. If the ultrasound showed some abnormality, this was usually not clinically important, with the exception of the occasional finding of acute obstruction.[8] Therefore, the question has been raised as to whether an excessive number of examinations are being performed unnecessarily and whether one should be more selective in identifying the children who require imaging.

Complications of UTI

In trying to identify the subgroup of children who need imaging, a number of investigators have focused on the complications after one or more episodes of UTI. They have studied the frequency of complications and the associated features. As a result, some conclusions on the relationship between UTI and their complications have been suggested.

Chronic Renal Failure

Although UTI is common (incidence of UTI in England and Wales is 24,000 per year), chronic renal failure (CRF) after acute pyelonephritis is rare. Data from the UK incident dialysis registry show that 167 patients out of 1 million people in a 5-year period (1996-2001) are on dialysis as a result of chronic pyelonephritis. A study in the primary care setting on long-term follow up of children with a history of UTI suggested no significant difference in GFR between children who had unilateral renal scarring and children with normal kidneys.[9] Children with severe scarring seem to have a greater risk of progressive renal damage and end-stage renal failure.[9] In Sweden, the incidence of CRF after pyelonephritis and reflux decreased from 5% in 1978 to 1985 to 0% in 1986 to 1994 after an active surveillance program monitoring signs and symptoms of acute pyelonephritis.[10,11]

The available reports suggest that the risk of CRF in the global population of children with UTI is very low. Unilateral renal damage seems to bear the same risk of developing CRF as the incidence in the general population. Bilateral renal damage and renal scarring in a solitary kidney are more likely to be associated with higher risk of developing CRF several years later; the risk seems to be linked to the level of the GFR and the blood pressure at the time of the UTI, and the number and size of renal scars.[12]

Hypertension

Data suggest that the risk of hypertension after a UTI in children treated in primary care is very low. Wennerstrom and coworkers[13] followed up for 16 to 26 years a cohort of 1221 children who had a first UTI diagnosed in the years 1970 to 1979. A total of 68 children had renal scarring, 57 of them were followed up and matched against a control group of 51 children with normal kidneys. Five out of 53 (9%) children with renal scarring had hypertension compared with 3 of 47 (6%) children in the group with normal kidneys: there was no significant difference in the incidence of hypertension between these groups. Patzer and coworkers[14] found that children with severe bilateral renal scarring following UTI were more likely to have hypertension. Another report suggests that children with no renal damage have the same incidence of hypertension as children with unilateral renal damage.[15] Children with bilateral renal damage and children with scarred solitary kidneys have higher risk of developing hypertension.[15]

In summary, it seems that the risk of hypertension in an unselected group of children with UTI is low. The risk is likely to be higher in children with a significantly reduced

number of functioning nephrons (ie, children with severe bilateral renal damage or children with scarred solitary kidneys). This data needs to be corroborated in a larger cohort of patients.

Pregnancy-Related Complications

A total of 111 women with a history of previous UTI had no significant difference in the incidence of preeclampsia, operative delivery, prematurity or low birth weight between women with renal scarring and women without scarring. Four women with renal scarring and persistent vesico-ureteric reflux had an episode of acute pyelonephritis during their pregnancy.[16] It seems however that the risk of serious complications during pregnancy in women with renal scars is low.

Who Needs Imaging? The Child at Risk

The current literature on the relationship among UTI and CRF, hypertension, and pregnancy complications suggests that the vast majority of children with UTI are not at risk of subsequent complications. Therefore, the indiscriminate use of imaging in every child with a first diagnosed UTI is unlikely to be effective in identifying the children who develop complications, as these are rare. With indiscriminately generous use of imaging, resources are wasted. Moreover, with a widespread use of prophylactic antibiotics in many children with abnormal imaging—used until the findings on imaging normalize, ie, reflux on cystography—there is an increased risk of urinary tract colonization with resistant micro-organisms. This may result in antibiotic resistant UTI with further imaging examinations required for assessment. It seems more sensible to reserve imaging tests for the children at risk of renal damage after UTI and treat promptly with appropriate antibiotic therapy, without imaging tests, the other children.

Who Are the Children at Risk?

A child is considered *clinically* at risk of developing renal damage if the following features are present:

- Clinical signs eg, poor urinary stream, palpable kidneys;
- Atypical organism (ie, not *E. coli*);
- High fever, septicemia;
- Failure to respond to antibiotic treatment within 48 hours; and
- Recurrent UTI.

In children with these features, imaging is justified. An imaging test may show some of the following features, which can explain the severity of the symptoms and direct further management:

- Urinary stasis, due to the following conditions: bladder dysfunction (incomplete bladder emptying; detrusor overactivity); outflow obstruction (pelvic-ureteric junction [PUJ], vesico-ureteric junction [VUJ], posterior urethral valves); constipation
- Renal scarring: congenital: renal dysplasia; acquired renal scarring
- Renal calculi; and
- Vesicoureteric reflux (VUR).

The aim of imaging in a child with UTI at risk of complications is to prevent further UTI by demonstrating structural or functional abnormalities that can be treated medically or surgically.

How Can Imaging Be Used?

In a child with UTI at risk of developing renal damage imaging tests can be used in the following ways:

- To localize the infection;
- To detect anatomical abnormalities;
- To detect vesico-ureteric reflux;
- To show renal scarring; and
- To study bladder function.

Imaging Localization of a UTI

A DMSA scan performed during an episode of suspected acute pyelonephritis is the gold standard to localize the site of infection. Ultrasound can occasionally show areas of nephronia using the power Doppler technique but is not sensitive at demonstrating areas of inflammatory infiltrate during an acute pyelonephritis. As clinical symptoms are often nonspecific, imaging tests can be useful in confirming or excluding the diagnosis. Several authors have shown that one in three patients with a clinically suspected acute pyelonephritis have a normal DMSA.[8,17-19] The DMSA scan performed during the acute pyelonephritis appears to have prognostic value. It has been shown that a normal DMSA during an acute pyelonephritis with or without reflux is associated with a 0% risk of renal scarring. Mild renal inflammatory involvement with or without reflux and extensive renal involvement without reflux are likely to be associated with an intermediate risk of developing renal scars after the UTI. Extensive renal inflammatory involvement with reflux is associated with a high risk of developing renal scars.[20]

A DMSA scan performed during the episode of acute pyelonephritis offers the following advantages: it can help in the diagnosis of acute pyelonephritis, which can be difficult especially if clinical symptoms are vague and urinary analysis is indeterminate. If the scan is normal, this can be reassuring as it suggests a low risk of renal damage after the infection. If the DMSA shows massive inflammatory involvement and reflux, the child is at high risk of renal scarring and appropriate treatment/follow-up can be organized.

An acute DMSA in hospitalized children with febrile UTI is not routinely performed in many institutions. The main objection to its use is that it does not change immediate management. It has been shown that there is no difference in terms of bacteriuria, persistence or recurrence of renal involvement between a short course of IV antibiotics followed

by oral antibiotics compared with a longer course of IV antibiotics (eg, 2 weeks of treatment).[21-23] What seems to make the difference in terms of prevention of renal scars in a child with UTI is prompt initiation of antibiotic treatment. If there is significant delay in starting antibiotic treatment, the number of scars is higher when a three-day IV treatment is given instead of a seven-day treatment.[18] However, the prognostic value of massive, bilateral inflammatory involvement during a clinical acute pyelonephritis in association with vesico-ureteric reflux in terms of identifying children at high risk of renal scarring[20] is probably worth investigating further.

Imaging to Detect Anatomical Abnormalities

A UTI can be the presenting symptom of an anatomical abnormality of the urinary tract. The imaging modalities that are most frequently used to clarify the anatomy of the urinary tract are ultrasound and fluoroscopy. MRI is occasionally necessary to better assess complex congenital abnormalities. Isotope imaging is used to assess regional renal parenchymal function and drainage. Conditions that can declare themselves with a UTI include obstruction, calculi, renal duplication, renal ectopia and crossed fused kidneys.

Obstruction to urinary outflow includes PUJ obstruction, VUJ obstruction, and obstruction at the bladder outlet (such as posterior urethral valves [PUV]). Ultrasound is normally the first modality to define these conditions antenatally. A MCUG is the investigation of choice in diagnosis of PUV in the neonatal period. Nuclear medicine is necessary in case of detection of pelvic or ureteric dilation: it provides data on the relative renal function and can help in distinguishing between urinary stasis (eg, a baggy renal pelvis) and resistance to urinary outflow (eg, PUJ obstruction). Also, isotope dynamic renography may help to assess the VUJ and distinguish between an obstructing VUJ and a dilated nonobstructing VUJ.

Renal calculi are not very common in children and are usually diagnosed with ultrasound. Isotope imaging is not routinely performed to assess drainage, as this is rarely impaired, but can be used to assess regional renal function. A DMSA scan at baseline and following treatment (eg, with percutaneous lithotripsy) is helpful in showing possible focal renal damage associated with renal calculi and/or their treatment.

A duplex kidney is normally diagnosed with ultrasound, which can also demonstrate if there is dilation of the collecting system of the upper or the lower moiety and of the ureters. The ultrasound will also detect the presence of an ureterocele (unless collapsed and adherent to the bladder wall) and the thickness of the renal cortex. Functional imaging with either DMSA or isotope dynamic renography provides information on the global relative function of each kidney and on the relative function of each moiety of a duplex kidney (Fig. 1). If a renal moiety is nonfunctional, there will be no tracer uptake. The isotope examination will have to be interpreted in the clinical context and in the light of the other imaging tests. This will help to make the diagnosis of a non-

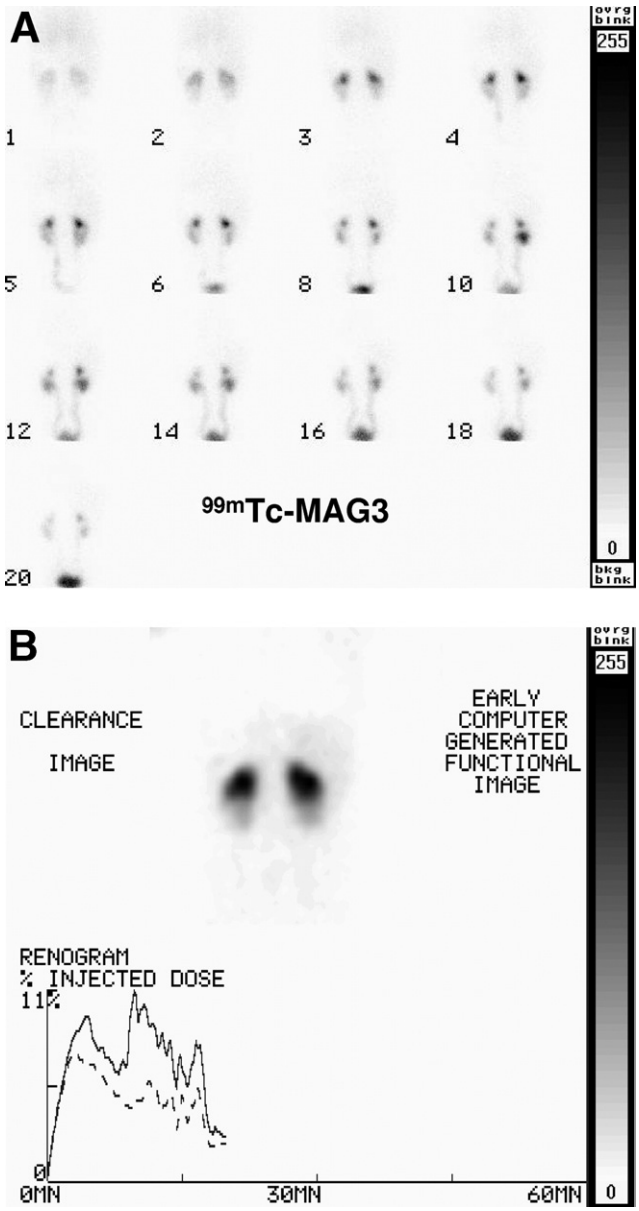

Figure 1 Shown is the dynamic renography with ^{99m}TC-MAG3 in a 5-year-old girl with UTI, bilateral duplex kidneys and right lower pole reflux on antibiotic prophylaxis. The MAG3 scan (A) shows symmetrically reduced function in the lower moiety bilaterally and good function in the upper moieties. Differential function: left kidney 47%, right kidney 53%. Drainage is satisfactory bilaterally. At minute 10 there is a clear evidence of reflux into the right lower moiety in coincidence with an episode of micturition in the nappy; this confirmed by a spike seen in the time activity curve of the right kidney (B). This case shows that on occasions VUR can be found during a dynamic renography in very young, nontoilet-trained children, either in coincidence with a micturition or even without bladder emptying; in the latter case, the finding raises the probability of detrusor overactivity.

functional renal moiety more definitive, when the isotope and ultrasound findings are reviewed in conjunction.

Ectopic kidneys can be diagnosed with ultrasound. Occasionally the ultrasound fails to demonstrate an ectopic kidney and functional imaging (often a DMSA scan) is very helpful.

An anterior view will have to be acquired in addition to the other standard views and the differential function will have to be calculated with the geometric mean. Horseshoe kidneys can be underdiagnosed with ultrasound and functional imaging (DMSA or MAG3) is again very helpful. Crossed fused renal ectopia often requires nuclear medicine examinations for regional renal parenchymal function and intravenous urography (IVU) to clearly define the anatomy of the collecting system.

However, in a primary care patient population the incidence of anatomical renal abnormalities is very low. Even in the subgroup of children presenting with a febrile UTI the presence of anatomical abnormalities is low and the majority of abnormalities found on ultrasound do not result in change in management.[8]

Imaging to Detect VUR

VUR is present in 1-3% of the general population. Among children with a UTI, however, VUR is present in 30-40%. VUR resolves spontaneously with age in the majority of children. VUR is likely to be an inherited condition: siblings of children with VUR have a significantly higher incidence of VUR than the general population. There are different grades of VUR as shown by the radiological features on the MCUG. Grade I VUR reaches the ureter only. Grade II outlines the ureter, pelvis, and calyces but no dilation is present. Grade III demonstrates ureteral dilation and slight blunting of the calyceal fornices. Grade IV shows more pronounced dilation, tortuosity of the ureter and marked blunting of the calyceal fornices. Grade V demonstrates marked dilation and tortuosity of the ureter with gross dilation of the upper system and clubbing of the calyces.

Several imaging investigations are available to demonstrate the presence of VUR. Imaging tests involving the use of a bladder catheter include the radiological MCUG and the direct isotope cystography (DIC). The first can provide an excellent anatomical definition of the urethra and a good outline of the bladder; if VUR is present, the MCUG can grade it according to its severity; it can also show if there is dilation and tortuosity of the ureters. With the new fluoroscopy equipment, the radiation burden given by a MCUG is very low. The DIC offers the advantage of a continuous monitoring of the kidneys during the bladder filling and emptying and a very low radiation burden. The disadvantage is a poor anatomical definition. The main technique that does not make use of a catheter is the indirect radionuclide cystography (IRC): this test requires that the child be toilet-trained. The child voids before the gamma camera at the end of a dynamic radionuclide renography, when the bladder is full of radioactive urine. The main advantage of the test is that it can detect VUR with a physiologically filled and emptying bladder.

The Debate on VUR

After the publication of the guidelines of the Royal College of Physicians and the American Academy of Pediatrics, VUR has been by and large considered a significant risk factor for renal damage. Children with a UTI are screened for VUR and, if present, they are commenced on prophylactic antibiotics until VUR has resolved.

In recent years, the relevance of VUR in predicting renal damage has been questioned. It has been noticed that many children with VUR do not necessarily get renal damage.[24] Also, approximately 50% of children with an acute pyelonephritis do not have demonstrable VUR.[17,25,26]

There seems to be a difference between low-grade VUR (grades I and II) and high-grade VUR (mostly grade IV) and the presence of renal scarring following a UTI. Low-grade VUR (the most common form seen in a child with UTI) is associated with a low risk of renal scarring; high-grade VUR is associated with a higher risk of scarring.[17,27,28] A possible explanation as to why high-grade VUR can be harmful to the kidney is that high-grade VUR of infected urine can bring bacteria directly into contact with the renal parenchyma via the papillae (intrarenal reflux).[29,30]

A recent systematic review of the literature and meta-analysis in children with UTI has shown that only 20% of children with VUR demonstrate renal damage on DMSA; in addition, scarred kidneys are seen in children with no demonstrable VUR. Therefore VUR seems to be a weak predictor of renal damage.[31,32]

VUR seems to have no prognostic significance in the majority of cases. Only a small subpopulation of children with UTI and VUR develop renal scarring. Children with VUR are therefore likely to be a heterogeneous group, with some children at risk of developing renal scars and others not.

Hansson[24] noticed that very few patients in a cohort of 303 children with high-grade VUR had a normal DMSA, the others having focal abnormalities. He therefore suggested that a DMSA performed during acute pyelonephritis would detect almost all cases with high-grade VUR and therefore could replace the MCUG (being less traumatic and invasive) as a first line investigation; the MCUG would be reserved for children with an abnormal DMSA and ultrasound. This observation deserves further evaluation because, if confirmed, it could shift the emphasis from reflux as a major risk factor for renal damage to inflammatory parenchymal involvement during acute pyelonephritis as the most important risk factor in determining renal damage.

In summary, the relationship between VUR and renal scarring is not simple. Not all children with VUR develop renal damage after UTI. Renal damage can occur in the absence of VUR. Further evaluation of VUR and UTI is necessary to identify subgroups of children with VUR and UTI who are at risk of subsequent renal scarring.

Imaging to Detect Bladder Dysfunction

Bladder dysfunction is associated with increased risk of recurrent UTI and slower resolution of VUR.[33] This condition can be due to detrusor muscle overactivity and detrusor–sphincter dyssynergia.[34] The former results in frequent but ineffective contractions of the detrusor muscle. The contractions can cause VUR with no bladder emptying. Eventually bladder emptying occurs. This condition is diagnosed with urodynamics, although an indirect radionuclide cystogram may demonstrate the bladder dysfunction. The latter is characterized by slow and incomplete bladder emptying with a large urinary residual.

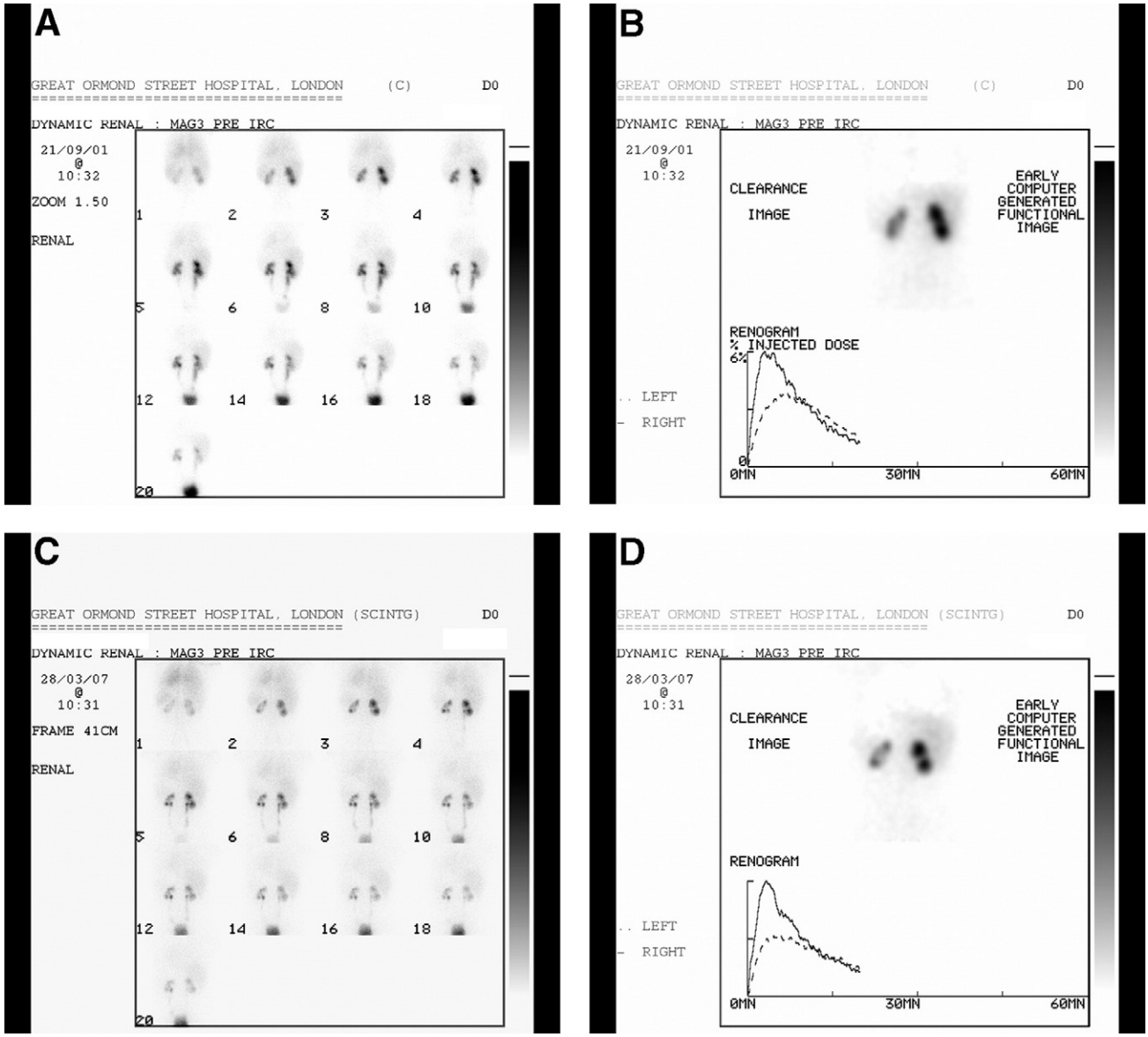

Figure 2 Shown are the nuclear medicine studies of a 10-year-old boy with a history of recurrent UTIs. Dynamic renal scintigraphy with ^{99m}Tc-MAG3 when the child was 4 years old (A and B) and follow-up scintigraphy at 10 years of age (C and D) with IRC after the more recent dynamic renography study (E-H) are shown. The renal scintigraphy shows 2 damaged kidneys (the left more than the right) and significantly reduced function in the left kidney (split function: left kidney 30%, right kidney 70%). Drainage is satisfactory. The IRC study (2 cystograms performed during the same visit to the nuclear medicine department, one after the other) shows incomplete bladder emptying at the end of the first cystogram, with a large urinary residual in the bladder (of approximately 250 mL, as it can be inferred from the time activity curves of the cystogram) (F). There are several episodes of mild left sided reflux, as shown by the first cystogram and the compressed images (E and F). The second cystogram shows almost complete bladder emptying with another episode of left sided reflux (G and H). The findings are compatible with a dysfunctional bladder with a large urinary residual, which is likely to cause increased pressure within the bladder and consequent reflux into the left kidney. A dysfunctional bladder is a recognized risk factor for recurrent UTI and can be associated with persisting reflux. The recurrent UTIs in this boy have damaged both kidneys (the left to a much greater extent than the right). Comparison between the two studies shows some progression of renal damage in the left kidney.

Children with bladder dysfunction and recurrent UTI and VUR are at high risk of developing renal scars and progressive scarring.[33] Bladder dysfunction can be diagnosed from the clinical history and with a voiding chart (with the times and volumes of bladder emptying). Ultrasound can sometimes demonstrate indirect signs of bladder dysfunction such as bladder volume, the presence of a thick bladder wall and a significant urinary residual volume following micturition. MCUG demonstrates bladder trabeculations and the possible presence of bladder neck hypertrophy. The IRC is a completely physiological test of bladder function as no catheterization is needed and the child voids when s/he wishes. The

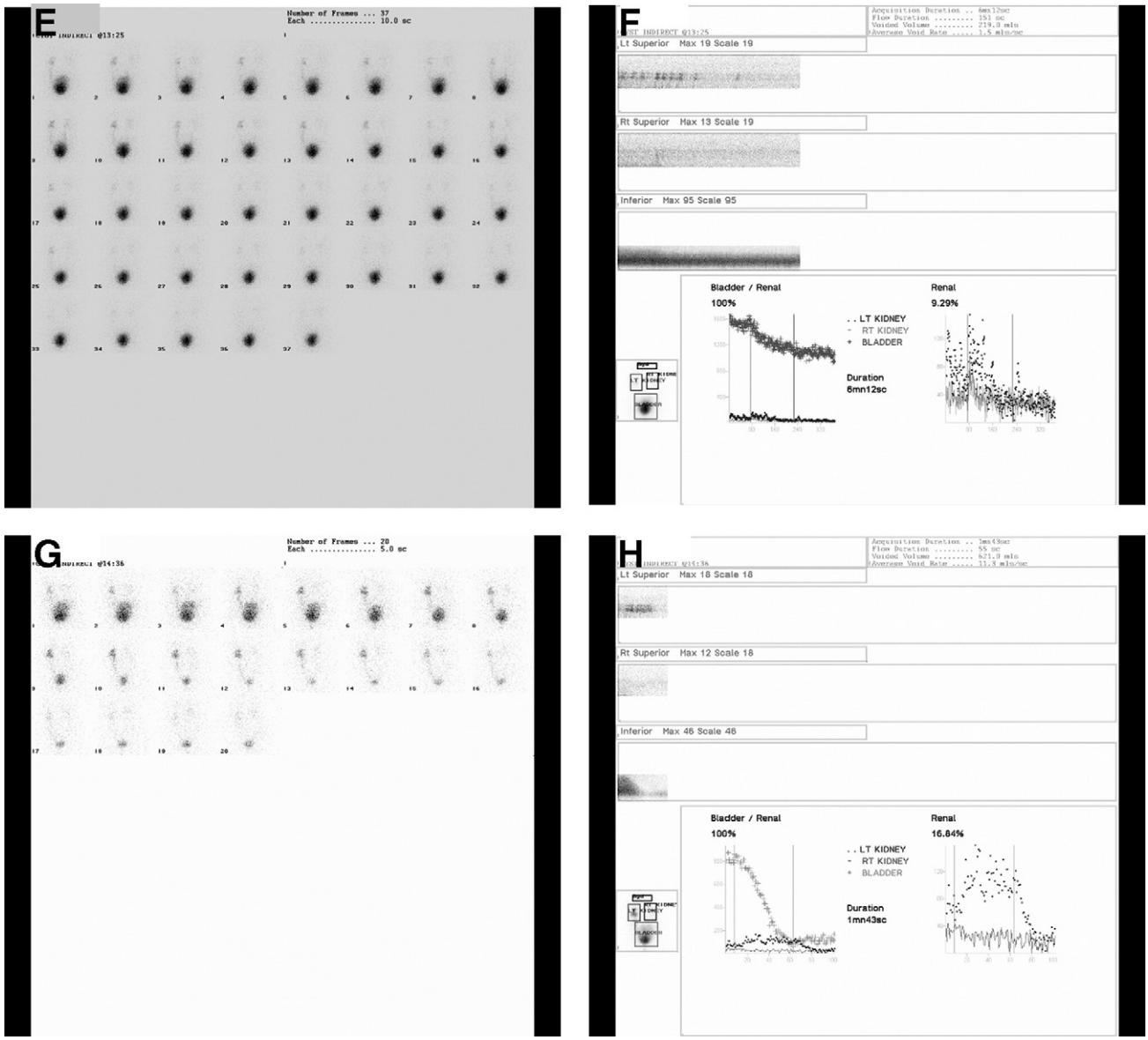

Figure 2 (continued)

child needs however to be toilet trained. The test demonstrates micturition in real time and documents the duration and the completeness of bladder emptying. The IRC can also show VUR. The sensitivity of the test for VUR is higher if the IRC is repeated (during the same visit to the nuclear medicine department) whenever the first cystogram shows persistent activity within the bladder/collecting system and until the bladder and the collecting system are empty.

It is important to identify bladder dysfunction in children with UTI as this condition is a significant risk factor for re-infection and further renal damage (Fig. 2). A simple test like the IRC after a dynamic radinuclide renography (with repeated cystograms during the same appointment until the bladder is empty and/or the collecting system has drained completely) provides an initial bladder function assessment in a completely physiological fashion in addition to the evaluation of the relative renal function and drainage. If the IRC suggests bladder dysfunction, further evaluation with urodynamics may confirm the IRC findings and direct specific therapy focused on the bladder pathology.

Imaging to Detect Renal Scarring

The gold standard to detect renal scarring is the DMSA scan, performed six months after the acute episode of UTI (Fig. 3). It is not advisable to perform a DMSA scan earlier than six months because if a focal defect is demonstrated, this may be due to persisting inflammatory infiltrate and therefore can be reversible. A repeat DMSA 6-8 months later to distinguish a reversible from a permanent scar is then required, with a consequent increased radiation burden to the child. A DMSA scan cannot distinguish between antenatal renal dysplasia, postnatal and acquired renal damage.

Recent studies have shed some light on the relationship between renal scarring and long-term complications (hypertension, CRF, complications in pregnancy). Unilateral

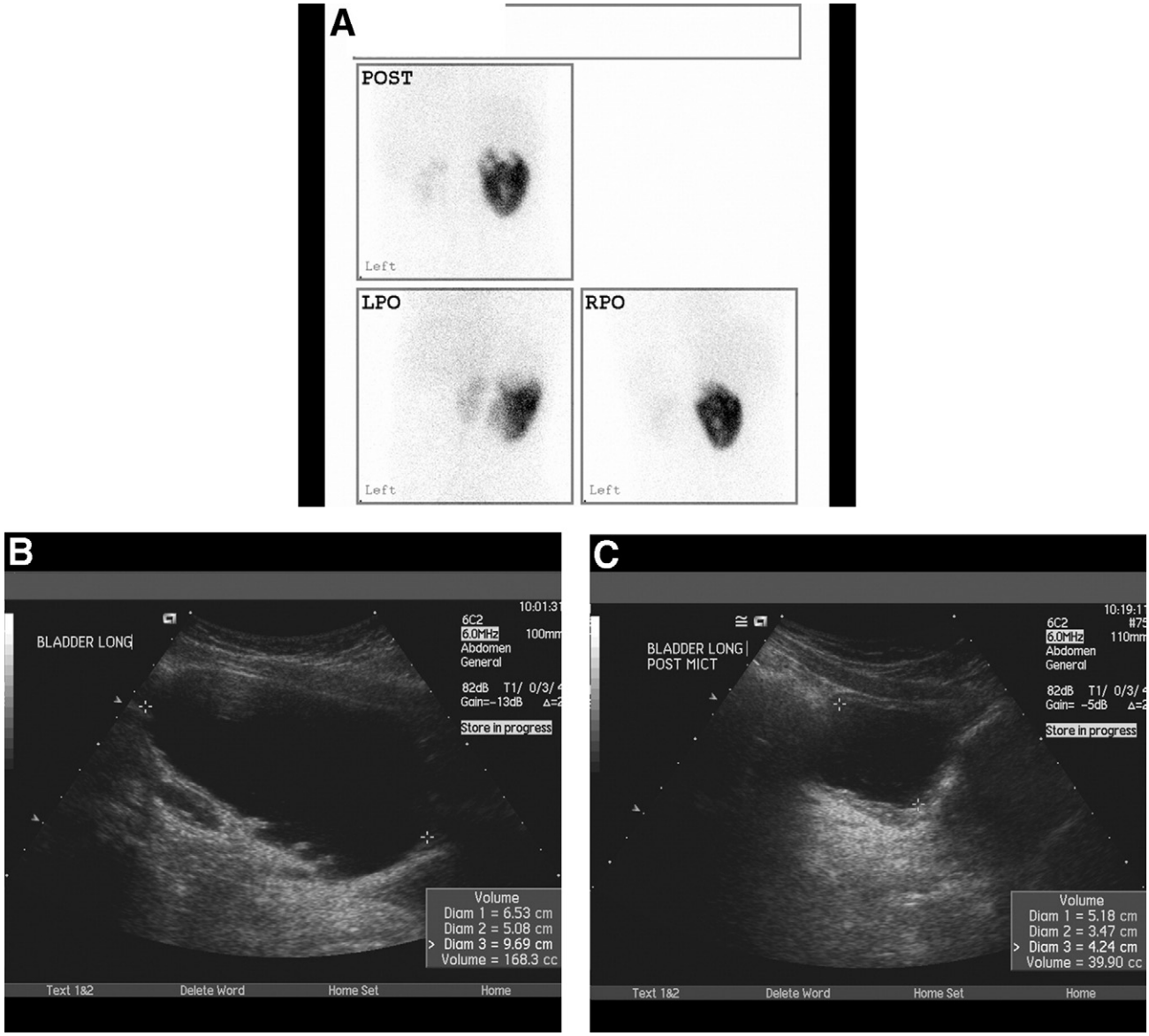

Figure 3 DMSA scan in a 12-year-old girl with spinal dysraphism, recurrent UTI, and bladder dysfunction. The ultrasound showed a thickened bladder wall with small diverticula and focal thinning at the upper pole of the left kidney. The DMSA scan shows several renal scars bilaterally with a very poorly functioning left kidney and a damaged but much better functioning right kidney. The differential function is left kidney <5%, right kidney >95%.

scarring seems to be associated with the same rate of long-term complications as the general population. Bilateral renal scarring (or scarring in a solitary kidney) has been found to be associated with higher risk of hypertension and CRF.[15] It seems that the strongest predictor in determining the risk of hypertension and CRF is the number of functioning nephrons in a kidney, once renal damage has occurred. Also, a scarred kidney is at higher risk of developing progressive renal damage after recurrent UTI and VUR.[35]

The advantage of performing a DMSA scan in all children with UTI is to see if the UTI has caused renal scarring. The disadvantage is that a very high number of children will have a normal DMSA, with consequent waste of resources and unnecessary radiation burden to the child. There is a gradual move toward a more focused use of DMSA in children who are at higher risk of damaging the kidneys after a UTI, such as children with systemic symptoms who fail to respond to first line antibiotics, children with symptoms suggestive of septicaemia, children with an unusual micro-organism in their urine and children with recurrent UTI.

The Different Imaging Strategies in Children With UTI

The existing imaging strategies in children with UTI are based on what are perceived to be the significant risk factors for renal damage and long-term complications.

The Traditional Approach: The Focus on Reflux

This strategy is focused on VUR as the main risk factor in children with UTI. Children with VUR are considered at high risk of developing renal damage and therefore they should be identified with a cystogram and commenced on prophylactic antibiotics until the VUR resolves. This approach is based on the RCP guidelines of 1991 and has been confirmed by the guidelines of the American Academy of Pediatrics. All children with an acute pyelonephritis should have a cystogram as part of their imaging work up.

We have already seen that more recent studies have shown that not all children with VUR are at risk of developing renal damage[24,31,32]; this approach selects a number of children who are not at risk of renal scarring and fails to identify other children, with no demonstrable VUR, who nevertheless do develop renal scarring.[24] Moreover, the MCUG is perceived as a traumatic and invasive test, especially in older children, with an additional associated risk of infection.

A New Approach: The Focus on Acute Renal Inflammatory Involvement

This is focused on detecting renal inflammatory involvement during the clinical episode of acute pyelonephritis and uses the acute DMSA, performed during the episode of infection, as its cornerstone. This approach has been tested in Sweden[24] but has been used in other countries as well.[20,28] The rationale for adopting this strategy is that children with a normal DMSA during the episode of acute pyelonephritis have 0% chances of developing renal scarring, even in the presence of VUR.[20] Conversely an abnormal DMSA scan during acute pyelonephritis will detect virtually all children with potentially harmful VUR.[24] Therefore, the supporters of this approach advocate the use of a cystogram only in children who have an abnormal DMSA (and/or anatomical abnormalities on ultrasound) during the episode of acute pyelonephritis, eliminating the use of the cystogram in children with clinical acute pyelonephritis but normal acute DMSA and normal anatomy at ultrasound. The advantages and disadvantages of the use of acute DMSA have already been discussed in the section on imaging localization of UTI.

A Different New Approach: Fewer Imaging Tests in the Child at Risk

From the available evidence, it seems reasonable to concentrate the use of imaging in those children at risk of renal damage and not in the larger population presenting with uncomplicated UTI. Thus, children with a first UTI with no systemic symptoms who are older than 6 months do not require imaging (children younger than 6 months should have an ultrasound to assess the urinary tract for possible anatomical abnormalities).

Imaging is reserved for children with recurrent UTI and children with systemic symptoms who do not respond to antibiotic treatment within 48 hours or who have severe symptoms or unusual micro-organisms. Children in this group who are younger than 1 year are referred for ultrasound, MCUG and late DMSA (six months after the UTI, assess for scarring). Children in this cohort older than 1 year have an ultrasound and a late DMSA (MCUG only if urinary tract dilation is demonstrated on ultrasound).

Further Research

Although in the last few years there has been significant progress in the assessment of the role of imaging in UTI, there is still immense controversy. Areas such as the role of VUR in causing renal damage, the risk of renal scarring and CRF in children with UTI, the effectiveness of antibiotic prophylaxis and/or surgical intervention in preventing recurrent UTI and renal damage still await a proper evaluation. Well-designed cohort studies with sufficient number of patients are needed to address these questions.

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