URINARY TRACT INFECTIONS IN JAMAICAN CHILDREN - OUR PROTOCOL

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URINARY TRACT INFECTIONS

THE WINDOW
TO EARLY DIAGNOSIS OF UROLOGICAL DISEASE
Obstruction / Reflux

Posterior urethral valves (PUV)  Vesico-ureteric reflux (VUR)
Terminology

- MCUG – micturating cystourethrogram
- VCUG – voiding cystourethrogram
- MCUG = VCUG
- VUR – vesico-ureteric reflux
- PUV – posterior urethral valves
- US – ultrasound
- KUB US – ultrasound of kidneys, ureters and bladder
Definitions - traditional

- **Urinary Tract Infection (UTI)** – significant bacteriuria +/- symptoms
- **Acute pyelonephritis**
  - UTI with fever, systemic symptoms, loin pain
- **Cystitis**
  - Afebrile UTI with lower tract symptoms / signs
  - Without systemic symptoms
Definitions - European Association of Urology 2014

- First infection – indicator of anatomical anomalies
- Unresolved infection
  - Bacteria remain despite treatment
  - Inadequate Rx, multiple organisms of differing sensitivities
- Persistent infection
  - Bacteria re emerging from occult sites
  - Infection always with the same organism
  - Intervening periods of sterile urine during and soon after antibiotic Rx
Definitions - European Association of Urology 2014

- Re infection
  - Each episode different organism
  - E coli – differing serotypes: recurrent E coli UTI is not persistent infection
Definitions

- Lower urinary tract infection (UTI) (cystitis)
  - Bladder mucosa
- Upper UTI (pyelonephritis)
  - Diffuse pyogenic infection of renal pelvis and parenchyma
  - Fever, systemic signs
  - +/- cystitis symptoms
IMPORTANCE

- UTI may be the first indication of underlying pathology
- Obstruction
  - Upper tracts PUJ
  - Lower tracts PUV
- Congenital abnormalities
- May result in renal scarring
JOURNEY

- Circa 1984 in Jamaica
  - UTI investigation
    - Girls recurrent UTI
    - Boys first UTI …maybe
    - No islandwide protocol
- Many children had recurrent UTI before any investigation was done
- Presentation with CKD from obstructive uropathy > age 5 years
- Girls reflux nephropathy scarring > 5 years
MCUG objections - VUR

- VUR uncommon in Blacks
- Not seen at all in Nigerian children (Eke et al)
- West et al 50 Jamaican children
  - MCUG for different reasons
  - 72% were UTI
  - VUR incidence was 10%.
  - Conclusion:
    - VUR was not common in Jamaican children
    - MCUG only if abnormal renal ultrasound.

VUR is not the only pathology detected on MCUG
Ultrasound is not reliable for lower tract evaluation
1985- to present

- Investigation of all children at first UTI
- Age < 5 years
  - MCUG and Renal US (+/- nuclear scan)
- MCUG – all males
- Age > 5 years
  - US
  - MCUG
    - abnormal history, examination or US
    - Recurrent UTI
  - +/- Renal scan
Result

- Congenital abnormalities diagnosed earlier
- Most in the first year of life
- CKD from obstructive uropathy
  - Majority onset in neonatal period
  - Vs late diagnosis and intervention
  - PUV is the most common urological pathology
  - Primary VUR uncommon as cause of CKD
New Foreign Guidelines

- NICE 2007
- AAP 2011
- Challenged
  - usefulness of investigation after the first UTI
  - need for MCUG
  - need for urine culture
  - value of UTI prophylaxis
- Local wave of unrest about 2011 Jamaican guidelines
NICE Guidelines 2007

- National
- Institute for Health and Clinical Excellence guidelines
- All ages
- Any UTI
NICE definitions – UTI risk factors

- Poor stream / large bladder/ abdominal mass
- History
  - previous UTI -suggested or proven
  - Recurrent PUO
- Constipation / dysfunctional voiding
- Spinal lesion / poor growth / hypertension
- Family history – renal disease, VUR
NICE - Culture criteria

- Acute Pyelonephritis (APN) (not cystitis)
- High to intermediate risk of serious illness
  - Age < 3 years
  - Positive Dipstix for wbc or nitrites
  - Recurrent UTI
  - Infection unresponsive to Rx within 24-48 hours if no previous culture
  - Symptoms and dipstick do not correlate
NICE problems

- Not all symptoms of cystitis are UTI related
  - Without culture misdiagnosis possible

- Culture:
  - With empiric treatment subsequent isolation of organism may be difficult if response poor
  - Without culture impossible to determine if “non E. coli” organism (requiring radiological study)

- Cystitis is not considered UTI and is neither cultured or investigated or followed up
Cystitis – NICE guidelines

- 3 day treatment
- No follow-up
- No investigation
- No culture unless poor response to treatment
- Culture then...
- BUT cystitis:
  - may be the precursor to pyelonephritis
  - May indicate urological pathology
AAP Guidelines 2011

American Association of Paediatrics

- Age 2-24 months
- First UTI
Definitions – AAP diagnosis and selection criteria – 2 months – 2 yrs

- **Diagnosis - AAP**
  - Pyuria $\geq 50,000$ colonies/ml single uropathogen
  - Catheter sample of urine - CSU

- **Culture children at high risk**
  - Fever $> 38.50 r 39.0^\circ C$ /Uncircumcised males
  - Ill appearance + /- other symptoms
  - White female $< 12$ months – fever $> 2$ days
  - no other source of fever

- **Low risk**
  - Circumcised males  Age $> 1$ year
  - Black race
  - Presence of obvious infection elsewhere
  - Fever $> 24$ hours
Culture

- Culture needed
- Supportive but not diagnostic
  - Urinalysis – leukocyte esterase, nitrite – limitations
  - Bacteria on unspun urine sample
Culture method - AAP

- CSU – less traumatic
- Greater success rate than SPA
- SPA success rate 23-90%
- CSU 83-78%
- Clean catch urine 85% false positive rate
- [MSU up to 20% false positive]
Follow-up cultures
AAP

- Urine cultures during and after treatment not beneficial

[BUT]

- Clinical response DOES NOT guarantee biological cure
TREATMENT
Treatment – AAP - new trends

- Oral = parenteral if able to tolerate *
- Once daily aminoglycosides
- No short courses
- 7-10 days minimum

*with exceptions
INVESTIGATION
INVESTIGATION - Purpose

- Anatomical abnormalities
- Role of antenatal ultrasound
- Renal / bladder ultrasound
- MCU
- Nuclear Renal Scan – scarring
  - DMSA (Dimercaptosuccinic Acid)
  - Glucoheptonate
NICE GUIDELINES

- Restricting renal US at diagnosis to infants <6 months
- MCUG if UTI atypical or recurrent
- No imaging in children > age 6 months if response in 48 hours
- Imaging only if Atypical UTI
- Imaging confined in most cases to KUB ultrasound
NICE guidelines assumptions

- Uropathology cannot present with cystitis
- Antenatal US detects most congenital urological abnormalities before first UTI
- First UTI presentation IS first UTI
- Cystitis symptoms are always due to infection
- Renal / bladder US – good predictors of pathology
- All ultrasonographers have paediatric experience
AAP guidelines for Investigation
AAP - Premises

- MCUG for detection of VUR
- Scarring may occur independently of VUR
- Antibiotic prophylaxis is ineffective in reducing frequency of UTI
- So early detection will not have therapeutic benefit
- Ultrasound KUB detect high grade reflux
- Antenatal ultrasound – diagnosis before birth
- No need for MCUG at first UTI
AAP 2011-
Investigation after first UTI

- **MCUG** –
  - Not needed after first UTI
  - Used if recurrent UTI

- **Ultrasound** – kidneys, ureters and bladder
  - Less invasive
  - Poor sensitivity

- **Antenatal ultrasound**
  - may miss pathology

Overlooks possibility of outflow tract obstructive uropathy (e.g. PUV)
OBJECTIONS to the new Guidelines
GUIDELINES not universally accepted

- European Society for Pediatric Urology 2014
- American Urological Society 2014
- ALANEPE
- Studies showing unreliability of KUB ultrasound in diagnosis VUR
- Do not endorse the new guidelines
RIVUR
Randomized Intervention for children with Vesico Ureteral Re reflux
RIVUR

- 2 year multisite randomized placebo-controlled trial
- 607 children with VUR
- Age 2mo-6 years
- 13% prophylaxis and 24% placebo
- Trimethoprim – sulfamethoxazole prophylaxis
RIVUR

- Trimethoprim – sulfamethoxazole prophylaxis
  - Reduced risk of symptomatic or febrile recurrent UTI by 50%
  - No difference in the rate of renal scarring**
  - Increased E coli antibiotic resistance rate in treated group 63% vs. placebo 19%

**? Related to the intensity of monitoring patients in study as early diagnosis and treatment reduces scarring risk!
RIVUR STUDY

- Questioned the rationale of delaying MCUG since study has shown that institution of antibiotic prophylaxis in VUR reduces risk of recurrent febrile infections

- Suggested that the AAP recommendation for delaying MCUG may need to be reconsidered
AAP CLINICAL PRACTICE GUIDELINE

“Is not intended to be a sole source of guidance…

Rather it is intended to assist clinicians in decision making.

It is not intended to replace clinical judgment or

To establish an exclusive protocol for the care of all children with this condition.”

Pediatrics 2011; 128: pg 596 AAP Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2-24 months
OUR GUIDELINES

From birth to age 18 years
MANAGEMENT GUIDELINES FOR URINARY TRACT INFECTIONS IN JAMAICAN CHILDREN
CONSENSUS DOCUMENT FOR MEDICAL PRACTITIONERS IN JAMAICA
SEPTEMBER 25TH 2014

Dr. Colin Abel – Paediatric Urologist – Bustamante Hospital for Children
Dr. Simone Dundas Byles – Paediatric Surgeon – University Hospital of the West Indies
Dr. Marsha Gooden – Paediatric Nephrologist – University Hospital of the West Indies
Dr. Maolynne Miller – Paediatric Nephrologist – University Hospital of the West Indies
Dr. Joy Williams – Paediatric Nephrologist – Bustamante Hospital for Children
Diagnosis of UTI

- Diagnosis should be made by urine culture in all cases if possible.

- Urine culture:
  - Neonates with suspected sepsis
  - Infants and children with unexplained fever
  - Symptoms and signs of UTI
  - Fever in a child with past history of UTI
Diagnosis

- Urine culture – gold standard
- Suggestive: +ve wbc, nitrites
- Urine collection: clean first
  - Bladder tap – percuss first (avoid bowel tap)
  - CSU - visualize urethral orifice
    - Do not aspirate with syringe / size 5 or 6 F feeding tube
- Voided urines: MSU, clean catch
  - High false positive rate / ideally 2 cultures
  - Clean perineum first
Diagnostic criteria

- Bladder tap – any growth
- CSU $\geq 10^4$/ml
- Voided urine
  - $> 100,000$ organisms /ml
  - Ideally same organism same sensitivity on 2 separate voided samples
  - Appropriate cleaning, storage and delivery of sample
  - **BAG urines only helpful if sterile**
- Bladder urines – if ill patient and treatment is imminent
Jamaican guidelines

- No distinction is made between the radiological investigation of a child with cystitis and a child with acute pyelonephritis.
History and examination:

- **History**
  - Dysfunctional elimination syndrome symptoms
  - Obstructive, neurological symptoms
  - Previous UTI, unexplained febrile illnesses
  - Family history of renal disease

- **Examination**
  - Growth parameters, anemia, bone disease, BP
  - Abdominal examination
  - Examination for sacral lesions, anal wink and lower limb reflexes
Sacral dimple

http://newborns.stanford.edu/PhotoGallery/SacralDimple2.html
Sacral tuft
INVESTIGATIONS
Investigations:

All children with UTI irrespective of age or sex should be investigated after the FIRST UTI.
Investigations age < 5 years

- **Renal ultrasound**
  - Use charts for normal renal lengths
  - Charts for premature infants available
  - Manual available

- **MCUG**

- +/- renal scan
Investigations:

- **MCUG**
  - Fluoroscopic

- Request MCUG films for review in patient with recurrent UTI and reportedly normal studies
Normal MCUG
Posterior urethral valves
Spinning top urethra with VUR
Christmas tree bladder
Vesico-ureteric reflux

Table 9: Grading of Vesico-ureteral reflux (VUR) - International Classification

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DEGREE OF REFUX</th>
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<tbody>
<tr>
<td>I</td>
<td>Into distal ureter</td>
</tr>
<tr>
<td>II</td>
<td>Up ureter into pelvis and calyces. No dilatation, normal calyceal fornices</td>
</tr>
<tr>
<td>III</td>
<td>Same as II, but with mild dilatation of pelvis and calyces</td>
</tr>
<tr>
<td>IV</td>
<td>Same as III, but with moderate dilatation and/or tortuosity of the ureter and moderate dilatation of the renal pelvis</td>
</tr>
<tr>
<td>V</td>
<td>Gross dilatation and tortuosity of ureter, pelvis and calyces with significant blunting of the majority of the fornices.</td>
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+/- Nuclear scans

- **DMSA** – dimercaptosuccinic acid
- **Tc99 Glucoheptonate (GC)** – scarring and function
- **Tc99 MAG3** – Mercapto-acetyl triglycine
- Use radiological Departments which allow communication with Radiologist
Investigations age > 5 years at diagnosis of first UTI

- Renal ultrasound
- MCUG
  - All males**
  - Abnormal history, examination or ultrasound
  - +/- Nuclear renal scan +/- Furosemide (Lasix™)
- Adolescent female – not sexually active
  - KUB ultrasound
Indications for nuclear scans in UTI

- Febrile UTI
  - Acutely or at 4-6 months post UTI if not done acutely
- Recurrent febrile UTI
- Abnormal MCUG or US
- Follow-up of urological abnormalities for scarring
- Repeat scan in 6 months if abnormal at onset
- Scan with Lasix if obstruction suspected
Miscellaneous investigations

- Urinalysis – nitrites, wbc, blood, protein
- Urine microscopy – unspun
- Blood urea, creatinine, electrolytes
- CBC
- +/- blood culture, septic screen if indicated
Patient and physician education

- Complications of UTI
- Reason for investigation and monitoring
- Symptoms of UTI
- Urine culture in febrile illnesses
- Further investigations if UTI recur
- Physician education
  - Diagnosis, Rx, investigation
  - Referral
Patient and physician education

Do not

- transmit your anxiety over bladder catheterization to the patient
- send your patient to a Radiologist who is uncomfortable catheterizing children
Patient and physician education

- **Do**
  - Ensure Radiologist catheterizes with 5 of 6 F feeding tube not Foley catheter
  - Send to Radiology services which have experience with paediatric MCUG
  - Be calm about the process
  - Ask Paed nephrologist for help if you need

- **If patient is anxious**
  - you may catheterize in your office and send to Radiology with capped feeding tube in situ
REFERRAL
Specialist referral
Paed urology, Paed surgery, Paed nephrology

- Congenital urological abnormalities
- Antenatally diagnosed uropathology
- Abnormal radiological investigations
- Renal scarring
- Recurrent UTI
- Poor response to treatment
- Dysfunctional elimination syndrome
- \textbf{ALL children with meningomyelocele at birth or soon after}
TREATMENT
Treatment: Afebrile, Asymptomatic bacteriuria

- Treat all confirmed UTI if diagnosed during monitoring of child on UTI prophylaxis for urological abnormality
- If UTI asymptomatic and not based on bladder urine – repeat voided urine or do CSU
- If parenteral antibiotics are the only option, confirm UTI with bladder sample
Treatment: Afebrile, Symptomatic UTI

- Offensive urine, haematuria, dysuria
- Oral broad spectrum antibiotics initially
- Empiric therapy for first UTI
  - Amoxil / clavulanic acid as sole agent outside neonatal period
  - Local study – Cotrimoxazole age 1-12 years
- Recurrent UTI – be guided by previous sensitivities
- Duration 10 days
Febrile UTI - Out patient treatment

- Age > 3 months – non toxic
- Expected compliance
- Initial –
  - 2 days parenteral 3\textsuperscript{rd} generation cephalosporin or \textit{od Aminoglycoside} then oral antibiotics based on sensitivity to complete 10 days of Rx
  - OR if not septic or vomiting ORAL antibiotics for 10 days
Febrile UTI - Inpatient treatment

- Age < 3 months, systemically ill, immunocompromized
- Vomiting
- Compliance concerns
- Parenteral drugs:
  - Amoxil/ clavulanic acid + aminoglycoside (once daily)
  - 3rd generation Cephalosporin
- Choice of antibiotic dependent on previous UTI history and co-morbid pathology
Febrile UTI - In patient treatment

- **Neonate:**
  - Parenteral 10 - 14 days
  - Not Ceftriaxone

- **Non neonate**
  - Parenteral till afebrile and non toxic after 2 days then orally depending on sensitivity to complete 10 days
  - Duration of parenteral therapy dependent on severity of illness and clinical response
Duration of therapy

- 10 days
- 14 days
- Shorter courses unreliable results
Aminoglycoside use

- May be given once daily
- Use lowest limit of dose range (usually 5mg/kg)
- Drug levels not measurable locally
- Urea, creatinine, electrolytes monitoring:
  - Day1, Day 3 and at end of course
- If urea and creatinine rising
  - Evaluate
  - Consider drug toxicity
- If used in renal failure – drug dose adjustment needed
FOLLOW-UP
Follow up

- Adjust antibiotic according to sensitivity and response
- Start prophylaxis as soon as treatment ends (day 11) till radiology completed and normal
- Culture
  - 2 days after starting, 2 days after ending
  - When symptoms or fever occur in future
  - Every 3 months if underlying abnormality
Follow up

- At diagnosis and follow-up, stress need for completing radiological investigations
- Monitor BP at visits
- Ensure that voided urines are collected properly
UTI prophylaxis – indications -

- First UTI – till studies completed
- Urological abnormalities
- Recurrent symptomatic UTI (≥ 2 within 6 months)
UTI prophylaxis - indications

- No UTI prophylaxis if imaging normal
- UTI prophylaxis TILL IMAGING COMPLETED
UTI prophylaxis - drugs

- Determined by sensitivity of uropathogen and age of patient
- Cotrimoxazole, Cefalexin, Cefadroxil, Nitrofurantoin
- Age 0-2 months – Amoxil, Cefalexin, Cefadroxil
UTI GUIDELINES

MUCH CONTROVERSY

LOCAL MANAGEMENT DECISIONS CANNOT ALWAYS BE BASED ON FOREIGN EXPERIENCE

REGULAR STATUS REVIEWS ESSENTIAL
AAP CLINICAL PRACTICE GUIDELINE

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Thank you