Preserving the Miracle of Antibiotics:
Urinary tract infections for Primary Care Physicians

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Objectives

- To review current evidence for prophylaxis, diagnosis, evaluation, treatment, management, and practice improvement of urinary tract infections.
- UTI in non-pregnant, pre-menopausal women, catheterized adult patients
- To depict the current antimicrobial crisis treating asymptomatic bacteriuria.
- To introduce new Antibiotic Stewardship Program initiatives
International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases

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IDSA GUIDELINES

Co-Sponsoring Organizations

- American College of Obstetricians and Gynecologists (ACOG)
- Society of Academic Emergency Medicine (SAEM)
- American Urological Association (AUA)
- Association of Medical Microbiology and Infectious Diseases - Canada
- European Society of Clinical Microbiology and Infectious Diseases (ESCMID)
Epidemiology of UTIs

- By age 24, 1 in 3 women will develop UTI requiring Abx
- 50% women experience at least 1 episode of UTI during their lifetime
- 8 millions UTI/year in the US
- $2.14 billions/year in the US
- Higher rate of recurrence
  - A second UTI within a 6-month period is 25% or within a 12-month period is 46%
  - Reasons: re-infection (OR) the establishment of protected, intracellular bacterial reservoirs within the bladder mucosa

Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Acute bacterial cystitis</td>
<td>A culture-proven infection of the urinary tract with a bacterial pathogen associated with acute-onset symptoms such as dysuria in conjunction with variable degrees of increased urinary urgency and frequency, hematuria, and new or worsening incontinence.</td>
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<tr>
<td>Uncomplicated urinary tract infection</td>
<td>An infection of the urinary tract in a healthy patient with an anatomically and functionally normal urinary tract and no known factors that would make her susceptible to develop a UTI.</td>
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</table>
| Complicated urinary tract infection       | An infection in a patient in which one or more complicating factors may put her at higher risk for development of a UTI and potentially decrease efficacy of therapy. Such factors include the following:  
  • Anatomic or functional abnormality of the urinary tract (e.g., stone disease, diverticulum, neurogenic bladder)  
  • Immunocompromised host  
  • Multi-drug resistant bacteria |
| Recurrent urinary tract infection         | Two separate culture-proven episodes of acute bacterial cystitis and associated symptoms within six months or three episodes within one year. |
| Asymptomatic bacteruria                   | Presence of bacteria in the urine that causes no illness or symptoms. |

The index patient for this guideline is an otherwise healthy adult female with an uncomplicated recurrent urinary tract infection.

AUA guidelines, Jennifer Anger, MD, MPH; Una Lee, MD; A. Lenore Ackerman, MD, PhD; Roger Chou, MD; Bilal Chughtai, MD; J. Quentin Clemens, MD; Duane Hickling, MD, MSCI; Anil Kapoor, MD; Kimberly S. Kenton; Toby C. Chai, MD, MS; MD, MS; Melissa K. Koulman, MD, PhD; Mary Ann Rondanino; Ann Stapleton, MD; Lynn Stothers, M.D.

Diagnosis of uncomplicated acute cystitis

- Women, with symptoms of cystitis and no vaginal discharge, have > 90% probability of acute cystitis
- Do not need to do a urinalysis
- Do not need a urine culture

Algorithm

- Woman with symptoms of UTI (acute onset dysuria, frequency, or urgency)
  - No complicating conditions (such as pregnancy, known voiding abnormalities, co-morbid conditions -> complicated UTI)
  - No back pain/systemic sx (if present -> consider pyelonephritis)
  - No vaginal discharge (if present -> consider STD)

- If Hx not clear → UA/urine dipstick
  - If positive → 80% cystitis (consider tx for UTI)
  - If negative → 20% cystitis (dipstick not very specific so 1/5th of these cases might still have real UTI – consider urine cx, close f/u, other diagnoses)


Table 1: Diagnostic criteria for UTI (18, 19)

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Clinical features</th>
<th>Laboratory investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acute uncomplicated UTI in women; acute uncomplicated cystitis in women</td>
<td>Dysuria, urgency, frequency, suprapubic pain, no urinary symptoms in 4 weeks before this episode</td>
<td>&gt;10 WBC/mm³</td>
</tr>
<tr>
<td>2</td>
<td>Acute uncomplicated pyelonephritis</td>
<td>Fever, chills, flank/flank graft pain; other diagnoses excluded; no history or clinical evidence of urological abnormalities (ultrasonography, radiography)</td>
<td>&gt;10 WBC/mm³</td>
</tr>
</tbody>
</table>

Urine Culture vs No Urine Culture

- Complicated UTI: Anatomic, functional or metabolic abnormality of the urinary tract
  - Women—pregnancy, bladder outlet obstruction
  - Men—BPH, prostatitis
  - Diabetes, immunocompromised, post-menopausal, elderly
  - Catheter, calculi, neurogenic bladder
- Hx Multi-drug resistance
- Pyelonephritis

Get a urine culture
Start empiric antibiotics
Tailor therapy based on culture


Recommended treatment for AUC

1. TMP-SMX (160/800) – 1 tab BID x 3 days
2. Nitrofurantoin macrocrystals - 100 mg BID x 5 days
3. Pivmecillinam 400 mg BID x 5 days
4. Fosfomycin trometamol sachet 3 g a single dose

Avoid if suspect pyelonephritis

*Pyelonephritis – fever, flank pain, or clinical suspicion

TMP-SMX – avoid if local resistance rate >20%
Nitrofurantoin – 40 times expensive than TMP-SMX; contraindicated if CrCl <60
Fosfomycin and Pivmecillinam – lower efficacy
Fosfomycin – Only approved for E. coli
Pivmecillinam – not available in the US and Canada

Other treatments for AUC

- Fluoroquinolones – Ciprofloxacin ER 1000 mg once daily (OR) Levofloxacin 750 mg once daily x 3 days
  - Should be reserved for more severe cases
  - High collateral damage
- Beta-lactam agents – 3-7 days
  - Augmentin
  - Cefdinir (Omice®)
  - Cefaclor (Ceclor®)
  - Cefpodoxime (Vantin®)
- Amoxicillin or ampicillin – should NOT be used.


Overview of Antibiotic Profiles for AUC

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Efficacy</th>
<th>Safety</th>
<th>Resistant prevalence</th>
<th>Collateral damage</th>
<th>Retail Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofuratoin</td>
<td>93% (84-95%)</td>
<td>Good</td>
<td>Low</td>
<td>Low</td>
<td>$110/30 = $3.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$36/5 days</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>93% (90-100%)</td>
<td>Good</td>
<td>Intermediate</td>
<td>Probable</td>
<td>$53/60 = $0.90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$5.4/3 days</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>91%</td>
<td>Good</td>
<td>Low</td>
<td>Low</td>
<td>$80/3g sachet</td>
</tr>
<tr>
<td>Pivmecillinam</td>
<td>55-82%</td>
<td>Good</td>
<td>Low</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>FQs</td>
<td>90% (85-98%)</td>
<td>Good</td>
<td>Intermediate</td>
<td>Probable</td>
<td></td>
</tr>
<tr>
<td>Beta-lactams</td>
<td>89% (79-98%)</td>
<td>Fair</td>
<td>Intermediate</td>
<td>Probable</td>
<td></td>
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</tbody>
</table>

Predictors of antibiotic resistance

- Most data is for TMP-SMX; some for FQ
  - Exposure in past 3-6 months
  - Hx of travel outside of the US
  - Previous MDR-microorganisms

Management of Acute Pyelonephritis

- Urine culture
- Fluoroquinolones
  - Resistance rate <10%
    - Oral cipro 500 mg q12 x 7 days
    - Oral Cipro ER 1000 mg once daily x 7 days
    - Oral Levofloxacin 750 mg once daily x 7 days
  - Resistance rate >10%
    - An initial 1-time IV antibiotics (eg. 1 g of ceftriaxone or a consolidated 24-h dose of an aminoglycoside), followed by cipro or levofloxacin
- Oral TMP-SMX (160/800) 1 tab BID x 14 days. Initial IV antibiotic is recommended if susceptibility is not known.
- Oral beta-lactam – less effective; initial IV antibiotic is recommended
Catheter-associated UTI in Adults

Scope

- Catheter-associated asymptomatic bacteriuria (CA-ASB)
- Catheter-associated symptomatic UTI (CA-UTI)

- Diagnosis
- Prevention
- Treatment

## Definition

- **Catheter-associated infection**
  - Infection occurring in a person whose urinary tract is currently catheterized or
  - Has been catheterized within the previous 48 h.

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## Diagnosis

<table>
<thead>
<tr>
<th>Signs &amp; symptoms of UTI*</th>
<th>CA-UTI (urethral, suprapubic, intermittent, condom catheter)</th>
<th>CA-ASB (urethral, suprapubic, intermittent, condom catheter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFU</td>
<td>$\geq 10^3$</td>
<td>$\geq 10^5$</td>
</tr>
<tr>
<td></td>
<td>$\wedge$ no value for condom catheter</td>
<td></td>
</tr>
<tr>
<td>Micro-organisms</td>
<td>$\geq 1$ species</td>
<td>$\geq 1$ species</td>
</tr>
<tr>
<td>Collection technique</td>
<td>- A single catheter urine specimen (OR)</td>
<td>- A single catheter urine specimen (OR)</td>
</tr>
<tr>
<td></td>
<td>- MSU within 48 h after removal of catheter</td>
<td>- A single urine specimen from a freshly applied condom catheter</td>
</tr>
</tbody>
</table>

- *Fever, rigors, malaise, lethargy, ams, flank pain, CVA tenderness, hematuria, pelvic discomfort
- After removal of catheter, dysuria, urgency, frequency, suprapubic pain/tenderness
- In patients with spinal cord injury, increased spasticity, autonomic dysreflexia, sense of unease

Collection technique of urine specimens

- For short-term catheterization
  - Through the catheter port
  - Puncture the catheter tubing with a needle and syringe

- For long-term catheterization
  - Replace the catheter
  - From a freshly placed catheter

Pyuria

- Pyuria is **NOT** diagnostic of CA-ASB or CA-UTI!
- The presence, absence or degree of pyuria should **NOT** be used to differentiate CA-ASB from CA-UTI.
- Pyuria in CA-ASB **NOT** an indication for Abx.
- Signs & symptoms of UTI without pyuria → CA-UTI!
Odorous or Cloudy Urine

- Its alone should NOT be used to:
  - Differentiate CA-ASB from CA-UTI
  - As an indication for urine culture
  - Initiate antibiotic therapy

Prevention of CA-UTI

- Limiting Unnecessary Catheterization
  - Not for urinary incontinence
  - Should develop a list of indications
  - A physician’s order
- Discontinuation of Catheter
  - Reminded by the nurse or EMR
  - Automatic stop-orders
Prevention of CA-UTI (contd.)

- **Alternatives to Indwelling Urethral Catheterization**
  - Condom catheter (men) – to reduce CA-ASB in cooperative patients (insufficient data for CA-UTI or cognitively impaired patients)
  - Intermittent and suprapubic catheterization – to reduce CA-ASB and CA-UTI
  - Data insufficient on which one is preferred.

Prophylaxis with Systemic Antimicrobials

- **NOT recommended.**

Prophylaxis with Methenamine Salts

- **NOT recommended.**
Prophylaxis with Cranberry Products

- Conflicting data
- NOT routinely recommended

Enhanced Meatal Care

- Povidone-iodine solution, silver sulfadiazine, poly-antibiotic ointment or cream, or green soap and water
- Insufficient data – NOT routinely recommended
**Catheter Irrigation with antimicrobials**

- NOT recommended.

**The Drainage Bag**

- Addition of antimicrobials or antiseptics - NOT recommended.

**Routine Catheter Change**

- Eg. Every 4-8 weeks.
- Include long-term indwelling urethral or suprapubic catheters.
- NOT recommended.

**Prophylactic Antimicrobials at Time of Catheter Removal or Replacement**

- NOT recommended.
Screening for and Treatment of CA-ASB in Catheterized Patients to Reduce CA-UTI

- NOT recommended.

Screening for and Treatment of CA-ASB at Catheter Removal to Reduce CA-UTI

- NOT recommended.

Duration of Treatment

- 7 days if rapid response
- 10-14 days if slow response
- 5 days for levofloxacin
- 3-day regimen (for women, age <65, no upper urinary tract symptoms and catheter removed.)
Recurrent UTI

- Two episodes of acute bacterial cystitis within six months or three episodes within one year.
- Separate infections with resolution of symptoms between episodes.

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AUA guidelines are applied to healthy adult female with an uncomplicated recurrent UTI

- Obtain a complete history and perform pelvic examination
- Document positive urine cultures associated with symptoms
- Omit surveillance urine testing
- Do not treat ASB

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PPX NITROFURANTOIN, BACTRIM, TMP, CEHALEXIN, FOSFOMYCIN 6-12 months

Antibiotic ppx supported by RTC studies publish prior to 1995, ppx might be less effective given the changing antibiotic resistance patterns that have occurred over time.

Abx ppx reduced the number of clinical recurrences when compared to placebo in pre and postmenopausal women with rUTI

Increase in mild, moderate and severe adverse events associated with abx use

The effect of abx lasted during the active intake however when stopped UTI recurred

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Obtain urine culture every time there is symptomatic episode prior to treatment

Straight catheterized sample to avoid skin and vaginal bacteria contamination in patients who may have a difficult time doing a clean catch. (obese, wheelchair bound )

Cystoscopy/urologic studies to asses for anatomical or structural abnormalities

Preventive methods: Offer cranberry juice, lactobacillus, increase water intake, D-mannose, methenamide

Vaginal estrogen therapy
Antibiotic resistance is a major threat to fighting and preventing infections in the United States. Overprescribing and inappropriate use of antibiotics are the driving factors for trends in resistance. Resistant organisms cause at least 2 million infections and 23,000 deaths each year. Antibiotic stewardship programs (ASP) have been implemented in many hospitals nationwide to combat these frightening trends.
ASPs have been shown to optimize treatment, reduce adverse effects, increase cure rates, decrease hospital-acquired infections, and reduce hospital costs.

UTI's are the most common bacterial infection encountered in ambulatory care, Emergency department, and inpatient care.

Catheter-associated UTIs are the most common type of healthcare-associated infection reported to the National Healthcare Safety Network (NHSN) and the most commonly treated infections in residents of long-term care facilities.

“In the past 20 years antimicrobial resistance among urinary pathogens is increasing in frequency in the community and hospital settings because of antibiotic overuse, inappropriate treatment of asymptomatic bacteriuria, and local differences in antibiotic use.”
The diagnosis of UTI is primarily based on signs and symptoms rather than isolated laboratory findings (ASB).

Urine cultures are often not useful for acute uncomplicated cystitis, are recommended for patients with uncomplicated pyelonephritis and complicated UTI, and with few exceptions, should not be collected in asymptomatic patients.

Antimicrobial therapy should be tailored to each patient taking into consideration the severity of disease, individual and local patterns of antimicrobial resistance and the potential for collateral damage associated with antimicrobial use.

Selecting the correct drug, dose, and shortest clinically effective duration of therapy when possible, is key to optimal antimicrobial stewardship.

Strategies to prevent recurrent UTIs and catheter-associated bacteriuria could greatly reduce the use of antimicrobials and are therefore key stewardship modalities.

It is the responsibility of all healthcare providers to practice antimicrobial stewardship and prescribe antimicrobials prudently, thoughtfully and rationally.
"the public will demand [the drug and] then will begin an era of abuses. The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed to other individuals and perhaps from there to others until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save.

In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope the evil can be averted."

Fleming A. New York Times 1945
Thank you