Faculty Disclosure

The Association of Public Health Laboratories adheres to established standards regarding industry support of continuing education for healthcare professionals. The following disclosures of personal financial relationships with commercial interests within the last 12 months as relative to this presentation have been made by the speaker(s):

Jared Spotkov, MD MPH
“Nothing to disclose”.
“UTI”

- 56,000 urine cultures/month in one large health system laboratory
- Bacterial UTI is one of the most commonly diagnosed infections in adults
  - 0.5-0.7 UTI per person-year (University cohort 796 women)
  - 0.07 UTI per person-year in postmenopausal women
  - Up to 10% women in the US have symptomatic UTI each year, up to 60% will experience a UTI at some time in their life
  - As such UTI/bacteriuria drives frequent antimicrobial use, emerging resistance, and complications such as Clostridium difficile diarrhea
- The choice of whom/when to treat is the critical step
A “Perfect Storm”: Diagnosis and Treatment of Urinary Tract Infections in Adults

- Lack of specificity (and sensitivity) of symptoms
- Lack of specificity of bacterial evaluation of urine
- Indwelling urinary devices in urinary instrumentation
- Tendency to treat (and retreat) all positive cultures
- Mounting burden of bacterial resistance
- Increasing occurrence of other antibacterial complications, chiefly Clostridium difficile infections
Clinical Questions in UTI Management

• Whom and how to test?
• Whom to treat?
• Which treatment regimens?
Diagnosis of Urinary Tract Infection
Symptoms

- Painful, urgent, frequent urination, increasing night time urination
- New or increased incontinence
- Macrohematuria
- Suprapubic pain
- “Offensive” smell, turbid urine
- Prior infections of the urinary tract
Diagnosis of UTI

• Complicated by the frequency of “asymptomatic bacteriuria”:
  – Asymptomatic bacteriuria prevalence in schoolgirls 1% to postmenopausal women (over 80 years) > 20%, men (over 75 years) 6-15%
  – Midstream urine collection:
    • $10^5$ cfu/mL common in true infection and of historical interest
    • IDSA recommends $10^2$ cfu/mL of uropathogen (sensitivity/specificity 90%)
    • Pyelonephritis usually associated with $10^4$ cfu/mL of uropathogen
Symptomatic UTI

Symptoms of pain (dysuria) and suprapubic pain, urinary frequency, urgency, incontinence, even hematuria are not specific for bacterial UTI

– Chemical or physical trauma
– Urolithiasis
– Neoplasm
– Viral infection
– Vaginitis, prostatitis
Symptomatic UTI

• Invasive complicated UTI (pyelonephritis) may lack specific urinary symptoms and consist of fever, signs of “sepsis,” and positive urinary or bloodstream bacterial cultures
Implications of UTI Diagnosis

- UTI diagnosis is often used as a reason for initiating antimicrobial therapy, solely based upon
  - Presence of pyuria
  - Presence of bacteriuria
  - Convenient explanation for changes in mental or physical status (“altered mental status,” “weakness,” etc.)
Role of the Microbiology Laboratory

• Not only to accurately report presence of microorganisms and susceptibility information
• Help in the interpretation of these results and guide appropriate management
  – Accurately describe the limitations of the laboratory tests
  – Dissuade unnecessary testing
• Method of collection and rapidity of plating/incubation are common factors in mistaken diagnoses
Diagnosis of Urinary Tract Infection

- **Pyuria** = at least 10 leukocytes/mm$^3$ of midstream urine by counting chamber
- A less reliable method uses a urine specimen that is centrifuged for 5 minutes at 2000 rpm and then the sediment examined under high power. With this method, 5 to 10 leukocytes/high-power field in the sediment is the upper limit of normal
- The dipstick leukocyte esterase test is a rapid screening test for detecting pyuria and has largely replaced microscopic methods. Although the sensitivity and specificity are high for detecting more than 10 white blood cells/mm$^3$ of urine (75% to 96% and 94% to 98%, respectively), a positive test by no means indicates UTI, and in patients with a negative leukocyte esterase test and UTI symptoms, a urine microscopic examination for pyuria or a urine culture should be considered.


Diagnosis of UTI – indirect methods

Rapid indirect methods to detect bacteriuria
- Dipstick that detect the presence of urine nitrite, which is formed when bacteria reduce the nitrate that is normally present; False-negative test results are common, especially in the detection of low-count bacteriuria (10^2 to 10^3/mL) and with certain microorganisms like Enterococci, Candida and others species), false-positive results are rare. When both leukocyte esterase and nitrite tests are negative, there is better correlation with absence of bacteriuria.
- In specific populations (like the elderly), reagent testing is an unreliable method of identifying patients with positive urine cultures.
- Positive urine culture rates are only slightly higher in patients with vague symptoms attributable to UTI than they are in (asymptomatic) patients treated for non-urologic problems = many positive cultures in elderly patients with non-focal systemic symptoms are false-positive tests reflecting asymptomatic bacteriuria.

More on Diagnosis

- Pyuria ($\geq 10$ WBC/mm³ uncentrifuged urine) is an insensitive and nonspecific indicator of infection.
- Nitrite insensitive (80% for bladder urine 4H) but more specific and organism dependent (Enterococcus faecalis, yeast and others).
- Method of collection and rapidity of plating/incubation are common factors in mistaken diagnoses.
Bacterial studies of urine

- However, it is important to remember that about one third of young women with cystitis have fewer than $10^5$ bacteria/mL of urine.
- Infectious Diseases Society of America consensus culture definition of cystitis for use in antibiotic treatment studies is $\geq 10^2$ colony-forming units (CFU)/mL or more of a uropathogen (sensitivity 90% and specificity 90%).
- Pyelonephritis, $10^4$ CFU/mL or more (sensitivity 90% and specificity 90%).
- Acceptable methods for urine collection include (1) midstream clean catch, (2) catheterization, and (3) suprapubic aspiration.
Midstream Urine Collection --
technique

• Women: The woman should wash her hands, straddle the commode (facing the back of the commode), wash her vulva from front to back four times with four different sterile gauze pads soaked in soap, and then rinse with two more sponges soaked in sterile distilled water. She should then spread her labia and void, discarding the first portion of urine and collecting the second. The urine should be processed immediately or, if refrigerated at 4° C, it can be cultured within 24 hours.

• Men: the prepuce should be retracted, the glans cleaned with sterile soap filled gauze pads, and then rinsed with two more sponges soaked in sterile distilled water. He then discards the first part of the urine stream, collects the second, and discards the final portion.
Asymptomatic Women

- $>10^5$ cfu/mL in a clean-catch urine specimen from an asymptomatic woman = 80% probability that this represents true bacteriuria
- $10^4 - 10^5$ cfu/mL in an asymptomatic woman, a confirmatory second specimen will contain $10^5$ or more cfu/mL in only 5% of cases.
- Asymptomatic women, 95% of the time $10^4$ to $10^5$ bacteria/mL represents contamination
- There is consensus that except in pregnancy, pre-urologic surgery or instrumentation, asymptomatic bacteriuria should NOT be treated
Asymptomatic Men

• 10^3 or more cfu/mL in one culture is suggestive of infection, and 10^5/mL defines bacteriuria.
• False-positive cultures are caused by contamination or incubation of urine before processing.
• There is consensus that except in pregnancy, pre-urologic surgery or instrumentation, asymptomatic bacteriuria should NOT be treated.
• False-negative cultures may be caused by the use of antimicrobial agents, soap from the preparation falling into the urine, total obstruction below the infection, infection with a fastidious or “atypical” organism (e.g., mycobacteria, fungus), and dilutional due to water loading or glucose or drug induced diuresis.
Bacteriology

• CFU/mL criteria apply only to the Enterobacteriaceae. Other organisms (gram positive bacteria, fungi, “fastidious” organisms may not reach $10^5$cg/mL. Pure cultures and those with pathogenic organisms should be reported.

• Pure growth of Enterobacteriaceae occurs in 90% of urine samples containing more than $10^5$ bacteria/mL. Mixed infection occurs in about 5% of cases.

• In patients with symptoms of UTI, one titer of $10^5$ or more bacteria/mL of urine carries a 95% probability of true bacteriuria. With titers below $10^5$/mL but in the presence of frequency, urgency, and dysuria, women have a 33% chance of having bacterial infection.
UTI with low colony counts

• Urethral syndrome: Up to 50% young women with symptomatic bacterial UTI have $<10^5$ cfu/ mL of urine

• Non gonococcal/chlamydial bacterial urethritis (often due to gram negative uropathogenic organisms) has also been reported in men
Signal Organisms

- Organisms which often indicate contamination, improper handling of specimen: diphtheroids, lactobacilli, Candida species, low colony counts of multiple organisms (> 2), Enterococci and *Streptococcus agalactiae*
Signal organisms

Signal Organisms

• Coagulase negative staphylococci
• *Staphylococcus saprophyticus* 5-15% lower tract UTI especially in young women
• Vancomycin resistant *Enterococcus faecium* and *faecalis*
• *Staphylococcus aureus*
• CTX-M-15 ESBL *E. coli* O25:H4 sequence type ST131
Should we culture?

UTI (cystitis) symptoms in low risk women may be treated without urine culture:

1. Delayed treatment with antimicrobial
2. Nonsteroidal anti-inflammatory agent for 2 days
3. Short-term antimicrobial treatment

Exclusions: increased risk of illness = pregnancy, prior history recurrent UTI, urinary obstruction, surgery, immune compromised = perform appropriate cultures
Don’t Report

Reducing Antimicrobial Therapy for Asymptomatic Bacteriuria Among Noncatheterized Inpatients: A Proof-of-Concept Study

Jerome A. Leis,1,2 Gabriel W. Rebick,1 Nick Daneman,1 Wayne L. Gold,1 Susan M. Poutanen,1,3,5 Pauline Lo,3 Michael Larocque,3 Kaveh G. Shojania,1 and Allison McGeer1,3,4

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(See the Editorial Commentary by Naik and Trautner on pages 984–5.)

This proof-of-concept study demonstrates that no longer routinely reporting urine culture results from noncatheterized medical and surgical inpatients can greatly reduce unnecessary antimicrobial therapy for asymptomatic bacteriuria without significant additional laboratory workload. Larger studies are needed to confirm the generalizability, safety, and sustainability of this model of care.

Keywords. asymptomatic bacteriuria; urine culture; antimicrobial stewardship.
Asymmetric paternalism: “The majority of positive urine cultures from inpatients without an indwelling urinary catheter represent asymptomatic bacteriuria”

‘Call the microbiology laboratory if UTI is “strongly suspected” ‘

Higher prevalence of asymptomatic bacteriuria (ASB) (86%) vs urinary tract infections (14%) among the 74 cultures from patients without urinary catheters (n=415)

48% patients whose urine cultures were reported openly with confirmed ASB received antibiotics vs 12% in the “closed reporting” group

Clinicians called the microbiology laboratory for only 14% (5 of 37) of suppressed culture results

4 urinary tract infections occurred in noncatheterized patients, and in each of these cases clinicians had empirically started therapy, with the presumption that clinically significant symptoms of urinary tract infection were present

No untreated patients had clinically significant signs of sepsis or urinary tract infection 72 hours after urine culture collection.

Other paternalistic approaches = “fast and frugal” “concurrent audit and feedback”
Don’t Even Culture

Correspondence

Optimizing Urine Culture Collection in the Emergency Department Using Frontline Ownership Interventions

To the Editor—The recent article by Leis et al. “Reducing antimicrobial therapy for asymptomatic bacteriuria among non-catheterized inpatients: a proof-of-concept study” [1], reveals a novel way to manage the problem of unnecessary urine collection. However, this laboratory-based solution proposed by Leis et al does not address the complex behaviors leading to the unnecessary urine collection. In their article, urine cultures are still being collected, and the laboratory is still processing the specimens, leading to unnecessary workload and costs.

An intervention that reduces the unnecessary ordering of urine cultures combined with the approach of Leis et al would be the ideal solution. Front-line ownership (FLO) has been used to change complex behaviors in a variety of settings in healthcare [2]. We implemented a quality improvement initiative utilizing FLO aimed at reducing the number of urine cultures (UCs) collected in the emergency department (ED) of our 515-bed community teaching hospital. We gathered data pre-intervention from January through June and after intervention from July to December 2013. All urine culture rates included both catheter and non-catheter specimens.

Our intervention consisted of an initial meeting highlighting unnecessary UCs to the Unit Based Council (a multidisciplinary team of ED frontline staff), ED managers, and ED physicians with an infection preventionist trained in FLO. Thereafter, thinking sessions involving the ED staff were facilitated by the same infection preventionist utilizing FLO principles. These sessions featured process reviews, policy assessments, and utilization dialogue aimed at understanding the ED staff barriers hindering the appropriate collection of UCs. Sessions noted that collection was happening related to poor compliance with published UC guidelines [3], staff practice patterns were based on outdated internal nursing policies that recommended frequent UC collection, and urine catheterization kits contained a sterile collection container that prompted urine collection. Automation of UC results on the hospital information technology system vs manual entry of point-of-care urine dips led to a preference for UC testing. Pressure to improve workflow also led staff to preemptively send urine for testing in case it was eventually needed to avoid subsequent
To Treat or Not to Treat

- No antimicrobials – placebo may cure 25-42% women (spontaneous resolution) albeit with small risk of more prolonged symptoms and even smaller risk of progression to pyelonephritis
- Antibacterial treatment of asymptomatic bacteriuria in young women may increase the frequency of symptomatic infection
- Forcing fluids
- Urinary pH acidification: mandelic, hippuric acid
- Cranberry juice, acidification and prevention of E coli adherence to uroepithelium (one mechanism may be coating of the fimbriae of E. coli with fructose and a proanthocyanidin
- Re establishment of protective vaginal microbiome (estrogen therapy, Lactobacillus spp, etc.)

Choosing an antibiotic:

- More difficult (and will be increasingly so) in this era of bacterial resistance
- Single dose treatments (particularly β lactams) high failure rate (except fosfomycin)
- Community resistance > 20% make amoxicillin, trimethoprim, trimethoprim-sulfamethoxazole, fluoroquinolones less reliable
- “collateral damage” of adverse effects of antimicrobials, superinfection
UTI and *Clostridium difficile*

- UTI is a frequent “excuse” to use antimicrobial therapy in persons at risk for *Clostridium difficile*
- Limit treatment to more certain diagnoses of UTI (high threshold of diagnosis)
- Limit duration of antimicrobials
- When treatment is necessary for UTI and gram negative bacilli are suspected pathogens, urine specific agents (e.g., nitrofurantoin) may be less likely to promote *Clostridium difficile* disease
- If systemic antimicrobials are necessary, consider other *Clostridium difficile* preventive measures
Antimicrobials Currently Recommended in UTI in the US

- **Nitrofurantoin** = bladder specific (not concentrated in kidneys or other tissues or fluids). Less effective when creatinine clearance is <50-60 mL/min. Ineffective against Pseudomonas aeruginosa, Proteus, Morganella, Providencia species. Should not be used chronically particularly in the elderly (short course treatment OK). Hepatotoxicity, pulmonary toxicity, vasculitis are uncommon but occur especially with prolonged use.

- **Fosfomycin** = organic phosphonate interfering with bacterial cell wall synthesis; has broad gram positive and Enterobacteriaceae activity, ineffective against *Pseudomonas* species; multiple treatments rapidly induce resistance.

- **Cephalexin** = adequate bladder concentration for susceptible organisms, inadequate for pyelonephritis or bloodstream infections.
Antimicrobials Currently Recommended in UTI

- Trimethoprim-sulfamethoxazole – broad spectrum for many gram negative bacilli except Pseudomonas aeruginosa, but increasing bacterial resistance noted (>20% E coli). For susceptible organisms in cystitis, 3 day treatment course often effective. No longer dependable for “empiric treatment”.

- Ciprofloxacin (and other fluoroquinolones) – broad spectrum for many gram negative bacilli, but overuse has contributed to emerging resistance (>20% E coli). For susceptible organisms in cystitis, 3 day treatment course often effective. No longer dependable for “empiric treatment”.
# Empiric Treatment of Cystitis (lower UTI)

<table>
<thead>
<tr>
<th>UTI</th>
<th>Organisms</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; line</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; line</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Cystitis – uncomplicated or low risk patient</td>
<td><em>E. coli</em> &lt;br&gt; <em>Staph. saprophyticus</em> and others</td>
<td>No abx indicated for asymptomatic bacteriuria in non-pregnant patients &lt;br&gt; NITROFURANTOIN 100 mg PO BID x 5 days <em>(In patients with CrCl &gt; 60 mL/min; not for pyelonephritis)</em> &lt;br&gt; -or-  &lt;br&gt; CEPHALEXIN 500 mg PO BID x 7 days &lt;br&gt; -or-  &lt;br&gt; FOSFOMYCIN TROMETHAMINE 3 grams orally single dose</td>
<td>CIPROFLOXACIN 250 mg PO BID x 3 days &lt;br&gt; -or-  &lt;br&gt; TMP/SMX DS: 1 tab PO BID x 3 days</td>
<td>Culture not necessary for low risk, uncomplicated cystitis. &lt;br&gt; If recent use of CIPROFLOXACIN or TMP/SMX (within 6 months) consider use of alternative abx. NITROFURANTOIN is less effective in renally impaired patients. Consider alternatives if CrCl &lt;60 mL/min. Avoid long-term use of NITROFURANTOIN in patients &gt;65 yrs old due to potential for toxicity.</td>
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# Empiric Treatment of Cystitis in Pregnancy

<table>
<thead>
<tr>
<th>UTI</th>
<th>Organisms</th>
<th>1(^{st}) line</th>
<th>2(^{nd}) line</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Cystitis in pregnancy    | *E. coli*  
*Staph. saprophyticus* and others | CEPHALEXIN  
500 mg PO BID x 7 days  
Or other broad spectrum oral cephalosporin | NITROFURANTOIN  
100 mg PO BID x 5 days  
-or-  
TMP/SMX DS: 1 tab BID x 7 days  
*(Note: avoid this agent in the 1\(^{st}\) and 3\(^{rd}\) trimesters of pregnancy)* | Culture recommended.  
NITROFURANTOIN is contraindicated at term or when labor is imminent |
# Empiric Treatment of Pyelonephritis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Organisms</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; line</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; line</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Pyelonephritis                | *E. coli* and others | CIPROFLOXACIN 500 mg PO BID x 7 days (see comments)                                 | CEFPODOXIME 200 mg PO BID x 10-14 days                                              | Urinalysis and culture recommended  
If recent fluoroquinolone or TMP/SMX use (within 6 months) or documentation of prior resistance by culture - strongly consider CEFTRIAXONE 1 g IV dose and alternative such as beta-lactam while waiting for sensitivities.  
If true PCN or cephalosporin allergy, a consolidated 24-hour IV dose of an aminoglycoside is an alternative to CEFTRIAXONE.   |
|                               |                   | *Consider initial IV dose of CEFTRIAXONE 1 g or other parenteral antimicrobial if resistance suspected* | *If oral beta-lactam is used an initial IV dose of long-acting abx (e.g., 1 g CEFTRIAXONE or other) is recommended -or-  
TMP/SMX DS: 1 tab PO BID x 14 days if organism is susceptible* |                                                                                                                                 |

Consider renal imaging to exclude urinary obstruction, anatomic abnormalities.
Principles of Management of UTI

• Establish diagnosis of UTI
• Differentiate from urethritis, vaginitis, bacterial/viral STI, prostatitis
• Acute uncomplicated vs recurrent vs complicated
• Anatomic predisposition (most importantly presence of urinary obstruction, abscess, or necrotizing infection)
Management of Severe Complicated UTI

- Support and stabilize patient
- Investigate possible urinary obstruction or alternate intra-abdominal infection
- Evaluate for possible antimicrobial resistance:
  - Recent (3-6 month) antimicrobials
  - History of resistant organisms
  - Geographic history (Skilled Nursing, Board and Care, from home)
- Presumptive treatment for resistant organisms would include ESBL, potential linked gentamicin resistance, or in some cases CRE
Welcome To The NEW SCPMG Infectious Disease Website 10.13.2014
Initiatives-click on links from this page:

Diagnosis and treatment of Urinary Tract Infections, a major cause of inappropriate antimicrobial use

CDC: severe respiratory illness among young and middle age adults due to influenza A (H1N1)

Appropriate Use of Laboratory Testing

Interferon Gamma Release Assay-TB (Quantiferon): NOT a routine replacement for PPD; not more sensitive or specific. See linked guidelines for use.

Clostridium difficile: prevention, early identification, appropriate isolation, early initiation of treatment, risk of relapse and early treatment of relapse

Influenza Guidance Page: Back for more: sporadic influenza in S California. IMMUNIZE YOUR PATIENTS AS SOON AS POSSIBLE AND YEARLY.

Feedback
Management of UTI

Guidelines

Low Risk UTI = Adult premenopausal women with cystitis (dysuria, urgency, frequency)

- No systemic symptoms (fever, rigors, etc)
- No symptoms of pyelonephritis (flank pain)
- No sexually transmitted infections (STI) or vaginitis
- Not pregnant
- Low-risk adult women (no recurrent UTI, diabetes mellitus, immune suppression, stone or structural urinary disease)
- No history of previous antibiotic resistant bacterial infections causing UTI or recent antimicrobial treatment
- History/examination if necessary to exclude vaginitis, STI
- NO URINE CULTURE NECESSARY for presumptive treatment (see guidelines)

Asymptomatic patients with positive urine cultures should not be routinely treated for UTI. "abnormal" urinanalysis alone does not constitute reason for antimicrobial
QUESTIONS???