Prevention of Ventilator-Associated Pneumonia

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pulmonary nodules or masses or undiagnosed pneumonia. This would seem to be a prudent approach, at least for patients able to produce adequate sputum for these preparations. Awareness and training of laboratory personnel would be another part of the equation, which would hopefully amount to a better chance of noninvasive diagnosis of pulmonary blastomycosis.

If bronchoscopy or thoracoscopy/thoracotomy must enter the diagnostic sequence, a couple of caveats should be kept in mind. First, lidocaine treatment has been shown to inhibit the growth of *B dermatitidis* in culture. Thus, limiting the concentration of lidocaine to 1 g/dL has been recommended in suspected cases to reduce the antifungal effect.[4] Second, *B dermatitidis* is frequently missed in standard hematoxylin and eosin-stained histologic specimens, so special stains, usually silver or periodic acid-Schiff stains, are often needed to identify the organism.

A serologic test, usually being inexpensive and noninvasive, might be an ideal way to screen for blastomycosis and direct the workup for possible active cases in endemic areas. Regrettably, Martynowicz and Prakash, like others, have found the currently available commonly used serologic techniques to have inadequate sensitivity for such an application. Yet work is ongoing in this area, and in the future, novel serologic or molecular biological techniques may make the job of uncovering veiled *B dermatitidis* infections easier.

Blastomycosis is not a common infection. The Centers for Disease Control and Prevention estimates the incidence in endemic areas to be one to two cases per 100,000 population. Yet, the consequences of missing the diagnosis can be significant, including not only an unfavorable clinical outcome, but also substantial distress to the patient as he or she faces potentially unnecessary tests and procedures while having to cope with the uncertainty of diagnosis. Understanding the various forms of this treatable infection, especially by clinicians who practice in endemic areas, is the first step to smooth diagnosis and treatment. Then, suspicion in patients whose exposure history and disease presentation put blastomycosis into the differential diagnosis should direct collection of adequate, and perhaps, multiple sputum specimens to be cultured and stained for fungal detection, including by Papanicolaou stain. Specimens from bronchoscopy and other more invasive procedures should also be appropriately collected and processed. With the proper knowledge and watchfulness, hopefully the true identity of this great masquerader will, in more cases than not, be promptly exposed.

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Selecting Interventions That Make a Difference

In this issue of *CHEST* (see page 858), Smulders et al describe the results from their randomized trial of intermittent subglottic drainage for the prevention of ventilator-associated pneumonia (VAP). They found that general ICU patients receiving intermittent subglottic drainage had a significantly lower incidence of VAP compared to patients in their control group (4% vs 16%; $p = 0.014$). The duration of mechanical ventilation, length of stay in the ICU and hospital, and mortality were similar for both groups.

The results of this study are in agreement with those of three previous randomized trials of subglottic drainage using specially designed endotracheal tubes.[1–3] Taken together, these studies all support the utilization of subglottic drainage to reduce the incidence of VAP. Unfortunately, other important clinical and economic outcomes, such as mortality and lengths of stay, did not appear to be significantly influenced by the use of this intervention. This may be explained, in part, by the design of the four randomized studies performed to date, which focused on the prevention of VAP during the first 5 to 7 days of mechanical ventilation. VAP occurring later during mechanical ventilation may be more important to prevent, as it is more likely to be due to "high-risk" antibiotic-resistant bacteria such as *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*.[4] VAP attributed to antibiotic-resistant pathogens has been associated with greater hospital mortality and longer lengths of stay

compared to VAP attributed to antibiotic-sensitive bacteria such as methicillin-sensitive *S aureus* and *Haemophilus influenzae*.[5,6] Therefore, additional larger studies focusing on the prevention of VAP due to antibiotic-resistant bacteria may be needed to demonstrate a mortality advantage for subglottic aspiration, as has been done for selective digestive decontamination.[7,8]

An important omission from the studies examining subglottic drainage has been the influence of this intervention on antibiotic utilization in the ICU setting. The findings of these trials suggest that reductions in the occurrence of VAP in patients receiving subglottic aspiration should be associated with fewer antibiotic days. Reducing the use of antibiotics in the ICU setting may result in a lower incidence of hospital-acquired infections due to antibiotic-resistant bacteria, as has been demonstrated by other strategies that have successfully decreased the use of empiric antibiotic therapy for VAP.[9] Noninvasive ventilation for acute respiratory failure is another example of an intervention associated with reductions in the incidence of VAP and antibiotic use.[10] In addition to reducing the use of antibiotics and the occurrence of antibiotic-resistant bacterial infections, pharmacy drug costs are decreased with implementation of antibiotic-sparing strategies.[9]

Interventions aimed at the prevention of VAP can be segregated into two broad categories (Table 1).

Table 1—*Interventions for the Prevention of VAP*

Interventions aimed at the prevention of colonization of the aerodigestive tract
Avoid unnecessary antibiotic use
Limit stress ulcer prophylaxis to high-risk patients
Use of sucralfate for stress ulcer prophylaxis
Selective digestive decontamination with antibiotic suspensions and pastes*
Chlorhexidine oral rinse
Oral hygiene and decontamination
Appropriate use of prophylactic antibiotics in high-risk patients
Routine hand disinfection before patient contacts
Isolation precautions for patients infected with high-risk antibiotic-resistant pathogens
Interventions aimed primarily at the prevention of aspiration
Discontinue nasogastric tube/endotracheal tube as soon as possible
Semirecumbent positioning
Avoid gastric overdistension
Oral (nonnasal) intubation
Subglottic drainage
Drainage of ventilator circuit condensate
Avoid unnecessary patient transports and reintubation
Noninvasive mask ventilation to prevent tracheal intubation
Avoid unnecessary use of sedation

*Should be used in patients at high risk for complications from VAP due to concerns regarding the emergence of antibiotic-resistant bacteria with routine use of antibiotic prophylaxis.

The first category includes pharmacologic strategies that aim to reduce colonization of the aerodigestive tract with pathogenic bacteria. The second category includes nonpharmacologic strategies attempting to decrease the occurrences of aspiration. Both of these approaches to VAP prevention appear to be important given our current understanding of the pathophysiology of VAP, which is thought to result from aspiration of contaminated secretions originating from the aerodigestive tract and ventilator circuit.[11] Additionally, infection control programs employing combinations of interventions aimed at preventing both colonization of the aerodigestive tract with pathogenic bacteria and aspiration have been shown[12,13] to be successful and cost-effective. These quality improvement studies further support the use of prevention strategies aimed at both processes involved in the pathogenesis of VAP.

There are a number of effective pharmacologic and nonpharmacologic interventions available to clinicians for the prevention of VAP.[14] Developing a VAP prevention program for use in a specific ICU should be based on careful consideration of the following factors. Focused infection control efforts with buy-in from all patient-care providers (physicians, nurses, respiratory therapists) are most likely to be successful.[15] The selection of interventions for a VAP prevention program depends on the available patient staffing, administrative resources, and the ability of the unit or infection control group to tract compliance with the program over time. Several studies[16–18] have shown the importance of unit staffing on compliance with interventions, such as hand washing and ventilator weaning, which should decrease the incidence of nosocomial infections. In units with suboptimal staffing, interventions requiring minimal effort from bedside nurses and respiratory therapists may be most applicable (*eg*, semirecumbent patient positioning, alcohol foam and gels for hand disinfection, subglottic drainage). Additionally, the influence of interventions on patient outcomes should be tracked over time to determine their success and cost-effectiveness.[12,13] This will help to determine whether these interventions should be continued and whether erosion in compliance with the VAP prevention program has occurred. The latter may necessitate further education and training of unit staff or implementation of alternative interventions to improve the effectiveness of the infection control program.

No simple, low-cost interventions currently exist that effectively prevent both colonization of the aerodigestive tract with pathogenic bacteria and aspiration. The intervention that comes closest to accomplishing this goal is the use of noninvasive positive-pressure ventilation administered via a face

mask as an alternative to tracheal intubation and mechanical ventilation.[10] Clinical studies[10,19,20] have demonstrated the ability of noninvasive ventilation to reduce the occurrence of nosocomial infections, including VAP, compared to the use of conventional mechanical ventilation. Unfortunately, the use of noninvasive ventilation may initially require more support from trained respiratory therapists that may impede its utilization locally.[21] Therefore, additional simple interventions for the prevention of VAP in patients requiring tracheal intubation are required.

Biofilm formation routinely occurs on endotracheal tubes and is considered an important factor promoting the occurrence of VAP.[22] Unfortunately, there are no current interventions that have the ability to prevent biofilm development on the endotracheal tube as well as within the airways of patients receiving mechanical ventilation. Chemicals aimed at blocking gene products from bacteria that form biofilms, antibodies that block fibronectin-binding protein adhesion of bacteria, and the use of specialized coatings that block bacterial adherence and communication offer the future possibility to block biofilm formation in patients receiving mechanical ventilation to further reduce the incidence of VAP.[23,24] One exciting approach would be to have a specially designed endotracheal tube that helps to prevent both colonization of the aerodigestive tract with pathogenic bacteria and aspiration. Until such devices are developed and shown to be clinically useful, clinicians should employ currently available measures for their patients receiving mechanical ventilation that have been shown to be safe and cost-effective.

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Is a Silver Coating a Silver Lining?

Infection and its major consequence, sepsis, are ever-increasing problems in the ICU environment. A recent study[1] by Angus and coworkers suggest that there are > 750,000 episodes of severe sepsis each year in the United States. Their projections suggest that the incidence will continue to increase at a rate of 1.5%/yr.[1] One of the most common ICU infections and the nosocomial infection associated with the highest mortality rate is hospital-acquired pneumonia.[2–6] Ventilator-associated pneumonia (VAP) is the term for hospital-acquired pneumonia that develops in an intubated patient receiving mechanical ventilatory support.[3–5] VAP presents multiple diagnostic and therapeutic challenges for the clinician.[3–5] One of the most controversial areas concerns the benefits of an aggressive diagnostic approach vs empiric treatment for VAP.[7–11] The aggressive diagnostic approach utilizes fiberoptic bronchoscopy along with a protected specimen brush or BAL coupled with quantitative cultures to ensure that sufficient thresholds of microorganisms are present.[7,8] Advocates of this approach point out the poor specificity of the clinical diagnosis of VAP and our need to use antibiotics judiciously in this time of increasing antibiotic resistance.[8,9,11,12] However, the supporters of empiric treatment contend that the aggressive invasive approach is more costly, and only defines treatment failure, and emphasize the need for additional randomized, prospective, multicentered controlled clinical trials to determine if either strategy is associated with a survival benefit.[7,10] Another controversial area surrounds the determination of the attributable mortality of VAP that typically develops in patients with comorbid conditions that are associated with significant mortality.[3,5]

Given the current difficulties with the clinical diagnosis, treatment, and assessment of attributable mortality of VAP, perhaps, the most prudent goal would be to channel our efforts toward prevention. Current prevention strategies include positioning patients with their heads elevated > 30°, selective digestive decontamination, rotational therapy, and continuous subglottic aspiration/suctioning, and early extubation with liberation from mechanical ventilatory support.[6,13–17] Indwelling catheters, such as Foley and central venous catheters, invade the normal body barriers and subsequently become coated with a "biofilm."[18] This biofilm is an excellent growth medium for bacteria and ultimately gives rise to infection. Specialized coatings have been used to retard the growth of the biofilm and to decrease the likelihood of subsequent colonization of the catheter surface with microorganisms.[18,19] Some common nosocomial infections, such as blood stream and urinary tract infections, have been prevented by the use of special coatings on the indwelling catheter.[19–21] A natural extension of this technology would be to coat the endotracheal tube in an attempt to decrease the development of VAP.

The report by Olson and coworkers in this issue of *CHEST* (see page 863) evaluated silver coated endotracheal tubes in an experimental animal model of VAP. The investigators evaluated the special coated endotracheal tube compared to a standard endotracheal tube in a prospective, randomized, double-blind, controlled trial in dogs receiving mechanical ventilation with Pseudomonas placed in the oropharynx. Serial swabs were obtained from the endotracheal tubes; at death, the endotracheal tube, tracheal, and lung parenchymal bacterial burdens were assessed. The silver coating was found to delay the appearance of bacteria on the inner surface of the endotracheal tube. In addition, there were significantly less aerobic bacteria in the lung parenchyma and less parenchymal inflammatory changes on histologic assessment.

While this was a small study of relatively short duration, the results suggest that silver coating endotracheal tubes may offer some help in the battle to prevent VAP. The investigators attempted to recreate "life in the ICU," where all too frequently patients are managed in a sedated, supine, flat position. The dogs involved in this trial were kept in this same state, which would tend to promote aspiration of the deposited oropharyngeal bacteria and potentiate the subsequent colonization of the lower airway and endotracheal tube. However, at present, there is little to no data to help us understand the significance of decreased numbers of colonizing bacteria on an endotracheal tube. It might be assumed that less is better, but it may be an all-or-none phenomenon. The same issues surround the implications of a decreased aerobic bacterial burden on the eventual development of pneumonia or, more importantly, on ultimate survival. Future trials will need to compare the coated endotracheal tube to our current preventive strategies (*ie*, elevated head of the bed, rotational/kinetic therapy, continuous subglottic suction, etc.) to see if there is continued or additional benefit. Nonetheless, VAP is an important cause of morbidity, mortality, and increased length and cost of care for the critically ill. If a strategy as simple and likely inexpensive as silver coating the endotracheal tube can prevent VAP, it is indeed the silver lining that we have been searching for. At this time,