EDITORIAL

Assessment of Pediatric Hydronephrosis Using Output Efficiency

The purpose of diuresis renography is to establish or rule out obstruction because hydronephrosis may occur with and without obstruction. Obstruction is not easily defined physiologically, but the best definition may be a restriction to urine flow that, left untreated, will cause progressive renal deterioration. The effects of obstruction are recognized as hydronephrosis, parenchymal atrophy and impaired renal function. These changes are the results of obstruction but do not define or predict the potential for progressive renal deterioration (*1*). What finally matters most is the effect of obstruction on the kidney (*2,3*).

Diuresis renography is accepted by many as the most accurate test for diagnosing uretero-pelvic junction (UPJ) obstruction. Let us examine the basis of this accepted teaching. First, one needs to look at the patient population, next the definition of obstruction, then the technique and analysis of the diuretic renogram and, finally, the interpretation of these results. Having been through this sequence, one may argue that the diuretic renogram may be a rather poor gold standard for diagnosing obstruction at the UPJ in children with an ultrasound diagnosis of prenatal UPJ dilatation.

Use of the terminology UPJ obstruction immediately implies that there is an abnormality that we, the medical profession, may be able to fix and, furthermore, that surgical reconstruction is both necessary and effective. The basis for this approach came from the fact that before 1979 patients presented with intermittent loin pain and/or hematuria and that these symptoms were secondary to a UPJ obstruction. Further evidence to support this approach was that after surgery the vast majority of these patients were symptom free. The urologists who operated did so to relieve symptoms and prevent any further renal damage but did not believe that the surgery was done to improve renal function. Tests undertaken to prove the obstruction were, at times, unhelpful, and this was attributed to the intermittent nature of the UPJ obstruction. This is the background that we inherited when prenatal ultrasound was introduced in the late 1970s and early 1980s. A new group of patients was presented, all asymptomatic, very young and, by definition, with immature renal function. Previously, all these children would have been regarded as normal. The history of the treatment of these asymptomatic infants with UPJ obstruction or, rather, UPJ dilatation, has changed from the situation of many centers operating early on most infants in the 1980s to a position where only about 25% have surgery in some teaching institutions. Many centers are attempting to develop indications for surgery, but these indications are still debated. One of the major problems is that before the natural history could be accurately established, many institutions were undertaking operations at different times for different reasons. Even now the follow up of those treated conservatively is less than 20 yr, which is a short period when one considers that these children have a projected life span of over 80 yr. Furthermore, one cannot simply extrapolate from the earlier clinical experience and suggest that the intermittent nature of the classical UPJ obstruction will occur in these children with prenatal UPJ dilatation. The ultrasound evidence from follow up in these infants suggests that the dilatation is persistent in the vast majority of children.

Received Apr. 23, 1997; accepted Apr. 30, 1997.

For correspondence or reprints contact: Isky Gordon, MD, Great Ormond Street Hospital for Children, London WC1N 3 JH, England.

Definition of Obstruction

Before turning to the diuretic renogram, there is a need to look critically at the definition of UPJ obstruction. In the patient with loin pain associated with a temporary reduction of renal function, dilatation of the calyces and renal pelvis and delayed excretion of contrast or radioisotope, there is no need to look further for a definition of obstruction. However, in an asymptomatic child or the incidental finding of a dilated renal pelvis, the definition is not so easy. The techniques used have fallen into three categories. The first category is obstruction based on a diagnostic test, such as the pressure/perfusion test (Whitaker), diuretic urogram, diuretic renogram, parenchymal transit time on radioisotope renography and, finally, the histology of the resected UPJ. The second category is loss of function seen on repeated studies over a period of time. The third technique, which is still used even in the late 1990s, is that the surgeon says it looked obstructed at the time of operation.

The only unequivocal definition of UPJ obstruction is loss of renal function with time if no surgery is undertaken. This definition is not universally used because the diagnosis is made after the renal function has fallen, and most surgeons prefer to operate in order to prevent this. The use of this definition has been suggested in this asymptomatic group of infants/children (*4*).

Let us examine the evidence for the definitions of obstruction based on the pressure/perfusion test and diuretic urogram/renogram. In 1965, Baklund et al. (*5*) described five symptomatic children who had pressure perfusion studies before surgery for UPJ obstruction. These authors described perfusion at different rates to maintain a constant pressure. The results did not allow any conclusion as to the definition of obstruction. Currently, the diagnosis of obstruction is said to occur when the pressure is above 23 cm water at a flow rate of 10 ml/min, yet the evidence to support this definition is minimal. In his original article, Whitaker (*6*) described 11 cases of UPJ obstruction in which the pressure equilibrated at 23 cm water when the vessel crossing the renal pelvis was lifted free. These cases were defined as obstruction on clinical and surgical grounds. Other studies are in children with a mixed group of diagnoses and use different pressure levels to define obstruction, yet the validation of the diagnosis of obstruction was the operative finding, an endpoint not accepted by many pediatric urologists. (*7–9*). Although the pressure/perfusion test is accepted by many as the reference technique, there is little evidence to support the values used, especially in this group of young infants with prenatal UPJ dilatation.

Diuretic Urogram. The diuretic urogram is based on an anatomical definition related to the increase in size of the calyx after a diuretic stimulus. In one study, 20 adult patients with urographic evidence of unilateral, moderately wide renal pelves were examined by routine and diuretic urography. Planimetry of the corresponding calyx system of the two examinations was performed. An increase in size by more than 20% after osmotic diuresis indicated an obstruction of the pelvi-ureteric junction in kidneys with moderately wide renal pelves. These authors did not, however, define the independent reference technique against

which to make the diagnosis of obstruction (*10,11*).

Diuretic Renogram. In the late 1970s, there were several articles on the value of the diuretic renogram technique. The diuretic response was divided into four groups: Type I, normal; Type II, obstructed; Type IIIa, atonic; and Type IIIb, partially obstructed (*12*).

Confirmation that the above four patterns are accurate requires careful analysis. In the article, by Lupton et al. (*13*), there is corroborative evidence from histology of the resected specimens while in the papers by Koff et al. (*14,15*), there is confirmation by pressure/perfusion studies. Both papers also state that at the time of surgery "the appearances were those of obstruction." There is debate in the pathological literature as to whether the histological changes reported are primary or secondary to the dilatation (*16*). The conclusion reached was that "the diuretic radionuclide urogram is a simple, rapid and noninvasive technique to determine whether true obstruction exists in dilated nephroureteral systems" (*17*).

Many early studies state that failure to wash out in the presence of either gross dilatation or a full bladder should be interpreted with caution (*18*). Poor washout can occur with poor renal function (*19,20*) or with renal immaturity. Koff et al. suggested that only after the age of 4 mo could one rely on the diuretic renogram (*21*). Renal maturation is an ongoing process with adult values of glomerular filtration (GFR) only reached at about 2 yr of age, although tubular maturation proceeds more rapidly with 80% of maturation occurring by the end of the first year of life (*22*). The diuretic renogram may be undertaken in many different ways. In pediatrics, the well-tempered diuretic renogram (WTDR) (*23*) has been suggested. Since it requires intravenous fluids before the injection of radioisotope and a bladder catheter, it accounts for most variables. As noted in O'Reilly et al. (*24*) the WTDR is aimed at the neonate, but very few children have diuretic renography during this very early period of life. Furthermore, the routine use of intravenous fluids and a bladder catheter "may result in an overkill" and are not routinely used in all departments. The analysis of the diuretic response is considered by O'Reilly et al. Visual interpretation of the curves is strongly recommended since it "is accurate in the overwhelming majority of cases." However, the statement that "an obstructed response... should be considered obstructive" shows the circular nature of the argument that is ongoing. Quantification of the diuretic washout curve is considered unhelpful since it may vary with radiopharmaceutical and the renogram technique, be institution specific and not easy to reproduce between departments (*24*).

Comparison of the diuretic renogram with other techniques gives differing results. O'Reilly et al. (*25*) showed close correlation with parenchymal transit times in 85% of cases, correlation in 78% with pressure perfusion measurements and 88% with morphological studies. However, there are numerous articles that fail to show close correlation between the results of pressure perfusion and the radionuclide diuretic washout. Poulsen et al. concluded that there was no correlation between the presence of organic stenosis or external compression and the outcome of the diagnostic tests. Furthermore, they claim that the currently used diagnostic procedures for hydronephrosis generally are insufficient to discriminate between significant and nonsignificant obstruction (*26,27*). Further doubt is cast by the possibility of a false-negative diuretic renogram. Hay et al. (*28*) report that the detection of a Type I or Type IIIa response in a dilated, painful system cannot be taken to exclude obstruction.

Interpretation of Results

In the asymptomatic infant who has been identified through prenatal ultrasound as having UPJ dilatation, there is no gold standard for the prospective diagnosis of obstruction. Follow-up studies in asymptomatic children with prenatal diagnosis of UPJ dilatation treated conservatively suggest that there is a small proportion of kidneys that deteriorate. Ransley et al. (*29*) suggested a figure of 25% while Koff et al. (*30*) suggested 7% and concluded that UPJ dilatation is a relatively benign condition. This latter work also showed the inaccuracy of the diuretic renogram in the diagnosis of obstruction; an observation made by other investigators (*31*). Bearing these factors in mind, how can the results of diuretic renography be applied to the infants and children who are asymptomatic with a prenatal diagnosis of UPJ dilatation? These results suggest that the definition of obstruction in the asymptomatic infant is unclear, especially since obstruction is a relatively uncommon occurrence in this group, and the diagnosis can only be established retrospectively if there is a fall in renal function.

The article by Saunders et al. in this month's journal tackles the important issue in diuretic renography of taking renal function into account when judging the response to a diuretic challenge. This approach is physiologically sound since renal function has been recognized as an important variable since the introduction of diuretic renography. If two kidneys have filtration rates in which one is half the other, then it is logical to expect that the kidney with the poorer function will clear the isotope from the blood slower and its response to a diuretic stimulus will be slower. This paper is therefore important and builds on the work of Chaiwatanarat (*32*). The quantification of the results also is useful and allows comparison both of sequential studies in the same patient as well as between patients. The problem that the authors face (and the community at large dealing with children with prenatal UPJ dilatation) is how to judge these results. If these results are simply compared to the classical four groups of washout curves and there is a difference, how do they know which test is correct? Since there is serious doubt whether obstruction exists, even when the "obstructed pattern" based on the classical method of analysis is observed, how can the authors evaluate these new results, especially if the two techniques give different answers? Since the incidence of obstruction in this group of children is very low, one should consider instead the diuretic renogram as providing essential information about renal function, as well as drainage, and so helps reveal the pathogenesis of UPJ dilatation in infants and children who have been identified on the basis of a prenatal diagnosis of UPJ dilatation. The diuretic renogram, thereby, allows the natural history to be written and management based on sound observations.

Isky Gordon
Great Ormond Street Hospital for Children
London, England

REFERENCES

1. Koff SA. Problematic ureteropelvic junction obstruction. *J Urol* 1987;138:390.
2. Whitaker RH. Some observations and theories on the wide ureter and hydronephrosis. *Br J Urol* 1975;47: 377–385.
3. Whitaker RH. The Whitaker test. *Urol Clin North Am* 1979;6:529–539.
4. Nonomura K, Yamashita T, Kanagawa K, Itoh K, Koyanagi T. Management and outcome of antenatally diagnosed hydronephrosis. *Int J Urol* 1994;1:121–128.
5. Backlund L, Groote G, Reuterskiold AG. Functional stenosis as a cause of pelvi ureteric obstruction and hydronephrosis. *Arch Dis Child* 1965;40:203–206.
6. Whitaker RH. Diagnosis of obstruction in dilated ureters. *Ann R Coll Surg Engl* 1973;53:153–166.
7. Whitaker RH. Methods of assessing obstruction in dilated ureters. *Br J Urol* 1973;45:15–22.
8. Whitfield HN, Britton KE, Fry IK, Hendry WF, Nimmon CC, Travers P, Wickham JE. The obstructed kidney: correlation between renal function and urodynamic assessment. *Br J Urol* 1977;49:615–619.
9. Whitfield HN, Harrison NW, Sherwood T, Williams DI. Upper urinary tract obstruction: pressure/flow studies in children. *Br J Urol* 1976;48:427–430.

10. Bratt CG, Aurell M, Nilson A, Nilsson S. Diuretic urography and renography in the diagnosis of hydronephrosis. *Contrib Nephrol* 1978;11:142–145.
11. Nilson AE, Aurell M, Bratt CG, Nilsson S. Diuretic urography in the assessment of obstruction of the pelvi-ureteric junction. *Acta Radiology Diagn Stockh* 1980;21:499–503.
12. O'Reilly PH, Lawson RS, Shields RA, Testa HJ. Idiopathic hydronephrosis–the diuresis renogram: a new noninvasive method of assessing equivocal pelviouretеral junction obstruction. *J Urol* 1979;121:153–155.
13. Lupton EW, Testa HJ, Lawson RS, Edwards EC, Carroll RN, Barnard RJ. Diuresis renography and the results of pyeloplasty for idiopathic hydronephrosis. *Br J Urol* 1979;51:449–453.
14. Koff SA, Thrall JH, Keyes JW Jr. Assessment of hydroureteronephrosis in children using diuretic radionuclide urography. *J Urol* 1980;123:531–534.
15. Koff SA, Thrall JH, Keyes JW Jr. Diuretic radionuclide urography: a noninvasive method for evaluating nephroureteral dilatation. *J Urol* 1979;122:451–454.
16. Gosling JA, Dixon JS. Functional obstruction of the ureter and renal pelvis. A histological and electron microscopic study. *Br J Urol* 1978;50:145–152.
17. O'Reilly PH, Testa HJ, Lawson RS, Farrar DJ, Edwards EC. Diuresis renography in equivocal urinary tract obstruction. *Br J Urol* 1978;50:76–80.
18. Gordon I, Mialdea Fernandez RM, Peters AM. Pelviuretic junction obstruction: the value of post-micturition view in ^{99m}Tc-DTPA diuretic renography. *Br J Urol* 1988;61:409–412.
19. Hjortso E, Fugleberg S, Nielsen L, Gjorup T, Hartling O, Munck O. Diuresis renography in patients with reduced renal function. *Dan Med Bull* 1988;35:294–295.
20. Kass EJ, Majd M. Evaluation and management of upper urinary tract obstruction in infancy and childhood. *Urol Clin North Am* 1985;12:133–141.
21. Koff SA, McDowell GC, Byard M. Diuretic radionuclide assessment of obstruction in the infant: guidelines for successful interpretation. *J Urol* 1988;140:1167–1168.
22. Lythgoe MF, Gordon I, Anderson PJ. Effect of renal maturation on the clearance of ^{99m}Tc MAG3. *Euro J Nucl Med* 1994;21:1333–1337.
23. Conway JJ, Maizels M. The "well tempered" diuretic renogram: a standard method to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis. A report from combined meetings of the Society for Fetal Urology and members of the Pediatric Nuclear Medicine Council, the Society of Nuclear Medicine. *J Nucl Med* 1992;33:2047–2051.
24. O'Reilly P, Aurell M, Britton K, Kletter K, Rosenthal L, Testa T. Consensus on diuresis renography for investigating the dilated upper urinary tract. Radionuclides in Nephrourology Group Consensus Committee on Diuresis Renography. *J Nuklearmedizin* 1996;37:1872–1876.
25. O'Reilly PH, Testa HJ, Lawson RS, Farrar DJ, Charlton Edwards E. Diuresis renography in equivocal urinary tract obstruction. *Br J Urol* 1984;56:84.
26. Poulsen EU, Frokjaer J, Taagehoj Jensen F, et al. Diuresis renography and simultaneous renal pelvic pressure in hydronephrosis. *J Urol* 1987;138:272–275.
27. Gonzalez R, Chiou R. The diagnosis of upper urinary tract obstruction in children: comparison of diuresis renography and pressure flow studies. *J Urol* 1985;133:646–649.
28. Hay AM, Norman WJ, Rice ML, Steventon RD. A comparison between diuresis renography and the Whitaker test in 64 kidneys. *Br J Urol* 1984;56:561–564.
29. Ransley PG, Dhillon HK, Gordon I, Duffy PG, Dillon MJ, Barratt TM. The postnatal management of hydronephrosis diagnosed by prenatal ultrasound. *J Urology* 1990;144:584–587.
30. Koff SA, Campbell KD. The nonoperative management of unilateral neonatal hydronephrosis: natural history of poorly functioning kidneys. *J Urol* 1994;152:593–595.
31. Gordon I, Dhillon HK, Gatanash H, Peters AM. Antenatal diagnosis of pelvic hydronephrosis: assessment of renal function and drainage as a guide to management. *J Nucl* Med 1991;32:1649–1654.
32. Chaiwatanarat T, Padhy AK, Bomanji JB, Nimmon CC, Sonmezoglu K, Britton KE. Validation of renal output efficiency as an objective quantitative parameter in the evaluation of upper urinary tract obstruction. *J Nuklearmedizin* 1993;34:845–848

Adrenal Glands Imaging with Indium-111-DTPA-D-Phe^1-Octreotide Following ACTH Therapy

Mordechai Lorberboym, Peter Rubin, Richard Warner and Josef Machac

Divisions of Nuclear Medicine and Gastroenterology, Departments of Radiology and Medicine, Mount Sinai School of Medicine, New York, New York

Somatostatin receptors have been identified in a variety of neuroendocrine tumors and activated leukocytes. A high density of somatostatin receptors is also present in most intestinal intramural veins of patients with inflammatory bowel disease. We present a case of a 25-yr-old female with severe Crohn's disease unresponsive to medical therapy, including adrenocorticotropic hormone (ACTH) administration. The patient underwent ^{111}In-DTPA octreotide scintigraphy to evaluate the potential role of somatostatin receptor imaging in inflammatory bowel disease. Despite the lack of significant somatostatin receptors in the affected bowel, an unexpected prominent activity of ^{111}In-DTPA octreotide was noted in the adrenal glands on the SPECT images, presumably resulting from excessive stimulation by ACTH. The expression of somatostatin receptors in the stimulated adrenals may be used to image other adrenal pathologies and could potentially indicate response to therapy.

Key Words: somatostatin receptors; adrenocorticotropic hormone; Crohn's disease

J Nucl Med 1997; 38:1489–1491

Somatostatin is a small regulatory peptide that exerts an inhibitory effect on a broad spectrum of physiologic functions. The somatostatin analog octreotide labeled with ^{111}In-DTPA-D-Phe^1 is used to localize a wide variety of neuroendocrine and non-neuroendocrine tumors that possess a high number of somatostatin receptors (*1–5*). In addition, tracer uptake in granulomas and inflammatory foci in autoimmune diseases was successfully imaged (*6*).

The known expression of somatostatin receptors in inflammatory cells was used in our patient to evaluate a potential role for octreotide scintigraphy in inflammatory bowel disease. A nonphysiologic stimulation by external adrenocorticotropic hormone (ACTH) in this patient revealed an unexpectedly high receptor expression in the adrenal glands.

CASE REPORT

A 25-yr-old woman with a history of Crohn's disease since 1981 underwent ileal resection in 1987 after developing a fistula to the bladder. In 1990, she had recurrent loose bowel movements, rectal pain, tightness and bleeding. Sigmoidoscopy revealed active Crohn's disease of the rectum and left colon. The patient was intolerant to steroids (developing psychosis) and was treated with cyclosporine, klotrix (potassium chloride) and ACTH 40 U intravenously every day. She underwent a secondary ileocolectomy and ileosigmoid anastomosis. However, the patient did not respond well to surgery. A ^{111}In-DTPA octreotide scan was performed to evaluate the potential role of somatostatin receptor imaging and determine the extent of residual inflammatory bowel disease. The patient was injected with 4 mCi ^{111}In-DTPA octreotide, followed by anterior and posterior whole-body images at 4 and 24 hr postinjection and a SPECT study of the abdomen. The planar images were unremarkable except for a large spleen (Fig. 1). The

Received Aug. 29, 1996; revision accepted Oct. 21, 1996.

For correspondence or reprints contact: Mordechai Lorberboym, MD, Department of Nuclear Medicine, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY 10029.