

# Renal Cortical Scintigraphy and Diuresis Renography in Infants and Children\*

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Renal scintigraphy is performed frequently in infants and children. Renal cortical scintigraphy using  $^{99m}\text{Tc}$  dimercaptosuccinic acid is predominantly performed to assess the renal sequelae of urinary tract infection. It is most commonly performed for the evaluation of chronic renal scars, although it is also undertaken in the assessment of acute pyelonephritis. Diuresis renography using  $^{99m}\text{Tc}$  mercaptoacetyltriglycine is of great use in the evaluation of renal tract obstruction, which may occur at a variety of levels, but most commonly occurs at the ureteropelvic junction. Consensus statements have been formulated in an attempt to standardize methods of performing these investigations. However, several areas of controversy exist in the performance of these studies, and these are outlined. Radionuclide cystography and renal function estimation using clearance calculations are not covered in this article.

**Key Words:** renal cortical scintigraphy; diuresis; renography  
**J Nucl Med 2001; 42:91-95**

**A** marked increase in the early detection of renal tract pathology in infants has accompanied the widespread use of ultrasound evaluation of the fetus during pregnancy. This has resulted in the investigation of many children with an antenatal diagnosis of hydronephrosis or other ultrasound abnormalities. The urinary tract pathologies diagnosed most frequently are vesicoureteric reflux and obstruction, which can occur at different levels in the urinary tract.

Vesicoureteric reflux, which is the abnormal flow of urine from the urinary bladder back toward the pelvicalyceal system, can have important sequelae, particularly in the presence of urinary tract infection. In the acute condition, this can result in pyelonephritis. Long-term risks include renal cortical scarring and reflux nephropathy. In severe cases, renal impairment may occur, even resulting in end-stage renal failure. Systemic hypertension also may develop. The renal complications of vesicoureteric reflux are

most accurately evaluated with renal cortical scintigraphy using  $^{99m}\text{Tc}$  dimercaptosuccinic acid (DMSA).

It is important to diagnose urinary tract obstruction, especially if the obstruction is of high grade, because it may ultimately result in the loss of function of the obstructed kidney. Diuresis renography using  $^{99m}\text{Tc}$  mercaptoacetyltriglycine (MAG3) is an established diagnostic tool in determining whether obstruction is present and assessing the severity of the obstruction. Radionuclide cystography and renal function estimation using clearance calculations are not covered in this article.

## RENAL CORTICAL SCINTIGRAPHY

### Clinical Indications

The clinical indications for undertaking renal cortical scintigraphy are varied. It is the investigation of choice in establishing the diagnosis of acute pyelonephritis (1,2). This condition cannot be diagnosed reliably on clinical grounds alone, particularly in children. The younger the child is, the more nonspecific the signs are. Neonates and infants frequently present with nonspecific clinical findings, such as failure to thrive. A child's complaint frequently is stomach pains. Although lower urinary tract infection usually resolves without significant sequelae, incorrectly diagnosed, delayed, or inappropriately treated upper tract infection can lead to renal scarring. Acute pyelonephritis may be unifocal, multifocal, or diffuse (1). There is histologic confirmation in the pig model of DMSA abnormalities in acute pyelonephritis (3-7).

DMSA is the most reliable technique in the diagnosis of chronic renal cortical scarring, compared with other imaging modalities, such as ultrasound examination and intravenous urography (8-11). Renal cortical scarring is the sequela of upper urinary tract infection. Vesicoureteric reflux may be a predisposing factor, although upper tract involvement with infection can occur even in the absence of demonstrable reflux. The detection of scarring is important because of the risk of the subsequent development of systemic hypertension and possible renal impairment. The DMSA findings in renal cortical scarring have been confirmed histologically in the pig model (12).

DMSA scintigraphy has also been used in the diagnosis of renal infarcts, horseshoe kidney, multicystic dysplastic

Received Mar. 20, 2000; revision accepted Aug. 22, 2000.

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kidney, and ectopic kidney (13). Segmental renal artery stenosis also may be diagnosed, especially when captopril is administered 1 h before the radiopharmaceutical.

### Technique

A consensus report on renal cortical scintigraphy in children with urinary tract infection was published by the Scientific Committee of Radionuclides in Nephrourology after a survey of 30 international experts (14). The radiopharmaceutical of choice is  $^{99m}\text{Tc}$  DMSA. Other, less-favored, radiopharmaceuticals are  $^{99m}\text{Tc}$  glucoheptonate (GH) and  $^{99m}\text{Tc}$  MAG3.  $^{99m}\text{Tc}$  dimethyltriamine pentaacetic acid (DTPA) is not recommended for cortical imaging. The recommended minimum dose of  $^{99m}\text{Tc}$  DMSA is 15–20 MBq (0.4–0.5 mCi), with a maximum adult dose of 110 MBq (3 mCi). Scintigraphy is performed 2–3 h after tracer injection and should include at least a posterior view, acquired for a minimum of 200,000 counts or 5 min using a high-resolution parallel-hole collimator, and both posterior oblique views. Many experts advocate the addition of pinhole images, using a 3–4-mm aperture insert (7,12,15). Pinhole views are acquired for 100,000–150,000 counts or for 10 min. Some workers add SPECT. SPECT may provide useful information but can increase the number of false-positive results and is more technically demanding during both acquisition and analysis (7,16,17). Motion artifacts constitute a problem related to the long acquisition time. Pinhole imaging is more easily repeated than is a SPECT study. Several workers recommend the addition of either pinhole or SPECT imaging to the planar studies to increase the level of certainty with which renal cortical scintigraphy is interpreted (12,15).

### Differential Function

Determination of left-to-right renal DMSA uptake should be performed on the posterior planar view using the parallel-hole collimator. Depth correction may be applied, either by using the lateral view to obtain the kidney depth or by determining the geometric mean using both the anterior and posterior views. Background correction may also be applied by using an area around the kidneys, although the signal-to-noise ratio is particularly favorable, making the need for background correction questionable (14). There is also no consensus on the need for depth correction. It is agreed that the lowest normal value of relative uptake is 45% (14).

### Patient Preparation

No special preparation is required. The question of drug sedation of young children during study acquisition is an issue that needs to be addressed by the nuclear medicine facility performing the examination. Details of pediatric sedation have been published by the Society of Nuclear Medicine (SNM), based on guidelines from the American Academy of Pediatrics (18,19).

Most centers perform the posterior parallel-hole collimated view with the patient in the supine position (i.e., the patient is placed above the gamma camera). Pinhole views

may be performed with the patient in either the supine or prone position.

### Image Interpretation

A DMSA study is considered abnormal if there is reduced relative function of a kidney (i.e., more than 10% difference between the two kidneys) and/or decreased or absent uptake of tracer in the renal cortex, causing distortion or indentation of the normal renal outline (20).

The Scientific Committee of Radionuclides in Nephrourology found a consensus on a variety of normal images that can be obtained on a DMSA study (14):

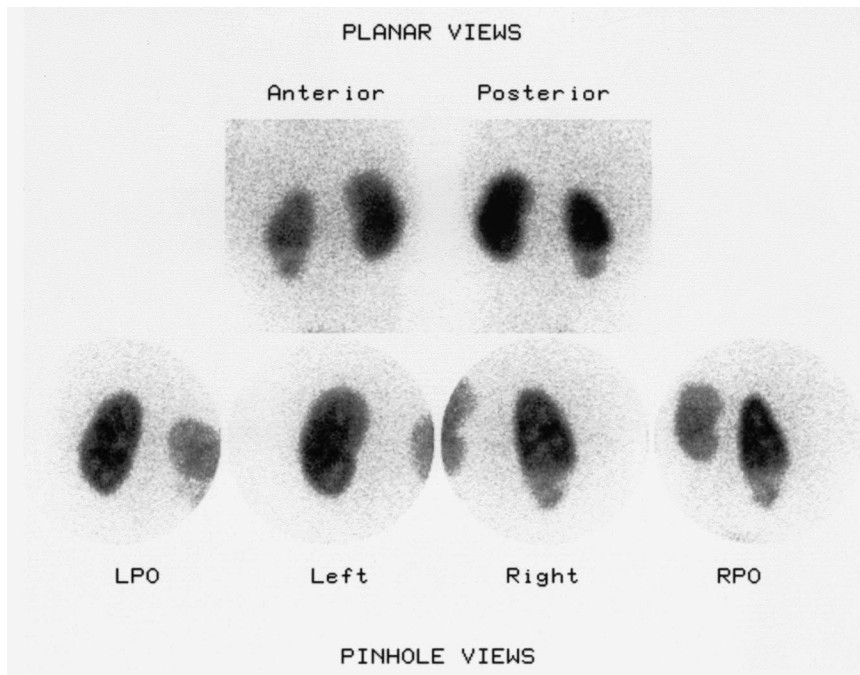
1. Kidney contours are generally round, and there is contrast between the active outer part and the less active inner part.
2. A contour can be flat without suggesting a lesion.
3. The lateral aspect of the superior half of the left kidney can be flattened and may even be concave.
4. In infants, a normal kidney may appear as a triangular shape with flattened external sides.
5. A slender kidney, characterized by a short transverse axis in the posterior view, is generally normal and corresponds to a rotated kidney.
6. The transverse axis may be shorter at either the upper or lower pole, giving a “pear-shaped” appearance.
7. A pole, especially the upper pole, can appear to be pathologically hypoactive, simply because of the contrast with the hyperactive columns of Bertin underlying the pole.
8. The number and size of the columns of Bertin may differ among patients.

Fetal lobulation classically occurs at the junction of a column of Bertin with the renal cortical rim. Hydronephrosis may cause a problem with image interpretation because of tracer retention in the collecting system. Delayed imaging at 6 or 24 h may help (14).

### Acute Pyelonephritis and Renal Cortical Scarring

Acute pyelonephritis may cause residual scan abnormalities for at least 3 mo after infection. In the detection of renal cortical scars, some workers advocate performing the DMSA study after 3 mo (21), and others have shown that 6 mo is the minimal time before a lesion can be considered permanent, although improvement can be noted up to 12 mo (2,22,23).

On the basis of the first scintigraphy performed at the time of an acute infection, it is possible to predict the late scintigraphic outcome in only a limited number of cases (14). Improvement is likely to occur when the DMSA study demonstrates a large hypoactive upper or lower pole, without deformity of the outlines, with indistinct margins, and with no volume loss. No improvement is likely to occur when there is a single defect resulting in localized deformity of the outline, indicating that there has been volume loss (Fig. 1).



**FIGURE 1.**  $^{99m}\text{Tc}$  dimercaptosuccinic acid study renal cortical scintigraphy performed on 5-mo-old boy with antenatal diagnosis of right hydronephrosis. Investigations performed postnatally revealed presence of right duplex kidney on ultrasound examination and high-grade vesicoureteric reflux into lower pole moiety of right duplex kidney on contrast cystogram. Boy had no history of urinary tract infection but had strong family history of vesicoureteric reflux. DMSA study demonstrates presence of extensive scarring in lower pole moiety of right duplex kidney.

Renal cortical scintigraphy is more frequently undertaken to assess the chronic sequelae of urinary tract infection. Its clinical utility during the acute infection is debated. Well-controlled prospective studies are needed to estimate whether early scintigraphy may influence the type and duration of the treatment when acute pyelonephritis is suspected or may modify later strategy (such as the indication for a micturating cystourethrogram or for delayed renal cortical scintigraphy).

#### DIURESIS RENOGRAPHY

The methodology for performing diuresis renography in the evaluation of neonatal hydronephrosis is a very controversial area in pediatric nuclear medicine. The problem is that there is no gold standard to apply when evaluating diuresis renography in the diagnosis of functionally significant obstruction in infants and children. Furthermore, the cause of obstruction at the ureteropelvic junction (UPJ) in infants is not only the result of classic fibromuscular hyperplasia, as is seen in adults. Infants may have tortuous ureters with a corkscrew appearance, and kinking may occur in the proximal ureter at the site of tortuosity, resulting in obstruction (24,25). It is also recognized that, especially in infants and children, obstruction may resolve spontaneously or develop over time. The postulated reason for this is the phenomenon of transitional hydronephrosis (26–29).

The Society of Fetal Urology and the Pediatric Nuclear Medicine Council–SNM developed the concept of the “well-tempered” diuretic renogram, which was a standard method to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis (30,31). Its aim was to enable standardized optimal data collection and analysis so

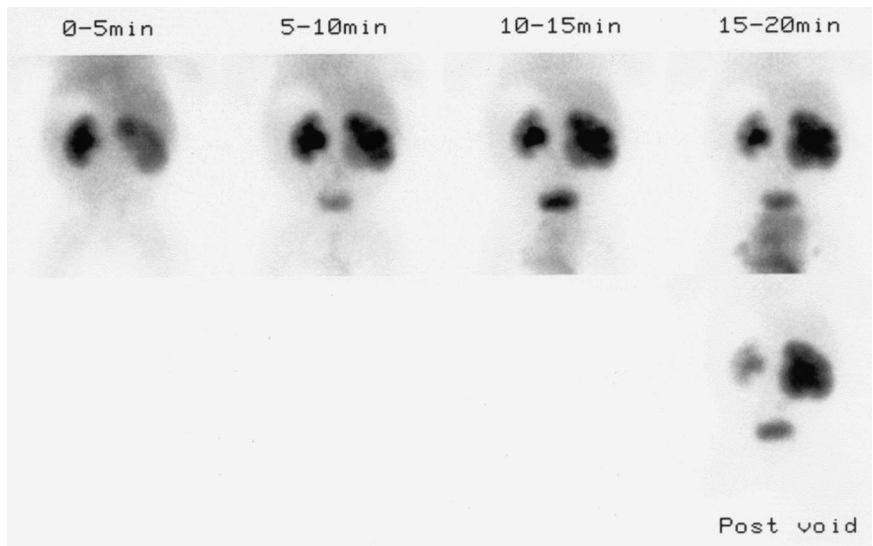
that the results of diuretic renography could be compared between institutions and so that a double-blinded multicenter prospective study could be undertaken. The main points of the “well-tempered” renogram follow.

#### Patient Preparation

The patient should be at least 1 mo of age. Serum creatinine should be measured to exclude azotemia. Oral hydration should be offered ad libitum, as formula or water, beginning 2 h before the study and throughout the study. Intravenous fluid should be given as dilute saline solution (D5.3NS or D5.25NS) at a rate to deliver 15 mL/kg over a 30-min interval, beginning 15 min before injection of the radiopharmaceutical. The infusion is continued for the remainder of the study at a maintenance fluid volume at a rate of 200 cc/kg/24 h. The patient’s bladder should be catheterized to ensure adequate drainage throughout the study. Bladder urine drainage should be measured at 10-min intervals to determine the diuretic response.

#### Technique

$^{99m}\text{Tc}$  MAG3 is the recommended radiopharmaceutical, at a dose of 1.85 MBq/kg (50  $\mu\text{Ci}/\text{kg}$ ) and a minimum dosage of 37 MBq (1 mCi).  $^{99m}\text{Tc}$  MAG3 has a higher extraction by the kidneys than  $^{99m}\text{Tc}$  DTPA, which is another less preferred agent used in diuresis renography. Renal uptake by  $^{99m}\text{Tc}$  MAG3 is 55% compared with 20% uptake by  $^{99m}\text{Tc}$  DTPA. This higher extraction results in better images for qualitative and quantitative analysis, and this is of particular benefit in the neonatal period, when renal function is immature. The patient should be supine. Both digital data acquisition, at 20 s/frame, and analog images should be collected. Digital data should be collected in a



**FIGURE 2.** Diuresis renography with  $^{99m}\text{Tc}$  mercaptoacetyltriglycine (MAG3) performed on 2-mo-old girl who had antenatal diagnosis of right hydronephrosis. Postnatal serial ultrasound examinations revealed increasing dilatation of right pelvicalyceal system. No reflux was demonstrated on cystogram. MAG3 study was F+0 examination, with furosemide given at same time as radiopharmaceutical. Diuresis renography confirms presence of significant right ureteropelvic junction obstruction. Drainage from left kidney was normal.

128 × 128 matrix for ease of region-of-interest (ROI) placement. Data should be acquired with magnification, ensuring that the heart, kidneys, ureters, and bladder are in the field of view. ROI for background subtraction should be 2 pixels wide around the outer perimeter of the ROI of the kidney.

#### Diuretic Phase

Furosemide is injected intravenously at a dose of 1 mg/kg at 20–30 min after radiopharmaceutical administration or when the entire collecting system is believed to be full.

#### Data Analysis

The total counts of the renogram curve for each kidney minus background during the interval between 60 s and the appearance of radioactivity in the calyces are used to determine differential renal function. Data analysis should also include: percentage differential cortical function; 20-min-to-peak ratios; renogram curve pattern categories of normal, immature, stasis, obstructive, or poor function; and clearance half-times for diuretic response analysis.

#### Areas of Contention

Several aspects of the “well-tempered” renogram have been questioned by some workers in the field (24,25,32–34). Neonates are by definition less than 1 mo old, so the “well-tempered” diuretic renogram recommendations really refer to infants (i.e., children less than 1 y old). However, MAG3 diuresis renography has been shown to be useful even in children aged 1 mo or less (35,36). The technique should be available for children less than 1 mo old.

The need for volume expansion with intravenous fluids in all neonates and infants has also been questioned. Reliable results have been obtained in studies involving children who have been normally hydrated with oral fluids before scintigraphy, with added postmicturition or post-gravity-assisted drainage images after the diuresis renography (24,25,33,37,38).

The necessity for routine bladder catheterization in all children also has been challenged (24,25,32–35,37,38). Most children do not have bladder outlet obstruction and will void spontaneously, especially because a diuretic has been administered. It would appear that the routine use of a bladder catheter is not indicated, as it is an invasive procedure associated with a risk of introducing infection. The post-gravity-assisted drainage or postmicturition image should overcome most diagnostic problems related to a full urinary bladder and its resultant back pressure (24,25,37,38). Workers who do not routinely insert bladder catheters acknowledge that bladder catheterization is required in some cases, such as in patients with urethral valves, neurogenic bladder, suspected ureterovesical junction obstruction, or grade II or higher vesicoureteric reflux demonstrated on a cystogram.

The timing of diuretic administration is also controversial. Several groups have reported the utility of early furosemide administration, either at F+ 0 (i.e., at the same time as radiopharmaceutical administration) (24,25) (Fig. 2) or 2–3 min after radiopharmaceutical administration (39,40).

#### CONCLUSION

The Procedure Guideline for Diuretic Renography in Children, developed by the SNM, is based on the “well-tempered” diuretic renogram (41,42), and comments have been encouraged. I support the Consensus on Diuresis Renography for Investigating the Dilated Upper Urinary Tract in its recommendation that the “well-tempered” diuretic renogram group revisit and update its report, addressing the areas of contention that have been outlined (32).

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