Antimicrobial Stewardship Initiatives for Asymptomatic Bacteriuria

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Objectives

- Discuss the consequences of antimicrobial misuse.
- Identify indications for antimicrobials for the management of asymptomatic bacteriuria (ASB).
- Describe antimicrobial stewardship interventions to minimize inappropriate antimicrobial use for ASB.

Disclosure

- I have no actual or potential conflict of interest in relation to this program or presentation.

Pretest Question 1

SL is a 34 y/o 24 week pregnant female who presents for routine prenatal assessment. Her UA is positive for bacteria and urine culture is sent. She denies urinary symptoms. Which of the following options is the best course of action for SL?

A. SL requires antimicrobial therapy with nitrofurantoin 100mg Q12h for 5-7 days.
B. SL requires antimicrobial therapy with ciprofloxacin 750mg Q12h for 7 days.
C. SL does not require antimicrobial therapy because she has reached 24 weeks.
D. SL does not require antimicrobial therapy because she is asymptomatic.

Pretest Question 2

MT is a 65 y/o male who is scheduled for an elective TKA in three days. As part of his pre-operative evaluation a UA with reflexive culture was performed. The urine culture grew 50,000 CFU *E. coli* resistant to ampicillin (sensitive to all other antimicrobials evaluated). He denies symptoms associated with UTI. Which of the following options is the best course of action for MT?

A. MT requires antimicrobial therapy with ciprofloxacin 750mg Q12h for 10 days.
B. MT requires gentamicin as part of his surgical prophylactic regimen.
C. MT did not require screening for asymptomatic bacteriuria as his surgical procedure does not involve the GU tract.
D. MT did not require screening for asymptomatic bacteriuria but, since positive should receive antimicrobial therapy for 3 days.

Pretest Question 3

GP is a 62 y/o female who presents to the ED with a 3-day history of urinary frequency and dysuria. During the last 24h, she has developed fever, nausea, vomiting, and flank pain. Her vitals are as follows: BP 140/75, HR 120, RR 16, T 39°C and she has a mild leukocytosis (12,000). Her UA is cloudy and demonstrates the presence of leukocyte esterase, nitrites, bacteria, and WBC. Which of the following options is the best course of action for MT?

A. GP does not require antimicrobial therapy as this is likely viral.
B. GP requires outpatient antimicrobial therapy with a beta-lactam for 3 days.
C. GP requires hospital admission with IV antimicrobials for 21 days for pyelonephritis.
D. GP requires hospital admission with IV antimicrobials at least for the first 24h followed by 10-14 days of oral therapy.

Pretest Question 4

- Which of the following antimicrobial stewardship interventions can be utilized to minimize inappropriate antimicrobial use for asymptomatic bacteriuria?

A. Guideline development and education
B. Prospective audit and feedback to providers
C. Laboratory intervention
D. All of the above

Case to Consider…

HF is a 79 y/o female who is bedridden and resides in a nursing home. She is chronically catheterized and her catheter was last changed three weeks ago. Upon presentation, her urine is cloudy, UA shows many bacteria, and the nurse reports foul-smelling urine. She denies symptoms. Vitals: BP 131/84, HR 78, WBC 10K, T 37.1° C Urine culture obtained.

Which of the following is the best option for HF?

A. No therapy because she is chronically catheterized and has no symptoms
B. No antibiotic therapy, but the catheter should be changed
C. Oral ciprofloxacin 500 mg twice daily for 7 days and a new catheter
D. Oral ciprofloxacin 500 mg twice daily for 14–21 days without a change in catheter

Reason for Action

- ~50% of all antimicrobials prescribed in US acute care hospitals are unnecessary or inappropriate

- Reduced number of antimicrobial agents approved in the past 25 years, with no clear recovery expected in the near future

Dellinger RP, et al. *Intern Care Med* 2013;39:165-228.
Dellit TH, et al. *Clin Infect Dis* 2007;44:159-177.

Consequences of Antimicrobial Misuse

Adverse Effects

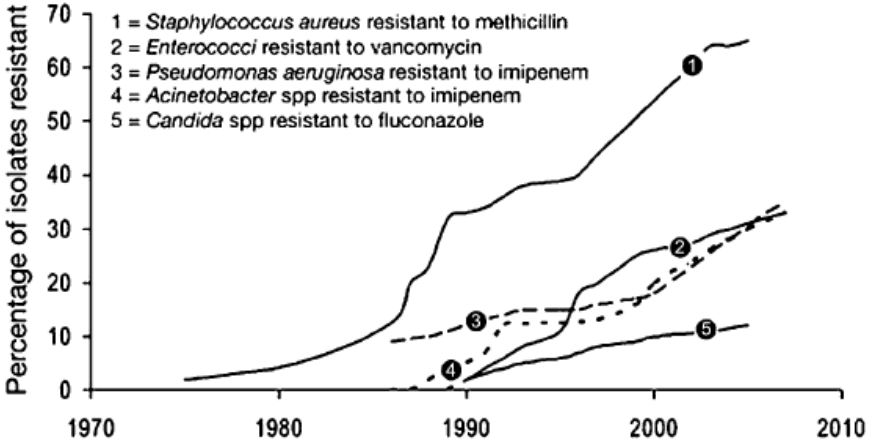
- Patients unnecessarily exposed to antimicrobials are at risk for serious adverse effects with no clinical benefit
  - Adverse drug effects
    - 25% of ADEs involve antimicrobials
    - May cause significant drug-drug interactions
    - Hypersensitivity reactions
    - Organ dysfunction
  - *Clostridium difficile* infection
    - Increasing in incidence and severity

Bates DW, et al., *JAMA*, 1995;274:29-34.
Chalasani N, et al. *Gastroenterology* 2008;135:1924-34.

Consequences of Antimicrobial Misuse

Antimicrobial Resistance

- Worldwide increase in the prevalence of antimicrobial-resistant pathogens



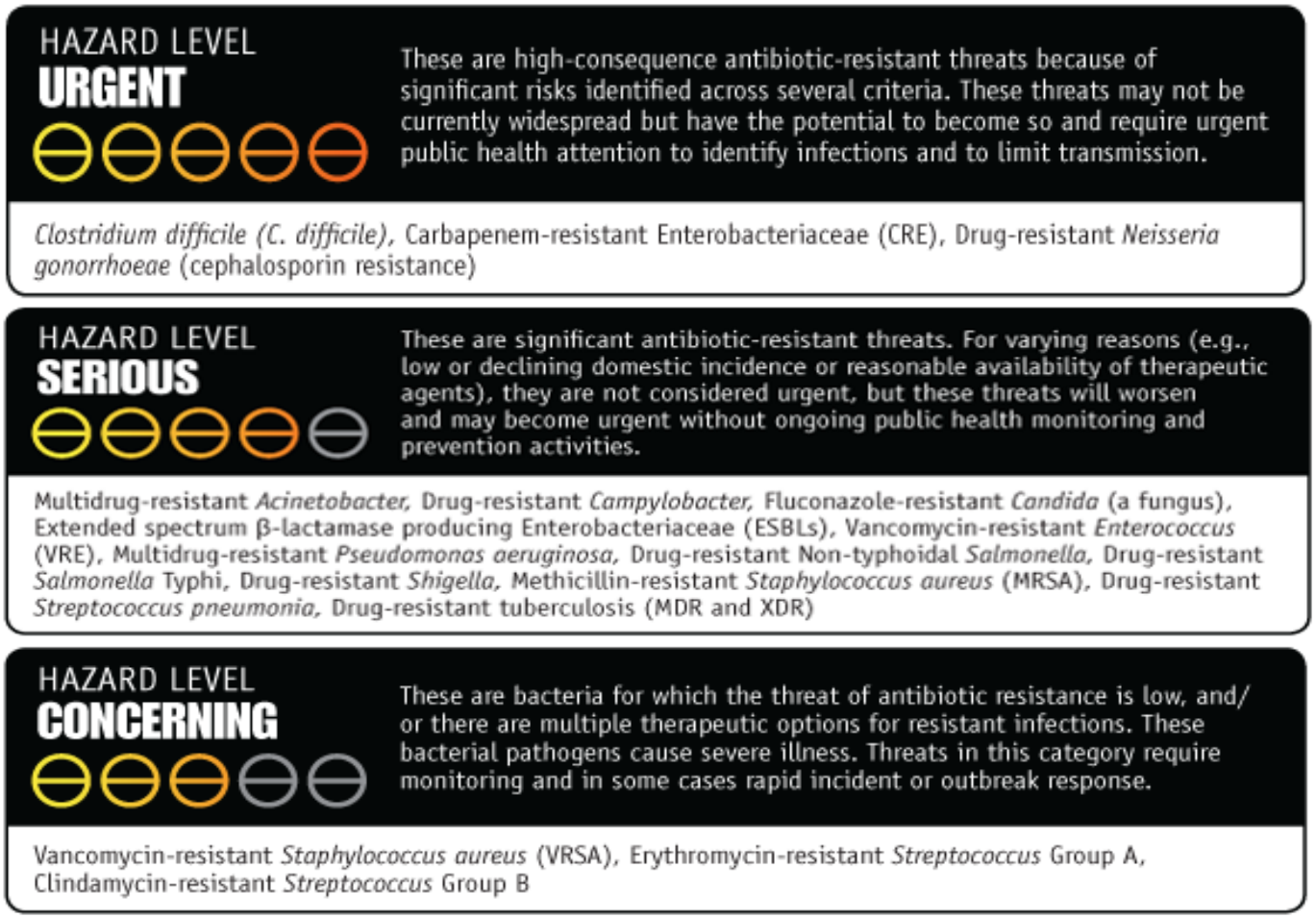
New Resistance Finding First colistin-resistant mcr-1 E. coli discovered in 2 U.S. samples
http://www.cdc.gov/drugresistance/index.html

Dellit TH, et al. *Clin Infect Dis* 2007;44:159-177.
Tacconelli E. *Curr Opin Infect Dis* 2009;22:352-8.
Septimus EJ, et al. *Clin Infect Dis* 2011;53:S8-S14.

Epidemiology: Antimicrobial Resistance Burden

Huttner A, et al. *Antimicro Res Infect Control* 2013;2:31.
CDC. Antibiotic Resistance Threats in the US, 2013. Atlanta, GA:CDC;2013.

CDC Drug-Resistant Threats to the US



CDC. Antibiotic Resistance Threats in the US, 2013. Atlanta, GA:CDC;2013.

Asymptomatic Bacteriuria (ASB)- Antimicrobial Stewardship Opportunity for Improvement

ASB Defined

- Bacteriuria without symptoms of a urinary tract infection (UTI)
- ASB remains one of the most common reasons for unnecessary antimicrobial use in hospitals
  - 45-65% of patients receive inappropriate therapy
- Driven by reflexive prescribing for positive urine cultures

Pavese P, et al. *Infect Control Hosp Epidemiol* 2009;30:596-599.
Chowdhury F, et al. *J Community Hosp Intern Med Perspect* 2012;2:17814.

ASB Recommendations

IDSA and US Preventive Services Task Force Recommendation Statement

- Screening and treatment
  - Has NO clinical benefit and predisposes patient to increased risks
  - Not recommended unless patient is:
    - Pregnant (AI)
    - Anticipating a urologic interventional procedure (AI-AIII)

Choosing Wisely®
An initiative of the ABIM Foundation

Nicolle LE, et al. *Clin Infect Dis* 2005;40:643-654.
Gupta K, et al. *Clin Infect Dis* 2011;52:e103-e120.
Lin K. *Ann Intern Med*. 2008;149(1):W20.

Evidence Supporting Interventions to Reduce Screening and Treatment of ASB

Ref	Urine collection	ASB Treatment
1	Pre: 2.6 urine cultures/ 1000 patient-days; Post: 0.9 urine cultures/1000 resident-days (p <0.001)	Pre: 68%; Post: 44% (p =0.22) DOT Pre: 167.7/1000 patient-days; DOT Post: 109/1000 patient-days (p <0.001)
2	Intervention: 2.03 urine cultures/1000 resident-days Control: 2.48 cultures/1000 resident-days Weighted mean difference: -0.51 (95% CI -1.38 to 0.35)	Intervention: 1.17 courses of antimicrobials/1000 resident-days prescribed; Control: 1.59 courses of antimicrobials/1000 resident-days prescribed -0.49 (95% CI -0.93 to -0.06)
3	Culture rate Pre: 73.6%; Post: 64.8% (p = NR)	Pre: 26%; Post: 26% (p = NR) Mean LOT Pre: 6.3 days; mean LOT Post: 2.2 days (p<0.001)
4	Number collected Pre: 3419; Post: 3127 (p<0.001)	Pre: 47%; Post: 15% (p = 0.036)
5	NR	Pre: 62% (66/107); Post: 26% (28/107) (p<0.0001) Median LOT Pre: 6.5 days; Median LOT Post: 5 days (p = NS)
6	NR	Pre: 73.5%; Post: 16.7% (p = 0.01)
7	Pre: 100% results reported; Post: 14% results reported	Pre: 48%; Post: 12% (95% CI, 5-27%) ARR 36% (95% CI, 15-57%; p = 0.02); NNT 3 (95% CI, 2-7)
8	Pre: 41.2/1000 bed days; Post: 23.3/1000 bed days (IRR, 0.57; 95% CI, 0.53-0.61; p <0.001); Maintenance: 12.0/1000 bed days (IRR, 0.29; 95% CI, 0.26-0.32; p <0.001)	Pre: 1.6/1000 bed days; Post: 0.6/1000 bed days (IRR, 0.35; 95% CI, 0.22-0.55; p <0.001); Maintenance: 0.4/1000 bed days (IRR, 0.24; 95% CI, 0.13-0.42; p <0.001)
9	104 prescriptions for UTI evaluated; 40 (38%) recommendations for change in therapy, 10 (25%) implemented, 8% of subjects started on antimicrobials met criteria for infection; 26% decrease in antimicrobials for UTI during intervention, 6% reduction continuing through intervention period (95% CI, -8 to -3%); No effect on CDI or antimicrobial resistance	

Zabarsky TF, *et al. Am J Infect Control* 2008;36:476-480.
Loeb M, *et al. BMJ* 2005;331:669-673.
Linares LA, *et al. Infect Control Hosp Epidemiol* 2011;32:644-648.
Chowdhury F, *et al. J Community Hosp Intern Med Perspect* 2012;2:17814.
Kelley, *et al. Infect Control Hosp Epidemiol* 2014;35:193-195.
Pavese P, *et al. Infect Control Hosp Epidemiol* 2009;30:596-599.
Leis JA, *et al. Clin Infect Dis* 2014;58:980-983.
Trautner BW, *et al. JAMA Intern Med* 2015;175:1120-1127.
Doernberg SB, *et al. Antimicrob Resist Infect Control* 2015;4:54.

Interventions Used to Reduce ASB Screening and Treatment

- Clinical Guidelines and Pathways
- Education
- Laboratory intervention
- Prospective audit and feedback to prescribers

Clinical Pathways and Guidelines

- IDSA ASB Guidelines

Infectious Diseases Society of America Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults

Lindsay E. Nicolle,[1] Suzanne Bradley,[2] Richard Colgan,[3] James C. Rice,[4] Anthony Schaeffer,[5] and Thomas M. Hooton[6]

- IDSA Treatment Guidelines

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

Kalpana Gupta,[1] Thomas M. Hooton,[2] Kurt G. Naber,[9] Björn Wullt,[10] Richard Colgan,[3] Loren G. Miller,[4] Gregory J. Moran,[5] Lindsay E. Nicolle,[8] Raul Raz,[11] Anthony J. Schaeffer,[6] and David E. Soper[7]

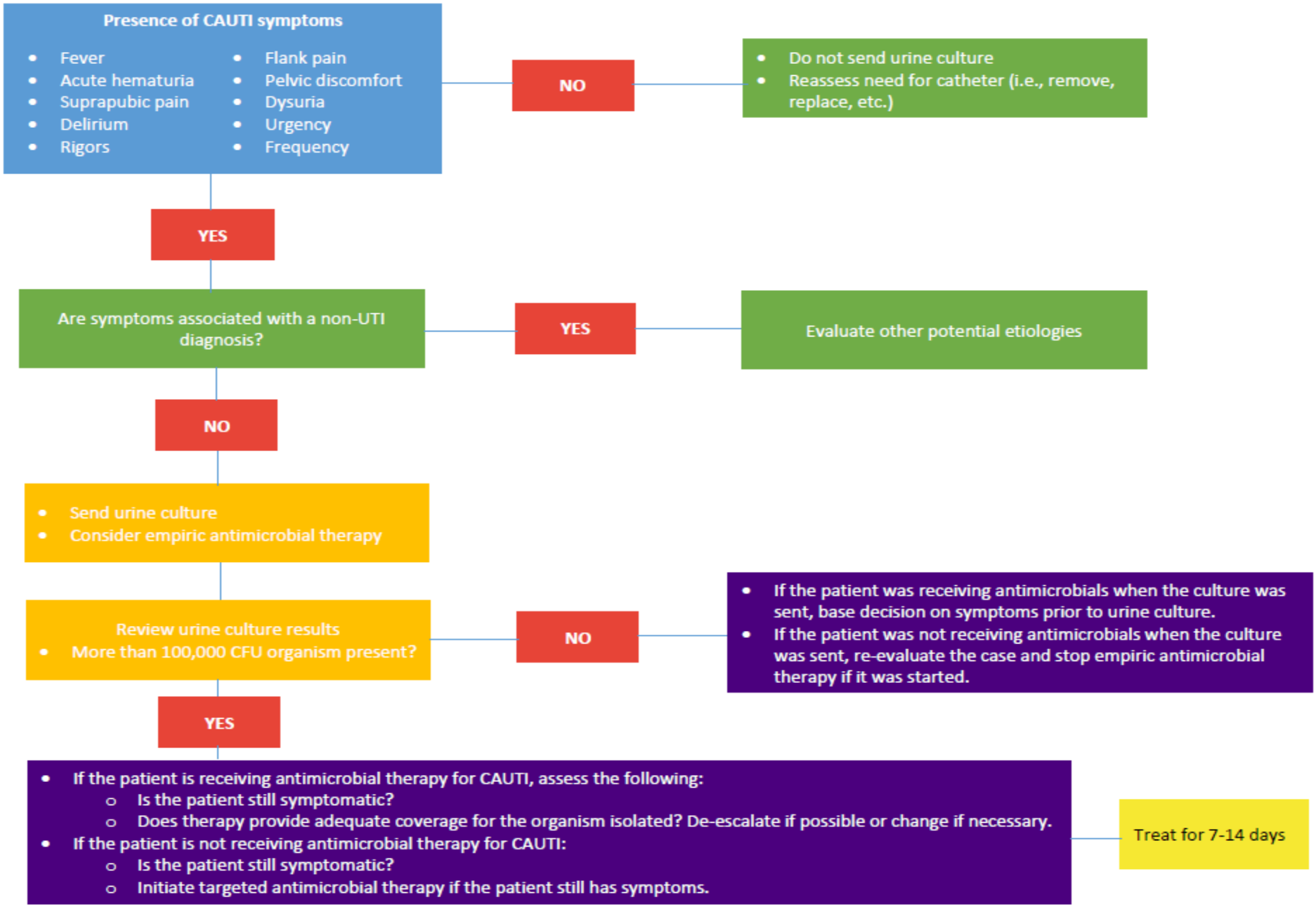
Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infection in Adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America

Thomas M. Hooton,[1] Suzanne F. Bradley,[3] Diana D. Cardenas,[2] Richard Colgan,[4] Suzanne E. Geerlings,[7] James C. Rice,[5,*] Sanjay Saint,[3] Anthony J. Schaeffer,[6] Paul A. Tambayh,[8] Peter Tenke,[9] and Lindsay E. Nicolle[10,11]

- Change the "culture of culturing"
  - Provide recommendations on appropriateness of urine cultures and reflexive cultures
  - Catheter care/maintenance
- Incorporate treatment recommendations
  - Symptoms
  - Empiric, definitive, length of therapy
  - Use site-specific antibiogram
- Embed clinical decision support within EMR

Advocate Health Care

Example Recommendations – Catheterized Patients



Education

- Dissemination of guidelines
  - Pocket cards with treatment algorithms
  - Posting information on site-specific intranet
- Prepare and present in-services to reinforce information
- Charter multidisciplinary teams for implementation and continuous education/feedback
- Develop a detailed communication plan to update physician leadership and other key stakeholders

Laboratory Intervention

- Require inclusion of indication in order for urine culture
  - Symptoms present and not first-episode acute, uncomplicated cystitis
  - Pregnancy
  - Transurethral resection of the prostate, or other urologic procedures
- Consider embedded clinical decision support
  - Suppression of culture results
  - E.g., “The majority of positive urine cultures from inpatients without an indwelling urinary catheter represent asymptomatic bacteriuria. If you suspect your patient has developed a UTI, please call the lab.”
- Restrict reflexive urine cultures

Laboratory Screening for Pyuria: Criterion for Performing Culture? NO!

- Few published data to support urinalysis (UA) with reflex to culture only if UA is positive
  - Criteria vary among labs
  - No outcome studies

- Several methods to evaluate for pyuria
  - Dipstick for leukocyte esterase (low sensitivity and specificity)
  - Manual microscopy
  - Automated microscopy (variable sensitivity 71-98% and specificity 55-92%)

- Clinical diagnosis may be a more reliable predictor than pyuria alone
  - Pyuria consistent with but, not diagnostic of UTI
  - Absence of pyuria does not exclude UTI in symptomatic patient
  - Pyuria with ASB does not indicate need for treatment

- Catheterized patients
  - Absence of pyuria in symptomatic patients suggests a diagnosis other than UTI

Burd EM. *J. Clin. Microbiol*. 2011. 49(9) S34-S38.
National Guidance Clearinghouse. 2008.
Hooton TM. IDSA. *Clin. Infect. Dis*. 50:625-663.

Cultures in Uncomplicated Cystitis (Adults)

- Cultures do not need to performed for patients with first-episode acute, uncomplicated cystitis
  - Empiric treatment can be initiated based on symptoms alone
  - Cultures have little impact on antimicrobial therapy
    - Pathogens are reasonably predictable, TMP-SMX as first line therapy

- Indications to order culture
  - No clinical improvement within 48 hours
  - Recurrence
  - Other complicating factors

ACOG. 2008. Practice Bulletin no 91. *Obstet Gynecol*. 111:785-794.
Gupta K. *Clin Infect Dis*. 2011. 52:e103-e120.
Mehnert-Kay SA. *Am Fam. Physician* 2005. 72:451-456.
National Guidance Clearinghouse. 2008.

Prospective Audit and Feedback

- Key element of antimicrobial stewardship
- Develop a process for case review
  - Relate back to site-specific guidelines
  - Develop a script to follow for consistency
- Educate pharmacists to assess commonly used urinary tract infection antimicrobials for earlier intervention
- Helpful to prevent initial treatment as opposed to stop therapy after administration

Barlam TF, *et al. Clin Infect Dis* 2016;62:e51-e77.

Case to Consider…

Pharmacist receives a call from a hospitalist for an antimicrobial recommendation for a multidrug-resistant organism isolated from the urine of a patient on a Medical-Surgical unit.

Before providing a recommendation for drug therapy, what is the first question the pharmacist should ask?

A. Does the patient have any drug allergies?
B. Is the patient currently receiving antimicrobial therapy?
C. Is the patient symptomatic?
D. Does the patient have any comorbidities?

Safety Concerns: Missed Diagnoses?

- Adults
  - ASB Prevalence ~1-20%
  - Women with ASB are more likely to develop subsequent symptomatic UTI

- Pediatrics – American Academy of Pediatrics
  - ASB not associated with subsequent infections
  - UTI symptoms may be missed on history and physical, or nonspecific symptoms, or inconvenient testing
  - Unnecessary treatment leads to increased likelihood of pyelonephritis
  - 12% of UTIs are missed on dipstick

Zorc J. *Clin Microbiol Rev*. 2005 Apr; 18(2):417-422.
Hellstrom A. *Arch Dis Child*. 66:232-234.
Huicho L. *Pediatr Infect Dis J*. 21:1-88.

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Post-test Question 1

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