

Vesicoureteral reflux

Summary

Vesicoureteral reflux (VUR) is the retrograde flow of urine from the bladder into the ureter. Primary VUR is the most common type and is due to a congenital defect of the terminal portion of the ureter. Bladder outlet obstruction, cystitis, and congenital ureteral anomalies (e.g., ureteral duplication, ectopic ureter) may cause secondary VUR. Children with VUR are usually asymptomatic until they develop a urinary tract infection (presenting with fever, dysuria, urgency, flank pain). Other manifestations include hypertension, uremia, and kidney failure in advanced cases of reflux nephropathy. The initial workup for VUR includes laboratory tests (creatinine levels, electrolytes) and renal ultrasound for evaluation of kidney function and possible structural damage. Voiding cystourethrogram is the diagnostic test of choice for demonstrating urinary reflux and the severity of the disease. Most cases of primary VUR resolve spontaneously as the child ages. Medical management with prophylactic antibiotics (e.g., trimethoprim-sulfamethoxazole, nitrofurantoin) and behavioral modification (timed micturition) has proven successful in treating and preventing complications. Patients with higher grades of primary VUR with ureteral dilation and hydronephrosis or with recurrent UTIs require endoscopic/surgical correction of the vesicoureteral junction. Treatment of the underlying cause corrects secondary VUR. Complications of VUR include hydronephrosis, obstructive nephropathy, pyelonephritis, and chronic kidney disease.

Epidemiology

- **Incidence:** ~ 1% of newborns^[1]
- **Age:** children < 2 years^[2]
- **Sex:** ♀ > ♂ (2:1)^[2]
- **Race:** more common in white children^[2]

Types:

- **low-pressure or passive reflux:** Reflux occurring during bladder filling. less likely to show spontaneous reflux resolution.
- **high-pressure or active reflux:** reflux during voiding.

Etiology

The intramural segment of the ureter is the terminal portion of the ureter, which runs obliquely through the bladder wall before it enters the bladder cavity. When the bladder contracts during micturition, the lumen of the intramural ureter is occluded due to its oblique position within the bladder wall (flap valve mechanism). If the intramural section of the ureter is too short, this mechanism fails.

Primary VUR (most common type)^[3]

- **Short intramural ureter** → vesicoureteric junction (VUJ) fails to close completely during bladder contraction → VUR^[3]

Secondary VUR

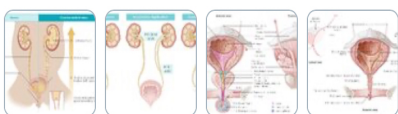
- **Bladder outlet obstruction** (anatomic/functional): high pressure within the bladder → reflux of urine through the VUJ

- Anatomic: **posterior urethral valves**^[4]; urethral meatal stenosis
 - Functional: bladder and bowel dysfunction^[4]; neurogenic bladder
 - Cystitis
- ~ 50% of children (mostly boys) with posterior urethral valves develop VUR. The valves are additional membranes in the urethra which block urinary flow.

- **Congenital anomalies of the ureter**

- Ureteral duplication (most common renal abnormality; 1% of the population)^[4]
- Ectopic ureter
- Ureterocele

- **Iatrogenic**^[4]



Clinical features

- Suspected in the prenatal period when **hydronephrosis** is detected on routine antenatal ultrasound
- Postnatal presentation
 - Recurrent febrile **urinary tract infections**
 - Neonates: irritability, fever, and listlessness
 - Older children: urinary urgency, frequency, incontinence, and dysuria associated with fever
 - **Reflux nephropathy**: renovascular hypertension, kidney failure, uremia^[5]
 - Flank or abdominal pain before or during voiding

! VUR is generally asymptomatic until it causes a urinary tract infection.

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Laboratory studies

- Urinalysis and urine culture: indicated in all children with hydronephrosis to rule out infection
- Renal function tests: serum creatinine, urea, and electrolytes

Imaging

Ultrasound

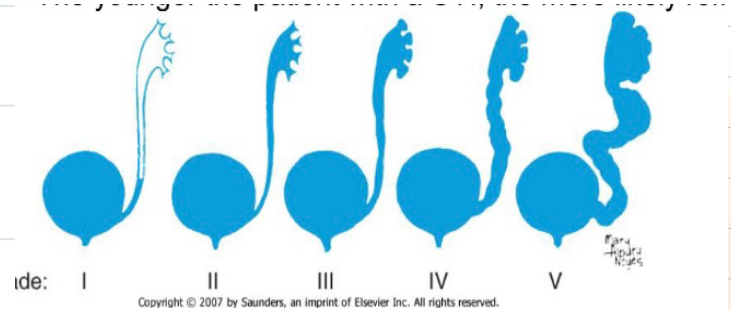
- Indicated in children with febrile UTI and for follow-ups
- Detection of hydronephrosis and dilated ureter

Contrast voiding cystourethrogram (micturating cystourethrogram)

- **Indications**
 - Children with ≥ 2 episodes of febrile UTIs or
 - First febrile UTI in a child and any of the following:
 - A renal anomaly detected on ultrasound
 - Fever $\geq 39^{\circ}\text{C}$ (102.2°F) and a pathogen other than *E. coli* detected in urine culture
 - Hypertension
- **Procedure:** Contrast is instilled into the bladder through a urethral catheter; images are obtained via fluoroscopy while the child is voiding.

Grading of vesicoureteral reflux^[6]

Grades	Findings on voiding cystourethrogram
Grade I	• Reflux limited to the ureter • No ureteral dilation
Grade II	• Reflux up to the renal pelvis • No ureteral dilation
Grade III	• Reflux up to the renal pelvis • Mild dilation of the ureter • Blunting of the calyces
Grade IV	• Reflux up to the renal pelvis • Gross dilation of the ureter • Moderate ureteral tortuosity
Grade V	• Gross dilatation of the ureter, pelvis, and calyces • Significant ureteral tortuosity • Loss of papillary impressions



- renal scarring in low grade VUR is low (15%) → increases with higher grades of reflux (grade IV or V) - 65%.
- Grade I or II VUR resolve without surgical intervention
- grade IV or V < 50% resolve without surgical intervention
- **Nuclear renal scanning best identifies renal scars.**

DMSA renal scan [7]

- Nuclear imaging method based on the injection of radioactive dimercaptosuccinic acid
- Assessment of cortical tissue, renal function, and scarring (indicated in the case of hypodense photopenic lesions)
- Further indicated for follow-ups and treatment monitoring

MAG3 scan (radionuclear cystourethrography)

- A nuclear medicine scan using the radiolabelled isotope MAG3 (mercaptoacetyl triglycine)
- Detects VUR, especially if caused by obstructions, measures renal function
- Follow-ups

Urodynamic testing

- Indicated in the evaluation of secondary VUR

Treatment

Conservative treatment

- Indications: VUR grades I-III in children < 5 years of age
- Long-term prophylactic **antibiotics**
 - Children > 3 months: trimethoprim-sulfamethoxazole, nitrofurantoin
 - Infants < 2 months: amoxicillin
- Correction of voiding dysfunction: behavior modification (e.g., timed voiding (every 3 hours), prevention of constipation)
- Close surveillance: urinalysis, renal imaging

Surgical treatment

- **Indications**
 - VUR ≥ grade IV
 - Bilateral grade III VUR, especially in children > 6 years
 - Worsening renal function/breakthrough urinary tract infections despite prophylactic antibiotics
- **Subureteric transurethral injection (STING procedure)**
 - Cystoscopy-guided injection of dextranomer/hyaluronic acid below the mucosa of the ureterovesical junction keeps the intravesical ureter in place, alters its angle, and, thereby, corrects the VUR.
 - Day-care procedure
 - Success rates of up to 90%
- **Surgery:** ureteral reimplantation (ureteroneocystostomy)

Urodynamics

A group of tests to assess function of the urinary tract and to identify sites of obstruction. Includes cystometry (evaluates bladder function during filling, storage, and voiding), uroflowmetry (evaluates rate of urine flow), and urethral tests (evaluate intrinsic sphincter function). Indicated in the diagnostic workup of lower urinary tract dysfunction and for the planning of surgical treatment.

Complications

- **Infections**
 - Urosepsis
 - Pyelonephritis
 - Perinephric abscess
- **Renal complications**
 - Ureteral dilation > 7 mm in children
 - Megaureter
 - Hydronephrosis
 - Renal scarring
 - Chronic kidney disease

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