Objectives

Pharmacist learning objectives:
• Summarize antimicrobial stewardship initiatives targeting asymptomatic bacteriuria
• Discuss interventions to improve utilization of antimicrobials for urinary tract infection (UTI) treatment

Technician learning objectives:
• Evaluate urinary tract laboratory values including urinalysis and urine culture
Agenda

• UTI treatment and screening definitions
• Stewardship interventions for inpatient and emergency department settings
• Opportunities and challenges in UTI management:
  - Asymptomatic bacteriuria (ASB)
  - Geriatric population
Urinary Tract Infections: Scope

• Ambulatory: 7 million office visits/year
• Emergency department: 1 million visits/year
• Inpatient: 400,000 hospitalizations/year
• Most common organisms: *E. coli*, gram-negative bacilli
• Antimicrobial utilization: up to 20-50% inappropriate

Antibiotics!!!!!
Diagnosing Urinary Tract Infection

• **Patient presentation**
  - Systemic signs/symptoms: white blood cell count (WBC), fever
  - Cystitis: dysuria, frequency, urgency
  - Pyelonephritis: flank pain, costovertebral angle pain
  - Indwelling catheter infection: suprapubic discomfort
  - Non-specific symptoms: altered mental status, delirium

• **Urinalysis (UA)**
  - Presence of white blood cell (WBC) count or pyuria, leukocyte esterase (LE), nitrites

• **Urine culture (UC)**
  - Indicated in patients with UTI signs/symptoms
  - Organism isolated and colony counts
Defining Asymptomatic Bacteriuria

• Positive urine culture in absence of urinary symptoms

<table>
<thead>
<tr>
<th></th>
<th>Bacterial colony count</th>
<th>Number of specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>≥ 10^5 cfu/mL</td>
<td>2 consecutive</td>
</tr>
<tr>
<td>Men</td>
<td>≥ 10^5 cfu/mL</td>
<td>1</td>
</tr>
<tr>
<td>Catheterized</td>
<td>≥ 10^2 cfu/mL</td>
<td>1</td>
</tr>
</tbody>
</table>

• 1-5% in healthy women, up to 40% in institutionalized elderly, 50% in spinal cord injury

• Risks of treating ASB
  - Increased *C. difficile* infection or antimicrobial resistance
  - Delay identification of correct diagnosis (ie geriatric patients)

UTI Stewardship Interventions

- **Educational Strategies**
- **Treatment and Screening Algorithms**
- **Leveraging Technology**
- **Culture Call Back**
- **UA Reflex to Culture**
- **Catheter Protocols**
- **Geriatric Population**

- **Common goals**
  - Improve culture of culturing
  - Reduce treatment of asymptomatic (Asx) bacteriuria
  - Reduce days of antibiotics

- **Multi-disciplinary approach**
  - Pharmacy: ID and team-based pharmacists
  - Physicians
  - Nursing
Educational Strategies and Algorithms

- Intensive training of medical and nursing staff
  - Presentations, clinical vignettes, letters to providers

- Development of screening and treatment algorithms
  - Antibiogram data to guide empiric therapy
  - Recommended treatment durations
  - Examples included at end of slide set

- Addition of message in positive urine culture results
  - “Antibiotic treatment is only indicated for symptomatic patients”
  - Prescribers call laboratory for culture and susceptibility data

5. Irfan N. Plos One 2015; DOI:10.1371/journal.pone.0132071
### Educational Strategies and Algorithms

<table>
<thead>
<tr>
<th>Study</th>
<th>Urine Cultures: Pre</th>
<th>Urine Cultures: Post</th>
<th>ASB treatment: Pre</th>
<th>ASB treatment: Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zabarsky TF: 2008¹ Cleveland VA LTAC</td>
<td>2.6/1000 pt-days (inappropriate UC)</td>
<td>0.9/1000 pt days (inappropriate UC)</td>
<td>1.7/1000 pt days</td>
<td>0.6/1000 pt days</td>
</tr>
<tr>
<td>Chowdjury F: 2012² Lutheran Medical Center, NY inpatient</td>
<td>3419 cultures collected in 30 days</td>
<td>3127 cultures collected in 30 days</td>
<td>64/109 (83%) cultures were ASB</td>
<td>13/55 (17%) cultures were ASB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30/64 (47%) treated</td>
<td>2/13 (15%) treated</td>
</tr>
<tr>
<td>Irfan N: 2015³ Hamilton Health Sciences, Ontario inpatient</td>
<td>Not reported</td>
<td>Not reported</td>
<td>160/341 (47%) cultures were ASB</td>
<td>24/93 (26%) cultures were ASB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>94/160 (59%) treated</td>
<td>2/24 (8%) treated</td>
</tr>
</tbody>
</table>

- Longest study showed 30 months of continued improvements¹
- Challenges: time intensive, changing engrained habits for culture ordering and UTI treatment

3. Irfan N. Plos One 2015; DOI:10.1371/journal.pone.0132071
Leveraging Technology

- **Stewardship alert software and UTI Care Bundle**
  - Generate alert when positive urine culture or UA and on antibiotics
  - Pharmacist review patient compliance with institutional criteria
    - Treatment approach in symptomatic patients, IV to PO switch at 72 hours, culture assessment for appropriate therapy

- **Clinical decision support (CDSS) with ED diagnosis of UTI**
  - Contains recommendations on diagnostic and therapeutic tools, antibiotic selection tailored to the patient, follow-up
  - Positive outcomes: improved diagnosis of asymptomatic bacteriuria

- **ED specific antibiogram to guide empiric therapy**

Culture Call Back

- Pharmacist or provider review of urine culture data
  - Recommendations for discontinuation, de-escalation, or continuation

<table>
<thead>
<tr>
<th></th>
<th>ASB treatment</th>
<th>Antibiotics</th>
<th>Factors associated with ASB treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhang X: 2017</td>
<td>58/136 (43%) patients treated</td>
<td>122/426 (29%) days saved with pharmacist intervention</td>
<td>+ leukocyte esterase, + nitrite, age ≥ 75 years</td>
</tr>
<tr>
<td>Multicare Auburn Medical Center, WA</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Pre-Intervention</th>
<th>Post-Intervention</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burchett P: 2015</td>
<td>8.8% called to discontinue abx with negative culture</td>
<td>74.4% called to discontinue abx with negative culture</td>
<td>30.3 (10.8-85.4)</td>
</tr>
<tr>
<td>Children’s Hospital of Colorado, CO</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Challenges
  - Lack of documentation of UTI symptoms in ED note
  - Over-culturing urine

UA Reflex to Culture

- UA results make automatic decision for further urine culture test
  - Nitrite, leukocyte esterase, white blood cell counts (> 5 or > 10), presence of bacteria

<table>
<thead>
<tr>
<th>UA characteristics</th>
<th>+ UC sensitivity</th>
<th>NPV</th>
<th>Eliminating UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones CW: 2014¹ UNC</td>
<td>+ nitrite, + LE, WBC &gt; 10, or bacteria</td>
<td>96.5% (93.6-98.1%)</td>
<td>98.2% (96.7-99%)</td>
</tr>
<tr>
<td>Hertz J: 2015² Vanderbilt</td>
<td>+ nitrite, + LE, WBC &gt; 10, or bacteria</td>
<td>95.3% (94.3-96.4%)</td>
<td></td>
</tr>
</tbody>
</table>

- Point/counterpoint
  - Concerns for missing UTI in immunocompromised, elderly
  - Symptomatic patients
  - Lacking data for catheterized patients

Urinary Catheter Protocols

- Insertion and maintenance
- Maintain a closed system
- Nursing protocol with catheter removal criteria
- Documentation electronically
- Correct specimen collection
- Assessing fevers in catheterized patients
  - Using the UA as guidance
  - Remove or replace catheter
- Decreased catheter-associated UTI rates
- Decreased UC numbers:
  - 4749 in 2013 to 2479 in 2014

Geriatrics: Challenges in UTI Assessment

- Comorbidities
  - Dementia, Alzheimer’s
  - Diuretic use for heart failure, hypertension

- Nonspecific signs and symptoms
  - AMS, changes in behavior
  - Malaise, lethargy

- Fall risk
  - General debility
  - Medication interactions, elevated doses
  - Dehydration
Expert Consensus Statements

• Define threshold for antibiotic initiation

• Loeb Criteria\(^1\)
  - Dysuria alone  \(\text{OR}\)
  - Fever \textit{with} urgency, frequency, suprapubic pain, hematuria, costovertebral tenderness, or incontinence

• McGreer Criteria\(^2\)
  - Need \(>3\) of the following
    - Fever, burning, frequency, new flank/suprapubic pain, worsening change/functional status, change in character of urine

• Problem: not validated tools
  - Positive predictive value of around 60\(\%\)^3

Nonspecific Symptom Reliability

- Review of clinical features that caused investigation of possible UTI
- Goal: Identify signs/symptoms associated with bacteria plus pyuria
  - > 100,000 CFU in culture and > 10 WBC’s on UA
- Results
  - Features not associated: falls, family requests workup, previous UTI, malaise, syncope, changes in behavior, gait, or voiding pattern
  - 3 statistically associated features
    - Dysuria, change in character of urine, change in mental status
    - Dysuria with change in urine character and/or change in mental status predicted 63% of patients with bacteria plus pyuria

Geriatrics: Opportunities

• Recommendations

- One piece of evidence for a potential UTI should not trigger treatment\(^1,2\)

- Watchful waiting\(^1,3,4\)

- Workup patient for other causes

Nursing Home Education Strategy

• Common theme: multifactorial approach
  - Nursing staff pocket cards – appropriate urine culture
  - Empiric therapy guides/algorithms – diagnostics and antibiotic guidance
  - Educational session on asymptomatic bacteriuria
  - Direct feedback to LIP’s

• Resulted in reduction in antibiotic use, inappropriate cultures, treatment of asymptomatic bacteriuria

Year of Urine

Medina Hospital

• Quality Assessment
• Antimicrobial Stewardship Initiative
ME Urine Cultures and Urinalysis for August 2017

• Goal of quality project
  - Describe patient population receiving urine cultures (UC) and/or urinalysis (UA) for diagnosis of urinary tract infection (UTI)
  - Evaluate potential impact of implementing an UA reflex to UC
  - Characterize antibiotic utilization for treatment of UTI

• Patient population
  - UC and/or UA drawn for diagnosis of UTI in August 2017 at Medina Hospital Emergency Department or inpatient service
  - 18 years and older
  - Only first UC included
ME Urine Culture and Urinalysis

• Data collection
  - Baseline demographics and urine culture risks factors
  - Signs and symptom of UTI
  - Urine culture: date/time, result, organism, organism load
  - Urinalysis: leukocyte esterase, nitrite, bacterial load, white blood cell count, protein
  - Antimicrobial utilization

• Statistical analysis
  - Descriptive
Opportunities and Next Steps

- Algorithm for urine culture ordering and treatment
- Empiric therapy guide
  - Duration of therapy definitions
  - Oral options
- Collaboration with emergency department (ED) team to determine workflow and challenges
- Provider education through inpatient and ED stewardship
  - Department of Medicine and Surgery meetings
Cleveland Clinic

Every life deserves world class care.
Supplemental Appendix 1: Algorithm for Bacteriuria Assessment

Assessment of Bacteriuria in Adults

A. Screen and appropriately treat ALL SYMPTOMATIC patients for bacteriuria

B. SCREEN AND TREAT the following ASYMPTOMATIC patients for bacteriuria
- Pregnant women
- Candidate for TURP (transurethral resection of the prostate)
- Candidate for urologic procedure that causes mucosal bleeding

C. DO NOT SCREEN OR TREAT all other ASYMPTOMATIC patients, including the following cases:
- Premenopausal, non-pregnant women
- Diabetic women
- Older persons living in the community
- Elderly, institutionalized subject
- Persons with spinal cord injury
- Catheterized patients while the catheter remains in situ

Screening includes performing a routine urine culture to diagnose bacteriuria.

Criteria for diagnosing bacteriuria:

1) Male patient (symptomatic and asymptomatic)—Need ONE:
- A single, clean-catch voided urine specimen with 1 bacterial species isolated in a quantitative count ≥ 10^5 cfu/ml
- A single, catheterized urine specimen with 1 bacterial species isolated in a quantitative count ≥ 10^5 cfu/ml

2) Female patient (symptomatic)—Need ONE:
- A single voided urine specimen with isolation of the same bacterial strain in quantitative counts ≥ 10^5 cfu/ml
- A single, catheterized urine specimen with 1 bacterial species isolated in a quantitative count ≥ 10^5 cfu/ml

3) Female patient (Asymptomatic)—Need ONE:
- Two (2) consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts ≥ 10^5 cfu/ml
- A single, catheterized urine specimen with 1 bacterial species isolated in a quantitative count ≥ 10^5 cfu/ml

Once clinically significant bacteriuria is diagnosed, treat appropriately.
Supplemental Appendix 2: Assessment Tool

- Assists providers in determining appropriate initiation of antibiotics for urinary tract infections
- Antibiogram was not available at this facility

Table 1: Gentiourinary Infections: Assessment Tool Snapshot

<table>
<thead>
<tr>
<th>Category</th>
<th>Asymptomatic Bacteriuria</th>
<th>Uncomplicated Community-Acquired UTI</th>
<th>Complicated Community-Acquired UTI</th>
<th>Health Care-Associated UTI/Urosepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
</tr>
<tr>
<td>Absence of fever</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
</tr>
<tr>
<td>Absence of flank pain</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
</tr>
<tr>
<td>No urological abnormalities</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
</tr>
<tr>
<td>Female</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
<td>Abnormality</td>
</tr>
<tr>
<td>Positive urine cultures ≥ 100,000 CFU/mL with no signs or symptoms</td>
<td>Positive urine cultures ≥ 100,000 CFU/mL</td>
<td>Positive signs and symptoms</td>
<td>Positive signs and symptoms</td>
<td>Positive signs and symptoms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment*</th>
<th>No treatment recommended</th>
<th>Oral</th>
<th>Oral</th>
<th>Oral</th>
<th>Oral</th>
<th>Intravenous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin 100 mg every 12 hours</td>
<td>Nitrofurantoin 100 mg every 12 hours</td>
<td>Cefuroxime 500 mg four times a day</td>
<td>Cefuroxime 500 mg four times a day</td>
<td>Cefuroxime 500 mg four times a day</td>
<td>Cefuroxime 500 mg four times a day</td>
<td>Cefuroxime 500 mg four times a day</td>
</tr>
<tr>
<td>Levofloxacin 250 mg once a day^</td>
<td>Levofloxacin 250 mg once a day^</td>
<td>Levofloxacin 250 mg once a day^</td>
<td>Levofloxacin 250 mg once a day^</td>
<td>Levofloxacin 250 mg once a day^</td>
<td>Levofloxacin 250 mg once a day^</td>
<td>Levofloxacin 250 mg once a day^</td>
</tr>
<tr>
<td>TMP-SMX DS every 12 hours</td>
<td>TMP-SMX DS every 12 hours</td>
<td>TMP-SMX DS every 12 hours</td>
<td>TMP-SMX DS every 12 hours</td>
<td>TMP-SMX DS every 12 hours</td>
<td>TMP-SMX DS every 12 hours</td>
<td>TMP-SMX DS every 12 hours</td>
</tr>
<tr>
<td>Ciprofloxacin 1g every eight hours</td>
<td>Ciprofloxacin 1g every eight hours</td>
<td>Ciprofloxacin 1g every eight hours</td>
<td>Ciprofloxacin 1g every eight hours</td>
<td>Ciprofloxacin 1g every eight hours</td>
<td>Ciprofloxacin 1g every eight hours</td>
<td>Ciprofloxacin 1g every eight hours</td>
</tr>
<tr>
<td>Gentamicin 1mg/kg every eight hours</td>
<td>Gentamicin 1mg/kg every eight hours</td>
<td>Gentamicin 1mg/kg every eight hours</td>
<td>Gentamicin 1mg/kg every eight hours</td>
<td>Gentamicin 1mg/kg every eight hours</td>
<td>Gentamicin 1mg/kg every eight hours</td>
<td>Gentamicin 1mg/kg every eight hours</td>
</tr>
</tbody>
</table>

* Doses should be adjusted as appropriate for patients with renal or hepatic abnormalities.
^ Dosed appropriate antibiotic therapy during study analysis and prior to FDA warning of quinolones use; contraindicated in pregnancy.
^ Agent serves as option in pregnant woman.
# Reserved for patients with penicillin allergies.
$ Reserved for patients with suspected extended-spectrum beta-lactamase infection.
Supplemental Appendix 3: Algorithm for Ordering Urine Culture

- Nursing home study
- Nurses primarily recommend ordering urine cultures
- Intervention targeted at nursing and physicians
- Nurses complete log of presenting symptoms when UTI suspected