Cultures and Ventilator-Associated Pneumonia

Not How, But How Many

Pneumonia remains a common yet vexing complication of critical illness. While it is the most common nosocomial infection in ICUs, and the one most commonly associated with death, its diagnosis remains the subject of ongoing investigations, heated debate, and a disquieting amount of “art of medicine.” The article by Wu and colleagues in this issue of CHEST (see page 662) does not, of itself, provide insight into how we may improve outcomes for our patients suspected of having nosocomial pneumonia (and specifically ventilator-associated pneumonia [VAP]). It does, however, add to an increasing body of evidence that suggests that, when cultured quantitatively, invasive and noninvasively obtained cultures should provide comparable information. Linking this with improved outcomes for our patients is more problematic and involves an assessment of the risks of inappropriate treatment, whether changing antibiotic therapy in response to culture data alters outcome, and the role that antibiotic use patterns play in the selection of drug-resistant pathogens in the ICU.

The number of studies1–4 indicating that the combination of qualitative cultures and clinical data has a high false-positive rate in diagnosing VAP is large and generally consistent. However, the lack of a “gold standard” or criterion standard for establishing a diagnosis of VAP is problematic. This is especially true in light of reports5–7 suggesting that reliance solely on invasively obtained and quantitatively cultured samples using rigid diagnostic cut points may result in underdiagnosis of VAP. Studies examining the impact on relevant clinical outcomes of using quantitative cultures to obtain a more accurate diagnosis have been contradictory, or at least difficult to interpret. Fagon et al.,8 in a multicenter prospective randomized trial in > 400 patients, found that the use of antibiotics and early mortality was lower in patients in whom the diagnosis of pneumonia was made using quantitative cultures of bronchoscopically obtained specimens, in contrast to patients in whom qualitative cultures of tracheal aspirates were used. While this study has been criticized for not demonstrating a reduction in mortality rate at 28 days, there was a significant reduction in 28-day mortality using a proportionate hazards multivariate analysis.

Several studies9–11 have found that inappropriate antibiotic therapy of VAP is associated with increased mortality rates. While this has not been a consistent finding, even in studies where there was no significant difference, the trend toward increased mortality with inadequate therapy is compelling and suggests the possibility of a type II statistical error.12 Interestingly, it appears that it is the initial, empiric, antibiotic therapy that has the greatest impact on outcome.9,13 Given this, why be concerned about specimens whose results will be unavailable for 48 to 72 h, long after empiric therapy has been started? There are two reasons. First, the use of quantitative cultures in an institution should permit a more accurate determination of the organisms responsible for VAP in that institution and thereby improve the accuracy of the initial antibiotic prescription. Second, the data of Fagon et al.8 strongly suggest that if quantitative culture findings are negative, antibiotics can be safely discontinued. This has important implications for the ICU. Antibiotic use patterns play an important role in the emergence of antibiotic-resistant organisms. This appears to be based on both the frequency and duration of antibiotic administration.14,15 Stopping empiric antibiotic therapy for VAP when quantitative culture findings are negative may facilitate decreased antibiotic use with attendant reductions in both cost and in the antibiotic-forced selection of resistant organisms.

Were bronchoscopy routinely employed to collect specimens from patients suspected of VAP, it would place a potentially untenable time and cost burden on health-care systems. Bronchoscopy, however, does not appear to be routinely necessary. Ruiz et al.16 found no difference in mortality or antibiotic use when comparing tracheal aspirates (TAs) with bronchoscopically obtained specimens, both of which were cultured quantitatively. However, the study was small, enrolling only 76 patients, and was probably underpowered to detect clinically relevant differences in outcomes. Similarly, Bregenon et al.,17 in a prospective, case-controlled study comparing outcomes in patients in whom a diagnosis of VAP was made using quantitative cultures obtained from invasively obtained vs noninvasively obtained samples, found no difference in outcomes among 76 pairs of patients matched on several clinical variables. The correlation between quantitatively cultured TA specimens and bronchoscopically collected specimens appears to be good. El-Ebiary and colleagues18 found very good correspondence between these techniques. This has been reconfirmed in the current study by Wu and colleagues in a population that is extraordinarily common in most ICUs: patients already receiving antibiotic therapy. Significantly, quantitative cultures of TA specimens were at least as sensitive and nearly as specific as bronchoscopically obtained specimens. Hence, use of a 105 threshold for TA cultures should minimize the po-
potential for not treating a pneumonia that is present, while maintaining reasonable specificity and permitting the discontinuation of antibiotic therapy in a large number of patients without pneumonia. Further, antibiotic sensitivities of species collected by invasive and noninvasive means were similar, arguing that there will be little difference in antibiotic use patterns or culture-directed changes in antibiotic therapy consequent to the use of one specimen or the other.

TAs are not routinely cultured quantitatively in most hospitals in the United States. The reasons for this are several and include increased cost and uncertainty as to how these data should be applied clinically. However, the cost of quantitative cultures should be more than offset by the decrease in antibiotic usage. Fagon et al8 found 4 more antibiotic-free days in the group being managed using quantitative culture; and, in the study of Wu and colleagues, nearly half of the quantitative TA cultures were below the threshold indicating pneumonia. While many of these patients may yet receive antibiotic therapy for nonpulmonary indications, it is hard to escape the conclusion that antibiotic administration can be reduced if quantitative cultures (of TAs) are employed and antibiotics discontinued if culture findings are negative. Hence, quantitative cultures can assist the physician in more accurately diagnosing VAP, permit an institution to better ascertain the organisms most commonly responsible for VAP, and permit physicians to more accurately target empiric antibiotic therapy, without increasing cost or adding procedure-related morbidity. It is hard to imagine more compelling arguments for the broad application of quantitative cultures of respiratory secretions in suspected VAP. However, we must now focus our research efforts, not on isolated aspects of the process of care of patients with VAP, but on the comparison of clinically relevant and well-delineated diagnostic and treatment algorithms on the important outcomes of mortality and cost of care.

David L. Bowton, MD, FCCP
Winston-Salem, NC

Dr. Bowton is Professor, Internal Medicine (Pulmonary and Critical Care) and Anesthesiology (Critical Care), Wake Forest University Baptist Medical Center.
Correspondence to: David L. Bowton, MD, FCCP, Pulmonary and Critical Care Medicine, Wake Forest University Baptist Medical Center, Winston-Salem, NC 27157-1054; e-mail: dbowton@wfubmc.edu

REFERENCES