favoring older adults with comorbidities and greater risk of antibiotic-resistant infection.[9] Antibiograms that accurately reflect the diverse ambulatory population that emergency physicians care for are needed to better inform empiric antibiotic prescribing practices. Their validity may be improved when urine culture is obtained as part of the evaluation for uncomplicated cystitis in both young, healthy patients without comorbid illnesses and those who may be colonized with antibiotic-resistant organisms. ED-specific antibiograms can effectively drive changes in antibiotic prescribing for urinary tract infection.[10]

Appropriately targeted antibiotic therapy at the patient level and data-driven empiric treatment strategies at the population level promote ED antibiotic stewardship. Antibiotic therapy tailored to urine culture and susceptibility testing reduces the likelihood of an incompletely treated infection. In situations in which uncomplicated cystitis is difficult to distinguish clinically from pyelonephritis, urine culture can guide adjustments in therapy should a therapeutic failure arise and increase the safety and acceptability of prescribing empiric antibiotics that achieve therapeutic levels only in the urine (eg, nitrofurantoin), even when pyelonephritis cannot be excluded according to history and physical examination (eg, subjective fever, borderline costovertebral angle tenderness). ED-specific antibiograms can further improve emergency physician confidence in the empiric use of narrow-spectrum antibiotics and increase treatment success on the first pass for a broader range of urinary tract infections. Cure of infection with a narrow-spectrum antibiotic or one that concentrates only in the urine minimizes collateral damage to the patient's gastrointestinal microbiome. Such disruptions, commonly associated with fluoroquinolones and broad-spectrum cephalosporins, can lead to the emergence of antibiotic-resistant organisms and *Clostridium difficile* infection. Thoughtful and deliberate use of antibiotics to treat uncomplicated cystitis allows us to be better stewards of finite and diminishing antibiotic resources.

In an era of mounting antibiotic resistance, urine culture remains our primary means of determining whether a prescribed antibiotic for uncomplicated cystitis will be effective against the infecting pathogen. It is also the backbone on which local antibiotic resistance rates are determined and reported to prescribers through antibiograms. Although a single urine culture may not change the management of uncomplicated cystitis in the ED, a population-focused approach to culture and susceptibility testing paints a bigger picture of the evolving epidemiology of urinary tract infection and antibiotic resistance, better and more accurately guiding clinical practice. Future research characterizing ED treatment failure rates for uncomplicated cystitis, the effect of ED-specific antibiograms on treatment success, and the true value of using empiric antibiotics that are narrow spectrum or that concentrate primarily in the urine in curbing antibiotic resistance in ED populations will help optimize our use of urine culture in the management of uncomplicated cystitis.

https://doi.org/10.1016/j.annemergmed.2018.06.012

REFERENCES

1. Gupta K, Hooton TM, Naber KG, et al. 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. *Clin Infect Dis*. 2011;52:e103-e120.
2. Dumkow LE, Kenney RM, MacDonald NC, et al. Impact of a multidisciplinary culture follow-up program of antimicrobial therapy in the emergency department. *Infect Dis Ther*. 2014;3:45-53.
3. Lingenfelter E, Drapkin Z, Fritz K, et al. ED pharmacist monitoring of provider antibiotic selection aids appropriate treatment for outpatient UTI. *Am J Emerg Med*. 2016;34:1600-1603.
4. Talan DA, Takhar SS, Krishnadasan A, et al. Fluoroquinolone-resistant and extended-spectrum β-lactamase-producing *Escherichia coli* infections in patients with pyelonephritis, United States. *Emerg Infect Dis*. 2016;22:1594-1603.
5. Fleming VH, White BP, Southwood R. Resistance of *Escherichia coli* urinary isolates in ED-treated patients from a community hospital. *Am J Emerg Med*. 2014;32:864-870.
6. Rosa R, Abbo LM, Raney K, et al. Antimicrobial resistance in urinary tract infections at a large urban ED: factors contributing to empiric treatment failure. *Am J Emerg Med*. 2017;35:397-401.
7. Grodin L, Conigliaro A, Lee SY, et al. Comparison of UTI antibiograms stratified by ED patient disposition. *Am J Emerg Med*. 2017;35:1269-1275.
8. Jorgensen S, Zurayk M, Yeung S, et al. Emergency department urinary antibiograms differ by specific patient group. *J Clin Microbiol*. 2017;55:2629-2636.
9. Hines MC, Al-Salamah T, Heil EL, et al. Resistance patterns of *Escherichia coli* in women with uncomplicated urinary tract infection do not correlate with emergency department antibiogram. *J Emerg Med*. 2015;49:998-1003.
10. Percival KM, Valenti KM, Schmittling SE, et al. Impact of an antimicrobial stewardship intervention on urinary tract infection treatment in the ED. *Am J Emerg Med*. 2015;33:1129-1133.

URINE CULTURE AND UNCOMPLICATED CYSTITIS: THE MINUSES OUTWEIGH THE PLUSES

Brit Long, MD
Department of Emergency Medicine
San Antonio Uniformed Services Health Education Consortium
Fort Sam Houston, TX

Alex Koyfman, MD
The University of Texas Southwestern Medical Center
Department of Emergency Medicine
Dallas, TX

Urinary tract infection consists of a spectrum of clinical infectious diseases. Acute, uncomplicated cystitis is an

infection of the lower urinary tract in nonpregnant premenopausal women.[1,2] Acute pyelonephritis and complicated urinary tract infections (structural or functional urinary tract abnormality, urinary instrumentation or obstruction, renal transplant, older age, male sex, pregnancy, immunosuppression, recent hospitalization or antibiotic therapy [within 30 days], renal failure, and patients with prolonged symptoms [>7 days]) are managed differently than uncomplicated cystitis. Urine cultures for these other urinary tract infections are recommended because of the higher rate of treatment failure.[1,2] Although recommendations advise against obtaining urine cultures in uncomplicated cystitis,[1] many physicians order these cultures perhaps because of concern about a resistant organism, fear of misdiagnosis, or as a component of an order set. However, urine cultures rarely lead to a meaningful change in management for acute uncomplicated cystitis because of the high efficacy of empiric treatment; laboratory costs and follow-up of routine urine cultures would add unnecessary expense and a time burden on emergency department (ED) personnel.

The most common causative organism in cystitis is *Escherichia coli*, responsible for 80% to 95% of infections.[1-3] Other common organisms include other Enterobacteriaceae and *Staphylococcus saprophyticus*.[1-3] Diagnosis of cystitis typically includes signs and symptoms (ie, dysuria, frequency, and urgency) in combination with urine assessment, with treatment focusing on common organisms. Female patients with at least 2 signs or symptoms of cystitis and no vaginal discharge or irritation possess a positive likelihood ratio of 24.6 for diagnosis of urinary tract infection.[4] In the proper clinical context, urinalysis and clinical findings can reliably diagnose cystitis, without urine culture.

The Infectious Diseases Society of America's guidelines for cystitis include nitrofurantoin, which is recommended for almost all cases of uncomplicated cystitis, unless the patient has an allergy (rare) or low renal function.[1] Empiric therapy is based on the bacteriology of cystitis in women and antibiotic pharmacokinetics and pharmacodynamics; it is associated with low risk of collateral damage, including effect on intestinal flora, increase in microbial resistance, and renal injury.[1,5,6] Urine cultures report 2 important components: a specific organism and the minimum inhibitory concentration, which is determined by testing against achievable blood levels of the antibiotic.[5,7] However, this testing does not reflect patient-specific factors, urine drug concentrations, or in vivo medication effects.[5,7] The minimum inhibitory concentration reported by a laboratory is based on blood minimum inhibitory concentration, not urine minimum inhibitory concentration. Antibiotic concentrations in the urine are high enough to overcome resistance reported by urine susceptibility testing, even with reported blood resistance to a particular antibiotic. Common cystitis pathogens are susceptible to the concentrations routinely achieved in the urine for nitrofurantoin and other recommended empiric treatments for cystitis.[1,5,8] There is no difference in cure rate when the urinary pathogen is not susceptible to the prescribed antibiotic according to the blood minimum inhibitory concentration.[5,9,10] Studies evaluating placebo for uncomplicated cystitis found clinical cure in 25% to 42% of patients who do not receive antibiotics or are treated with antibiotics without in vitro activity against the specific uropathogen.[1,5,11] Thus, in vitro susceptibility does not necessarily predict the clinical effectiveness of antibiotics that are concentrated in the urine.[5,7,9]

Routine cultures can present several challenges to ED care because they increase total cost and time spent by clinicians following up culture results.[5,12,13] A very low proportion of urine cultures lead to a meaningful modification in management or follow-up, with studies suggesting less than 2%.[12,13] Urine cultures in uncomplicated cystitis are associated with increased costs (>$50/patient, based on location and local costs). Urine culture results do not return in a sufficient time to affect initial empiric therapy as well.[1,13] The potential for contaminated specimens and false-positive results can also result in confusion when urine cultures are interpreted and may confound management. Greater than 25% of urine cultures are falsely positive, potentially exposing patients to adverse medication effects.[14,15]

Rather than obtaining routine urine cultures for patients with cystitis, we recommend empiric therapy with nitrofurantoin, providing return precautions, and obtaining urine cultures for those who fail to improve with antibiotics.[1,5,15] Uncomplicated cystitis is rarely associated with progression to sepsis or sudden death, even if organisms are resistant to prescribed antibiotics at concentrations found in blood or tissue.[1,5] If symptoms continue, other conditions should be considered such as a sexually transmitted infection, and we recommend a urine culture at this time. Ordering urine cultures only for patients who have failed empiric treatment would result in a large reduction in the number of cultures performed, without significantly increasing the risk of treatment failure. Clinical response, rather than culture and minimum inhibitory concentration results, should be the criterion for successful treatment of uncomplicated cystitis.

This review does not reflect the views or opinions of the US government, Department of Defense, US Army, US Air Force, or SAUSHEC EM Residency Program.

https://doi.org/10.1016/j.annemergmed.2018.06.008

REFERENCES

1. Gupta K, Hooton TM, Naber KG, et al. 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. *Clin Infect Dis*. 2011;52:E103-E120.
2. Hooton TM. Uncomplicated urinary tract infection. *N Engl J Med*. 2012;366:1028-1037.
3. Hooton TM, Scholes D, Hughes JP, et al. A prospective study of risk factors for symptomatic urinary tract infection in young women. *N Engl J Med*. 1996;335:468-474.
4. Bent S, Nallamothu BK, Simel DL, et al. Does this woman have an acute uncomplicated urinary tract infection? *JAMA*. 2002;287:2701-2710.
5. Wenzler E, Danziger LH. Urinary tract infections: resistance is futile. *Antimicrob Agents Chemother*. 2016;60:2596-2597.
6. Mavromanolakis E, Maraki S, Samonis G, et al. Effect of norfloxacin, trimethoprim-sulfamethoxazole and nitrofurantoin on fecal flora of women with recurrent urinary tract infections. *J Chemother*. 1997;9:203-207.
7. Doern GV, Brecher SM. The clinical predictive value (or lack thereof) of the results of in vitro antimicrobial susceptibility tests. *J Clin Microbiol*. 2011;49:S11-S14.
8. Drago L, Nicola L, Mattina R, et al. In vitro selection of resistance in *Escherichia coli* and *Klebsiella* spp. at in vivo fluoroquinolone concentrations. *BMC Microbiol*. 2010;10:119.
9. Hooton TM, Scholes D, Gupta K, et al. Amoxicillin-clavulanate vs ciprofloxacin for the treatment of uncomplicated cystitis in women: a randomized trial. *JAMA*. 2005;293:949-955.
10. Cole KA, Kenney RM, Perri MB, et al. Outcomes of aminopenicillin therapy for vancomycin resistant enterococcal urinary tract infections. *Antimicrob Agents Chemother*. 2015;59:7362-7366.
11. Christiaens TC, De Meyere M, Verschraegen G, et al. Randomised controlled trial of nitrofurantoin versus placebo in the treatment of uncomplicated urinary tract infection in adult women. *Br J Gen Pract*. 2002;52:729-734.
12. Poon E, Self L, Mcleod SL, et al. Do urine cultures in the emergency department change management of young women with symptoms of uncomplicated urinary tract infection? *CJEM*. 2016;18:S77.
13. Johnson JD, O'Mara HM, Durtschi HF, et al. Do urine cultures for urinary tract infections decrease follow-up visits? *J Am Board Fam Med*. 2011;24:647-655.
14. Khawcharoenporn T, Vasoo S, Ward E, et al. Abnormal urinalysis finding triggered antibiotic prescription for asymptomatic bacteriuria in the ED. *Am J Emerg Med*. 2011;29:828-830.
15. Pallin DJ, Ronan C, Montazeri K, et al. Urinalysis in acute care of adults: pitfalls in testing and interpreting results. *Open Forum Infect Dis*. 2014;1:ofu019.