Pediatric Urinary Tract Infection: How New Guidelines Will Change Your Practice

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Objectives

- Recognize the clinical manifestations of UTI
- Identify common pathogens in UTI and renal abscess
- Define common complications of UTI
- Identify new practice guidelines in the management of pediatric urinary tract infection

Pediatric Urinary Tract Infections

- Common and if missed: renal scarring, hypertension, and end-stage renal dysfunction
- Nonspecific signs and symptoms

Practice Parameter: The Diagnosis, Treatment, and Evaluation of the Initial Urinary Tract Infection in Febrile Infants and Young Children

- Diagnosis of UTI
  - appropriately collected urine specimen
  - presence of pyuria as well at least 50,000 colonies per mL
  - single uropathogenic organism
- Follow-up monitoring after rx for 7 to 14 days
- Ultrasonography of the kidneys and bladder should be performed
- Antimicrobial prophylaxis not recommended
- VCUG is not recommended routinely after the first UTI unless ultrasonography results show hydronephrosis, scarring, or other evidence of high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances OR in setting of recurrence of a febrile UTI

How common and who gets UTI?

- The overall prevalence of UTI is approximately 5 percent in children w/ UFI
- Higher in preterms than term infants
- Circumcision
  - Uncircumcised boys in first year of life >10 fold higher incidence than girls or circ boys
- Females have a two- to fourfold higher prevalence of UTI than do circumcised males
- Caucasian females with UFI (temp >39°) 16% prevalence

http://aappolicy.aappublications.org/cgi/content/full/pediatrics;103/4/843

No disclosures
Pathogenesis of UTI
- Colonization of periurethral mucosa with GI bacteria
- Ascending infection
- Microbe/host factors
  - E. coli isolates from UTI more commonly express virulence factors
  - Adhesins mediate attachment to uroepithelial receptors, aerobactin which enhance bacterial growth
  - Bladder emptying, obstruction, indwelling FB, VUR

Historical features of importance
- Chronic constipation
- Incontinence
- Lack of proper stream
- Frequency, urgency
- Withholding maneuvers
- Previous UTIs, prior febrile illnesses
- Known VUR

Clinical Manifestations of UTI
- Nonspecific signs/sxs in neonates
- Infants with fever/vomiting
- Fever/abdominal pain in 2-5 year olds
- Nocturnal abdominal pain in school aged girls
- Dysuria, urgency, flank pain in those >5 years

Case 1
- A 19 month old girl presents w/ fever and vomiting
- She went to local ED last pm and received IM ceftriaxone after a bagged urine specimen showed pyuria
- In your office today and looks good
- WBC is 20K
- What is your next step?

Bag urine culture
- Cultures of urine specimens obtained by clean voided bag →60-85% false positive
- Adverse outcome common
  - delayed diagnosis and treatment
  - unnecessary recall
  - unnecessary treatment
  - unnecessary hospital admission
  - unnecessary additional testing including radiologic investigations

Is bag urine ever okay?
- YES!
  - 2 months~2 years
  - Unexplained fever and not ill
  - Antibiotics not prescribed
- If you send the bag urine and it is abnormal, cannot use it for culture if antibiotics are given**
- Properly collected culture if
  - Positive leukocyte esterase or nitrite test
  - Greater than 5 white blood cells per high-power field
  - Presence of bacteria on Gram stained urine (unspun urine)
Diagnostic Approach to UTI: Use of the laboratory and interpretation of testing

- Obtaining the correct specimen
- Routine Urinalysis
  - WBC
  - Nitrites
  - Leukocyte esterase
  - Bacteria
- Differentiating asymptomatic bacteriuria
  - 1-2% of preschool girls; 5% of girls by 15 years
  - In setting of urinary catheter, will abate if catheter removed

Interpretation of Quantitative Urine Culture Results

- Specimen dependent
- Refrigerate and process within 24 hours if not immediately
- Sensitivity of urinalysis
  - LE 75-85%
  - Nitrites 29-70%
  - Negative microscopy for bacteria combined with negative dipstick has high negative predictive value

Interpretation of Quantitated Urine Culture (Hellerstein, PIDJ, 1982)

<table>
<thead>
<tr>
<th>Collection method</th>
<th>Colony Count</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suprapubic</td>
<td>&gt;10^3</td>
<td></td>
</tr>
<tr>
<td>Catheterized</td>
<td>&gt;10^5</td>
<td>?Repeat cx 10^3-4</td>
</tr>
<tr>
<td>Clean voided</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girl</td>
<td>&gt;10^5</td>
<td></td>
</tr>
<tr>
<td>Boy</td>
<td>&gt;10^4</td>
<td>Infx unlikely &lt;10^4</td>
</tr>
</tbody>
</table>

In general, at least 50,000 CFU/ml of appropriately obtained urine=infection

Contamination in urine cultures using catheterized specimens

- Children younger than 6 months with significant adhesions
- Uncircumcised boys or those with severe phimosis
- Suprapubic aspiration
- Use fresh, sterile catheter if repeated attempt at catheterization*


Differential Diagnosis of Bacteruria

- Urethritis
- Vaginitis
- Cervicitis
- Prostatitis
- Foreign body
- Nephrolithiasis
- Renal abscess
- Vaginovesical or entervesical fistulae

Etiologic Agents in UTI

<table>
<thead>
<tr>
<th>Organism</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>80</td>
</tr>
<tr>
<td>Klebsiella/Enterobacter</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td></td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>most common Gram pos</td>
</tr>
<tr>
<td>Proteus, Providencia, Morganella</td>
<td>&gt;1 y, nosocomial</td>
</tr>
<tr>
<td>Staphylococcus saprophyticus</td>
<td>15% in adol ♀</td>
</tr>
<tr>
<td>Serratia/Citrobacter</td>
<td>other site</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>NICU</td>
</tr>
<tr>
<td>Fungi</td>
<td></td>
</tr>
</tbody>
</table>
Traditional Antimicrobial Approach to UTI

- Cefixime 8 mg/kg once daily or equivalent for outpatient uncomplicated UTI for 10 days
  - Consider using most narrow spectrum drug available
- Ceftriaxone for uncomplicated UTI in child requiring admit
- Ampicillin (200 mg/kg/d divided 4 doses) plus gentamicin 7 mg/kg/d divided 3 doses) for those with recurrent infection or underlying UT abnormality

Following child w/ UTI

- Assess clinical response
- Use of inflammatory markers for the hospitalized patient
- Consider complicated disease and assess microbiologic response (re-culture urine) for those with persistent fever
- Recurrences
  - Highest risk first few months after infection
  - Rate is high whether or not UT abnormality
  - Usually new organism rather than relapse

Vesicoureteral Reflux

- Grades
  - I—does not reach renal pelvis
  - II—to renal pelvis without dilatation
  - III—to kidney with mild dilatation
  - IV—moderate dilatation of ureter with obliteration of calyces
  - V—gross dilatation of ureter, renal pelvis, calyces
- Grades I-III often resolve by age 5 years, IV, V in 40%

CONCEPTUAL BASIS FOR VCUG

- Since the mid-1970s the management of children after a 1st febrile UTI has been based on the theory of a cause-and-effect relationship:
  - UTI + VUR → kidney damage.
- More recent data, using cortical imaging, shows that renal scarring occurs as frequently in children without VUR as in those with VUR.

Case 2

- A 5 year old girl was treated for the last 4 days with amoxicillin after strep throat was diagnosed on the basis of fever and abdominal pain (w/ positive rapid strep testing)
- She has persistent fever, and abdominal pain, the latter is severe enough that she has received fentanyl during her ED evaluation
- Marked leukocytosis is noted w/ peripheral WBC of 35K and urinalysis and liver function studies are normal. CT examination is performed with the suspicion of acute appendicitis
Complicated UTI

- Pyelonephritis
- Acute lobar nephronia: confined to single renal lobe and tissue necrosis without liquefaction
- Renal abscess
- Perinephric abscess
- Reflux nephropathy

WOTF is the most likely cause of her clinical illness?

- S. aureus
- E. coli
- Enterobacter cloacae
- Pseudomonas aeruginosa
- Enterococcus faecalis

Renal and Perinephric Abscess

- 80% in preantibiotic era: S. aureus
  - Remains an important etiologic agent
- Enterobacteriaceae especially E. coli
- Other: Pseudomonas, Enterococcus, CoNS, Streptococcus spp, Actinomyces spp, Anaerobes, Fungi, M. TB

Conditions at increased risk for renal abscess

- UT Conditions
  - Infection, anomaly, stones, tumor, neurogenic bladder, PCD, peritoneal dialysis
- Primary infection w/ bacteremia
  - Multiple sites, Indwelling central catheter, IVDU
  - Endocarditis
- Surgery
- Immunodeficiency
- Renal trauma
- Diabetes mellitus (adults)

Clinical and laboratory manifestations

- Most abscesses unilateral and flank pain is common presentation, splinting
- Infants can have palpable mass
- Consider renal abscess in setting of FUO, failure to respond to rx for UTI, OR fever in the setting of dialysis, surgery, obstructed tract, after renal trauma
  - Remember that urine culture can be negative in ~1/2

15 year old with abnormal voiding, fever, flank/abdominal pain
**Case 3**

- A 2 year old girl has a temperature of 40° and vomiting.
- Urinalysis from a bag specimen shows pyuria, positive LE and nitrites.
- A catheterized specimen is sent for urine culture and grows *E. coli* which is susceptible (surprise) to ampicillin.
- Does she need further imaging?

**Imaging?**

- Yes, she needs cystogram and renal ultrasound.
- Yes, renal ultrasound only is sufficient.
- No imaging is needed.
- It depends….

**Do we still need to order IMAGING STUDIES for 1st time UTI?**

**NO**

- Combining data from 3 good studies (Alon, Hoberman, Zamir) RUS findings changed management in only 2 of 687 patients (0.03%).
- More recent data, using cortical imaging, shows that renal scarring occurs as frequently in children without VUR as in those with VUR.

**Is imaging necessary in UTI?**

- **YES**
  - Poor response to therapy
  - Good follow up not assured
  - Voiding abnormality
  - Abdominal mass

- Not necessary for 1st time UTI and good response to therapy in those w/o voiding issues or abdominal mass AND who have undergone prenatal ultrasonography in an experienced center after 30 to 32 weeks gestation.

**Case 4**

- A 3 year old has her second urinary tract infection.
- She has no constipation or voiding dysfunction and a previously normal renal u/s.
- Cystogram is performed and shows Grade 2 VUR on the left.
- Does she need antibiotic prophylaxis?

**What about antibiotic prophylaxis?**

- Recurrent urinary tract infections (UTIs) are observed in 30-50% of children after the first UTI.
  - 90% occur within 3 months of the initial episode.
  - Risk high in infants <3 months.
Who needs antibiotic prophylaxis following UTI?

- Urinary antibiotic prophylaxis among patients with mild to moderate VUR (Grades I-III) did not decrease the overall incidence of recurrent UTI, the rate of pyelonephritis, or the formation of renal scars

Antibiotic prophylaxis

- Drug choice
- Discussion with parents on risk/benefit
- Follow up
- If fever, no new antibiotics without evaluation of urine

Recurrent UTI and pathogens

- In children with recurrent UTIs and in those treated with antibiotic prophylaxis there is a greater incidence of UTI due to Proteus spp., Klebsiella spp. and Enterobacter spp.,
- Pseudomonas spp., Serratia spp. and Candida spp. are more frequent in children with urogenital abnormalities and/or undergoing invasive instrumental investigations

Who gets recurrent febrile UTI despite normal urinary tract?

- 264 children with UTI (J Urol. 2004 Oct)
- 119 had a negative ultrasound and voiding cystourethrogram
- Among those with good f/u, 16/84 (19%) had recurrent UTI.
- Mean followup was 4.4 years (range 1.9 to 7.0).
- Risk may be highest in young infants
- Some recommend evaluation and treatment of phimosis, treatment of constipation and voiding dysfunction

Case 5

- A 3 month old girl has had fever for the last 5 days. She has no localizing findings but she is irritable and seems to have abdominal pain; pyuria is noted.
- She is given oral amoxicillin at a local ED and the next day breaks out in a rash.
- On her 8th day of fever, she is admitted to your institution.

You also note
Differential diagnosis: pyuria
Not always UTI
- Group A streptococcal infection
- Appendicitis
- Kawasaki disease
  - Definition of incomplete KD
  - Echocardiogram

AN IMPORTANT POINT

- The most effective way to reduce the risk of renal scarring associated with a UTI is *early diagnosis and effective treatment of a febrile UTI*. “This is more effective than a stereotyped policy”
  - Stan Hellerstein.