UTI In Children

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Introduction

- Predisposition to UTI
- Diagnosis
- Investigations
- Treatment
Why important

- UTI → Pyelonephritic scarring (reflux nephropathy) → chronic renal failure
  - Leading cause of end stage renal failure in children worldwide
- UTI → renal scarring → Hypertension
Therefore:

investigations: identifying those children with UTI's that are at risk of developing chronic renal failure

Treatment aimed at hopefully preventing damage/further damage
What predisposes someone to a UTI

- Residual urine

- Nidus for infection:
  - Stones crystals
  - Foreign body

- Bacterial factors

- Host Factors
  - Systemic diseases
    - Malnutrition (Kwashiorcor)
    - Diabetes mellitus
    - Immune deficiency diseases and immunosuppression (steroids)
  - Local Host defences
Regular and complete emptying...

- **Residual urine**
  - Reflux
  - Obstruction: PUJ, VUJ, PUV
  - Bladder dysfunction
    - Constipation
    - Dysfunctional voiding
    - Neurogenic bladder
Bacterial Factors

- Bacteria must be able to
  - Colonise gut
  - adhere to the perineum or prepuce
  - Adhere to urothelium
  - Grow well in urine double rapidly
Bacterial factors

- **Bacterial properties**
  - O Ag, K Ag
  - Adhesive capacity: p-fimbria toxins
  - Inflammation → alters ureteral peristalsis

- **Periurethral bacterial flora**
  - Normally colonized by aerobic and anaerobic organism
  - First years of life

- **Increased No of pathogenic organism**
  - Presence of prepuce
  - Antibiotic eradication of normal vaginal/periurethral flora
Local host defence

- Increase susceptibility to bacteria
  - Antibactericidal activity of bladder wall
  - Increased receptivity to bact fimbria

- Antiadherence mechanisms
  - Differences in secretion of the molecules: IgA, Tamm horsfall

- Trauma to external urethral meatus
  - Bubble bath
  - Wiping method
Symptomatic UTI

- Upper tract Pyelonephritis
  - TEMP > 38.5
- Lower tract
Epidemiology

- Overall incidence 1-3% of all children
- Female > males except first months of life

Hansson S Acta Paediatrica 1999
Jakobsson B Pediatrics 1999
“Don’t worry darling, you didn’t burn the beer!”
Epidemiology(2)

- $\frac{1}{2}$ girls and $\frac{1}{3}$ boys
- Have demonstrable underlying renal abnormalities
  - vesico-ureteric reflux
  - Obstructive lesion
Factors which predispose to renal scarring include:

- **Young age with acute pyelonephritis**, Berg 1989 Pediatr Neph; Smellie JM 1985 BMJ
  
  Questionable Benador 1997 Hewitt IK,

  
  Questioned: Pediatrics 2008; Doganis D, Pediatrics 2007


- **Severe VUR (Grade III-V)** Ransley PG Br J Radiol 1978 Nuutinen2001 Pediatr Nephrol, Merrick 1995 Arch Dis Childhood
  

- **VUR causing renal dysplasia in utero** Blumenthal

- **Congenital obstructive uropathy** Rushton 1992 J Urol
How to make a Paediatrician grumpy

- Is this really a UTI!
- Extensive investigations
- Unpleasant procedures
- Expensive
- Long term consequences/follow up for child
How to collect urine and diagnose UTI correctly

- Careful attention to detail – NB
- Methods
  - Bag method
  - Clean catch
  - Suprapubic pucture
  - In and out catheter
Bag specimen

- Clean genitalia with sterile water
- Remove immediately after micturition
- **Unacceptable** for culture - only good for screening
- If positive (dipstix leuc or nitrite) then send another specimen using other collection method
Positioning of the patient for suprapubic bladder aspiration  The child is restrained in the supine and frog leg position. This permits adequate stabilization of the pelvis. The site for needle insertion is in the midline, approximately one to two centimeters above the pubic symphysis. Adapted from King, C, Henreting, FM. Pocket Atlas of Pediatric Emergency Procedures, Lippincott Williams and Wilkins, Philadelphia 2000.
Gentle traction of the labia majora in females to visualize the urethra. Gentle traction of the labia majora in girls facilitates the visualization of the urethra for transurethral bladder catheterization.
Proper position for penis in transurethral bladder catheterization in
﻿

Processing urine

- Send to lab within 1 hour
  - Bact count doubles every 20 min
- In refrigerator <4 degrees for 24 hours
  ie do not leaving urine specimens lying around will result in false positive’s
“Real” Urine collection

- Bag specimen is a reasonable screen
- Bag collection adequate in circumcised boys
- In girls and uncirc. Boys invasive collection is cost effective but traumatic
  - Urgent vs. Screen
  - Sedation
  - U/S guidance
Clinical Picture

- Very varied.
- High index of suspicion often necessary.
- In babies often not related to urinary tract.
Clinical picture: newborn + infants

- Often a picture of septicaemia.
- Prolonged neonatal jaundice.
- Renal failure.
- Hypo- or hyperthermia.
- Apathy or irritability.
- Convulsions.
- Poor feeding or development.
- Diarrhoea, vomiting.
- Acidosis.
- Poor urine stream in boys. (Posterior urethral valve).
Clinical picture: older child

- **Upper urinary tract (Pyelonephritis)**
  - mostly systemic signs.
  - Fever above 38.5°C.
  - Rigors/convulsions.
  - Vomiting.
  - Abdominal pain. Tender renal angles
  - Dysuria

- **Lower urinary tract (Cystitis)** – few systemic signs.
  - Minimal or no fever.
  - Lower abdominal/bladder tenderness.
  - Dysuria and frequency.
  - Malodorous urine – sometimes bloody.
  - Crying on micturition.
  - Chronic nappy rash.
  - Secondary enuresis.
Symptoms Miming UTI's

- Dysfunctional voiding
- Local irritants
  - Foam baths, detergents, soap, chlorine, pin worm, foreign bodies, injury and meatal ulceration.
- Vulvitis
  - Relative oestrogen deficiency. Frequently associated with a discharge. Treat with Premarin cream nightly for 7 days. Antibiotic if the culture is positive.
- Emotional problems with or without secondary enuresis.
  - Often attention-seeking or adaptation problem.
- Constipation
- Unusual organisms. Chlamydia & mycoplasma.
Side room investigations: Urine dipstix

- Blood/protein: non-specific; many other causes.
- Leukocyte esterase test:
  - Sensitive for leukocytes but not specific for UTI’s – especially in girls.
- Nitrite test for bacteria:
  - High specificity (99%) but low sensitivity 50%.
- pH: alkaline urine - Proteus infection.

- Urine with any positive parameters should be sent for culture
- Negative we accept as negative
Bacteria:
- Uncentrifuged: 2-3 moving organisms/h.p.f.
- Centrifuged: 15-20 organisms/h.p.f
  - Correlate well with a bacterial count of 100,000 organisms/ml

White blood cells: Traditional, but may also give false positive and false negative results.
- **Centrifuged:**
  - < 5 WBC/h.p.f = negative
  - > 5-10 WBC/h.p.f. = suggestive, but not diagnostic.
- **Uncentrifuged:**
  - < 4000 WBC/ml = negative

Microscopy: wbc + bacteria = 99% specificity
Other causes of wbc in urine

- Fever
- Acute systemic/virus infections
- Dehydration
- Vulvovaginitis & urine reflux in vagina. Balanitis
- glomerulonephritis, interstitial nephritis
- Half treated UTI’s (Antibiotic)
- Appendicitis
- Tuberculosis (Relatively uncommon in children)
- Kidney stones (Usually infective in children)
- Cystic diseases of the kidneys
- After polio vaccination
Culture: When do you have proof of infection?

- >10 to 5 CFU
  - Clean catch
- >10 to 4 CFU
  - Catheter
- Any growth
  - Suprapubic collection
Bacteriology

- Gram-negative bacilli, of which Escherichia Coli most common (± 80%).
- Klebsiella spp,
- Enterococci (Enterococcus faecalis)
- Proteus spp in boys (urine alkaline)
- Pseudomonas and Serratia.
- Candida albicans
  - occurs especially in premature babies
  - may present with an obstructive picture due to the Candida-balls.
Further investigation:

- Want to find underlying abnormality of urinary tract
- Balance this against over investigating every child with a UTI and cost issues
Investigations

- Ultrasound
- Micturating cystogram
- Nuclear medicine studies DMSA, Mag 3
- IVP
- Magnetic resonance
Rationalization of Investigations

- **Whiting; Westwood 2005 review** on cost effectiveness of Investigations of UTI
  - no evidence to support the clinical effectiveness of routine investigations in a child with confirmed UTI

- Risk of scarring after 1 UTI almost negligible
<table>
<thead>
<tr>
<th></th>
<th>Responds well to treatment within 48 h</th>
<th>Atypical UTI</th>
<th>Recurrent UTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 6 months</td>
<td>Ultrasound</td>
<td>Ultrasound, DMSA and VCUG</td>
<td>Ultrasound, DMSA and VCUG</td>
</tr>
<tr>
<td>Age 6 months–3 years</td>
<td>None</td>
<td>Ultrasound and DMSA</td>
<td>Ultrasound and DMSA</td>
</tr>
<tr>
<td>Age &gt; 3 years</td>
<td>None</td>
<td>Ultrasound</td>
<td>Ultrasound and DMSA</td>
</tr>
</tbody>
</table>
CONFIRMED UTI
All patients have ultrasound (U/S) as soon as possible

Refer if no further imaging available

Normal U/S

No further infections

Normal

No further investigations

Abnormal U/S

2nd UTI or 'Atypical' UTI

Repeat U/S

Dilatation of system *

Normal

Abnormal

Normal

Abnormal

Dilated Kidney only – PUJ (pelvi-ureteric junction) obstruction need MAG3 Nuclear study

DMSA & DMSA in our setting best early as compliance better + if bad 'defect' proceed with investigations

Indirect Cystogram (Nuclear Medicine)

Boys > 3yrs or Girls Potty-trained (exclude VUR/bad scar)

MCUG

Boys < 3yrs or Girls not potty trained (exclude valve/reflux)

Refer and investigate appropriately
Atypical UTI includes:

- seriously ill
- poor urine flow
- abdominal or bladder mass
- raised creatinine
- septicaemia
- failure to respond to treatment with suitable antibiotics
- within 48 h
- infection with non-E coli organisms
Branches
Sometimes they appear out of nowhere
Screening for Posterior urethral valves?

- U/S of kidney and bladder high sensitivity (93-95%) for excluding PUV
  
  Williams Cr J Urol 2001

  Ismaili K J Pediatr 2002
Treatment

**Early treatment** can prevent or diminish renal damage!

- Adjust antibiotic dosage in renal failure.
Oral Vs IVI antibiotics

- IVI only vs IVI then oral
  - 4 trial comparing
    - IVI 7-14 days vs IVI 3-4 days then oral
    - “no differences in recurrence or scars.”
      Bloomfeild P Cochrane database syst rev 2003

- Only oral vs IV then oral
  - 2x RCT 306+387 children 1-24 months febrile UTI:
    - IV cefotax /oral cefixime or augmentin total duration 10-14 days
      HobermanA 1999 Paediatrics
      Montini G Nephrol Dial Transplant 2003
  - “...safe and effective...and cheaper”

Recommendation: 1) Oral antibiotics should be used
                  2) IVI for seriously ill or vomiting
Duration of Therapy

- Lower urinary tract infection
  - Short course (3-4 days) vs long course (7-10 days)
  - 10 trials comparing this
    “.. Short course treatment as effective as long course..”

  *Systematic review Michael M Arch Dis Child 2002*

- Pyelonephritis
  - no trials comparing this alternative

**RECOMMENDATION:**

1) Short course for lower UTI
2) Standard RX for PN until more trials
What antibiotic?

- Depends on local sensitivities
Prophylaxis – very controversial

1. Does it reduce number of infections?

2. Does it reduce progression of pyelonephritic scarring?

3. Is Acute Therapy of recurrent PN episodes superior to prophylaxis in reducing scars?

4. Is it superior or inferior to surgery?
Before considering prophylaxis/surgery

Rx underlying problem:

- Dysfunctional voiding
  - Urotherapy
    - Constipation
    - Toileting advice
    - Psych
    - Physio –biofeedback TENS

- Neurogenic bladder
Prophylaxis

- **Cochrane Database of Systematic Reviews 2007 Issue**
  - "Review of trials found some evidence that long term antibiotics did prevent some infections, but these infections occurred without the child being unwell and may not be real illnesses and thus don’t need prevention"
  - Large, properly randomised double blinded studies are required

- **BMJ 2007;335(21 July)**
  - Prophylaxis was associated with an increased likelihood of antibiotic resistance and is not associated with a reduced risk in recurrent infection.
  - Alternative is close surveillance without antibiotics
Prophylaxis - controversial

- Prophylaxis has been repeatedly documented to decrease symptomatic recurrences of uncomplicated UTI in women

## Prophylaxis

<table>
<thead>
<tr>
<th>Author and year</th>
<th>Patient age</th>
<th>Total number of patients in study</th>
<th>VUR status</th>
<th>Number of patients with VUR</th>
<th>VUR grade</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garin et al. 2006</td>
<td>1 month-18 years</td>
<td>218</td>
<td>±VUR</td>
<td>113</td>
<td>I-III</td>
<td>12</td>
</tr>
<tr>
<td>Craig et al. 2009</td>
<td>0-18 years</td>
<td>576</td>
<td>±VUR</td>
<td>243</td>
<td>I-V</td>
<td>12</td>
</tr>
<tr>
<td>Montini et al. 2008</td>
<td>2 months-7 years</td>
<td>338</td>
<td>±VUR</td>
<td>128</td>
<td>I-III</td>
<td>12</td>
</tr>
<tr>
<td>Roussey-Kesler et al. 2008</td>
<td>1 month-3 years</td>
<td>225</td>
<td>+VUR</td>
<td>225</td>
<td>I-III</td>
<td>18</td>
</tr>
<tr>
<td>Pennesi et al. 2008</td>
<td>0-30 months</td>
<td>100</td>
<td>+ VUR</td>
<td>100</td>
<td>II-IV</td>
<td>24-48</td>
</tr>
<tr>
<td>Swedish Reflux Trial 2010</td>
<td>1-2 years</td>
<td>203</td>
<td>+VUR</td>
<td>203</td>
<td>III-IV</td>
<td>24</td>
</tr>
</tbody>
</table>
Prophylaxis: does it reduce infections and scarring in children with dilatation of upper Urinary Tract (PUJ, VUJ)

- Commonly recommended in at least the first year of life
  - Dillon et J Urol 1990

- Single trial: “.. Antibacterial prophylaxis in children with PUJ obstruction was not useful..” Madden NP Br J Urol 1993
Prophylaxis: does it **reduce infections** in children with neurogenic bladder

- Several studies showed positive effect
  
  *Beiring-Sorensen FJ Urol ’94; Johnson HW Paed 1993*

- Many authors found no superiority
  
  *Kuhlemeier KV J Uro 1985; Mohler JL J Urol 1987*

- Meta –analysis of 15 studies
  
  “.. There is no significant reduction of symptomatic UTI’s under antibiotic prophylaxis in neurogenic bladder..”

  *Morton SC 2002 Arch Phys Med Rehabil*
International Guidelines

- **NICE**: “do not use antibiotic prophylaxis routinely in infants and children following first time UTI, and only selectively in recurrent UTI”

- **AUA**: recommend Px after febrile UTI c reflux in children < 1yr
  In children >1 yr –optional unless recurrent or high grade
WONG FOOK HING BOOK STORE
Problems with studies in Prophylaxis

- Poor stratification according to risk or recurrence
  - No of previous Uti
  - Bladder dysfx
  - Anomalies urinary tract
  - Other factors

- Poor definitions of UTIs
- Poor info on patient compliance
Prophylactic chemotherapy: Individualize

- *Dont use in isolation – Rx dysfunctional voiding*
- *Step up approach ie if recurrent UTI’s may try it*
- *High grade reflux - optional*
Reflux: to operate or not

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**Important studies**


- 225 children
- Grade III/ IV reflux GFR > 70
- Renal growth UTI recurrence rate similar
- Febrile UTI > Px group
- No differences
  - Somatic growth
  - Nuclear imaging
Swedish Reflux Study 2010

- High rate of recurrent febrile UTI in Girls with dilating reflux
- Antibiotics and deflux decreased infection rate
- Scarring
Surgical treatment

- Usually when other Rx fail
- AUA still offer as first line rx after consultation with parents
  - Ie individualize
- Endoscopic procedures now considered first line management
STOP

IN THE NAAAAME OF LOVE
Prophylaxis: Is it superior or inferior to surgery in VUR

- **Important study 2006**: Ten year results of RCT of treatment with **severe VUR (III/IV)** 306 children
  - 47% high grade reflux disappeared over 10yrs
  - Number or new scars renal growth and function were identical in both groups
  - Medical pts had more **febrile UTI**

- Jodal U Pediatr Nephrol 2006
So what should we do

- Surgery
  - High success rate
  - Immediate cure
  - But unnecessary in 50% of cases

- Medical Management
  - Prolonged medication
  - Repeated imaging
  - Persistence of reflux anyway in 50%
  - Risk of PN in pregnant women

→ individualized strategy
So what should we do

- Surgery
  - High success rate
  - Immediate cure
  - But unnecessary in 50% of cases

- Medical Management
  - Prolonged medication
  - Repeated imaging
  - Persistence of reflux anyway in 50%
  - Risk of PN in pregnant women

→ individualized strategy
RESULTS

- 125 MCUG’s
- Black:
  - 53 boys: 13 girls
- Non black:
  - 31 boys: 28 girls
- Age:
  - 1 month - 13 yrs
  - (100 patients < 2 yr)
URINE RESULTS

- Adequate samples 54%
- Diagnosis doubtful 24%

Cultures:

- E. coli
- Klebsiella
- Proteus
- Enterobacter
- Pseudomonas
- no growth
- ?
ULTRASOUND RESULTS

- Large/echogenic kidneys (9)
- Hydronephrosis / hydroureter (7)
- Mild pelvicalyceal dilation (4)
- Absent kidney / hypoplastic kidney (2)
- Horseshoe / duplex / ureterocele (1)
CONCLUSIONS

In black patients:

- Low incidence of VUR in particularly girls
- High incidence of PUV

Role of ultrasound:

- Poor correlation with Vesico-ureteric reflux (VUR)
- Good correlation with posterior urethral valves (PUV)

Confirms poor urine collection technique is common.

- No results can be ignored
MCUG RESULTS

17 Abnormal

5 Black
- 3 PUV
  - Abnormal US in all
- 2 VUR
  - All US normal
    - 1 grade III / IV
    - 1 grade II

12 Non-black
- 10 VUR
  - 6 normal US
    - grade II reflux or less
    - 1 lost to follow up
    - 1 required surgery
- 1 PUV
- 1 Residual
  - Abnormal US
  - Normal
MCUG RESULTS

- 125 MCUG’s
  - 17 abnormal
    - 12 VUR
    - 4 PUV
    - 1 increased residual
E. Radiological Study

- This is a study of a 3 day old boy baby who presented with bilateral renal masses and respiratory distress
The following is a renal ultrasound of a newborn baby with a palpable abdominal mass.
### Test Characteristics of Tests Used to Diagnose Urinary Tract Infections in Children

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive likelihood ratio</th>
<th>I/negative likelihood ratio</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dipstick</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocyte esterase (LE)</td>
<td>84 percent</td>
<td>78 percent</td>
<td>4</td>
<td>0.2</td>
<td>†</td>
</tr>
<tr>
<td>Nitrite</td>
<td>50 percent</td>
<td>98 percent</td>
<td>25</td>
<td>0.5</td>
<td>†</td>
</tr>
<tr>
<td>Nitrite or LE</td>
<td>88 percent</td>
<td>93 percent</td>
<td>13</td>
<td>0.1</td>
<td>†</td>
</tr>
<tr>
<td>Nitrite and LE</td>
<td>72 percent</td>
<td>96 percent</td>
<td>18</td>
<td>0.3</td>
<td>†</td>
</tr>
<tr>
<td><strong>Microscopy</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td><strong>Uncentrifuged</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyuria (&gt;10/mm³) (all ages)</td>
<td>77 percent</td>
<td>89 percent</td>
<td>7</td>
<td>0.4</td>
<td>†</td>
</tr>
<tr>
<td>Pyuria (&gt;10/mm³) (&lt;2 yr)</td>
<td>90 percent</td>
<td>95 percent</td>
<td>18</td>
<td>0.1</td>
<td>◊ †</td>
</tr>
<tr>
<td>Bacteriuria (gram stained)</td>
<td>93 percent</td>
<td>95 percent</td>
<td>19</td>
<td>0.1</td>
<td>†</td>
</tr>
<tr>
<td>Overall (P+B) = enhanced</td>
<td>85 percent</td>
<td>99.9 percent</td>
<td>85</td>
<td>0.1</td>
<td>†</td>
</tr>
<tr>
<td>Overall (P or B)</td>
<td>95 percent</td>
<td>89 percent</td>
<td>9</td>
<td>0.1</td>
<td>†</td>
</tr>
<tr>
<td><strong>Centrifuged</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyuria (&gt;5/hpf)</td>
<td>67 percent</td>
<td>79 percent</td>
<td>3</td>
<td>0.4</td>
<td>†</td>
</tr>
<tr>
<td>Bacteriuria</td>
<td>81 percent</td>
<td>83 percent</td>
<td>5</td>
<td>0.2</td>
<td>†</td>
</tr>
<tr>
<td>Overall (P+B)</td>
<td>66 percent</td>
<td>99 percent</td>
<td>7</td>
<td>0.4</td>
<td>◊ †</td>
</tr>
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</table>


CONFIRMED UTI TREATED WITH APPROPRIATE ANTIBIOTICS

ALL PATIENTS HAVE ULTRASOUND AS SOON AS POSSIBLE

< 2 YEARS

MCUG
Once urine clear (2-3 weeks later) on prophylaxis

+ / -

DMSA if available (assess upper tract/renal involvement)

> 2 YEARS

NORMAL ULTRASOUND

"MILD" INFECTION
Not Recurrent

"SEVERE" INFECTION (T >38, vomiting, abdominal pain) OR "RECURRENT" INFECTION

NO FURTHER INVESTIGATIONS

MCUG

DMSA Scan

INVESTIGATE APPROPRIATELY

ABNORMAL ULTRASOUND

MCUG's are unpleasant but should be used initially especially in young kids to define anatomy
Subsequent Indirect Mag 3 scans can be used for followup of proven reflux once potty trained
DMSA scans in older children can be used instead of MCUG i.e. if U/S & DMSA Normal then no further investigations. If defect, need followup 3-6mths later.

NB - ensuring that UTI's are CONFIRMED UTI's will cut down on unnecessary and costly investigations
Prophylaxis: does it reduce infections in children with Reflux

- No representative prospective studies comparing recurrence rate of infection in children with reflux versus those without.
- 2006 Garin 113 children reflux 1-3. No difference in recurrence or scarring.

- One study published only as an abstract:
  - Reddy PP 1997 Paediatrics (suppl)

- Studies on scarring:
- No
Prophylaxis with Other

  - Probiotics are as effective as antibiotic prophylaxis in children with persistent 1y VUR
  - Small group 120 kids with 1y VUR
  - Incidence of UTI
    - Probiotic gp 18.3% and Antibiotic 21.6%
Antibiotic prophylaxis was not associated with a reduction in recurrent UTIs but was associated with increased bacterial resistance.

APA recommends prophylaxis!!
Risk of scarring

Committee on Quality Improvement, Subcommittee on Urinary Tract Infection, Pediatrics 1999;103:843-852
Prevention of scarring??

- No results available which compare children on and of Prophylaxis.

Review Beetz Ped Nephrol 2006