Utility of Technetium-99m-MAG3 Diuretic Renography in the Neonatal Period

Joseph C.H. Wong, Monica A. Rossleigh and Robert H. Farnsworth

Departments of Nuclear Medicine and Urology, The Prince of Wales Hospital, Sydney, Australia

Diuretic renography performed in the neonatal period has been reported to be unreliable in diagnosing obstruction. **Methods:** The scans of 27 neonates (age up to 28 days; mean 17 days) with a total of 53 renal units were reviewed; a renal unit being defined as comprising a kidney and its ureter. All were referred following perinatal ultrasound diagnosis of hydronephrosis or hydroureteronephrosis. The neonates had standard diuretic renography using MAG3 with a frusemide dose of 1 mg/kg followed by another image obtained after gravity-assisted drainage. **Results:** There were 17 normal undilated renal units showing excellent diuretic responses with clearance half-times of 0.6–7.7 min. Eighteen renal units were diagnosed as having pelvi-ureteric junction (PUJ) obstruction, with surgical confirmation in all. Eight were diagnosed as unobstructed and of these seven were confirmed nonobstructed by serial imaging using ultrasound and MAG3, but one subsequently had pyeloplasty performed for PUJ obstruction. One unit was indeterminate for PUJ obstruction but had good clearance with gravity-assisted drainage and was shown to be unobstructed on repeat studies. Of nine units diagnosed as having vesico-ureteric junction (VUJ) obstruction, eight had surgical confirmation and one remains of uncertain final diagnosis. Co-existing VUJ obstruction could not be diagnosed in two units with PUJ obstruction because of insufficient radiotracer drainage through the tight stenosis into the ureter. **Conclusion:** An adequate diuretic response is present in the neonatal period using MAG3 and this allows for reliable diagnosis of obstruction. An unobstructed or indeterminate result necessitates follow-up imaging to ensure obstruction does not develop. Co-existing VUJ obstruction may be missed in a scan showing PUJ obstruction.

Key Words: technetium-99m MAG3; neonate; pelvi-ureteric; vesico-ureteric obstruction

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The use of perinatal ultrasonography has resulted in an increased recognition of hydronephrosis and hydroureteronephrosis (*1*). The primary concern is differentiating obstructive from nonobstructive causes. With obstruction, the levels commonly involved are at the pelvi-ureteric (PUJ) and vesico-ureteric junctions (VUJ). The management varies from a conservative approach in nonobstructed kidneys to different operative procedures for PUJ and VUJ obstructions (*1*).

Diuretic renography provides an important diagnostic tool in assessing for functional obstruction of urinary drainage that is safe and relatively noninvasive. Due to its dependence on glomerular filtration, ^{99m}Tc-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) has been reported to be unreliable in the neonatal period due to immature renal function, with reduced glomerular filtration rate (GFR) and reduced responsiveness to a diuretic stimulus (*2–5*). Technetium-99m mercaptoacetyltriglycine (^{99m}Tc-MAG3) is a radiopharmaceutical that has advantageous properties over DTPA in diuretic renography, especially in the neonatal period, in that it is actively secreted predominantly by the anionic tubular transport system with only about 11% filtered at the glomeruli. It therefore has a higher extraction ratio resulting in a higher kidney-to-background ratio giving improved images for qualitative and quantitative analysis (*6*).

Previous studies have examined the use of MAG3 and/or DTPA in diuretic renography with broad age ranges (*7–10*). More recently, Chung et al. (*11*) demonstrated diuretic renography to be reliable in evaluating hydronephrosis during the neonatal period using either ^{99m}Tc-DTPA or ^{99m}Tc-MAG3.

Our study is limited to the neonatal period at initial scanning, defined as age up to 28 days, using solely ^{99m}Tc-MAG3. The aim is to document an adequate diuretic response in the normal neonatal kidney and to demonstrate its accuracy in the diagnosis of obstruction at the PUJ or the VUJ levels in the kidney with a dilated collecting system.

MATERIALS AND METHODS

Twenty-seven neonates had MAG3 renal scans performed over a 31-mo period. This cohort consisted of 21 boys and 6 girls with an age range of 6 to 28 days at the time of initial scanning. The mean age was 17 days. All were term neonates (between 37–42 completed weeks' gestation) except for 4 whom were pre-term at between 28 to 35 wk. The serum creatinine ranged from 0.02–0.09 mmol/liter, with a mean of 0.05 mmol/liter (normal ≤0.05 mmol/liter). Five patients had creatinine levels greater than 0.05 mmol/liter.

All neonates were referred from the Pediatric Urology Depart-

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For correspondence contact: Joseph C.H. Wong, MBBS, Department of Nuclear Medicine, The Prince of Wales Hospital, High Street, Randwick, NSW 2031, Australia.

For reprints contact: Monica A. Rossleigh, MBBS, Department of Nuclear Medicine, The Prince of Wales Hospital, High Street, Randwick, NSW 2031, Australia.

ment on the basis of perinatal ultrasound results suggestive of either PUJ or VUJ obstruction. All patients had prior evaluation for vesico-ureteric reflux with micturating cystograms. The clinical notes and radiological investigations were reviewed. Each kidney and ureter were considered as a renal unit for data analysis.

Preceding the scan, the neonates were breast- or bottle-fed by the mother to achieve adequate hydration. The lighting in the scanning room was dimmed to facilitate sleep in the neonate following the feed. Only neonates with suspected vesico-ureteric junction obstruction or known vesico-ureteric reflux had urinary catheters inserted under gentamicin cover to avoid any back pressure effect on the pelvic or ureteral washout.

A gamma camera with LEAP collimation was used. The patients were studied supine and positioned so that the heart, kidneys and bladder were in the field of view. Images were obtained in a posterior projection. Following the intravenous administration of 20 MBq ^{99m}Tc-MAG3, initial dynamic images were acquired at forty 1-sec frames followed by sixty-two 20-sec frames. Intravenous frusemide was administered at a dose of 1 mg/kg at 20 min into the study, provided that there was sufficient radiotracer in the collecting systems and further acquisition of 120 10-sec frames were obtained. The patient was then held upright for about 5 min to achieve gravity-assisted drainage followed by a 5-min static image. Differential renal function was calculated using the total counts of the renogram curve for each kidney minus background during the interval between 2 to 3 min following the injection of the radiopharmaceutical. The frusemide half-time clearance values were generated from the exponential fit of the maximal slope of the washout curves during frusemide-induced diuresis.

Two independent observers interpreted the images and the diagnoses were made based on the following criteria (*2,3,9,10,12*):

- PUJ obstruction was diagnosed if:

1. Visual analysis showed no significant drainage or progressive accumulation of radiotracer in the pelvi-calyceal system in the diuretic phase or a pelvic frusemide clearance half-time of greater than 15 min.
2. Visual comparison of the pre- and postgravity-assisted drainage images showed no significant change.

A limitation of the above criteria exists, however, in the presence of a VUJ obstruction as it is recognized that VUJ obstruction causes delay in pelvic drainage and clearance half-times due to back pressure. A resultant potential pitfall is that concomitant PUJ obstruction may be missed in a patient with a VUJ obstruction.

- VUJ obstruction was diagnosed if:

1. Visual analysis showed no significant drainage or progressive accumulation of radiotracer in ureter in the diuretic phase or a pelvic frusemide clearance half-time of greater than 15 min.
2. Visual comparison of the pre- and postgravity-assisted drainage images showed no significant change.

- A nonobstructed renal unit was diagnosed if:

1. Visual analysis showed good drainage of the pelvi-ureteric system in the diuretic phase or a pelvic frusemide clearance half-time of less than 10 min.
2. Visual comparison of the pre- and postgravity-assisted drainage images showed further drainage.

- Renal units diagnosed as being indeterminate for obstruction were those not satisfying the criteria groups as described above.

The differential function was used in providing supportive evidence of obstruction. Reduction in relative function has not been included in the diagnostic criteria because reduced as well as increased (supranormal) function may be encountered with obstruction (*3,13*).

RESULTS

Of the 27 patients, there were a total of 53 renal units for data analysis, because one patient had unilateral renal agenesis (Table 1).

There were 17 normal undilated renal units all showing good drainage in the diuretic phase. In 15 units, the clearance half-times ranged from 0.6 to 7.7 min. Two units (Patients 14 and 24) had falsely elevated half-times due to near complete clearance of radiotracer prior to the administration of frusemide, which was obvious on visual analysis (*14*).

Thirty-six units had hydronephrosis or hydroureteronephrosis on ultrasonography. Following evaluation with MAG3 diuretic renography, the final diagnoses were achieved in 27 units at the time of surgery and in 8 units with follow-up imaging, including ultrasonography and a repeat MAG3 study. A follow-up ultrasound finding of decreasing pelvi-calyceal size or a repeat MAG3 result of nonobstruction was taken to confirm a nonobstructed state. The final diagnosis for one unit remains uncertain.

Eighteen renal units were diagnosed as having obstruction at the PUJ level (Fig. 1). All were confirmed at subsequent surgery and had pyeloplasty performed. Bilateral disease accounted for six units. Two renal units (Patients 14 and 15) with documented PUJ obstruction had co-existing VUJ obstruction discovered at the time of surgery (Fig. 2).

One unit (Patient 22) was indeterminate for PUJ obstruction and was subsequently demonstrated not to have obstruction on repeat ultrasound and MAG3. This patient had delayed drainage from the left pelvi-calyceal system and a frusemide clearance half-time of 58.4 min. This patient was diagnosed as indeterminate because there was good clearance with gravity-assisted drainage.

Of the eight units meeting the criteria for being unobstructed (Fig. 3), seven were confirmed with serial imaging using ultrasound and MAG3, with the follow-up period ranging from 13 to 17 mo (mean 14.4 mo). One subsequently had pyeloplasty performed 7 mo later for a PUJ obstruction. Three of the unobstructed units had prolonged frusemide clearance half-times. In Patient 27 ($t_{½}$ = 39.4 min), this was because most of the radiotracer had been discharged from the pelvic system prior to the administration of frusemide. Patients 10 and 21 had clearance half-times of 11.8 and 15 min, respectively, but because there was visually good drainage with frusemide and following gravity assistance, this was diagnosed as unobstructed and confirmed on follow-up studies.

Of the nine units classified as having VUJ obstruction on

TABLE 1
Patient Data and Results

Patient no.	US	Initial scan $t_{1/2}$ (min) L	Initial scan $t_{1/2}$ (min) R	Poor drainage with GAD	Differential function	Scan result	Final diagnosis (If different from scan result)
1	L HN	∞	2.7	L	34:66	L PUJO	
2	L HN	59.3	2.4	L	69:31	L PUJO	
3	L HN	26.7	2.0	L	43:57	L PUJO	
4	L HN	∞	7.7	L	47:53	L PUJO	
5	L HN	∞	1.7	L	41:59	L PUJO	
6	L HN	∞	3.1	L	29:71	L PUJO	
7	L HN	88.3	5.5	L	44:56	L PUJO	
8	R HN	3.2	37.1	R	46:54	R PUJO	
9	R HN	6.5	11.6	R	48:52	R PUJO	
10	Bilat HN	11.8	34.1	R	46:54	R PUJO L No obs	
11	Bilat HN	345.0	82.0	R + L	47:53	Bilat PUJO	
12	Bilat HN	20.7	201.0	R + L	45:55	Bilat PUJO	
13	Bilat HN	14.9	23.8	R + L	46:54	Bilat PUJO	
14	L HN	68.0	22.2	L	51:49	LPUJO	LPUJO + VUJO
15	R HN	3.4	220.0	R	61:39	R PUJO	RPUJO + VUJO
16	L HU	19.2	—	L	100:0	L VUJO	
17	L HU	18.1	7.0	L	54:46	L VUJO	
18	L HN	um 164.0 lm 2.1	0.6	L um	65:35	L um VUJO	
19	R HU	3.5	∞	R	72:28	R VUJO	
20	R HU	NR	NR	R	59:41	R VUJO	
21	R HU L HN	15.0	100.0	R	42:58	R VUJO L No obs	
22	R HU L HN	58.4	33.0	R	48:52	R VUJO Ind L PUJO	R uncertain L No obs
23	Bilat HN	37.7	301.0	R + L	49:51	Bilat VUJO	
24	L HN	6.5	28.6		49:51	L No obs	
25	L HN	7.9	7.2		50:50	L No obs	L PUJO
26	Bilat HN	2.5	2.7		48:52	Bilat No obs	
27	Bilat HN	8.8	39.4		49:51	Bilat No obs	

US = ultrasound; Bilat = bilateral; HN = hydronephrosis; HU = Hydroureteronephrosis; um = upper moiety of duplex system; lm = lower moiety of duplex system; NR = not recorded due to patient motion; PUJO = pelvi-ureteric junction obstruction; VUJO = vesico-ureteric junction obstruction; Ind = indeterminate study; No obs = no obstruction.

MAG3 diuretic renography (Fig. 4), eight had later surgical confirmation, with bilateral disease accounting for two of these units. The last unit remains of uncertain final diagnosis. This patient has persistent hydroureteronephrosis on ultrasound and similar results on repeat MAG3 scans suggestive of a VUJ obstruction. Due to the presence of multiple congenital anomalies requiring more urgent attention and as the differential renal function and serum creatinine has remained stable, more invasive renal investigations have been deferred.

Five of the patients studied (nine renal units because one patient has unilateral renal atresia) had mild elevation of serum creatinine between 0.06–0.09 mmol/liter. Six renal units were correctly diagnosed as obstructed, with one patient having bilateral disease. One of these units was the case with PUJ obstruction and an undiagnosed co-existing VUJ obstruction. The remaining three uninvolved renal units showed good drainage with pelvic clearance half-times between 3.4–7.0 min.

Postoperative MAG3 scans were available for 21 units

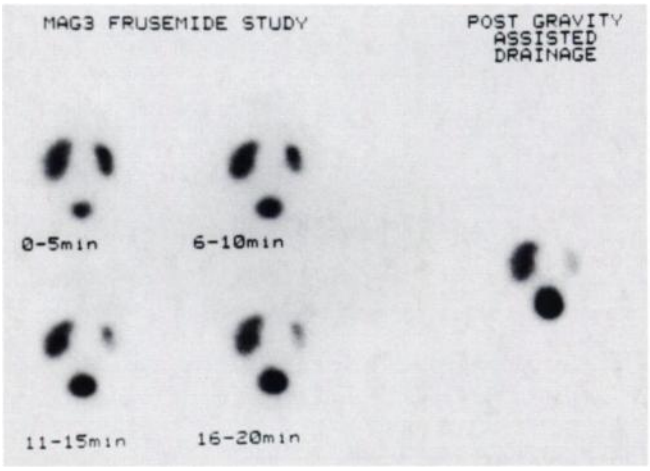

FIGURE 1. Left PUJ obstruction. Posterior views show a dilated left pelvi-calyceal system which drains poorly during the diuretic phase and which remains essentially unchanged following gravity assisted drainage. Good drainage is seen from the normal right kidney. The pelvic clearance half-time was infinity for the left and 7.7 min for the right.

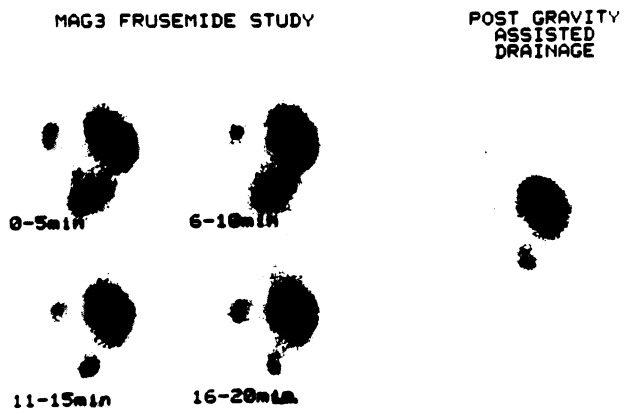

FIGURE 2. Posterior views demonstrate a right PUJ obstruction which was subsequently shown to have a co-existing VUJ obstruction at surgery. A markedly dilated right pelvi-calyceal system is present which drains very poorly in the diuretic phase and with gravity assisted drainage. A normal drainage pattern is seen with the left kidney. There is increased background activity due to mild renal impairment (serum creatinine of 0.06 mmol/liter). The pelvic clearance half time for the right was 220 min and 3.4 min for the left. The tight right PUJ stenosis resulted in insufficient drainage of radiotracer into the ureter to enable diagnosis of co-existing VUJ obstruction.

(Table 2). Of these, 16 had PUJ obstruction, 2 had both PUJ and VUJ obstruction and 3 had VUJ obstruction. Analysis of the postoperative studies showed that 14 units had pelvic clearance half-times of less than 10 min, 4 units in the range between 10 to 15 min and 3 units greater than 15 min. All had showed improvement in drainage and clearance half-times compared with the preoperative studies except for one unit (Patient 9) with mild elevation of clearance half-time of 11.6 min remaining effectively unchanged at 12.6 min but with visually improved drainage with gravity assistance.

Finally, there were three units showing the phenomenon

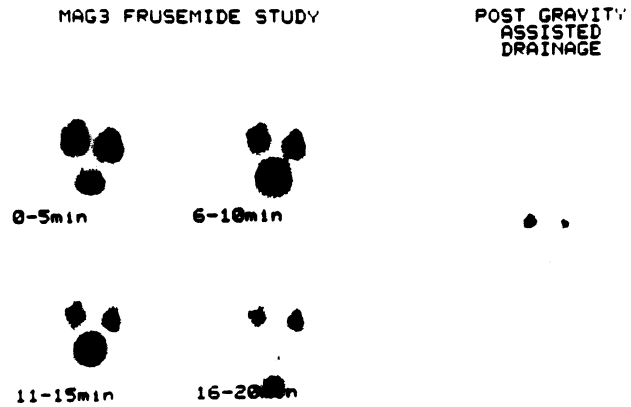

FIGURE 3. Bilateral dilated pelvi-calyceal systems discovered with antenatal ultrasonography. The posterior images show dilated pelvic systems but good drainage in both the diuretic phase and with gravity assisted drainage indicating absence of functional obstruction. The pelvic clearance half-time for the left was 2.5 min and 2.7 min for the right.

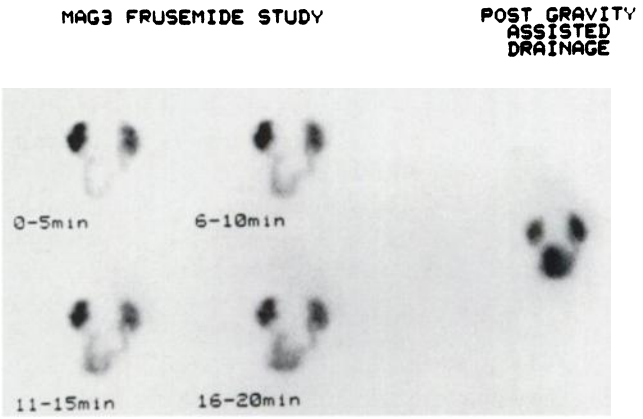

FIGURE 4. Bilateral VUJ obstruction. Posterior images demonstrate significant accumulation of radiotracer in both pelvi-ureteric systems with poor drainage seen in the diuretic phase and following gravity-assisted drainage. The pelvic clearance half-time for the left was 37.7 min and 301.0 min for the right.

of hyperfunctioning of the obstructed kidney with the relative function ranging from 58% to 69%.

DISCUSSION

Routine antenatal ultrasonography has resulted in an increased antenatal diagnosis of hydronephrosis and hydroureteronephrosis requiring differentiation of obstruction from nonobstruction. A unique problem exists in the neonatal group with immature renal function and report-

TABLE 2
Comparison of Pre- and Postoperative Pelvic Clearance Half-Times*

Patient no.	Final diagnosis	Initial scan t½ (min) L	Initial scan t½ (min) R	Postoperative scan t½ (min) L	Postoperative scan t½ (min) R
1	L PUJO	∞		0.7	
2	L PUJO	59.3		4.1	
3	L PUJO	26.7		7.8	
4	L PUJO	∞		11.3	
5	L PUJO	∞		9.6	
6	L PUJO	∞		2.9	
7	L PUJO	88.3		5.1	
8	R PUJO		37.1		11.8
9	R PUJO		11.6		12.6
10	R PUJO		34.1		17.7
11	Bilateral PUJO	345.0	82.0	11.5	6.6
12	Bilateral PUJO	20.7	201.0	15.1	9.4
13	Bilateral PUJO	14.9	23.8	8.1	4.3
14	LPUJO + VUJO	68.0		16.7	
15	RPUJO + VUJO		220.0		8.9
17	L VUJO	18.1		2.5	
19	R VUJO		∞		6.6
21	R VUJO		100.0		5.3

*Only the prolonged initial half-times and subsequent postoperative values are presented.

PUJO = pelvi-ureteric junction obstruction; VUJO = vesico-ureteric junction obstruction.

edly reduced tubular response to a diuretic stimulus. The glomerular filtration rate has been documented at 38 ml/min/1.73m^2 at birth, rising to 103 ml/min/1.73m^2 at 6 mo of age and eventually reaching adult levels at 1 to 2 yr of age (*15*). As a result, several investigators (*3–5*), including members of the Society for Fetal Urology and the Pediatric Nuclear Medicine Council of the Society of Nuclear Medicine (*2*), have found diuresis renography to be unreliable in the neonatal period. The "well tempered diuretic renogram" has as part of its protocol recommendation that patients undergoing diuresis renography should be at least 1 mo of age for reliable interpretation of data.

Our data show adequate diuretic responses in the neonatal kidneys as seen by the responses in normal kidneys as well as the dilated unobstructed kidneys and absence of false-positives for obstruction. This indicates perhaps that low GFR is a more important factor causing unreliability with neonatal DTPA imaging and this may be nullified using MAG3 which is predominantly actively secreted.

MAG3 diuresis renography appears reliable in the diagnosis of unilateral and bilateral PUJ and VUJ obstruction. No false-positives were encountered for either unilateral or bilateral disease. The ability to diagnose bilateral obstruction is important, as it has been suggested that in this age group, evaluation for obstruction can only be reliably made if the contralateral uninvolved kidney is functionally mature (*4*). Although only four of our patients had bilateral obstruction, our data would suggest that there is an adequate diuretic response obtained with MAG3 renography to allow for reliable diagnosis of bilateral disease.

Although small numbers also exist in the subgroup of patients with mild renal impairment (serum creatinine between 0.06–0.09); nevertheless the data also suggest that there is sufficient diuretic response in these patients and, together with the good quality images possible with MAG3, an accurate assessment for obstruction is possible. Of note is that the clearance half-times of the uninvolved kidneys remain under 10 min, which is the normal or unobstructed range. Caution must be taken, however, when interpreting renography results in patients with more severe renal impairment.

Postoperative scans are useful to demonstrate improvement in drainage following the surgical procedures. All renal units except one showed improvement in pelvic clearance half-time values, with two-thirds (14/21) returning to unobstructed values. The single unit (Patient 9) that did not show any change in the clearance half-times did demonstrate good drainage following gravity assistance, confirming the usefulness of this view in the postoperative period (*12*).

There are few papers focused on diuretic renography and vesico-ureteric junction obstruction. Jamar et al.(*10*) have described a good agreement between pelvic and ureteric clearance half-times. We have not calculated the ureteric washout times in our study, but the pelvic clearance half-times ranged from 19.2 min to infinity in our patient group with VUJ obstruction. The most likely cause of the delayed pelvic clearance of radiotracer is the back pressure effect from the obstructed VUJ. Hence, the ability to diagnose a PUJ obstruction is limited in the presence of a existing VUJ obstruction. We did not encounter this situation. Instead we had two patients showing PUJ obstruction which were subsequently diagnosed to have co-existent VUJ obstructions at surgery. The likely explanation is that there was severe PUJ obstruction causing poor radiotracer drainage resulting in inadequate visualization of the ureter.

There was one renal unit classified as unobstructed which required pyeloplasty 7 mo later. This has been noted in other studies (*9,16,17*). The reason for this may be due to the phenomenon of transitional hydronephrosis, in which progressive renal maturation may result in either progression or resolution of the obstruction (*16,17*). Therefore, it is imperative for follow-up imaging in patients with an unobstructed picture. We use monthly ultrasonographic evaluation and if there is no evidence of involution of the dilated pelvis or if there is increasing dilatation, a repeat MAG3 diuretic renography is performed, usually in 3 to 6 mo.

The relative function of the involved kidneys were elevated (range of 58%–69%) in one unit with PUJ obstruction and two units with VUJ obstruction. There has been documented general observation that the percent differential function is frequently normal or even increased over the opposite normal kidney especially in the neonates. The mechanism for this hyperfunctioning phenomenon is unknown (*3,13*).

We have relied upon follow-up ultrasound findings of decreasing pelvi-calyceal size and repeat MAG3 studies showing nonobstruction to confirm a nonobstructed state. We acknowledge that while there is a possibility of reproducing false-negative studies, it does seem unlikely because repeat imaging with two different modalities were used.

Finally, we have utilized breast- or bottle-feeding prior to the study as the means of achieving hydration rather than intravenous fluid expansion. We have found this to lessen the invasiveness of the test without compromising the reliability of the test (*14*). In addition, feeding calms the neonate who then frequently drifts off to sleep. This subsequently allows for good image acquisition without motion artifacts.

CONCLUSION

Our study using MAG3 diuretic renography indicates that there is sufficient diuretic response in the neonatal kidney for accurate assessment of obstruction in perinatal hydronephrosis and hydroureteronephrosis. These findings confirm the results of Chung et al. (*11*). There appears to be reliable assessment of both unilateral and bilateral obstruction. Our data also suggest that there are high-resolution images and sufficient diuretic responses obtained in patients showing mild elevation of serum creatinine to allow for accurate diagnosis of obstruction. MAG3 diuretic renography is useful in the follow-up of postsurgical pa-

tients to document improved clearance. An obstructed result has a high level of correlation with surgical findings, whereas an unobstructed or indeterminate result necessitates further follow-up imaging with sequential ultrasonography and diuretic renography to ensure obstruction does not develop. Tandem lesions pose a diagnostic problem. Co-existing VUJ obstruction may be missed in a scan showing PUJ obstruction and vice versa.

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