Influence of Ureteral Status on Kidney Washout During Technetium-99m-DTPA Diuresis Renography in Children

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To assess the influence of the ureter on renal washout during ^{99m}Tc-DTPA diuresis renography, ureteral images were reviewed in 42 children (median age: 5 mo) referred for hydronephrosis. Sixty-minute acquisitions were obtained in hydrated patients under bladder drainage. Furosemide was injected at 30 min. An abnormal ureter was defined as an intense and continuous image of >10 min. A washout index was determined on renal (KT½) and ureteral (UT½) curves. Curve patterns corresponding to normal (type I), obstructive (II) and nonobstructive (III) cases were described. Compared with the x-ray data, diuresis renography was highly sensitive (91%) and specific (98%) for detecting any abnormality. Despite an obstructive KT½ (>20 min), no patient with an abnormal ureter underwent therapy at the ureteropelvic junction. After surgery at the lower level, hydronephrosis regressed. Our data indicate that abnormal ureter findings at diuresis renography have to be recognized before planning therapy for children with hydronephrosis.

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For the last 10 years, diuresis renography has been widely used as a valuable diagnostic tool for hydronephrosis, particularly when obstruction at the pelviureteric junction was questionable (*1–3*). More recently, the assessment of global and relative renal function with ^{99m}Tc-DTPA has become of major concern in nuclear pediatric urology (*4,5*). Diuresis renography was described in 1967 by Rado et al. (*6*) in cases of ureteropelvic junction (UPJ) obstruction and also in one case of ureteral obstruction secondary to ureterolithiasis. Since then, many papers have stressed interest in the test for evaluating ureteral or infraureteral lesions but few focused on the problem raised by ureteral dilatation (*1,7–15*). Unfortunately, most authors have mixed data about UPJ obstruction with various other ureteral dysfunctions without any particular emphasis on the latter conditions.

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The functional assessment of the ureters remains difficult. When the ureters are dilated, the question about obstruction is raised. Ultrasonography, intravenous pyelography or other radiological procedures do not always provide appropriate information, while the Whitaker test (pressure-perfusion study), though direct and probably more accurate, is necessarily invasive, not always suitable in day-to-day pediatric applications and has not been validated in children (*15–17*). Moreover, reference values in the normal pediatric population are not available. The aims of this study were: (1) to determine the significance of the visualization of the ureter during diuresis renography performed in a random pediatric population referred for hydronephrosis as compared to the morphological data provided by the radiological procedures; (2) to evaluate from a functional point of view, the relationship between the kidney and the ureter washout, especially when an obstructive process was suspected; and (3) to estimate the impact of the scintigraphic findings on therapeutic choice.

MATERIALS AND METHODS

Patients

Forty-two patients referred for hydronephrosis were investigated (29 boys and 13 girls). Their ages ranged from 8 days to 15 yr (median: 5 mo). In 19 cases, the diagnosis of hydronephrosis was antenatally established and postnatally confirmed by ultrasonography. A total of 45 consecutive diuretic renographies were reviewed after functional imaging of the ureters had been performed.

Diuresis renography results were compared to those from other diagnostic procedures, such as ultrasonography, intravenous pyelography, micturating cysto-uretrography and in some instances, ante- or retrograde direct pyelography. A radiologically abnormal ureter was defined from the observation of any ureteral abnormality except for those related to isolated vesicoureteral reflux (VUR), a feature whose scintigraphic detection would normally not be possible because of the continuous bladder emptying through the catheter. Thus, isolated VUR with a negative scan should be considered as a true-negative result and inversely, a positive scan with the same radiological abnormality, as a false-positive. The different radiological procedures were performed within 2 wk of the radioisotopic investigation and without knowledge of the results of the different studies.

Methods

Radioisotopic studies were performed after intravenous injection of 18.5–55.5 MBq (according to body weight) freshly prepared ^{99m}Tc-DTPA (Amerscan, Amersham International plc, UK). Correct hydration of the patients was maintained by constant infusion of fluids (glucose 5% in lactate-Ringer solution (Viaflex® Baxter SA, Belgium) 300 ml/m^2 for at least 2 hr starting 30 min before the scan). An indwelling catheter was inserted into the bladder to avoid any deleterious effect of bladder distension on the pelvic or ureteral washout and possible superimposition of the bladder on the ureteral image. Data were collected for 60 min (15 sec/frames for 6 min and 1 min/frame for an additional 54 min) by means of a computer-linked gamma camera (Apex 410, Elscint, Haïfa, Israel) equipped with a low-energy high-resolution collimator (APC-4, Elscint, Haïfa, Israel). Furosemide (1 mg /kg; max: 20 mg) was administered intravenously at 30 min. Studies were performed in the supine position on a plexiglas table and under light sedation for the children up to 2 yr to ensure immobility for 60 min. Renograms and ureteral curves were obtained on ROIs drawn on a 60-min summed frame. The following parameters were determined for the kidneys: T_{max} (n < 7 min), RA_{30}, namely, the residual activity at the 30th min (n < 60%), and a washout index (KT½) calculated from the exponential fit of the steepest negative slope of the renogram after furosemide-induced diuresis. According to Kass et al. (*1*), a KT½ higher than 20 min was considered to reflect obstructive process, a value below 15 min excluded any obstruction and a KT½ between 15 and 20 min remained inconclusive. A washout index was also determined for the ureter when it was visually abnormal (UT½). Finally, when T½ could not be calculated because of the appearance of an upsloping curve after diuresis injection, a standard value of 100 was arbitrarily used for the statistics.

This analysis was performed without knowledge of the final diagnosis, nor of the ureteral status as determined by previous workup or by recent radiological procedures. Diuretic renography was analyzed in each case with regards to the kidney washout. In this study, however, the results have only been presented in detail for those cases where abnormal visualization of the ureter(s) was observed. Abnormal visualization was defined as a continuous and intense ureteral image lasting for more than 10 min.

Statistical Analysis

Unpaired Student's t-test and linear regression analysis were applied.

RESULTS

Persistent ureteral visualization was found in 17 examinations performed in 16 patients. In four cases, it was present bilaterally giving 21 kidney-ureter units for further evaluation. The diagnostic performance of the diuretic scan in the detection of an ureteral dilatation as compared to the radiological procedures is summarized in Table 1. Seven poor or nonfunctional kidneys were withdrawn from the calculations. Our results allow us to conclude that the positive predictive value was 95%, while the negative predictive value was 97%. The overall diagnostic accuracy was 96%.

TABLE 1
Diagnostic Performance of Diuresis Renography to Detect an Ureteral Abnormality Versus Radiological Findings

	RX +	RX −	Total
Scan +	20	1	21
Scan −	2	60	62
Total	22	61	83

Sensitivity = 91%; Specificity = 98%.

False-negative scans were represented by a case of slight stenosis of the ureteral orifice and a case of "adult type" ureterocele. The only false-positive case resulted from the image of a juxtavesical accumulation of the tracer associated to a different filling and emptying pattern than that of the bladder, in a patient with controlateral UPJ obstruction. In this case, x-rays failed to demonstrate any abnormality of the bladder and of the ureter.

Table 2 shows the characteristics and the scintigraphic findings of these 16 patients. As illustrated in Figure 1, the ureteral curve presents several patterns. Type I curve corresponds to the well recognized normal curve, with a sharp peak, dependent or not on the administration of a diuretic. An obstructive pattern, without any washout after furosemide, is represented by type IIa and IIb curves and, in case of a quantitatively insufficient washout (UT½ > 20 min), by a type IIc curve. These curves and the corresponding scintigraphic images are illustrated in Figure 2. Finally, a nonobstructive ureteral pattern is present either without any tracer accumulation before furosemide, with a sharp peak of radioactivity after pelvis emptying and a prompt ureteral washout (type IIIa), or with accumulation before diuresis and a rapid washout afterwards (type IIIb, Figure 3). It should be noted that the pattern of the type IIIa curve is similar to that of the normal curve (type I), but in the latter case, the ureter is visually considered as normal.

A good agreement was found between the KT½ and the UT½. Indeed, in 21 analyzed kidney-ureter units, 13 had a normal T½ and 6 a T½ >20 min for both the kidney and the ureter. There was a disagreement between the values in only one case. In another case, the UT½ was within the indeterminate range (16 min), while the KT½ was clearly of the obstructive type (29.2 min). The correlation between the two calculated T½ was significant ($r = 0.66$; $p < 0.01$). If the other quantitative parameters between the patients with an obstructive UT½ or a nonobstructive value were compared, a significantly lower T_{max} was observed in the nonobstructive cases (30.5 versus 17.8 min; $p < 0.001$). Conversely, the RA_{30} was not statistically different between these two groups (98.4% versus 88.4% = ns).

Table 3 indicates the type of therapy decided in those cases. Although no patient with both an obstructive UT½ and KT½ underwent corrective surgery of the upper tract, follow-up studies demonstrated a spontaneous regression of the hydronephrosis after successful surgery of the lower urinary tract abnormality. In the group of patients with a nonobstructive UT½, five ureters were surgically treated

TABLE 2
Clinical and Scintigraphic Findings of the Children with Persistent Ureteral Image

Patient no.	Age	Side	T½ kidney (min)	T½ ureter (min)	Ureteral curve	Diagnosis
1	9 d	L	20.6	≫	IIa	Primary megaureter
2	13 d	R	4.1	3.8	IIIb	Primary megaureter
3	14 d	R	5.4	12.1	IIIa	Ureterocele
4	1.5 mo	R	9.3	8.4	IIIb	Bilateral primary megaureter
	—	L	8.9	13.8	IIIb	
5	1.5 mo	R	3.6	2.2	IIIa	UPJ, hypospadias
6	3 mo	R	≫	≫	IIb	PUV
	—	L	26.3	68.1	IIc	
7	3 mo	L	4.0	2.4	IIIb	Primary megaureter
8	4 mo	L	29.2	16.0	IIc	PUV, renal failure vesicostomy, residual dilatation
	9.5 mo	L	14.6	8.5	IIIb	
9	5 mo	L	5.1	9.1	IIIb	Primary megaureter
10	6 mo	L	3.0	3.1	IIIb	Primary megaureter
11	10 mo	R	12.4	23.4	IIc	PUV, bilateral vesicoureteral reimplantation
	—	L	22.7	≫	IIa	
12	1.5 yr	R	4.3	8.6	IIIb	UPJ, ureter (−)
13	3.5 yr	R	7.1	8.0	IIIa	Postsurgery (VUR)
14	4.5 yr	L	27.1	28.4	IIc	Primary megaureter
15	8.5 yr	R	5.6	4.2	IIIb	Sigmoid kidney, ectopia
16	8.5 yr	R	5.0	3.5	IIIb	Neurogenic bladder, chronically infected
	—	L	23.9	≫	IIa	

PUV = posterior urethral valve; UPJ = ureteropelvic junction; and VUR = vesicoureteral reflux.

and eight did not receive any treatment. Two of these patients were later operated on for an UPJ obstruction (Patient 5, for intermittent UPJ obstruction and Patient 3 for progressive renal atrophy secondary to pelvis dilatation). In these two cases, it was clear that the progression of renal disease was not related to the ureteral abnormality which was only an accessory diagnosis. Finally, two pa-

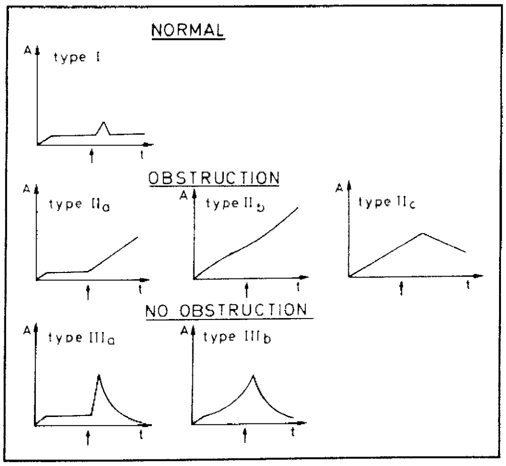

FIGURE 1. Schematic time-activity curves representing the different ureteral patterns. The time is on the horizontal axis (from 0 to 60 min); the arrow indicates furosemide injection (30 min).

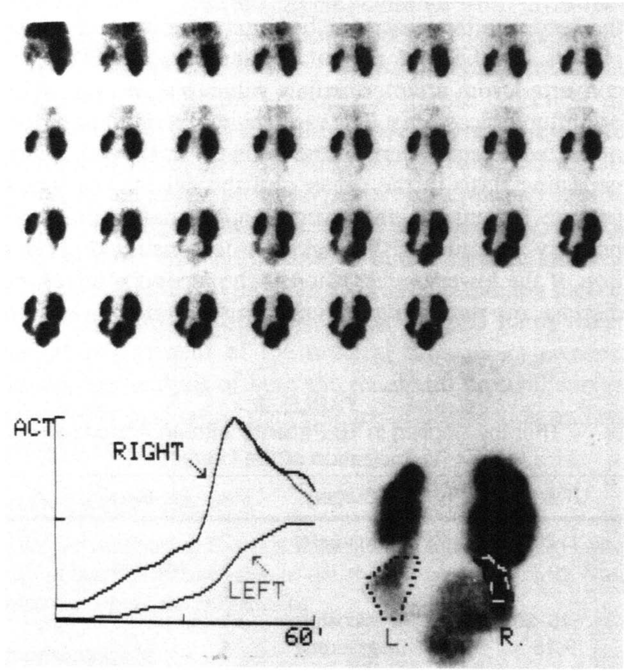

FIGURE 2. Typical example of bilateral obstructive megaureter (2-min grouped frames, posterior view). The ROIs are shown on a summed image in the right lower quadrant. The right ureteral washout is delayed (UT½ = 23 min) and the activity increases progressively after furosemide injection (30 min) in the left ureter. The right ureter has a type IIc curve and the left a type IIa.

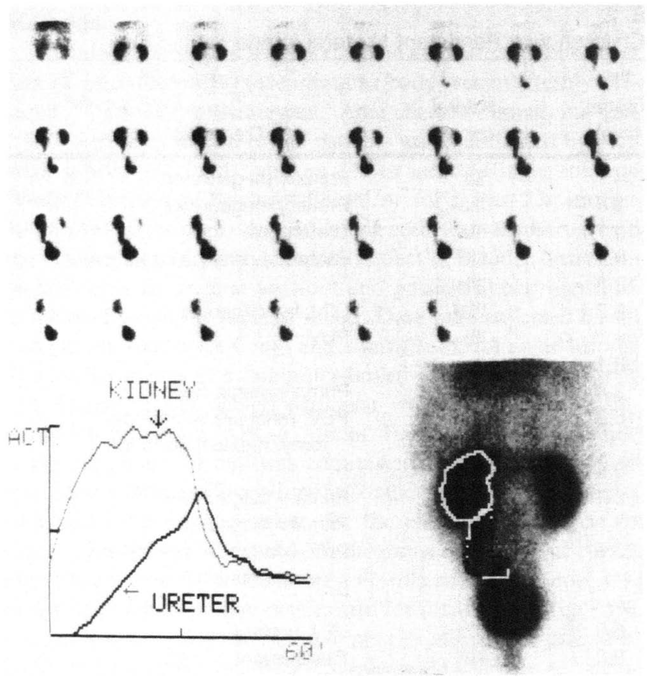

FIGURE 3. Nonobstructive left primary megaureter (2-min grouped frames, posterior view). The ROIs are shown in the right lower quadrant. The renal activity decreases rapidly after furosemide (30 min). The ureter fills progressively and empties promptly after furosemide injection. The renal curve is clearly of the nonobstructive type (KT½ = 5.1 min) and the ureteral curve is of the IIIb type (UT½ = 9.1 min).

tients were studied twice, the first for initial diagnosis and the second after treatment because of residual hydronephrosis. In the first patient (Patient 8), the UT½ was converted from an intermediate value to a nonobstructive one after vesicostomy. The radiological examination demonstrated improvement of the drainage in spite of a slight persisting stasis in the ureter and the pelvis. The second patient (Patient 14) underwent surgical management of a primary megaureter; the first scan demonstrated obstruction of the lower ureter, whereas the second scan did not disclose any remaining ureteral stasis in spite of a residual

TABLE 3
Therapy Applied in 16 Patients with an Abnormal Visualization of the Ureter

UT½ (min)	n	Surgery	n	No surgery	n
>20	7	Megaureter	2		
				Medical	1
		PUV	4		
15–20	1	Vesicostomy	1	—	—
<15	13	Megaureter	4		
				Abstention	8
		Urethral stricture	1		
Total	21		12		9

PUV = posterior urethral valve and n = number of ureters.

dilatation of the pelvis that was confirmed by subsequent x-ray procedures.

DISCUSSION

Over the last 10 years, diuresis renography has become a popular method for the differential diagnosis between obstructive and nonobstructive hydronephrosis, especially in pediatrics (*1,3,18*) and between obstructive and nonobstructive dilatation of collecting systems. Additionally, it is a simple and safe way to determine relative renal function as well as absolute glomerular filtration rate (*2,4*). Technetium-99m-DTPA is now the radiopharmaceutical of choice in the diagnosis of obstructive nephropathy (*3,19*). Iodine-123-hippurate is not readily available everywhere, while hippurate labeled with ^{131}I is not the optimal tracer for gamma camera imaging. Thus, the availability of a suitable ^{99m}Tc-labeled compound with excellent physical properties for the gamma camera and low radiation burden to the patient allows for the imaging of the ureters during diuresis renography (*15*), a diagnostic approach previously not feasible with probe renography.

Although the most common indication for diuresis renography is hydronephrosis due to UPJ obstruction, the problem raised by dilated ureters requires particular attention as presented by Koff et al. (*8,15*). These authors have published typical ureteral curves, corresponding to normal, dilated nonobstructive and obstructive patterns (*8*). In our studies, though the three main patterns were similar, it should be remembered that ureteral stasis can occur before or after furosemide administration as well. Furthermore, an additional pattern has been described which corresponds to a poor furosemide-responding system (type IIc). This pattern correlates well with a kidney response type IIIb, as previously described by O'Reilly (*17*).

The use of a quantitative washout index allows one to differentiate patients with type III (nonobstructive) from those with type IIc (obstructive) urinary tracts. The good agreement and the correlation between the T½ calculated for the kidneys and for the ureters demonstrate the close dependence of kidney drainage when the ureter appears to be dilated. Particular attention should therefore be directed to the ureteral image when obstruction is suspected at the kidney level. Indeed, none of our patients actually presented an UPJ obstruction despite a KT½ of >20 min. These cases could have been misinterpreted without knowledge of the ureteral washout as demonstrated not only by radiological procedures but also by diuresis renography itself. On the other hand, if the analysis is limited to the renal curve, in cases with a good response of the kidney to furosemide but impaired ureteral drainage (*20*) false-positives may result. Koff et al. emphasized the importance of examining the scan itself, not only the curves, when performing a diuretic urogram (*8*). They also stressed the importance of generating curves on ROIs as close as possible from the suspected site of obstruction. Our data confirm the need for defining time-activity curves for both the kidney and the ureter and of comparing them separately to obtain a more accurate and valid assessment of urinary tract drainage.

Our investigation has been limited to the pediatric population and more particularly to neonates and young infants: 62% of the patients were under the age of 1 yr. In these patients, ureteral obstruction can be the cause of hydronephrosis in up to 50% of cases (*21*). This feature is often detected by sonography but can also sometimes be missed because of the incomplete filling of the ureter at the time of sonography or because of poor contrast during IVP. Maizels recognized this potential pitfall and raised the question of associated disorders (as UPJ obstruction and an ureterocele) or tandem obstruction, a condition which was not encountered in our series (*13*).

Our results demonstrate that any abnormal visualization of an ureter represents a highly sensitive indicator of significant abnormality or dysfunction at this level which should be corroborated by radiological investigation to improve the morphological informations. At the opposite end, a negative scan would, in this respect, virtually eliminate a dilated ureter, except for those related to vesicoureteral reflux. This latter disease should be more appropriately investigated by a x-ray micturating cysto-urethrography or an isotopic cystography. The observation of a false-positive case in the bladder region is not surprising and again stresses the need to be cautious in the interpretation of any additional bladder image as recently described by Orzel and Weinberger (*22*). As mentioned above, the definition of "abnormal visualization" has been empirically stated, based on the experience of normal transient ureteral image. No attempt was made to modify retrospectively the cutoff time of 10 min in order to optimize the sensitivity or the specificity of the visualization.

Three practical lessons can be learned from this type of study. First, the use of a bladder catheter is essential to avoid artifactual effects of bladder distension (*23*) and to distinguish true upper urinary tract obstruction (UPJ or vesicoureteral junction) from lower urinary tract obstruction (posterior urethral valves, neurogenic bladder . . .), especially in sedated children (*24,25*). It could be argued that catheterization is invasive and causes infection, particularly when studying dysplastic and/or dilated systems, but it is routinely used in voiding cystography and prophylactic antibiotics can be administered in these cases. However, in selected cases, it may be of great value to first perform the scan without catheterization in order to assess the importance of the bladder filling/emptying cycle and its impact on the upper urinary tract drainage. In other selected cases, it is of interest to document the usefulness of improving bladder emptying in patients with neurogenic bladder (*26*), posterior urethral valves (*11*) or after surgery at the vesicoureteral level. In these cases, a postmicturition view as proposed by Gordon and others will complete the study (*27*). It should be noted that in our experience, despite continuous bladder drainage, activity in the bladder can be apparent even if there is passive drainage and overdistension of the bladder is avoided. This is particularly true in very young patients, as in patients with posterior urethral valves. Such an observation can be related to low hydrostatic pressure in the supine position and to the inhibition of the bladder reflexes under sedation. On a technical note, the position of the catheter must be carefully verified and when drawing ROIs caution is needed in order not to include the bladder or bladder-scattered activity in the ureteral ROIs. Second, all examinations have been performed in a supine position as generally observed in the literature. This position is indeed the most comfortable for infants. No child with massive nephroureteral dilatation was incorrectly diagnosed as being obstructive. However, when technically feasible, a sitting or erect image should be adopted (*28*). A third comment is related to the problem of severely impaired renal function with limited furosemide-induced diuresis, as we encountered in one neonate with posterior urethral valves, right renal dysplasia and left questionable dilatation. In this case, despite a possible false-positive obstructive pattern, a vesicostomy was performed followed by regression of the dilatation and the reversibility to a non-obstructed $KT_{1/2}$, while renal function showed little improvement at short-term follow-up.

In conclusion, several important facts arise from our study. First, ^{99m}Tc-DTPA diuretic renography using the gamma camera is a sensitive and specific method for detecting ureteral pathology in children with hydronephrosis if there is a continuous, intense visualization of the ureter for at least 10 min. We would again stress that such a method is not appropriate in the detection of vesicoureteral reflux, which has to be investigated by more adequate methods and that, to avoid an artifactual visualization of the ureter secondary to a vesicoureteral reflux, the use of an open bladder catheter is necessary. Second, one should be especially cautious in the interpretation of obstruction at the pelviureteric level and no therapy should be selected without knowledge of the ureteral status when evident impairment of the ureteral drainage is present. Finally, the analysis of both the renal and ureteral curves is helpful in evaluating the presence of obstruction and its precise location.

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EDITORIAL

Effects of Ureteral Function on Assessment of Hydronephrosis

The need for assessment of ureteric function in the patient with an obviously dilated ureter has increased particularly with the added spectrum of asymptomatic patients presenting with hydronephrosis and hydroureter on antenatal and perinatal ultrasound. Early detection provides both a potential for prophylaxis against urinary tract infection with subsequent renal parenchymal damage, and prophylaxis against atrophy or developmental delay from pressure effects secondary to obstruction. At present, our knowledge of the natural history of hydronephrosis continues to be defined. Prior surgical interventions were planned on anatomical findings in symptomatic patients with urinary tract infection, pain, hematuria or stone formation with detection methods that were more invasive and gave anatomical rather than physiological or functional information. It is thus important that documentation of renal function, functional effects of obstruction and response to therapy be fully evaluated, particularly in the asymptomatic patient. Correlations will maximize the advantages of early detection and minimize the effects of unwarranted intervention on the developing urinary tract, as well as providing accurate information to the family and the primary caretaker to guide decision making.

Twenty years experience with diuretic renography has allowed definition of obstructive patterns, renal and bladder function and differential clearance data. Reproducible results depend on meticulous technique, with diagnostic accuracy of diuretic renography depending upon renal function (glomerular filtration rate), as well as the distention characteristics of the pelvis and ureteric function (*1*). Adequate hydration must be assured and there should be sufficient residual renal function to allow diuretic response to define the distensibility and volume of the collecting system. Urinary bladder volume and drainage can also affect the pattern of response and the ability to interpret drainage of the lower ureter, hence the practice of bladder catheter drainage during study. Standard testing protocols are required with study design and interpretation requiring close collabora-

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