BEST PRACTICES FOR WOMEN WITH UTIs

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Disclosures
• None

Objectives
1) review guidelines for diagnosis and management of uncomplicated UTIs
2) discussion of evidence based recommendations for prevention of UTIs
3) diagnosis, work up and management of complicated UTIs (pyelonephritis, recurrent UTI, chronic UTI)
4) initial diagnosis, work up and management of non-infectious bladder pain

Sources

Endorsed by:
American College of Obstetrics and Gynecology
American Urology Association
Society for Academic Emergency Medicine
Definitions

Urinary Tract Infection (UTI or cystitis)
- Positive urine culture and symptoms
  - Urgency/frequency
  - Dysuria
  - Hematuria
  - Urinary incontinence
  - Suprapubic pain

Not a UTI
- Asymptomatic bacteriuria

Epidemiology

- ~50% of 32yo women report having had at least 1 UTI
- 25% of young healthy women will have a recurrence within 6 months of their initial UTI episode
- 20% of women >65yo have asymptomatic bacteriuria

Sources


Microbiology

• 75-95% of Uncomplicated UTIs are caused by *E. coli*
  • Uropathogenic *E. coli* are a specific subset of extraintestinal pathogenic *E. coli* that have the potential for enhanced virulence.

• But there are plenty of others: *Enterobacter*, *Klebsiella*, *Pseudomonas*, *Proteus*, *Streptococcus faecalis*, *Morganella*, *Staphylococcus*, *Chlamydia*

Risk Factors for UTI

Catheters

• Cause 30-40% of nosocomial infections
• One catheterization → 2% risk of bacteriuria
• Every day of an indwelling catheter → 3-10% risk of bacteriuria
• Only treat for symptoms
• Place indwelling cath only for clear indications (not for incontinence)
• Antibiotic prophylaxis should not be done routinely

Risk Factors for UTI

• Gender (female)
• Menopausal status
• Intercourse
• New sex partner
• Previous urinary tract infection
• Hx of UTIs in a 1st degree relative

Not Risk Factors for UTI

• Post coital (or pre-coital) voiding
• Fluid intake
• Delaying voids
• Wiping patterns
• Type of underwear
Diagnosis of Cystitis

- Urgency/frequency
- Dysuria
- Hematuria
- Urinary incontinence
- Suprapubic pain

- Caution
  - Recent UTI?
  - Recurrent UTI?
  - Not UTI?

Then check UA/Cx


Urinary Microbiome

- Urine is NOT sterile
  - 16S rRNA
  - Expanded Quantitative Urine Culture

- Positive urine culture = Dysbiosis


Diagnosis of Cystitis - UA

- Nitrite

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- 87/148 (59%) women with pos LE or nitrite had pos UCx
- 63/66 with neg UCx were given Abx.

Diagnosis of Cystitis - UA

- In patients with urgency/frequency
- Pyuria (>10 WBC /hpf) had negative LE in 60%
- Pyuria for predicting positive Urine Culture

<table>
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Diagnosis of Cystitis - UCx

- If patient is symptomatic any growth of 1 or 2 bacteria should be considered a positive result
- On ‘Contamination’
  - Squamous cells in 99/105 cath samples but no samples had bacterial ‘contamination’ (mixed growth or <10K)
  - Squamous cells in 101/105 clean catch samples; 21% had bacterial ‘contamination’.


Asymptomatic Bacteriuria

- No benefit in treating
  - Institutionalized Elderly
  - Ambulatory Elderly
  - Premenopausal Women
  - Diabetic Women
  - Renal transplant patients
- Only group in which treatment is recommended is pregnant women


Asymptomatic Bacteriuria

- Common in older people
- Not associated with decline in renal function


Asymptomatic Bacteriuria

Treatment may cause UTI?


- 673 women 18-40yo randomized to Abx vs. no Tx
- At 12 months 73% in the Abx vs. 15% in no Tx had symptomatic UTI ($P<.0001$)

Treatment of Uncomplicated UTI

Collateral Damage: ecological adverse effects of abx
- Selection of drug resistant bacteria
- Colonization or infection with multi-drug resistant bacteria

Possibly due to effect on fecal flora
- Fluoroquinolones
- Broad spectrum cephalosporins
- Trimethoprim
- Ampicillin

Treatment of Uncomplicated UTI

2 reasons to consider collateral damage in choosing antibiotic treatment

1) minimal risk of progression (<1% progress to pyelo) spontaneous resolution in 25%–42% of women

2) UTI is common use for Abx many small increments amplify collateral damage
Treatment of Uncomplicated UTI

Nitrofurantoin monohydrate/macrocrystals 100 mg bid X 5 days
Minimal risk of 'collateral damage'
Avoid if pyelonephritis suspected
Considerations: ≥64yo, renal insufficiency

Trimethoprim-sulfamethoxazole (one DS tablet) bid X 3 days
Note increasing resistance

Fosfomycin 3 gm single dose (mix powder in ½ cup water)
Minimal risk of 'collateral damage'
Avoid if pyelonephritis suspected

Second Line Tx of Uncomplicated UTI

Fluoroquinolones x 3 days
Propensity for collateral damage
Should be reserved for uses other than acute cystitis
Longer course has large increase in AE with same efficacy

FDA Fluoroquinolone Warning

- Associated with disabling and potentially permanent side effects of the tendons, muscles, joints, nerves, and central nervous system
- For some serious bacterial infections the benefits of fluoroquinolones outweigh the risks, and it is appropriate for them to remain available as a therapeutic option.
- Health care professionals should not prescribe systemic fluoroquinolones to patients who have other treatment options for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, and uncomplicated urinary tract infections because the risks outweigh the benefits in these patients.
Second Line Tx of Uncomplicated UTI

**Fluoroquinolones x 3 days**
- Propensity for collateral damage
- Should be reserved for uses other than acute cystitis
- Longer course has large increase in AE with same efficacy

**β-lactams**
- Generally have inferior efficacy and more adverse effects, compared with other UTI antimicrobials
- Does this include cephalexin?

Other Treatment Considerations

- Phenazopyridine
  - Urinary pain reliever
  - Nitrite positive (or UA indeterminate)

- Bladder pain may persist after infection is treated

- Clinical efficacy of any antibiotic regimen ~90%

So check UA/Cx for persistent or recurrent Sx

**Diagnosis of Pyelonephritis**

- fever
- chills
- flank pain
- CVA tenderness
- nausea or vomiting
- urgency/frequency
- dysuria
- hematuria
- urinary incontinence
- suprapubic pain

For any suspicion of pyelo always collect UA/Cx before starting antibiotics

**Outpatient Treatment of Pyelonephritis**

- ciprofloxacin 500 mg PO bid x7d
  - May add initial one dose IV agent
    - Ciprofloxacin 400mg
    - Ceftriaxone 1 g of ceftazidime
    - Consolidated 24-h dose of an aminoglycoside

- trimethoprim-sulfamethoxazole (DS) PO bid x14d
  - Recommended to add initial one dose IV agent if sensitivities are unknown

- β-lactam agents are less effective than other agents
  - Recommended to add initial one dose IV agent
Outpatient Treatment Of Pyelonephritis

• What does standard of care treatment achieve?

• In women receiving 7 days of ciprofloxacin for pyelonephritis, 6% had another symptomatic UTI within 30 days
  - (as did 7% of women treated with TMP-SMX for 7d)

• 2 patients in ciprofloxacin group developed C difficile
• 1 patient in TMP-SMX group developed a rash

Fox MT, Mela MT, Same RG, Conley AT, Tenima PO. A Seven-Day Course of TMP-SMX May Be as Effective as a Seven-Day Course of Ciprofloxacin for the Treatment of Pyelonephritis. Am J Med. 2017 Jul;130(7):842-845

Inpatient Treatment of Pyelonephritis

• When unable to tolerate PO

• IV antibiotics
  - Fluoroquinolones
  - Aminoglycoside, with or without ampicillin
  - Extended-spectrum cephalosporin or extended-spectrum penicillin, with or without an aminoglycoside
  - Carbapenem (ertapenem)

International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women

Yeast on urine micro or culture?

If asymptomatic then no further workup or treatment is indicated

If pt has UTI symptoms check a new urine specimen
  - Clean catch OK, cath if not possible.
  - If indwelling cath present, change and collect new specimen
  - If immunocompromised she may not be able to mount a response that would cause UTI symptoms
  - If critically ill, yeast in urine may be a marker of fungemia \( \rightarrow \) collect blood cultures


Recurrent UTIs

• Recurrent cystitis should be managed with prophylactic antimicrobial therapy only when nonantimicrobial preventive strategies are not effective.

Prevention 1) Vaginal Estrogen
- Post-menopausal women are at significantly increased risk of urinary tract infection
- Oral estrogen does not protect
- Vaginal estrogen does protect

Prevention 2) Cranberry
- 28 studies in 4,947 patients: significant reduction in the risk of repeat UTIs with cranberry
  - WRR = 0.68, 95% CI 0.55-0.80, p <0.0001
  - Inhibits binding of E coli to urothelium
  - Juice or capsules but pts tend to stop drinking juice

Prevention 3) Probiotics
- Randomized patients post-op to cranberry capsules vs. placebo bid x6w
- UTI definition: clinically diagnosed and treated
- UTIs
  - 19% in Cranberry group
  - 38% in Placebo group p=0.008


Prevention

3) Probiotics

- Vaginally place *L. crispatus* significantly decreased recurrent UTI (27% → 15%) in young women after 1 UTI
  

- Vaginally placed *L. rhamnosus* and *L. reuteri* decreased recurrent UTIs (although not oral dosing)
  

Prevention - Antibiotics

- **Methenamine (add vitamin C)**
  
  Lee BS, Bhuta T, Simpson JM, Craig JC. Methenamine hippurate for preventing urinary tract infections. *Cochrane Database of Systematic Reviews* 2012, Issue 10. Art. No.: CD003265.

- **Post-coital or Fixed Dosing**

<table>
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<th>Less than Daily</th>
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<td>Nitrofurantoin 100mg</td>
<td>TPM-SMX 40/200 tw</td>
</tr>
<tr>
<td>Trimethoprim 100mg</td>
<td>Fosfomycin 3g q 10d</td>
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<tr>
<td>Cephalexin 250mg</td>
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Recurrent UTI Management

- **Standing UA/Cx**

- **Prevention strategies**

- Cranberry bid

- Vaginal estrogen on peri or post-menopausal

- Vaginal probiotics

- **Antibiotic prophylaxis**
Recurrent UTI Management

- Referral to FPMRS specialist

*Same bacteria repeatedly (by sensitivities) may indicate nidus in urinary tract / chronic UTI

A special note about…

Hematuria, frequency, urgency, pyuria, pelvic pain, suprapubic pain

Also sound like **Bladder Pain Syndrome**

Bladder Pain Syndrome

**Symptomatic diagnosis** based on the presence of three key symptoms: pain, urgency, and frequency, as well as exclusion of a short list of other conditions that cause the same symptoms.

- Epidemiology of Interstitial Cystitis Interstitial Cystitis Epidemiology Task Force Meeting NIDDK Executive Committee Summary and Task Force Meeting Report 2003

Bladder Pain Syndrome Diagnosis

An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes.

Treatment: First steps

1) Identify and avoid Bladder Irritants
2) Ibuprofen +/- acetaminophen
3) Phenazopyridine (Azo Standard or Uristat)

So…

- Prevent
  - Minimize indwelling catheter
- Diagnose
  - Symptoms
  - Watch for frequent episodes
  - Limitations of urinalysis and culture
- Treat
  - Appropriate selection of antibiotics
- Prophylaxis
  - Cranberry, Estrogen, Probiotics, Antibiotics (as last resort)

Consider

- Is this a Recurrent UTI?
  - Are we optimizing non-antibiotic prophylaxis?
- Is this the same bacteria over and over?
- Is this not a UTI?

Thank you!

- Questions?