TABLE 153-9 EMPIRICAL ANTIBIOTIC TREATMENT OF HEALTH CARE–ASSOCIATED PNEUMONIA

Patients without Risk Factors for MDR Pathogens
Ceftriaxone (2 g IV q24h) or cefotaxime (2 g IV q6–8 h) *or*
Moxifloxacin (400 mg IV q24h), ciprofloxacin (400 mg IV q8h), or levofloxacin (750 mg IV q24h) *or*
Ampicillin/sulbactam (3 g IV q6h) *or*
Ertapenem (1 g IV q24h)
Patients with Risk Factors for MDR Pathogens
1. A β-lactam:
Ceftazidime (2 g IV q8h) or cefepime (2 g IV q8–12h) *or*
Piperacillin/tazobactam (4. 5 g IV q6h) *or*
Imipenem (500 mg IV q6h or 1 g IV q8h), or meropenem (1 g IV q8h)
plus
2. A second agent active against gram-negative bacterial pathogens:
Gentamicin or tobramycin (7 mg/kg IV q24h) or amikacin (20 mg/kg IV q24h) *or*
Ciprofloxacin (400 mg IV q8h) or levofloxacin (750 mg IV q24h)
plus
3. An agent active against gram-positive bacterial pathogens:
Linezolid (600 mg IV q12h) *or*
Vancomycin (15 mg/kg q12h initially with adjusted doses)

Abbreviation: MDR, multidrug-resistant.

The standard recommendation for patients *with* risk factors for MDR infection is for three antibiotics: two directed at *P. aeruginosa* and one at MRSA. The choice of a β-lactam agent provides the greatest variability in coverage, yet the use of the broadest-spectrum agent—a carbapenem, even in an antibiotic combination—still represents inappropriate initial therapy in 10–15% of cases.

SPECIFIC TREATMENT

Once an etiologic diagnosis is made, broad-spectrum empirical therapy can be modified to specifically address the known pathogen. For patients with MDR risk factors, antibiotic regimens can be reduced to a single agent in more than one-half of cases and to a two-drug combination in more than one-quarter of cases. Only a minority of cases require a complete course with three drugs. A negative tracheal-aspirate culture or growth below the threshold for quantitative cultures, especially if the sample was obtained before any antibiotic change, strongly suggests that antibiotics should be discontinued. Identification of other confirmed or suspected sites of infection may require ongoing antibiotic therapy, but the spectrum of pathogens (and the corresponding antibiotic choices) may be different from those for VAP. If the CPIS decreases over the first 3 days, antibiotics should be stopped after 8 days. An 8-day course of therapy is just as effective as a 2-week course and is associated with less frequent emergence of antibiotic-resistant strains.

The major controversy regarding specific therapy for VAP concerns the need for ongoing combination treatment of *Pseudomonas* infection. No randomized controlled trials have demonstrated a benefit of combination therapy with a β-lactam and an aminoglycoside, nor have subgroup analyses in other trials found a survival benefit with such a regimen. The unacceptably high rates of clinical failure and death for VAP caused by *P. aeruginosa* despite combination therapy (see "Failure to Improve," later) indicate that better regimens are needed—including, perhaps, aerosolized antibiotics. VAP caused by MRSA is associated with a 40% clinical failure rate when treated with standard-dose vancomycin. One proposed solution is the use of high-dose individualized treatment, although the risk of renal toxicity increases with this strategy. In addition, the MIC of vancomycin has been increasing, and a high percentage of clinical failures occur when the MIC is in the upper range of sensitivity (i.e., 1. 5–2 μg/mL). Linezolid appears to be 15% more efficacious than even adjusted-dose vancomycin and is clearly preferred in patients with renal insufficiency and those infected with high-MIC isolates of MRSA.

FAILURE TO IMPROVE

Treatment failure is not uncommon in VAP, especially that caused by MDR pathogens. In addition to the 40% failure rate for MRSA infection treated with vancomycin, VAP due to *Pseudomonas* has a 50% failure rate, no matter what the regimen. Causes of clinical failure vary with the pathogen(s) and the antibiotic(s). Inappropriate therapy can usually be minimized by use of the recommended triple-drug regimen (Table 153-9). However, the emergence of β-lactam resistance during therapy is an important problem, especially in infection with *Pseudomonas* and *Enterobacter* species. Recurrent VAP caused by the same pathogen is possible because the biofilm on endotracheal tubes allows reintroduction of the microorganism. However, studies of VAP caused by *Pseudomonas* show that approximately half of recurrent cases are caused by a new strain. Inadequate local levels of vancomycin are the likely cause of treatment failure in VAP due to MRSA.

Treatment failure is very difficult to diagnose. Pneumonia due to a new superinfection, the presence of extrapulmonary infection, and drug toxicity must be considered in the differential diagnosis of treatment failure. Serial CPIS calculations appear to track the clinical response accurately, while repeat quantitative cultures may clarify the microbiologic response. A persistently elevated or rising CPIS by day 3 of therapy is likely to indicate treatment failure. The most sensitive component of the CPIS is improvement in oxygenation.

COMPLICATIONS

Apart from death, the major complication of VAP is prolongation of mechanical ventilation, with corresponding increases in length of stay in the ICU and in the hospital. In most studies, an additional week of mechanical ventilation resulting from VAP is common. The additional expense of this complication often warrants costly and aggressive efforts at prevention.

In rare cases, some types of necrotizing pneumonia (e.g., that due to *P. aeruginosa*) result in significant pulmonary hemorrhage. More commonly, necrotizing infections result in the long-term complications of bronchiectasis and parenchymal scarring leading to recurrent pneumonias. The long-term complications of pneumonia are underappreciated. Pneumonia results in a catabolic state in a patient already nutritionally at risk. The muscle loss and general debilitation from an episode of VAP often require prolonged rehabilitation and, in the elderly, commonly result in an inability to return to independent function and the need for nursing home placement.

FOLLOW-UP

Clinical improvement, if it occurs, is usually evident within 48–72 h of the initiation of antimicrobial treatment. Because findings on chest radiography often worsen initially during treatment, they are less helpful than clinical criteria as an indicator of clinical response in severe pneumonia. Seriously ill patients with pneumonia often undergo follow-up chest radiography daily, at least until they are being weaned off mechanical ventilation.

Prognosis VAP is associated with significant mortality. Crude mortality rates of 50–70% have been reported, but the real issue is attributable mortality. Many patients with VAP have underlying diseases that would result in death even if VAP did not occur. Attributable mortality exceeded 25% in one matched-cohort study, while more recent studies have suggested much lower rates. Patients who develop VAP are at least twice as likely to die as those who do not. Some of the variability in VAP mortality rates is clearly related to the type of patient and ICU studied. VAP in trauma patients is not associated with attributable mortality, possibly because many of the patients were otherwise healthy before being injured. However, the causative pathogen also plays a major role. Generally, MDR pathogens are associated with