Challenges in the Evaluation and Management of Urinary Tract Infection

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What Challenges?

- Properly defining UTI
- Growing antimicrobial resistance and appropriate antibiotic choices
- What to do with asymptomatic bacteriuria
- Managing recurrent UTI
- The patient needing long-term catheterization

Urinary Tract Infection – What is It?

Definition of “UTI”

- “Urinary tract” - Easy!
- “Infection” - Ambiguous
  - Presence of micro-organisms in normally sterile site? (urinary tract?)
  - Local host inflammatory response?
  - Evidence of harm to host? (= disease)
  - Implies a need to treat

> 10^5 cfu/mL ≠ “Significant Bacteriuria”

- Clinical vs. microbiological significance
  - Microbiological: bacteria are truly coming from the bladder
  - Clinical: bacteria causing dz, need treatment

- ≥ 10^5 cfu/mL criterion for “significance” - Microbiological
  - Designed for voided samples in ax patients to distinguish vaginal and urethral contamination from bacteria truly from the bladder
  - Not informative re. clinical significance of bacteria
  - Unsuit for symptomatic or catheter-associated UTI

Comparison of Diagnostic Tests for Acute Symptomatic Lower Urinary Tract Infection

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>1.00</td>
<td>0.48</td>
<td>0.52</td>
<td>NA</td>
</tr>
<tr>
<td>Pyuria</td>
<td>0.91</td>
<td>0.50</td>
<td>0.67</td>
<td>0.83</td>
</tr>
<tr>
<td>MSU, any coliforms</td>
<td>1.00</td>
<td>0.71</td>
<td>0.79</td>
<td>1.00</td>
</tr>
<tr>
<td>MSU, ≥ 10^5/ml coliforms</td>
<td>0.95</td>
<td>0.85</td>
<td>0.88</td>
<td>0.94</td>
</tr>
<tr>
<td>MSU, ≥ 10^6/ml coliforms</td>
<td>0.51</td>
<td>0.99</td>
<td>0.98</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Stamm et al. NEJM 1982
**Significance of Pyuria**

- Pyuria = >10 WBCs/hpf in spun urine
- Useful in patient with symptoms, decent NPV
- Not useful in asymptomatic patients
- Degree of pyuria of no significance ("packed", "clumps",">150 per field")
- Urine dipstick detects leukocyte esterase from WBCs or nitrite from *Enterobacteriaciae*. Surrogate for pyuria and bacteriuria.
- Many variables can affect diagnostic accuracy
- Modestly useful if confirming a strong clinical suspicion either way (68-88% sensitivity, 66% specificity) but inadequate alone to rule in or out true UTI

**UTI Definitions (IDSA)**

- **Asymptomatic Bacteriuria**: >10^5 cfu/mL voided specimen (7 X2) or chronic Foley, or >10^5 cfu/mL from a new catheterized specimen
- **Acute uncomplicated cystitis and pyelonephritis**: typical symptoms in an otherwise healthy non-pregnant adult. Dx confirmed with + UA and/or >10^5 cfu/mL on UC
- **Complicated cystitis or pyelonephritis**: lower or upper tract UTI in patient with underlying risk of treatment failure (diabetes, pregnancy, renal failure, obstruction, anatomic abnormality, indwelling device, recent instrumentation, transplant, immunosuppression, hospital-acquired)
- **Catheter-associated UTI**: presence of symptoms or signs of UTI with no other identifiable source with >10^5 cfu/mL.

**Bacteriology of UTIs**

- Be suspicious of Group B strep, lactobacillus, and *Enterococcus*. Tend to correlate poorly with repeat cultures or catheterized specimens. Frequent contaminants. To be "real" should be pure growth at higher #s (10^5)

**Empiric Antimicrobial Management of UTI**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Antibiotic</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uncomplicated Cystitis</strong></td>
<td>Nitrofurantoin 100 mg bid</td>
<td>5 days</td>
<td>First choice, low resistance, Avoid if GFR &lt; 60</td>
</tr>
<tr>
<td></td>
<td>TMP-SMX DS bid</td>
<td>3 days</td>
<td>Avoid if regional resistance &gt; 20% or recent use</td>
</tr>
<tr>
<td></td>
<td>Fosfomycin 3 gm</td>
<td>Single dose</td>
<td>Minimal resistance, avoids if any suspicion of pyelonephritis</td>
</tr>
<tr>
<td></td>
<td>Cipro or Levo 250 mg bid</td>
<td>3 days</td>
<td>2nd line agents, should be reserved if can’t take above</td>
</tr>
<tr>
<td><strong>Pyelonephritis</strong></td>
<td>Cipro 500 mg bid</td>
<td>7 days</td>
<td>Definitive therapy should be based on C&amp;S data. Consider ceftazidime if ESBL risk is high</td>
</tr>
<tr>
<td></td>
<td>IV FQ, CP or ES-PCN</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Complicated Cystitis</strong></td>
<td>Cipro 500 mg bid</td>
<td>5-10 days</td>
<td>Need to empirically cover for <em>Pseudomonas</em> and consider ESBL. Definitive based on C&amp;S data.</td>
</tr>
<tr>
<td></td>
<td>IV CR, ES-PCN, FQ</td>
<td>5-14 days</td>
<td></td>
</tr>
</tbody>
</table>

**What Actually Happens: Choice of Antibiotics for Uncomplicated Cystitis in FP Clinics in Dallas**

![Graph showing choice of antibiotics for uncomplicated cystitis in FP Clinics in Dallas]

**What Actually Happens: Duration of Antibiotics for Uncomplicated Cystitis in FP Clinics in Dallas**

![Graph showing duration of antibiotics for uncomplicated cystitis in FP Clinics in Dallas]
Risks with Use of the Quinolones

<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achilles tendon rupture</td>
<td>4.3 (95% CI, 2.4-7.8)</td>
</tr>
<tr>
<td>Current exposure overall Age 60-79</td>
<td>6.4 (95% CI, 3.0-13.7)</td>
</tr>
<tr>
<td>Age &gt; 80</td>
<td>20.4 (95% CI, 4.6-90.1)</td>
</tr>
<tr>
<td>Serious arrhythmia</td>
<td>2.43 (95% CI, 1.6-3.8)</td>
</tr>
<tr>
<td>Death 1-5 d after Levofloxacin</td>
<td>2.49 (95% CI, 1.7-3.6)</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>2.43 (95% CI, 1.8-3.2)</td>
</tr>
<tr>
<td>C. Diff infection</td>
<td>12.7 (95% CI, 2.6-61.6)</td>
</tr>
</tbody>
</table>

Van Den Linden, J Antimicrob Chemother 2008
McCusker, Emerg Infect Dis 2003
Chien-Chang, JAMA Int Med 2015
Gowtham, Ann Fam Med. Apr 2014
Van Der Linden, JAMA Int Med 2003

Antibiotic Resistance Trends in E. coli Urinary Isolates

Where Can you Get Local and Regional Data?

- Start with your local Antibiogram
- For “big” data try: the Epcoracids Bugs + Drugs app

Asymptomatic Bacteriuria

<table>
<thead>
<tr>
<th>Population</th>
<th>Bacteriuria %</th>
<th>Pyuria w Bacteriuria %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Adult Women</td>
<td>2-5%</td>
<td>32%</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>2-11%</td>
<td>50%</td>
</tr>
<tr>
<td>Diabetic Women</td>
<td>8-14%</td>
<td>70%</td>
</tr>
<tr>
<td>Elderly: Nursing Home Female</td>
<td>25-53%</td>
<td>90%</td>
</tr>
<tr>
<td>Spinal Cord Injury Male</td>
<td>15-35%</td>
<td>90%</td>
</tr>
<tr>
<td>Indwelling urinary catheter</td>
<td>50%</td>
<td>33-86%</td>
</tr>
</tbody>
</table>


Asymptomatic Bacteriuria ≠ UTI

- Common, esp. elderly women and compromised pts
- 20-50% of treated “UTI” is actually Asx Bacteriuria
- Good evidence that Rx gives no benefit and causes harm (ADEs, resistance, more UTI)
Asymptomatic Bacteriuria: When to Treat

- Urologic procedures where urinary mucosa expected to be breached
- Pregnancy
- Kids with VUR?
- Early post renal transplant?
- NOT: elderly, diabetics, nursing home residents, spinal cord injury, impending joint replacement, indwelling urethral catheter

A Case of a “UTI”

Edna S. is an 85 y.o. female NH pt with dementia and urinary incontinence managed with diapers. Nursing staff noted yesterday that she had more pungent urine than usual and was acting a little more confused. They took the liberty to send a U/A and UCx via straight cath which showed 25 WBCs/HPF, many bacteria, and Cx is growing >100k gram negative rods. Nurses are calling for antibiotic orders.

Do you wait for final cx results? Do you give empiric amoxicillin? sulfa? a cephalosporin? a quinolone? nothing?

Antibiotic Use in LTCFs

- Prevalence of NH residents on an antibiotic at any given time: 6 – 10%
- 60-70% will receive an antibiotic over the course of a year
- Majority of antibiotics are given for UTIs followed by URIs
- Estimated that over half of antibiotic prescriptions are unnecessary and/or inappropriately long duration
UTI is #1 reason for Abx in LTCFs

**Problem:** What constitutes symptoms in an elderly, incontinent, and demented patient with limited ability to communicate?

Near Mythical Belief that “UTIs” are the Cause of:

- Unexplained falls
- Weakness
- Delirium
- Any other non-specific symptoms in the frail elderly, without definitive urinary symptoms

Evidence for this is of very poor quality

Nicolle, L. J Amer Geri Soc 2008;56:103-108
Juthani-Mehta M. J Amer Geri Soc 2009;57:963-70
Sundvall P. BMC Family Practice 2011, 12:36
Nicolle, L. J Amer Geri Soc 2009;57:113-114
Maki, M. Infect Control and Hosp Epi 2009;30:646-648
Gupta K. JAMA 2010;303:864-864

Diagnosing UTI in the Cognitively Impaired NH Patient

<table>
<thead>
<tr>
<th>Table 1 Comparison of expert consensus criteria for the diagnosis of acute symptomatic UTI for non-catheterized residents in the nursing home</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGee</td>
</tr>
<tr>
<td>3 of the following signs or symptoms:</td>
</tr>
<tr>
<td>Fever or chills</td>
</tr>
<tr>
<td>New or increased dysuria, frequency, or urgency</td>
</tr>
<tr>
<td>New flank or suprapubic pain</td>
</tr>
<tr>
<td>Change in character of the urine</td>
</tr>
<tr>
<td>Worsening of mental or functional status</td>
</tr>
<tr>
<td>Urinary incontinence</td>
</tr>
</tbody>
</table>

Must have a positive urine culture with $\geq 10^5$ bacteria and $\leq 2$ organisms

Proposed Algorithm for Management of Suspected UTI in LTCF Residents

Selected UTI Symptom

- Urine Dipstick
  - Leuko Est
  - Nitro
  - ESR
  - TMP-SMX x 3d
  - Nitrofurantoin x 5d
- If the patient has no UTI symptoms, send for urine culture

Non-specific Symptom

- Vaginal irrit', incont, change in urine, change in mental status
- Hold abx
- Hydrate
- Monitor symptoms
- UTI Symptom and Change in Urine character

Evidence for this is of very poor quality

Loeb, BMJ 2005

Validation Study of the Loeb Criteria

Findings: Significant decrease in overall antimicrobial use with no increase in admissions, complications, or mortality

Recurrent UTIs in Women
Recurrent UTIs

- > 2 infections in 6 mos or > 3 in 1 year
- Most are due to re-infection rather than relapse
- Incidence: 27% of college women with 1st UTI experience 2nd infection within 6 mos. 2.7% will have a 3rd episode

Recurrent UTIs: Risk Factors

- Genetic risk factors: P1 blood group phenotype and non-secretors of AB or B blood group antigens are susceptible to vaginal colonization with pathogenic E coli
- Behavioral risks: frequent sex, new sexual partner, use of diaphragm-spermicide
- Post-menopausal women: impaired bladder emptying
  - Urinary incontinence (OR 5.79)
  - Cystocele (OR 4.85)
  - Non-secretor status (OR 2.9)

Prevention Strategies

- Stop spermicides and diaphragm
- Increased fluids, post-coital voiding, probiotics, cranberry juice?
  - No harm but little to no evidence for benefit
- Topical estrogen for post-menopausal women
- Antibiotics
  - Post-coital
  - Intermittent self-treatment
  - Continuous

Antibiotic Management of Recurrent UTIs

<table>
<thead>
<tr>
<th>Method</th>
<th>Antibiotic</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-coital</td>
<td>Nitrofurantoin</td>
<td>SS or DS 100 mg</td>
<td>1 yr – indefinite</td>
</tr>
<tr>
<td></td>
<td>Cipro</td>
<td>250 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cephalexin</td>
<td>250 mg</td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>Nitrofurantoin</td>
<td>SS qd or 3x/wk 50-100 mg qd</td>
<td>6 mos – 2 yrs</td>
</tr>
<tr>
<td></td>
<td>Cipro</td>
<td>125 mg qd</td>
<td></td>
</tr>
<tr>
<td>Intermittent</td>
<td>TMP-SMX</td>
<td>125 mg qd</td>
<td></td>
</tr>
</tbody>
</table>

Long-Term Urinary Catheters and Infection

- 5-10% of LTCF residents are catheterized
- Essentially all are bacteriuric (CA-ASB) – defined as ≥ 10^5 cfu/mL
- CA-UTI defined as ≥ 10^3 cfu/mL with ass’d symptoms
- Associated with increased upper urinary inflammation at autopsy
- Accounts for 45-55% of bacteremias in LTCFs
- Incidence of febrile episodes is 1.1 per 100 catheter-days, most are low grade and resolve without abx
- Symptom correlation with bacteruria is v poor and nonspecific. Order cultures with: new CVA tenderness, high temps, rigors, or delirium
Levels of Bacteria with a Catheter in Place

Once bacteria introduced into urinary tract with a catheter in place, rapidly rises to “significant” levels ( >10^5 / mL) of bacterial colonization.

Incidence of Significant Bacteriuria by Catheter Days

Incidence of CA-ASB and CA-UTI in Male Spinal Cord Injury Patients

Long-term Urinary Catheters – Don’ts

- Don’t place unless definitive indication
- Don’t obtain a U/A or U/C with nonspecific symptoms
  - (esp don’t obtain for “cloudy”, “malodorous” urine or encrusted catheter)
- Don’t use pyuria to distinguish CA-ASB from CA-UTI (although absence of pyuria suggests not CA-UTI)
- Don’t use methenamine salts or cranberry juice as preventative
- Don’t use prophylactic antibiotics

Long-term Urinary Catheters – Dos

- Frequently review for necessity and remove when possible
- Acceptable indications: Urinary retention
  - Not indicated for incontinence unless terminally ill or failing all other management methods
- Diapering > Condom Cath > Intermittent straight cath > Suprapubic catheter? > Indwelling foley catheter
- If suspect UTI, replace catheter, then send UA/UC

Incidence of CA-ASB and CA-UTI in Male Spinal Cord Injury Patients

My love for you burns stronger than any urinary tract infection.