

# Medical versus Surgical Management of Vesico Ureteral Reflux

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## Abstract

Vesico ureteral reflux is the abnormal retrograde flow of urine from the bladder into the ureter and possibly the kidney. There are 2 types of reflux:

**Primary reflux** – which is caused by a congenital abnormality at the ureterovesical junction

**Secondary reflux** – occurs when high pressure in the bladder causes a breakdown of the normal antireflux mechanism at the ureterovesical junction that occurs in children with posterior urethral valves or neurogenic bladders. This also happens in children who have complete ureteral duplication with or without a ureterocoele.

This article focuses on primary vesico ureteral reflux and the approach to this entity. Primary vesico ureteral reflux can and should be treated conservatively (except Grade V bilateral reflux) with very selective indications for surgical intervention. The advantages and the disadvantages are discussed in detail together with details of both these modes in the treatment of reflux, and recommendations for therapy, follow up and the future.

The choice for conservative or surgical therapy for vesico ureteral reflux (VUR) applies only to primary VUR. In order to understand the arguments for and against the type of therapy –one must understand the basics of what is VUR and its natural course, hence a brief summary of VUR follows and then the actual details of medical or surgical intervention.

VUR refers to the retrograde flow of urine

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from the bladder into the upper urinary tract. Reflux may be congenital or acquired. Reflux can be basically divided into 2 types – primary and secondary.

The incidence of reflux in asymptomatic children is anywhere between 0.5% and 18.5%. In children who present with urinary tract infection, reflux has been found in 29 – 50% cases.<sup>1,2</sup> Though VUR is more common in girls, boys with urinary infections have a higher incidence of VUR. The incidence of VUR is also found to be inversely proportional to the age.

**Primary VUR** is caused by a congenital inadequacy of the valvular mechanism at the uretero-vesical junction(UVJ), and secondary reflux is the result of anatomic abnormalities (posterior urethral valves(PUV), prune belly syndrome, ano rectal malformations(ARM); or due to functional obstructive phenomenon (myelodysplasia, dysfunctional voiding)

**Primary VUR** : The main factors that keep the UVJ valve mechanism intact are:

- Oblique entry of ureter into the bladder and ratio of submucosal tunnel length to ureteral diameter of 4:1.<sup>3,4</sup>

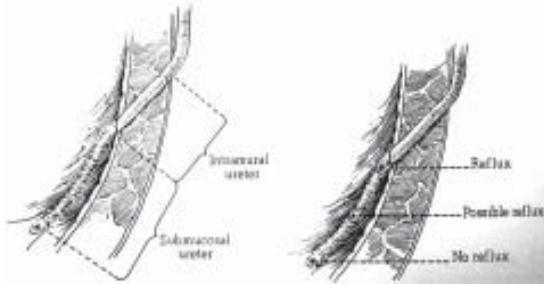


Fig. 1 : Anatomy of vesico ureteral junction.

- An active component is the ureterotrigonal longitudinal muscles that close the ureteral meatus and submucous tunnel during the detrusor contraction.<sup>4</sup>
- Active ureteral peristalsis during diuresis also prevents reflux.<sup>5</sup>

The debate for medical vs Surgical therapy for VUR is essentially restricted to primary reflux and will not hold in patients with :

### Secondary Reflux

Reflux associated with urinary tract anomalies (duplication, diverticulum, PUJ, horseshoe kidney, ureterocoele etc)

The natural history of primary reflux is that with continuous antibiotics, lower grades of reflux resolve spontaneously in 5 years from the time it has been diagnosed. Thus care needs to be taken for that period with a close and proper follow up on a regular basis.

Vesico ureteral reflux has been graded as per International classification for the sake of uniformity from Grade I – Grade V as follows (Fig. 2).

Grade I: Wisp of reflux into ureter

Grade II: Reflux into ureter, renal pelvis and calyces; but normal delicate cupping of calyces present

Grade III: Reflux with mild or moderate dilatation and /or tortuosity of ureter and mild or moderate dilatation of renal pelvis with slight or no blunting of calyceal fornices

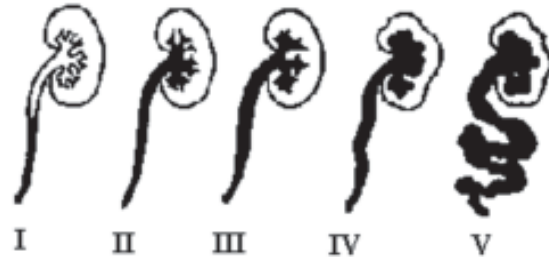


Fig. 2 : International grades of vesicoureteral reflux.

Grade IV: Reflux with moderate dilatation and/or tortuosity of ureter and moderate dilatation of renal pelvis and calyces with complete obliteration of sharp angle of fornices but with maintenance of papillary impressions in majority of calyces

Grade V: Reflux with gross dilatation and tortuosity of ureter and renal pelvis and calyces with disappearance of papillary impressions in the majority of calyces.

### Effects of Reflux

VUR predisposes an individual to Pyelonephritis by facilitating the transport of bacteria from the bladder to the upper urinary tract

Immunologic and inflammatory reaction caused by pyelonephritic infection results in renal injury or scarring. Renal scarring is radiologically diagnosed and is almost always due to reflux. On the other hand, 30 – 60% children with VUR have renal scars.<sup>2,5</sup> It has been said sterile reflux alone may be sufficient to cause renal scars. Continuous low dose chemoprophylaxis that keeps the urine sterile prevents development of new scars.<sup>6</sup> Short courses of antibiotics is not effective and about 20% of children develop scars during the treatment.

Extensive scarring causes reduced renal function and may lead to renin mediated hypertension.<sup>7</sup> Smellie and Normand found progressive renal damage in patients with hypertension. In fact hypertension may not

always be due to renal failure, rather to associated vascular lesions. Other effects of renal scarring are renal insufficiency, end stage renal disease, reduced growth and morbidity during pregnancy.<sup>8,9</sup>

Recent reports confirm that renal damage like scarring, parenchymal thinning, diminished renal size has been found some infants in whom reflux was antenatally detected, and this damage can occur in the absence of urinary tract infection.<sup>10</sup>

### **Principles of management**

The primary goals of therapy in VUR in children are :

- Avoid infection – symptomatic pyelonephritis
- Prevent renal injury
- Prevent renal hypertension secondary to effects of reflux
- Allow proper and normal renal growth

There are 2 types of therapy – Medical or conservative and surgical or operative.

Medical therapy is based on certain assumptions and principles.

- Reflux resolves given adequate time – spontaneous resolution
- Reflux without infection does not cause scarring, and complications
- Renal damage due to reflux occurs prenatally and cannot be prevented, no new damage occurs after birth
- Damage to the kidneys that occurs on medical or after surgery is almost the same percentage as explained further in the chapter.

The mean age of reflux resolution is 4.6 to 6.8 years of life. The overall spontaneous resolution rates are as follows<sup>11</sup>

- Grade I: 90%
- Grade II: 75%

- Grade III: 50%
- Grade IV: 25%
- Grade V: 0-5%

Detailed studies have also give an insight to the ultimate prognosis

Grade I and II: Age at presentation and laterality have no effect on resolution rates

Grade III: Increasing age and bilaterality shows a poorer prognosis

Grade IV: Resolution of VUR is about 10% at 5 years in bilateral cases, but 40% at 5 years in unilateral cases

### **Medical therapy** consists of

The medication used should achieve a high urinary concentration

The medication should have a broad spectrum of activity

The antibiotic is administered at half the standard dose

Antibiotic must be changed at regular intervals to avoid resistance, cumulative side effects

Follow up radiological investigations like MCU, USG and renal DMSA scans must be done at yearly intervals

The success of medical line of therapy can only be judged on the basis of its results and these can be grouped in many ways and based on multiple studies

- *Reflux resolution:* Though spontaneous resolution of reflux is an accepted fact, an in-depth study will clarify and prognosticate the chances of resolution in a given case. In general a lower grade reflux has a better chance of resolving.<sup>11</sup>
  - Grade I and II: No difference in resolution rate with respect to age or laterality.
  - Grade III: Both age and laterality altered the resolution rate. Higher the age at presentation(or diagnosis), and / or

bilaterality of reflux lessor the chances of resolution and surgical intervention may be required.

Grade IV: A very low chance of resolution if bilateral at time of presentation irrespective of the age of the child and surgery may be opted for earlier.

- *Renal scarring*: Most studies having a minimum 5 years follow up show there is no statistical difference in the rate of new scarring in patients treated medically or surgically. The Birmingham Reflux Study identified new scars after 5 years in 6% of medically treated and 5.2% of surgically treated patients
- *Renal growth and Function*: There is no evidence to show that renal growth is impaired in unscarred kidneys exposed to sterile reflux of any grade. Surgical correction of VUR does not facilitate growth of the kidney postoperatively. However, surgical correction stabilizes the glomerular filtration rate but has not lead to a long term improvement
- *Urinary Tract Infection*: In children with grade II – IV VUR, the incidence of pyelonephritis was 2.5 times higher in medically treated patients than those surgically treated.
- *Hypertension*: There is no statistically significant difference in the risk of hypertension related to medical or surgical therapy
- *Uraemia*: With severe bilateral reflux nephropathy – neither therapy can prevent progressive renal failure and uraemia.
- *Somatic growth*: There is no evidence to show the effect of therapy of VUR on growth of the child – thus medical therapy is as good as surgical therapy.

In order to get the best results of non

surgical therapy, a comprehensive medical line of therapy will involve not only the medication – antibiotic to be given but in addition two other things which have to be individualized, that is bladder training and Anticholinergics medications in selected cases.<sup>12</sup>

**Comprehensive Medical therapy** for VUR is always started in any child diagnosed to have Primary VUR except Grade V bilateral reflux where surgery may be advisable at diagnosis unless the child is few months old. Another point of importance is the presence of scars at the diagnosis, if present, the therapy and changeover to surgery may be earlier. This therapy may consist of one or more of the following

- *Bladder training*: this consists of a number of steps
  - Regular, volitional and complete emptying of the bladder
  - Voiding schedule –about 5 – 7 times per day
  - Reeducation – proper voiding dynamics to be taught to the child
  - Elimination of constipation that may be concomitantly present
  - Genital and perineal hygiene – cleaning and keeping dry emphasised
- *Continuous antibiotic prophylaxis*: this involves
  - Giving antibiotic once a day – usually at night
  - Dose is 1/3 of the dose required for acute infection
  - Long term for years till reflux resolves or the risk of reflux is considered low
- *Anticholinergic medication*: this is required in cases who have
  - Bladder instability, frequency, urgency
  - Urge incontinence

Drugs used – Oxybutynin,  
propantheline Bromide

The above used judiciously will give the best results in a given child

Success of Medical therapy is when:

Child is free of infection

Develops no new renal scars during follow up

No progress of existing scars during follow up

Reflux resolves spontaneously

**Failure** of medical therapy is:

Break thorough urinary infection when child is on antibiotics

Development of new scars

Progress of existing scars

Failure of reflux to resolve

Non compliance of drugs and instructions by the patient

Allergic or side effects of the medication prescribed to the patient

I have treated over 25 patients of primary reflux with low grade medically with excellent results. The only patients I had to operate were due to non compliance, breakthrough infections, or children from out of Mumbai, where, follow up was erratic.

**Surgical Intervention** in cases of VUR is the alternative mode of treatment and this can be divided into 3 types of interventions<sup>13</sup>

□ **Open surgery** – Reimplantation of ureter - Extravesical, transvesical or a combination. Ureteral reimplantation surgery is an extremely successful procedure, with the elimination of VUR in over 95% operated cases. There is no fixed surgical procedure for all reflux but should be tailored for the individual case. The various techniques described are concerned with the intravesical or

extravesical lengthening of the intramural ureter, or with advancing the ureteral orifice towards the bladder neck. It is always better to operate when there is no active infection, and not sooner than 3 weeks after an acute urinary infection has been treated. I shall describe in short some of the commonly used methods of surgical correction.

**Politano – Leadbetter Technique:** This is a transvesical technique – a circular incision is taken around the ureteral opening, and free it from the trigone. The intravesical ureter is dissected and then brought inside the bladder through a new hiatus above and lateral to the original one. A submucosal tunnel is dissected from the new hiatus to the original one and the ureteral orifice is sutured back in its original position. A long intravesical ureteral segment lies submucosally and is supported by intact and unincised vesical detrusor (Fig. 3).

**Cohen Advancement Procedure:** This is very commonly used all over and has excellent results uniformly. In this, sufficient mobilization of the ureters is done transvesically. Separate submucosal tunnels are made for each ureter across the bladder base, so that each ureter opens on the opposite side from its hiatus (Fig.4).

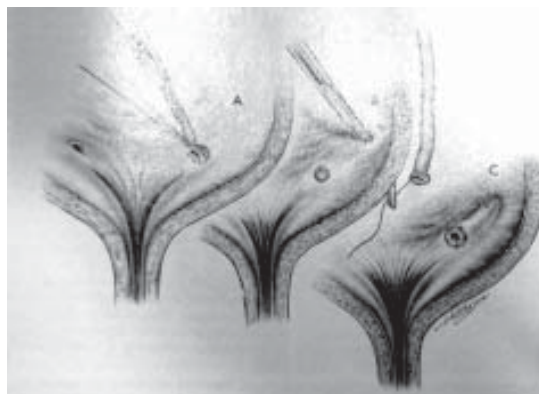


Fig. 3 : Politano leadbetter technique.

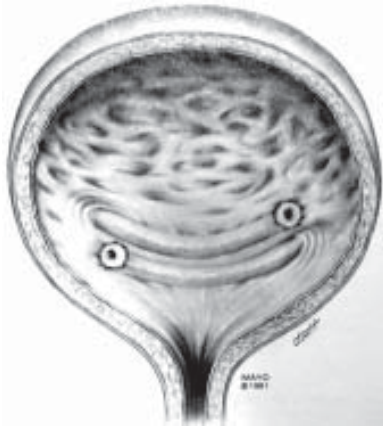


Fig. 4 : Cohen technique.

Other techniques are : Lich Gregoir, Glenn Anderson, Paquin, etc. (Fig.5).

- Endoscopic Injection of Teflon, Collagen etc. This procedure is a relatively non invasive method of therapy where Endoscopically a substance is injected in subureteric region. This has been popularised and used extensively by O'Donnell and Puri in Europe.<sup>14</sup> They have injected Polytetra-fluoroethylene(Teflon) paste. In their series, of 216 refluxing ureters that were injected, reflux resolved in only 76.3% after one injection, and overall resolution increased to 84% after 2 injections. However, pulmonary migration of Teflon particles was of concern to USA and hence the FDA banned the use of this drug. Recently use of another molecule (Diflux) is being done with more or less similar results and it is considered safer than Teflon. However, this result compares poorly with operative results of 95 – 99% success. Additionally, the cost of the Diflux material is at present Rs. 20,000 which does not include the cost of the scopy, the operation theatre, the anaesthesia and one day stay that is required.
- **Laparoscopic** reimplantation of ureter.

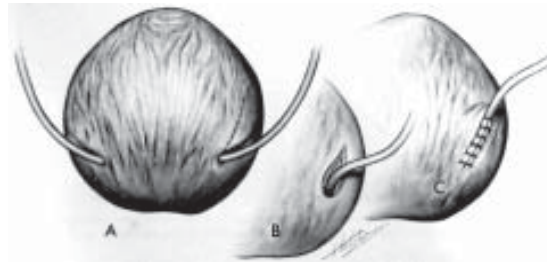


Fig. 5 : Lich gregoir method.

This is a relatively new approach with limited success and no definite results are available to compare with open surgery. Long term results will be important to know the effectiveness.<sup>15</sup>

The results of surgical intervention can also be based on certain criteriae:

- *Reflux resolution* : Surgical reimplantation for reflux has shown an overwhelming success rate with a single surgical procedure<sup>16</sup>
  - Grade I: 99%
  - Grade II: 99.1%
  - Grade III: 98.3%
  - Grade IV: 98.5%
  - Grade V: 80.7%

For endoscopic surgery overall reflux correction is about 77.1% in single injection.<sup>16</sup>

- *Renal Scarring*: statistically insignificant difference in scarring following surgical or medical therapy
- *Renal growth and Function*: surgical correction of the reflux stabilizes the glomerular filtration rate but does not show any long term improvement
- *Urinary tract infection*: Grade II - IV – pyelonephritis is 2.5 times higher in those treated medically than those treated by surgery
- *Hypertension*: No difference statistically for the risk of hypertension following medical or surgical intervention

- *Complications of surgery* : Obstruction about 2%. Contralateral reflux incidence of 9.1% and this usually resolves with time about 1 year.

The indications for surgery in general are<sup>13,16</sup>

Reflux with upper urinary tract anomalies – duplication, ureterocoele etc.

Bladder diverticulum with ureteral reflux  
Reflux in a solitary kidney

Break through infection in a child on antibiotic prophylaxis

Appearance of new scar	} Failure of medical therapy
or progress of existing scar(s)	
Grade V reflux in older child	

Bilateral Grade IV – V reflux in any child

Non compliance of medical line of therapy

Persistent secondary reflux in cases like Posterior urethral valves

Having now defined the difference between medical and surgical therapy, the actual question comes that in a given child diagnosed to be having VUR, what should be the ideal approach and when to choose to change from medical to surgical.

In children with VUR, the initial evaluation may differ from case to case.

In all children, urine must be examined to look for infection and proteinuria. The child's height, weight and blood pressure must be noted before proceeding further.

If the child shows evidence of renal scarring, hydronephrosis, has a single kidney or has some known underlying renal disease – a serum creatinine must be done. In children who have a definite history of voiding dysfunction, a urodynamics study is of great value – since, if this problem remains untreated or is ignored even the best treatment will fail.

The socio economic and interest of the parents and family may also change the type of therapy option. For example if the child is from a village outside a main metropolis and is unlikely to follow up regularly or get investigated as advised, or may not be relied upon to take the oral medications regularly – then surgical intervention may have to be suggested earlier than normally one would. In boys, diagnosed to have VUR, circumcision would be advisable in order to decrease the incidence of recurrent UTI. Urine collection for routine, and more important in culture specimen proper collection makes a lot of difference as well as the quality and reliability of the laboratory doing the cultures.

Follow up evaluation needs to be done yearly – this should include clinical as well as investigative. Height, weight, blood pressure and urinalysis from clinical standpoint. History suggestive of urinary infections in that year, any pain in loin to suggest attack of pyelonephritis etc. Feedback on voiding schedule, low pressure volitional voiding is also very important. Micturating Cystourethrogram must be carefully done to compare the VUR grade, DMSA scan for either new scars or increase of old scars. Current recommendations are slightly different – and less aggressive. Imaging every 2 years in children with Grade I and II VUR and children younger than 2 years with unilateral Grade III. Older children with Grade III and all children with Grade IV VUR should be imaged every 3years.<sup>16</sup> This recommendation is based on the relatively slow rate of VUR resolution, balanced with the morbidity and cost of repeated imaging studies compared with the side effect of long term antibiotic prophylaxis.

### Conclusions

The initial therapy in all primary reflux irrespective of grade and presence of scars is

conservative. The advantages are that with this non invasive therapy, results are almost as good as surgery, easily accepted by the child and parents. Medical therapy has few short term risks. It is proved beyond doubt that of Grade I – III reflux at least 50% cases resolve within 3 – 5 years with continuous antibiotic prophylaxis. Girls need to be treated more aggressively than boys because girls have a higher risk of acquiring UTI than boys. If there is no resolution of reflux, or breakthrough infections or non compliance by the child and family, then this would be the right time to go in for surgical correction of reflux to prevent further damage to the kidney(s). Grade IV reflux may be initially treated medically with close follow up in younger age group and unilateral, but if bilateral and persists on follow up, surgery is advised without any further delay.

Aggressive therapy i.e. surgery for Grade V is based on the accepted finding that such cases are unlikely to resolve spontaneously on antibiotic therapy, same is true for children having scars at diagnosis, since these cases face a higher risk of progressive scarring and decreased renal functional reserve.<sup>17</sup>

In short, the therapy recommended depends on multiple parameters like

- age of the child at diagnosis,
- the grade of the reflux,
- the sex of the child,
- presence or absence of scars
- presence of voiding dysfunction

Thus choosing the correct treatment - medical or surgical is crucial at each stage to give the best result in terms of renal function, growth, scarring, pyelonephritis and recurrent urinary infections and hypertension.

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#### **IS IT TIME TO SCREEN AND TREAT H PYLORI TO PREVENT GASTRIC CANCER?**

Despite classification of *Helicobacter pylori* as a carcinogen, screening for and treatment of infected people to prevent gastric cancer is not generally accepted. Yet globally, gastric cancer is the second leading cause of cancer deaths annually. Up to 80% of non-cardiac gastric adenocarcinomas are attributable to this bacterium, probably through the development of gastric atrophy followed by intestinal metaplasia.

The results are clear: in a high-risk population, gastric cancer rates are substantially reduced, but not abolished, by *H. pylori* eradication.

Data from randomized trials suggest that the relative risk of developing gastric cancer after *H. pylori* eradication in other high-risk populations is reduced. An Asia-Pacific consensus conference in 2007 concluded that population-based screening and antibiotic treatment of *H. pylori* in high-risk populations is now recommended.

Population based screening by double-contrast barium radiography or upper endoscopy is used in Japan and Korea to detect early gastric cancer.

*H. pylori* eradication has potential risks in a population setting. For example, the strategy could increase risk of gastro-oesophageal reflux disease (GORD), Barrett's oesophagus, and oesophageal adenocarcinoma. A meta-analysis concluded that presence of *H. pylori* (pooled odds ratio 0.52, 95% CI 0.37-0.73) and more virulent *H. pylori* strains (0.51, 0.31-0.82) were protective against oesophageal adenocarcinoma.

Disappearance of *H. pylori* might unmask asthma and atopy, although a causal association has not been established.

Compelling evidence now exists to show that *H. pylori* eradication reduces risk of subsequent gastric adenocarcinoma irrespective of age.

**Nicholas J Talley, *The Lancet*, 2008; 372 : 350-51.**