enhanced by principles learned from quantitative-culture studies. The most recent IDSA/ATS guidelines for HAP/VAP suggest that either approach is clinically valid.

QUANTITATIVE-CULTURE APPROACH The essence of the quantitative-culture approach is to discriminate between colonization and true infection by determining the bacterial burden. The more distal in the respiratory tree the diagnostic sampling, the more specific the results and therefore the lower the threshold of growth necessary to diagnose pneumonia and exclude colonization. For example, a quantitative endotracheal aspirate yields proximate samples, and the diagnostic threshold is 10^6 cfu/mL. The protected specimen brush method, in contrast, obtains distal samples and has a threshold of 10^3 cfu/mL. Conversely, sensitivity declines as more distal secretions are obtained, especially when they are collected blindly (i.e., by a technique other than bronchoscopy). Additional tests that may increase the diagnostic yield include Gram's staining, differential cell counts, staining for intracellular organisms, and detection of local protein levels elevated in response to infection.

The Achilles heel of the quantitative approach is the effect of antibiotic therapy. With sensitive microorganisms, a single antibiotic dose can reduce colony counts below the diagnostic threshold. Recent changes in antibiotic therapy are the most significant. After 3 days, the operating characteristics of the tests are almost the same as if no antibiotic therapy has been given. Conversely, colony counts above the diagnostic threshold during antibiotic therapy suggest that the current antibiotics are ineffective. Even the normal host response may be sufficient to reduce quantitative-culture counts below the diagnostic threshold if sampling is delayed. In short, expertise in quantitative-culture techniques is critical, with a specimen obtained as soon as pneumonia is suspected and before antibiotic therapy is initiated or changed.

In a study comparing the quantitative with the clinical approach, use of bronchoscopic quantitative cultures resulted in significantly less antibiotic use at 14 days after study entry and in lower rates of mortality and severity-adjusted mortality at 28 days. In addition, more alternative sites of infection were found in patients randomized to the quantitative-culture strategy. A critical aspect of this study was that antibiotic treatment was initiated only in patients whose gram-stained respiratory sample was positive or who displayed signs of hemodynamic instability. Fewer than one-half as many patients were treated for pneumonia in the bronchoscopy group, and only one-third as many microorganisms were cultured.

CLINICAL APPROACH The lack of specificity of a clinical diagnosis of VAP has led to efforts to improve the diagnostic criteria. The Clinical Pulmonary Infection Score (CPIS) was developed by weighting of the various clinical criteria usually used for the diagnosis of VAP (Table 153-8). Use of the CPIS allows the selection of low-risk patients who may need only short-course antibiotic therapy or no treatment at all. Moreover, studies have demonstrated that the absence of bacteria in gram-stained endotracheal aspirates makes pneumonia an unlikely cause of fever or pulmonary infiltrates. These findings, coupled with a heightened awareness of the alternative diagnoses possible in patients with suspected VAP, can prevent inappropriate overtreatment for pneumonia. Furthermore, data show that the absence of an MDR pathogen in tracheal aspirate cultures eliminates the need for MDR coverage when empirical antibiotic therapy is narrowed. Since the most likely explanations for the mortality benefit of bronchoscopic quantitative cultures are decreased antibiotic selection pressure (which reduces the risk of subsequent infection with MDR pathogens) and identification of alternative sources of infection, a clinical diagnostic approach that incorporates such principles may result in similar outcomes.

Other large randomized studies that did not demonstrate a similar beneficial impact of quantitative culture on outcomes did not tightly link antibiotic treatment to the results of quantitative culture and other tests. Given the conflicting results only partially explained by methodologic issues, the IDSA/ATS guidelines therefore suggest that the choice depends on availability and local expertise.

TABLE 153-8 CLINICAL PULMONARY INFECTION SCORE (CPIS)

Criterion	Score
Fever (°C)	
≥38.5 but ≤38.9	1
>39 or <36	2
Leukocytosis	
<4000 or >11,000/μL	1
Bands >50%	1 (additional)
Oxygenation (mmHg)	
Pa_{O_2}/FI_{O_2} <250 and no ARDS	2
Chest radiograph	
Localized infiltrate	2
Patchy or diffuse infiltrate	1
Progression of infiltrate (no ARDS or CHF)	2
Tracheal aspirate	
Moderate or heavy growth	1
Same morphology on Gram's stain	1 (additional)
Maximal score[a]	12

[a]At the time of the original diagnosis, the progression of the infiltrate is not known and results of tracheal aspirate culture are often unavailable; thus, the maximal score is initially 8–10.

Abbreviations: ARDS, acute respiratory distress syndrome; CHF, congestive heart failure.

TREATMENT VENTILATOR-ASSOCIATED PNEUMONIA

Many studies have demonstrated higher mortality rates with initially inappropriate empirical antibiotic therapy. The key to appropriate antibiotic management of VAP is an appreciation of the resistance patterns of the most likely pathogens in a given patient.

ANTIBIOTIC RESISTANCE

If not for the higher risk of infection with MDR pathogens (Table 153-1), VAP could be treated with the same antibiotics used for severe CAP. However, antibiotic selection pressure leads to the frequent involvement of MDR pathogens by selecting either for drug-resistant isolates of common pathogens (MRSA and Enterobacteriaceae producing extended-spectrum β-lactamases or carbapenemases) or for intrinsically resistant pathogens (*P. aeruginosa* and *Acinetobacter* species). Frequent use of β-lactam drugs, especially cephalosporins, appears to be the major risk factor for infection with MRSA and extended-spectrum β-lactamase–positive strains.

P. aeruginosa has demonstrated the ability to develop resistance to all routinely used antibiotics. Unfortunately, even if initially sensitive, *P. aeruginosa* isolates also have a propensity to develop resistance during treatment. Either de-repression of resistance genes or selection of resistant clones within the large bacterial inoculum associated with most pneumonias may be the cause. *Acinetobacter* species, *Stenotrophomonas maltophilia*, and *Burkholderia cepacia* are intrinsically resistant to many of the empirical antibiotic regimens employed (see later in this chapter). VAP caused by these pathogens emerges during treatment of other infections, and resistance is always evident at initial diagnosis.

EMPIRICAL THERAPY

Recommended options for empirical therapy are listed in Table 153-9. Treatment should be started once diagnostic specimens have been obtained. The major factor in the selection of agents is the presence of risk factors for MDR pathogens. Choices among the various options listed depend on local patterns of resistance and—a very important factor—the patient's prior antibiotic exposure.

The majority of patients *without* risk factors for MDR infection can be treated with a single agent. The major difference from CAP is the markedly lower incidence of atypical pathogens in VAP; the exception is *Legionella,* which can be a nosocomial pathogen, especially with breakdowns in the treatment of potable water in the hospital.