RACP Lecture Series

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Urinary Tract Infections

- Epidemiology
- Pathogenesis
- Controversies
  - Investigations
  - Treatment
  - Anatomical associations

Clinical features UTI

- Neonate
  - Fever without focus
  - Poor feeding
  - Lethargy
  - Irritability
  - Vomiting
  - Prolonged jaundice
  - Collapse/septicaemia/meningitis

- Infant
  - Irritability
  - Fever
  - Abdominal pain
  - Vomiting
  - Anorexia

- Child
  - Dysuria, frequency
  - Enuresis
  - Fever
  - Loin/abdominal pain

Collection of urine

- Older child
  - Dysuria, frequency
  - Wetting – day or night
  - Little abdominal pain
  - Fever, loin pain, systemic symptoms
Midstream urine

- Reliable sample if well collected
- Must be continent and have reasonable voluntary control
- Clear instructions
- Assess number of squames on Urine report

Collection of urine - bag

- High risk of contamination
  - Better than no sample
  - Technique
    - Clean perineum with water then dab dry with cotton wool
    - Stick on bag, leave nappy off
    - Give baby a feed
    - Once voided
      - Remove immediately
      - Cut lower corner of bag
      - Pour into specimen container
      - Lots of contamination

Collection of urine - suprapubic aspiration

- Give feed/fluid load
- Have open specimen container to catch urine if voids (clean catch)
- 1cm above symphysis pubis
- Directly into bladder

Collection of urine - catheterization

- Give feed/fluid load
- 5FG soft feeding tube
- Insert only till get urine back
  - Soft tubes may knot if inserted several centimetres

Urine dipstix - leukocytes

- Leukocyte esterase
  - in PMN, mono, eosin, baso
  - $\ + $ = 5 - 15 WBC/HPF (N<5)
  - false +ve
    - chlorine bleach, formalin
  - false -ve
    - high glucose, high S.G.
    - cephalaxin, cephalothin
    - tetracycline, gentamicin
    - ++ ascorbic acid

PMN in urine

Nitrite

- gram neg bacilli
- Convert nitrate to nitrite
- positive = > 100,000 org/mL
- false positives
  - sample errors
  - macrohaematuria
- false negatives
  - urine in bladder < 4hrs
  - needs adequate nitrate (veg diet)
  - ascorbic acid
  - urine pH<6
Haematuria & proteinuria

- Haematuria (eumorphic)
  - 20 - 25% macroscopic with acute cystitis
  - Of no additional diagnostic value
- Proteinuria
  - Common with UTI
  - No additional diagnostic value

Dysmorphic RBC suggest glomerular bleeding - not with UTI's

UTI - epidemiology

- 2nd most common bacterial infection after otitis media
- Overall prevalence - approximately 7% in febrile infants and young children
- Varies by
  - Age
  - Race/ethnicity
  - Sex
  - Circumcision status
- White children: two- to four-fold higher prevalence than black children.
- Girls: two- to four-fold higher prevalence of UTI than circumcised boys.
- White girls with a temperature of >39°C have a UTI prevalence of 16 percent.

Bacteriology of UTI's

- Uncomplicated UTI
  - Usual gram neg aerobic bacilli
    - E. coli 80%
    - Klebsiella
    - Enterobacter,Citrobacter
    - Proteus,Providencia,Morganella
  - Pseudomonas - usu low virulence, little tissue invasion
- Gram positive:
  - Staph, enterococcus
- Anaerobes:
  - May cause UTI despite high fecal numbers
- Fungi
- Viruses

Absolute and relative accuracy of rapid urine tests for urinary tract infection in children: a meta-analysis

- 0.3 - 1.3% of all infants have UTI
- Males = females < 12 months of age
- Males > females < 3 months of age
- Females > males after 12 months
- Symptomatic UTI before puberty
  - Girls – 3-5%
  - Boys - 1-2%
- Recurrence
  - Girls – 50%
  - Boys – uncommon, rare after 2 years

- Bacteriuria
- Bacteria in urine
- Infection
  - Polymorphs in urine
  - Bacteria count
    - 1 x 10^9 cfu/mL - msu
    - 1 x 10^9 cfu/mL - clean catch
    - 1 x 10^9 cfu/mL - catheter
    - Any pure growth - suprapubic

Gram neg E. coli on human blood agar
UTI - pathophysiology

- Defense against bacterial invasion
- Physical
  - Unidirectional urinary flow
  - Uroepithelium
  - Local proteins that inhibit/impede bacterial attachment - Tamm Horsfall protein
- Innate and adaptive immunity
  - Uroepithelial cell activation and transmembrane signalling
  - Production of distinct inflammatory mediators, and inflammatory cell recruitment
  - Cell and bacterial destruction

UTI - pathogenesis

- Bacterial properties
  - Attachment - fimbriae - E. coli - internalised in transitional epithelial cells in vacuoles equivalent to phagocytosis
  - Induces inflammatory response - this response results in renal damage

UTI - pathogenesis

- Toll like receptors - recognise pathogen associated molecule patterns
  - TL 2 - detect lipoproteins from Gram positive bacteria
  - TL 4 - lipopolysaccharide signalling receptor - lower urinary tract and bladder
  - TL 11 - kidney - recognises uropathogenic E. coli (UPEC) and inhibits ascent of micro-organisms
- Tamm Horsfall protein - ascending Loop of Henle - prevents UPEC colonization, impedes fimbrial attachment, activates innate and adaptive immunity

UTI - Imaging

- Ultrasound of kidneys
  - Kidneys
    - Presence & number
    - Shape & size
    - Echotexture of renal parenchyma
    - Hydronephrosis
  - Ureters
  - Hydroureters
  - Bladder & urethra

- Normal renal ultrasound
  - Kidney cortex
  - Hydronephrosis
  - Renal pelvis, no hydronephrosis
Hydronephrosis U/s
- Hydronephrosis
  - Dilated renal pelvis and ureters on both sides
  - Normal bladder

Micturating cystourethrogram
- Insert catheter into bladder
  - Fill with radio opaque dye
  - X ray during filling & voiding
  - Catheter may be inserted under sedation, then awake for voiding phase
  - MMC only

Vesicoureteric reflux
- Renal pelvis
  - Dilated
  - Calyceal dilatation or clubbing
- Ureters
  - V-U reflux (severity)
  - Dilatation/tortuosity
- Bladder
  - Size, shape, thickened wall
- Urethra
  - Obstruction, stenosis

Classification of VUR severity

Importance of VUR
- Recurrent UTI's
  - Often pyelonephritis
    - Fever, dysuria, urinary frequency, loin pain,
    - Septicaemia
  - Associated reflux nephropathy
    - Hypertension, renal impairment,
    - Occasional kidney failure

Reflux nephropathy
- Congenital
  - Abnormal development as ureteric bud penetrates metanephric blastema
- Acquired
  - from pyelonephritis
DMSA

- Dimercaptosuccinic acid scan
- Radio isotope injected IV
- Taken up by renal distal tubular cells
- Areas of poor uptake = tubular atrophy & interstitial fibrosis = renal scarring or reflux nephropathy

Reflux nephropathy

- Majority of VUR resolves or improves with bladder growth
  - Reduce UTI (lower & upper) whilst resolution occurs
  - Importance during own pregnancies

- Renal impairment
- Severely reflux nephropathy
- 20% of children and adolescents with ESRF have reflux nephropathy
- 5-10% of adults with ESRF have reflux nephropathy
- Hypertension
- Reflux nephropathy most common cause in kids

Reflux nephropathy

- Medical
  - Prophylactic antibiotics
    - Trimethoprim Cotrimoxazole
    - Nitrofurantoin
    - Not Keflex, Amoxil, Augmentin
  - Urinary surveillance
    - Regular P&V urine for leukocytes & nitrites
    - Urine M & C
    - Commercial Antibiotics immediately
    - Review for sensitivities
  - How long for?
    - At least till fully toilet trained

- Surgical
  - Reimplantation of ureters

Lower urinary tract vs upper urinary tract infection

- Clinical
- Radiological
- Serum markers – procalcitonin

Controversies

- Treatment
  - Which antibiotic?
  - How delivered?
  - How long to treat?
Controversies

• Imaging
  • What imaging?
  • Who?
  • When
  • Do you need to image?

Post UTI imaging

• AAP – US and VCUG (MCU) in all children up to 2 years of age

• NICE
  • US if less than 6 months or older if atypical UTI or recurrent UTI
  • MCU – if less than 6 months and atypical or recurrent UTI

Post UTI imaging

• What are we trying to diagnose?
  • Renal damage (40% post UTI)
  • VUR – 30%
  • Obstruction 1%

• ? Best test for those indications
  • DMSA
  • MCU
• High Risk
  • Recurrent UTI
  • Clinical signs – poor stream, palpable kidneys/ Bladder
  • Unusual organism
  • Bacteraemia/ sepsicaemia
  • Prolonged clinical course
  • Unusual presentation eg older boy
  • Known antenatal abnormality
Vesico-ureteric reflux – does it matter?

- CKD – chronic malformed kidneys
- Obstructive uropathy – 22%
- Hypoplasia/ dysplasia/ aplasia – 18%
- Reflux nephropathy – 8%

Preventing recurrence
- Do not prescribe antibiotic prophylaxis routinely.

**Box 3: Main characteristics of patients with asymptomatic recurrent urinary tract infection**
- Age (up to 6 years)
- Persistent pain during urination
- Poor urine flow
- Microscopically or culturally significant urine
- Recurrent urinary tract infections
- Failure to respond to treatment with suitable antibiotic within 48 hours
- Failure to respond to treatment with suitable antibiotic within 48 hours
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- Vesico-ureteric reflux plus recurrent urinary tract infection
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### VUR, reflux nephropathy

- **Prevalence**
  - 24% - 30% of young people < 21 years with UTI
  - 8% Grade IV or V

- **Resolution**
  - 13% per year – Grade I, II, III
  - 73% of children have no VUR or Grade I after 10 years

### UTI/ VUR/ RN

- **Long term complications**
  - CKD
  - Hypertension
  - Pregnancy associated complications

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**Plain Language Summary**

Short course of antibiotics (2-4 days) are as effective as longer treatment for bladder infection in children. However, there is no consensus on the duration of treatment. The antibiotics can be varied according to the age of the child and severity of infection. A single dose of antibiotics is often used in children under the age of two. However, if the infection persists, a longer course of antibiotics may be necessary. The duration of treatment should be adjusted according to the severity of the infection and the response to treatment. Additional testing may be necessary to rule out other causes of the infection, such as reflux or other congenital anomalies.
PLAIN LANGUAGE SUMMARY

Cranberries for preventing urinary tract infections (Review)

Jepson RG, Craig JC

Methods

We randomly assigned children under the age of 18 years who had had one or more microbiologically proven urinary tract infections to receive either daily cranberry-juice concentrate (30 mL) or placebo for 12 months. The primary outcome was microbiologically confirmed symptomatic urinary tract infection. Arteriovenous-aneurysm surgery was performed with the use of ultrasonography data.

RESULTS

From December 1996 to March 2007, a total of 175 children (710 placebo- and 710 cranberry-juice concentrators) were recruited. The treatment was effective in reducing the number of urine cultures positive for bacteria, but there was no difference in the incidence of symptomatic urinary tract infections. The intervention was well tolerated, and there were no side effects.
Renal Aplasia

- Bilateral
  - 1 in 4000 births
  - Incompatible with life
  - Males > females (70%)
  - Oligohydramnios
  - Pulmonary hypoplasia
- Unilateral
  - 1/1000, M: F – 1.8:1
  - ? Associated genitourinary conditions

Kidney Position

- Malrotation
- Ectopy
  - Pelvic
  - Thoracic
  - Associated abnormalities
  - UTI, abdominal pain, renal calculi, VUR, obstruction, hydronephrosis

Kidney Position

- Kidney – Ectopia - Crossed

- Kidney - Horseshoe

- 1 in 400
- Male > female
- Asymptomatic – complicated
  - UTI,
  - Haematuria,
  - Obstruction,
  - Hydronephrosis,
  - Calculi
- Associated anomalies – VATER/ VACTERL etc
Horseshoe Kidney

- PUJ
- Obstruction
- 1 in 40 live births
- Male > Female
- Abdominal Mass
- UTI
- Abdominal pain
- Haematuria

Renal Collecting System

PUJ

- ? Other anomalies
- Antenatal finding
- Ix –
  - US, Nuclear medicine
  - Antegrade/retrograde study
  - Surgery

Pressure effects of obstruction

- Kidneys begin to struggle if storage pressure within bladder consistently above 35 cm H$_2$O
- Usu around 10 cm H$_2$O

Kidney – Vascular malformations

- Renal Artery Stenosis
- Renal AVM
- Renal artery aneurysm
- Mid aortic syndrome
### Ureter - Duplication

- 1 in 125 births
- 40% bilateral
- F>M
- Complete duplication
- Incomplete duplication
- Bifid Ureter
- Clinically – asymptomatic, UTI, Mass, VUR, Obstruction

### Duplex Kidney

- Upper Moiety
- Lower Moiety
- Associated
  - VUR – usu lower
  - Obstruction – usu upper

### Duplex ureters - IVP

### Ectopic ureters

- Ureter may be part of a duplex but may be single system
- Ureter may end in
  - bladder (N continence)
  - Urethra
  - Seminal vesicle/vagina
- If bypass sphincter = incontinence (dribbling)
Ectopic ureter

- May be seen on IVP
- May be missed
- If strong clinical suspicion (persisting dribbling)
- Cystoscopy
- Dye IV to pass into urine
  - Identify ectopic ureter
  - Surgery can be curative

Ectopic ureter – possible insertion – male, female

Ureterocoele

- Balloon like dilatation of distal ureter with pin-hole opening
- Usu upper half of duplex system
- Bladder consequences
  - Decreased functional bladder capacity
  - Obstruction to emptying
  - Distortion of bladder neck after surgery
  - Assoc VUR --- UTI's

Ureterocoele

Hypospadias and Epispadias

- Bladder open
  - Lower ant abdo wall absent
  - Bladder visible through "hole"
  - May turn inside out
  - Small bladder
  - Detrusor, bladder neck, ext sphincter abn
  - Assoc abn pelvis
  - Symphysis pubis widely separated

Bladder extrophy

- Perineum usu short
  - Anus more anterior
  - Occ anal stenosis
- Male>female
  - Undescended testes
  - Short penis
  - Usu N uterus, ovaries
  - Short vagina, ura multipsis
Posterior Urethral Valve

- Proximal male urethra blocked by fine membrane (valve)
- Presentation
  - Antenatal hydronephrosis
  - UTI in boy
  - Delayed day time continence

Posterior Urethral Valve

- Incontinence
  - Urethral sphincter distorted
  - Bladder
    - Noncompliant hypertonic bladder
    - Incomplete emptying
    - High pressure storage
  - Ureters
    - Vesicoureteric reflux (often high grade) - UTI's
  - Kidneys
    - Obstructive uropathy - high volume urine prod'n

Posterior urethral valve

- Management
  - Remove obstruction
  - Mx VUR/UTI's
  - Mx renal damage
  - Renal impairment
  - Salt & bicarb wasting
  - Bladder compliance
    - Ditropan
    - Bladder augmentation
      - CIC/ostomy