

# Radionuclide Voiding Cystography

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Abstract. Radionuclide voiding cystography is a sensitive and accurate method for diagnosing vesicoureteric reflux. This method allows for continuous monitoring of bladder filling and emptying, permits detection of reflux at any time during the study, and evaluates its dynamics. Since it results in very low amounts of radiation to the patient, it is an ideal method for the diagnosis and followup of children with reflux.

Key words: Radionuclide voiding cystogram – Children – Vesicoureteric reflux.

Study of the ureters and bladder in pediatric nuclear medicine is limited to the use of radionuclide cystography for evaluation of suspected vesicoureteric reflux. This failure of the ureterovesical valve mechanism may be caused by a congenital variation, pathologic process, or immaturity that distorts the anatomy or function of the ureterovesical junction. The principal long-term consequence of vesicoureteric reflux of infected urine is development of pyelonephritic scars that, in turn, may lead to hypertension and chronic renal failure.

Several passive and active factors characterize a normal valve mechanism of the ureterovesical junction. The passive factors include: an oblique entry of the ureter into the bladder; an adequate length of intramural ureter, particularly of its submucosal segment; and an adequate ratio of the length of the submucosal tunnel to the diameter of the ureter. The active factors are contraction of the ureterotrigonal muscles, which close the ureteral meatus and the submucosal tunnel; and active ureteral peristalsis, as during diuresis.

The incidence of vesicoureteric reflux in the general population (noninfected) is not known. In a study by Ransley [1], only 7 (1%) of 535 apparently normal neonates, infants, and children had vesicoureteric reflux. We reviewed radionuclide voiding cystograms in 37 siblings of patients with known vesicoureteric reflux and found that 12 (32%) of them exhibited reflux. The reflux was unilateral in 8 patients and bilateral in 4 patients. Jerkins and Noe [2] found a similar incidence among siblings using radiographic cystography.

The intramural ureter becomes longer with age, often producing sufficient length to convert a refluxing ureterovesical junction into a nonrefluxing one. Normand and Smellie in 1979 reported spontaneous cessation of reflux in 71% of children and 79% of the ureters in their patients. The most important factor in the spontaneous resolution of reflux seemed to be the diameter of the ureter: resolution took place in 85% of ureters of normal caliber but only in 41% of dilated ureters. These authors also reported that 63% of ureters associated with scarred kidneys ceased to reflux spontaneously [3].

Follow-up radiographic voiding cystograms approximately every 12 months are often obtained in patients with reflux to evaluate its evolution. Cessation of reflux usually eliminates the need for continuing antiinfectious prophylaxis. Because of the concern about gonadal radiation to children from these multiple studies, radionuclide cystography, with its much lower radiation dose, has become a desirable alternative.

In view of the tendency of vesicoureteric reflux to resolve spontaneously, its management remains controversial. Persistent reflux, depending on the

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individual patient, may require further antibiotic treatment with continuation of monitoring, or surgical correction. The degree of ultimate damage to the kidneys or subsequent pathology does not appear to change with the treatment chosen.

## Technique

Radionuclide cystography was introduced in the late 1950s by Winter [4], and since then several reports on this topic have appeared [5-12]. Conway and his coworkers refined the method for application to pediatric patients [13-16].

Radionuclide cystography permits continuous monitoring of bladder filling and emptying. Reflux can be detected and its dynamics recorded at any time during the study. Using computerized gamma cameras, estimates of the capacity of the bladder and the volume of reflux can be made. Simultaneous recording of intravesical pressure permits assessment of reflux dynamics and analysis of the relationship between intravesical volume, pressure, and reflux.

#### Indications

In our institution radionuclide cystography is used in the following situations: follow-up a few months to a year after the initial diagnosis (by conventional VCUG) of vesicoureteric reflux in patients on long-term antibiotic treatment; following antireflux surgery; in siblings of patients with known vesicoureteric reflux; and occasionally as a screening test to detect reflux in children who have had urinary infection.

## **Patient Preparation**

A complete explanation of the procedure should be given to the patient and/or the parents. When conducted with patience and understanding, such a conversation will reduce anxiety about the examination. In addition, we find it helpful to give or mail to our patients a brochure with information and instructions for preparation [17, 18]. If a patient is unusually apprehensive about the procedure, we perform the study on another day. We do not use sedation.

The patient is instructed to void in the bathroom before the examination if possible, and then to lie supine on the examination table for the entire study. The examination table is covered with absorbent paper to avoid contamination.

#### Equipment

A computerized gamma scintillation camera with a field of view sufficiently large to include both kidneys and the bladder should be used. The camera should be equipped with a high-sensitivity or diverging collimator.

# **Radiopharmaceuticals**

The radionuclide used is technetium-99 m as sodium pertechnetate: 1 mCi dissolved in a 500-ml bottle of sterile saline. This bottle is connected to the intravesical catheter by means of standard intravenous tubing at the beginning of the study.

#### Catheterization

Sterile urethral catheterization trays prepared for each study contain the following items: 3 small containers, cotton, and a sterile towel with a central opening. Other materials needed include: antiseptic solution, Povidone-Iodine, (Betadine<sup>®</sup>); sterile water; anesthetic jelly (lidocaine); a bright light source; a 10-ml syringe with a blunt, tapered adapter; and aqueous lidocaine (0.5%). Two sizes of catheters are used: a 2.6-mm diameter catheter for most patients and a 1.5-mm diameter catheter for babies. For simultaneous pressure recordings, we use a 3-mm diameter, double-lumen catheter (Fr 9, Reusch, West Germany).

Success of the examination depends on a careful catheterization technique. Inexperience is the most frequent cause of iatrogenic damage to the male urethra. If necessary, a parent or aide assists in restraining the patient, who lies supine and is encouraged to relax. The so-called frog position is useful in catheterizing females. The periurethral area (girls) or the glans penis (boys) is carefully cleansed with antiseptic solution and sterile water. These fluids should be warmed to body temperature before use. The catheter is lubricated with the anesthetic jelly to facilitate smooth insertion. The urethral orifice in girls is identified before attempting catheterization.

In girls, the catheter should be introduced easily in one motion without hesitation. Any additional contact with the area surrounding the urethral orifice should be avoided because it causes discomfort. This cannot be emphasized enough; a child who has had a bad first experience with this procedure is not likely to cooperate in the future.

In males, the urethra is anesthetized. The penis is held with one hand, while lidocaine (5–10 ml is slowly injected into the urethra using the blunt adaptor. Slow and deep breathing helps to relax the sphincter and allows anesthesia of the entire urethra. Slightly squeezing the anterior portion of the penis for a minute prevents the lidocaine from draining out. The catheter is then gently and continuously introduced into the bladder. Deep breathing and/or instructions to the patient to void may relax the sphincter. If the sphincter remains closed, the catheter should be kept under continuous and mild pressure against it. In the majority of cases, the catheter will eventually glide through the sphincter.

Do not try to overcome a closed or spastic sphincter by repeated back-and-forth motions of the catheter; this may result in urethral injury. In the rare instance when it is necessary to repeat the urethral anesthesia, a second attempt at catheterization is virtually always successful.

Once the catheter has been advanced beyond the sphincter, the majority of children will cooperate. In girls, the catheter is fixed with adhesive surgical tape to the inner thigh; in boys, to the dorsal shaft of the penis. Leaving the catheter in place until the end of the study has the advantage of allowing a repeat examination in case of failure as well as additional filling of the bladder, if necessary, in order to initiate voiding. It is important to ensure that there is no skin contamination of the radionuclide as it may be confused with reflux during analysis.

#### Recording

The radionuclide cystogram is recorded on the computer in a series of 5-second frames for the duration of the study. An analog record is also made at 1 frame per 30 seconds for the entire study.

#### Filling and Voiding

The bottle with the radionuclide is suspended 70–90 cm above the examination table and is connected to the catheter. The child is encouraged to lie quietly on the table (Fig. 1). Sand bags along-side the patient's body help to maintain positioning, and dim light during the procedure seems to have a quieting effect.

The entire examination is monitored on the persistence osciloscope by the operator. The end of the filling phase is indicated by a bladder volume appropriate for the patient's age (Fig. 2) and a reduction of the rate of flow of the infusate.

With filling of the bladder to its capacity, voiding is usually initiated without delay. Careful and complete collection of the voided fluid is necessary for quantitation. We use a plastic urinal for both girls and boys. In girls, its lower border is gently pressed against the perineum and inner thighs.

#### Analysis

The sequential images of the cystogram are displayed on the computer monitor and evaluated visually. Contrast enhancement is helpful in identifying small volumes of reflux. If reflux is present, regions of interest are drawn over the kidneys and bladder. In addition, another region equidistant from the bladder is selected to correct for background scatter.

It is important to determine if there has been any patient motion during the study since this will invalidate any attempts at quantitation. If motion has not occurred, time-versus-activity curves are calculated for each region of interest (Fig. 3).

To obtain an estimate of the volume of reflux, bladder capacity, and residual capacity, a relationship between activity and volume is obtained. Assuming that attenuation of the gamma rays is constant, that the isotope is well-mixed with the solution of saline, and that a negligible amount of urine is produced by the kidneys during the study, the counts recorded will be proportional to the volume(s)

$$V = RC \tag{1}$$

where V is volume, R is constant, and C is counts. Note that 0 counts represents zero volume.

The constant R is calculated by relating the voided volume to the drop in total vesical counts during the voiding phase of the study. At the beginning of the voiding phase, the volume is Vo and the counts are Co. At the end of the voiding phase, the volume will be Ve and the counts Ce. Substituting these values into equation (1) yields:

$$Vo = RCo, \tag{2}$$

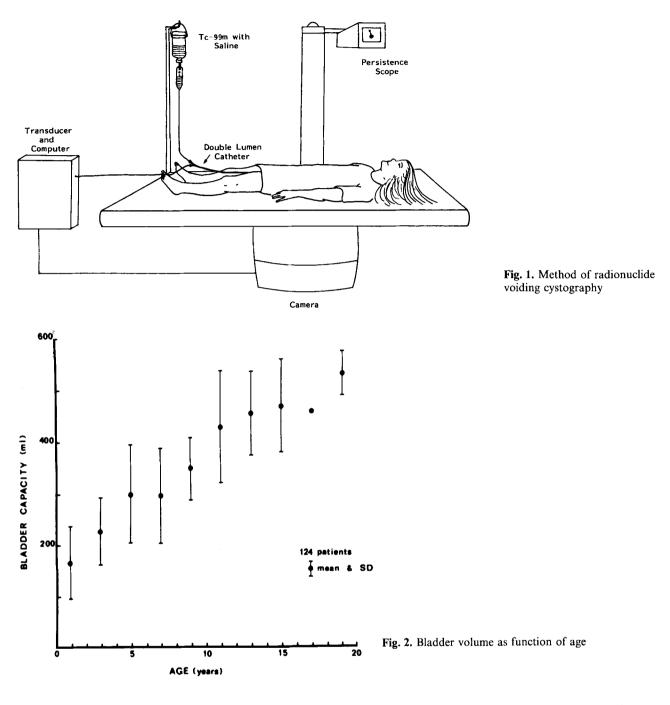
$$Ve = RCe. \tag{3}$$

Subtracting Eq. (3) from Eq. (2) yields:

$$R = \frac{Ve - Vo}{Ce - Co} = \frac{V}{C} = \frac{\text{change in volume}}{\text{change in counts}}$$
(4)

Once the ratios are calculated, it is easy to obtain any volume of interest for any particular time of the study (e.g., maximum volume of reflux). One simply has to multiply the ratio R by the number of counts over a particular region for a given frame.

After the counts in each region are converted to volumes, it is possible to calculate rates of flow.



To obtain the average voiding flow rate, the count loss during voiding must be divided by the time of voiding and multiplied by the constant R.

Average Flow Rate =  $R \frac{V}{T}$  (5)

Variables obtained in this way include the following:

1. Volume of the bladder at the first occurrence of reflux and at the time of maximum reflux during filling and/or voiding; 2. Maximum bladder volume (end of filling);

3. Volumes of reflux (initial, maximum, residual);

4. Average voiding flow rate.

# Interpretation

## Radiologic Grading

We agree with Ransley [1] that grading of vesicoureteric reflux is convenient for communication but need not be applied too rigidly in an individual

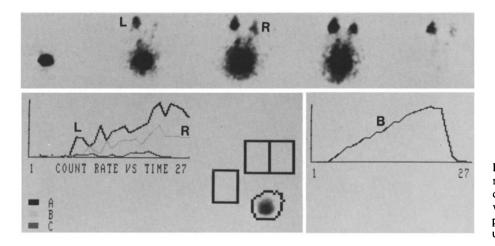


Fig. 3. Bilateral vesicoureteric reflux in a 5-year-old girl first discovered by conventional voiding cystography 1 year previously. L, left ureter; R, right ureter; B, bladder

case. Recently a report by an international group studying vesicoureteric reflux adopted a classification of reflux based on its radiographic appearance [19] (Fig. 4). This classification represents a continuum, and some cases may not fall precisely within 1 of its 5 grades. Further, the same patient may have grade II reflux during one examination and grade I or III during another.

Typically, patients with reflux of low grade (I through III) are candidates for nonsurgical treatment and continuous antibiotic therapy. With higher grades of reflux (significant ureteral and pelvicalyceal dilatation), spontaneous resolution of reflux can occur but is less likely. Continuous antibiotic therapy may be given to these patients provided that their urine remains sterile, that frequent urine cultures are performed, and that serial radiologic evaluation is carried out. This routine requires careful compliance by the patient and parents.

Surgical treatment in experienced hands has a high degree of success  $(\pm 95\%)$ , offers an immediate correction of the anatomic problem, and reduces the risk of pyelonephritis. Neither medical nor surgical treatment, however, offers a clear advantage as far as subsequent development of hypertension or impairment of renal growth. Whichever form of therapy is chosen, long-term followup and observation are essential to assess the patient's progress and the presence of complicating factors, such as residual vesicoureteric reflux, new scars, pyelonephritis, hypertension, or obstruction.

# Reflux

An analysis of 135 consecutive radionuclide studies in our hospital revealed a 32% incidence of vesicoureteric reflux, usually of mild to moderate degree. Reflux was present in 47% of the nonsurgical patients and in 11% of the patients evaluated following surgery. It was unilateral in 60% and bilateral in 40%. Unilateral reflux occurred in the right and the left ureter with equal frequency. In the 59 refluxing renal units, reflux occurred during filling and voiding in 80% while reflux during voiding only was present in 17% of the ureters. The remaining 3% of ureters refluxed during bladder filling only. Almost 80% of those patients with reflux during filling and voiding exhibited an increase in the refluxed volume during voiding of 2–34 ml (average, 7 ml).

Comparing the 5 radiographic grades of reflux with radionuclide cystography is not easy and may not be appropriate due to inherent technical peculiarities of each method. In radionuclide cystography, however, it is possible to distinguish degrees of severity. In the least severe degree, activity is seen in the ureter without reaching the renal pelvis (Fig. 5). This corresponds to grade I reflux. When a small volume refluxes into the renal pelvis with minimal or no visualization of the ureter (Figs. 6, 7, 8 and 9) it corresponds to radiographic grades II to III. It is not possible, by radionuclide technique, to assess the diameter of either the ureter or the pelvicalyceal system. Finally, the radionuclide cystogram can reveal a large volume of reflux reaching a dilated pelvicalyceal system with definite dilatation (and even redundancy) of the ureter. This corresponds to radiologic grades IV or V (Figs. 10 and 11).

The radionuclide cystogram is more sensitive than conventional radiographic voiding cystography for the diagnosis of vesicoureteric reflux [15]. It also permits an estimation of the refluxed volume. Experiments with phantoms using volumetric flasks to represent bladders, small containers of various volumes to simulate reflux and also using several scatter thicknesses were carried out to de-

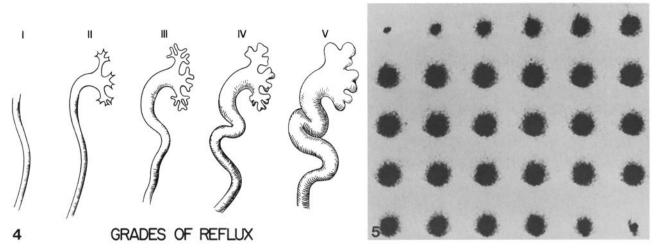


Fig. 4. Radiographic classification of reflux, International Study Classification. I, ureter only, II, ureter, pelvis, and calices; no dilatation, normal caliceal fornices. III, mild or moderate dilatation and/or tortuosity of ureter and mild or moderate dilatation of renal pelvis but no or slight blunting of fornices; IV, moderate dilatation and/or tortuosity of ureter and moderate dilatation of renal pelvis and calices. Complete obliteration of sharp angle of fornices but maintenance of papillary impressions in majority of calices. V, gross dilatation and tortuosity of ureter. Gross dilatation of renal pelvis and calices. Papillary impressions are no longer visible in majority of calices

Fig. 5. Small volume of intermittent left vesicoureteric reflux in an 8-year-old girl with previously documented left grade I–II reflux. At the end of the top row, vesicoureteric reflux is within the ureter and appears to reach the left renal pelvis. The last frame (bottom right) shows reflux into the distal left ureter

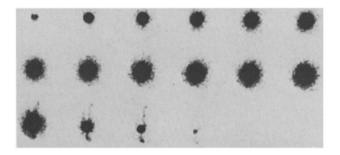


Fig. 6. Bilateral vesicoureteric reflux in a 6-year-old observed mainly during voiding. A year previously, she showed unilateral reflux. Left reflux is minimal and does not seem to reach the renal pelvis. The reflux into the right ureter is greater than the left, is still small in volume, and reaches the renal pelvis

termine the sensitivity of this technique. The same radiopharmaceutical-specific activity, collimator, and frame rate as used in the clinical studies were employed. Under these conditions, it was determined that the minimum detectable volume of reflux was 0.20 ml (240-ml flask and 3.5 cm of scatter); the minimum distance from the projected edge of the flask at which 0.20 ml of reflux was detectable was 2 cm. Actual estimate of the volume of reflux if it was less than 1 ml yielded a greater than 50% error. Volumes in the smaller container (reflux) of 1 ml or greater yielded an error in the estimated volume of 10% when using 3.5 cm of scatter and 20% with 6 cm of scatter. Three cadaveric kidneys containing 1.0, 5.0, and 10.0 ml of test solution in their pelvicalyceal system were imaged along with a 240-ml flask (bladder) using 3.5 cm of scatter. Estimations of simulated reflux volume under these conditions carried an error of 10%.

# Patterns of Reflux

The ability to monitor continuously during radionuclide cystography permits observation of several dynamic patterns of reflux. Continuously increasing reflux characteristically occurs during the early or mid filling phase, supposedly through a patulous ureteral orifice that allows the bladder and ureter(s) to behave as a single chamber (Fig. 10). Occurrence of reflux in this condition appears to be independent of intravesical pressure, which is usually low during the beginning of bladder filling. This corresponds to Lattimer's group 3: reflux at low pressures and low volumes [20].

Most commonly, vesicoureteric reflux does not start until a certain bladder volume has been reached and then either continues to increase until the end of the filling phase or shows intermittent increases and decreases in volume (Fig. 12). In some patients, however, there may be only transient episodes of reflux during the filling phase

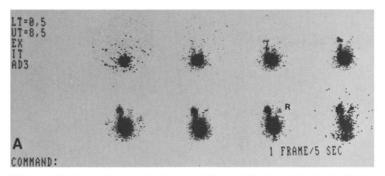
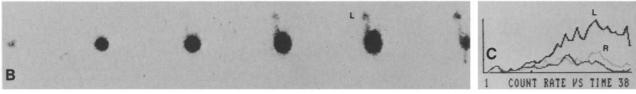
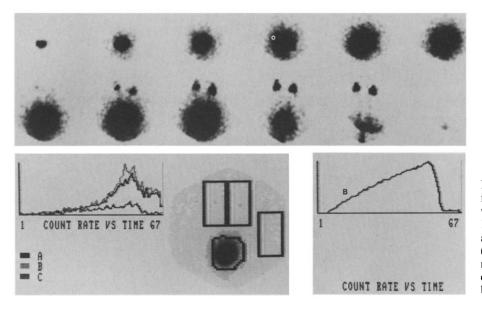
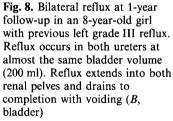


Fig. 7. Bilateral vesicoureteric reflux 6 months after surgical repair of megaureters. Left ureter is larger than right. Enhanced computer images (A) reveal the right reflux clearly while analog images (B) show only left reflux. Time-activity curves (C) over the ureters reveal the dynamics of reflux (L, left ureter; R, right ureter)







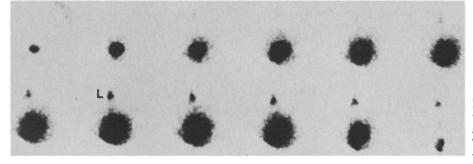


Fig. 9. Five-year-old girl with left vesicoureteric reflux 4 months after right ureteral reimplantation. There is no evidence of right vesicoureteric reflux

(Fig. 5). Some children who are unwilling or unable to void during the cystogram are asked to urinate in the bathroom and a post-voiding image is obtained. In some cases the postvoid image will show the only evidence of vesicoureteric reflux (Fig. 13). In certain cases of bilateral reflux, one ureter can be seen to begin refluxing at a certain bladder volume and then reflux begins into the contralateral ureter at a greater bladder volume (Figs. 3, 7, 12 and 15).

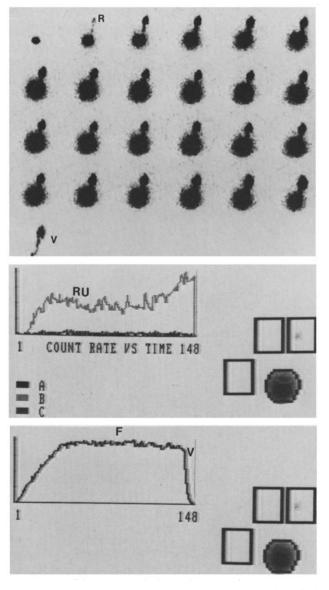


Fig. 10. Five-year-old girl with previous pyelonephritis and bilateral vesicoureteric reflux. Previous left ureteral reimplantation. There is right vesicoureteric reflux only (R) which occurs at a small bladder volume (150 ml) and increases at the end of bladder filling (F) and during voiding (V)

If reflux has occurred during the filling phase, it usually increases (Fig. 10) in volume during the voiding phase, but occasionally it may decrease or disappear altogether during voiding (Figs. 8 and 12). In other cases reflux only occurs during or after voiding (Figs. 6 and 14). Refluxed fluid may continuously drain into the bladder immediately after completion of voiding, despite the intravesical pressure frequently reaching its maximum at this time. Reflux may not have as much to do with intravesical pressure as with the state of bladder filling and contraction insofar as they affect the ureterovesical junction.

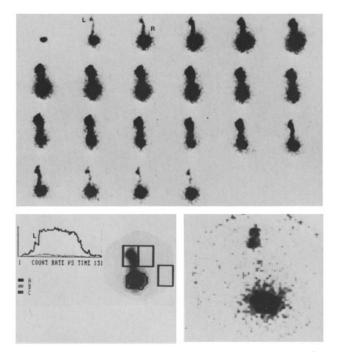


Fig. 11. Four-year-old boy with severe left (L) vesicoureteric reflux. Reflux occurs at a relatively small bladder volume (150 ml). A post-void image (below right) reveals retention of radiotracer within the left renal pelvis. On the third image (above) there is evidence of right (R) vesicoureteric reflux to the distal ureter only

## **Bladder** Capacity

Information about bladder capacity on previous studies, mean standard values, and observation of the infusion flow rate should aid the operator in filling the patient's bladder to its approximate capacity. These and other guides are highly variable, however. For example, bladder capacity generally increases with the age of the patient (Fig. 2). However, at a given age or in a given patient it may vary by 100% or more from the mean volume. Subjective signs of complete bladder filling shown by the patient (upgoing toes, restless legs, urgency) should be noted, but their value is questionable.

Influences operating at the time of examination may cause the functional capacity to be quite different from the actual capacity. Mechanical factors, such as rapid filling of the bladder, irritation from the catheter, or low temperature of the instilled fluid, can induce high bladder tonus and thus lower bladder capacity. Apprehension may provoke the same response. Uninhibited bladder contractions due to irritability from severe inflammation characteristically cause intermittent pain and urgency and tend to keep bladder capacity low. In most children with urinary tract infection in our series, however, bladder capacity seemed

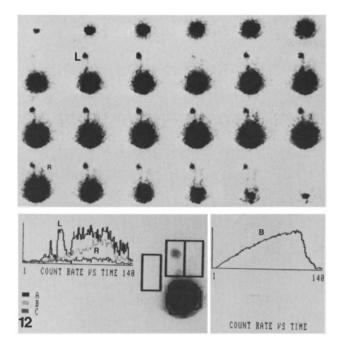
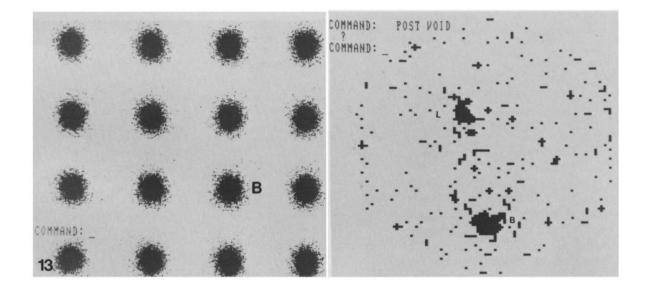


Fig. 12. Bilateral vesicoureteric reflux in a 9-year-old girl at 1-year follow-up. Reflux in the left ureter (L) occurs at a bladder volume of 230 ml while right reflux (R) occurs at nearly 400 ml of bladder capacity. Note the dynamic nature of the reflux and the complete emptying of activity from the renal pelves after voiding. *B*, bladder time-activity curve

Fig. 13. Left vesicoureteric reflux detected only after voiding (right panel). During the filling phase (left panel), no reflux is demonstrated. This study was done in a 5-year-old girl with a left refluxing duplex system



not to be affected. Starfield [21] established values of functional bladder capacity in nonenuretic and enuretic children and showed that the bladder capacity was significantly lower in the latter group.

## Intravesical Pressure

Our method of examination permits simultaneous recording of the radionuclide cystogram and intravesical pressures in the computer. Using a doublelumen catheter, one channel is used for infusion while the other is connected to a pressure transducer. The pressure transducer output is connected through an analog-to-digital converter to the computer. Time-activity and time-pressure waves can then be displayed on the same computer monitor and on the same time scale.

In a study designed to establish normal and abnormal ranges of intravesical pressure, measurements during radionuclide cystography were obtained in 40 patients. There were 16 normal children, 15 children with reflux, and 9 children who had had surgery previously. In the normal children, maximum intravesical pressures during filling were 15–80 cm H<sub>2</sub>O (average, 42 cm H<sub>2</sub>O) and during voiding or postvoiding 24–136 cm H<sub>2</sub>O (av-

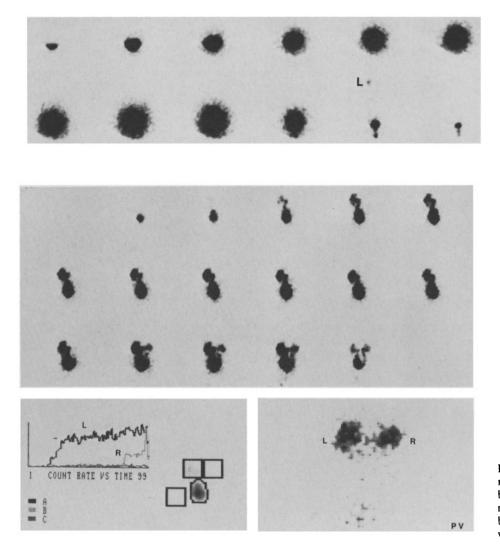


Fig. 14. Small volume of left (L) vesicoureteric reflux during voiding only, in a 9-year-old girl with previously demonstrated bilateral grade II reflux

Fig. 15. Bilateral vesicoureteric reflux beginning at different bladder volumes (below left) with retention of radiotracer within both renal pelves (L, R) after voiding (below right)

erage, 78 cm  $H_2O$ ). There was no significant difference between the patients with reflux and those who had prior reimplants. The initial voiding pressure was always higher than the maximum filling pressure. Intravesical pressures decreased with increasing bladder capacity. During filling of the bladder, the intravesical pressure showed a continuous increase until full bladder capacity was reached. Toward the end of voiding, a pressure peak that occurred after contraction characterized the pressure curve. In most instances, the highest recorded intravesical pressure was reached just at the end of micturition.

A relationship between intravesical pressure and cortical renal damage in the absence of infection remains widely debated [22]. However, in patients with vesicoureteric reflux there are alterations in renal blood flow during voiding [23]. Renal damage from pyelotubular backflow of contrast material has also been considered [24]. It has been clearly demonstrated that in children under 6 years of age, but mainly in infants, massive reflux in the presence of urinary tract infection leads to renal damage [25–29].

Intrarenal reflux seems to play an important role in the etiology of renal damage [30]. Since intravesical pressure is higher in younger children than in older ones and since renal damage mainly occurs in younger children, some relationship between intravesical pressure, infected urine, intrarenal reflux, and reflux nephropathy seems likely. In the absence of a barrier at the ureterovesical junction, the upper urinary system and the bladder act as a single chamber. Studies in our laboratory seem to indicate that intravesical pressure is probably least important in terms of etiology, management, and prognosis of reflux provided that no distal obstruction or neurogenic dysfunction coexists. The majority of our patients exhibited reflux during filling at a relatively large bladder volume.

The increasing bladder volume during the cystogram probably influences the competence of the ureterovesical junction more than the increase in pressure.

In the growing child, maturation of the ureterovesical junction probably implies not only lengthening of the intravesical ureter but also strengthening of the specific musculature related to the ureterovesical junction. Therefore, decreasing occurrence of reflux with age is to be expected [15, 31-33]. Controversy still exists about maturation of the ureterovesical junction [34, 35]. Reflux during voiding only may be related to the changing anatomic condition of the ureterovesical junction during bladder contraction.

## Bladder Emptying

We calculated the voiding flow rates in 75 patients [36, 37]. The average flow rate in 26 normal children was 10.2 ml/sec (range, 2-21 ml/sec  $\pm 4.5$  SD). In 49 abnormal patients (reflux with or without infection or previous surgery), the voiding flow rates averaged 10.5 ml/sec (range, 1.4-31 ml/sec  $\pm$ 5.7 SD). In all 75 patients, the average voiding flow rate was 10.4 ml/sec (range, 1.4-31 ml/sec  $\pm$ 5.3 SD). The average voiding flow rate seemed to relate to the initial bladder volume and thus to age. The greater the initial bladder volume, the higher the voiding flow rate. The presence of an indwelling catheter did not seem to reduce the voiding flow rate significantly [41]. In patients with an indwelling catheter, it averaged 10.7 ml/sec (range, 2.0-31 ml/sec), while in those without a catheter, the average flow rate was 9.8 ml/sec (range, 1.4–25 ml/sec). The voiding time was 10-116 seconds with an average of 35 seconds. With the exception of a few extreme values, the voiding time in normal patients is comparable to that in patients with reflux.

Gierup observed that children usually do not use abdominal straining during voiding [38]. When they do, the urinary flow either increases or decreases, probably in relation to whether or not the external sphincter is being contracted along with the abdominal muscles [39]. Thus, urging the child to strain in order to void may be counterproductive.

# Residual Bladder Volume

Residual volumes measured by catheterization and by radionuclide cystography may or may not be the same (Fig. 16), and in many instances there is gross discrepancy between these two measure-

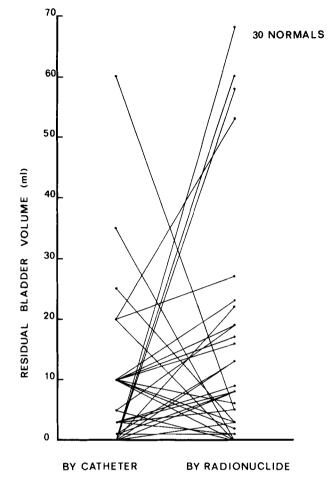


Fig. 16. Residual bladder volumes measured in the same patients by catheterization and by radionuclide cystography in 30 normal children

ments. The reasons for such inconsistency are many. The patient may not adequately empty the bladder because of some underlying abnormality such as aberrant micturition (as in some cases of reflux) or dysuria [40, 41]. The bladder may not be properly drained due to the placement of the tip of the catheter against the bladder wall [42], or the patient may simply be unwilling or unable to void due to the unnatural situation [43].

We have observed more complete emptying of the bladder in patients who have had their bladder filled to a maximum or optimal volume during cystography. Apparently a high tonicity of the bladder wall induced adequate contraction and more complete emptying. A large residual volume in children either at the beginning or at the end of the study does not necessarily mean that the patient has a significant abnormality. Demonstration of an empty bladder, on the other hand, is useful [44].

# Urine Cultures

We reviewed the results of urine cultures in 113 consecutive children referred for radionuclide cystography. Urinary infection with *Escherichia coli* or *Streptococcus fecalis* was found in 11% of our patients in spite of their allegedly being on continuous antibiotic treatment and being carefully evaluated by their physician. There was a nearly equal incidence of urinary infection in patients on conservative treatment and in those who had undergone surgery. Our experience agrees with that of other workers indicating that reflux and infection are independent of one another [25, 35, 45–48].

## Dosimetry

For children between 1 and 10 years of age undergoing radionuclide cystography, the absorbed radiation dose estimates are 18-27 mrad for the bladder and 1-2 mrad for the ovaries. The testicular dose is less than the dose to the ovaries. The dose to the kidneys is estimated to be 0.02-0.04 mrad/ml of reflux per minute of residence in the collecting system. The estimated dose to the ureter in reflux is 1.3 mrad/min, which is the same as the dose to a sphere of 1 ml filled with Tc-99 m at a concentration of 2 mCi/liter.

Comparing our results to those published by Conway et al. [44], the dose to the bladder is similar. With regard to the doses to which the gonads of a girl are exposed during conventional voiding cystourethrography, there is approximately 50– 200 times less radiation with computerized radionuclide voiding cystography [49, 50].

The residence time for the activity in the bladder was determined from the duration of the study in patients of various age groups. The average bladder capacities were taken from the data of Fig. 2. The empty bladder mass was estimated by extrapolation from data in adults using growth curves [51].

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#### References

 Ransley PG: Vesicoureteric reflux. In Williams DI, Johnston JH (eds): *Pediatric Urology*, 2nd ed. London: Butterworth Medical, 1982

- Jerkins GR, Noe HN: Familial vesicoureteral reflux: a prospective study. J Urol 128:774-778, 1982
- 3. Normand ICS, Smellie J: Vesicoureteric reflux: the case for conservative management. In Hodson J, Kincaid-Smith (eds): *Reflux Nephropathy*. New York: Masson, 1979
- 4. Winter CC: A new test for vesicoureteral reflux: an external technique using radioisotopes. J Urol 81:105–111, 1959
- 5. Apperson JW, Atkins H, Fleming R: The value of the isotope cystogram in determining pressure and volume at which ureteral reflux ccurs. J Urol 89:405-413, 1963
- 6. Blaufox MD, Gruskin A, Sandler P, Goldman H: Radionuclide scintigraphy for detection of vesico-ureteral reflux in children. J Pediatr 79:239-246, 1971
- 7. Dodge EA, Vesico-ureteric reflux, diagnosis with iodine-131 sodium ortho-iodohippurate. *Lancet 1*:303-304, 1963
- Handmaker H, McRae J, Buck EG: Intravenous radionuclide voiding cystography (IRVC). Radiology 108:703-705
- Rosenthall L: Residual urine determination by roentgenographic and isotope means. *Radiology* 80:454–459
- Timmermans L, Collard M, Merchie G: Le diagnostic de reflux vesicoureteraux par la cystometrie associée au radiocinema et aux radioisotopes. Acta Clin Belg 19:23-37, 1964
- 11. Timmermans L, Merchie G: Une nouvelle methode d'exploration des reflux vesico-uretero-renaux. Acta Urol Belg 37:105-110, 1969
- 12. Winter CC: Pediatric urological tests using radioisotopes. J Urol 95:584-587, 1966
- Conway JJ, Belman AB, King LR: Direct and indirect radionuclide cystography. Semin Nucl Med 4: 197-211, 1974
- Conway JJ, Belman AB, King LR, Filmer RB: Direct and indirect radionuclide cystography. J Urol 113:689-693, 1975
- Conway JJ, Kruglik GD: Effectiveness of direct and indirect radionuclide cystography in detecting vesicoureteral reflux. J Nucl Med 17:81-83, 1976
- Nasrallah PF, Conway JJ, King LR, Belman AB, Weiss S: Quantitative nuclear cystogram. Urology 6:654-658, 1978
- 17. Hass EA, Solomon DJ: Telling children about diagnostic radiology procedures. *Radiology* 124:521, 1977
- Lebowitz RL: Voiding cystourethrography in children. In: Contemporary Diagnostic Radiology. Baltimore: Williams & Wilkins, 1978
- Report of the International Reflux Study Committee: Medical versus surgical treatment of primary vesicoureteral reflux. *Pediatrics* 67: 392–400, 1981
- Lattimer JK, Apperson JW, Gleason DM, Baker D, Fleming SS: The pressure at which reflux occurs, an important indicator of prognosis and treatment. J Urol 89:395-404, 1963
- Starfield B: Functional bladder capacity in enuretic and nonenuretic children. J Pediatr 111:167–172, 1974
- 22. Bailey RR: Sterile reflux: is it harmless? In Hodson J, Kinkaid-Smith P (eds) *Reflux Nephropathy*. New York: Masson, 1979
- Orr WA, Kimbrough H, Gillenwater JY: Alterations in renal blood flow with voiding in the presence of vesicoureteral reflux. J Urol 106:214–219, 1971
- 24. King LR: Vesicoureteral reflux: history, etiology, and conservative management. In Kelalis PD, King LR, Belman AB (eds) Clinical Pediatric Urology. Philadelphia: WB Saunders, 1976
- Cremin BJ: Observations on vesico-ureteric reflux and intrarenal reflux: review and survey of material. *Clin Radiol* 30:607-621, 1979
- Hodson CJ, Edwards D: Chronic pyelonephritis and vesicoureteric reflux. Clin Radiol 11: 219-231, 1960

- 27. Rolleston GL, Shannon FT, Utley WLF: Relationship of infantile vesicoureteral reflux to renal damage. Br Med J 70:460-463, 1970
- Rolleston GL, Shannon FT, Utley WLF: Follow-up of vesicoureteric reflux in the newborn. *Kidney Int 8 (Suppl* 4): S59-S64, 1975
- 29. Smellie J, Edwards D, Hunter N, Normand ICS, Prescod N: Vesicoureteral reflux and renal scarring. *Kidney Int 8 (Suppl 4)*: S65–S72, 1975
- 30. Rolleston GL, Maling TMJ, Hodson CJ: Intrarenal reflux and the scarred kidney. Arch Dis Child 49:531-539, 1974
- 31. Hutch JA: Theory of maturation of the intravesical ureter. J Urol 86: 534-538, 1961
- 32. Tanagho EA, Meyers FH, Smith DR: Urethral resistance: its components and implications. I. Smooth muscle component. Invest Urol 7:136–149, 1969
- Tanagho EA, Meyers FH, Smith DR: Urethral resistance: its components and implications. II. Striated muscle component. Invest Urol 7:195-205, 1969
- 34. Lyon RP, Marshall S, Tanagho EA: Theory of maturation: a critique. J Urol 103:795-800, 1970
- 35. Stephens FD, Lenaghan D: The anatomical basis and dynamics of vesicoureteral reflux. J Urol 87:669-680, 1962
- 36. Spencer RP, Treves S: Bladder emptying flow rates as a function of bladder volume. *Yale J Biol Med* 44:199-205, 1971
- 37. Strauss BS, Blaufox MD: Estimation of residual urine and urine flow rates without urethral catheterization. J Nucl Med 11:81-84, 1970
- Gierup P: Micturition studies in infants and children. Scand J Urol Nephrol 4:191-207, 1970
- Whitaker J, Johnston GS: Urinary flow rate with two techniques of bladder pressure measurement. *Invest Urol* 4:235-238, 1966
- 40. Hutch JA: Aberrant micturition. J Urol 96:743-745, 1966
- Willi UV, Lebowitz RL: The so-called megaureter-megacystis syndrome. AJR 133:409–416, 1979
- 42. Lebowitz RL, Avni FE: Misleading appearances in pediatric uroradiology. *Pediatr Radiol* 10:15-31, 1980
- 43. Poznanski E, Poznanski A: Psychogenic influences on void-

ing: observations from voiding cystourethrography. Psychosomatics 10:339-342, 1969

- 44. Conway JJ, King LR, Belman AB, Thorson T: Detection of vesicoureteral reflux with radionuclide cystography. AJR 115:720-727, 1972
- 45. Faure C: Le reflux vesico-ureteral. In: Lefebvre J (ed). Traite de Radiodiagnostic, XVIII Paris: Masson et Cie, 1973
- 46. Friedland GW: Recurrent urinary tract infections in infants and children. Radiol Clin North Am 15:19-35, 1977
- Gross GW, Lebowitz RL: Infection does not cause reflux. AJR 137:929-932, 1981
- 48. Stephens FD: Urologic aspects of recurrent urinary tract infections in children. J Pediatr 80:725-737, 1972
- 49. Fendel H: Radiation exposure due to urinary tract disease. In: Progress in Pediatric Radiology. Vol 3: Genitourinary Tract. Basel: Karger, 1970
- Leibovic SJ, Lebowitz RL: Reducing patient dose in voiding cystourethrography. Urol Radiol 2:103-107, 1980
- 51. Snyder WS, Cook MJ, Nasset ES: Report of the Task Group on Reference Man. Oxford: Pergamon Press, by The International Commission on Radiological Protection, 1975
- 52. Dilman LD, Van der Lage FC: Radionuclide decay schemes and nuclear parameters for use in radiation dose estimation. In MIRD Pamphlet no. 10. New York: Society of Nuclear Medicine, 1975
- 53. Loevinger R, Berman M: A revised schema for calculating the absorbed dose from biologically distributed radionuclides. In MIRD Pamphlet no. 1 (revised). New York: Society of Nuclear Medicine, 1975
- Ransley PG: Vesicoureteral reflux: continuing surgical dilemma. Urology 12:246, 1978
- 55. Smith JC: Urethral resistance to micturition. Br J Urol 40:125-155, 1968
- 56. Snyder WS, Ford MR, Warner GG: Estimates of specific absorbed fractions for photon sources uniformly distributed in various organs of heterogenous phantom. In MIRD Pamphlet no. 5 (revised). New York: Society of Nuclear Medicine, 1978
- 57. Timmermans L, Merchie G: Les radionuclides dans le diagnostic de maladies des reins et des voies urinaires: reflux vesicoureterorenaux. Acta Urol Belg 35:254-259, 1967