

# Diagnostic significance of $^{99m}\text{Tc}$ -dimercaptosuccinic acid (DMSA) scintigraphy in urinary tract infection

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## Abstract

A total of 106 children with symptomatic urinary tract infection (73 girls and 33 boys, 0-15.9 years of age) were studied by means of a dimercaptosuccinic acid (DMSA) scan, renal ultrasound, and a desmopressin test during infection and at follow up approximately two months later. At follow up they were also investigated by means of intravenous urography (IVU) and micturition cystourethrography (MCU).

During infection 23 children had a normal DMSA scan while 83 children had an abnormal one. The median C reactive protein and SD score for renal concentration capacity in the former group were 15 (range <10-178) mg/l and -1.0 SD score (range -2.4 to 1.8), respectively, and in the latter group 98 (range <10-320) mg/l and -3.1 SD score (range -5.7 to 1.1), respectively. In the former group there was no significant finding in any child on ultrasound or IVU and only one had significant vesicoureteric reflux (VUR) (grade 3).

At follow up 51 children had a normal DMSA scan while 55 children showed persistent changes. The median SD score for renal concentration capacity in the former group was -0.9 SD score (range -3.2 to 1.4) and in the latter group -1.6 SD score (range -4.6 to 2.5). No significant changes were found in the former group on ultrasound or IVU and only two children had significant VUR (grade 3). In the latter group 20 children showed changes on ultrasound, 15 showed changes on IVU, and 23 had VUR.

These results suggest that a normal DMSA scan during or approximately two months after urinary tract infection in children indicates a low risk of finding significant pathology of the urinary tract.

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The cumulative risk of contracting a symptomatic urinary tract infection during childhood is 3% for girls and 1% for boys.<sup>1</sup> If not treated and controlled properly a urinary tract infection may have serious long term consequences.<sup>2</sup> The protocol for the investigation and follow up of children with urinary tract infection has recently been the subject of debate.<sup>3,4</sup> Most authors, however, recommend some combination of renal ultrasound, intravenous urography (IVU), a dimercaptosuccinic acid (DMSA) scan, and micturition cystourethrography (MCU).<sup>5-7</sup> Children with urinary tract infection therefore require great resources in the health care system. At times when economic resources are

limited, ways to simplify and rationalise the investigations and follow up of these children without sacrificing safety would be of value. Moreover, diagnosis of urinary tract infection in small children is not always easy with the available indirect parameters. A more direct approach to the diagnosis in these cases could be helpful in identifying children at risk. It has been shown previously that a DMSA scan is a sensitive method to diagnose and localise acute pyelonephritis in children<sup>8</sup> and to detect renal scars.<sup>9,10</sup> This raises the question of to what extent the DMSA scan can replace other radiological methods as a routine investigation in children with urinary tract infection. The significance of a normal or an abnormal DMSA scan during or shortly after infection is not well documented, however. The purpose of this study was to find out if a DMSA scan was more sensitive to distinguish between upper and lower urinary tract infection than other commonly used parameters and to evaluate the predictive value of a normal DMSA scan in children with urinary tract infection.

## Patients and methods

A total of 106 children admitted to the hospital with symptomatic urinary tract infection (33 boys and 73 girls, 0-15.9 (median 0.7) years of age) were included in the study after obtaining informed consent from the parents. The age and sex distribution of the children is shown in fig 1. The primary symptoms were fever, failure to thrive, or feeding difficulties. The children were investigated according to the following protocol. On admission a blood sample was taken for the determination of C reactive protein. Ultrasound, a DMSA scan, and a desmopressin test were performed within five

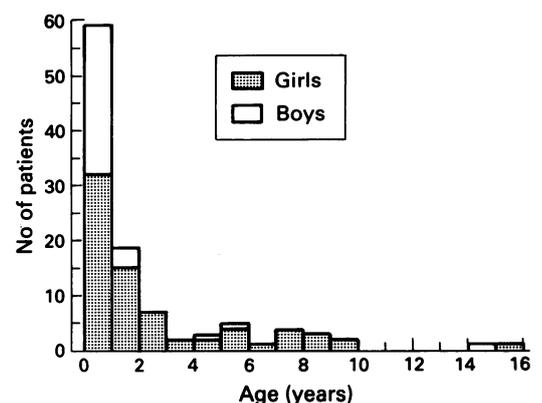


Figure 1 Children grouped by age and sex.

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days after admission. After 6–20 (median 8) weeks these investigations were repeated and IVU and MCU were also performed. All children were treated with antibiotics for at least 10 days and after this prophylactic low dose antibiotic treatment was administered until the follow up investigation. No child had a breakthrough infection during the interval between the first and second investigations.

#### DMSA SCAN

The children were examined supine and immobilised in a vacuum pillow.  $^{99m}\text{Tc}$ -DMSA was given in a dose of 0.5 MBq/kg body weight (minimum 10 MBq). At least three hours after injection one anterior and one posterior picture with a 10 minute acquisition time ( $n=24$ ) or a 500 000 count posterior picture ( $n=82$ ) was taken. All DMSA scans were evaluated visually and each kidney was subjectively judged to be normal or abnormal.

#### ULTRASOUND

Ultrasound was performed with 3.5 or 5 MHz sector scanners. Changes on ultrasound were considered present if changes in parenchymal echogenicity and/or dilatation of the pelvis were observed.

#### IVU

IVU was performed according to standard procedures and changes were considered present if renal scarring, hydronephrosis, ureteric dilatation, or malformations were observed. Renal scarring was defined as a combination of parenchymal reduction and deformities of calices.<sup>11</sup>

#### MCU

The presence of reflux was noted at MCU and graded on a scale from 0 to 5 in accordance with the International Reflux Study.<sup>12</sup>

#### DESMOPRESSIN TEST

Desmopressin (Minirin, Ferring) was administered intranasally, 10  $\mu\text{g}$  for infants and 20  $\mu\text{g}$  for children over 1 year of age. One hour later three consecutive urine samples were collected and the highest urine osmolality was taken as a measure of the maximum urinary concentration ability. A SD score was calculated according to Mårild *et al.*<sup>13</sup>

#### STATISTICS

Mann-Whitney's non-parametric test was used for statistical analyses, a  $p$  value  $<0.05$  being considered significant.

This study was approved by the local ethics committee.

#### Results

During infection 23 children (13 boys and 10 girls, 0–3.6 (median 0.2) years of age) had a

normal DMSA scan. Eighty three children (20 boys and 63 girls, 0.1–15.9 (median 1.0) years of age) had an abnormal DMSA scan (130 kidneys). The age distribution of children below 1 year of age in relation to findings on DMSA scan during infection is shown in fig 2. At follow up no child in the normal group showed changes in the DMSA scan and 28 children originally with an abnormal DMSA scan had become normal. Thus at follow up 51 children had a normal DMSA scan and 55 children had persistent changes in 68 kidneys.

#### LABORATORY PARAMETERS

The C reactive protein concentration during infection in the two groups is shown in fig. 3. The median C reactive protein in the patients with normal DMSA scan was 15 mg/l, significantly lower than in those with abnormal scans where the median was 98 mg/l ( $p<0.001$ ). In the normal group, 10 out of 23 children had a C reactive protein concentration  $>20$  mg/l, which might indicate that they had acute pyelonephritis. In seven of these children, all with C reactive protein  $>32$  mg/l, there was, however, an ongoing upper respiratory tract infection that might have been responsible for the raised C reactive protein. In the abnormal group, six children had a C reactive protein concentration  $<20$  mg/l, indicating a lower urinary tract infection. Therefore, the C reactive protein did

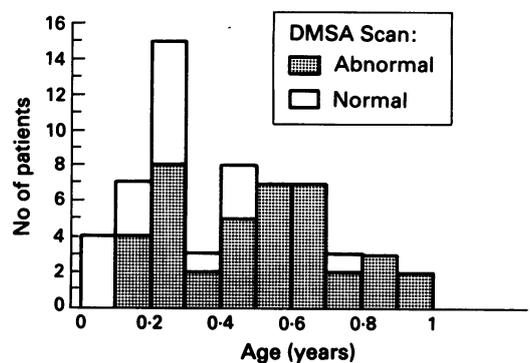


Figure 2 Distribution of findings on DMSA scan in children below 1 year of age.

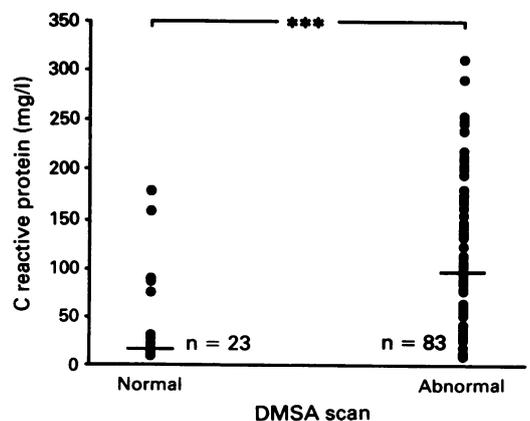


Figure 3 C reactive protein concentration in children with a symptomatic urinary tract infection and a normal or abnormal DMSA scan. The lines indicate the median values. \*\*\*= $p<0.001$ .

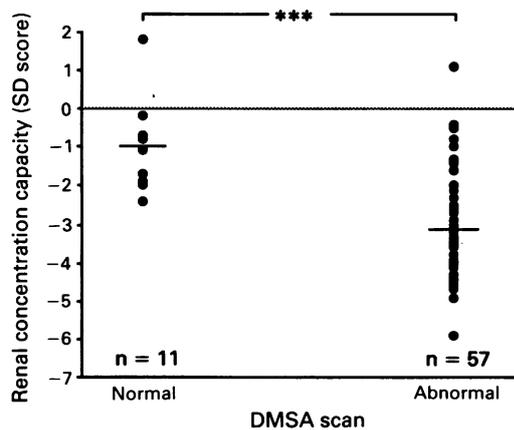


Figure 4 The SD score for renal concentration capacity according to Mårild et al<sup>13</sup> in children with a symptomatic urinary tract infection and a normal or an abnormal DMSA scan. The lines indicate the median values. \*\*\* =  $p < 0.001$ .

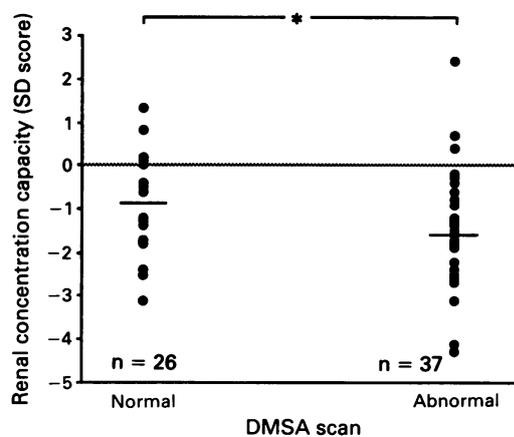


Figure 5 The SD score for renal concentration capacity according to Mårild et al<sup>13</sup> approximately two months after a symptomatic urinary tract infection in children with a normal or an abnormal DMSA scan performed at the same time. The lines indicate the median values. \* =  $p < 0.05$ .

Table 1 Children investigated with a DMSA scan during infection who showed changes in ultrasound during infection and IVU and MCU at follow up. Figures are number of children (kidneys)

DMSA scan	During infection		Abnormal at follow up	
	Normal	Abnormal on ultrasound	IVU	MCU
Normal	23	5 (6)	2 (3)	3 (6)
Abnormal	83 (130)	20 (22)	15 (20)	23 (34)

Table 2 Changes found on ultrasound, IVU, and MCU in children with a urinary tract infection and investigated with a DMSA scan during infection and at follow up after approximately two months. Figures are number of children (kidneys)

	During infection		At follow up	
	Normal	Abnormal	Normal	Abnormal
Findings on ultrasound:				
Changes in echogenicity		10 (11)		1 (1)
Hydronephrosis		2 (2)		1 (1)
Slight dilatation	5 (6)	8 (9)	3 (4)	2 (2)
Findings on IVU:				
Renal scarring		5 (8)		5 (8)
Hydronephrosis		2 (2)	1 (1)	1 (1)
Double ureters		6 (8)	1 (1)	5 (7)
Slight dilatation	2 (3)	2 (2)	2 (3)	2 (2)
Findings on MCU:				
VUR grade $\geq 3$	1 (2)	14 (19)	2 (3)	13 (18)
VUR grade $< 3$	2 (4)	9 (15)	3 (5)	8 (14)

not agree with findings on the DMSA scan in 16 children (15%).

During infection the SD score for renal concentration capacity was available for 68 children and is shown in both groups in fig 4. The median SD score for the abnormal group was significantly lower than in the normal one ( $p < 0.001$ ), but there was overlapping between the two groups. In the normal group, one child had an SD score  $< -2$  SD score, while in the abnormal group, 10 children had a normal SD score ( $> -2$  SDS). Thus in 16% of the children there was a disagreement between findings in the DMSA scan and the desmopressin test. At follow up, the SD score for renal concentration capacity was available for 63 children. It was significantly lower in the children with DMSA changes than in those without ( $p < 0.05$ ), but there was a large overlap between the two groups.

RADIOLOGICAL FINDINGS

DMSA scan during infection

The number of children investigated with a DMSA scan during infection and with abnormal findings on ultrasound at the same time is shown in table 1. The findings are specified in table 2. Five children with a normal DMSA scan showed changes on ultrasound, but these changes were only a slight dilatation of the renal pelvis without clinical significance (table 2). Altogether 24% of children (17% of kidneys) with changes in the DMSA scan during infection showed abnormal changes on ultrasound (table 1). In the normal group no child was found to have significant changes at IVU (tables 1 and 2). All children with renal scarring on IVU showed severe changes in the DMSA scan (table 2). Among the children with a normal DMSA scan during infection, only one child was found to have a significant vesicoureteric reflux (VUR) (bilateral grade 3). This was a 5 month old boy who had a prominent renal pelvis on ultrasound during infection.

DMSA scan at follow up

The number of children in each group with findings on ultrasound, IVU, and MCU is shown in table 3 and the findings are specified in table 2. In the normal group no child had significant changes on ultrasound or IVU. The one child with hydronephrosis on IVU and a normal DMSA scan at follow up did not have a significant obstruction and required no intervention. All kidneys with established scars at IVU showed changes in the DMSA scan. The overall frequency of VUR was 25%. Five children with a normal DMSA scan at follow up

Table 3 Children investigated with a DMSA scan at follow up who showed changes in ultrasound, IVU, and MCU at follow up. Figures are number of children (kidneys)

DMSA scan at follow up	Abnormal at follow up		
	Ultrasound	IVU	MCU
Normal			
51	3 (4)	4 (5)	5 (8)
Abnormal			
55 (68)	4 (4)	13 (18)	21 (32)

had VUR, but it was significant in only two children (grade 3 reflux in three kidneys).

### Discussion

It is important to bear in mind that all children in the present study were hospitalised and investigated because of a symptomatic urinary tract infection. The primary symptoms were therefore those commonly associated with an upper urinary tract infection: fever, feeding difficulties, and failure to thrive. The median age of the children with a normal DMSA scan during infection was very low (fig 2). The normal DMSA scan in this group could therefore have two explanations. Either the DMSA scan may not be a sufficiently sensitive method to diagnose acute pyelonephritis in infants or these infants had in fact a lower urinary tract infection. However, seven of the 10 children in this group with clinical and laboratory parameters suggesting the presence of acute pyelonephritis had an ongoing upper respiratory tract infection. We believe that these children actually had a primary upper respiratory tract infection with concomitant bacteriuria.  $^{99m}\text{Tc}$ -DMSA is taken up by the proximal tubular cells by an active process.<sup>14 15</sup> The normal DMSA scans seen in the smallest infants suggest that this process already is mature in these infants, although this may vary between individual infants. In our experience, however, the quality of the DMSA scan in infants under 2–3 months of age is not always satisfactory and it would seem wise not to rely on this method to diagnose acute pyelonephritis in these young infants.

The renal concentration capacity is often used to differentiate an upper urinary tract infection from a lower one.<sup>16</sup> In the present study the renal concentration capacity was significantly lower in the children with changes in the DMSA scan both during infection and at follow up. However, there was a marked overlapping between the two groups at all times, making it difficult to predict changes in the DMSA scan from the desmopressin test. Moreover, for children under 6 months of age, normal values for the concentration capacity are not available.<sup>17</sup> Therefore, although the desmopressin test shows a difference between the two populations with a normal and an abnormal DMSA scan, it is not a reliable test to differentiate an upper urinary tract infection from a lower one in individual cases. A non-invasive direct method for diagnosing an upper urinary tract infection in children is needed. The use of ultrasonography in this respect has not turned out to be as successful as was initially hoped, as shown by the present study and others.<sup>8 18</sup> In the majority of cases the differentiation between lower and upper urinary tract infection can be made on a clinical basis, however. We therefore believe that in children over 3 months of age in whom acute pyelonephritis is suspected but clinical and laboratory parameters are ambiguous, a DMSA scan should be performed in order to verify the diagnosis. This procedure could help to identify the children who are at risk and spare many children unnecessary investigations and follow ups.

Abnormal findings in other radiological investigations were scanty in children with a normal DMSA scan. The most common finding on ultrasound or IVU in these children was a slight dilatation of the renal pelvis or ureter that was considered to be of no significance. In these cases the presence of VUR was suggested and this was the case in five out of six kidneys. The presence of double ureters was easily detected by IVU but was not detected by the DMSA scan. Although this finding is usually considered to be of no significance, it is interesting to note that all these kidneys showed defects in the DMSA scan during infection and all but one at follow up. This suggests that these kidneys are at risk in children with a urinary tract infection and is in agreement with a previous report.<sup>19</sup>

The overall frequency of VUR in the present study was 25%, which is similar to that reported by others.<sup>5 20 21</sup> During infection VUR was associated with DMSA changes in all but three children and in only one child was the reflux significant (grade 3). This child showed a slight dilatation of the renal pelvis on ultrasound. At follow up the DMSA scan had become normal in an additional two children with VUR, one of whom had a significant reflux (grade 3). The children with significant reflux were boys aged 3 and 5 months. MCU is the definitive method of demonstrating VUR, although radio-nuclides are being used more frequently.<sup>22</sup> MCU is a rather unphysiological investigation and is often a cause of great distress in children and parents. Most authors agree that an MCU should be carried out in all children with urinary tract infection under the age of 1 year as these children are at high risk of developing renal damage.<sup>23 24</sup> Whether this investigation should be performed routinely in older children with a urinary tract infection is a matter of debate.<sup>3 4 25</sup> In the present study, a normal DMSA scan indicated a low risk of finding a significant pathology of the urinary tract. It would therefore seem safe not to perform MCU as a routine investigation in children with a urinary tract infection over 1 year of age, provided that they have a normal DMSA scan either during or approximately two months after infection and a normal ultrasound during infection.

In conclusion, our present results indicate that a DMSA scan is a sensitive method to distinguish between upper and lower urinary tract infection in children and we suggest that it should be used to verify the diagnosis in children in whom there is a suspicion of acute pyelonephritis but the clinical and laboratory parameters are ambiguous. Moreover, the results indicate that an MCU may be safely omitted as a routine investigation in children over 1 year of age with a urinary tract infection who have a normal DMSA scan during infection or at follow up approximately two months after infection and a normal ultrasound during infection.

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