Urinary Tract Infections

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April 2016

Disclosures
Outline

- Asymptomatic bacteriuria
- UTIs in the young
- UTIs in the elderly
- UTIs in special populations
- Prevention of UTIs
- Catheter-associated UTIs

Asymptomatic Bacteriuria Is Common

Up to:
- 5% healthy premenopausal women
- 19% healthy elderly people
- 27% diabetic women, 11% diabetic men
- 50% institutionalized patients
- 89% spinal cord injury patients w/intermittent self-cath
- 100% long-term catheters
Asymptomatic Bacteriuria

Do NOT treat!!

unless...

Asymptomatic Bacteriuria: Treatment = Harm

- 673 young women w/recurrent UTIs
- Screened for bacteriuria at 3, 6, 12 months
- 1 group treated if +, other not
- Treated group more infections at 6 and 12 months (47% vs 13%)
- More *E. coli* in treated group, more *enterococcus* in untreated group
- Protective effect of bacteriuria?

Cai 2012
UTIs in the Young and Old

Case 1

• It’s Sunday at 5pm. You are on call for the weekend. Miss Jones, a healthy 26 year old regular clinic patient, complains of dysuria and frequency without vaginal discharge or other symptoms. She says this feels “just like when I had a UTI before.”
• You decide to...
Case 2

• It’s Sunday at 5pm. You are on call for the weekend. Mrs. Watson’s nursing home is calling because her urine is cloudy and she is “not herself.” She seems more withdrawn, even with her baseline dementia. She has no vital sign changes. They are requesting an order for a UA and/or treatment of her UTI.
• You decide to...

Young and Old= Different!
Uncomplicated Cystitis: Young Women

• Self-diagnosis (recurrent UTI): likelihood ratio (LR) 4
• If seeking care for symptoms: LR 19
• Specific signs and symptoms affect probability
  – Positive LR: Dysuria, frequency, back pain, or CVA tenderness
  – Negative LR: vaginal discharge, vaginal irritation, no dysuria, no back pain
    • Vaginal discharge or irritation: LR 0.3, 0.2
  – Strongest combination = dysuria and frequency without vaginal discharge: LR 25

JAMA 287:2701, 2002

UTI Symptoms and Rx: Young Women

• Symptoms good predictors
  – Dysuria + frequency without vaginal discharge
• Treat without testing
  – Testing won’t change pre-test probability
• Treatment approaches
  – Clinic visit
  – Telephone
  – Patient-Initiated
Treatment Approaches: Young Women

- Telephone Management: Rx without office visit
  - No difference in return visits, pyelonephritis, other dx as clinic visits
  - 1 study showed preferred over office visit
- Patient-Initiated Therapy: Patient has Rx available
  - Must have had prior dx of UTI
    - 3 studies: correct diagnosis > 90%
  - Need established relationship with clinician
    - Accuracy of dx only 61%
    - High rate of chlamydia (17-21%)


Young and Old = Different!
UTI Symptoms: Elderly Women

• Elderly women: symptoms not easy to interpret
  – Multifactorial cause of symptoms
    • Baseline urinary symptoms
    • Medications
    • Changes in perineum
  – Need “UTI-specific symptoms”

UTI-Specific Symptoms: Elderly

• One or more of following:
  – Acute dysuria
  – New or worsening urgency
  – New or worsening frequency
  – Suprapubic tenderness
  – Costovertebral tenderness
  – Fever (≥ 38°C)

WITH...

• Lab confirmation: > 10⁵ CFU of no more than 2 uropathogens

Mody 2014
UTI-Specific Symptoms: Elderly

- One or more of following:
  - **Acute dysuria**
    - LR 1.31 (CI 1.12-1.50)
  - New or worsening urgency
  - New or worsening frequency
  - Suprapubic tenderness
  - Costovertebral tenderness
  - Fever ($\geq 38^\circ$)

**WITH...**

- Lab confirmation: > $10^5$ CFU of no more than 2 uropathogens

Medina-Bombardo 2003

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Dipstick in Older Patients?

- “Positive” definition: presence of leukocyte esterase, nitrites, or both
  - Depends on study population
- Sensitivity 82%, specificity 71%
- Negative Predictive Value (NPV) 92-100%

**Conclusion:**
- High false positives
- Use to rule out, NOT to confirm diagnosis

Fight the Urge

Elderly woman

Vague symptoms

Hydrate, evaluate meds

Symptoms resolve

UTI-specific symptoms

Send urine sample, treat

Mody, JAMA, 2014

Young vs Old Comparisons

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Dysuria + frequency + no vaginal discharge</td>
<td>Acute dysuria + culture</td>
</tr>
<tr>
<td>UA needed?</td>
<td>No</td>
<td>To rule out, not in</td>
</tr>
<tr>
<td>Culture?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Timing of Rx</td>
<td>Treat upon clinical dx</td>
<td>Consider waiting</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Nitrofurantoin, tmp/smz, fosfomycin</td>
<td>Nitrofurantoin, tmp/smz, fosfomycin</td>
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</tbody>
</table>
Uncomplicated Cystitis: Preferred Agents

- Nitrofurantoin 100 mg BID x 5 days
- TMP/SMZ 1 DS tab PO BID x 3 days
- Fosfomycin 3gm PO once
  - Inhibits bacterial wall synthesis by inactivating pyruvyl transferase
  - Comes in powder mixed in water
  - Can require prior authorization

Uncomplicated Cystitis: Preferred Agents with Caveats

- Nitrofurantoin
  - Not if upper tract disease
  - Not in men (poor tissue penetration of prostate)
- TMP/SMZ
  - Not if E coli resistance > 20%
    - PPMC: 18% (outpt + inpt)
  - Significant interactions with warfarin (increases INR)
- Fosfomycin
  - Not if upper tract disease
  - Data in men limited
Nitrofurantoin in the Elderly

- Per FDA contraindicated if GFR < 60
  - Based on decrease in urine excretion
  - No clinical efficacy endpoints, small numbers of patients, poor definition of creatinine clearance, old studies

- Recent data: okay to use if GFR >= 40
  - “Data supporting the contraindication are non-existent”

**Summary of Benefits:**
low plasma concentrations, high urine excretion, low rates of resistance after 60 yrs, cost effective

Bains 2009, Oplinger 2013, Singh 2015

Nitrofurantoin and Pulmonary Toxicity

- Associated with long-term use
  - Case reports of short-term use: recovery with cessation of drug
- J Antimicrobial Ther: systematic review and meta-analysis
  - 27 trials, over 4800 patients
  - No pulmonary toxicity
  - No hepatotoxicity

Huttner 2015
Return to the Cases

• Case 1: young woman w/UTI symptoms → treat empirically

• Case 2: elderly woman with nonspecific UTI symptoms → wait to treat, evaluate causes, give short didactic to nursing home staff about UTIs in the elderly

Special Populations
UTIs in Diabetics

• At greater risk for UTIs
• Little data to support or refute longer Rx than non-diabetics
• Recommend: Treat similarly to those without diabetes

Gupta, IDSA, 2010

UTIs in Men

• Consider alternative diagnoses
  – BPH symptoms
  – STDs
• Difficult to delineate prostatitis from cystitis
• Drug penetration into prostate unclear
  – Tmp/smz and fluoroquinolones penetrate prostate best
    • May be moot point if inflammation present
UTIs in Men

• Drug duration unclear
  – Ranges from 7 days to 6 wks
  – Few studies
  – Acute symptoms:
    • 1 RCT: 2 wks vs 4 wks of ciprofloxacin equivalent
    • 1 observational trial: 33,000 veterans with UTIs
      – ≤ 7 days of rx same recurrence rates as longer rx
      – Longer rx with more C difficile

Summary: 1 wk probably enough

Ulleryd 2003, Drekonja 2013

Upper Tract Disease: Pyelonephritis

• Can Rx as outpatient if clinically stable
• Obtain culture
• Rx fluoroquinolones
  – If E coli resistance > 10%, consider starting with one
dose of IM ceftriaxone
    • PPMC resistance 13%
• Duration 5 days
  – ≥ 8 RCT: 5-7 days = 10-14 days
  – Meta-analysis: 7-14 days = 14-42 days
  – This includes hospitalized days of Rx

CID 52:e103,2011
Recurrent UTIs

Prevention of Recurrent UTIs: What Works?

<table>
<thead>
<tr>
<th>Reasonable – no proven benefit</th>
<th>Reasonable – controversial or needs data</th>
<th>Recommend – data to support</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Post-coital voiding</td>
<td>-Probiotics</td>
<td>-Avoiding spermicides</td>
</tr>
<tr>
<td>-Increased fluid intake</td>
<td>-Cranberry products</td>
<td>-Abx prophylaxis</td>
</tr>
<tr>
<td>-Wiping front to back</td>
<td></td>
<td>-Vaginal estrogen</td>
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<tr>
<td>-Avoiding tight clothes</td>
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</table>
The Probiotic Buzz

- Lactobacillus: 1 of 4 RCT studies showed reduced rates
- Oral lactobacillus versus Tmp/smz for prevention
  - RCT of 252 postmenopausal women
  - Results: lactobacillus group with increased UTIs and more side effects, less resistance; no lactobacillus in vaginal flora identified
- Vaginal lactobacillus vs placebo
  - RCT of 100 women
  - Results: lactobacillus group with 15% vs 27% UTI rate; well tolerated; had vaginal colonization
- More to come...
  Barrons 2008; Beerepoot 2012; Stapleton 2011

The Cranberry Controversy

- Cochrane Review 2008: benefit
- Cochrane Review July 2012: no benefit (added 14 studies)
- Wang 2012 in Annals: benefit
  - Pooled risk ratio 0.6 (CI 0.49-0.8), esp in women, women with recurrent UTIs, juice drinkers, higher doses
- Why different?
  - 24 (Cochrane) vs 13 (Wang) RCTs
  - Wang excluded cranberries vs antibiotics
  - Wang excluded one study of recurrent UTIs b/c of heterogeneity that showed no effect
- Verdict: Who knows! But minimal effect if present. Consider its use.
Recurrent UTIs: Abx Prophylaxis

• Consider if ≥ 2 infections in 6 mo or ≥ 3 in 1 yr
• Eradicate current infection first
• Post-coital, continuous, self-treatment all effective
• No abx better than another
  – Depends on prior resistance patterns
• Risk of resistance to chosen drug

Stamm 1993; Nicolle 1987; Chew 1999; Pfau 1989; Melekos 1997

Still Some Goodness in Estrogen

• Oral replacement no help
• Topic estrogen for postmenopause
  – Intravaginal estriol cream nightly x 2 wks then BIW for 8 months versus placebo
    • Increased lactobacillus, decreased E coli colonization
    • Decreased UTIs (0.5 versus 5.9/year)
    • Few side effects

Raz, 1993
Alternative Solution to Recurrent UTIs: The Extended Office Visit

• Talk to the patient about risks/benefits
• Consider not treating if simple cystitis
  – May clear on own (up to 50%)
  – Complications rare (2-3% develop pyelonephritis)
  – Symptomatic relief possible
    • Hydration, Acetaminophen, Pyridium
  – Stop spermicides, consider vaginal estrogen
  – Discuss resistance concerns
• Stop checking the urine!

Knotterus 2013

Complicated UTIs: Catheter-Associated
Catheter-Associated UTIs: Precautions

• Virtually 100% colonization rates
• Color and cloudiness of urine NOT predictive
• Catheters only indicated for:
  — Urinary retention
  — Urinary incontinence in terminally ill patient
  — Accurate urine output measurements in critically ill patient
  — Prolonged surgical procedures

Complicated UTIs: Catheter-Associated

Symptomatic infection=

• **Symptoms/signs**
  — new fever, rigors, altered mental status, or lethargy with NO other cause
  — CVA tenderness
  — acute hematuria
  — pelvic pain
  — increased spasticity or autonomic dysreflexia in spinal cord injury pts

  **PLUS**

• **Culture data**
  — >$10^5$ CFU of single organism
Catheter-Associated UTIs: Treatment

- Obtain culture
  - From freshly replaced catheter
  - From midstream urine if catheter removed
- Treatment
  - Antibiotics...choice depends
    - Prior organisms
    - Prior abx
    - Resistance rates
  - Fluoroquinolones, ceftriaxone, ceftazidime

Remove catheter if possible!

Preventing UTIs with Catheters: What helps?

<table>
<thead>
<tr>
<th>Helps</th>
<th>Unclear</th>
<th>Doesn’t help or harms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bag below urethra</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changing Foley after infection (if &gt; 2 wks in place)</td>
<td>Changing Foley monthly</td>
<td>Antibiotic flushes Scheduled urine cultures</td>
</tr>
</tbody>
</table>

Hooton, IDSA, 2009
Stop Checking the Urine!

• Do NOT check if:
  – Cloudy
  – Different color
  – For test of cure
  – With catheter change
  – With general malaise or different behavior

Summary

• Asymptomatic bacteriuria is common
  – Don’t treat!
• UTIs in young and old are different
  – Immediate treatment for young vs delayed treatment for old
• Consider an extended office visit to reframe the approach to recurrent UTIs
• Stop checking the urine!