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Improving the Culture of Culturing: Critical Asset to Antimicrobial Stewardship

To the Editor—We read with interest the study by Mullin et al[1] to reduce catheter-associated urinary tract infections (CAUTIs) in intensive care units (ICUs). The authors focused on optimizing the use of urine cultures and urinary catheter care. The effort led to a reduction in urine culturing in adult ICUs of 41%–80% and more than one-third in the National Healthcare Safety Network (NHSN) defined CAUTI between 2013 and 2014, without much change in device utilization. Compliance with appropriate testing was not reported. These findings highlight 2 important issues: (1) the link between the NHSN surveillance definition and culturing practices and (2) the importance of appropriate testing for CAUTI as a pillar for antimicrobial stewardship.

Nationally, the NHSN CAUTI definition has been used to evaluate quality initiatives to reduce urinary catheter infectious harm, and these definitions have been linked to financial penalties for underperforming hospitals. However, the reliance of this definition on fever and a positive urine culture makes it susceptible to changes in culturing practices.[2] The artificial improvements in NHSN-defined events based on reductions in culturing do not necessarily equate to preventing clinical CAUTIs. They may even provide a false sense of success in combatting CAUTI in ICUs where we have seen little movement.[3] Other measures such as device utilization are not susceptible to testing practices and may better reflect care.[2]

Asymptomatic bacteriuria is common among catheterized patients.[4] Orders for obtaining urine cultures are influenced by the clinician's "practice culture." Practices that utilize "screening cultures on admission," "standing orders," or "reflex" urine cultures based on urinalysis results may lead to inappropriate diagnoses and/or antimicrobial use. In addition, clinicians often order urine cultures in catheterized patients based on pyuria, urine odor, color, or turbidity, actions that are discouraged by the Infectious Diseases Society of America guidelines.[5] Such actions also increase utilization of additional resources (eg, testing, antibiotics, consultations) and adversely expose patients to unnecessary testing and treatments.[6] More importantly, inappropriately obtained urine cultures may lead to the wrong diagnosis. Ensuring that frontline physicians and nurses are aware of the indications for testing as well as the risks associated with inappropriate testing are good first steps to improving care (Table 1).[7]

We suggest a 2-pronged approach to reducing unnecessary urine cultures in catheterized patients. First, we recommend the establishment of an optimized process for obtaining urinalyses and urine cultures. A thorough review of pathways, order sets, policies, and institutional guidelines is needed to ensure best-practice integration. Such a review must include any orders or testing processes embedded into the electronic medical records. For example, pathways or order sets geared toward specific conditions (eg, pneumonia or congestive heart failure) should avoid incorporating tests such as urine cultures to help curb unnecessary use. Moreover, preoperative urine cultures should be avoided in asymptomatic patients that are not undergoing urologic procedures. Testing in populations with a high prevalence of asymptomatic bacteriuria (eg, the elderly or those with urinary catheters) often results in identifying colonized patients, placing them at risk to be exposed to antibiotics unnecessarily. Reflex cultures in catheterized patients based on abnormal urinalysis results (with no consensus on what constitutes abnormal urinalysis to trigger a culture) are frequently used as a convenience to avoid submitting a second

TABLE 1. When to Obtain or Not Obtain a Urine Culture in a Patient With an Indwelling Urinary Catheter

Appropriate Urine Culture Use
• Part of an evaluation of sepsis without a clear source (ie, CAUTI is often a diagnosis by exclusion)
• Based on local findings suggestive of CAUTI (eg, pelvic discomfort or flank pain)
• Prior to urologic surgeries where mucosal bleeding anticipated or transurethral resection of prostate
• Early pregnancy (ie, avoid urinary catheters if possible)
Inappropriate Urine Culture Use
• Urine quality: color, smell, sediments, turbidity (ie, they do not constitute signs of infection)
• Screening urine cultures, whether on admission or before nonurologic surgeries
• Standing orders for urinalysis or urine cultures without an appropriate indication
• "PAN" culturing (ie, mindfulness in evaluating the site of infection is key)
• Obtaining urine cultures based on pyuria in an *asymptomatic* patient
• *Asymptomatic* elderly and diabetics (cf, high prevalence of asymptomatic bacteriuria)
• Repeat urine culture to document clearing of bacteriuria after treatment (cf, no clinical benefit to patients)

urine sample for culture. However, urinalyses are often performed without clinical suspicion of urinary infection, and discovery of pyuria may lead to unnecessary cultures. Pyuria is a common occurrence in patients with urinary catheters and has a low positive predictive value for bacteriuria.[8] Urine cultures based on urinalysis results should only be pursued in symptomatic patients and when CAUTI is suspected in a sepsis workup with no obvious sources.[9] Reflex urine cultures, without clinical assessment, may undermine antimicrobial stewardship efforts. The solution is to integrate only established best practices into the work flow, underscoring "no testing without clinical evaluation."

Second, clinician engagement is of paramount importance in changing a culture of inappropriate testing. Physicians and nurses should be educated on best practices, and clinical leaders should be role models to their peers.[7] Culturing stewardship needs to be viewed as a necessity by all stakeholders, and the benefits should be relayed in a language that resonates with the different teams.[10] For example, "PAN" culturing is frequently used without understanding that certain sites are colonized and that the value of the cultures depend on the suspected site of infection. Infectious diseases specialists and infection preventionists often focus on the risk of *Clostridium difficile* infection and multidrug resistance. We must also highlight the risk of misdiagnosis, which may better capture the attention of other stakeholders such as hospitalists and intensivists. Antimicrobial stewardship teams should also consider incorporating testing stewardship in their efforts to achieve the correct diagnosis, the optimal antimicrobial choice, and the appropriate duration of antimicrobial use. Short of establishing benchmarks for culturing stewardship to gauge success, periodic audits of urine culture use are necessary to identify trends and provide feedback on performance.

In summary, "improving the culture of culturing" should be viewed as an integral component of antimicrobial stewardship. Such an approach is likely to encourage clinicians to use their clinical judgment in their patient evaluations and to move from a reflexive process to a more reflective one, leading to better care.

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Detection of Piperacillin-Tazobactam-Resistant/Pan-β-Lactam-Susceptible *Escherichia coli* with Current Automated Susceptibility Test Systems

TABLE 1. *In vitro* Susceptibility profile of *E. coli* Against Piperacillin-Tazobactam Using Broth Microdilution (BMD) and 3 Automated Susceptibility Test Systems

	Phenotypic Profile Method[a]			
E. coli	BMD (TZP MIC)	MicroScan	Phoenix	Vitek 2
EC C1-6	S (16)	S	S	S
EC C2-9	R (512)	**I**	R	R
EC C3-23	R (≥2048)	R	R	R
EC C1-7	S (4)	S	S	S
EC C1-23	S (16)	S	S	S
EC C6-25	R (2048)	R	R	R
EC C7-1	R (256)	**S**	**I**	**I**
EC C10-11	R (≥2048)	**I**	R	R
EC C11-14	R (≥2048)	R	R	R
EC C2-5	S (4)	S	S	S
EC C12-1	R (512)	**S**	R	**I**
EC C14-26	R (≥2048)	R	R	R
EC C18-6	R (≥2048)	R	R	R
EC C30-5	R (256)	**I**	R	R

NOTE. TZP, piperacillin-tazobactam; EC, *Escherichia coli*; MIC, minimum inhibitory concentration (μg/mL), S, susceptible; I, intermediate; R, resistant.
[a]Data shown in bold are erroneous results.

To the Editor—The determination of phenotypic antimicrobial resistance via currently available automated susceptibility systems is well established worldwide. Phenotypic testing is continuously challenged by ever-changing alterations in gene expression, genetic mutation, or new gene acquisition from another bacterium.[1] The development of antibiotic resistance increases the risk of clinical failure in infected patients, especially if such resistance is unknown to the clinical practitioner.[2] The global use of automated microbiology test systems, such as MicroScan (Beckman Coulter, Brea, CA), Phoenix (Becton Dickinson Diagnostic Systems, Sparks, MD), and Vitek 2 (bioMérieux, Durham, NC), for the identification and antimicrobial susceptibility testing (AST) of bacteria has grown, but these systems have had serious reporting errors with certain organism-antibiotic combinations.[3–5] We have recently identified 43 *Escherichia coli* isolates from 29 US hospitals that are pan-β-lactam-susceptible (ie, all cephalosporins, monobactams and carbapenems [PBL-S]) but are resistant to piperacillin-tazobactam (TZP-R), a broad-spectrum β-lactamase inhibitor.[6–8] In this study, we assessed the accuracy of the aforementioned systems in determining the susceptibility profile of this unique phenotype.

We sent 14 unidentified clinical isolates of *E. coli*, 4 piperacillin-tazobactam susceptible (TZP-S)/PBL-S and 10 genotypically confirmed TZP-R/PBL-S to 3 sites for AST using MicroScan, Phoenix, and Vitek 2. To assess the accuracy of the categorical results provided by these systems (ie, susceptible, intermediate, or resistant), piperacillin-tazobactam minimum inhibitory concentrations (MICs) were determined in triplicate by broth microdilution (BMD) according to the 2016 Clinical Laboratory Standards Institute guidelines. AST data were determined via specific manufacturer and laboratory guidelines for each system. Categorical errors reported by the automated systems in relation to BMD were classified as very major (false susceptibility), major (false resistance), or minor (involving the intermediate category interpretation).[9]

The MICs of these isolates against piperacillin-tazobactam and the interpretive classification generated by each system are reported in Table 1. Notably, none of the systems demonstrated 100% accuracy in reporting the phenotypic profile when compared with the BMD reference method. Phoenix reported 1 minor error, Vitek 2 demonstrated 2 minor errors, and MicroSca produced the most inconsistent results, with 2 very major errors and 3 minor errors.

These findings are relevant considering that piperacillin-tazobactam is used empirically in compromised hosts or as directed therapy for *E. coli* infections given the retention of high susceptibility rates compared with other available antibiotics.[6,10] Therefore, the detection of this TZP-R/PBL-S phenotype is vital to providing appropriate antimicrobial therapy and optimal patient care. Furthermore, the use of cascade reporting has been implemented in many hospitals to control antibiotic use, which often involves reporting the susceptibilities of broad-spectrum agents only when the organism is resistant to more narrow-spectrum agents. Therefore, cascade reporting may misrepresent the susceptibility of this organism if it is overlooked due to its susceptibility to more narrow-spectrum antimicrobial agents. Although further studies are needed to determine the clinical relevance of these TZP-R/PBL-S strains, the high use of piperacillin-tazobactam and the prevalence of *E. coli* infections make the recognition of this phenotype

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