Vesicoureteric reflux

#2 presentation in paediatric urology
a/w renal scarring, hypertension, reflux nephropathy and occasionally ESRF
Incidence ~ 1-2% 'normal' paediatric population
Commoner in male infants and girls > 12 months (5:1 female:male)
White > blacks
VUR in boys
- Clinical presentation or prenatal
- Age 0-2 yrs
- Moderate to high grade
- Anatomical factors important

VUR in girls
- Clinical presentation
- Age 2-7 yrs
- Low grade
- Functional factors important (dysfunctional voiding/ defaecation)

Classification
- Primary
  - Congenital
  - Defect in longitudinal muscle of intravesical ureter and lateral insertion of UO short transmural tunnel – inadequate valvular mechanism
  - Genetic predisposition
    - 50% offspring of women with VUR
    - 33% sibling with VUR
    - Autosomal dominant with variable penetrance/expression
- Secondary
  - Neuropathic bladder (#1 cause)
  - Posterior urethral valves
  - Non-neurogenic dysfunctional voiding (DSD, OAB, constipation: often contributes to so-called primary VUR)
  - Urinary tract infection - due to reduced compliance, increased intravesical pressure, distortion of VUJ secondary to oedema and paralysis of ureteric smooth muscle due to bacterial endotoxins

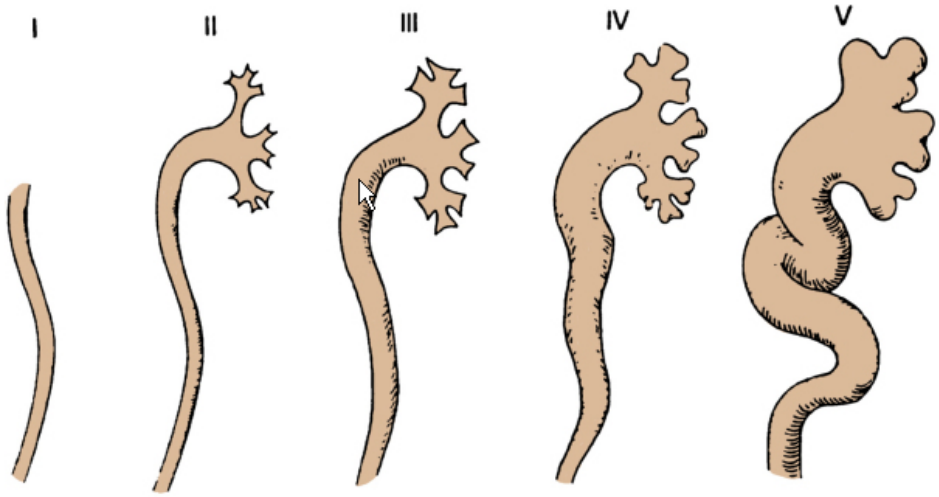
VUR and renal damage
- One third of refluxing units a/w renal scarring at presentation
- Risk of nephropathy/hypertension
  - 10% with unilateral scarring
  - 20% with bilateral scarring
- ESRF < 0.1% of those with scars
- Renal damage may be 'aquired' prenatally, presenting with globally small kidneys or associated with post-natal infective episodes
- Pioneering animal work by Hodson, Ransley identified the importance of reflux of infected urine – reflux of sterile urine not a/w scars. Also:
  - Renal scarring occurs maximally after first episode pyelonephritis
  - Conical renal papilla protect against reflux. Compound papillae at renal poles most susceptible to renal scarring

Natural growth of bladder + ureter causes elongation of transmural ureter – therefore greater risk of scarring before 4 yrs of age
Asymptomatic bactiuria not associated with renal scarring – only febrile UTI causing pyelonephritis

Imaging

USS	poor sensitivity: can miss up to 75% of cases
DMSA	good for renal scarring/split function, poor for reflux
MCUG	Gold-standard. Allows grading (see below) and anatomy
MAG-3	Follow-up only. Lower sensitivity, no grading, no anatomy

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



Management

Because sterile urine not a/w scarring and VUR has the tendency to spontaneously resolve over time (see below), conservative medical management primarily indicated.

Grade of reflux	Distribution of different grades of reflux (%)	Spontaneous resolution rate for each grade (%)
I	7	83
II	53	60
III	32	46
IV	6	9
V	2	0

<u>International reflux committee values</u>

I	90% resolution
II	80% resolution

III 50% resolution
IV 20% resolution
V <10% resolution

Medical management comprises:
(i) Continuous antibacterial prophylaxis until 4yrs old
(ii) Urine dipstick surveillance
(iii) Management of underlying dysfunctional voiding (drill, double void, oxybutynin etc.)
(iv) Treatment of chronic constipation

NB. Recently some authors have criticised antibiotic therapy because:
a. Poor compliance [one large study of US kids showed compliance rates of ~ 40%]
b. High incidence of breakthrough infection even when 100% compliant (~60%)
c. Promotes bacterial resistance without reducing the incidence of UTI (Conway JAMA 2007)

<u>Indication for surgical intervention</u>
Failure to comply with Abx
Breakthrough infections of Abx
Grade IV/V reflux
Hutch diverticulum
? persistent reflux in girls > 5 years
? parental choice

Surgical management comprises:
(i) Endoscopic subureteric injection therapy (PTFE, collagen, dextranomer/hyaluronic acid co-polymer (Deflux – only treatment approved by US FDA), polydimethylsiloxane (Macroplastique))
Success rates for correction of VUR grades I and II, III, IV and V were 78.5%, 72%, 63% and 51% after one treatment; second treatments had an overall success rate of 68% (Elder 2006)
Advantages that day-case procedure, cheap, repeatable.
Observational studies suggest that subureteric injection a/w lower UTI frequency than prophylaxis alone(Elder 2007), but no randomized studies. Appears inferior to re-implantation
(ii) Ureteric re-implantation (neoureterocystostomy)
Length 5 x diameter of re-implanted ureter
Numerous methods
Cohen-Ahmed
cross-trigonal
low complication rate (preservation of detrusor hiatus reduced risk of obstruction)
Politano-Leadbetter

- Most comon worldwide
- Extension of tunnel superolaterally and inferomedially
- Length to diameter ration follows Paquin's 5:1 rule (determined on normal children)
- Often requires psoas hitch
- Good for megaureter (in concert with Starr plication)
- New detrusor hiatus can obstruct however

Glenn-Anderson
- Modified Politano-Leadbetter
- Not good for dilated ureters

Lich-Gregoir
- Extramucosal advancement
- Minimal haematuria and pain
- Not good for dilated ureters
- ? precipitates voiding dysfunction (2' to extravesical mobilisation)

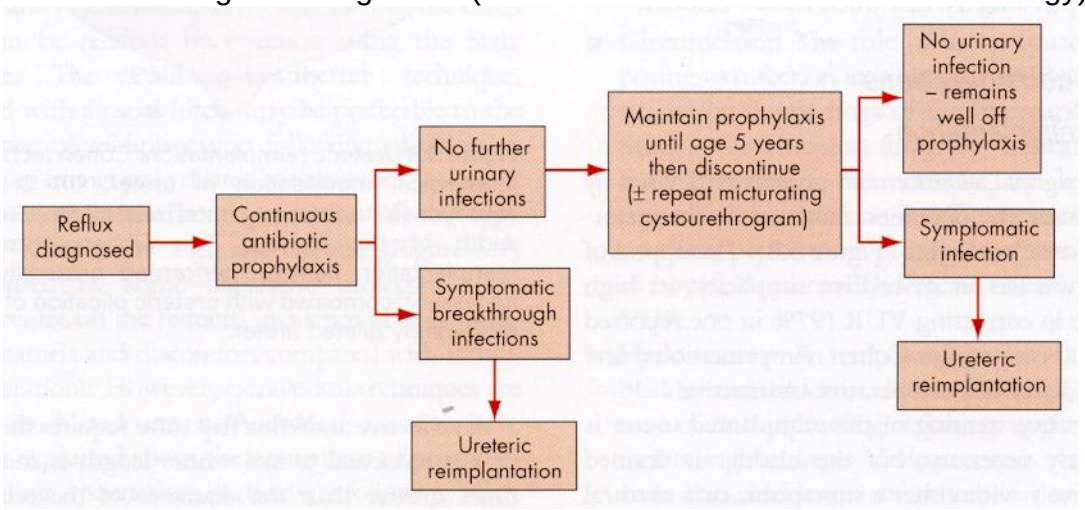
(iii) Other surgical alternatives
- Circumcision – controversial
- Vesicostomy or SPC
- Nephroureterectomy (non-function)
- TUU (previous failed open re-implant)

Medical management or surgical intervention - evidence

Number of trials assessed outcome including Birmingham Reflux Study Group and International Reflux Study. The outcome of these studies and other assessed by Cochrane review (Hodson 2007). Findings:

1. No Rx vs. ABx prophylaxis
   - Small, underpowered, large confidence intervals
   - No difference in UTI frequency
2. ABx + re-implant vs. ABx alone
   - Majority of studies including big 2 above
   - No difference in UTI frequency up to 10 yrs (still 40-50% in each group)
   - Reduced frequency of febrile UTI/pyelonephritis in surgical group (NNT 10-15 to prevent one febrile UTI)
   - No difference in scarring or nephropathy up to 10 yrs
3. Surgery alone vs. Abx
   - Never been performed
4. Subureteric injection vs. ABx
   - Never been performed. Observational data suggest that subureteric injection a/w lower rate of UTI but no RCT data
5. Subureteric injection vs. surgery
   - Never been performed

Practical management algorithm (D Thomas – essentials Paediatric Urology)

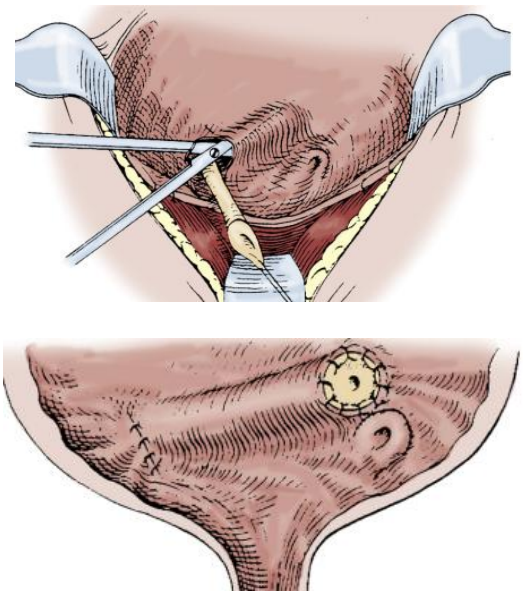


Screening

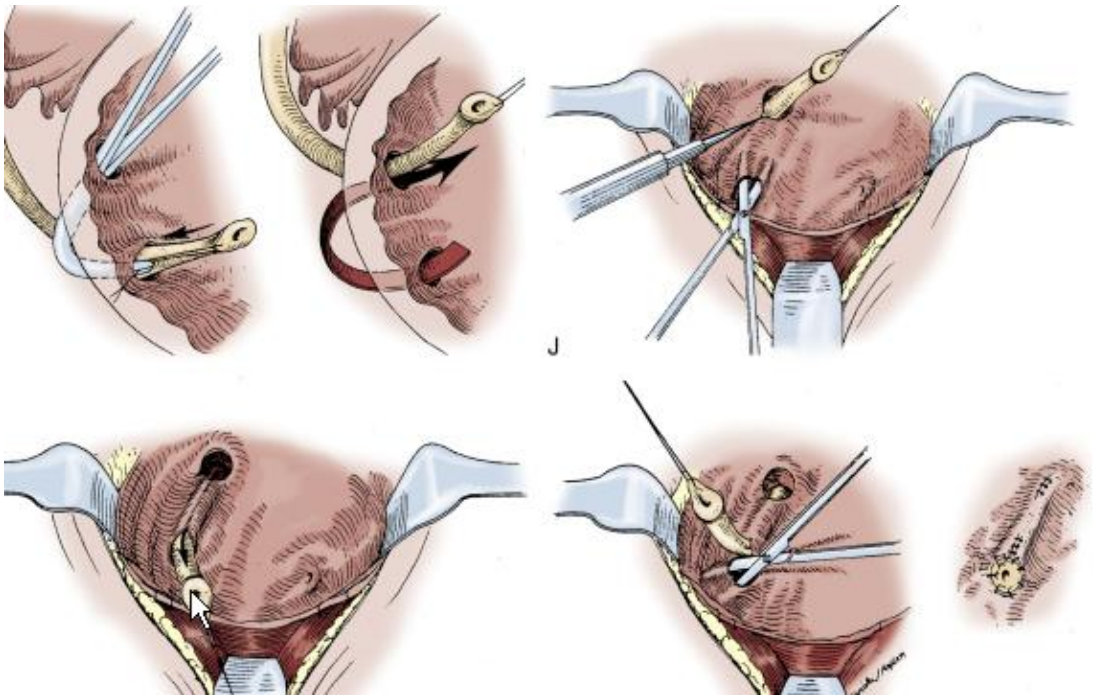
DMSA and MCUG too invasive and expensive for routine screening
USS cheap and acceptable but high false negative rate
Benefit of intervention not conclusively proven
Siblings of index case < 4 yrs recommended ?USS/MCUG/indirect cystography to be characterized.

Appendix

Cohen-Ahmed cross-trigonal ureteric reimplantation (neoureterocystostomy)



Leadbetter –Politano



Lich-Gregoir