Evidence-Based Algorithms for Diagnosing and Treating Ventilator-Associated Pneumonia

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BACKGROUND: Ventilator-associated pneumonia (VAP) is widely recognized as a serious and common complication associated with high morbidity and high costs. Given the complexity of caring for heterogeneous populations in the intensive care unit (ICU), however, there is still uncertainty regarding how to diagnose and manage VAP.

OBJECTIVE: We recently conducted a national collaborative aimed at reducing health care–associated infections in ICUs of hospitals operated by the Hospital Corporation of America (HCA). As part of this collaborative, we developed algorithms for diagnosing and treating VAP in mechanically ventilated patients. In the current article, we (1) review the current evidence for diagnosing VAP, (2) describe our approach for developing these algorithms, and (3) illustrate the utility of the diagnostic algorithms using clinical teaching cases.

DESIGN: This was a descriptive study, using data from a national collaborative focused on reducing VAP and catheter-related bloodstream infections.

SETTING: The setting of the study was 110 ICUs at 61 HCA hospitals.

INTERVENTION: None.

*Figures and Appendix can be found online at www.interscience.wiley.com/jhm
MEASUREMENTS AND RESULTS: We assembled an interdisciplinary team that included infectious disease specialists, intensivists, hospitalists, statisticians, critical care nurses, and pharmacists. After reviewing published studies and the Centers for Disease Control and Prevention VAP guidelines, the team iteratively discussed the evidence, achieved consensus, and ultimately developed these practical algorithms. The diagnostic algorithms address infant, pediatric, immunocompromised, and adult ICU patients.

CONCLUSIONS: We present practical algorithms for diagnosing and managing VAP in mechanically ventilated patients. These algorithms may provide evidence-based real-time guidance to clinicians seeking a standardized approach to diagnosing and managing this challenging problem.

KEYWORDS: critical care, health care–associated infection, pneumonia diagnosis, quality of health care, ventilator-associated pneumonia.

Ventilator-associated pneumonia (VAP) is a serious and common complication for patients in the intensive care unit (ICU).\textsuperscript{1} VAP is defined as a pulmonary infection occurring after hospital admission in a mechanically-ventilated patient with a tracheostomy or endotracheal tube.\textsuperscript{2,3} With an attributable mortality that may exceed 20% and an estimated cost of $3000-$20,000 per episode,\textsuperscript{4–9} the management of VAP is an important issue for both patient safety and cost of care.

The diagnosis of VAP is a controversial topic in critical care, primarily because of the difficulty distinguishing between airway colonization, upper respiratory tract infection (eg, tracheobronchitis), and early-onset pneumonia. Some clinicians insist that an invasive sampling technique (eg, bronchoalveolar lavage) with quantitative cultures is essential for determining the presence of VAP.\textsuperscript{10} However, other clinicians suggest that a noninvasive approach using qualitative cultures (eg, tracheal suctioning) is an acceptable alternative.\textsuperscript{11} Regardless, nearly all experts agree that a specimen for microbiologic culture should be obtained prior to initiating antibiotics. Subsequent therapy should then be adjusted according to culture results.

Studies from both Europe and North America have demonstrated considerable variation in the diagnostic approaches used for patients with suspected VAP.\textsuperscript{12,13} This variation is likely a result of several factors including controversy about the best diagnostic approach, variation in clinician knowledge and experience, and variation in ICU management protocols. Such practice variability is common for many ICU behaviors.\textsuperscript{14–16} Quality-of-care proponents view this variation as an important opportunity for improvement.\textsuperscript{17}

During a recent national collaborative aimed at reducing health care–associated infections in the ICU, we discovered many participants were uncertain about how to diagnose and manage VAP, and considerable practice variability existed among participating hospitals. This uncertainty provided an important opportunity for developing consensus on VAP management. On the basis of diagnostic criteria outlined by the Centers for Disease Control and Prevention (CDC), we developed algorithms as tools for diagnosing VAP in 4 ICU populations: infant, pediatric, immunocompromised, and adult ICU patients. We also developed an algorithm for initial VAP treatment. An interdisciplinary team of experts reviewed the current literature and developed these evidence-based consensus guidelines. Our intent is that the algorithms provide guidance to clinicians looking for a standardized approach to the diagnosis and management of this complicated clinical situation.

METHODS

Our primary goal was to develop practical algorithms that assist ICU clinicians in the diagnosis and management of VAP during daily practice. To improve the quality and credibility of these algorithms, the development process used a stepwise approach that included assembling an interdisciplinary team of experts, appraising the published evidence, and formulating the algorithms through a consensus process.\textsuperscript{18}
We developed these diagnostic algorithms as part of a national collaborative effort aimed at reducing VAP and central venous catheter–related bloodstream infections in the ICU. This effort was possible through a 2-year Partnerships in Implementing Patient Safety grant funded by the Agency for Healthcare Research and Quality (AHRQ). The voluntary collaborative was conducted in 61 medical/surgical and children's hospitals across the Hospital Corporation of America (HCA), a company that owns and/or operates 173 hospitals and 107 freestanding surgery centers in 20 states, England, and Switzerland. HCA is one of the largest providers of health care in the United States. All participating hospitals had at least 1 ICU, and a total of 110 ICUs were included in the project. Most hospitals were in the southern or southeastern regions of the United States.

Interdisciplinary Team

We assembled an interdisciplinary team to develop the diagnostic algorithms. Individuals on the team represented the specialties of infectious diseases, infection control, anesthesia, critical care medicine, hospital medicine, critical care nursing, pharmacy, and biostatistics. The development phase occurred over 3–4 months and used an iterative process that consisted of both group conference calls and in-person meetings.

Our goal was not to conduct a systematic review but rather to develop practical algorithms for collaborative participants in a timely manner. Our literature search strategy included MEDLINE and the Cochrane Library. We focused on articles that addressed key diagnostic issues, proposed an algorithm, or summarized a topic relevant to practicing clinicians. Extra attention was given to articles that were randomized trials, meta-analyses, or systematic reviews. No explicit grading of articles was performed. We examined studies with outcomes of interest to clinicians, including mortality, number of ventilator days, length of stay, antibiotic utilization, and antibiotic resistance.

We screened potentially relevant articles and the references of these articles. The search results were reviewed by all members of the team, and an iterative consensus process was used to derive the current algorithms. Preliminary versions of the algorithms were shown to other AHRQ investigators and outside experts in the field, and additional modifications were made based on their feedback. The final algorithms were approved by all study investigators.

RESULTS

Literature Overview

Overall, there is an enormous body of published literature on diagnosing and managing VAP. The Medline database has listed more than 500 articles on VAP diagnosis in the past decade. Nonetheless, the best diagnostic approach remains unclear. The “gold standard” for diagnosing VAP is lung biopsy with histopathologic examination and tissue culture. However, this procedure is fraught with potential dangers and impractical for most critically ill patients. Therefore, practitioners traditionally combine their clinical suspicion (based on fever, leukocytosis, character of sputum, and radiographic changes), epidemiologic data (eg, patient demographics, medical history, and ICU infection surveillance data), and microbiologic data.

Several issues relevant to practicing clinicians deserve further mention.

Definition of VAP

Although early articles used variable criteria for diagnosing VAP, recent studies have traditionally defined VAP as an infection occurring more than 48 hours after hospital admission in a mechanically ventilated patient with a tracheostomy or endotracheal tube. In early 2007, the CDC revised their definition for diagnosing VAP. These latest criteria state there is no minimum period that the ventilator must be in place in order to diagnose VAP. This important change must be kept in mind when examining future studies.

The term VAP is more specific than the term health care–associated pneumonia. The latter encompasses patients residing in a nursing home or long-term care facility; hospitalized in an acute care hospital for more than 48 hours in the past 90 days; receiving antibiotics, chemotherapy, or wound care within the past 30 days; or attending a hospital or hemodialysis clinic.

The CDC published detailed criteria for diagnosing VAP in its member hospitals (Tables 1 and 2). Because diagnosing VAP in infants, children, elderly, and immunocompromised patients is often confusing because of other conditions with similar signs and symptoms, the CDC published alternate criteria for these populations. A key objective during development of our algorithms was to consolidate and simplify these diagnostic criteria for ICU clinicians.
# TABLE 1
CDC Criteria for Diagnosing Ventilator-Associated Pneumonia (VAP),3 Defined as Having Been on a Mechanical Ventilator in the Past 48 Hours

<table>
<thead>
<tr>
<th>Radiology</th>
<th>Signs/symptoms/laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two or more serial chest radiographs with at least 1 of the following*:</td>
<td>CRITERIA FOR ANY PATIENT</td>
</tr>
<tr>
<td>- New or progressive <em>and</em> persistent infiltrate</td>
<td>At least 1 of the following:</td>
</tr>
<tr>
<td>- Consolidation</td>
<td>- Fever (&gt;38°C or &gt;100.4°F) with no other recognized cause</td>
</tr>
<tr>
<td>- Cavitiation</td>
<td>- Leukopenia (&lt;4000 WBC/mmm³) or leukocytosis (≥12,000 WBC/mmm³)</td>
</tr>
<tr>
<td>- Pneumatoceles, in infants ≤ 1 year old</td>
<td>- For adults ≥70 years old, altered mental status with no other recognized cause</td>
</tr>
</tbody>
</table>

Note: In patients without underlying pulmonary or cardiac disease (eg, respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), 1 definitive chest radiograph is acceptable.*

At least 2 of the following:
- New onset of purulent sputum,§ or change in character of sputum,§ or increased respiratory secretions, or increased suctioning requirements
- New-onset or worsening cough or dyspnea or tachypnea§
- Rales§ or bronchial breath sounds
- Worsening gas exchange (eg, O₂ desaturation [eg, PaO₂/FiO₂ ≤ 240],** increased oxygen requirement, or increased ventilation demand)
- Any laboratory criterion from Table 2

ALTERNATE CRITERIA FOR INFANTS ≤ 1 YEAR OLD
Worsening gas exchange (eg, O₂ desaturation, increased ventilation demand or O₂ requirement) and

At least 3 of the following:
- Temperature instability with no other recognized cause
- Leukopenia (<4000 WBC/mm³) or leukocytosis (≥15,000 WBC/mm³) and left shift (≥10% bands)
- New-onset purulent sputum,§ change in character of sputum,§ increased respiratory secretions, or increased suctioning requirements
- Apnea, tachypnea,§ nasal flaring with retraction of chest wall, or grunting
- Wheezing, rales,§ or rhonchi
- Cough
- Bradycardia (<100 beats/min) or tachycardia (>170 beats/min)

ALTERNATE CRITERIA FOR CHILD >1 OR ≤12 YEARS OLD
At least 3 of the following:
- Fever (>38.4°C or >101.1°F) or hypothermia (<36.5°C or <97.7°F) with no other recognized cause
- Leukopenia (<4000 WBC/mm³) or leukocytosis (≥15,000 WBC/mm³)
- New-onset purulent sputum,§ change in character of sputum,§ increased respiratory secretions, or increased suctioning requirements
- New-onset or worsening cough or dyspnea, apnea, or tachypnea§
- Rales§ or bronchial breath sounds
- Worsening gas exchange (eg, O₂ desaturation <94%, increased ventilation demand or O₂ requirement)
- Any laboratory criterion from Table 2

ALTERNATE CRITERIA FOR IMMUNOCOMPROMISED PATIENTS***
At least 1 of the following:
- Fever (>38.4°C or >101.1°F) with no other recognized cause
- For adults > 70 years old, altered mental status with no other recognized cause
- New-onset purulent sputum,§ change in character of sputum,§ increased respiratory secretions, or increased suctioning requirements
- New-onset or worsening cough, dyspnea, or tachypnea§
- Rales§ or bronchial breath sounds
- Worsening gas exchange (eg, O₂ desaturation [eg, PaO₂/FiO₂ ≤ 240],** increased oxygen requirement, or increased ventilation demand)
- Hemoptysis
- Pleuritic chest pain
- Matching positive blood and sputum cultures with Candida spp.†††
- Evidence of fungi or Pneumocystis from minimally contaminated LRT specimen‡‡ (eg, BAL or protected specimen brushing) from 1 of the following:
  - Direct microscopic exam
  - Positive culture of fungi
- Any laboratory criterion from Table 2

(continued)
TABLE 1 (continued)

CDC, Centers for Disease Control and Prevention.

In nonventilated patients, the diagnosis of pneumonia may be quite clear based on symptoms, signs, and a single definitive chest radiograph. However, in patients with pulmonary or cardiac disease (eg, congestive heart failure), the diagnosis of pneumonia may be particularly difficult because other noninfectious conditions (eg, pulmonary edema) may simulate pneumonia. In these cases, serial chest radiographs must be examined to help separate infectious from noninfectious pulmonary processes. To help confirm difficult cases, it may be useful to review radiographs on the day of diagnosis, 3 days prior to the diagnosis, and on days 2 and 7 after the diagnosis. Pneumonia may have rapid onset and progression but does not resolve quickly. Radiographic changes of pneumonia persist for several weeks. As a result, rapid radiographic resolution suggests that the patient does not have pneumonia but rather a noninfectious process such as artefact or congestive heart failure.

Note that there are many ways of describing the radiographic appearance of pneumonia. Examples include but are not limited to air-space disease, focal opacification, and patchy areas of increased density. Although perhaps not specifically delineated as pneumonia by the radiologist, in the appropriate clinical setting these alternative descriptive wordings should be seriously considered as potentially positive findings.

Purulent sputum is defined as secretions from the lungs, bronchi, or trachea that contain >25 neutrophils and ≥10 squamous epithelial cells per low-power field (>X100). If your laboratory reports these data quantitatively (eg, many WBCs or few squames), be sure their descriptors match this definition of purulent sputum. This laboratory confirmation is required because written clinical descriptions of purulence are highly variable.

A single notation of either purulent sputum or change in character of the sputum is not meaningful; repeated notations over a 24-hour period would be more indicative of the onset of an infectious process. Change in the character of sputum refers to the color, consistency, odor, and quantity.

Care must be taken to determine the etiology of pneumonia in a patient with positive blood cultures and radiographic evidence of pneumonia, especially if the patient has invasive devices in place such as intravascular lines or an indwelling urinary catheter. In general, in an immunocompetent patient, blood cultures positive for coagulase-negative staphylococci, common skin contaminants, and yeasts will not be the etiology of the pneumonia. An endotracheal aspirate is not a minimally contaminated specimen. Therefore, an endotracheal aspirate does not meet the laboratory criteria.

**This measure of arterial oxygenation is defined as the ratio of arterial tension (PaO2) to the inspiratory fraction of oxygen (FiO2).**

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In adults, tachypnea is defined as respiration rate >25 breaths/min. Tachypnea is defined as >75 breaths/min in premature infants born <37 weeks’ gestation and until the 40th week; >60 breaths/min in patients <2 months old; >50 breaths/min in patients 2–12 months old; and >30 breaths/min in children >1 year old.

Notes may be described as crackles.

Blood and sputum specimens must be collected within 48 hours of each other.

Semi-quantitative or nonquantitative cultures of sputum obtained by deep cough, induction, aspiration, or lavage are acceptable. If quantitative culture results are available, refer to algorithms that include such specific laboratory findings.

**Etiology**

The most commonly isolated VAP pathogens in all patients are bacteria.21 Most of these organisms normally colonize the respiratory and gastrointestinal tracts, but some are unique to health care settings. Tracheal intubation disrupts the body’s natural anatomic and physiologic defenses and facilitates easier entry of these pathogens. Typical organisms include Staphylococcus aureus, Pseudomonas aeruginosa, Enterobacter species, Klebsiella pneumoniae, Acinetobacter species, Escherichia coli, and Haemophilus influenzae.22,23 Unfortunately, the prevalence of antimicrobial resistance among VAP pathogens is increasing.24 Risk factors for antibiotic resistance are common to ICU patients and include recent antibiotics, hemodialysis, nursing home residence, immunosuppression, and chronic wound care.5 Polymicrobial infections are frequently seen in VAP, with up to 50% of all VAP episodes caused by more than 1 organism.25

Viral VAP is rare in immunocompetent hosts, and seasonal outbreaks of influenza and other similar viruses are usually limited to nonventilated patients.26 However, influenza is underrecognized as a potential nosocomial pathogen, and numerous nosocomial outbreaks because of influenza have been reported.27–31 Although herpes simplex virus is often detected in the respiratory tract of critically ill patients, its clinical importance remains unclear.32

Fungal VAP is also rare in immunocompetent hosts. On the other hand, pulmonary fungal infections are common in immunocompromised patients, especially following chemotherapy and transplantation. Candida species are often isolated from the airways of normal hosts, but most cases traditionally have been considered clinically unimportant because these organisms are normal oropharyngeal flora and rarely invade lung tissue.33,34 It is unclear whether recent studies suggesting Candida colonization is associated with a higher risk for Pseudomonas VAP will change this conventional wisdom.35–37

Immunocompromised patients with suspected VAP are unique because they are at risk not only for typical bacteria (which are the most common causes of VAP) but also for rarer opportunistic
TABLE 2

Laboratory Criteria Supporting Diagnosis of VAP

- Positive growth in blood culture* not related to another source of infection
- Positive growth in culture of pleural fluid
- Positive quantitative culture from minimally contaminated LRT specimen (e.g., BAL) \(^3\)
- \(>5\%\) BAL-obtained cells contain intracellular bacteria on direct microscopic exam (e.g., gram stain)
- Histopathologic exam shows at least 1 of the following:
  - Abscess formation or foci of consolidation with intense PMN accumulation in bronchioles and alveoli
  - Positive quantitative culture of lung parenchyma
  - Evidence of lung parenchyma invasion by fungal hyphae or pseudohyphae
- Positive culture of virus or Chlamydia from respiratory secretions
- Positive detection of viral antigen or antibody from respiratory secretions (e.g., EIA, FAMA, shell vial assay, PCR)
- Fourfold rise in paired sera (IgG) for pathogen (e.g., influenza viruses, Chlamydia)
- Positive PCR for Chlamydia or Mycoplasma
- Positive micro-IF test for Chlamydia
- Positive culture or visualization by micro-IF of Legionella spp. from respiratory secretions or tissue
- Detection of Legionella pneumophila serogroup 1 antigens in urine by RIA or EIA
- Fourfold rise in L. pneumophila serogroup 1 antibody titer to \(\geq 1:128\) in paired acute and convalescent sera by indirect IFA

* Care must be taken to determine the etiology of pneumonia in a patient with positive blood cultures and radiographic evidence of pneumonia, especially if the patient has invasive devices in place such as intravascular lines or an indwelling urinary catheter. In general, in an immunocompetent patient, blood cultures positive for coagulase-negative staphylococci, common skin contaminants, and yeasts will not be the etiologic agent of the pneumonia.

\(^3\) An endotracheal aspirate is not a minimally contaminated specimen. Therefore, an endotracheal aspirate does not meet the laboratory criteria.

Infections and noninfectious processes that mimic pneumonia. While assessing these patients, clinicians must consider the status of the underlying disease, duration and type of immunosuppression, prophylactic regimens, and risk factors for noninfectious causes of pulmonary infiltrates. Common opportunistic infections include viruses, mycobacteria, fungi, and Pneumocystis. Noninfectious processes include pulmonary edema, drug toxicity, radiation pneumonitis, engraftment syndrome, bronchiolitis obliterans organizing pneumonia, alveolar proteinosis, transfusion-related lung injury, alveolar hemorrhage, and progression of underlying disease. In general, diagnosing VAP in the immunocompromised patient requires a prompt, comprehensive, and multidisciplinary approach.

In preterm and term infants, the most common VAP pathogens are gram-negative organisms such as E. coli and P. aeruginosa. Other less common pathogens are Enterobacter, Klebsiella, Acinetobacter, Proteus, Citrobacter, and Stenotrophomonas maltophilia. Infants with a preceding bloodstream infection or prolonged intubation are more likely to develop VAP. Unfortunately, gram-negative bacteria often colonize the airways of mechanically ventilated infants, and tracheal aspirate culture data are difficult to interpret in this population.

Children are more likely to develop VAP if they are intubated for more than 48 hours. The most common pathogens isolated from tracheal aspirates in mechanically ventilated children are enteric gram-negative bacteria, P. aeruginosa, and S. aureus. Few studies have precisely delineated the pathogenesis of VAP in the pediatric ICU population.

Overall, the causes of VAP vary by hospital, patient population, and ICU type. Therefore, it is essential that ICU clinicians remain knowledgeable about their local surveillance data. Awareness of VAP microbiology is essential for optimizing initial antibiotic therapy and improving outcomes.

**“Early” Versus “Late” VAP**

Distinguishing between “early” and “late” VAP is important for initial antibiotic selection because the etiologic pathogens vary between these 2 periods. Early VAP (days 1–4 of hospitalization) usually involves antibiotic-sensitive community-acquired bacteria and carries a better prognosis. In contrast, late VAP (≥5 days after hospital admission) is more likely to be caused by antibiotic-resistant nosocomial bacteria that lead to increased morbidity and mortality. All patients who have been hospitalized or have received antibiotics dur-
ing the prior 90 days should be treated as having late VAP because they are at much higher risk for colonization and infection with antibiotic-resistant bacteria.47 Of note, 2 recent studies suggest that pathogens in the early and late periods are becoming similar at some institutions.50,51 Overall, the distinction between early and late VAP is important because it affects the likelihood that a patient has antibiotic-resistant bacteria. If antibiotic-resistant pathogens are suspected, initial therapy should include empiric triple antibiotics until culture data are available.

Culturing Approaches
Because clinical criteria alone are rarely able to accurately diagnose VAP,52,53 clinicians should also obtain a respiratory specimen for microbiologic culture. Despite the convenience of blood cultures, their sensitivity for diagnosing VAP is poor, and they rarely make the diagnosis alone.54 Two methods are available for culturing the lungs—an invasive approach (eg, bronchoscopy with bronchoalveolar lavage) and a noninvasive approach (eg, tracheal aspirate).

Some investigators believe that adult patients with suspected VAP should always undergo an invasive sampling of lower-respiratory-tract secretions.55 Proponents of the invasive approach cite the frequency with which potential pathogens colonize the trachea of ICU patients and create spurious results on tracheal aspirates.22 In addition, several studies have shown that clinicians are more likely to narrow the spectrum of antibiotics after obtaining an invasive diagnostic sample.56 In other words, the invasive approach has been associated with better antimicrobial stewardship.

Other investigators believe that a noninvasive approach is equally safe and effective for diagnosing VAP.57 This “clinical” approach involves culturing a tracheal aspirate and using a pneumonia prediction score such as the clinical pulmonary infection score (CPIS; Table 3). The CPIS assigns 0–12 points based on 6 clinical criteria: fever, leukocyte count, oxygenation, quantity and purulence of secretions, type of radiographic abnormality, and results of sputum gram stain and culture.58 As developed, a CPIS > 6 has a sensitivity of 93% and a specificity of 100% for diagnosing VAP.58 However, the CPIS requires that nurses record sputum volume and that the laboratory stains the specimen. When the CPIS has been modified based on the unavailability of such resources, the results have been less impressive.59–61 Despite studies showing that a noninvasive clinical approach can achieve adequate initial antibiotic coverage and reduce overuse of broad-spectrum agents,62,63 clinicians who use the CPIS must understand its inherent limitations.
A meta-analysis\textsuperscript{56} comparing the utility of an invasive versus a noninvasive culturing approach identified 4 randomized trials examining this issue.\textsuperscript{66–69} Overall, an invasive approach did not alter mortality, but patients undergoing bronchoscopy were much more likely to have their antibiotic regimens modified by clinicians. This suggests that the invasive approach may allow more directed use of antibiotics. Recently, the Canadian Critical Care Trials Group conducted a multicenter randomized trial looking at this issue.\textsuperscript{11} There was no difference between the 2 approaches in mortality, number of ventilator days, and antibiotic usage. However, all patients in this study were immediately treated with empiric broad-spectrum antibiotics until culture results were available, and the investigators did not have a protocol for stopping antibiotics after culture data were available.

In summary, both invasive and noninvasive culturing approaches are considered acceptable options for diagnosing VAP. Readers interested in learning more about this topic should read the worthwhile Expert Discussion\textsuperscript{70} by Chastre and colleagues\textsuperscript{55} at the end of this article. In general, we recommend that ICU clinicians use a combination of clinical suspicion (based on the CPIS or other objective data) and cultures ideally obtained prior to antibiotics. Regardless of the chosen culturing approach, clinicians must recognize that 1 of the most important determinants of patient outcome is prompt administration of adequate initial antibiotics.\textsuperscript{71–75}

\textbf{Initial Antibiotic Administration}

Delaying initial antibiotics in VAP increases the risk of death.\textsuperscript{71–75} If a patient receives ineffective initial therapy, a later switch to appropriate therapy does not eliminate the increased mortality risk. Therefore, a comprehensive approach to VAP diagnosis requires consideration of initial empiric antibiotic administration.

Whenever possible, clinicians should obtain a lower respiratory tract sample for microscopy and culture before administering antibiotics because performing cultures after antibiotics have been recently started will lead to a higher rate of false-negative results.\textsuperscript{76} Unless the patient has no signs of sepsis and microscopy is completely negative, clinicians should then immediately start empiric broad-spectrum antibiotics.\textsuperscript{57} Once the culture sensitivities are known, therapy can be deescaled to a narrower spectrum.\textsuperscript{77} Recent studies suggest that shorter durations of therapy (~8 days) are as effective as longer courses and are associated with lower colonization rates by antibiotic-resistant bacteria.\textsuperscript{62,78}

Initial broad-spectrum antibiotics should be chosen based on local bacteriology and resistance patterns. Clinicians must remain aware of the most common bacterial pathogens in their local community, hospital, and ICU. This is essential for both ensuring adequate initial antibiotic coverage and reducing overall antibiotic days.\textsuperscript{65} Unrestricted use of broad-spectrum antibiotics increases the risk of resistant pathogens. Clinicians must continually deescalate therapy and use narrow-spectrum drugs as pathogens are identified.\textsuperscript{79}

\textbf{Prevention of VAP}

In 2005, the American Thoracic Society published guidelines for the management of adults with VAP.\textsuperscript{5} These guidelines included a discussion of modifiable risk factors for preventing VAP and used an evidence-based grading system to rank the various recommendations. The highest evidence (level 1) comes from randomized clinical trials, moderate evidence (level 2) comes from nonrandomized studies, and the lowest evidence (level 3) comes from case studies or expert opinion. Others have also published their own guidelines and recommendations for preventing VAP.\textsuperscript{80–82} Table 4 shows the key VAP preventive strategies.

Some strategies are not recommended for VAP prevention in general ICU patients. Selective decontamination of the digestive tract (ie, prophylactic oral antibiotics) has been shown to reduce respiratory infections in ICU patients,\textsuperscript{113} but its overall role remains controversial because of concerns it may increase the incidence of multi-drug-resistant pathogens.\textsuperscript{114} Similarly, prophylactic intravenous antibiotics administered at the time of intubation can reduce VAP in certain patient populations,\textsuperscript{115} but this strategy is also associated with an increased risk of antibiotic-resistant nosocomial infections.\textsuperscript{116} Using kinetic beds and scheduled chest physiotherapy to reduce VAP is based on the premise that critically ill patients often develop atelectasis and cannot effectively clear their secretions. Unfortunately, neither of these modalities has been shown to consistently reduce VAP in medical ICU patients.\textsuperscript{117–119}
Algorithms for Diagnosis and Treatment of VAP

We present algorithms for diagnosing VAP in 4 ICU populations: infant (<1 year old), pediatric (1-12 years old), immunocompromised, and adult ICU patients (Figs. 1–4). Because clinicians face considerable uncertainty when diagnosing VAP, we sought to develop practical algorithms for use in daily ICU practice. Although we provided the algorithms to collaborative participants as a tool for improving care, we never mandated use, and we did not monitor levels of adherence.

In Figure 5, we present a guideline for the initial treatment of VAP. The key elements in this algorithm include: (1) obtaining cultures prior to administering antibiotics, (2) starting empiric antibiotics promptly, (3) assessing whether the patient has risk factors for antibiotic-resistant pathogens, and (4) modifying or stopping the initial therapy based on culture results. If the patient has any risk factors for antibiotic-resistant pathogens, he or she should be initially treated with 3 drugs: an antipseudomonal beta-lactam, an antipseudomonal quinolone, and linezolid or vancomycin. The empiric use of 2 antipseudomonal medications is essential because of the high rates of antibiotic resistance among *Pseudomonas* and other gram-negative organisms. Likewise, the empiric use of linezolid or vancomycin will cover antibiotic-resistant gram-positive organisms such as methicillin-resistant *S. aureus* (MRSA).

Five teaching cases are presented in the Appendix. We demonstrate how to utilize the diagnostic algorithms in these clinical scenarios and offer tips for clinicians wishing to employ these tools in their daily practice. These cases are useful for educating residents, nurses, and hospitalists.

Overall, our intent is that the combined use of these VAP algorithms facilitate a streamlined diagnostic approach and minimize delays in initial antibiotic administration. A primary focus of any VAP guideline should be early and appropriate antibiotics in adequate doses, with deescalation of therapy as culture data permit. In general, the greatest risk to a patient with VAP is delaying initial adequate antibiotic coverage, and for this reason, antibiotics must always be administered promptly. However, if culture data are negative, the clinician should consider withdrawing unnecessary antibiotics. For example, the absence of gram-positive organisms on BAL after 72 hours would strongly suggest that MRSA is not playing a role and that vancomycin can be safely stopped. We agree with Neiderman that “the decision point

### Table 4: Strategies for Preventing VAP

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Level of evidence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>General infection control measures (hand hygiene, staff education, isolate MDR pathogens, etc.)</td>
<td>1</td>
<td>2,83,84</td>
</tr>
<tr>
<td>ICU infection surveillance</td>
<td>2</td>
<td>2,83–85</td>
</tr>
<tr>
<td>Avoid reintubation if possible, but promptly reintubate if a patient inanerably fails extubation</td>
<td>1</td>
<td>2,83,86,87</td>
</tr>
<tr>
<td>Use NPPV when appropriate (in selected patients)</td>
<td>1</td>
<td>88</td>
</tr>
<tr>
<td>Use oral route for endotracheal and gastric tubes (vs. nasal route)</td>
<td>2</td>
<td>89</td>
</tr>
<tr>
<td>Continuous suctioning of subglottic secretions (to avoid pooling on cuff and leakage into LRT)</td>
<td>1</td>
<td>90–92</td>
</tr>
<tr>
<td>Maintain endotracheal cuff pressure &gt; 20 cm H$_2$O (to prevent secretion leakage into LRT)</td>
<td>2</td>
<td>93</td>
</tr>
<tr>
<td>Avoid unnecessary ventilator circuit changes</td>
<td>1</td>
<td>94</td>
</tr>
<tr>
<td>Routinely empty condensate in ventilator circuit</td>
<td>2</td>
<td>95</td>
</tr>
<tr>
<td>Maintain adequate nursing and therapist staffing</td>
<td>2</td>
<td>96–98</td>
</tr>
<tr>
<td>Implement ventilator weaning and sedation protocols</td>
<td>2</td>
<td>99–101</td>
</tr>
<tr>
<td>Semi-rect patient positioning (vs. supine)</td>
<td>1</td>
<td>102</td>
</tr>
<tr>
<td>Avoid aspiration when using enteral nutrition</td>
<td>1</td>
<td>103,104</td>
</tr>
<tr>
<td>Topical oral antiseptic (e.g., chlorhexidine)</td>
<td>1</td>
<td>105–108</td>
</tr>
<tr>
<td>Control blood sugar with insulin</td>
<td>1</td>
<td>109</td>
</tr>
<tr>
<td>Use heat-moisture exchanger (vs. conventional humidifier) to reduce tubing condensate</td>
<td>1</td>
<td>95</td>
</tr>
<tr>
<td>Avoid unnecessary red blood cell transfusions</td>
<td>1</td>
<td>110</td>
</tr>
<tr>
<td>Use of sucralfate for GI prophylaxis</td>
<td>1</td>
<td>111,112</td>
</tr>
<tr>
<td>Influenza vaccination for health care workers</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

MDR, multidrug resistant; NPPV, noninvasive positive pressure ventilation; LRT, lower respiratory tract.
is not whether to start antibiotics, but whether to continue them at day 2–3.”57

DISCUSSION
In this article, we introduce algorithms for diagnosing and managing VAP in infant, pediatric, immunocompromised, and adult ICU patients. We developed 4 algorithms because the hospitals in our system care for a wide range of patients. Our definitions for VAP were based on criteria outlined by the CDC because these rigorously developed criteria have been widely disseminated as components of the Institute for Healthcare Improvement’s “ventilator bundle.”120 Clinicians should be able to easily incorporate these practical algorithms into their current practice.

The algorithms were developed during a collaborative across a large national health care system. We undertook this task because many clinicians were uncertain how to integrate the enormous volume of VAP literature into their daily practice, and we suspected there was large variation in practice in our ICUs. Recent studies from other health care systems provided empirical evidence to support this notion.12,13

We offer these algorithms as practical tools to assist ICU clinicians and not as prescriptive mandates. We realize that the algorithms may need modification based on a hospital’s unique bacteriology and patient populations. We also anticipate that the algorithms will adapt to future changes in VAP epidemiology, preventive strategies, emerging pathogens, and new antibiotics.

Numerous resources are available to learn more about VAP management. An excellent guideline from the Infectious Diseases Society of America and the American Thoracic Society discusses VAP issues in detail,5 although this guideline only focuses on immunocompetent adult patients. The journal Respiratory Care organized an international conference with numerous VAP experts in 2005 and subsequently devoted an entire issue to this topic.81 The Canadian Critical Care Trials Group and the Canadian Critical Care Society conducted systematic reviews and developed separate guidelines for the prevention, diagnosis, and treatment of VAP.80,121

In summary, we present diagnostic and treatment algorithms for VAP. Our intent is that these algorithms may provide evidence-based practical guidance to clinicians seeking a standardized approach to diagnosing and managing this challenging problem.

REFERENCES


