

EDITORIALS



Diagnosis of Ventilator-Associated Pneumonia

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In this issue of the *Journal*, Heyland et al., writing for the Canadian Critical Care Trials Group, report the results of a multicenter, randomized trial comparing the use of bronchoalveolar lavage and endotracheal aspiration for the diagnosis of ventilator-associated pneumonia.¹ This study was part of a larger 2-by-2 factorial design also comparing empirical antimicrobial monotherapy (a carbapenem) and combination therapy (a carbapenem plus a fluoroquinolone). The authors conclude that bronchoalveolar lavage and endotracheal aspiration are associated with similar clinical outcomes and similar overall use of antibiotics. However, several important limitations of the study must be appreciated in order to place it into proper context.

Heyland et al. restricted the patient population and the pathogens evaluated in their study. Of the 2531 screened patients, 307 (12.1%) were excluded because they were already colonized or had a respiratory tract infection with an organism not sensitive to one of the study drugs, and 706 (27.9%) were excluded because they were immunocompromised, had already received one of the study drugs, or had a chronic disease. Therefore, at least 40% of the screened patients who were excluded had risk factors for colonization or infection with potentially antimicrobial-resistant bacteria. Unfortunately, these exclusions probably represent the majority of patients undergoing real-time evaluation for suspected ventilator-associated pneumonia.²⁻⁵

Initial administration of an appropriate antimicrobial regimen (i.e., one to which the pathogens are sensitive, on the basis of *in vitro* susceptibility testing) in patients with suspected ventilator-associated pneumonia should be regarded as one of the primary determinants of in-hospital outcome. Use of an initial antimicro-

bial regimen that is inappropriate for the microorganisms causing ventilator-associated pneumonia has been associated with a significantly greater risk of death than use of an appropriate initial regimen.^{6,7} These findings strongly suggest that initial antimicrobial therapy for ventilator-associated pneumonia and other serious infections should be selected according to the presence or absence of risk factors for infection associated with health care (e.g., recent hospitalization, admission from a chronic care environment, current hemodialysis, immunocompromised state, late-onset infection, or prior use of antimicrobial agents during the current period of hospitalization).^{5,8} Initial antimicrobial regimens in patients with suspected ventilator-associated pneumonia who have these risk factors should appropriately treat potentially resistant pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*.⁸

The guidelines for the management of nosocomial pneumonia, recently published by the American Thoracic Society and the Infectious Diseases Society of America, propose a de-escalation approach to treatment that attempts to address the need for balancing appropriate initial antimicrobial therapy and emerging antibiotic resistance.⁸ In patients with clinically suspected ventilator-associated pneumonia, specimens should be obtained from the respiratory tract for microbiologic processing, followed by the timely administration of an empirical antimicrobial regimen selected according to the presence or absence of risk factors for infection with antimicrobial-resistant bacteria. Microorganism identification and antibiotic susceptibility testing should also be conducted so that the use of antimicrobial agents can be deescalated when appropriate. An important caveat in applying this guideline is that

hospitals should use their own local microbiologic data to formulate appropriate initial treatment regimens.⁹

In addition to administering an initial antimicrobial regimen that is likely to be active against the pathogens causing infection, the clinician has the obligation to minimize future emergence of antimicrobial resistance. De-escalation promotes both the narrowing of the initial antimicrobial regimen once the microbiologic data become available and the use of antimicrobial therapy for the shortest duration that is clinically effective. Bronchoalveolar lavage is a tool used to facilitate modification of initial antimicrobial treatment regimens for ventilator-associated pneumonia. The airway of a patient receiving mechanical ventilation is commonly colonized with potentially pathogenic bacteria. Consequently, the testing of secretions obtained from an endotracheal tube or tracheostomy tube cannot consistently differentiate between upper airway colonization and lower respiratory tract infection.¹⁰ Sampling methods that minimize contamination from the upper airway (e.g., bronchoalveolar lavage or protected brush catheter sampling) offer the advantage of establishing a more precise microbiologic diagnosis of ventilator-associated pneumonia to guide subsequent changes in antimicrobial therapy.¹¹

Heyland et al. found that the use of bronchoalveolar lavage did not influence in-hospital mortality or length of stay as compared with endotracheal aspiration. However, the main potential effect of bronchoalveolar lavage is to permit the de-escalation or cessation of unnecessary antimicrobial therapy on the basis of microbiologic findings, especially when initial broad-spectrum antimicrobial agents are prescribed for patients at risk for infection with resistant bacteria.^{8,10} The exclusion of patients colonized or infected with MRSA, *P. aeruginosa*, and other multidrug-resistant pathogens diminishes the usefulness of the results of Heyland et al. for clinical decision making. There is less concern about administering inappropriate initial antimicrobial therapy when the risk of infection with resistant pathogens is low, thus allowing for the initial use of more narrow-spectrum antimicrobial agents. The culture of bronchoalveolar-lavage fluid is more likely to result in modification of prescribed broad-spectrum regimens than is the culture of an endotracheal aspirate.

Clinicians appear to be confident that the cul-

ture of bronchoalveolar-lavage fluid, as compared with endotracheal aspirate, for the microbiologic diagnosis of ventilator-associated pneumonia actually reflects the presence or absence of ventilator-associated pneumonia and the etiologic agents of the infection.¹⁰ A meta-analysis was recently conducted of four randomized trials comparing lower respiratory tract sampling and quantitative culture with clinical criteria for the diagnosis of ventilator-associated pneumonia; the likelihood of modifying initial antimicrobial therapy in the sampling group was almost three times that in the clinical-criteria group.¹² However, in patient populations with a low prevalence of infection or colonization with antibiotic-resistant bacteria, the use of endotracheal aspiration should suffice, since initial empirical treatment with broad-spectrum antimicrobial agents is not required.

In addition to the narrowing of initially prescribed broad-spectrum antimicrobial regimens on the basis of microbiologic data, the shortening of the duration of antibiotic treatment is an important component of de-escalation. Patterns of excess administration of antibiotics, especially beyond 7 or 8 days in patients receiving mechanical ventilation, have been linked with subsequent infection with potentially resistant bacteria.⁸ These findings suggest that clinicians caring for patients with suspected ventilator-associated pneumonia should use antimicrobial treatment strategies that minimize the prolonged and potentially unnecessary administration of antibiotics, in order to curtail resistance.^{8,10,11}

In summary, given the rapid emergence of antimicrobial resistance and the limited number of new antimicrobial agents, clinicians treating patients with suspected ventilator-associated pneumonia not only must prescribe appropriate initial antimicrobial regimens to optimize outcomes but also must minimize the development of resistance by rigorously using a de-escalation strategy. When applied properly, bronchoalveolar lavage and endotracheal aspiration are tools that can facilitate de-escalation.

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Carbapenems for Surgical Prophylaxis?

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In this issue of the *Journal*, Itani and colleagues¹ describe a study in which 1002 patients were randomly assigned to receive either ertapenem or cefotetan in a single dose before elective colorectal surgery. Many experienced surgeons and hospital epidemiologists will probably be surprised that the overall rate of failure in the modified intention-to-treat analysis was approximately 40% for patients receiving ertapenem and 50% for those receiving cefotetan. A possible explanation for these high failure rates is that the authors of the study, unlike those of most previous trials, included unexplained use of postoperative antibiotics and anastomotic leaks in their definition of prophylaxis failure. However, this fact does not explain why nearly one in six patients receiving ertapenem and approximately one in four patients receiving cefotetan had a surgical-site infection. These rates are substantially higher than those reported by the National Nosocomial Infections Surveillance System and our infection-control network of 36 community hospitals.² Although the authors cite previous reports with similarly high rates of surgical-site infection with cefotetan, most studies examining outcomes of colorectal surgery have reported lower rates of infection.³

The high rates of surgical-site infection reported by Itani et al. may relate to a combination of factors. For example, more than a quarter of the patients were obese, and as in other

studies,^{4,5} obesity was identified as an independent risk factor for surgical-site infection. Failure of antibiotic therapy in many obese patients may be related both to technical factors, such as inadequate obliteration of nonvascularized "dead space" during wound closure, and to inadequate administration of antibiotics and subsequent low drug levels in serum and tissue at the end of long procedures.⁶ Other surgery-related factors that could have contributed to the high rates of postoperative infection were inappropriate (or inappropriately early) removal of hair, technical errors (such as bowel perforation or spillage of fecal material), the failure to maintain normothermia, and uncontrolled hyperglycemia during the perioperative period. The Surgical Infection Prevention and Surgical Care Improvement Projects have emphasized the need for careful management of these factors in preventing infections after colorectal surgery.⁷ Thus, it is important to remember that the selection of an antimicrobial agent as prophylaxis is only one of many considerations in reducing rates of postoperative infection.

Even though the authors demonstrated that ertapenem was superior to cefotetan in this trial, is it reasonable to conclude that ertapenem should be a preferred agent for prophylaxis before colorectal surgery? Only one third of Medicare patients undergoing colorectal surgery currently receive cefotetan as prophylaxis,⁷ and there are numerous