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^{99m}Tc dimercaptosuccinic acid (DMSA) scan as first investigation of urinary tract infection

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SUMMARY A total of 115 children under 5 years who presented with a first symptomatic urinary tract infection and who had a ^{99m}Tc dimercaptosuccinic acid (DMSA) scan were studied to assess its value and compare the findings with those of other imaging techniques. Renal cortical defects were detected in 65 kidneys by DMSA scan, intravenous urogram, and ultrasound scan combined; 62 (95%) being seen on DMSA scan. The finding of reflux on micturating cystourethrography showed a highly significant correlation with renal defects seen on DMSA scanning, a less close but still significant correlation with abnormalities on intravenous urography, but none with ultrasound scan findings. The sensitivity of the DMSA scan in screening for all grades of reflux is estimated as 0·66, which is higher than that previously reported for the intravenous urogram or ultrasound scan. DMSA scans were less likely to miss grade 3 reflux than the other two methods.

DMSA scans are more useful than other upper renal tract imaging techniques in detecting renal defects. Consideration should be given to their use as a first investigation in place of routine intravenous urograms. Ultrasound scans alone will overlook potentially serious urinary tract abnormalities.

Despite the acknowledged importance of investigating symptomatic urinary tract infection in children[1] there is still considerable disagreement as to which investigations should be undertaken after the first infection in different age groups of children. The aims of investigation should be to detect the presence of renal damage and the presence of those conditions that may predispose to renal damage, that is, vesicoureteric reflux, obstruction, and renal stones. Recent papers have compared the use of ultrasonography with intravenous urography[2] or have considered the ^{99m}Tc dimercaptosuccinic acid (DMSA) scan as only a second line investigation.[3] It has now been suggested, however, that DMSA scans should be used in the 1–7 year age group together with ultrasound scans.[4]

It is believed that most renal scars are established by 5 years of age.[5] From 1982 onwards we have been using the DMSA scan as a first line investigation in children presenting with their first symptomatic urinary tract infection under this age; this paper reports our initial experience of the scans alongside other imaging techniques.

Patients and methods

Over a three year period (1982–4) 115 children under the age of 5 years presented with symptomatic urinary tract infection that had been proved with a urinary culture of greater than 10^5 organisms/ml of urine in the presence of pyuria on one occasion or in the absence of pyuria on two occasions as suggested by Kass.[6] A group of paediatricians were invited to refer children for a DMSA scan as part of an investigation protocol in which the upper renal tract was investigated before considering a micturating cystourethrogram. The criteria for performing these investigations were not rigidly defined. In general micturating cystourethrography was performed if upper tract imaging was abnormal, although some paediatricians performed them in all children below 1 year of age. Intravenous urograms or ultrasound scans, or both, were performed according to the paediatricians' preference. All 115 children had DMSA scans, 92 had intravenous urograms, 57 had ultrasound scans, and 65 had micturating cystourethrograms.

The characteristics of the study population are shown in table 1 where they are divided into two groups depending on whether or not they had a micturating cystourethrogram. There was no significant difference between the two groups in terms of mean age, age grouping, or sex ratio.

Intravenous urograms were performed after a laxative the previous evening and restricted fluid for five to eight hours before the examination depending on age. They consisted of a full length control film, films of the renal area at 5 and 10 minutes after injection of 20–40 ml Hypaque or Niopam, and full length films before and after micturition. Renal scarring and renal size were recognised by the criteria of Hodson[7]; significant dilatation of the collecting system or the ureter on the post-micturition film and other features associated with reflux, such as striation of the renal pelvis, were recorded.

Ultrasound scans of the kidneys were performed in anterior and posterior sagittal and transverse planes using a 5 mHz transducer and a static B scanner (Philips) or latterly a real time scanner (Advanced Diagnostic Research) in which coronal planes were also obtained. Transverse scans of a full bladder were employed to visualise dilatation of the ureters. Renal length was measured and any focal cortical abnormality recorded. Separation of the renal sinus echoes by more than 0·5 cm was recorded as a dilated upper tract.

DMSA scans were performed two to three hours after the intravenous injection of 2 MBq/kg ^{99m}Tc DMSA (minimum dose 20 MBq; maximum dose 160 MBq) (Compagne Oris Industry). Images were acquired in the posterior and both posterior oblique projections, with the child lying supine directly on the collimator of a large field of view gamma camera (International General Electric) for 500 000 counts or five minutes per view. Analogue images were used for reporting, although enhanced digital images could highlight focal abnormalities of the cortex. Defects were reported if there was a clear interruption in the renal outline on the posterior or oblique projections. Care was taken in the interpretation of movement artefacts at the renal poles and the variation in medullary uptake was ignored. Any appreciable discrepancy in renal size was noted

Table 1 *Age, age group, and sex of children in study*

	No micturating cystourethrogram	*Micturating cystourethrogram*
No of children	50	65
Male/female	14/36	21/44
Age:		
0–11 months	22	24
12–35 months	18	24
36–59 months	10	17
Mean age (years) (95% confidence intervals)	1·68 (1·30 to 2·05)	1·70 (1·36 to 2·04)

Table 2 *No of abnormalities detected on imaging in 115 children (230 kidneys)*

DMSA scan		*Intravenous urography*		*Ultrasound scan*		*Micturating cystourethrography*	
Micturating cystourethrography performed (65 children, 130 kidneys)							
Cortical defects	55	Cortical defects	6	Cortical defects	5	Grade 1 reflux	8
Patchy uptake	5	Dilated upper tract	33	Dilated upper tract	12	Grade 2 reflux	31
Contracted kidney	6	Contracted kidney	2	Contracted kidney	2	Grade 2 reflux	21
Enlarged kidney	2	Enlarged kidney	7	Enlarged kidney	4		
		Duplex upper tract	3	Duplex upper tract	2		
		Wide ureter post-micturition	7				
Total:							
Abnormal*	66		39		17		60
Normal	64		69		45		70
Not done	0		22		68		0
Micturating cystourethrography not performed (50 children, 100 kidneys)							
Cortical defects	7	Cortical defects	1	Cortical defects	2		
Patchy uptake	1	Dilated upper tract	7	Dilated upper tract	9		
Contracted kidney	0	Contracted kidney	1	Contracted kidney	1		
Enlarged kidney	1	Enlarged kidney	3	Enlarged kidney	1		
		Duplex upper tract	3	Duplex upper tract	0		
		Wide ureter post-micturition	1				
		Stone	1				
Total:							
Abnormal*	9		12		13		
Normal	91		64		39		
Not done	0		24		48		100

*Some kidneys had more than one abnormality.

as well as relative renal uptake outside the range of 45–55% calculated by region of interest analysis after background subtraction.

Micturating cystourethrograms were performed after bladder catheterisation with a 4·5–6 FG feeding tube. Hypaque was run into the bladder slowly by gravity from a height of 100 cm. The bladder was screened intermittently during filling and the catheter removed before continuous screening during micturition. Reflux was recorded on a scale of 1 to 3 (grade 1 confined to the ureter, grade 2 reaching the renal calyces without distension, and grade 3 with distension; after Bailey[8]).

Results

Table 2 shows the abnormalities of kidneys that were detected by the four different types of investigation in the 115 children. Because micturating cystourethrograms were only performed in 65 children these results are shown separately to allow comparison of the results of upper renal tract imaging with the 50 children who did not proceed to micturating cystourethrography.

Table 3 compares the detection of cortical defects by DMSA scans and intravenous urograms in the 92 children who had both investigations. This shows that DMSA scans are significantly more sensitive at detecting defects than intravenous urograms ($p<0·05$ by McNemar's test).

Table 4 considers only those children who had micturating cystourethrograms. The results of DMSA scans, intravenous urograms, and ultrasound scans in kidneys with reflux are compared with those without reflux. There was a highly significant correlation between the presence of cortical defects on the DMSA scan and detection of reflux on the micturating cystourethrogram ($p<0·001$ by χ^2 with Yates's correction). There was a less pronounced but still significant correlation beteen reflux and parenchymal defects or upper tract dilation on the intravenous urograms ($p<0·05$) but no significant correlation with the ultrasound scan findings.

Table 5 shows the results of upper tract investigations in the 21 kidneys which showed grade 3 reflux on micturating cystourethrograms. The superior correlation between grade 3 reflux and the DMSA scan ($p<0·001$, χ^2) compared with grade 3 reflux and the intravenous urogram or ultrasound scan ($p>0·05$) is clearly seen in this group of patients.

Table 3 *Detection of renal defects in DMSA scans compared with intravenous urograms*

	With DMSA scan	*Without DMSA scan*	*Totals*
With intravenous urography	32	2	34
Without intravenous urography	23	35	58
Totals	55	37	92

$p<0·05$ by McNemar's test.

Discussion

DETECTION OF SCARRING

We believe that a DMSA scan is at present the most sensitive method to detect renal defects. The find-

Table 5 *Screening investigations in 21 kidneys with grade 3 reflux*

	Normal	*Abnormal*	*Not done*
DMSA scan	3	18	0
Intravenous urography	9	7	5
Ultrasound scan	10	6	5

Table 4 *Comparison of screening investigations with results of micturating cystourethrography. Results are number of kidneys*

	DMSA scan		*Intravenous urography*		*Ultrasound scan*	
Micturating cystourethrography						
No reflux (n=70)	Normal	44	Normal	44	Normal	25
	Abnormal	26	Abnormal	16	Abnormal	9
			ND	10	ND	36
Reflux (n=60)	Normal	20	Normal	25	Normal	20
	Abnormal	40	Abnormal	23	Abnormal	8
			ND	12	ND	32

ND=not done.

ings on DMSA scans have been shown to correlate closely with findings on intravenous urograms,[9] though we detected far more cortical defects on DMSA scanning than by intravenous urography (table 3). A recent publication by Monsour *et al* of a series of children with proved reflux has further confirmed the accuracy of DMSA scans in detecting early renal scarring in the under 5 year age group.[10] Serial observations of intravenous urograms have suggested that it can take up to two years for scars to become evident by this method.[11 12] In our series 95% (62/65) of defects that we saw by any method were seen on DMSA scans. Of the remaining three cortical defects one was detected by ultrasonography and two, as shown in table 3, by intravenous urography. These other investigations were not performed in all kidneys with normal DMSA scans and we cannot be certain how many more cortical defects might otherwise have been detected by these means. The most favourable estimate of the results of performing urograms on all our patients, however, suggests that we would have detected nine cortical defects in the 168 kidneys reported as normal on DMSA scan at the cost of missing 26 of the 62 defects that were detected by DMSA scan.

Our total figure of cortical defects in 28% of the kidneys investigated is similar to other reported series (24–35%),[9 13] although their study populations included children over 5 years. It is likely that these cortical defects indicate renal involvement in the infective process and kidneys at risk of scarring are therefore identified soon after the infection. It has yet to be shown that all these defects will go on to develop into renal scars but Merrick *et al* have shown that in a group of children with established pyelonephritis the DMSA scan was more sensitive than the intravenous urogram in the detection of scarring.[13] It has been reported that ultrasound scans are poor at detecting small cortical defects[14] and our experience supports this view.

DETECTION OF REFLUX

As it is well recognised that there is a strong association between the presence of reflux and parenchymal scarring,[15 16] we expected that there would be a strong correlation between cortical defects on DMSA scans and reflux on micturating cystourethrograms and this is indeed the case (table 4). Previous authors have proposed that the intravenous urogram or ultrasound scan should be used to screen for significant reflux.[14 17 18] We have found the DMSA scan to be a better predictor of the presence of reflux than either of these methods.

The favourable results we obtained with the DMSA scan are open to criticism on the grounds that we are using an unrepresentative sample. Although we have shown (table 1) that there was no difference in mean age, age distribution, and sex between those children who had an micturating cystourethrogram and those who did not, the criteria used in selecting those children who proceeded to micturating cystourethrography resulted in an overrepresentation of kidneys with defects in this group. To reduce this bias we have looked at those patients who had only unilateral reflux and compared the results of the screening tests in each kidney. There were 17 such patients all of whom had a DMSA scan, 15 an intravenous urogram, and eight an ultrasound scan. There was a highly significant correlation between the finding of defects on the DMSA scan and reflux on the micturating cystourethrogram (14 of 17 in refluxing kidneys compared with three of 17 in non-refluxing kidneys; $p=0{\cdot}00028$, by Fishers's exact test, two tailed). The correlation for dilatation or scarring, or both, on intravenous urogram (eight of 15 with reflux compared with three of 15 without) and ultrasound scan (five of eight compared with two of eight) did not reach significance.

We then considered the patients who had unilateral cortical defects on the DMSA scan and went on to have a micturating cystourethrogram as these patients act as their own controls. In 37 patients with unilateral defects on the DMSA scan, 22 had reflux on the affected side and 11 on the non-affected side. If it is assumed that the micturating cystourethrogram does not give false negative results and that this group of patients are representative of the whole group this gives a sensitivity of 0·66, a specificity of 0·63, an accuracy of 0·65, and a significant correlation ($p<0{\cdot}025$, χ^2). Reported series quote intravenous urograms and ultrasound scan findings in both refluxing and non-refluxing kidneys that show a sensitivity of 0·54 and a specificity of 0·86 for the intravenous urogram in the largest series,[15] and other series show sensitivities of less than 0·5.[17 18] These last two series, however, show a sensitivity approaching 1·0 for the detection of grade three reflux; this is not borne out by our findings (table 5) or in other series.[19–21] In only seven of 16 kidneys with grade 3 reflux were there clues on intravenous urography that reflux might be present.

Our figures suggest that the DMSA scan is more sensitive than either intravenous urogram or ultrasound scan at predicting the presence of reflux. Although the intravenous urogram may be more selective, its lower sensitivity makes it less suitable as a screening test. It has been suggested that ultrasonography is not able to exclude the presence of appreciable reflux and this is confirmed by our experience in this series.[14 22] With newer equipment and greater experience the sensitivity of ultraso-

nography may be improved in the future. It remains true that the only way of ensuring that reflux is never missed is to perform a micturating cystourethrogram on every child and this approach has been recommended,[20] but we wonder whether this remains appropriate in view of the recent evidence that scarring rather than reflux *per se* is a more important factor in determining long term renal outlook.[23 24]

Only two children out of 14 under 1 year of age with reflux had no evidence of renal cortical defects on the DMSA scan. This confirms that young infants are particularly vulnerable to renal involvement if reflux and infection are present and we would recommend micturating cystourethrogram on all children under 1 year with a confirmed urinary tract infection.

Twenty six kidneys in 23 children showed cortical defects in the absence of reflux and these deserve further consideration as reflux should be present in over 90% of scarred kidney units.[18] We found reflux in only 57% of kidneys with defects seen on the DMSA scan. These scans were performed soon after the presentation of urinary tract infection and it has been reported that acute pyelonephritis can cause temporary abnormalities on DMSA scan for up to three months.[9] Follow up scans in 18 of these 26 kidneys, however, have now been performed at least six months after the original scan and in only six kidneys have the defects disappeared. We believe therefore that previous estimates of the occurrence of scarring in non-refluxing kidneys are an underestimate as they have relied on intravenous urography alone for the detection of scarring. Even if early scans identify one in three children whose defects are only temporary this would not weaken the argument for the DMSA scan as a screening test to detect those children who require a micturating cystourethrogram. The percentage of children who would have had a negative micturating cystourethrogram was only 43% which compares with 63% in a series using no preselection.[20] Those 12 kidneys with persistent defects suggest that scarring does occur in the absence of reflux more often than previously reported and these cases were only detected by a DMSA scan performed soon after the presenting infection.[25]

DETECTION OF OBSTRUCTION AND RENAL STONES

Ten cases of unilateral dilatation of the urinary tract were detected by intravenous urography. The DMSA scan was abnormal in all 10 cases, showing cortical defects in five, enlarged kidneys in three, and appreciably reduced split function in two. Seven of these cases also had an ultrasound scan of which five showed pronounced dilatation, one showed cortical scarring, and one was reported to be normal.

One patient in our series had a renal stone detected on the control film of the intravenous urogram. In this case the DMSA scan showed a cortical defect, although we would not expect the DMSA scan to be a reliable method of detecting stones.

CONCLUSIONS

We believe that given the available equipment and expertise DMSA scans are a most useful first investigation of urinary tract infection. In view of the non-invasive nature of ultrasonography and the increasing experience in its use we would recommend its retention also as a first line investigation as it is a reliable method of detecting structural abnormalities of the urinary tract. In our view, however, the use of ultrasound alone in the under 5 age group will overlook potentially serious urinary tract abnormality. We would suggest that those children who have abnormal DMSA scans proceed to micturating cystourethrography as two thirds of them will have reflux. If this approach is adopted the role of the intravenous urogram as a primary modality of investigation becomes questionable. Undoubtedly the occasional child with reflux will be missed but this would be true whatever combination of screening tests was used. Further prospective studies are needed to establish whether reflux in the absence of scarring is ever of any long term importance but we are reluctant to subject all children with urinary tract infection to micturating cystourethrography in our present state of knowledge. As well as being an unpleasant procedure it exposes the gonads to about 10 times the irradiation of a DMSA scan.[26] The unique ability of the DMSA scan in detecting the presence of kidney defects makes it a valuable research tool in defining those children who sustain renal damage with urinary tract infection and thus helps clarify the factors that put them at risk; newly developed methods for image presentation may further enhance sensitivity.[27] More widespread use of this technique should lead to a better understanding of the natural history of renal scars and allow earlier detection of children at risk of progressive renal damage.

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