Vesicoureteric reflux, when and how to treat?

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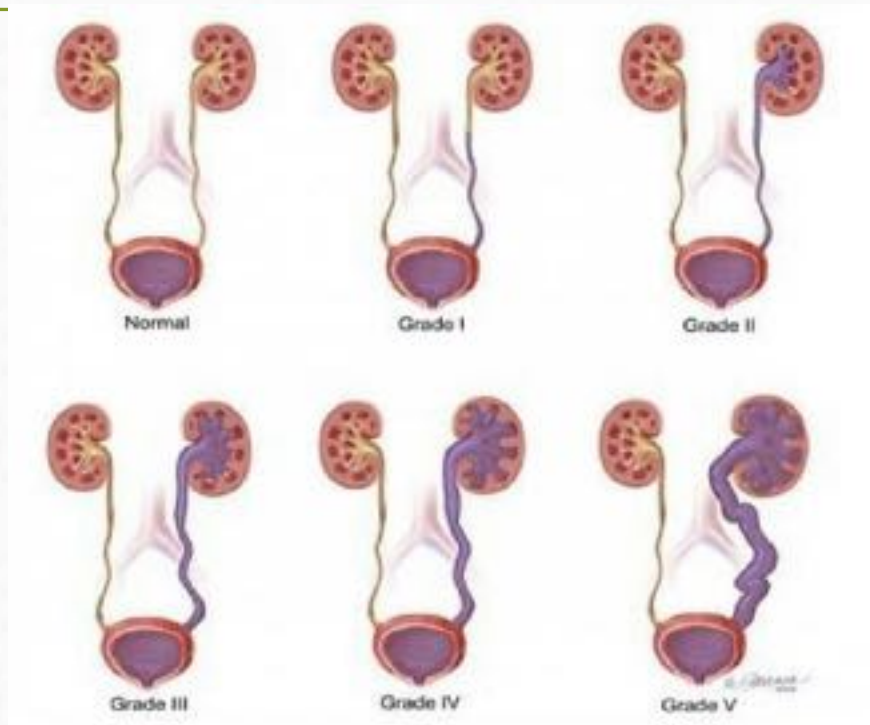
Agenda

- Definition and classification of VUR.
- Prevalence of VUR.
- When to suspect?.
- Diagnosis of VUR.
- Management of VUR.

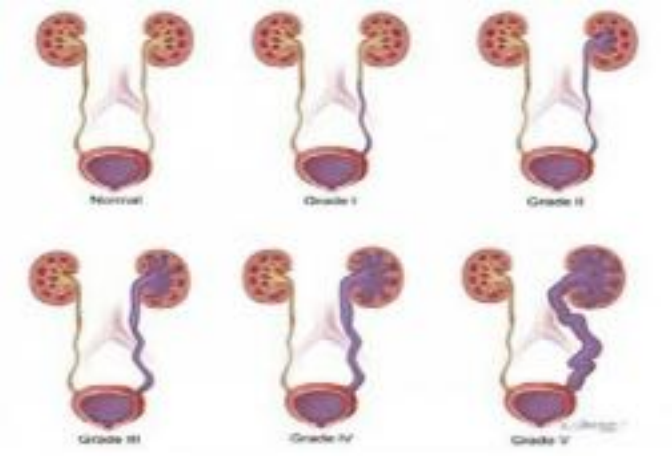
Definition of VUR

- Retrograde flow of urine from the bladder back into the ureter(s) because of immaturity of the preventive mechanism against reflux or failure as a result of anatomical or functional abnormalities.
- This retrograde flow can distend (dilating VUR) or not (non dilating VUR) the pelvicalyceal system.
- Isolated VUR in the absence of obstruction or infection is not an illness and has not been documented to have adverse outcomes. However, VUR has been recognized as a risk factor for recurrent febrile UTIs.



Classification of VUR

1ry VUR	2ry VUR
▪ Most of cases. ▪ They are born with an abnormal ureter (the valve between the ureter and the bladder does not close well, so urine comes back up the ureter toward the kidney). ▪ Either unilateral or bilateral. ▪ Get better or go away as a child gets older.	▪ Due to blockage or narrowing in the bladder neck or urethra or neurogenic bladder, so the urine goes back up the urinary tract. ▪ Mostly is bilateral reflux. ▪ Worsen with time.



Magnitude of the problem

- **0.4-1.8% in children without a history of UTI has VUR.**
- **About 1 in 3 children who has febrile UTI has VUR.**
- **34 to 45% of siblings and 1st order relatives of VUR patients have VUR (*75% of them had no previous UTI*).**
- **VUR with UTI is more prevalent in younger ages.**
- **It is more common in girls and infants younger than 2 years.**
- **The prevalence declines with age (10% by age 12 years).**

Magnitude of the problem

- **Grade IV–V VUR** was found in the following settings:

88% >> examination was for UTI

7 % >> examination was for familial VUR

4% >> examination was for symptoms of bladder/ bowel dysfunction.

1% >> examination for fetal hydronephrosis

When to suspect?

- Patients with fUTI.
- Screening infants with fetal hydronephrosis detected by US.
- Infant health checks using US.
- Screening for familial VUR.
- Presence of bladder/ bowel dysfunction (BBD).
- In patients with advanced renal dysfunction.
- During school health checks that reveal proteinuria or symptoms of kidney failure.

VUR and UTI

- For many years, VUR has been considered a risk factor for acute pyelonephritis and renal damage as urine, is an excellent culture medium, allowing bacterial multiplication in the bladder. During voiding, VUR transports infected urine to the renal parenchyma.
- This concept led to the clinical practice of obtaining a VCUG to evaluate for the presence of VUR after UTI and to use long-term daily low-dose antibiotics or surgical correction of VUR.

VUR and fetal hydronephrosis

- Improved antenatal US led to the recognition that VUR was not a single entity but 2 distinct conditions:

- 1- Rarer congenital “reflux disease” often with abnormal renal parenchyma and dilating IV-V VUR on VCUG following birth.
- 2- More common form of VUR “reflux symptom” which is usually detected in investigations after UTI in young girls with I-III VUR and normal kidneys.

VUR and fetal hydronephrosis

	VUR disease	VUR symptom
Predominant gender	Male	Female
Commonest age of Presentation	Newborn/Infant	Child
Common US features: ▪ Renal Parenchyma ▪ Urinary Tract	 Abnormal Dilatation	 Normal Normal
Typical grade of reflux	IV-V	I–III
Spontaneous resolution within the 1st years of life	Around 50%	80–90%
Possible etiopathogenesis	Abnormal vesicoureteral junction	Bladder dysfunction (?)
Frequency	Rare	Common

VUR and lower urinary tract dysfunction

Difficult and prolonged resolution of VUR

VUR and BBD

- **BBD is a condition where either of the following exist:**

(i) **a symptom of lower urinary tract dysfunction, which is basically identified with objective assessment tools, such as uroflowmetry or voiding diary, without clear organic factors (neurogenic bladder, external injury and congenital malformation) in patients aged ≥5 years who have achieved toileting independence**

AND / OR

(ii) **an abnormal abdominal and intestinal finding (frequency of bowel movement ≤2/week, recurring absence of bowel movement for ≥5 days, frequent but small quantity of feces or fecal impaction [size of a hen's egg or larger] in the rectum**

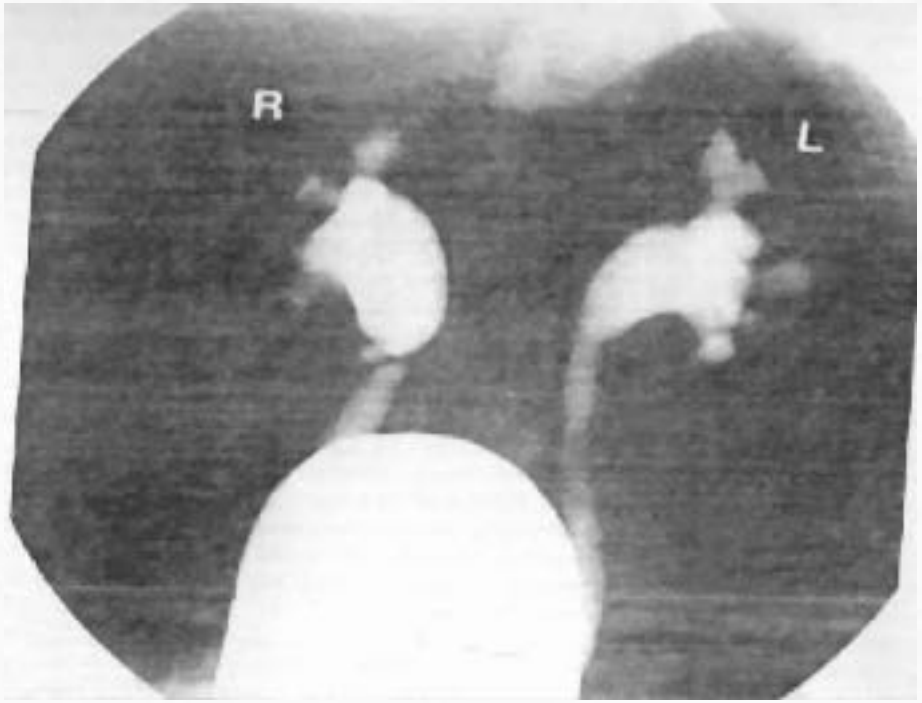
Diagnosis

US

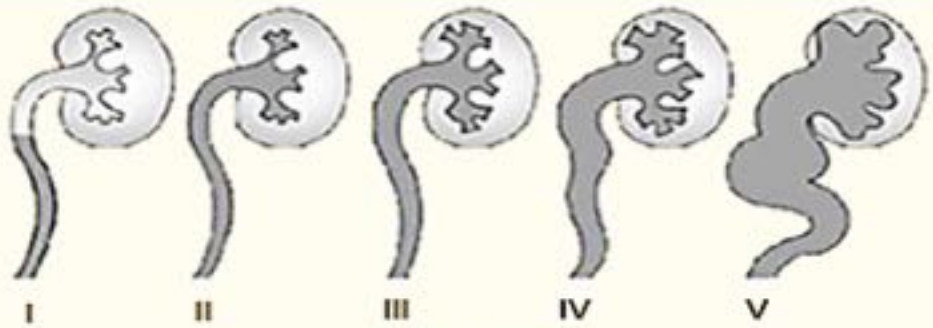
Sensitivity of 18–46%, specificity of 76–88%.

Diagnosis

- **Voiding cysto-urethrogram (VCUG) is the gold standard for the *diagnosis* and *grading* of VUR.**



Diagnosis of VUR



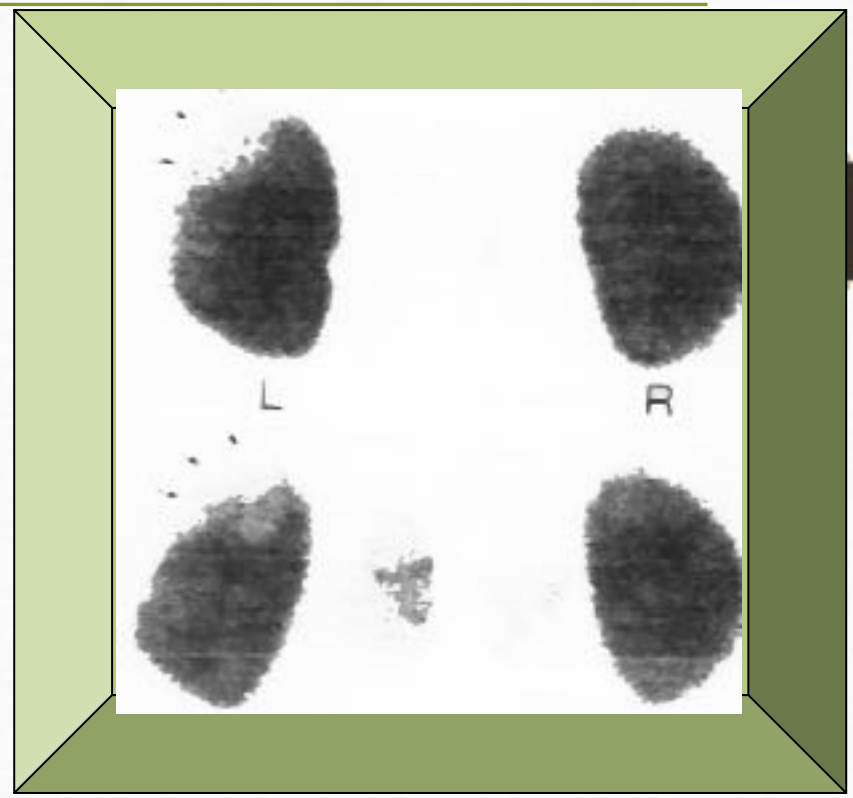
Grade	Description
I	Into a nondilated ureter
II	Into the pelvis and calyces without dilation
III	Mild to moderate dilation of the ureter, renal pelvis, and calyces with minimal blunting of the fornices
IV	Moderate ureteral tortuosity and dilation of the pelvis and calyces
V	Gross dilation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity

Diagnosis of VUR

- The NICE (2007) and the AAP (2011 & 2015) have recommended that VCUG should not be performed routinely after first fUTI in patients less than 24 months old unless renal ultrasound reveals abnormalities, or other atypical or complex clinical circumstances such as atypical/recurrent febrile UTI. In contrast, the American (2012) and European (2015) Urological Associations have continued to recommend performing a VCUG after first febrile UTI in children less than 2 years of age

Role of DMSA

- **Tc 99-DMSA** renal scintigraphy is a standard imaging test used for diagnosis of renal parenchymal damage and **scarring** in patients with VUR.
- Guidelines from the American Urology Association (AUA) suggest that DMSA renal scan is advised for patients at **risk for significant abnormalities** that may affect their care.



Natural course

- It improves and resolves spontaneously with time.
- Resolution is higher in grades (I,II) and less in those in grades (III-V).
- Time to resolution varies according to the degree of VUR, with median of 2.7 years for grade I, up to 9.5 years for grade IV.
- VUR following investigation of febrile UTIs represent a benign condition, with spontaneous resolution and excellent long-term outcome.
- Unlike, high-grade dilating VUR often with hypo-dysplastic scarred kidneys now detected by antenatal US, represent the "at-risk" group for CKD/ ESKD, not because of the VUR per se but rather the poorly functioning congenitally abnormal kidneys present from the outset.

Management

- The European Association of Urology (EAU) guidelines on the management of VUR state that "there is no consensus on the optimal management of VUR (diagnostic procedures, treatment options, or most effective timing of treatment).
- VUR guidelines from the American Urological Association (AUA) 2017, state that "the data were not sufficient to permit development of strict 'standards of care' in many instances".

Management

- **Goals:**
  - Prevention of recurrent urinary tract infections (UTIs).
  - Prevention of worsening renal damage (eg, renal scarring).
  - Minimization of morbidity of treatment and follow-up.
  - Identification and treatment of children with bladder and bowel dysfunction (BBD).

Management (general rules)

- Children with (grade I and II) are at a low risk for pyelonephritis and renal scarring and are more likely to have spontaneous resolution of their VUR than severe VUR (grade IV-V).
- For patients with BBD, measures to improve bladder and bowel function are initiated (laxatives, timed frequent voiding, pelvic floor exercises, behavioral modification, and, in some cases, anticholinergic therapy) with follow-up to see whether VUR spontaneously resolves.
- If symptomatic breakthrough infection occurs, a change in the treatment regimen should be considered. As an example, a child who is managed by observation may be changed to prophylactic antibiotics, whereas surgical correction may be considered in a child already on antibiotic prophylaxis.

Management

- **Therapeutic Options:**
  - Watchful waiting (surveillance).
  - Continuous antibiotic prophylaxis.
  - Surgical correction.
  - Other adjuvant therapies.

Surveillance (watchful waiting).

- When?
  - Low grade reflux (I, II)
  - Toilet trained (can express symptoms of UTI)
- Why?
  - To avoid risk of antibiotic resistance, deleterious effect on the gut flora, higher cost and patient none adherence.
- How?
  - Regular follow-up visits to the clinic.
  - In addition, we must ensure that all UTIs are reported and managed.
  - Antibiotic therapy should be administered promptly to treat febrile UTIs.

Continuous Antibiotic prophylaxis (CAP)

- Daily prophylactic administration of an antibiotic agent.
- It is based on the assumptions that use of continuous antibiotics results in sterile urine and the continued reflux of sterile urine does not cause renal damage, as well as the observation that reflux spontaneously resolves in most cases.
- Controversy still exists, heterogeneous data (age, degree of reflux, number of recurrent and febrile UTI, adherence to chemoprophylaxis, and the urine collection method).

Continuous Antibiotic prophylaxis (CAP)

Indications:

- Patients with a history of UTI
- All non toilet-trained patients with VUR regardless of the grade, unless the family/caregiver prefers surveillance and is compliant with medical advice and care.
- All patients with bladder and bowel dysfunction (BBD) regardless of the severity of VUR
- All patients with high-grade reflux (grade III to IV)

Continuous Antibiotic prophylaxis (CAP)

Age	Antibiotics option	Doses
≤2months	Ampicillin Amoxicillin Cephalexin	20 mg/kg/dose once 10 mg/kg/dose once 10 mg/kg/dose once
≥ 2 months	TMP-SMX Nitrofurantoin	2 mg/kg TMP/dose, once daily 1-2 mg/kg/day once daily.
SMX, sulfamethoxazole, TMP; trimethoprim		

Once daily at bed time

Timing of discontinuation of CAP

- At confirmation of spontaneous resolution – or surgical correction-of VUR (documented by VCUG).
- Other options are considered:

1- At completion of toilet training.

2- After CAP for 1–2 years, even if toilet training has not yet been completed (if patients have residual VUR of grade I–II without recurrent episodes of fUTI during follow up).

3-At new onset or recurrence of breakthrough UTI to start therapeutic regimen .

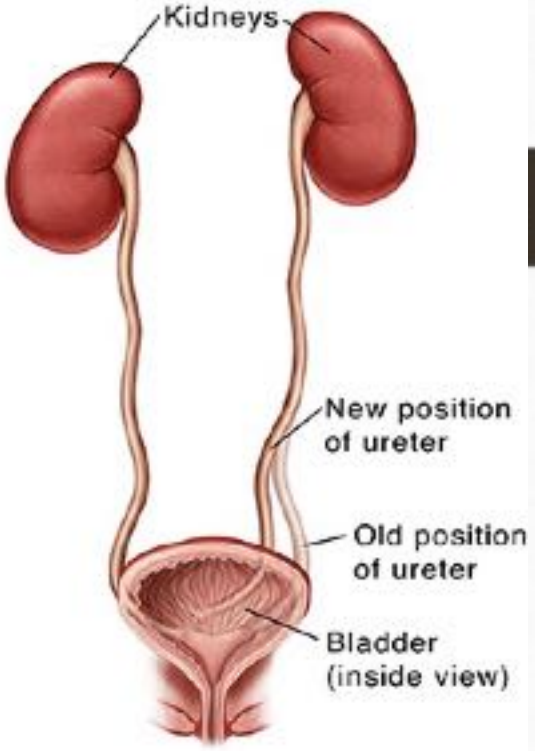
Follow up while on medical treatment

- General evaluation includes measurements of height, weight, and blood pressure.
- Mandatory urine cultures and urinalysis are required whenever there are urinary symptoms suggestive of UTI or unexplained fever
- Monitoring of reflux by (VCUG) or (RNC) usually every 18 to 24 months.
- Renal ultrasonography can be used to monitor renal growth.
- DMSA at the time of presentation in patients with grade III to V reflux - may perform initial baseline scans in all children, even those with lower VUR grades (I and II). Follow-up DMSA can be obtained to document renal involvement after a breakthrough UTI. New renal scarring or evidence of pyelonephritis would be a reason to suggest a change in management.

Role of surgery

- **When?**

  - **Children with persistent grade IV/V reflux beyond two or three years of age (age of spontaneous resolution).**
  - **Children with grade III to IV reflux who cannot tolerate / not compliant to CAP or with breakthrough infections on prophylactic antibiotic therapy**



Role of surgery

- **How?**
  - **Ureteral reimplantation: The connection between the ureter and bladder is corrected so that urine flows only in one direction. Either open or laparoscopic or Robot-assisted surgery.**
  - **Endoscopic correction: injects a periureteral bulking agent via a cystoscope which changes the angle and perhaps the fixation of intravesical ureter.**
- **These procedures are common, generally very safe, and have excellent long-term success.**

Follow up after surgery

- Both renal ultrasound and VCUG are usually repeated approximately six months after open surgical correction.
- Renal ultrasounds obtained too soon after correction demonstrate hydronephrosis that is transitory and of no clinical concern.
- Similarly, a renal ultrasound and VCUG are performed several months after endoscopic correction. In other centers, VCUG is not performed unless there is a documented UTI following endoscopic reimplantation.

Adjuvant therapy

- **Avoid constipation: most children get constipated. It makes it harder to empty the bladder and increases the risk of a UTI.**
- **Discourage "holding it." Drinking enough water and eating a high-fiber diet may prevent or treat constipation, gentle daily laxative. Children should have a soft bowel movement every day.**
- **It is also important that children completely empty their bladder every 2-3 hours when they are awake. Children should avoid holding their urine for long periods.**

long term follow up

- Annual assessments through adolescence, which include measurements of growth (height/ weight) and blood pressure, and urinalysis to detect proteinuria or bacteria.
- Renal ultrasound performed every two or three years to monitor renal growth, especially for patients with significant scarring.
- The need for DMSA renal scan is determined on a case-by-case basis, dictated by if information would affect clinical management. For example, nephrectomy may be considered for a patient with severe hypertension

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Guideline

Guidelines for the medical management of pediatric vesicoureteral reflux

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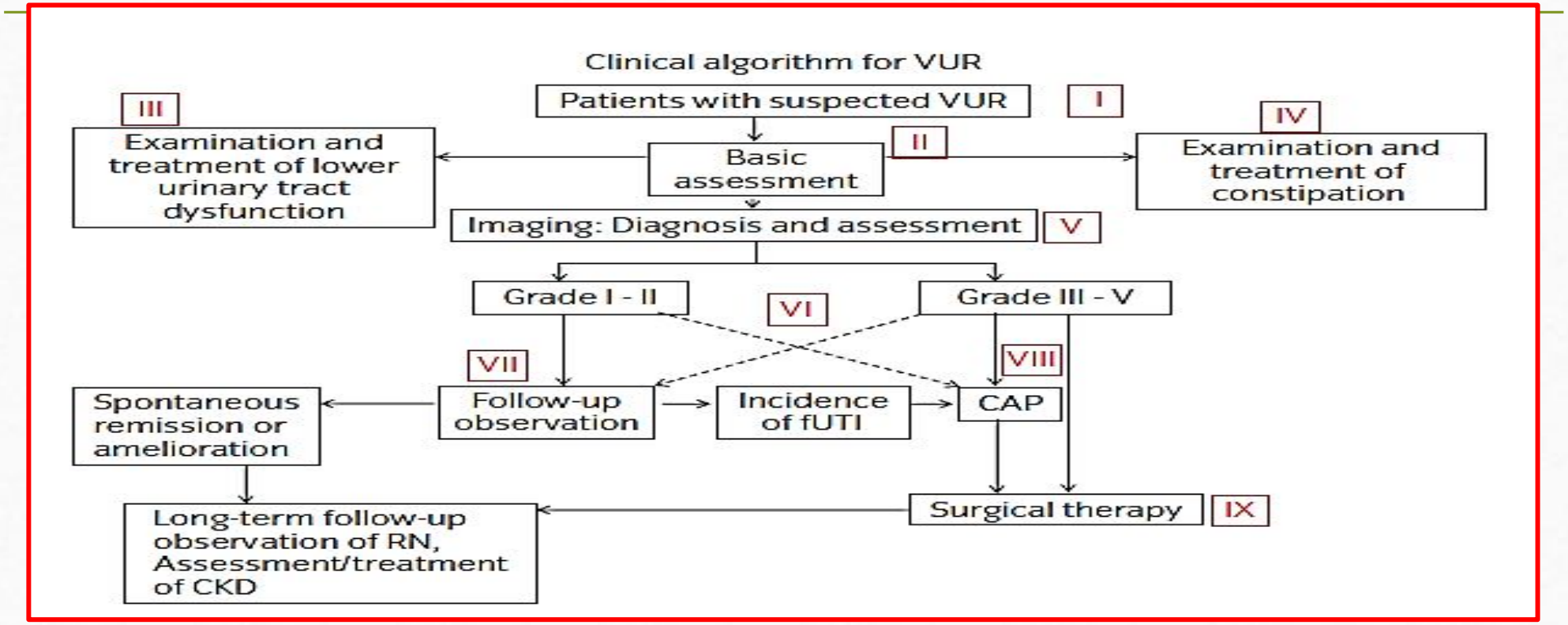

1. **The gold standard radiologic tool for diagnosis of VUR in infants is:**

a. Renal ultrasound.
b. VCUG.
c. DMSA scan.
d. Plain x ray abdomen.

2- According to the American Academy of pediatrics recommendations; VCUG should be performed in all the following situations except:

a. All Infants less than 24 months age after their first febrile UTI.
b. Infants less than 24 months age after recurrent febrile UTIs.
c. Infants less than 24 months age after their first febrile UTI if renal ultrasonography was abnormal.
d. Infants less than 24 months age after their first febrile UTI if urine culture revealed pseudomonas infection.

3-Continuous antibiotic prophylaxis is indicated in all of the following situations except:

a. VUR secondary to posterior uretheral valve.
b. VUR associated with BBD.
c. Patients with primary high grade VUR.
d. All non toilet trained children with VUR regardless of the grade.


THANK YOU!