

SPECIAL ARTICLE

Reflux Nephropathy and Vesico-Ureteric Reflux in Children - Radionuclide Technique

by

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Introduction

Reflux nephropathy is defined as 'renal scarring' associated with vesico-ureteral reflux (VUR) and consists of calyceal clubbing or deformity with overlying cortico-medullary scarring. The older terms chronic pyelonephritis and chronic atrophic pyelonephritis should be strictly defined as a persistent or recurrent bacterial infection of the kidney involving the renal parenchyma and the pelvi-calyceal system with exudation of inflammatory cells.

Reflux nephropathy and chronic atrophic pyelonephritis begin with reflux at the vesico-ureteral junction. VUR is the abnormal regurgitation of urine back into the kidneys. It is found in 30 to 50 percent of children who have urinary tract infections and in younger children rather than older children. Reflux

nephropathy occurs in only one-third of patients who have both reflux and urinary tract infections.

Radionuclide studies are particularly well suited to paediatrics as renal problems in children are part of a dynamic process which often requires a serial number of assessment. Nuclear medicine, the absence of side-effects, low radiation dose and ready acceptance by children and parents have added to their popularity. A number of different physiological and functional parameters can be evaluated using the appropriate radiopharmaceuticals and methods of analysis. The techniques are complementary to radiological investigations and add important functional parameters not obtained by those investigations.

Radionuclide investigations

With current gamma cameras and dedicated nuclear medicine computers, 7 radionuclide studies are applicable.

1. Direct Radionuclide cystogram (DRC)

This technique is used for the detection of VUR. The bladder is catheterised and normal saline with Tc-99m Sulphur Colloid (37MBq) instilled into the bladder until filled. The patient then voids. Continuous collection of data onto computer allows reflux to be detected and its dynamics recorded at any and all times

during the study. Estimates of bladder capacity, volume of reflux, residual volume, average voiding flow rate and simultaneous recording of intravesical pressure can be made. Reflux occurs at different phases of the DRC. Conway (1974) and Treves (1985) described VUR during filling only in 3% and 21%; during voiding only in 17% and 9%; and during filling and voiding in 80% and 70% respectively [1,2]. The interpretation of reflux is based on the international grading [3]. The schema is shown in Figure 1.

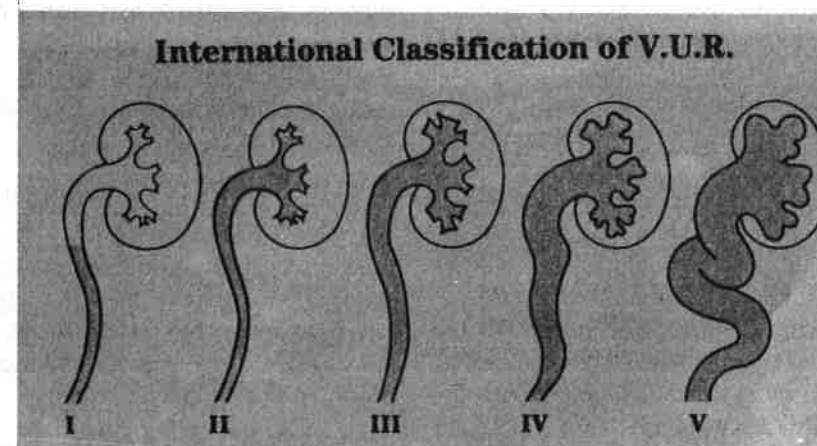


Figure 1.

- Grade I : Ureter only
 Grade II : Ureter, pelvis and calyces ; no dilatation, normal calyceal fornices.
 Grade III : Mild or moderate dilatation and/or tortuosity of the ureter and mild or moderate dilatation of the renal pelvis. No or slight blunting of the fornices.
 Grade IV : Moderate dilatation and/or tortuosity of the ureter with moderate dilatation of the renal pelvis and calyces and complete obliteration of the sharp angles of the fornices, but maintenance of papillary impressions in the majority of calyces.
 Grade V : Gross dilatation and tortuosity of the ureter, renal pelvis, and calyces; papillary impressions are not visible in the majority of calyces.

The ability to define the configuration of the collecting system is not as accurate as the radiographic study. A major advantage of the DRC is the low radiation dose which is approximately 1/20th of the contrast micturating cystourethrogram (MCU) [4] (see Table 1).

2. Indirect Radionuclide Cystogram (IRC)

This technique is developed so the patient did not need to be catheterised. It is not as accurate as the direct methods. In two series the IRC missed 20% of high grade reflux, 40% of low grade reflux and had a sensitivity of 68% [5]. We do not recommend the IRC unless the patient refuses or cannot be catheterised.

3. Differential Renal DMSA Scan (Tubular Mass)

Tc-99m Dimercaptosuccinic acid (DMSA) once injected intravenously accumulates in the proximal tubules. After three hours differential function is calculated and images are taken in the posterior, left posterior oblique, right posterior oblique and anterior positions. Scarred kidneys are indentified as polar, focal and diffuse. Mild scarring is considered if there is no more than 2 areas involved, severe scarring is more generalised with more calyces involved but with some normal areas. Diffuse scarring shows a generalised thinning of the renal parenchyme usually with marked prominence of calyces. It may be difficult to differentiate between a small diffusely scarred kidney and a dysplastic kidney. DMSA is an amino acid analogue, and is handled by the kidney in much the same way as amino acids are. It is taken up and retained by the cortical tubular cells and only a small amount is excreted in the urine. If the function of these cells is compromised, either temporarily because of acute inflammation,

or permanently because of scarring, that fact will show up as a photon-deficient area on the scan [6,7].

4. Differential Renal Scan +/- Diuretic Stress

This technique uses Tc-99m Diethylene triamine pentaacetic acid (DTPA), as an analogue of creatinine or inulin; it is filtered by the glomerulus and neither absorbed nor secreted by the tubules. Its excretion, therefore reflects the glomerular filtration rate which allows measurement of perfusion, differential renal function and quantitation of urine clearance. The major indication is determining whether dilatation is obstructive or non-obstructive in nature. The technique is very accurate, reproducible and useful in serial assesment. It has been used at the Childrens Hospital, Camperdown, Sidney with a sensitivity of 92%, specificity of 97% and an accuracy of 96% .

5. Single Photon Emission Computed Tomography (SPECT)

More recent gamma cameras are able to rotate around the patient and the computer reconstructs the study in transaxial, coronal and sagittal scans. This increases the sensitivity of DMSA and Gallium 67 studies.

6. Volume Expansion Diuretic Renal Scan (VEDRS)

This study is a modification of a differential renal scan. In some patients there is marked dilatation of the pelvicalyceal system or ureter e.g. posterior urethral valves and large megaureters. If other studies are equivocal or abnormal a VEDRS is recommended. This involves intravenous hydration of the patient with 360 ml.sq.m of 0.9% normal saline prior to the diuretic renal scan. This stresses the urinary system over a longer period of time

and with administration of a diuretic during the renal scan further excentuates any obstruction. If there is a coexisting reflux or a large neurogenic bladder a catheter should be placed in the bladder prior to the study.

7. Gallium - 67 Study

The Gallium 67 scan is used in the detection of acute inflammatory processes. It is also used in detecting acute renal infection or perinephric abscesses.

Clinical Indications For Radionuclide Studies In V.U.R

1. Vesico-Ureteric Reflux

The DRC is the most sensitive method for the continuous detection of VUR during filling and voiding phases. The DRC is more sensitive than the MCU. Conway (1974) in 100 patients found agreement in 86 cases, while 9 had positive DRC and negative MCU. Five patients had a positive MCU and negative DRC [1]. More recently Nasrallah (1982) described in 86 patients an agreement in 78% , positive DRC and negative MCU in 13%, bilateral VUR on DRC and unilateral VUR on MCU 4.5% and a positive MCU and negative DRC in 4.5% [8]. The DRC is recommended in : a. The follow up of VUR in patients managed non-operatively; b. Screening of VUR in female patients with UTI; c. Follow up after anti-reflux surgery; d. Detection of VUR in siblings (familial reflux).

2. Renal Scars

The most sensitive and accurate test for the detection of renal scarring is by the Tc-99m DMSA scan [9,10]. Merrick (1980) compared DMSA and glucoheptonate renal scans with intravenous pyelography in 79 children who had proved urinary tract infection and had been followed for a period of 1 to 4 years [11]. The sensitivity for detection of pyelonephritic scarring on intravenous pyelography in this group of patients was 86 % and the specificity 92 %, whereas renal cortical scintigraphy had a sensitivity of 96% and a specificity of 98%.

DMSA is a radionuclide agent which is fixed by the renal tubules with only minimal excretion. Therefore, it is optimal for morphological visualization of the functioning of the renal parenchyme and is considered the cortical scanning agent of choice for demonstrating postinflammatory renal scars [12]. Data from Prince of Wales Children Hospital and Wesmead Centre, Sydney found in 197 kidneys concordant results in 78% and dicordant results in 22%. Of this latter results 27 were abnormal on DMSA but normal or equivocal on IVP and 4 which were abnormal or equivocal on IVP or USG were normal on DMSA. The addition of SPECT to DMSA studies increases the sensitivity [13]

3. Acute Pyelonephritis (APN)

APN is often difficult to diagnose. Tc-99m DMSA and Gallium 67 are sensitive in the detection of acute inflammation. DMSA studies show distinctive striated flare defects which usually return to normal with treatment.

4. Post Surgical Assessment

Several complications may occur after reimplantation of the ureters.

- Residual VUR can be assessed by DRC.
- Renal function and significance of dilatation of the pelvi-calyceal system and

ureters should be assessed by the differential renal scan with diuretic stress.

- c. Development or progression of renal scars should be assessed by DMSA.

5. *Vesico-Ureteric Reflux and Co-Existing Pelvic Ureteric Junction (PUJ) Obstruction*

This is a difficult diagnostic problem where there is VUR diagnosed on MCU or DRC and

severe dilatation of the pelvicalyceal system. The differential renal scan with diuretic stress and a catheter placed in the bladder will usually be able to diagnose whether significant obstruction is present. The differential or not a functional estimate and quantitation of urine clearance are important parameters to determine prior to surgery and in serial post-operative assessment.

Table 1. Comparison of radiation dosage sustained in the course of various imaging procedures of the urinary tract in childhood

	MCU	DRC	IVP	DMSA 80 MBq
EDE	5.4 mSv	0.3 mSv	4.4 mSv	1 mSv
Gonad dose	6.0 mSv (M)	<0.02 mSv (M)	4.34 mSv (M)	0.96 mSv (M)
	1.0 mSv (F)	0.02 mSv (F)	3.58 mSv (F)	0.48 mSv (F)
Kidney dose	2 mSv	Negligible	5.6 mSv	13.4 mSv

EDE : Effective dose equivalent

(Chantler et al., 1991) [4]

M/F : Male/ female

mSv : Milli Sievert

MBq : Mega Backquerel

Legends

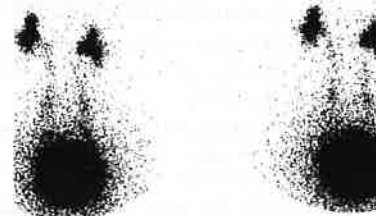


Figure 2. Direct radionuclide cystogram.



Figure 3 : Radionuclide DMSA study.

This 7-year-old girl presented with vomiting and intermittent temperatures to 39,5° C. A urine culture of *Escherichia coli* was obtained. The patient was catheterized and 120ml of saline with tracer instilled into the bladder. Mid-way through the filling phase of the study there was right sided vesico-ureteric reflux and soon after left sided vesico-ureteric reflux. This occurred to the level of the renal pelvis in both kidneys and that did appear to be mild dilatation of the renal pelvis bilaterally. This persisted during the voiding phase of the study and in the post-void study there was residual activity in the pelvi-calyceal system of both kidneys. Findings are consistent with bilateral grade 3 vesicoureteric reflux.

This 6-year-old girl had vesico-ureteric reflux on the left and intermittent UTIs for several years. The most recent UTI occurred 1 month before this examination. Large focal defects in tracer uptake are seen throughout the left kidney on posterior projection (arrows). The left kidney is small compared to the right. The differential function (tubular mass) revealed right kidney 65% , left kidney 35% .

Conclusion

Nuclear Medicine has many advantages in the investigation of genito-urinary disorders. The techniques described are accurate, reproducible, readily accepted by patients

and parents and are complimentary to radiological investigations in the management of reflux nephropathy and vesico-ureter reflux.

REFERENCES

1. Conway JJ, Belman AB, King LR. Direct and indirect radionuclide cystography. *Semin Nucl Med* 1974;4(2):197-211.
2. Treves ST. *Pediatric Nuclear Medicine*. Chs 4 and 5. Springer-Verlag 1985; 63-120.
3. Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Mobius TE.: International system of radiographic grading of vesicoureteric reflux. *Pediat radiol* 1985; 15 :105-9.
4. Chantler C, Berman LH, Collen-Jones F et al. Guidelines for the management of acute urinary tract infection in childhood. *J. R Coll Phys Lond* 1991; 25 (1):37-41.
5. Bower G, Lovergrove FT, Geijssel H. Comparison of direct and indirect radionuclide cystography. *J Nucl Med* 1985; 26 : 465-8.
6. Knight JF. Urinary tract infection. Current opinion in pediatrics. 1991; 3: 42-7.
7. Majd M. Radionuclide renal imaging in pediatrics, selected topics. *Pediatrics Imaging Update 1991*, Berns Congress Stockholm, Sweden, May 27-31, 1991.
8. Nasrallah PF, Nara S, Crawford J. Clinical indications of nuclear cystography. *J Urol* 1982; 128: 550-3.
9. Smellie JM. The DMSA scan and intravenous urography in detection of renal scarring. *Pediat Nephrology* 1989; 3: 6-8.
10. Slovis TL, Sty JR, Haller JO. *Reflux Nephropathy in Imaging of the pediatric urinary tract*. Philadelphia: W.B.Saunders. 1989: 202-4.
11. Merrick MV, Utterly WS, Wild SR. The detection of pyelonephritic scarring in children radioisotop imaging. *Brit J Radiol* 1980; 53: 544-56.
12. Rushton HG. Work-up of the child presenting with urinary infection in Alan J. Wein. *Common Problems in Urology*, St. Louis: Mosby Year Book, 1991: 423-47.
13. Howman-Giles R.: Personal communication, 1991.