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ORIGINAL ARTICLE

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Percutaneous direct radionuclide cystography in children: description of technique and early experience

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Abstract *Aims*. To describe a new test for vesicoureteric reflux in children and assess patient preference compared to indirect radionuclide cystography.
Materials and methods. One hundred and three toilet-trained children aged between 2.1 and 15.6 years underwent percutaneous injection of 10–20 MBq of 99m-technetium-labelled mercapto-acetyl-triglycine (MAG3) into the full bladder after the application of anaesthetic cream. Gamma camera images of the bladder and renal areas were recorded during a 5-min resting period and during micturition.
Results. All procedures were successful, 97 with a single stab. Fifty-four of the 66 children who expressed a preference preferred percutaneous suprapubic injection to intravenous injection. Images were easy to interpret and there were no indeterminate results. Of 200 renal units, 33 refluxed during the resting phase and 31 during micturition. In 24 renal units, reflux was only demonstrated during the resting phase. Reflux was significantly associated with abnormalities on dimercaptosuccinic acid (DMSA) scans ($P < 0.00\,1$).
Conclusions. The new technique of direct percutaneous radionuclide cystography is described. It was well tolerated by patients. It detects reflux during the resting phase that would be missed on the indirect study and avoids doubt as to whether activity in the renal areas is due to reflux or excretion. Free pertechnetate could be used and would be much cheaper.

Keywords Radionuclide cystography · Vesicoureteric reflux · Vesicorenal reflux · Children

Introduction

Indirect radionuclide cystography (IRC) has been one of the cornerstones of investigation of renal tract infection for more than two decades, and good overall agreement between micturating cystography (MCU) and IRC has been demonstrated [1, 2, 3, 4]. Direct radionuclide cystography (DRC) has been compared to IRC and found to be preferable because of ease of assessment and lower radiation dose [5]. DRC is not widely used because it involves catheterisation, which is poorly tolerated in older children and carries a risk of introducing infection. No reports could be found in the literature of DRC by percutaneous injection, which would obviate the need for catheterisation.

This study was performed to assess patient acceptability of percutaneous injection of radionuclide using the suprapubic approach, which is widely used clinically to obtain urine samples for culture. Small volumes of radionuclide can be introduced into the bladder percutaneously by suprapubic puncture, which is easily performed when the bladder is full, so this approach is only reliable in the toilet-trained child. This route of access to the bladder minimises the risk of infection and should be

better tolerated than catheterisation in this age group. Vesicoureteric reflux can be evaluated under physiological conditions of resting and micturition without the presence of a catheter. In a direct radionuclide cystogram the presence of any activity in the ureters or kidneys indicates reflux, making the study easier to interpret than an indirect study when upper-tract activity may be due to excreted radionuclide.

Materials and methods

One-hundred and three children (34 boys, 69 girls) aged between 2.1 and 15.6 years (mean 7.6 years) underwent percutaneous DRC. Most of the children had been referred by paediatric surgeons for the assessment of suspected vesicoureteric reflux prior to, or following cystoscopic submucosal injection of Macroplastique (Uroplasty BV, Hertogsingel, 54, 6214 AE Maastricht, The Netherlands) adjacent to the vesicoureteric junction. An information sheet was given to all the parents beforehand and consent obtained by the consultant paediatric radiologist (A.G.W.) who performed all the procedures. The children attended at least 45 min prior to their appointment time for application of EMLA cream to the suprapubic area. During this period the children who had recently micturated were encouraged to drink so that the bladder would be full, thus facilitating the injection. When the children said they needed to micturate, the fullness of the bladder was checked with US; if the bladder was not full, the procedure was delayed. When the bladder was considered to be adequately distended, the distance from the skin surface to the bladder lumen was measured by US (which was usually performed on the gamma camera couch using a portable ultrasound machine). The size of needle used for the injection depended on the skin-lumen distance: if less than 12 mm, a 25-gauge 25-mm needle was used; if 12–18 mm, 23-gauge 30-mm; if 18–30 mm, 22-gauge 4-cm; and if over 30 mm, 21-gauge 15-cm. A 25-gauge needle was used in 77 children, 23-gauge needle in 18, 22-gauge needle in 6 and a 21-gauge needle in 2. A sharp stab was used to insert the needle into the bladder in a position previously selected by US. A flexible connecting tube was attached to the needle hub and urine was aspirated to check the correct position of the needle tip in the lumen of the bladder.

Approximately 10 MBq of ^{99m}Tc-labelled MAG3 in a volume of 1–2 m1 was injected if the child was less than 5 years old and 20 MBq if the child was 5 years or older. Injection was performed whilst observing the gamma camera screen to check that activity spread throughout the bladder without local extravasation. The needle was then withdrawn and imaging commenced (Scintag Berthold Ltd gamma camera model GRC 1 with general-purpose collimator, MICAS Sparcstation 5 computer system). Posterior resting-phase images of the bladder and renal areas were acquired in 10-s frames for 5 min with the child supine on the couch. The camera was then placed erect and the patient seated in front of the camera for a standard micturition study (100 frames of 5 s). At the end of the procedure the children were asked whether they preferred an IV injection (which they had all had previously) or the suprapubic puncture. This was by questionnaire (Appendix) in 34 and direct questioning in 69. The form of the question was identical whether written or verbal.

Analysis of the data was performed with regions of interest being drawn around the bladder and the kidneys and time-activity curves constructed for both phases. A single consultant paediatric radiologist (A.G.W.) reported the examinations after review of the analogue images, the time activity curves and the cine images.

Details of previous imaging were obtained: 65 of the 103 children had undergone previous IRC and 87 had undergone dimercaptosuccinic acid (DMSA) scanning. The mean delay between previous IRC and the DRC was 12.4 months. Mean age for the indirect study was 6.95 years and 7.98 years for the direct study. In the interval between indirect and direct studies, 48 renal units in 32 children were subject to an antireflux procedure (STING procedure in 46, reimplantation of vesicoureteric junction in 2) and 76 renal units in 47 children did not undergo any procedure.

Results

There were no technical failures. In 97 children the bladder was punctured with a single stab, 5 children required two stabs and 1 child three stabs. All injections were intravesical without perivesical leakage of activity. No complications, such as haematuria or urinary tract infection, were reported. Fifty-four children preferred suprapubic puncture to IV injection, 31 had no preference and 12 preferred IV injection; a response was not obtained from 6 children.

Five children failed to micturate, in three of whom bilateral reflux was demonstrated at rest.

The number of renal units in which reflux was demonstrated is shown in Table 1. Of 200 renal units in 103 children, 55 renal units in 39 children showed reflux. Thirty-three units refluxed during the resting phase and 31 before or during the act of micturition. Nine units refluxed both at rest and during micturition. Twenty-four renal units showed reflux only during the resting phase. Vesicoureteric reflux, not reaching the kidney, was demonstrated in four units; in all cases this occurred during micturition. There were no equivocal results. Twenty-five of the refluxing units were right-sided and 30 left-sided. Reflux was unilateral in 23 children and bilateral in 16.

Five different types of reflux were demonstrated:

- Type 1: Episodic at rest with clearance (Fig. 1)
- Type 2: Episodic at rest persisting (Fig. 2)
- Type 3: Continuous at rest
- Type 4: Prior to micturition (Fig. 3)
- Type 5: During micturition (Fig. 4)

Some renal units showed more than one type of reflux. The distribution of the types of reflux is shown in Table 2.

DMSA scan results were available for 169 renal units in 87 children. Abnormal DMSA scans (either focal scarring or divided function less than 45%) were

Table 1. Reflux demonstrated by resting and micturition phases of study in 55 renal units

	Rest only	Micturition only	Rest and micturition	Total
Vesicorenal	24	18	9	51
Vesicoureteric	0	4	0	4
	24	22	9	55

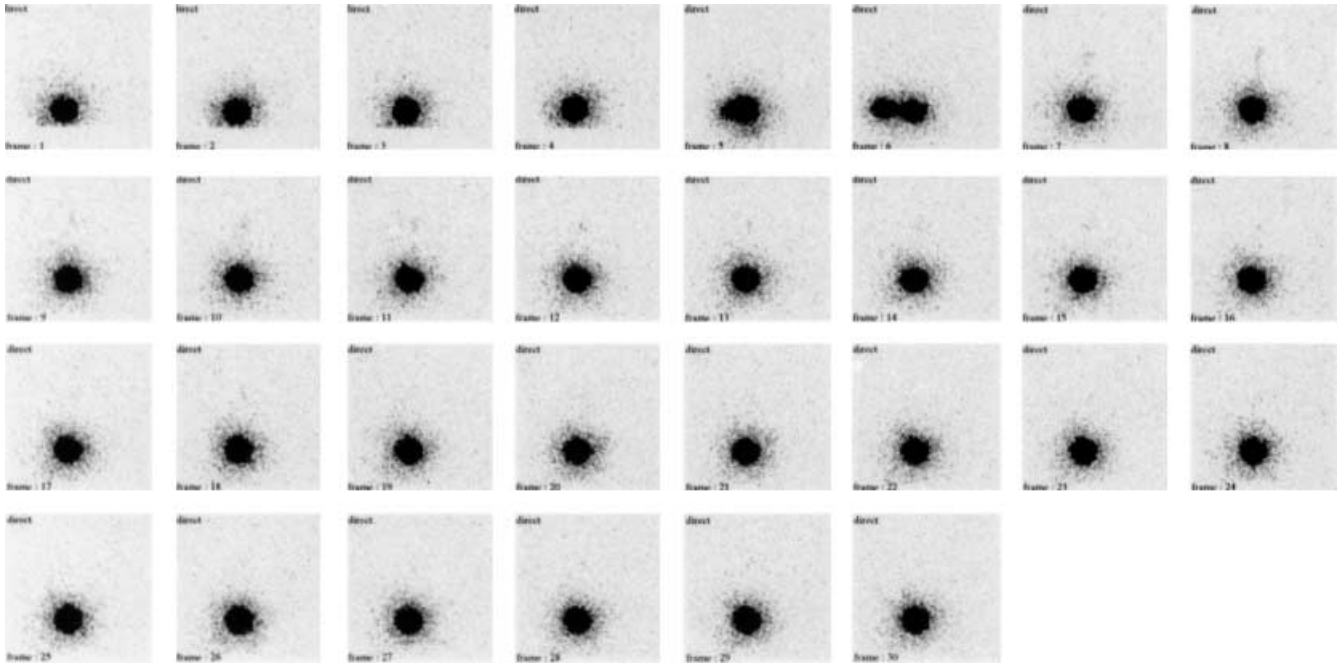


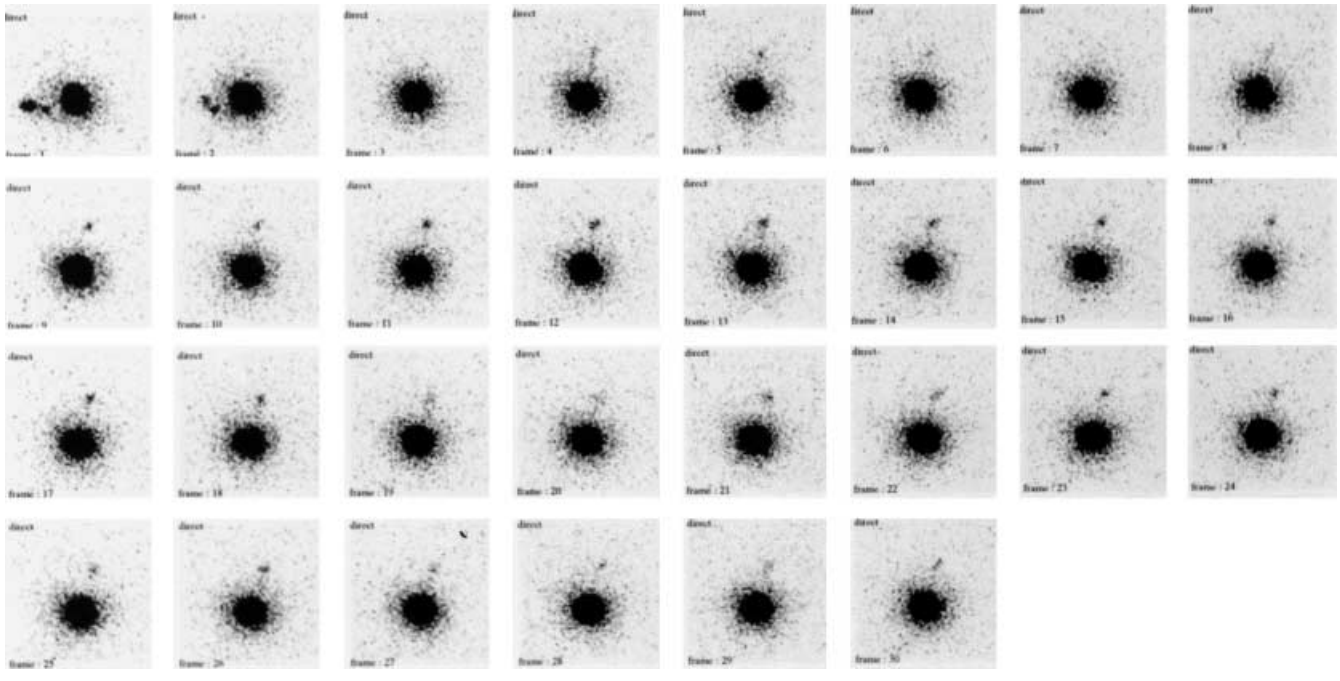
Fig. 1. Analogue images demonstrating reflux at rest into the right kidney which subsequently cleared. Repositioning artefact on frame 6. Reflux seen on frames 7–18

found in 31 (64.6%) of 48 refluxing units and 35 (28.9%) of 121 non-refluxing units. The relationship between reflux and abnormal DMSA was significant ($P < 0.001$, $\chi^2 = 18.36$).

Fig. 2. Analogue images showing persisting reflux into the right kidney from frame 4

Of 124 renal units in 65 children examined by previous MAG3 IRC, 61 (49.2%) were reported as showing definite reflux, 21 (16.9%) possible reflux and 42 (33.9%) as showing no reflux.

Of 120 renal units for which DMSA and IRC results were available, definite reflux was reported in 59 (49%) and possible or no reflux reported in 61 (51%). Abnormal DMSA scans (either focal scarring or divided function less than 45%) were found in 26 (44%) of 59 units with definite reflux and 20 (33%) of 61 units with



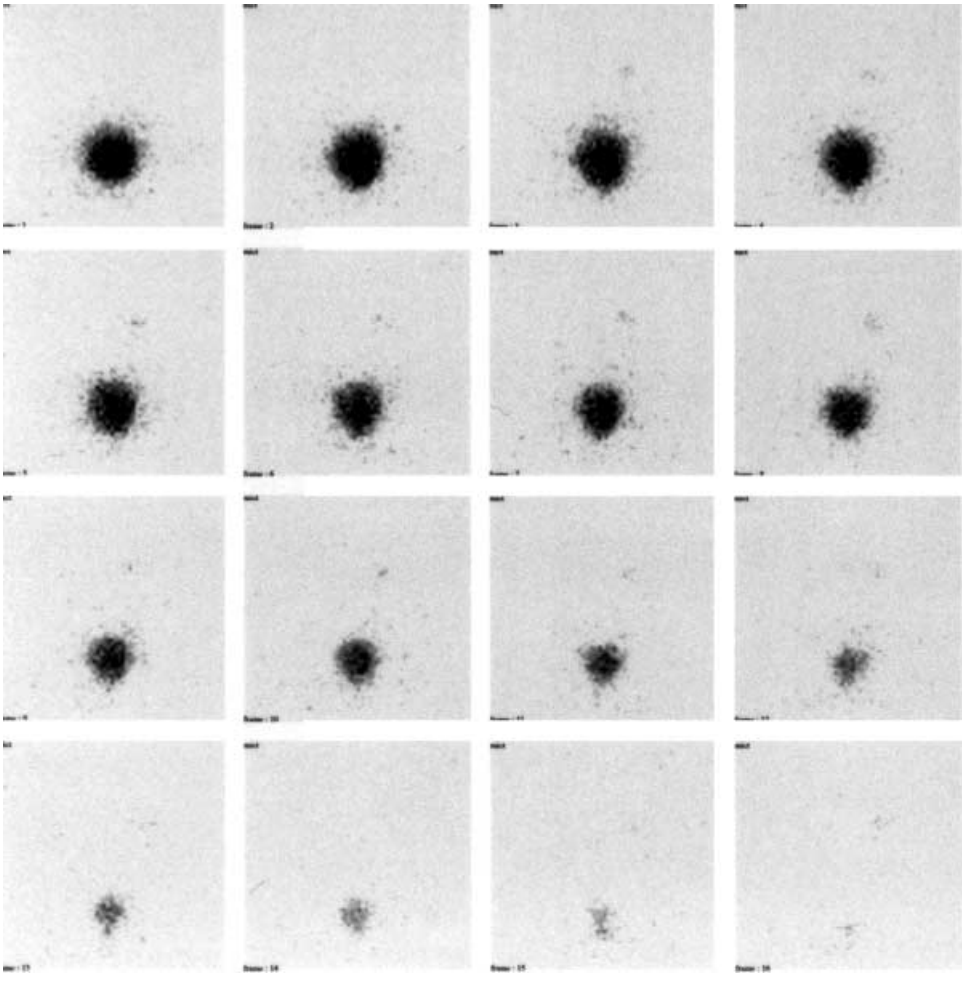


Fig. 3. Reflux into the right kidney at the onset of micturition

possible or no reflux. The relationship between reflux detected by IRC and abnormal DMSA scan was not significant ($P > 0.1$, $x^2 = 1.61$).

The results of indirect and direct studies with respect to interval surgery are shown in Table 3.

Discussion

Despite many years of research there is no clear consensus as to the investigation of urinary tract infection in children. In particular, there is controversy about the importance of demonstrating vesicoureteric reflux, although animal experiments indicate that the combination of reflux and infection causes scarring [6]. A highly significant correlation between reflux on radiographic MCU and renal defects on DMSA scanning has been demonstrated in children with urinary tract infection [7].

MCU is usually used to investigate reflux in babies and children who are not yet toilet-trained. Older, continent children can be investigated by IRC – in which labelled DTPA or MAG3 is injected IV, DRC – in which radionuclide is instilled into the bladder via a urethral catheter, or MCU. Children do not like catheterisation [3], which also carries the risk of introducing infection, so IRC, which has been shown to have broadly similar results to MCU [1, 2, 3], is widely favoured. IRC detects reflux in some children in whom reflux was not demonstrated on MCU [1, 2, 3], and these may be false-positive results. Others have preferred the DRC on the basis of accuracy and lower radiation dose [5, 8, 9], accepting the need for catheterisation. Reflux into the lower ureter may be missed on DRC, but this is not thought be of clinical significance [9]. The low radiation dose and accuracy of the catheter-DRC have been used as justification for using this technique for the screening of siblings of children known to have reflux [10]. Examination of the filling phase of a DRC detects reflux that would have been missed on IRC [11]. Intravesical pressure can be monitored during a catheter-DRC in those with clinical voiding abnormality [12].

This is the first report of percutaneous DRC (PDRC), although percutaneous injection has been described for contrast cystography [13]. The examinations in this

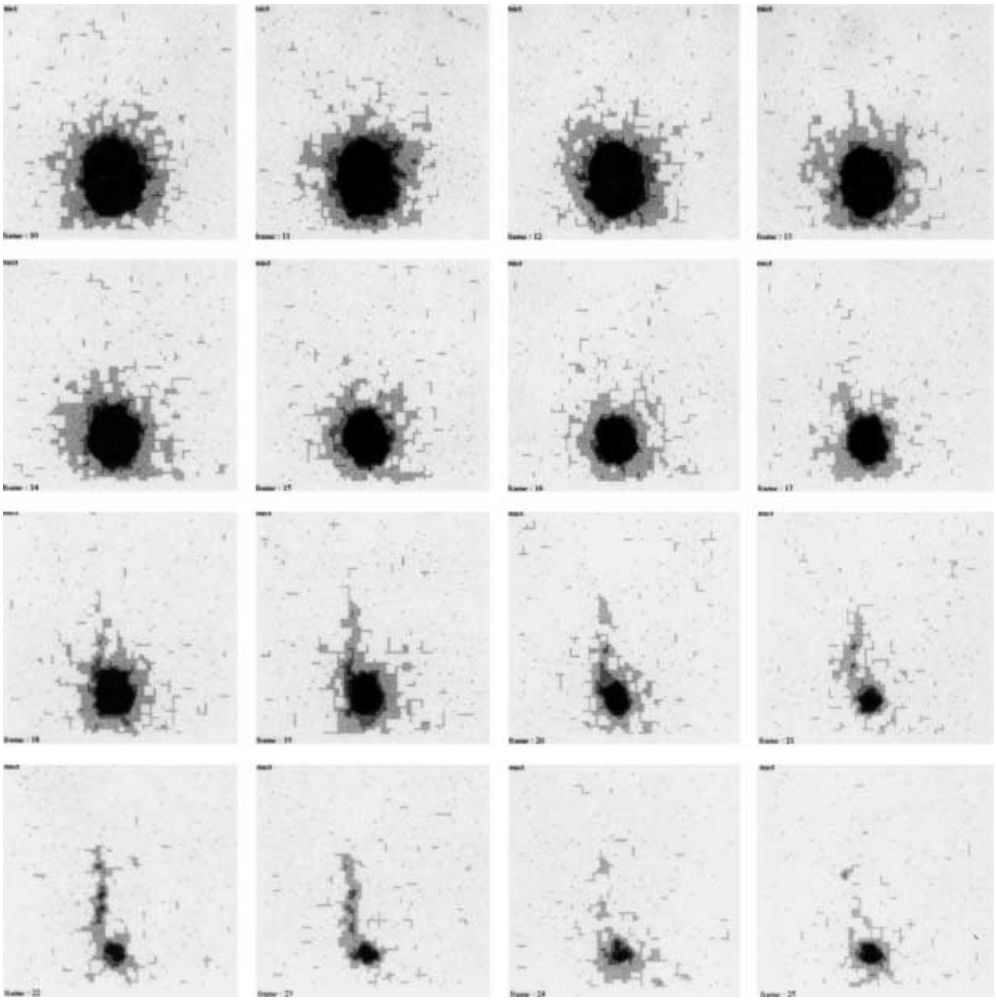


Fig. 4. Reflux into the left kidney during micturition

study were performed with the single aim of detecting vesicoureteric reflux in those children who were known to have had positive tests for reflux in the past (some of whom had undergone submucosal Macroplastique injection) and children in whom there were strong clinical reasons to suspect reflux. It is recognised that children in whom there is a possibility of obstruction of the upper tracts should have renography in addition to PDRC. PDRC is of particular benefit in children with poor renal function and/or upper tract dilatation since in these children IRC is difficult to interpret because of retained activity in the upper tracts. Children in whom bladder or urethral abnormalities are a possibility should still have MCU to demonstrate anatomical detail [13].

In no other type of reflux examination is reflux assessed in the physiological resting state. Although MCU and catheter-DRC can assess reflux in the filling phase, infusion is performed at rates faster than physiological

Table 2. Distribution of types of reflux in 55 refluxing units

Type 1. Resting study: episodic, clearing	9
Type 2. Resting study: episodic persisting	8
Type 3. Resting study: continuous	20
Type 4. Micturition study: before micturition	2
Type 5. Micturition study: during micturition	30
	69

Table 3. Results of indirect and direct cystograms for 124 renal units undergoing operative and conservative management

Management between indirect and direct studies	Refluxing units on indirect study[a]	Refluxing units on indirect study[b]	Refluxing units on direct study
Conservative ($n=76$)	37(48.7%)	23(30.3%)	18(23.6%)
Operative ($n=48$)	45(93.7%)	38(79.2%)	15(31.2%)

[a] Includes units with definite and possible reflux
[b] Includes only units with definite reflux

filling, and therefore reflux, if detected, is of uncertain clinical significance. In this study, 24 of 55 refluxing units showed reflux only in the resting phase, and this may not have been detected during IRC because of the presence of excreted radionuclide in the upper tracts. Assessment of clearing of refluxed urine from the upper tracts is possible during DRC, and this is likely to be of clinical significance. Prolonged retention of refluxed activity following voiding in DRC was found to correlate with decreased renal function [14]. The significance of the different types of reflux described here is uncertain, and with relatively small numbers conclusions should not be drawn from this study. The renal units with continuous reflux were found to have gaping ureteric orifices at cystoscopy for repeat submucosal injection.

The preference of patients for percutaneous injection of radionuclide directly into the bladder in comparison to IV injection was unexpected. MAG3 was chosen as the radiopharmaceutical agent because IRC could still have been performed had any of the children refused percutaneous injection; free pertechnetate would be a cheaper alternative. It had been anticipated that children would prefer percutaneous injection to catheterisation, but abdominal injection was found to be preferred to intravenous in most cases in which a preference was expressed. This was mainly due to the rapidity of the percutaneous bladder puncture, although several patients indicated it was completely painless.

In comparison to previous IRC performed on the same patients when definite or possible reflux was demonstrated in 66% of renal units, PDRC demonstrated reflux in 27.5% of renal units with no equivocal results. This could have several explanations:

1. There may be false-positive results in the indirect study as suggested by previous articles [1, 2, 3]. When those reported as possible reflux on the indirect study are excluded, the results of indirect and direct studies agree more closely (Table 3).
2. There may be false-negative results in the direct studies. While there are theoretical reasons (no background activity, no excreted activity in the upper tracts) why the direct study should be more accurate, false negatives cannot be completely excluded.
3. Reflux is an intermittent phenomenon (although this might be expected to affect direct and indirect studies similarly).
4. Success of antireflux procedures performed in the interval between indirect and direct procedures (although a lower incidence of reflux in the direct study was also detected in those renal units not undergoing antireflux procedures – see Table 3).
5. The natural history of decreasing prevalence of reflux with age.

This study considers only children who were toilet trained. Although the technique could be used for younger children who are not toilet trained, this may be difficult because a full bladder is required for easy injection and voluntary and controlled micturition must take place when requested to allow micturition images to be obtained within a reasonable time scale.

The population examined by this study is a selected population with a high prevalence of reflux. We have not used this technique to screen a population with low prevalence, for example all those children presenting with a single urinary-tract infection. It is probably only necessary to perform a reflux study on those children with abnormal DMSA scans whose management is altered by the demonstration of reflux. This group includes children being considered for antireflux surgery, those having a repeat examination following surgery and children being treated with prophylactic antibiotics because of reflux. A reflux study is also useful in the investigation of children with dilatation of the upper tracts when either reflux or obstruction may be the cause of the dilatation.

A minor disadvantage of PDRC is the necessity for US to assess bladder filling before injection. In our institution we keep a portable US machine in the nuclear medicine room, although the child can be examined in the US department immediately prior to injection and a suitable site marked on the skin. We have made no attempt to estimate the cost of this percutaneous procedure compared to DRC performed by catheterisation; however, it seems likely that the cost of the US examination (which takes only a few seconds) is no greater than the cost of consumables used for sterile catheterisation. The need for a full bladder to facilitate injection is a second disadvantage of the technique, although most of our children were able to say when they felt the need to micturate. Although some time is taken for the bladder to fill, this is less time consuming than with the indirect MAG3 voiding study since the indirect studies are commenced with an empty bladder. This article describes the new technique of percutaneous DRC, and early experience suggests that it is the best test for vesicoureteric reflux in continent children, having the benefits of accuracy, low radiation dose, speed and patient acceptability.

Appendix: Questionnaire

Direct radionuclide cystography

Your child has just had an injection directly into the bladder through the tummy wall.

1. Has your child had an injection into the hand or foot for a kidney scan before?
   - Yes ❑
   - No ❑
2. Which injection did he or she find easier?
   - Hand ❑
   - Tummy ❑
   - No difference ❑

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