Lower respiratory tract infections in intubated patients include ventilator-associated tracheobronchitis (VAT) and ventilator-associated pneumonia (VAP). These infections are increasingly caused by multidrug-resistant bacteria, which colonize the patient's oropharynx and enter the lower respiratory tract around the endotracheal tube cuff or through the lumen. Progression of colonization to VAT and, in some patients, to VAP is related to the quantity, types, and virulence of invading bacteria versus containment by host defenses. Diagnostic criteria for VAT and VAP overlap in terms of clinical signs and symptoms, and they share similar microbiologic criteria when endotracheal sputum aspirate samples are used. In addition, the diagnosis of VAP requires a new and persistent infiltrate on a chest radiograph, which may be difficult to assess in critically ill patients, and a significant bacterial culture of an endotracheal aspirate or bronchoalveolar lavage specimen. Current guidelines for the management of VAP strongly recommend the use of early, appropriate empirical antibiotic therapy based on patient risk factors for multidrug-resistant pathogens. An alternative model focused on VAT, using serial surveillance of endotracheal aspirate specimens to identify multidrug-resistant pathogens and their antibiotic susceptibilities, would allow earlier, targeted antibiotic treatment that could improve outcomes in patients, prevent VAP, and provide an attractive model for clinical research trials.

Intubation with mechanical ventilation increases the risk of pneumonia 6–20-fold among patients and is associated with crude mortality rates of 20%–40% [1, 2]. Lower respiratory tract infections in these patients include ventilator-associated tracheobronchitis (VAT) and ventilator-associated pneumonia (VAP). Diagnostic criteria for VAT and VAP overlap in terms of clinical signs and symptoms, and they share similar microbiologic criteria based on the quantitative or semiquantitative assessment of endotracheal aspirate specimens (Table 1) [1–5]. In contrast to VAT, VAP requires evidence of a new and persistent infiltrate on a chest radiograph, which may be difficult to interpret in some critically ill patients, and a significant result of quantitative culture of an endotracheal aspirate, bronchoalveolar lavage, or protected brush specimen.

Over the past decade, the incidence of lower respiratory tract infection due to multidrug-resistant (MDR) pathogens, such as methicillin-resistant Staphylococcus aureus, and gram-negative bacilli (eg, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, and Acinetobacter baumannii) has been increasing [1, 2]. On the basis of these data, the 2005 American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines for management of VAP emphasized the importance of early, appropriate, empirical antibiotic therapy based on patient risk factors for infection due to MDR pathogens to improve patient outcomes [1]. This empirical regimen was followed by deescalation when specific microbiologic data became available 48–72 h later. Potential disadvantages of the empirical ATS/IDSA model include excessive use of multiple empirical antibiotic therapy, which may increase antibiotic resistance; toxicity; and failure to properly deescalate when culture data become available.
Although many studies have investigated the management and prevention of VAP, few studies have focused on VAT as a model for earlier diagnosis, treatment, and prevention [4, 5]. In the VAT model, serial, quantitative assessment of endotracheal aspirate specimens can be used to identify MDR pathogens and their antibiotic susceptibilities, to diagnose VAT, and to initiate earlier, targeted antibiotic therapy [3–10]. By thinking outside the box, we briefly review the epidemiology, pathogenesis, and diagnostic criteria for VAT and VAP. We present data suggesting that the VAT model provides simpler, less subjective definitions and that the use of earlier, targeted (rather than empirical) antibiotic therapy appears to improve patient outcomes and prevent VAP. The VAT definition may be an objective tool for clinical trials.

**Epidemiology and Pathogenesis**

By definition, both VAT and VAP occur 48 h after intubation [1–3, 5]. VAP is associated with high crude mortality rates (range, 20%–50%) and health care costs estimated to be up to $40,000 per episode, which emphasizes the need for prevention and better outcomes [1, 2, 11]. The incidence of VAT is 2.7%–10% [3]. Medical and surgical patients who receive a diagnosis of VAT also experience a significantly longer length of intensive care unit (ICU) stay and duration of mechanical ventilation.

**Table 1. Comparison of Diagnostic Criteria Frequently Used for the Diagnosis of Ventilator-Associated Pneumonia (VAP) and Tracheobronchitis (VAT)**

<table>
<thead>
<tr>
<th>Criterium type</th>
<th>VAP</th>
<th>VAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs and symptoms</td>
<td>At least one of temperature (&gt;38°C), leukocyte count &gt;12,000 leukocytes/mm³, or leukopenia (leukocyte count &lt;4000 leukocytes/mm³) plus new onset of purulent endotracheal secretions or change in character of sputum or increases in respiratory secretions, suctioning requirements, new rales, bronchial breath sounds, or worsening oxygen requirements (increasing FiO₂ or PaO₂/FiO₂)</td>
<td>At least one of temperature (&gt;38°C), leukocyte count &gt;12,000 leukocytes/mm³, or leukopenia (leukocyte count &lt;4000 leukocytes/mm³) plus new onset of purulent endotracheal secretions or change in character of sputum or increases in respiratory secretions, or suctioning requirements</td>
</tr>
<tr>
<td>Radiologic criteria: chest radiograph or CT</td>
<td>New or progressive and persistent infiltrate on chest radiograph or consolidation or cavitation</td>
<td>Transient infiltrate, no new infiltrate, or nondiagnostic chest radiograph or CT (eg, atelectasis, ARDS, or CHF)</td>
</tr>
<tr>
<td>Microbiologic criteria</td>
<td>ETA Gram stain with PMNL with or without bacteria (note morphology and color), semiquantitative ETA (moderate-to-heavy growth) or quantitative ETA &gt;1 × 10⁶ cfu/mL; bronchoscopic or nonbronchoscopic samples; cytospin: PMNL with or without bacteria, BAL &gt;1 × 10⁶ cfu/mL or PSB &gt;1 × 10⁶ cfu/mL</td>
<td>ETA Gram stain with PMNL with or without bacteria (note morphology and color), semiquantitative ETA (moderate-to-heavy growth) or quantitative ETA &gt;1 × 10⁶ cfu/mL; bronchoscopic or nonbronchoscopic samples (usually not done or &lt;1 × 10⁶ cfu/mL criteria for VAP</td>
</tr>
</tbody>
</table>

**Figure 1.** Pathogenesis of bacterial lower respiratory tract infections. Bacterial pathogens usually enter the lower respiratory tract from the oropharynx by leakage of bacteria and secretions around the endotracheal tube (ETT) tube cuff. The black arrow represents the battle between the bacterial pathogen(s) and different host defenses. The black boxes represent potential patient outcomes over time: colonization, ventilator-associated tracheobronchitis (VAT), or ventilator-associated pneumonia (VAP).

The MDR pathogens most frequently isolated from patients with VAT and VAP are methicillin-resistant *S. aureus*, *P. aeruginosa*, *A. baumannii*, *E. coli*, and *K. pneumoniae* (with or with-
out extended-spectrum β-lactamases or carbepenemases) [1, 3].

Understanding the pathogenesis of VAT and VAP is crucial for establishing principles for therapy and prevention (Figure 1) [1, 2, 5]. Intubation with mechanical ventilation increases the risk of bacterial pneumonia by 6–20-fold [1, 2]. The endotracheal tube facilitates bacterial entry into the lower respiratory tract and tracheal colonization, which may progress, in some patients, to VAT or VAP (Figure 2) [1, 2, 5]. Bacteria usually enter the lower respiratory tract by leakage around the endotracheal tube cuff or through the endotracheal tube lumen [2, 5, 12]. The endotracheal tube cuff and intraluminal biofilm formation also prevent the exit of bacteria and secretions from the lower airway, increasing the need for manual tracheobronchial suctioning. The numbers and virulence of types of pathogens entering the trachea are important in disease progression and vary among and within bacterial species [13]. Host lung defenses, including cilia, mucous, polymorphonuclear leukocytes, and macrophages and their respective cytokines, antibodies (IgM, IgG, and IgA), and complement, help prevent progression of tracheal colonization to VAT or VAP [1, 14].

**DIAGNOSIS AND DEFINITIONS**

Similarities and differences in methods for the diagnosis of VAT and VAP are summarized in Table 1. Some of the clinical criteria, microbiologic methods, and end points for the diagnosis of VAT and VAP have been debated [1–6, 15–17]. Major components needed for diagnosis of both VAT and VAP include at least one of the clinical signs in Table 1, microbiologic confirmation, and interpretation of pulmonary infiltrates (discussed in greater detail below). Of these, microbiologic assessment of endotracheal aspirate specimens is crucial.

**Microbiologic issues.** Sputum endotracheal aspirate specimens from intubated patients receiving mechanical ventilation can be easily obtained for Gram staining and culture to help establish a diagnosis of lower respiratory tract infection and to help discriminate between tracheal colonization and VAT or VAP. Gram-stained smears of endotracheal aspirate specimens help evaluate lower airway inflammation by the presence of polymorphonuclear leukocytes and macrophages, as well as provide information on the bacterial morphology (gram-positive cocci may suggest *S. aureus*, and gram-negative bacilli may suggest *E. coli*, *Klebsiella* species, or *P. aeruginosa*). The presence of bacteria on the Gram stain roughly correlates with an endotracheal aspirate specimen having >1 × 10^5 organisms/mL.

For the diagnosis of VAT and VAP, endotracheal aspirate specimens with >1 × 10^5 colony-forming units (cfu)/mL are required, which appears to correlate well with moderate-to-heavy growth of a respiratory tract pathogen with use of the semiquantitative assessment of endotracheal aspirate specimens that is frequently used for the diagnosis of lower respiratory tract infections in many hospital microbiology laboratories [4–6]. Bacterial pathogens include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Stenotrophomonas maltophilia*, and *Burkholderia cepacia* or one of the other MDR pathogens discussed in Epidemiology and Pathogenesis. Coagulase-negative staphylococci, diphtheroids, anaerobes, and *Candida albicans* are usually lower respiratory tract colonizers in patients receiving mechanical ventilation. Of note, *Legionella pneumophilia* requires special culture media or diagnosis by urine antigen.

Although more data are needed, quantitative assessment of endotracheal aspirate specimens may provide a better, reproducible standard, compared with semiquantitative assessment of endotracheal aspirate specimens, for discriminating between tracheal colonization and lower respiratory tract infection. Greater diagnostic specificity for confirming VAP can be achieved using quantitative assessment of distal airway samples obtained by bronchoscopic or nonbronchoscopic bronchoalveolar lavage (BAL; >1 × 10^5 cfu/mL) or protected specimen brush samples (≥1 × 10^4 cfu/mL). However, BAL and protected specimen brush methods are not routinely available over a 24-h period in many hospitals. It is important to emphasize that quantitative microbiologic assessment is routinely used in microbiology laboratories to help discriminate between urinary tract colonization and infection, which is defined as ≥1 × 10^5 cfu/mL in a voided urine specimen [5].
Figure 3. Portable chest radiograph of an intubated patient with onset of clinical signs and symptoms consistent with ventilator-associated tracheobronchitis (VAT) and/or ventilator-associated pneumonia (VAP). The endotracheal aspirate Gram stain had many polymorphonuclear leukocytes and many gram-negative bacilli. Because of preexisting changes on chest radiograph, no new infiltrate could be detected on the chest radiograph to establish or confirm a diagnosis of VAP. The quantitative endotracheal aspirate had $>1 \times 10^6$ colony-forming units/mL, indicating VAT, and antibiotic therapy was initiated.

Radiographic issues. Further complicating differences between VAP and VAT is the difficulty in defining a new and persistent infiltrate on chest radiograph or lung CT in critically ill patients, which is essential for the diagnosis of VAP [1, 16, 17]. As shown in Figure 3, many critically ill patients often have preexisting lung infiltrates on their chest radiograph that are related to noninfectious causes, such as chest trauma, atelectasis, mucous plugs, congestive failure, or adult respiratory distress syndrome; these prevent accurate identification of a new infiltrate due to VAP. This problem is compounded by the use of portable chest radiographs. For decades, it has been emphasized that the quality, sensitivity, and specificity of a portable chest radiograph in critically ill ICU patients are often poor, and the findings may be difficult to interpret [16, 17]. For example, Nseir et al [4] reported that 38% of study patients receiving mechanical ventilation had abnormal chest radiograph findings at the time of admission to the ICU, and similar results have been noted by others [16–18].

Interpretation of chest infiltrates in critically ill patients could be improved with the use of lung CT, but this may be impractical for many ICU patients and is associated with a dose of radiation that is equivalent to $>100$ portable chest radiographs [19]. In addition, the availability of CT is limited in many ICUs, and if available, CT may still not confirm a diagnosis of VAP and would also increase health care costs significantly [20].

Figure 4. Example of serial monitoring with surveillance cultures using quantitative endotracheal aspirate (Q-ETA) specimens. *Pseudomonas aeruginosa* culture was performed on day 2, and *P. aeruginosa* was identified on day 4 after intubation. Changes in tracheal colonization increased over time to $>1 \times 10^6$ colony-forming units (cfu)/mL or (6 log$_{10}$) on day 8. At this time, the patient had a low-grade fever (37°C) with an increase in peripheral blood leukocyte count from 7300 cells/mm$^3$ to 11,500 cells/mm$^3$, but findings on the portable chest radiograph remained normal. Targeted antibiotic therapy was initiated for ventilator-associated tracheobronchitis on the basis of earlier antibiotic susceptibility data obtained from the Q-ETA sample obtained on day 4 and a Gram stain demonstrating polymorphonuclear leukocytes and gram-negative bacilli. Appropriate antibiotic therapy was followed by a rapid decrease in numbers of *P. aeruginosa* to $\sim 1800$ cfu/mL on day 10 and extubation on day 14. However, some patients may continue to have low levels of persistent tracheal colonization (gray ovals) over time, which should be monitored but not treated unless there are signs of infection, relapse, or a significant increase in bacterial counts.

Microbiologic surveillance in the trachea

Quantitative assessment of serial endotracheal aspirate specimens has been used for microbiologic surveillance after intubation to identify MDR pathogens before the development of clinical disease and appears to be a useful way to monitor the dynamics of the battle between the invading bacteria and the host defenses in the lower respiratory tract (Figure 4) [3–6, 9, 21]. Three studies have examined the use of serial, respiratory surveillance culture specimens collected at different times. Michael et al [22] obtained endotracheal aspirate specimens for quantitative assessment twice weekly in an intubated cohort, and when compared with a culture of BAL specimens performed at the time of VAP, the causative organism was identified a priori by quantitative assessment of endotracheal aspirate specimens in 83% of study patients. VAP was most frequently late onset, and the most common offending organism was *P. aeruginosa*. Depuydt et al [23] used weekly quantitative assessment of endotracheal aspirate specimens to detect VAP due to MDR pathogens and found that VAP was due to MDR pathogens in 69% of the episodes and that surveillance cultures led to the appropriate antibiotic therapy in 96% of patients.
a similar study with VAP confirmed by testing of BAL samples, Hayon et al [24] reported that quantitative endotracheal aspirate surveillance cultures identified at least one of the pathogens isolated by culture of BAL specimens, with the highest predictive value of culture of samples obtained within 72 h after the VAP diagnosis. Finally, Yang et al [25] used daily quantitative endotracheal aspirate cultures to identify patients infected with MDR P. aeruginosa and reported that colonized patients were more likely to develop VAP. Additional studies are clearly needed to expand and confirm these results in different populations of patients receiving mechanical ventilation, because VAT could provide a new and better gold standard for assessing the efficacy of new antibiotic agents for the treatment of lower respiratory tract infections in this high-risk patient population.

Increasing numbers of lower respiratory tract pathogens over time are likely to be a sign of increased bacterial dominance, greater inflammation, and risk of progression from colonization to VAT or VAP (Figure 4). Therefore, the use of serial surveillance cultures to identify MDR pathogens may be more important for the management of late-onset VAP (occurring >5 days after intubation) because of the greater risk of infection due to MDR pathogens and a significantly higher mortality rate, compared with early-onset VAP [1, 2, 26, 27]. In addition, multiple studies have reported that modification of an initial inappropriate antibiotic regimen on the basis of the results of antibiotic susceptibility testing 48–72 h later does not improve mortality [28]. In contrast to VAT, VAP is also more likely to involve an increased ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen, suggesting greater lung parenchymal damage.

RATIONALE FOR TREATING VAT

A’Court et al [9] studied tracheal colonization in 150 patients receiving mechanical ventilation with use of serial quantitative assessment of nonbronchoscopic bronchial lavage samples and found increases in lower respiratory tract colonization over time that appeared to peak ~2 days before the onset of clinical signs of VAT. In a prospective, observational cohort of medical and surgical patients, VAT was associated with increased length of ICU stay, longer duration of mechanical ventilation, and higher mortality in medical but not surgical ICU patients [3]. However, in a later study of patients with chronic obstructive pulmonary disease, Nseir et al [29] reported that patients with VAT, when compared with matched control subjects, had significantly lower median duration of mechanical ventilation and longer duration of ICU stay, but antibiotic therapy did not appear to protect against VAP. In a later prospective, observational case-control study involving patients with VAT, patients who were treated with antibiotics had significantly shorter durations of mechanical ventilation and ICU stay, but no difference was noted in mortality rates [30].

Two randomized studies of antibiotic therapy for VAT have recently been conducted. Palmer et al [7] performed a double-blind, randomized, placebo-controlled study involving medical ICU and surgical ICU patients that compared aerosolized antibiotic treatment (gentamicin every 8 h if gram-negative bacilli were present, vancomycin every 8 h if gram-positive bacteria were detected, or both for those with mixed infections) for 14 days or until extubation (n = 19) with a saline placebo (n = 24). VAT was defined as the production of >2 mL of purulent endotracheal aspirate over a 4-h period, with a Gram stain showing bacteria. Systemic antibiotics were given at the discretion of the treating physician and were frequently prescribed in both groups. Compared with the placebo group, the antibiotic group had significantly lower numbers of clinical signs and symptoms of VAP, faster weaning, reduced numbers of MDR pathogens, and lower use of systemic antibiotic (all end points, P < .05) [7]. Notable limitations of this study included the definition of VAT, lack of quantitative assessment of endotracheal aspirate specimens, high numbers of patients who had prior VAP, lack of data on radiographic signs of VAP, small numbers of study patients, and potential confounding by the use of systemic antibiotics.

The second study was a randomized, controlled, unblinded trial involving 58 patients who had received a clinical diagnosis of VAT defined by an endotracheal aspirate specimen with >1 × 10^6 cfu/mL and who received targeted intravenous antibiotic therapy or no therapy [4]. The antibiotic-treated group had more mechanical ventilation–free days (median, 12 vs 2 days; P < .001), lower ICU mortality (18% vs 47%; P < .05), and a significant decrease in VAP episodes (47% vs 14%; P < .02). The same microorganisms were identified in each group, supporting the concept that VAT appears to progress to VAP and that earlier therapy appears to improve patient outcomes and prevent or reduce the risk of VAP. Notable limitations included low numbers of patients, an imbalance in the numbers of patients randomized to each group, and lack of an independent, blinded evaluation of end points, such as interpretation of chest radiographs to exclude early VAP. Both of these studies on VAT are provocative, consistent with our current concepts of VAP pathogenesis and prevention, but have limitations and several additional questions that need to be addressed in future studies, some of which are summarized in Table 2.

VAT: A NEW PARADIGM FOR CLINICAL RESEARCH

Limited aforementioned data suggest that patients with VAT may benefit from early, appropriate antibiotic therapy, which parallels principles advocated in the 2005 ATS/IDSA guidelines.
for the management of VAP. Surveillance of quantitative assessment of endotracheal aspirate specimens appears to be important for early identification of MDR pathogens and antibiotic sensitivity profiles and as a clinical marker for earlier, targeted antibiotic therapy. VAT may also be a valuable, reproducible, microbiologic end point measure for research trials evaluating new antibiotics, as outlined in Figure 5 and summarized in Table 3 [1, 4, 5]. Other relevant clinical end points include duration of mechanical ventilation, ICU stay, and antibiotic use. We also suggest monitoring serial clinical (ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen) and microbiologic responses to therapy until extubation, 14-day and 28-day mortality, morbidity using quality-of-life markers, and data on health care costs in the study groups.

Advantages of using serial quantitative assessment of endotracheal aspirate specimens to identify VAT as an end point for clinical research trials are numerous, but more data are needed to address the concerns and limitations summarized in Tables 2 and 3. Examples include the impact of targeted therapy, the threshold for diagnosis (\(1 \times 10^5\) vs \(1 \times 10^6\) cfu/mL), and the impact of current prevention strategies on the incidence of VAT. In addition, treatment of VAT may allow shorter courses of treatment, because therapy is initiated earlier, before extensive lung damage occurs and when there are lower numbers of pathogens [31].

On the basis of our current understanding of VAP pathogenesis, serial quantitative assessment of endotracheal aspirate specimens may provide a means to monitor the lower respiratory tract and provide a trigger to initiate therapy and to optimize prevention [1, 4, 7]. Other benefits include a standard definition for lower respiratory tract infection for comparing hospitals, a new target for VAP prevention, improved patient outcomes in terms of reduced antibiotic use, duration of mechanical ventilation, duration of ICU stay, morbidity, and mortality. All of these should translate into decreased health care expenditures.

Several new areas for future research on VAP and VAT are possible by thinking outside the box. Greater success could probably be achieved by using a large, collaborative national and international network of interested experts funded by different pharmaceutical companies, similar to the AIDS Clinical Trials Group model. A group of investigators who are dedicated and interested could develop well-designed clinical trials involving a spectrum of patient populations coupled with independent data collection and statistical analyses to assess the risk, benefit, and impact of new antibiotic regimens, devices, and prevention strategies. Such a network could save millions of dollars, could reduce confusion, and would be more likely

### Table 2. Summary of Advantages, Limitations, and Questions of a Model Based on Serial Quantitative Assessment of Endotracheal Aspirate (Q-ETA) Samples for Early Diagnosis and Targeted Antibiotic Therapy of Ventilator-Associated Tracheobronchitis (VAT) and Prevention of Ventilator-Associated Pneumonia (VAP)

<table>
<thead>
<tr>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantages of VAT</td>
</tr>
<tr>
<td>Standardized microbiologic criteria for Q-ETA easy to perform</td>
</tr>
<tr>
<td>Serial Q-ETA identifies tracheal pathogens and their antibiotic susceptibilities</td>
</tr>
<tr>
<td>Diagnosis does not rely on radiographic changes</td>
</tr>
<tr>
<td>Targeted earlier, appropriate antibiotics rather than empirical therapy and deescalation</td>
</tr>
<tr>
<td>Reduces ambiguity of chest radiograph findings for VAT diagnosis</td>
</tr>
<tr>
<td>In contrast to VAP, VAT is not considered as a preventable health care–associated infection or medical error</td>
</tr>
<tr>
<td>Improved patient outcomes and reduced health care costs</td>
</tr>
<tr>
<td>An additional strategy for VAT prevention</td>
</tr>
<tr>
<td>VAT limitations and questions</td>
</tr>
<tr>
<td>Specific diagnostic threshold for Q-ETA needed ((&gt;1 \times 10^5) vs (1 \times 10^6) cfu/mL)</td>
</tr>
<tr>
<td>Thresholds for different pathogens and for immunocompromised patients</td>
</tr>
<tr>
<td>Frequency of surveillance Q-ETA not well established; increased volume of work for microbiology laboratories</td>
</tr>
<tr>
<td>Comparison data on Q-ETA and SQ-ETA for diagnosis</td>
</tr>
<tr>
<td>Predictive value of serial Q-ETA for identifying a pathogen</td>
</tr>
<tr>
<td>Current data on VAT impact on VAP prevention needed</td>
</tr>
<tr>
<td>Confirmation and validation needed in larger databases</td>
</tr>
<tr>
<td>VAT not a current standard of care</td>
</tr>
</tbody>
</table>

**NOTE.** cfu, Colony-forming units; SQ, semiquantitative.
to answer our current vexing clinical questions and provide better, evidence-based recommendations for future guidelines and current clinical management of lower respiratory tract infections in patients receiving mechanical ventilation.

CONCLUSIONS

Prevention of VAP has been a priority for hospitals that has achieved great success, but many critical care and infectious diseases specialists and pulmonologists do not believe that the use of the VAP bundle and checklists alone will produce a zero-VAP situation, especially in referral hospitals caring for patients with serious underlying diseases and multiple risk factors [14, 32]. In addition, in public reporting of health care infections, some persons believe that VAP should be considered as a medical error; focus on VAT may provide a better tool for comparing hospitals and quality-improvement efforts.

The definition of VAT is simpler, more reproducible, and more quantitative than the definition of VAP, and it is not currently considered to be a medical error. The VAT model could be advantageous for clinical research trials of new treatments and interventions by facilitating patient enrollment and providing more standardized comparisons of study patients, with tighter definitions based on quantitative microbiology. There would also be interesting data on bacterial burden and eradication rates over time, as well as better information on clinical failures and causes of relapse (Table 3). The use of serial surveillance cultures to identify and monitor MDR pathogens over time, coupled with the use of VAT as a trigger for initiating earlier appropriate therapy, could provide interesting data on the efficacy of an investigational antibiotic. The VAT model could also better assess the benefit of many different prevention strategies advocated for VAP. Focusing on VAT should also reduce the enormous costs of current clinical trials and confusion associated with outcome data based on poor definitions. Clearly, this is time to think outside the box and invest in better clinical research using VAT as a model for future clinical trials and for clinical management.

Acknowledgments

We thank Kathleen A. Craven for her suggestions and review of the manuscript.

Potential conflicts of interest. D.E.C. has received research funding from Bard and Pfizer; is a member of the speaker’s bureau for Pfizer, Merck, Covidien, Sanofi Pasteur, and Astellas; has received honoraria for speaking from Pfizer, Merck, Covidien, Wyeth, Sanofi Pasteur, Ortho McNeil, and Bard Pharmaceuticals; was a member of a data safety monitoring board for a Johnson & Johnson study of a new antibiotic for pneumonia; and has been a consultant to Arpida, Cubist, and Bayer-Nektar.

K.I.H.: no conflicts.

Supplement sponsorship. This article was published as part of a supplement entitled “Workshop on Issues in the Design of Clinical Trials for Antibacterial Drugs for Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia,” sponsored by the US Food and Drug Administration, Infectious Diseases Society of America, American College of Chest Physicians, American Thoracic Society, and the Society of Critical Care Medicine, with financial support from the Pharmaceutical Research and Manufacturers of America, AstraZeneca Pharmaceuticals, and Forest Pharmaceuticals.

References