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 ‘acquired’ 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**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
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<tbody>
<tr>
<td>USS</td>
<td>Poor sensitivity: can miss up to 75% of cases</td>
</tr>
<tr>
<td>DMSA</td>
<td>Good for renal scarring/split function, poor for reflux</td>
</tr>
<tr>
<td>MCUUG</td>
<td>Gold-standard. Allows grading (see below) and anatomy</td>
</tr>
<tr>
<td>MAG-3</td>
<td>Follow-up only. Lower sensitivity, no grading, no anatomy</td>
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</table>

**Grade Description**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>Into a nondilated ureter</td>
</tr>
<tr>
<td>II</td>
<td>Into the pelvis and calyces without dilatation</td>
</tr>
<tr>
<td>III</td>
<td>Mild to moderate dilatation of the ureter, renal pelvis, and calyces with minimal blunting of the fomices</td>
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<tr>
<td>IV</td>
<td>Moderate ureter tortuosity and dilatation of the pelvis and calyces</td>
</tr>
<tr>
<td>V</td>
<td>Gross dilatation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity</td>
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**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.

<table>
<thead>
<tr>
<th>Grade of reflux</th>
<th>Distribution of different grades of reflux (%)</th>
<th>Spontaneous resolution rate for each grade (%)</th>
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<tbody>
<tr>
<td>I</td>
<td>7</td>
<td>83</td>
</tr>
<tr>
<td>II</td>
<td>53</td>
<td>60</td>
</tr>
<tr>
<td>III</td>
<td>32</td>
<td>46</td>
</tr>
<tr>
<td>IV</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>V</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

**International reflux committee values**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Resolution</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>90%</td>
</tr>
<tr>
<td>II</td>
<td>80%</td>
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</table>
Paediatrics - VUR

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)

Indication for surgical intervention
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
t      cross-trigonal
      low complication rate (preservation of detrusor hiatus reduced risk of obstruction)
      Politano-Leadbetter
Most common worldwide
Extension of tunnel superolaterally and inferomedially
Length to diameter ratio 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)

[Image of surgical procedure]

Leadbetter–Politano

[Image of surgical procedure]
Lich-Gregoir