Complicated Urinary Tract Infections

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Disclosure: Dr. Lynch has no significant financial interest in any of the products or manufacturers mentioned.
50 year man with quadraplegia x 15 years complicated by sacral and ischial decubitus ulcers, chronic pelvic pain, and autonomic dysfunction

To keep the wounds dry, he is switched from intermittent urinary catheterization to an indwelling catheter....
>100000 Col/mL Pseudomonas aeruginosa. This bacterial species is known to produce a chromosomal AmpC inducible beta-lactamase. Penicillin or cephalosporin monotherapy for serious infections may result in the emergence of high-level resistance.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MICM Interp</th>
<th>Microtiter MIC (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>S</td>
<td>&lt;=16</td>
</tr>
<tr>
<td>Cefepime</td>
<td>S[comment]</td>
<td>4</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>S</td>
<td>4</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>R</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>S</td>
<td>&lt;=4</td>
</tr>
<tr>
<td>Imipenem</td>
<td>S</td>
<td>2</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>R</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Meropenem</td>
<td>S</td>
<td>2</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>S</td>
<td>16</td>
</tr>
<tr>
<td>Ticarcillin/clavulanic Acid</td>
<td>R</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>S</td>
<td>&lt;=2</td>
</tr>
</tbody>
</table>
Table 1. Features of Uncomplicated versus Complicated Cystitis and Pyelonephritis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Uncomplicated</th>
<th>Complicated*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical patient</td>
<td>Otherwise healthy, ambulatory women with no history suggestive of anatomical</td>
<td>Men, women, or children</td>
</tr>
<tr>
<td></td>
<td>or functional abnormality of the urinary tract</td>
<td>with functional, metabolic,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or anatomical conditions that</td>
</tr>
<tr>
<td></td>
<td></td>
<td>may increase the risk of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment failure or serious</td>
</tr>
<tr>
<td></td>
<td></td>
<td>outcomes (e.g., obstruction,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>stone, pregnancy, male sex,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>diabetes, neurogenic bladder,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>renal insufficiency, immunosup-</td>
</tr>
<tr>
<td>Clinical spectrum</td>
<td>Mild cystitis to severe pyelonephritis</td>
<td>Mild cystitis to life-threatening</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Infection suspected on the basis of typical symptoms; urinalysis and urine</td>
<td>urosepsis</td>
</tr>
<tr>
<td></td>
<td>culture not routinely needed for suspected cystitis but recommended for</td>
<td></td>
</tr>
<tr>
<td></td>
<td>pyelonephritis</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial resistance</td>
<td>Common but generally predictable (antimicrobial resistance alone does not</td>
<td>Multidrug resistance common and</td>
</tr>
<tr>
<td></td>
<td>warrant the designation complicated UTI</td>
<td>less predictable; fluoroquinolone</td>
</tr>
<tr>
<td>Empirical antimicrobial</td>
<td>For cystitis: first-line short-course antimicrobial regimen; for pyelonephritis</td>
<td>For cystitis: 7-day or longer</td>
</tr>
<tr>
<td>treatment</td>
<td>first-line oral or intravenous antimicrobial regimen for 5 to 14 days,</td>
<td>course of fluoroquinolone</td>
</tr>
<tr>
<td></td>
<td>depending on severity and need for hospitalization</td>
<td>preferred†</td>
</tr>
<tr>
<td>Response to treatment</td>
<td>Predictable with appropriate agent for recommended treatment duration;</td>
<td>Less predictable regardless of</td>
</tr>
<tr>
<td></td>
<td>persistent symptoms or early recurrence suggests presence of a complicating</td>
<td>antimicrobial susceptibility;</td>
</tr>
<tr>
<td></td>
<td>factor</td>
<td>may require instrumentation for</td>
</tr>
</tbody>
</table>

* Complicated urinary tract infections (UTIs) are heterogeneous in that the risks of infection and of treatment failure vary. Current classification schemes are overly simplistic, especially for patients with complicated infections, but the value of more complex classification schemes has not yet been shown. MRSA denotes methicillin-resistant *Staphylococcus aureus*.

† Short-course regimens are likely to be effective for mild-to-moderate cystitis in healthy, ambulatory, compliant women who are elderly, have catheter-associated UTIs, are pregnant, or have mild diabetes.
Uncomplicated Cystitis

- Healthy
- Non-pregnant
- Not recently hospitalized
- Women

Common pathogens
- E coli (70-90%)
- S saprophyticus (5-15%)
- Klebsiella
- Proteus

Complicated Cystitis

- Urological/structural abnormalities
- Pregnancy
- Very young/old
- Diabetic
- Catheter use

Resistant pathogens
- Klebsiella
- Pseudomonas
- Enterococcus
- And more…
Consider alternative dx (pyelo or complicated UTI)

Fluoroquinolones (3d) (although resistance is high in some areas)

Or

Beta-lactams (3-7d)
(Avoid amoxicillin or ampicillin alone)

**Woman with uncomplicated cystitis**
- No flank pain, fever, e/o pyelo
- Able to take PO abx

**Can take one of the below?**
- Nitrofuratoin (5d)
- TMP/SMX (3d)*
- Fosfomycin (1 dose)
- Pivmecillinam (3-7d)

**NO**
Drugs

- *E coli* Drug Resistance
  - Ampicillin, >20%
  - TMP/SMX, >20%
  - Fluoroquinolones, <10%, but rising
  - Nitrofurantoin, fosfomycin, mecillinam retain good activity

- Predictors of resistance
  - TMP/SMX use in previous 6 months
  - Travel outside the US (for US women) in preceding 3-6 months
  - Hospital antibiograms not terribly useful
30 year old woman with dysuria and frequency for 2 days. This is her 4th UTI in 6 months.
Recurrent UTI in Women

- A leading cause of morbidity in women
- No single accepted definition of recurrent UTI exists
  - 3 episodes in 12 months or 2 in 6 months
  - 4 or more in 12 months
- Should be distinguished from persistent UTI
- ACOG uses the terms reinfection and relapse
  - Relapse: UTI with same organism after adequate tx
  - Reinfection: different organism or another UTI after neg cx
Recurrent UTI in Women

- 25% experience a recurrence
  - Among women >55 y- recurrent *E coli* cystitis occurs in 53%
  - Among women 18-55 y- recurrent *E coli* cystitis in 36%

- Majority are believed to be *reinfections*

- *E coli* is most common pathogen and is also associated with an increased likelihood of recurrent UTI

Nosseir et al, J of Women’s Health, 2012
Risks for Recurrent UTI

- **Biological**
  - Mother with a history of UTI
  - Early age of 1st UTI
  - Anatomic
  - Post-menopause
  - DM
  - GU surgery/cystocele

- **Behavioral**
  - Sexual intercourse (new sex partner, frequency)
  - Spermicide use
  - Perineal hygiene (dementia)

- Virulence of the pathogen
Strategies for Recurrent UTI

- Postcoital prophylaxis
  - Works very well (10-fold fewer infections)
  - Single dose
  - Minimizes antibiotic exposure

- Continuous prophylaxis
  - Works very well (between 1-6 fold fewer infections)
  - More GI disturbance and candidiasis
  - Not necessarily better than postcoital prophylaxis

- Intermittent self-treatment
  - Women are very good at UTI self diagnosis (85-95%)
  - Short course antibiotics are effective
  - Since not really prophylaxis, more overall UTIs
<table>
<thead>
<tr>
<th>Drug</th>
<th>Continuous prophylaxis</th>
<th>Postcoital</th>
<th>Acute self-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP/SMX</td>
<td>40/200 mg daily or 40/200 mg 3 times/week</td>
<td>40/200 mg or 80/400 mg</td>
<td>160 mg TMP/800 mg SMX twice daily for 3 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TMP</td>
<td>100 mg daily</td>
<td></td>
<td>100 mg twice daily for 3 days</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>50–100 mg daily</td>
<td>50–100 mg</td>
<td>50–100 mg 4 times daily for 7 days</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>125–250 mg daily</td>
<td>125–250 mg</td>
<td></td>
</tr>
<tr>
<td>Norfloxacin&lt;sup&gt;*&lt;/sup&gt;</td>
<td>200 mg daily</td>
<td>200 mg</td>
<td>400 mg twice daily for 3 days</td>
</tr>
<tr>
<td>Ciprofloxacin&lt;sup&gt;*&lt;/sup&gt;</td>
<td>125 mg daily</td>
<td>125 mg</td>
<td>250 mg twice daily for 3 days</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td></td>
<td></td>
<td>3 g single dose</td>
</tr>
</tbody>
</table>

<sup>a</sup>TMP/SMX, trimethoprim-sulfamethoxazole.

<sup>*</sup>Avoid in childbearing years.
22 year old man with 10 days of fevers and flank pain

H/o skin and soft tissue abscesses

Active methamphetamine IVDU

UA: leukocytes and bacteria
What are you worried about?

- Descending/hematogenous dissemination leading to pyelonephritis
- Bacteremia
- Transverses from capillary to tubular lumen
- Most likely pathogen: Staphylococcus aureus
46 year old man with 5 days of dysuria and frequency

Risk factors for UTI?
  MSM, uncircumcised, obstruction/BPH

Differential diagnosis?
Differential Diagnoses

- Cystitis
- Urethritis - usually + discharge and sexually active
- Prostatitis - fever, abd and prostatic pain
  - Acute, chronic infection vs. prostatitis, asymptomatic inflammatory, granulomatous
- Nephrolithiasis: hematuria, no bacteria
- Epididymitis - tender, swollen scrotum, +/- discharge
- Orchitis - uncommon, mumps, coxsackie B, bacterial
Treatment

- Cystitis - 7 days TMP/SMX or fluoroquinolone
- Urethritis - depends on pathogen, but usually treat GC and CT together
- Prostatitis - can be difficult and very frustrating, long course of abx, not always successful
Catheter-associated UTI

- UTI is the most common hospital-acquired infection- ~5% of residents in US SNFs
- Majority of nosocomial UTI are associated with in-dwelling urinary catheters
- Each episode = $600
- Medicare target for elimination
- CDC 2009: symptoms + 105 CFU/ml or sx ± 103 CFU/ml + positive urinalysis
Prevention

- Not treating asymptomatic bacteriuria (ASB)
- Closed urinary drainage system
- Removing the catheter
- Impregnated catheters
- Condom catheters*
- Intermittent catheterization
- Suprapubic catheters
- Change it out prior to treatment
- Treat! Duration? PO/IV? 3-14 days
UTI in the ICU

- Insert aseptically and for appropriate indications
- Closed drainage systems recommended
- Remove ASAP
- Consider impregnated catheters (antimicrobial or antiseptic) (but only decreases bacteriuria/funguria)*
- Prophylactic abx: RCT 239 surgical pts, 3 doses TMP/SMX*

<table>
<thead>
<tr>
<th></th>
<th>Hospital-acquired (n = 71)</th>
<th>Community-onset (n = 327)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>59.2 ± 18.1</td>
<td>62.6 ± 17.5</td>
<td>.148</td>
</tr>
<tr>
<td>Female</td>
<td>39 (54.9)</td>
<td>237 (72.5)</td>
<td>.004</td>
</tr>
<tr>
<td>Underlying disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid tumor</td>
<td>23 (32.4)</td>
<td>47 (14.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Liver disease</td>
<td>8 (11.3)</td>
<td>21 (6.4)</td>
<td>.154</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>16 (22.5)</td>
<td>78 (23.9)</td>
<td>.813</td>
</tr>
<tr>
<td>Neurologic disease</td>
<td>23 (32.4)</td>
<td>43 (13.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Renal disease</td>
<td>12 (16.9)</td>
<td>60 (18.3)</td>
<td>.774</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (26.8)</td>
<td>100 (30.6)</td>
<td>.524</td>
</tr>
<tr>
<td>Comorbid condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>8 (11.3)</td>
<td>8 (2.4)</td>
<td>.003</td>
</tr>
<tr>
<td>Recent operation</td>
<td>9 (12.7)</td>
<td>9 (2.8)</td>
<td>.001</td>
</tr>
<tr>
<td>Corticosteroid use</td>
<td>9 (12.7)</td>
<td>8 (2.4)</td>
<td>.001</td>
</tr>
<tr>
<td>Immunosuppressant use</td>
<td>11 (15.5)</td>
<td>20 (6.1)</td>
<td>.008</td>
</tr>
<tr>
<td>Indwelling urinary catheter</td>
<td>36 (50.7)</td>
<td>48 (14.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Tube insertion</td>
<td>11 (15.5)</td>
<td>7 (2.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Inappropriate initial antimicrobial therapy</td>
<td>13/69 (18.8)</td>
<td>37/307 (12.1)</td>
<td>.133</td>
</tr>
</tbody>
</table>
67 year old woman with diabetes and secondary chronic renal insufficiency presents with fever, left sided flank pain and looks “sick”

You are consulted after the following radiology is obtained:
Emphysematous Pyelonephritis

Which of the following is correct:

- Percutaneous drainage + IV abx
- Immediate nephrectomy
- Patients with diabetes and good glucose control are not risk
- Usually Staphylococcus aureus
- More common in men than women
Emphysematous Pyelonephritis

- Rare, gas-forming infection of renal parenchyma
- Almost all reported cases in people with diabetes with poor glucose control
- Most common organisms are GNR (E. coli and Klebsiella)
- Mortality is 40-70% with abx alone
Classification

- Class 1: Gas in the collecting system only (i.e., emphysematous pyelitis)
- Class 2: Gas in the renal parenchyma without extension to the extrarenal space
- Class 3A: Extension of gas or abscess to the perinephric space, Class
- 3B: Extension of gas or abscess to the pararenal space, Class
- 4: Bilateral emphysematous pyelonephritis or a solitary functioning kidney with emphysematous pyelonephritis

Classification

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- Class 3A: Extension of gas or abscess to the perinephric space, Class
- 3B: Extension of gas or abscess to the pararenal space, Class
- 4: Bilateral emphysematous pyelonephritis or a solitary functioning kidney with emphysematous pyelonephritis
Don’t Forget Schistosomiasis

- S. Haematobium causes severe urinary tract pathology and renal complications
- Affects nutritional status and hemoglobin concentrations (anemia)
- In a study from Mali (2009) in an endemic region, overall prevalence of infection ~90% in children aged 7-14. Hematuria in ~25%. Pathological changes seen in 20%.

Guidelines

Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infection in Adults:
2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America

Thomas M. Hooton,1 Suzanne F. Bradley,1 Diana D. Cardenas,2 Richard Colgan,4 Suzanne E. Geerlings,7
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