Complicated Urinary Tract Infections: A Case-Based Discussion

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Disclosures

• I have no relevant financial relationships with commercial interests.
Outline & Objectives

• By the end of this session, participants will be able to:
  – Recognize the criteria that justify a diagnosis of complicated urinary tract infection (cUTI).
  – Discuss strategies for managing and preventing catheter-associated UTI (CA-UTI).
  – Recognize symptoms of incomplete bladder emptying and describe the relevant work-up.
  – Name circumstances under which recovery of organisms from the urine of an asymptomatic person warrants treatment.
Definitions

• Acute, uncomplicated cystitis:
  – symptomatic lower urinary tract infection
  – structurally normal genitourinary tract
• Acute, nonobstructive pyelonephritis:
  – renal infection with above plus CVA pain ± fever
  – structurally normal genitourinary tract

More Definitions

• Asymptomatic bacteriuria
  – isolation of a specified quantitative count of bacteria from the urine of a person without symptoms referable to the GU tract

• Complicated urinary infection:
  – UTI in persons with structurally or functionally abnormal urinary tract

Classification of Complicated UTI

• Structural Abnormalities
  – Obstruction
  – Prostatic infection
  – Calculi
  – Urinary diversion procedures
  – Infected cysts
  – External drainage
    • urinary catheters
    • nephrostomy tubes
  – Stents
  – Vesicoureteral reflux
  – “Neurogenic bladder”
  – Bladder or renal abscesses
  – Fistulae

• Metabolic/Hormonal
  – Diabetes mellitus
  – Pregnancy
  – Renal impairment
  – Xanthogranulomatous pyelonephritis
  – Malakoplakia
  – Primary biliary cirrhosis

• Impaired Host Responses
  – Transplant recipients
  – Neutropenia
  – Immunodeficiency syndromes

• Unusual Pathogens
  – Yeasts and fungi
  – *Mycoplasma spp.*
  – Resistant bacteria
  – Calculi-producing bacteria

Ronald & Harding. *Infect Dis Clin N Amer* 1997;11:583-592
Case #1

- A 78-year-old male resident of a long-term care facility is brought in to see you for evaluation of mild confusion and low-grade fevers to 100.8°F.
- His exam is unremarkable, save a bladder catheter placed ten weeks ago for management of incontinence.
- Urine culture shows <10,000 cfu/mL of vancomycin-resistant (but ampicillin-susceptible) *E. faecalis*.
- CXR is unremarkable, and you find no explanation for his confusion and fevers other than the possible UTI.
- What should you do next?
Case #1 continued

a) remove his catheter, repeat a urine culture, and if the same *Enterococcus* isolate is cultured, prescribe amoxicillin 500 mg TID x10 days

b) recommend that his catheter be exchanged for a new one and prescribe linezolid 600 mg BID x10 days

c) leave his catheter *in situ* and prescribe nitrofurantoin monohydrate macrocrystals 100 mg BID x14 days; exchange his catheter only if his post-treatment urine culture remains positive

d) leave his catheter *in situ* and repeat his urine culture and prescribe TMP/SMX one DS tablet BID x10 days only if >100,000 cfu/mL of bacteria are found
Catheter-Associated UTI

- Most common healthcare-associated infection
  - Up to 40% of nosocomial infections
  - Up to 69% considered avoidable
- Many people receive bladder catheters
  - 15-25% of inpatients
  - 5-10% of nursing home residents
- Bacteriuria incidence rate: 3-8% per day
  - By one month, nearly all have bacteriuria

Catheter-Associated UTI: Pathogens

• More diverse than uncomplicated infection
  – *E. coli* still predominates, but <33% of isolates
  – Other Enterobacteriaceae
  – *Pseudomonas spp.*
  – Gram-positive cocci (e.g., *Enterococcus spp.*)
  – *Candida spp.*

• Infection is often polymicrobial among persons with long-term catheters

• Drug resistance is a significant problem

Catheter-Associated UTI: Diagnosis

• If signs or symptoms consistent with UTI are present: $\geq 10^3$ cfu/mL bacteria
• Pyuria is generally necessary but not sufficient
• Diagnosis is very challenging.
  – Most patients with bacteriuria do not have symptoms referable to the GU tract.
  – Most patients with bacteriuria do not develop UTI.

Table 2. Symptoms Referable to the Urinary Tract, Fever, Leukocytosis, and Quantitative Pyuria in a Subset of 1034 Hospitalized Patients With Urinary Catheters*

<table>
<thead>
<tr>
<th></th>
<th>Without CAUTI (n = 945)</th>
<th>With CAUTI (n = 89)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Proportion with symptoms, %</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pain</td>
<td>5.9</td>
<td>4.8</td>
<td>.81</td>
</tr>
<tr>
<td>Urgency</td>
<td>7.6</td>
<td>6.0</td>
<td>.68</td>
</tr>
<tr>
<td>Dysuria</td>
<td>8.0</td>
<td>6.0</td>
<td>.66</td>
</tr>
<tr>
<td>Temperature &gt;38.5°C</td>
<td>19.8</td>
<td>17.7</td>
<td>.77</td>
</tr>
<tr>
<td>Highest temperature, mean ± SD, °C</td>
<td>38.1 ± 0.7</td>
<td>37.8 ± 0.5</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peripheral white blood cell count, mean ± SD, ×10⁶/L</td>
<td>11.3 ± 4.1</td>
<td>10.7 ± 3.6</td>
<td>.14</td>
</tr>
<tr>
<td>Highest urine white blood cell count, mean ± SD, /μL†</td>
<td>11 ± 100</td>
<td>309 ± 1065</td>
<td>.009</td>
</tr>
</tbody>
</table>

*Other than catheter-associated urinary tract infection (CAUTI), which was detected in 89 patients, no infections were identified. The proportion of patients with and without CAUTI who could respond to daily questions regarding symptoms was identical in the 2 groups: 94%.

†Excludes kidney transplant patients, whom we have found show a burst of sterile pyuria following transplantation.
Lack of Relationship between Pyuria and Bacteriuria in CA-UTI

Catheter-Associated UTI: Diagnosis

• Signs and symptoms suggestive of UTI:
  – fever, rigors, malaise, lethargy, ΔMS
  – flank pain and/or tenderness
  – acute hematuria
  – pelvic discomfort

• Patients with spinal cord injury:
  – Above plus increased spasticity or unease

• Not odor or color change

Catheter-Associated UTI: Management

• IDSA: “CA-bacteriuria results in considerable antimicrobial use (often inappropriate)... and comprises a large reservoir of antimicrobial-resistant organisms.”

• Caveat: “Most signs and symptoms... are non-specific and place a burden on the clinician who wishes to use antimicrobials appropriately.”

Catheter-Associated UTI: Management

• Consider condom catheters for men.
• Consider clean intermittent catheterization.
• Insert indwelling catheters only when indicated.
• Get the catheter out.
• Get the catheter out!
## Acceptable Catheter Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Comment(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically significant urinary retention</td>
<td>Temporary relief or longer-term drainage if medical therapy is not effective and surgical correction is not indicated.</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>For comfort in a terminally ill patient; if less invasive measures (eg, behavioral and pharmacological interventions or incontinence pads) fail and external collecting devices are not an acceptable alternative.</td>
</tr>
<tr>
<td>Accurate urine output monitoring required</td>
<td>Frequent or urgent monitoring needed, such as with critically ill patients.</td>
</tr>
<tr>
<td>Patient unable or unwilling to collect urine</td>
<td>During prolonged surgical procedures with general or spinal anesthesia; selected urological and gynecological procedures in the perioperative period.</td>
</tr>
</tbody>
</table>

**NOTE.** Adapted from [30, 120 121].
Do you know who has a catheter?

<table>
<thead>
<tr>
<th>Category</th>
<th>Observations of Patients with a Catheter (Number)</th>
<th>Observations in Which Provider Was Unaware of Catheter (Number)</th>
<th>Appropriate versus Inappropriate Urinary Catheters</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
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<td>476-80.</td>
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<td>88 (28)</td>
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<td>211</td>
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<td>44 (21)</td>
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<td>44 (41)</td>
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<td>All providers</td>
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<td>211</td>
<td>44 (41)</td>
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<td>44 (21)</td>
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<td>211</td>
<td></td>
<td>44 (41)</td>
<td>&lt;0.001</td>
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<tr>
<td>Medical students</td>
<td>39</td>
<td>8 (21)</td>
<td>26</td>
<td>5 (19)</td>
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<td></td>
<td>8 (21)</td>
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<td>5 (19)</td>
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<td>Interns</td>
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<td>19 (22)</td>
<td>58</td>
<td>9 (16)</td>
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<td>9 (16)</td>
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<td>58</td>
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<td>30</td>
<td>10 (33)</td>
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<td>30</td>
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<td>10 (33)</td>
<td>0.06</td>
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<td>Residetns</td>
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<td>70</td>
<td>13 (19)</td>
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<td>70</td>
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<td>15 (44)</td>
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<td>70</td>
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<td>34</td>
<td>15 (44)</td>
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<td></td>
<td>15 (44)</td>
<td></td>
<td>15 (44)</td>
<td>0.006</td>
</tr>
<tr>
<td>Attending physicians</td>
<td>88</td>
<td>33 (38)</td>
<td>57</td>
<td>17 (30)</td>
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<td></td>
<td>33 (38)</td>
<td></td>
<td>17 (30)</td>
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<td>57</td>
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<td>31</td>
<td>16 (52)</td>
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<td>57</td>
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<td>31</td>
<td>16 (52)</td>
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<td></td>
<td>16 (52)</td>
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<td>16 (52)</td>
<td>0.04</td>
</tr>
<tr>
<td>P value</td>
<td>0.06</td>
<td></td>
<td>0.09</td>
<td>0.29</td>
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</tbody>
</table>

Catheter Surveillance

• Only 39% of hospitals routinely monitor catheter duration and/or discontinuation

• Aside from aseptic insertion, most hospitals don’t implement CA-UTI prevention practices

• Other important factors:
  – Lack of physician and nurse buy-in
  – Patient request
  – Placement in ED

National CA-UTI Prevention Program

• Key interventions
  – Daily assessment for presence & need
  – Consider alternative collection methods
  – Emphasis on aseptic technique during insertion
  – Emphasis on proper maintenance
  – Feedback to physicians and nurses on rates*
  – Training to address gaps*

National CA-UTI Prevention Program

• In non-ICU settings:
  – Catheter use from 20.1% to 18.8%
  – CA-UTI rates decreased from 2.28 to 1.54 infections per 1000 catheter days

• [www.ahrq.gov/cautitools](http://www.ahrq.gov/cautitools)
• [www.catheterout.org](http://www.catheterout.org)
• [www.ahrq.gov/professionals/education/curriculum-tools/cusptoolkit](http://www.ahrq.gov/professionals/education/curriculum-tools/cusptoolkit)

Catheter-Associated UTI: Management

• Obtain a urine culture before antibiotics
  – If the catheter has been in place for >2 weeks, exchange the catheter and *then* culture the urine
  – If possible, remove the catheter completely and then obtain a clean-catch midstream specimen

• Tailor antibiotics based upon culture results

Johns Hopkins Hospital Inpatient
*E. coli* Antibiotic Susceptibilities

- Urine isolates only:
  - cefazolin 77%
  - ceftriaxone 92%
  - ciprofloxacin 71%
  - nitrofurantoin 96%
  - TMP/SMX 67%

Data courtesy of Dr. Sara Cosgrove
Johns Hopkins Hospital Non-ICU
*E. coli* Antibiotic Susceptibilities (All)

- ampicillin 45%
- amp/sulbactam 50%
- pip/tazobactam 94%
- cefazolin 73%
- cefoxitin 88%
- ceftriaxone 92%
- cefepime 96%
- aztreonam 93%
- meropenem 99%
- ertapenem 98%
- ciprofloxacin 68%
- gentamicin 86%
- amikacin 99%
- tetracycline 67%
- TMP/SMX 68%

Data courtesy of Dr. Sara Cosgrove
Catheter-Associated UTI: Management

• Data on duration of therapy are sparse
  – 7 days if prompt resolution of symptoms
  – 10-14 days otherwise
• Consider levofloxacin 750 mg x5d
• Consider treating as for uncomplicated cystitis in women <65 without upper tract symptoms who have the catheter removed

Other Catheter Consequences

- Trauma prompting intervention was as common as UTI in one study
- Infectious and non-infectious complications equally likely with short-term use
  - Urethral stricture or erosion 3-17%
- Non-infectious complications 4x more likely with long-term use
  - Blockage 26-57%
  - Bladder cancer, stones, gross hematuria...

Case #2

• A 72-year-old woman seeks attention regarding increased urinary frequency.
• You have diagnosed three UTI in the past five months, all seemingly with the same *E. coli*.
• On further questioning, she endorses urinary dribbling and hesitancy on a regular basis.
• After confirming an infection with the same *E. coli*, what should you include as part of the next step in her evaluation & management?
Case #2 (continued)

a) Make arrangements for PICC placement and start treatment with ertapenem 1 gram IV every 24 hours x14 days.

b) Obtain a pelvic CT scan to assess for a colovesicular fistula.

c) Treat with amoxicillin 500 mg by mouth every eight hours x21 days, followed by chronic suppression with nitrofurantoin.

d) Assess a post-void residual volume.
Incomplete Bladder Emptying?

• Symptoms
  – dribbling
  – continuous leakage
  – weak stream
  – hesitancy
  – frequency
  – nocturia

• Possible causes
  – Bladder outlet obstruction
    • men > women
  – Impaired detrusor contractility
  – Spinal cord injury

Possible Vicious Cycle of Detrusor Underactivity

Evaluation for & Management of Incomplete Emptying

• Measure post-void residual (PVR) volume
  – Rough guide: <50 normal, >200 abnormal
• Address obstructing lesions
• Clean intermittent catheterization

Clean Intermittent Catheterization

• Fewer complications than indwelling catheters
• Clean OK; does not need to be sterile
• Multiple-use catheters OK
• Individualize frequency for each patient
  – Roughly every four hours
• Goal bladder volume <500 cc
• Consider urology consultation and/or urodynamic testing as appropriate

Treatment

• Systemic antibiotics based on culture data
• Duration of therapy
  – 7 days if prompt resolution
  – 10-14 days if more delayed resolution and/or prolonged symptoms prior to treatment
• Methenamine salts?

Hooton TM et al. *Clin Infect Dis* 2010;50:625-663
Cranberry

- Data are limited
- Study quality is not great
- Results are conflicting
  - Most studies are negative
- Concerns: cost, fluid volume, side effects
- No published data among patients who are catheterized for reasons other than spinal cord injury

Hooton TM et al. *Clin Infect Dis* 2010;50:625-663
Case #3

- Annual visit for 89-year-old diabetic female assisted living resident with stage III chronic kidney disease and remote kidney stones who has had two UTI in the past five years.
- She feels well and denies urinary symptoms.
- U/A: 18 WBC/hpf.
- Culture: >100,000 TMP/SMX-resistant *E. coli*.
- How should these findings be managed?
Case #3 continued

a) TMP/SMX DS twice daily for seven days
b) No antibiotics are needed
c) Ciprofloxacin 250 mg twice daily for three days
d) Nitrofurantoin monohydrate macrocrystals 100 mg twice daily for seven days, followed by repeat U/A and UCx one week later
Asymptomatic Bacteriuria

- Women: Two consecutive voided urine specimens containing $\geq 10^5$ CFU/mL of the same bacterial strain
- Men: One voided urine specimen containing $\geq 10^5$ CFU/mL of one bacterial species
- Catheterized specimen: $\geq 10^2$ CFU/mL of one bacterial species

Table 2. Prevalence of asymptomatic bacteriuria in selected populations.

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence, %</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy, premenopausal women</td>
<td>1.0–5.0</td>
<td>[31]</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>1.9–9.5</td>
<td>[31]</td>
</tr>
<tr>
<td>Postmenopausal women aged 50–70 years</td>
<td>2.8–8.6</td>
<td>[31]</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>9.0–27</td>
<td>[32]</td>
</tr>
<tr>
<td>Men</td>
<td>0.7–11</td>
<td>[32]</td>
</tr>
<tr>
<td>Elderly persons in the community(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>10.8–16</td>
<td>[31]</td>
</tr>
<tr>
<td>Men</td>
<td>3.6–19</td>
<td>[31]</td>
</tr>
<tr>
<td>Elderly persons in a long-term care facility</td>
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<td></td>
</tr>
<tr>
<td>Women</td>
<td>25–50</td>
<td>[27]</td>
</tr>
<tr>
<td>Men</td>
<td>15–40</td>
<td>[27]</td>
</tr>
<tr>
<td>Patients with spinal cord injuries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermittent catheter use</td>
<td>23–89</td>
<td>[33]</td>
</tr>
<tr>
<td>Sphincterotomy and condom catheter in place</td>
<td>57</td>
<td>[34]</td>
</tr>
<tr>
<td>Patients undergoing hemodialysis</td>
<td>28</td>
<td>[28]</td>
</tr>
<tr>
<td>Patients with indwelling catheter use</td>
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<td></td>
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<tr>
<td>Short-term</td>
<td>9–23</td>
<td>[35]</td>
</tr>
<tr>
<td>Long-term</td>
<td>100</td>
<td>[22]</td>
</tr>
</tbody>
</table>

\(^a\) Age, \(\geq 70\) years.
Asymptomatic Bacteriuria Rx

• Whom should you treat?
  – Pregnant women
    • 20-30x increased risk of pyelonephritis
  – Persons about to undergo urologic procedures (e.g., TURP) wherein disruption of the uroepithelium is anticipated

• Others should not be screened or treated

• Pyuria, odor, and color change are NOT indications for treatment

Over-Treatment of ASB

• There’s lots of inappropriate treatment of ASB
  – 70% of CA-ASB in one study
  – 33% of Enterococcus ASB treated in another
    • No adverse downstream effect of not treating it

• One study showed increased rates of UTI among women with a history of recurrent UTI who received Rx for ASB

Case #4

• Your 83-year-old male inpatient has had *Candida glabrata* cultured from his urine. He has no symptoms referable to the GU tract.
• He is here with a CHF exacerbation; a catheter was placed for monitoring of fluid balance.
• Comorbidities include hypertension, dyslipidemia, and diabetes mellitus.
• You wish to leave the catheter *in situ* for now.
• How should his candiduria be managed?
a) Exchange the catheter now, then repeat a urine culture and treat with fluconazole if the candiduria persists.

b) Exchange the catheter now, then repeat a urine culture and treat with caspofungin if the candiduria persists.

c) Obtain a bladder ultrasound to exclude a “fungus ball.”

d) No interventions are needed.
Indications for Treating Candiduria

• Treatment not recommended unless high risk for dissemination
  – Neutropenia; very low birth weight infants
    • Treat these two as you would Candidemia
  – Anticipated invasive urologic procedures

• Fungus ball
  – Keep this in mind for patients with persistent Candiduria and no other apparent explanation

Treatment of Candida UTI

• Fluconazole 200-400 mg/d x2w
  – not other azoles
• Fluconazole-resistant *C. glabrata*
  – Cystitis
    • Amphotericin 0.3-0.6 mg/kg/d x1-7d
    • Flucytosine (5-FC) 25 mg/kg 4x/d x7-10d
  – Pyelonephritis
    • Amphotericin 0.3-0.6 mg/kg/d ± Flucytosine (5-FC) 25 mg/kg 4x/d
• *C. krusei* cystitis or pyelonephritis
  – Amphotericin 0.3-0.6 mg/kg/d x1-7d
• Not echinocandins
  – although there are case reports of success (& failure)

Review

• Complicated UTI are a heterogeneous group of infections
• Diagnosis needs to be made thoughtfully and carefully to minimize unnecessary antibiotic use for treatment of asymptomatic bacteriuria
• Assessments for functional and anatomical abnormalities of the GU tract should be considered for patients with cUTI