Quantitative SPECT of ^{99m}Tc-DMSA Uptake in Kidneys of Infants with Unilateral Ureteropelvic Junction Obstruction: Assessment of Structural and Functional Abnormalities

David Groshar, Moshe Wald, Boaz Moskovitz, Elias Issaq and Ofer Nativ

Departments of Nuclear Medicine and Urology, Bnai Zion Medical Center, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

We evaluated individual renal function using quantitative SPECT of dimercaptosuccinic acid (DMSA) uptake by the kidneys (QDMSA) in infants with unilateral ureteropelvic junction (UPJ) obstruction and compared our findings with infants without obstruction. **Methods:** QDMSA was performed on 13 infants (mean age of 2.8 ± 2.8 mo) with unilateral UPJ obstruction and on 15 age-matched controls without obstruction. **Results:** Control kidneys (n = 30) had a volume of 43.5 ± 8.8 mL, a percentage injected dose (%ID)/mL 0.62 ± 0.12 and uptake of 26.1% ± 3.9%. Kidneys with UPJ obstruction (n = 13) had a volume of 61.2 ± 19.3 mL, a %ID/mL of 0.42 ± 0.11 and uptake of 25.4% ± 8.2%. Contralateral kidneys (n = 13) had a volume of 44.0 ± 11.9 mL, a %ID/mL of 0.57 ± 0.16 and uptake of 24.2% ± 4.6%. The uptake in obstructed kidneys was similar to that observed in contralateral and control kidneys ($t = -0.77$, $P = 0.45$; $t = -0.37$, $P = 0.71$; respectively). UPJ kidneys had a statistically significant increased volume and decreased %ID/mL, compared with contralateral kidneys ($t = 3.35$, $P < 0.006$ and $t = 3.75$, $P < 0.003$, respectively) and control kidneys ($t = -4.2$, $P < 0.001$ and $t = 4.7$, $P < 0.001$, respectively). There was no significant difference between contralateral kidneys and control kidneys regarding volume ($t = -0.16$, $P = 0.87$), %ID/mL ($t = 0.98$, $P = 0.33$) and uptake ($t = -1.41$, $P = 0.16$). Of 13 infants, 11 (85%) showed large kidneys with thinning of the renal cortex. In 1 infant, there was no difference between the obstructed and contralateral kidneys regarding volume, %ID/mL and uptake, and 1 infant showed significant decreased uptake in the UPJ kidney compared with the contralateral kidney. **Conclusion:** Although the overall renal function of the obstructed kidneys remained unchanged, there was a statistically significant decrease in the %ID/mL of renal tissue in UPJ kidneys, which may represent renal dysfunction. Increased functional volume with a thin cortex may represent a compensatory mechanism of the obstructed kidney. Such changes may contribute to the understanding of pathophysiologic mechanisms and may be an early sign of obstruction in infants with hydronephrosis. Further longitudinal studies with an extended number of infants and serial measurements of kidney volumes and %ID/mL are warranted to assess the significance of QDMSA in the management of infants with asymptomatic unilateral renal pelvic dilatation.

Key Words: SPECT; dimercaptosuccinic acid; ureteropelvic junction obstruction; hydronephrosis; infants

J Nucl Med 1999; 40:1111–1115

Ureteropelvic junction (UPJ) obstruction is the most common cause of hydronephrosis in children (*1*). Prenatal sonography detects hydronephrosis in 1.4% of fetuses, and as many as half of these cases persist postnatally (*2*). However, pelvic dilatation may occur without clinically significant obstruction. The inability to establish or rule out obstruction has caused controversy in the management of infants with asymptomatic hydronephrosis (*3*). A test able to demonstrate the kidney's response to obstruction will be useful both for understanding the pathophysiology and for evaluating renal pelvic dilatation in asymptomatic infants.

Quantitative SPECT of dimercaptosuccinic acid (DMSA) uptake by the kidneys (QDMSA) is a method to evaluate individual renal function (*4–6*). QDMSA is a relatively simple reproducible technique that is easily standardized and allows determination of individual and global renal function (*7,8*). The aim of this study was to evaluate the renal volume and individual renal uptake measured by QDMSA in infants with unilateral UPJ obstruction and compared with infants with normal kidneys.

MATERIALS AND METHODS

Patient Population

^{99m}Tc-DMSA quantitative SPECT study of the kidneys was performed on 13 infants (10 males, 3 females; mean age 2.8 ± 2.8 mo, range 3 wk–10 mo). All infants had moderate to severe unilateral hydronephrosis on sonography, a diuretic renogram showing an obstructive curve pattern on the kidney with hydronephrosis and a nonobstructive curve pattern on the contralateral kidney. None had vesicoureteral reflux on voiding cystoureterogram; thus, all were considered as having unilateral UPJ obstruction. Fifteen age-matched infants (11 females, 4 males; mean age

Received Jul. 13, 1998; revision accepted Dec. 7, 1998.

For correspondence or reprints contact: David Groshar, MD, Department Nuclear Medicine, Bnai Zion Medical Center, 47 Golomb St., POB 4940, Haifa, Israel, 31048.

3.1 ± 2.1 mo, range 3 wk–10 mo) served as a control group. QDMSA was performed as part of the workup in children with previous urinary tract infection and no hydronephrosis or structural abnormalities of the urinary tract on sonography. All infants had normal values of serum creatinine, blood urea nitrogen and urinalysis.

Quantitative SPECT

QDMSA was measured using the same method as in previous studies (*7–9*). The infant was injected with 27.8–55.5 MBq (0.750–1.5 mCi) ^{99m}Tc-DMSA, and SPECT was performed after 4–6 h. In brief, studies were performed with a rotating gamma camera and an all-purpose, low-energy collimator. Data acquisition lasted 20 min and required 120 projections (3° apart), and the entire study accumulated 3–5 × 10^5 counts. Raw data were reconstructed by filtered backprojection with a Hann filter (cutoff point 0.5 cycle/cm). After reconstruction, each image was sectioned at 1-pixel (0.68-cm) intervals in the transaxial, coronal and sagittal planes using a 64 × 64 byte matrix. Kidney volumes and radioactive concentration measurements were calculated on the reconstruction data with the threshold method (*10*).

Threshold is the most used method for organ or tumor segmentation in SPECT studies (*11,12*). The threshold selection depends on the level of the surrounding activity and the organ size (*11,12*). The high target-to-nontarget ratio of DMSA in the kidney and kidney size (>30 mL) makes this method suitable for QDMSA (*10,11*). A threshold value of 43% was found to be optimal for ^{99m}Tc after performing a series of phantom measurements with known volumes and concentrations (*4,10*). The method does not deny that tissue attenuation is present but assumes that cancellation of attenuation effects occurs. Consideration of the theoretic role of attenuation and the inability to correct for it has led us to use the empirical threshold method and to demonstrate its usefulness and reliability by extensive phantom studies and by the only meaningful gold standard—the in vivo/in vitro correlation (*10*).

The operator chooses the slice to define the kidney and draw a region of interest (ROI) around the organ. For volume measurements (mL), the number of pixels in all sections multiplied by the slice thickness is summed. For concentration measurements, the threshold value is subtracted from all pixels in the ROI in all slices. All the nonzero pixels that have higher counts than the threshold value are used to calculate the concentration. Counts per voxel are converted into concentration units (μCi/mL) using the regression line obtained previously by phantom measurements (*10*). The percentage of injected dose per milliliter of renal tissue (%ID/mL) is calculated using this value corrected for radioactivity decay. Kidney uptake is then obtained by multiplying kidney volume (mL) and %ID/mL (*4*).

Statistical Methods

Values are expressed by their mean ± 1 SD (95% confidence intervals for the mean). The paired Student *t* test was used to compare left versus right kidneys in controls and to compare obstructed versus contralateral normal kidneys in infants with UPJ obstruction. Unpaired Student *t* test was performed for comparison between age-matched groups.

RESULTS

The results of the QDMSA study are presented in Table 1. In the control group, there was no statistically significant difference between right and left kidneys concerning the volume, %ID/mL and uptake; thus, they were grouped together. Control kidneys (n = 30) had a volume of 43.5 ± 8.8 mL (CI = 40.2–46.8 mL), a %ID/mL of 0.62 ± 0.12 (CI = 0.57–0.66) and an uptake of 26.1% ± 3.9% (CI = 24.7%–27.6%). Kidneys with UPJ obstruction (n = 13) had a volume of 61.2 ± 19.3 mL (CI = 49.5–72.9 mL), a %ID/mL of 0.42 ± 0.11 (CI = 0.36–0.49) and an uptake of 25.4% ± 8.2% (CI = 20.4%–30.4%). Contralateral kidneys (n = 13) had a volume of 44.0 ± 11.9 mL (CI = 36.8–51.2 mL), a %ID/mL of 0.57 ± 0.16 (CI = 0.47–0.67) and an uptake of 24.2% ± 4.6% (CI = 21.4%–27.0%).

TABLE 1
QDMSA Data in Unilateral UPJ Obstruction

		Quantitative SPECT					
		Obstructed (n = 13)			Contralateral (n = 13)		
Patient no.	Age	Vol (mL)	%ID/mL	Uptake	Vol (mL)	%ID/mL	Uptake
1	2 mo	86	0.42	36.1	39	0.64	25.0
2	1 mo	67	0.37	24.5	43	0.57	24.8
3	3 mo	44	0.47	20.7	37	0.47	17.4
4	5 mo	65	0.48	31.2	65	0.49	31.8
5	6 mo	86	0.22	18.9	63	0.41	26.2
6	1 mo	43	0.66	28.4	32	0.83	26.6
7	3 wk	47	0.43	20.1	37	0.51	19.0
8	4 mo	54	0.38	20.5	45	0.44	19.8
9	3 wk	43	0.46	19.5	33	0.67	22.8
10	1 mo	97	0.45	43.5	33	0.96	32.2
11	10 mo	74	0.37	27.4	63	0.43	27.1
12	3.5 wk	48	0.58	27.9	39	0.56	21.8
13	3.5 wk	42	0.29	12.2	41	0.49	20.1
Mean ± SD		61.2	0.42	25.4	44.0	0.57	24.2
		19.3	0.11	8.2	11.9	0.16	4.6
Control subjects (n = 30)							
Mean ± SD		43.5	0.62	26.1			
		8.8	0.12	3.9			

QDMSA = quantitative SPECT of dimercaptosuccinic acid uptake; UPJ = ureteropelvic junction; vol = volume; %ID/mL = percentage of injected dose per milliliter; uptake = kidney uptake (%).

The uptake in obstructed kidneys was similar to that observed in contralateral and control kidneys ($t = -0.77$, $P = 0.45$, $t = -0.37$, $P = 0.71$, respectively). UPJ kidneys had a statistically significant increased volume and decreased %ID/mL, compared with contralateral kidneys ($t = 3.35$, $P < 0.006$ and $t = 3.75$, $P < 0.003$, respectively) and control kidneys ($t = -4.2$, $P < 0.001$ and $t = 4.7$, $P < 0.001$, respectively). There was no statistically significant difference between contralateral kidneys and control kidneys regarding volume ($t = -0.16$, $P = 0.87$), %ID/mL ($t = 0.98$, $P = 0.33$) and uptake ($t = -1.41$, $P = 0.16$).

DISCUSSION

The use of maternal sonography, which easily detects fetal hydronephrosis, has increased the cases of asymptomatic

infants with this condition. The management of these patients after birth remains controversial. The question lies not in whether obstruction requires surgery but in distinguishing obstructive from nonobstructive renal pelvic dilation (*1,13*).

The best definition of a clinically significant obstruction is one that may cause renal function impairment, increases the risk of urinary tract infection and causes symptoms (stone formation, hypertension, pain or hematuria) (*1*). Currently, there is no gold standard technique to assess obstruction or predict an obstructive condition in asymptomatic infants with renal pelvic dilatation. The single factor that may have a continuous relationship to obstruction is renal function (*1*). It has been shown that elevated renal pelvic pressure due to obstruction results in renal dysfunction and renal cellular injury, leading to irreversible renal damage over time (*14*). There is a need for a method that is able to provide objective information on renal changes related to UPJ obstruction before irreversible damage occurs.

To evaluate the clinical significance of obstruction, Whitaker introduced the pressure-flow study in 1973 (*15,16*). This is an invasive test that measures the response of the renal pelvis to distention (measured by pressure) produced by an unphysiologically constant high flow rate of fluids. However, not all obstructions are constant, and the pressures observed during the study may never occur at other times, especially if the renal pelvis is dilated or highly compliant. This test is invasive and cumbersome and has not gained general acceptance as a routine method to evaluate obstruction.

The more simple diuretic renogram study involves the injection of a radiopharmaceutical, mainly diethylenetriamine pentaacetic acid or mercaptoacetyltriglycine, and the monitoring of its diuretic augmented passage through the upper urinary tract to obtain a time-activity curve. Different patterns of this washout curve can be obtained and the time to half drainage measured (*1,17–19*). Unfortunately, these measurements and curve patterns are affected by several technical factors, such as hydration status, individual response to furosemide, bladder drainage, size and compliance of the collecting system. In addition, they do not define the presence or absence of partial urinary obstruction (*1,20–23*).

Radionuclide differential renal function is also used to evaluate hydronephrosis. A differential renal function below 30%–40% or deterioration of the relative function over time has been advocated to indicate the need for surgical correction of unilateral UPJ obstruction. However, this technique is dependent on the background selection, giving inaccurate results especially in children younger than 1 y with hydronephrosis (*24,25*). Furthermore, several studies have shown that differential renal function for assessing obstruction has no prognostic value in neonatal hydronephrosis (*1,16,17–19,25–27*).

Morphologic abnormalities demonstrated on excretory urography, CT and sonography are usually late findings secondary to sequelae of obstruction and neither specifically define obstruction nor predict the risk for progressive renal deterioration (*28,29*).

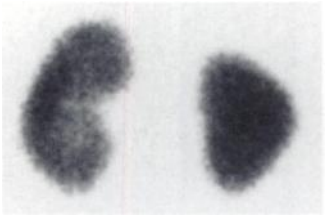

FIGURE 1. Planar posterior view of patient 11 shows large left kidney due to UPJ obstruction.

Renal cortical scintigraphy using ^{99m}Tc-DMSA has been used for detecting renal cortical defects (*30–33*). Functional imaging of the proximal renal tubular mass is obtained and is dependent on the renal blood flow and proximal tubular cell membrane transport function (*32,34*). The quantitation of ^{99m}Tc-DMSA uptake in each kidney separately provides a practical index of renal function (*4–6,34*). Planar and SPECT techniques have been used for measurement of the percentage uptake of injected radioactivity of ^{99m}Tc-DMSA by the kidneys (*4–6,34,35*).

In this study, QDMSA was performed in 13 infants with unilateral hydronephrosis as a result of UPJ obstruction and compared with 15 age-matched infants without obstruction. Unlike reflux nephropathy (*7,8*), obstructed kidneys showed a large cortical volume and total uptake similar to the contralateral normal kidneys. For that reason no contralateral adaptive changes occurred. Of 13 infants, 11 (85%) showed large kidneys with thinning of the renal cortex (Figs. 1 and 2). In 1 patient (patient 4), there was no difference in the volume, %ID/mL and uptake between the obstructed and contralateral kidneys (Fig. 3). Only 1 patient (patient 13) showed significant decreased uptake in the UPJ kidney compared with the contralateral one (Fig. 4), indicating impairment of renal function. These findings are in agreement with the work of Peters et al. (*36,37*), who found in a fetal ovine model study that hydronephrosis due to partial obstruction produced ipsilateral large kidneys with thin but structurally intact cortex (*37*).

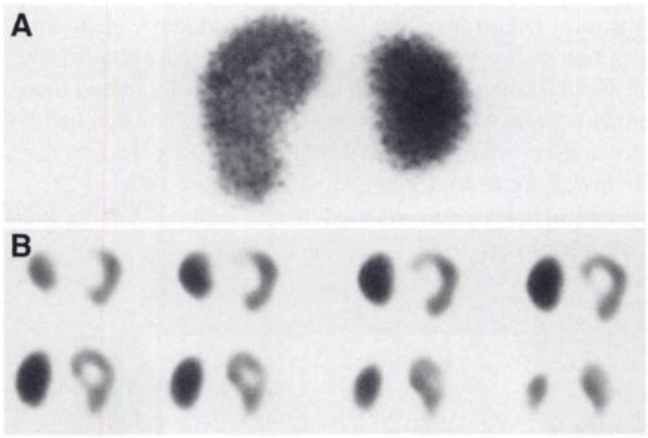

FIGURE 2. Planar posterior view (A) and SPECT coronal view (B) of patient 10 show large left kidney with thin cortex due to UPJ obstruction.

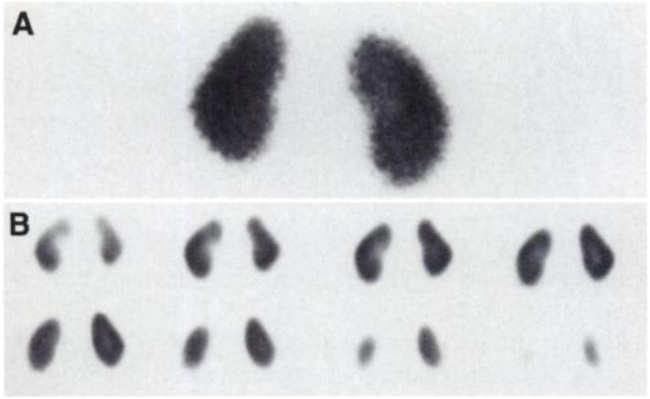

FIGURE 3. Planar posterior view (A) and SPECT coronal view (B) of patient 4 with right UPJ obstruction show no differences between kidneys.

UPJ obstruction can be characterized as a restriction to urine flow resulting in an elevated renal pelvic pressure, which, if left untreated, will cause progressive renal function deterioration (*1,3*). Elevated renal pelvic pressure has been shown to induce an increase in renal tubular pressure, a decrease in renal blood flow, a decrease in glomerular filtration rate and renal tubular dysfunction (*14*). However, the renal pelvic pressure does not stay continuously elevated and varies with other compensatory changes (*15*). Thus, functional impairment in UPJ obstructed kidneys is gradual, prolonged and not promptly recognized.

In this study, there was a statistically significant decrease in the %ID/mL of renal tissue in UPJ kidneys compared with contralateral normal kidneys and to control kidneys. This may represent renal dysfunction caused by elevated renal pelvic pressure. However, there was no significant loss of the individual renal function measured by the kidney uptake of DMSA that remained similar to the contralateral kidneys and to control kidneys. This was due to an increase in the functional renal volume.

CONCLUSION

This study recognizes the ability of QDMSA in detecting structural and functional changes in kidneys with UPJ obstruction. Although the overall renal function of the obstructed kidneys remained unchanged, the increased functional volume with a thin cortex may represent a compensatory mechanism of the obstructed kidney. Such changes may contribute to the understanding of pathophysiologic mechanisms and may be an early sign of obstruction in infants with hydronephrosis.

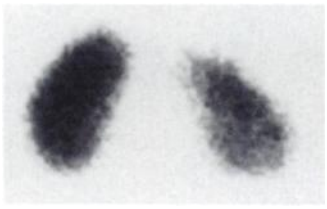

FIGURE 4. Planar posterior view of patient 13 with right UPJ obstruction and decreased uptake of ^{99m}Tc-DMSA.

We believe this study raises new issues in the application of QDMSA in infants with pelvic dilatation. Further longitudinal studies with an extended number of infants and serial measurements of kidney volumes and %ID/mL are warranted to assess the significance of QDMSA in the management of infants with asymptomatic unilateral renal pelvic dilatation.

REFERENCES

1. Peters CA. Urinary tract obstruction in children. *J Urol.* 1995;154:1874–1884.
2. Duckett JW Jr. When to operate neonatal hydronephrosis. *Urology.* 1993;42:617–619.
3. Gordon I. Assessment of pediatric hydronephrosis using output efficiency. *J Nucl Med.* 1997;38:1487–1489.
4. Groshar D, Frankel A, Iosilevsky G, et al. Quantitation of renal uptake of technetium-99m DMSA using SPECT. *J Nucl Med.* 1989;30:246–250.
5. Murase K, Tanada S, Ishine M, Yokoyama M, Hamamoto K. Methods for measuring the renal uptake rate of 99m-Tc-dimercaptosuccinic acid (DMSA): a comparative study. *Eur J Nucl Med.* 1990;16:725–731.
6. Groshar D, Embon OM, Frenkel A, Front D. Renal function and Tc-99m-DMSA uptake in single kidneys: the value of in vivo SPECT quantitation. *J Nucl Med.* 1991;32:766–768.
7. Groshar D, Moskovitz B, Gorenberg M, et al. Quantitative SPECT of technetium-99m-DMSA uptake in the kidneys of normal children and in kidneys with vesicoureteral reflux: detection of unilateral kidney disease. *J Nucl Med.* 1994;35:445–449.
8. Groshar D, Gorenberg V, Weissman I, Livne PM, Front D. Detection of permanent renal damage in kidneys with vesicoureteral reflux by quantitative SPECT uptake of Tc-99m-DMSA. *J Urol.* 1996;155:664–667.
9. Groshar D, Issaq E, Nativ O, Livne PM. Increased renal function in kidneys with UPJ obstruction: fact or artifact? Assessment by quantitative SPECT of DMSA uptake by the kidneys. *J Urol.* 1996;155:844–846.
10. Iosilevsky G, Israel O, Frenkel A, et al. A practical SPECT technique for quantitation of drug delivery to human tumors and organ absorbed radiation dose. *Semin Nucl Med.* 1989;19:33–46.
11. Erdi YE, Wessels BW, Loew MH, Erdi AK. Threshold estimation in single photon emission computed tomography and planar imaging for clinical radioimmunotherapy. *Cancer Res.* 1995;55:5823s–5826s.
12. Tauxe WN, Soussaline F, Todd-Pokropek A, et al. Determination of organ volume by single-photon emission tomography. *J Nucl Med.* 1982;23:984–987.
13. Saunders CAB, Choong KKL, Larcos G, Farlow D, Gruenewald SM. Assessment of pediatric hydronephrosis using output efficiency. *J Nucl Med.* 1997;38:1483–1486.
14. Fung LCT, Atala A. Constant elevation in renal pelvic pressure induces an increase in urinary N-acetyl-b-d-glucosaminidase in a nonobstructive porcine model. *J Urol.* 1998;159:212–216.
15. Koff SA. Pathophysiology of ureteropelvic junction obstruction. Clinical and experimental observations. *Urol Clin North Am.* 1990;17:263–272.
16. King LR. Hydronephrosis. When is obstruction not obstruction? *Urol Clin North Am.* 1995;22:31–42.
17. Koff SA, Campbell KD. The nonoperative management of unilateral neonatal hydronephrosis: natural history of poorly functioning kidneys. *J Urol.* 1994;152:593–595.
18. Upsdell SM, Gupta S, Gough DCS. The radionuclide assessment of pre-natally diagnosed hydronephrosis. *Br J Urol.* 1994;74:31–34.
19. Rickwood AMK, Godiwalla SY. The natural history of pelvic-ureteric junction obstruction in children presenting clinically with the complaint. *Br J Urol.* 1997;80:793–796.
20. MacNeily AE, Maizels M, Kaplan WE, Firlit CF, Conway JJ. Does early pyeloplasty really avert loss of renal function? A retrospective review. *J Urol.* 1993;150:769–773.
21. Salem YH, Majd M, Rushton HG, Belman AB. Outcome analysis of pediatric pyeloplasty as a function of patient age, presentation and differential renal function. *J Urol.* 1995;154:1889–1893.
22. Maizels M, Mitchell B, Kass E, Fernbach SK, Conway JJ. Outcome of nonspecific hydronephrosis in the infant: a report from the Registry of the Society for Fetal Urology. *J Urol.* 1994;152:2324–2327.
23. Palmer LS, Maizels M, Cartwright PC, Fernbach SK, Conway JJ. Surgery versus observation for managing obstructive grade 3 to 4 unilateral hydronephrosis: a report from the Society for Fetal Urology. *J Urol.* 1998;159:222–228.

24. Nguyen HT, Gluckman GR, Kogan BA. Changing the technique of background subtraction alters calculated renal function on pediatric mercaptoacetyltriglycine renography. *J Urol.* 1997;158:1252–1256.
25. Woolfson RG, Neild GH. The true clinical significance of renography in nephro-urology. *Eur J Nucl Med.* 1997;24:557–570.
26. Elder JS, Stansbrey R, Dahms BB, Selzman AA. Renal histological changes secondary to ureteropelvic junction obstruction. *J Urol.* 1995;154:719–722.
27. Stock JA, Krous HF, Heffernan J, Packer M, Kaplan GW. Correlation of renal biopsy and radionuclide renal scan differential function in patients with unilateral ureteropelvic junction obstruction. *J Urol.* 1995;154:716–718.
28. Koff SA, Peller PA, Young DC, Pollifrone DL. The assessment of obstruction in the newborn with unilateral hydronephrosis by measuring the size of the opposite kidney. *J Urol.* 1994;152:596–599.
29. Brandell RA, Brock JW, Hamilton BD, Cartwright PC, Snow BW. Unilateral hydronephrosis in infants: are measurements of contralateral renal length useful? *J Urol.* 1996;156:188–189.
30. Gordon I. Indications for 99m-technetium dimercapto-succinic acid scan in children. *J Urol.* 1987;137:464–467.
31. Yen TC, Chen WP, Chang SL, Liu RS, Yeh SH, Lin CY. Technetium-99m-DMSA renal SPECT in diagnosing and monitoring pediatric acute pyelonephritis. *J Nucl Med.* 1996;37:1349–1353.
32. Majd M, Rushton HG. Renal cortical scintigraphy in the diagnosis of acute pyelonephritis. *Semin Nucl Med.* 1992;22:98–111.
33. Crabbe DCG, Thomas DFM, Gordon AC, Irving HC, Arthur RJ, Smith SEW. Use of 99m-technetium-dimercaptosuccinic acid to study patterns of renal damage associated with prenatally detected vesicoureteral reflux. *J Urol.* 1992;148:1229–1231.
34. Taylor A. Quantitation of renal function with static imaging agents. *Semin Nucl Med.* 1982;12:330–344.
35. Groshar D, Moskovitz B, Issaq E, Nativ O. Quantitative SPECT of DMSA uptake by the kidneys: assessment of reproducibility. *Kidney Int.* 1997;52:817–820.
36. Peters CA, Gaertner RC, Carr MC, Mandell J. Fetal compensatory renal growth due to unilateral ureteral obstruction. *J Urol.* 1993;150:597–600.
37. Peters CA, Carr MC, Lais A, Retik AB, Mandell J. The response of the fetal kidney to obstruction. *J Urol.* 1992;148:503–509.