Predisposing factors to urinary tract infections in children

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UTI: Predisposing factors

• Virulent bacteria
• Sensitive host

• For a successful treatment one should consider all (known) predisposing factors, in order to
  – Eliminate the infection
  – Prevent recurrences
  – Prevent late complications
Acute pyelonephritis US (1)

Enlarged kidneys,
Blurred structure, abscess?
Acute pyelonephritis CT (2)

Enlarged kidney,
Multiple abscesses
Prune-belly syndrome
Meningomyelocele
Intrarenal reflux

Posterior urethral valve
Kidney fibrosis

a: small hyperechogenic kidney
b: normal kidney
UTI: Predisposing factors

Virulent bacteria

Sensitive host
Bacteria (1)

- Definitions
  - bacteriuria
  - significant bacteriuria
  - cystitis
  - pyelonephritis
  - unspecified
  - asymptomatic bacteriuria

- Sampling techniques
  - collecting bag
  - midstream urine
  - catheter urine
  - suprapubic puncture
Bacteria (2)

• ERRORS
  – Inappropriate sampling – misleading bacteriology – misleading sediment

  – Bacteriology should be considered together with urine sediment and the clinical syndrome

  – Controls should not rely solely on bacteriology, use urine sediment instead routinely
Bacterial virulence

• Virulence=factors that enable bacteria to invade the urinary tract

• Surface antigens
  – O: lipopolysaccharides with endotoxin properties. Induces fever, local inflammation
  – K: (capsular) antigen, prevents phagocytosis

• “P” fimbriae: bind to glycolipid receptors of the P blood group family

• A number of additional factors not routinely checked
Bacterial virulence

- Pyelonephritis: 3-4 (known) virulence factors
- Cystitis: 0-2 factors
- CAVE: OBSTRUCTION !! MALFORMATION !!
Bacterial virulence

Acute pyelonephritis (APN)
- Severe local and systemic inflammation, may become life-threatening.
- 30% bacteremia in adults.
- Progression to chronic infection and renal failure.

APN strains
- Fimbriae
- Toxins
- Capsules
- Iron binding molecules
- Inhibitors of innate immunity

Asymptomatic bacteriuria (ABU)
- A model of commensalism in the bladder

ABU strains
- Attenuated pathogens
- Smaller genome size
- Virulence genes contain deletions or mutations

Bacterial virulence

Bacterial spectrum at the 1st Dept. of Pediatrics

N=7850 (%)

- E. coli 49
- Enterococcus faecalis 13
- Proteus indol neg. 10
- Klebsiella 7
- Pseudomonas spp 7
- Enterobacter spp 6
- Proteus indol pos 3
- Staphylococcus 3
- Other 2
UTI: Predisposing factors

• Virulent bacterium

• Sensitive host
Sensitive host

• Age related factors
  – Anatomy (short urethra, phymosis and adhesio cellularis preputii et labia minora, diaper, obesity)
  – colonization
  – Immunological susceptibility
    – Mucosal barrier
    – Age related immununresponse
      » Inherited/acquired
Innate rather than adaptive immunity is essential for bacterial clearance during UTIs.

- T, B cell or RAG mutant mice are fully resistant to UTI.
- Tlr4−/− mice become asymptomatic carriers with low innate immune responses.
- mCxcr2−/− (IL-8 receptor deficient) mice develop acute, lethal septic pyelonephritis and surviving mice develop chronic renal damage.

Sensitive host

- Anatomical malformations
  - obstruction
  - VUR
  - meningomyelocele
  - prune-belly syndrome
  - Stone disease, etc
VUR (1)
anatomy of the ureteral orifice

Grade 1 VUR
Normal orifice

Grade 2 VUR
Stadium orifice

Grade 3 VUR
Golf hole orifice
VUR (2)

grading of reflux
Mucosa barrier

Innate immunity
IgA deficiency
P1 blood group
Previous infection
Stasis
Dysbacteriossis (antibiotics)
Age-related incidence of UTI

Relative risk vs age (years)

- Boys (dashed line)
- Girls (solid line)

Age (years):
- 0
- 10
- 20
- 30
- 40
- 50
- 60
- 70
- 80

Relative risk:
- Low
- Moderate
- High

Legend:
- Boys
- Girls
Sequence of kidney damage 1.

- UTI
- Parenchymal damage
- Fibrosis
- Loss of function
- Renal insufficiency

- Anatomic malformations
  - Subvesical Obstruction
  - VUR
  - UV - stenosis
  - PU - stenosis
  - Meningomyelocele
  - Prune-Belly-Syndrome

- Immun deficiency
- Virulent bacteria

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Sequence of kidney damage 2.

Primary bilateral parenchymal defect (hypoplasia/dysplasia) → Low nephron number → Secondary lesion hyperfiltration → Fibrosis → Loss of function → Renal insufficiency

- Hypoplastic kidneys, low nephron number

- UTI
  - Subvesical Obstruction
  - VUR
  - UV - stenosis
  - PU - stenosis
  - Meningomyelocele
  - Prune-Belly-Syndrome
  - Immun deficiency
  - Virulent bacteria

- Vitious cercle

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Causes and course of UTI

Gut flora **Bacterial virulence**
- Uropathogenic strain
- Colonisation of the urethra and the perineum (in females the vagina)

**Mucosa barrier**

**Host**
- Increased adherence
- Immunstatus (Innate and adaptive)
- VUR
- Obstruction
- Foreign body
- Previous inflammations

Cystitis

Akute pyelonephritis

Healed

Urosepsis

Scar and low nephron number

Hypertension, CKD...
Summary

• UTI is a frequent condition in children
• There are a number of predisposing factors to UTI, that are not related to pathological anatomy
• Primary renal hypoplasia with reduced nephron number accompanying the most severe anatomical malformations is a major factor leading to deterioration of kidney function
Reflux nephropathy

scar