

LETTERS TO THE EDITOR

Improving Compliance With Antibiotic Stewardship: What Is the Role of Initial Microscopy on the Management of Mechanically Ventilated Patients?

To the Editor—Ventilator-associated pneumonia (VAP) is one of the most serious healthcare-associated infections; it has a high mortality rate, especially in intensive care units (ICUs).¹

Diagnosing VAP is a complex issue, and the precise role of microbiologic parameters such as cultures (if qualitative or quantitative), as well as Gram stain, remain unclear.^{1,2} Microscopic evaluation by Gram stain of easily obtained respiratory secretions, such as endotracheal aspirate (EA), could provide a potentially useful guide to appropriate antimicrobial therapy in patients with suspected VAP.^{2,3}

To evaluate the performance of microscopic examinations by Gram staining of endotracheal aspirates (EAs) recovered from intensive care patients, a prospective study was performed.

Endotracheal aspirates were consecutively recovered from mechanically ventilated patients in an adult ICU in a tertiary hospital of Porto Alegre, southern Brazil, between January 1 and October 3, 2016. Smears were stained with Gram stain and were then cultured quantitatively. As selection criteria, only specimens with <10 squamous epithelial cells by microscopic examination in a low-power field were included in the study. Also, microorganisms presenting growth $\geq 10^6$ colony forming units (CFU) per milliliter of sample plated were considered a positive culture. Results from microscopy and culture were obtained independently and carried out by double-blind analysis.

A total of 717 EAs were obtained. Among them, 52 EAs were excluded due to the presence of >10 epithelial cells, and 13 (1.8%) were excluded due to inconsistent results in the culture (growth of non-pathogenic organisms such as yeasts). In the remaining 652 samples, a negative culture (ie, no bacterial growth $\geq 10^6$ CFU/mL) was observed in 415 (63.6%). Among the 237 positive cultures, gram-negative rods were recovered from 218 (92%) and gram-positive cocci were recovered from

19 (8%). For gram-positive cocci, only *S. aureus* were recovered in sufficient numbers to meet study criteria; only 2 of these (10.5%) were methicillin-resistant (MRSA).

Overall, 560 of 652 (85.9%) samples showed agreement between Gram stain and culture results. The sensitivity, specificity, positive and negative predictive values, and their confidence intervals (95% CI) for clustered gram-positive cocci and gram-negative rods are shown in Table 1.

Fast and accurate microbiological diagnosis of VAP is a major challenge, and no generally accepted gold standard exists for its diagnosis. In recent guidelines by the Infectious Diseases Society of America and the American Thoracic Society on the management of adults with hospital-acquired pneumonia and VAP, noninvasive sampling with semi-quantitative cultures has been suggested instead of invasive sampling with quantitative cultures.¹

Although universally accepted as a useful tool for evaluating clinical specimens, the real value of the Gram stain to guide an empirical approach is also controversial. Detection of gram-positive cocci in clusters on direct microscopic examination of EAs would constitute an important tool in antimicrobial stewardship and the use of anti-gram-positive agents, especially when *S. aureus* is recovered. On the other hand, several studies have pointed to the low sensitivity and positive predictive values of the Gram stain, contradicting its use as a presumptive guide to therapy.²⁻⁵

At our institution, a prior study showed a very high predictive negative value of the Gram stain of EAs when gram-positive cocci in clusters were considered;⁶ this study confirmed a virtually 100% negative predictive value (Table 1). To avoid inappropriate and empirical use of vancomycin, it is important to know when not to use this drug especially in a setting with very low MRSA prevalence, such as ours. For this purpose, the Gram stain serves a crucial purpose, particularly when gram-positive cocci in clusters are concerned.

In conclusion, Gram staining of EAs showed a very high negative predictive value in this study, contributing to a more conservative use of antimicrobials. In healthcare institutions with a low VAP prevalence due to MRSA, a Gram stain of EAs without the presence of gram-positive cocci may be the strongest reason to avoid the use of vancomycin.

TABLE 1. Sensitivity, Specificity, Positive and Negative Predictive Values of Gram-Stain Findings in Relation to the Quantitative Cultures of 652 Endotracheal Aspirates

Variable	Gram Stain Findings Presenting Distinct Bacterial Morphotypes, % (95% CI)		
	Gram-Positive Cocci in Clusters	Gram-Negative Rods	Total
Sensitivity	94.7 (74.0–99.9)	87.6 (82.5–91.7)	88.6 (83.9–92.3)
Specificity	97.1 (95.5–98.3)	90.8 (87.7–93.3)	84.3 (80.5–87.7)
Positive predictive value	50 (32.9–67.1)	82.7 (77.2–87.3)	76.4 (70.9–81.2)
Negative predictive value	99.8 (99.1–100)	93.6 (90.8–95.7)	92.8 (89.7–95.2)

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REFERENCES

1. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016;63:e61–e111.
2. Albert M, Friedrich JO, Adhikari NK, et al. Utility of Gram stain in the clinical management of suspected ventilator-associated pneumonia. Secondary analysis of a multicenter randomized trial. *J Crit Care* 2008;23:74–81.
3. O'Horo JC, Thompson D, Safdar N. Is the gram stain useful in the microbiologic diagnosis of VAP? A meta-analysis. *Clin Infect Dis* 2012;55:551–561.
4. Davis KA, Eckert MJ, Reed RL 2nd, et al. Ventilator-associated pneumonia in injured patients: do you trust your Gram's stain? *J Trauma* 2005;58:462–466.
5. Raghavendran K, Wang J, Belber C, et al. Predictive value of sputum gram stain for the determination of appropriate antibiotic therapy in ventilator-associated pneumonia. *J Trauma* 2007;62:1377–1382.
6. Victorino JA, Dias CG, Ribas EO, et al. Microscopic examination by Gram stain versus quantitative culture of endotracheal aspirates in mechanically ventilated patients. In: 9th Congress of the World Federation of Societies of Intensive and Critical Care Medicine. Buenos Aires, Argentina, 2005.

Improving the Culture of Culturing: Critical Asset to Antimicrobial Stewardship

To the Editor—We read with interest the study by Mullin et al¹ 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