

Antimicrobial Stewardship Hot Topics 2022

Antimicrobial Stewardship Committee

March – Asymptomatic Bacteriuria (ASB)

What is ASB?

Urinary tract infections (UTI) are the fifth most common type of healthcare-associated infection and account for 9.5% of infections in hospitals. National Healthcare Safety Network data from 2015 estimated 62,700 reports of UTIs in acute care hospitals.¹ While treatment of UTIs is commonplace, these are oftentimes misdiagnosed due to ambiguity of diagnosis. Many traditional definitions of UTI, such as presence of bacteriuria, are uninformative in identifying patients who would benefit from treatment. Common misconceptions of diagnostic criteria such as bacteriuria, pyuria, discolored urine, nitrites, leukocyte esterase and delirium can lead to overtreatment and harm associated with antibiotic use.²

ASB refers to isolation of bacteria in an appropriately collected urine specimen in the absence of urinary symptoms (e.g., suprapubic pain, urinary urgency, dysuria, and increased frequency). While there is lack of data supporting benefits of treatment and data supporting potential harms of treatment, practitioners often treat these as true infections.³ This perhaps stems from the desire to actively treat disease and from the fear of error or omission of treatment; however, this often leads to overuse of antibiotics, which in turn increases risk for adverse effects and *Clostridioides difficile* infections.⁴ Increased antimicrobial use increases antimicrobial resistance, and therefore bacteria isolated from UTIs have evolved to now include more extended-spectrum beta-lactamase-producing and carbapenemase-producing Enterobacteriaceae.³

ASB is common and the prevalence changes according to different patient factors (Table 1). ASB is more common in females compared to males and prevalence increases with age, diabetes, hemodialysis, and catheter use. Of note, patients with long-term catheter use will virtually all experience ASB as well as pyuria, making both the presence of bacteria and/or pyuria poor positive predictors of a true UTI.

While clinicians may be inclined to treat ASB due to presence of bacteria in the urine, the 2019 IDSA guidelines recommend against treatment in most clinical scenarios, as large cohort studies have demonstrated no adverse outcomes with untreated ASB.⁵⁻⁷ Further, randomized studies of treatment versus no treatment report a decrease in bacteriuria at 6 months but no difference in number of symptomatic episodes.⁸ Additional studies in elderly patients report higher adverse events with treatment, higher rates of re-infection, and increases in infections due to resistant organisms. The two patient populations with ASB that should be treated, as recommended by the IDSA guidelines, include pregnant patients or those undergoing urologic procedures.³

Table 1. Prevalence of asymptomatic bacteriuria in selected	
Population	Prevalence (%)
Healthy, premenopausal women	1.0-5.0
Pregnant women	1.9-9.5
Postmenopausal women (age 50-70 years)	2.8-8.6
Diabetic Patients	
Women	10.8-16
Men	0.7-11
Elderly persons in the community	
Women	10.8-16
Men	3.6-19
Elderly persons in a long-term care facility	
Women	25-50
Men	15-50
Patients with spinal cord injuries	
Intermittent catheter use	23-69
Sphincterotome and condom catheter	57
Patients undergoing hemodialysis	28
Patients with indwelling catheter use	
Short-term (<30 days)	3-5(per day)
Long-term (>30 days)	100

Common Misconceptions:

Treatment of ASB does not improve clinical outcomes in most patients, with the exception of pregnant women and patients undergoing urologic procedures.³ Further, treatment with antibiotics may increase the risk of adverse events such as *Clostridioides difficile* infection.⁹ However, despite these risks, a report from the Centers for Disease Control and Prevention (CDC) in 2014 stated that UTI treatment was avoidable 39% of the time.¹⁰ There are a variety of misconceptions and ideas surrounding what constitutes a UTI, how it is diagnosed, and how it is treated, which make avoidance of treatment difficult.

One common symptom that often gets attributed to a UTI is altered mental status in elderly patients, especially when patients arrive to the Emergency Department. This, along with falls in elderly patients, can lead clinicians to obtain a urine culture and treat if there is bacterial growth. However, studies suggest that even in the presence of pyuria or bacteriuria, it is reasonable to monitor elderly patients that are clinically stable off antibiotics for 24-48 hours while ruling out other diagnoses.¹¹ Other potential causes of altered mental status include polypharmacy, adverse drug reactions, hypoxia and dehydration and should be thoroughly assessed prior to attributing these symptoms to a UTI. One study by Langford et al reviewed 11,014 antimicrobial stewardship recommendations and found that recommendations surrounding limiting duration of therapy or stopping antibiotics were less likely to be accepted than recommendations aiming to increase antibiotic exposure. This demonstrates that it may be difficult to stop antibiotics once they are started; therefore, initial monitoring should be carefully considered prior to starting antibiotics in those that are clinical stable.¹²

Another common misconception is that cloudy or foul-smelling urine indicate UTI; however, these characteristics should not be used to diagnose a UTI. Urine odor is often due to patients' hydration status and concentration of urea in the urine, rather than a bacterial infection.¹¹ Advani et al describes knowledge gaps and practices of physicians versus nursing in terms of adherence to the IDSA guidelines. They found that nurses were more likely to consider a change in appearance of urine as an indication to get a urine culture and physicians were more likely to order urine cultures if there was pyuria present. Neither of these characteristics are always indicative of a UTI, and urine cultures are only necessary if symptoms are present. This study highlights the importance of education regarding guideline-recommended practices to different members of the team.¹³

Utility of the Urinalysis (UA)

The UA is often performed prior to a urine culture, which clinicians will use to assist in their diagnosis of a UTI; however, the different components have varying sensitivity and specificity (Table 2).¹⁴ This may be done by two methods: the clean-catch and the urine dipstick. The clean-catch method is adequate for both men and women and involves cleansing external genitalia and collecting urine in a cup midstream. Squamous epithelial cells are large and irregularly shaped cells which indicate a contaminated specimen when present. The urine dipstick on the other hand involves dipping test strips into a cup of urine to determine if certain components of the UA are present. It is often associated with high rates of false positives.¹⁴

Often, urine cultures have been obtained without any documented signs or symptoms infection which can influence clinical decision making and lead to antibiotic treatment. Several studies have demonstrated decreases in unnecessary urine cultures through reflex or “conditional” urine culturing.^{16,17} This means that urine cultures are only performed when certain criteria in the UA indicate inflammation or presence of bacteria. One study out of the several Veterans Affairs (VA) hospitals sought to decrease urine culturing and treatment by implementing a reflex urine culture if the UA was positive. Several sites (intervention sites) implemented a UA reflex to urine culture whereas other sites (control sites) did not. They found a 5.9% decrease in urine cultures at intervention sites ($p = 0.8$) and a 21% decrease relative to control sites that did not make this implementation ($p < .01$). There were no differences in rates of gram-negative bloodstream infections among intervention and control sites. This study demonstrates the impact of UA reflex to culture in diagnostic stewardship.¹⁵

Any amount of bacteria present in the urine may suggest a UTI in a symptomatic patient but presence of bacteria alone is not indicative of a UTI. The classic threshold for the definition of bacteriuria is 5+, which equates to 100,000 colony-forming-units (CFU), although lower counts in addition to urinary symptoms can still constitute a UTI. In fact, 30-50% of women with cystitis will have colony counts of 10^2 to 10^4 . Therefore, a culture with no growth reported in a woman with a symptomatic UTI should be interpreted cautiously.¹⁵ While bacteria in the urine alone should not be used to diagnose a UTI, it does have a high sensitivity and specificity for detection of pyuria.³

Pyuria is defined by a white blood cell count (WBC) in the urine of >10 /high power field (HPF) and is associated with a low specificity and positive predictive value. The absence of pyuria on the other hand is associated with a strong negative predictive value (90%) and its absence virtually eliminates the possibility of UTI. Leukocyte esterase is another component of the UA that can be used as a surrogate for pyuria. Nitrites in the urine indicate that bacteria in the urine is reducing nitrates to nitrites. Many gram-negative organisms are capable of this conversion. One notable exception is *Pseudomonas aeruginosa*, which cannot reduce nitrates and therefore contributes to the low sensitivity for this component of the UA.

While all of these UA findings may be present in a true urinary tract infection, positivity of some/all of these components of the UA do not imply a UTI is present. Therefore, it is important to critically evaluate the UA in conjunction with patient-reported symptoms to truly diagnose a UTI.¹⁴

Test	Usual Range	Indicators of Infection	Accuracy
Bacteria	Absent	Any Amount	Low Sensitivity (46-58%) High Specificity (89-94%)
Leukocyte esterase	Absent	Positive = pyuria, presence of WBC in the	High Sensitivity (72-97%) Low Specificity (41-86%)
WBC	<5/hpf	Pyuria = >10/hpf WBC	High Sensitivity (90-96%) Low Specificity (47-50%)
RBC	<5/hpf	Hematuria common in infection	Low Sensitivity (18-44%) High Specificity (88-89%)
Epithelial Cells	<5/hpf	<5 = good urine sample	High epithelial cells indicate contamination with skin flora
Nitrite	Absent	Positive = presence of certain bacteria in the urine	Low sensitivity (19-48%) High specificity (92-100%)
pH	4.5-8	pH increased if urea- splitting organism is present (<i>Proteus mirabilis</i>)	Does not indicate UTI - many causes for change in urine pH (diet, urine glucose, etc.)

Tools for antimicrobial stewardship and de-escalation

The CDC has a guidance document for implementation of Antibiotic Stewardship Elements at Small and Critical Access Hospitals, which outlines several potential strategies for minimizing treatment of ASB.¹⁰ They suggest implementing policies surrounding urine culture orders to ensure that positive urine cultures are more likely representative of true infection.

1. **Avoid Culturing:** only order urine cultures if a patient has symptoms of a UTI (dysuria, urgency, frequency, flank pain, or pelvic discomfort). Additionally, they recommend avoiding urine cultures in patients with catheters with foul-smelling or cloudy urine in the absence of signs/symptoms of UTI.
2. **Avoid Prescribing:** only treat with antibiotics if a patient endorses symptoms (dysuria, increased frequency/urgency, suprapubic pain, fever, or flank pain). Avoid prescribing in the absence of these symptoms when bacteriuria is present unless the patient is pregnant or undergoing invasive urologic procedures
 - a. **Pregnant Patients:**¹⁸ the US Preventative Services Task Force (USPSTF) updated recommendations in 2019 and down-graded their recommendation to screen and treat pregnant patients from a level A evidence to B evidence for screening and treating ASB

in pregnant patients due to previous studies using outdated regimens and new studies showing potential harms. They conclude with moderate certainty that there is moderate net benefit.

i. **Benefits:** Previous studies showed benefit of treating ASB in pregnant patients by reducing rates of pyelonephritis, however all of these studies were conducted in the 1960s and 1970s with the two most recent studies in 1987¹⁹ and 2015²⁰. Rates of pyelonephritis were considerably higher in the older studies vs. the newer studies (7-36% vs. 2.2 and 2.5% respectively).¹⁸⁻²⁰ These newer data suggest that the magnitude of the benefit may be reduced compared to earlier studies.

ii. **Harms:** Earlier studies did not account for potential harms such as adverse effects of antibiotics or changes to the microbiome.¹⁸

iii. **Positive Test:** >100K CFU of a uropathogen or >10K CFU of group B Streptococcus

b. **Patients Undergoing Endourological Procedures (i.e. TURP, ureteroscopy, percutaneous stone injury):**³ Guidelines recommend obtaining urine culture in patients undergoing endoscopic urologic procedures due to associated mucosal trauma and avoidance of serious postoperative complication of sepsis.

i. Obtain culture prior to procedure and prescribed targeted antimicrobial therapy (rather than empiric) x 1 or 2 doses (rather than prolonged therapy) administered 30-60 minutes prior to the procedure.

3. **Targeting Audit and Feedback:** Use the shortest duration of therapy possible with the narrowest spectrum agent when treating UTIs. This is based on pathogen, susceptibility results and resolution of signs/symptoms of infection.

Diagnostic stewardship can be implemented to target cases of ASB and reduce unnecessary treatment with antibiotics. Since urine cultures are non-specific for infection, these can lead to misdiagnosis and overtreatment. One study used a RAND-modified Delphi approach which characterized expert opinion best practices for utilizing diagnostics as stewardship tools. The best practices for urine culture identified were requiring a presence and documentation of signs of symptoms of UTI when ordering urine cultures and replacing stand-alone urine cultures with reflex urine cultures.²¹

At Duke University Hospital, our antimicrobial stewardship team has attempted to target interventions related to ASB through best practice alerts (BPA). Clinical decision support system (CDSS)

implementation is an effective strategy to improve stewardship-related outcome measures and may be useful to quickly identify ASB-treated patients. A BPA was created to identify patients with possible ASB for antimicrobial stewardship (AS) review. AS pharmacists received a BPA for patients with the following:

- 1) a new inpatient antibiotic order, AND
- 2) an associated genitourinary indication, AND
- 3) a preceding urinalysis within 7 days with 0-5 WBC/HPF .

We later performed a pre- and post-BPA retrospective review to determine median time to target intervention and number of stewardship interventions documented in EPIC I-vents. Three hundred twenty-seven antibiotic orders met BPA criteria (245 orders in the pre-BPA group and 82 in the post-BPA group). The median time to intervention was shorter in the post-BPA group compared to the pre-BPA group (13.5 hours vs. 28 hours ($p = 0.03$)). Pre-BPA UTI-related intervention rate was also lower compared to post-BPA (11.0% vs. 20.7%, $p = 0.04$).

Automatic identification of antibiotics targeting UTI with urinalysis showing absence of pyuria reduced the time to AS intervention and increased rate of UTI-specific interventions. Therefore, the use of CDSS may aid in efficiency of AS reviews and syndrome-targeted impact.

Significant bacteriuria is common and generally does not require antibiotics. It is important to critically evaluate clinical data such as a urinalysis in combination with patient symptoms when assessing who will benefit from treatment versus those who may experience harm from treatment. Educating healthcare providers on diagnostic approaches and common misconceptions may help prevent overtreatment. In addition, diagnostic stewardship may be a way to quickly identify patients who warrant discontinuation of antibiotic therapy.

References:

1. Centers for Disease Control and Prevention. Urine culture stewardship in patients without indwelling urinary catheters. [Urinary Tract Infection \(Catheter-Associated Urinary Tract Infection \[CAUTI\] and Non-Catheter-Associated Urinary Tract Infection \[UTI\]\) Events](#). Accessed February 20, 2022.
2. Finucane TE. "Urinary Tract Infection"-Requiem for a Heavyweight. *J Am Geriatr Soc*. 2017;65(8):1650-1655. doi:[10.1111/jgs.14907](https://doi.org/10.1111/jgs.14907)

3. Nicolle LE, Gupta K, Bradley SF, et al. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. Published online March 21, 2019. doi:[10.1093/cid/ciy1121](https://doi.org/10.1093/cid/ciy1121)
4. Kim JH et al. Observations on spiraling empiricism: its causes, allure, and perils, with particular reference to antibiotic therapy. *Am J Med*. 1989 Aug;87(2):201-6. doi: [10.1016/s0002-9343\(89\)80697-7](https://doi.org/10.1016/s0002-9343(89)80697-7)
5. Gustafson D, Lissner L, Bengtsson C, Björkelund C, Skoog I. A 24-year follow-up of body mass index and cerebral atrophy. *Neurology*. 2004 Nov 23;63(10):1876-81. doi: [10.1212/01.wnl.0000141850](https://doi.org/10.1212/01.wnl.0000141850).
6. Tencer J. Asymptomatic bacteriuria--a long-term study. *Scand J Urol Nephrol*. 1988;22(1):31-4. doi: [10.1080/00365599.1988.11690380](https://doi.org/10.1080/00365599.1988.11690380).
7. Evans DA, Kass EH, Hennekens CH, Rosner B, Miao L, Kendrick MI, Miall WE, Stuart KL. Bacteriuria and subsequent mortality in women. *Lancet*. 1982 Jan 16;1(8264):156-8. doi: [10.1016/s0140-6736\(82\)90393-2](https://doi.org/10.1016/s0140-6736(82)90393-2).
8. Boscia JA, Kobasa WD, Knight RA, Abrutyn E, Levison ME, Kaye D. Therapy vs no therapy for bacteriuria in elderly ambulatory nonhospitalized women. *JAMA*. 1987 Feb 27;257(8):1067-71. PMID: [3806896](https://pubmed.ncbi.nlm.nih.gov/3806896/).
9. Johnson S et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. *Clinical Infectious Diseases*. 2021;73(5):e1029-e1044. doi:[10.1093/cid/ciab549](https://doi.org/10.1093/cid/ciab549)
10. Centers for Disease Control and Prevention. Urine culture stewardship in patients without indwelling urinary catheters. [Patients without Indwelling Urinary Catheters | Urine Culture Stewardship | HAI | CDC](#). Accessed February 20, 2022.
11. Schulz L et al. Top Ten Myths Regarding the Diagnosis and Treatment of Urinary Tract Infections. *The Journal of Emergency Medicine*. 2016;51(1):25-30. doi:[10.1016/j.jemermed.2016.02.009](https://doi.org/10.1016/j.jemermed.2016.02.009)
12. Langford BJ, Nisenbaum R, Brown KA, Chan A, Downing M. Antibiotics: easier to start than to stop? Predictors of antimicrobial stewardship recommendation acceptance. *Clin Microbiol Infect*. 2020 Dec;26(12):1638-1643. doi: [10.1016/j.cmi.2020.07.048](https://doi.org/10.1016/j.cmi.2020.07.048). Epub 2020 Aug 6.
13. Advani SD, Gao CA, Datta R, Sann L, Smith C, Leapman MS, Hittelman AB, Sabetta J, Dembry LM, Martinello RA, Juthani-Mehta M. Knowledge and Practices of Physicians and Nurses Related to Urine Cultures in Catheterized Patients: An Assessment of Adherence to IDSA Guidelines. *Open Forum Infect Dis*. 2019 Aug 1;6(8):ofz305. doi: [10.1093/ofid/ofz305](https://doi.org/10.1093/ofid/ofz305).

14. Simerville JA et al. Urinalysis: a comprehensive review. *Am Fam Physician*. 2005 Mar 15;71(6):1153-62. Erratum in: *Am Fam Physician*. 2006 Oct 1;74(7):1096. [PMID: 15791892](#).
15. Claeys KC, Zhan M, Pineles L, et al. Conditional reflex to urine culture: Evaluation of a diagnostic stewardship intervention within the Veterans' Affairs and Centers for Disease Control and Prevention Practice-Based Research Network. *Infect Control Hosp Epidemiol*. 2021;42(2):176-181. doi:[10.1017/ice.2020.400](#)
16. Stagg A, Lutz H, Kirpalaney S, et al. Impact of two-step urine culture ordering in the emergency department: a time series analysis. *BMJ Qual Saf* 2018;27:140–147. 15. doi:[10.1136/bmjqs-2016-006250](#)
17. Epstein L, Edwards JR, Halpin AL, et al. Evaluation of a novel intervention to reduce unnecessary urine cultures in intensive care units at a tertiary-care hospital in Maryland, 2011–2014. *Infect Control Hosp Epidemiol* 2016;37:606–609. doi: [10.1017/ice.2016.9](#)
18. US Preventive Services Task Force, Owens DK, Davidson KW, et al. Screening for Asymptomatic Bacteriuria in Adults: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2019;322(12):1188. doi:[10.1001/jama.2019.13069](#)
19. Foley ME, Farquharson R, Stronge JM. Is screening for bacteriuria in pregnancy worthwhile? *Br Med J (Clin Res Ed)*. 1987;295(6592):270. doi:[10.1136/bmj.295.6592.270](#)
20. Kazemier BM, Koningstein FN, Schneeberger C, et al. Maternal and neonatal consequences of treated and untreated asymptomatic bacteriuria in pregnancy: a prospective cohort study with an embedded randomised controlled trial. *Lancet Infect Dis*. 2015;15(11):1324-1333. doi:[10.1016/S1473-3099\(15\)00070-5](#)
21. Claeys KC et al. Optimal Urine Culture Diagnostic Stewardship Practice– Results from an Expert Modified-Delphi Procedure. *Clinical Infectious Diseases*. Published online November 29, 2021:ciab987. doi:[10.1093/cid/ciab987](#)

Prepared by: Elizabeth Keil, PharmD, PGY2 Infectious Diseases Pharmacy Resident, Duke University Hospital

Reviewers

Rebekah Wrenn, PharmD, BCIDP, Residency Program Director, Infectious Diseases Pharmacy Programs, Duke University Hospital

Connor Deri, PharmD, BCIDP, Residency Program Coordinator, Infectious Diseases Pharmacy Programs, Duke University Hospital

Carla J Walraven, PharmD, BCIDP, Antimicrobial Stewardship/Infectious Diseases Pharmacist,
University of New Mexico Hospital

Ethan A. Smith, PharmD, BCIDP, Program Coordinator – Antimicrobial Stewardship, Cedars-Sinai
Medical Center

Disclaimer: The information contained in this document is intended for informational purposes for members of the Vizient Pharmacy Network Antimicrobial Stewardship Community Group only and is in no way intended to be a substitute for or in any manner to be construed as direct medical or clinical advice. Please feel free to share within your institution, but we request that you do not distribute to non-Vizient members or affiliates. For additional distribution permissions, or for more information, please contact gretchen.brummel@vizientinc.com, ethan.smith@cshs.org, or cwalraven@salud.unm.edu.