

Clinical Practice

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA

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A 65-year-old man with hypertension and degenerative joint disease presents to the emergency department with a three-day history of a productive cough and fever. He has a temperature of 38.3°C (101°F), a blood pressure of 144/92 mm Hg, a respiratory rate of 22 breaths per minute, a heart rate of 90 beats per minute, and oxygen saturation of 92 percent while breathing room air. Physical examination reveals only crackles and egophony in the right lower lung field. The white-cell count is 14,000 per cubic millimeter, and the results of routine chemical tests are normal. A chest radiograph shows an infiltrate in the right lower lobe. How should this patient be treated?

THE CLINICAL PROBLEM

There are approximately 4 million cases of community-acquired pneumonia in the United States each year, resulting in about 1 million hospitalizations.¹⁻³ Inpatient management of pneumonia is more than 20 times as expensive as outpatient care and costs an estimated \$9 billion a year.^{2,3} The length of hospitalization is the key determinant of inpatient costs.^{2,4} Previous studies have found wide variations in the rates and lengths of hospitalization among patients with pneumonia that are not explained by differences in the characteristics of the patients or the severity of disease.⁵⁻¹⁰ This article focuses on the initial management of community-acquired pneumonia in immunocompetent adults.

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STRATEGIES AND EVIDENCE

Diagnosis and Treatment of Pneumonia

Patients with pneumonia usually present with cough (more than 90 percent), dyspnea (66 percent), sputum production (66 percent), and pleuritic chest pain (50 percent), although nonrespiratory symptoms can also predominate.^{11,12} Elderly patients may report fewer symptoms.^{13,14} Unfortunately, information obtained from the history or physical examination cannot rule in or rule out the diagnosis of pneumonia with adequate accuracy.¹⁵ All rigorous definitions of pneumonia require the finding of a pulmonary infiltrate on a chest radiograph.¹⁶

The initial antibiotic regimen should be chosen empirically to cover common typical and atypical pathogens (Table 1). Pneumonia due to atypical organisms (*Mycoplasma pneumoniae*, legionella species, and *Chlamydia pneumoniae*) accounts for 20 to 40 percent of cases and cannot be differentiated from cases due to typical bacteria on the basis of the patient's history, the results of the physical examination, or findings on chest radiographs.^{17,18} Two large observational cohort studies found that antibiotic regimens that cover both typical and atypical organisms are associated with a lower risk of death than regimens that cover just typical bacteria.^{19,20}

Although rigorous data regarding the duration of therapy are limited, most experts recommend a total of 10 to 14 days. Intravenous therapy with antibiotics that have a high level of oral bioavailability (e.g., fluoroquinolones) may be no better than oral therapy with such antibiotics in patients with uncomplicated infections who have a functioning gastrointestinal tract.^{21,22}

Risk Stratification and the Decision to Hospitalize

Between 30 percent and 50 percent of patients who are hospitalized with pneumonia have low-risk cases, many of which could potentially be managed at home.²³⁻²⁵ Indeed, most low-risk patients would prefer to be treated as outpatients.²⁶ Although physicians base the decision about admission on their overall assessment of the severity of illness, they tend to overestimate the risk of death.²⁷ The average 30-day mortality rate among patients with pneumonia is 13.7 percent, but it ranges from 5.1 percent in studies involving ambulatory and hospitalized patients to 36.5 percent in studies involving patients who required intensive care.²⁸

The decision regarding hospitalization should be based on the stability of the patient's clinical condition,

TABLE 1. RECOMMENDATIONS FOR THE INITIAL EMPIRICAL TREATMENT OF PNEUMONIA.

HOSPITAL SETTING	ANTIBIOTIC THERAPY*	COMMON ORGANISMS
General inpatient ward	Third-generation cephalosporin plus a macrolide or doxycycline Antipneumococcal fluoroquinolone β -Lactam- β -lactamase inhibitor plus a macrolide or doxycycline	Typical pathogens: <i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> Atypical pathogens: <i>Mycoplasma pneumoniae</i> , legionella species, <i>Chlamydia pneumoniae</i>
Intensive care unit		
No risk of <i>Pseudomonas aeruginosa</i> infection	Third-generation cephalosporin plus an antipneumococcal fluoroquinolone or a macrolide β -Lactam- β -lactamase inhibitor plus antipneumococcal fluoroquinolone or macrolide	Same as above plus <i>Staphylococcus aureus</i> , drug-resistant <i>S. pneumoniae</i> , other gram-negative rods
At risk for <i>P. aeruginosa</i> infection	Antipseudomonal β -lactam plus aminoglycoside plus antipneumococcal fluoroquinolone or macrolide Antipseudomonal β -lactam plus ciprofloxacin	Same as above plus <i>P. aeruginosa</i> , other resistant gram-negative rods

*Third-generation cephalosporins include ceftriaxone (1 to 2 g per day), ceftizoxime (1 to 2 g every 8 to 12 hours), and cefotaxime (1 to 2 g every 6 to 8 hours). Doxycycline is given at a dose of 100 mg every 12 hours. Antipneumococcal fluoroquinolones include levofloxacin (500 mg per day), gatifloxacin (400 mg per day), and moxifloxacin (400 mg per day). Macrolide antibiotics include azithromycin (500 mg per day), erythromycin (500 mg every 6 hours), and clarithromycin (500 mg every 12 hours). A β -lactam- β -lactamase inhibitor is ampicillin-sulbactam (1.5 to 3.0 g every six hours). Antipseudomonal β -lactams include piperacillin-tazobactam (3.375 g every 6 hours) and cefepime (1 to 2 g every 12 hours).

the risk of death and complications, the presence or absence of other active medical problems, and psychosocial characteristics. Disease-specific prediction rules are available that can be used to assess the initial severity of pneumonia and predict the risk of death. Such instruments can help inform the decision to hospitalize a patient. The most widely used and rigorously studied prediction rule — the Pneumonia Severity Index — has been validated in more than 50,000 patients from a variety of inpatient and outpatient populations (Fig. 1).^{23,29}

The Pneumonia Severity Index is based on data that are commonly available at presentation and stratifies patients into five risk classes in which 30-day mortality rates range from 0.1 percent to 27.0 percent. The higher the score, the higher the risk of death, admission to the intensive care unit, and readmission and the longer the length of stay. Easy-to-use versions of the index are now available on the Internet (<http://ursa.kcom.edu/CAPcalc/default.htm>, <http://ncemi.org>, and <http://www.emedhomom.com/dbase.cfm>)³⁰⁻³² and handheld computers.

An algorithm that uses the Pneumonia Severity Index to judge the appropriateness of admission is shown in Figure 2. Patients in risk classes I, II, and III are at low risk for death, and most can be safely treated as outpatients in the absence of extenuating circumstances.

The availability of oral antibiotics that attain high serum levels has made outpatient treatment even easier to recommend than in the past. An algorithm based on the Pneumonia Severity Index deviates most

from traditional teaching in emphasizing that an age of more than 65 years alone is not an indication for admission.

Some low-risk patients, especially those who are elderly or in class III of the Pneumonia Severity Index, may look sick or be reluctant to be treated at home. Many of these patients may be appropriate candidates for a short stay or 23 hours of inpatient observation. This strategy allows them to receive antibiotic therapy and any needed hydration while their condition is monitored for deterioration. The risk of worsening, although very low, is highest on the day of presentation and decreases considerably thereafter,³³ so patients whose condition is stable throughout the first hospital day should subsequently do well. The few patients who do not have a favorable response to this approach can then be admitted as traditional inpatients.

Patients at moderate risk (class IV of the Pneumonia Severity Index) and high risk (class V) should be hospitalized, given their much higher rates of death and complications. In general, most such patients are elderly and have two or more additional poor prognostic factors, such as serious coexisting conditions, abnormal vital signs, and abnormal laboratory values. All patients with hypoxemia (defined by an oxygen saturation of less than 90 percent or a partial pressure of arterial oxygen of less than 60 mm Hg in a patient who is breathing room air) or serious hemodynamic instability should be hospitalized regardless of their score on the Pneumonia Severity Index. Other indications for admission include suppurative or metastatic disease (empyema, lung abscess, endocarditis, meningitis).

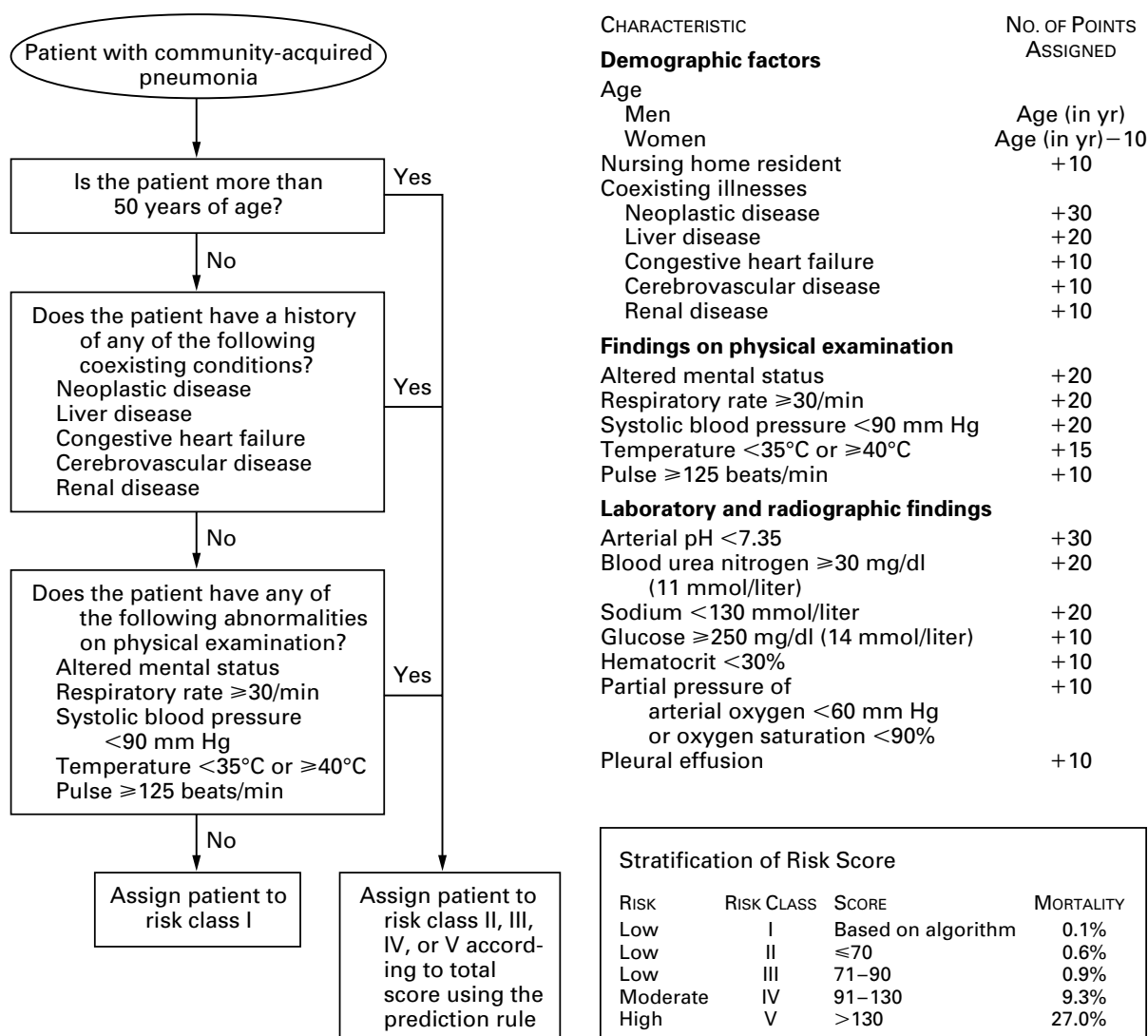


Figure 1. The Pneumonia Severity Index.

The Pneumonia Severity Index is used to determine a patient's risk of death. The total score is obtained by adding to the patient's age (in years for men or in years - 10 for women) the points assigned for each additional applicable characteristic.

Data have been adapted from Fine et al.²³

gitis, or osteomyelitis) or infection due to high-risk pathogens (e.g., *Staphylococcus aureus*, gram-negative rods, and anaerobes).

Several studies have established the safety and effectiveness of an approach involving an admission-decision algorithm that is based on the Pneumonia Severity Index. The strongest evidence comes from a randomized, controlled trial involving 19 hospitals.²⁵ The hospitals that were randomly assigned to implement the protocol admitted fewer low-risk patients than did the control hospitals (31 percent vs. 49 per-

cent). There were no significant differences between groups in the hospitalization rates among moderate- and high-risk patients for whom the protocol recommended admission. The intervention reduced the overall number of hospital bed-days per patient without any increase in deaths, complications, use of the intensive care unit, or readmissions or any decrement in the health-related quality of life.

This trial confirmed the findings of a study in which a similar triage protocol decreased the initial hospitalization rates among low-risk patients, from 58 per-

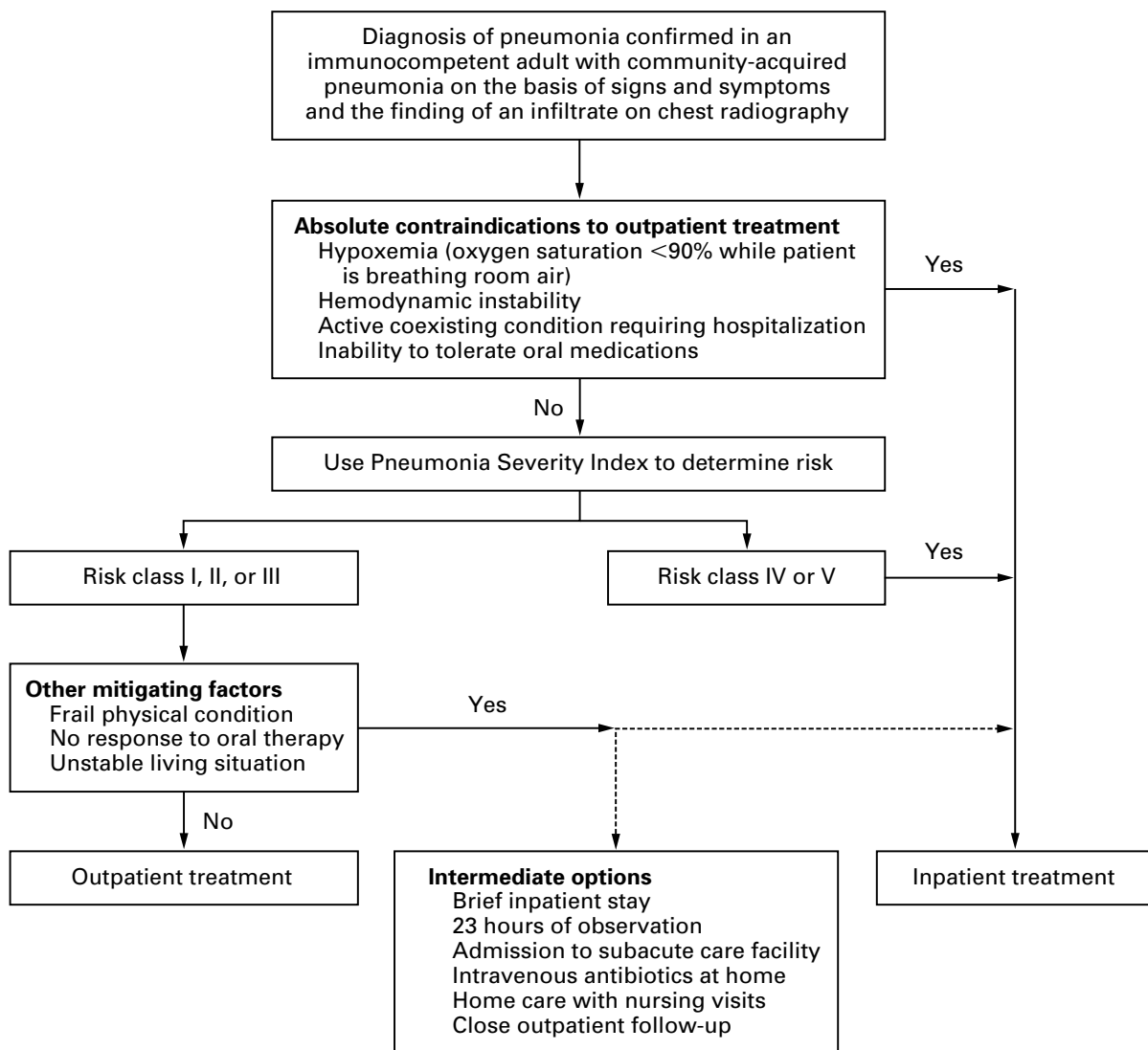


Figure 2. Algorithm for Determining Whether a Patient with Community-Acquired Pneumonia Should Be Admitted or Treated as an Outpatient.

cent to 43 percent, without any change in the rates of death, symptom resolution, functional recovery, or patient satisfaction.²⁴ The implementation of a somewhat different (but related) algorithm in urgent care clinics also increased the proportion of low-risk patients who were treated at home without compromising patient outcomes.^{34,35} These studies also confirm that selected low-risk elderly patients with pneumonia can be treated as outpatients with good results. Though this research shows that many low-risk patients who have traditionally been hospitalized can safely be treated at home, many still require or desire

hospitalization. The most common reasons for admitting low-risk patients include the presence of coexisting conditions, patients' preferences, and inadequate home support.³⁶

Criteria for Clinical Stability and Discharge

Once a patient is hospitalized and has received appropriate antibiotic therapy, the most important decision is determining when their condition is clinically stable and they are ready to go home. To be considered ready for discharge, patients should have stable vital signs, have adequate oxygenation while breathing

TABLE 2. CRITERIA FOR DETERMINING THE APPROPRIATENESS OF DISCHARGE.

Patient's vital signs are stable for 24-hour period (i.e., temperature $\leq 37.8^{\circ}\text{C}$ [100°F], respiratory rate ≤ 24 breaths per minute, heart rate ≤ 100 beats per minute, systolic blood pressure ≥ 90 mm Hg, and oxygen saturation $\geq 90\%$ while patient is breathing room air or at base line for patients with chronic obstructive lung disease or those receiving oxygen therapy at home).
Patient is able to take oral antibiotics.
Patient is able to maintain adequate hydration and nutrition.
Patient's mental status is normal (or at his or her base-line level).
Patient has no other active clinical or psychosocial problems requiring hospitalization.

room air, be able to take oral antibiotics and maintain their oral intake, and have returned to their base-line mental status (Table 2). They should also have no other active medical or psychosocial problems that require inpatient management.

Overall, the median time to clinical stability is three days among low-risk patients, four days among moderate-risk patients, and six days among those at high risk.³³ Once a patient's condition becomes stable, the risk of serious clinical deterioration is 1 percent or less, even among the sickest subgroup of patients. Conversely, patients who are discharged before their condition has stabilized have higher risk-adjusted rates of death or readmission and return more slowly to their usual activities.³⁷ Several randomized controlled trials and observational studies corroborate the safety of this type of discharge criteria.^{25,38-43} Although these studies used various designs and ways of defining clinical stability, they all stressed the importance of the resolution of fever, improving respiratory signs or symptoms, the ability to take oral antibiotics, and the absence of other active medical problems.

Similar stability criteria can be used to determine when patients can be switched from parenteral to oral antibiotics. This topic has recently been systematically reviewed.⁴³ In brief, data from randomized controlled trials and prospective studies indicate that early conversion from intravenous to oral therapy does not adversely affect outcomes.^{25,38-41,44-46} In addition, evidence from observational studies suggests that there is no need to observe patients for 24 hours after a switch to oral therapy.^{47,48}

The condition of individual patients will stabilize at different times depending on the initial severity of pneumonia, the presence or absence of coexisting conditions, and the response to therapy. Therefore, practice guidelines, critical pathways, and utilization-management rules should use objective criteria to

determine the appropriateness of discharge rather than rigidly specifying the number of days of hospitalization.

Though the condition of the average patient will become clinically stable on the third or fourth day of hospitalization,³³ patients need to be told that they will probably feel sick for a while. One week after presenting with pneumonia, 80 percent of patients report fatigue and cough and 50 percent report dyspnea and sputum production.¹² It is often a few weeks before all their symptoms resolve and they return to their usual activities.^{11,12,49}

GUIDELINES

Two national subspecialty organizations have published guidelines for the management of community-acquired pneumonia. The guidelines of the Infectious Diseases Society of America (updated in 2000) endorse the use of the Pneumonia Severity Index as providing "a rational foundation for the decision regarding hospitalization."⁵⁰ The recommended admission-decision algorithm is similar to that depicted in Figure 2. The guidelines state that patients in class I or II do not usually require hospitalization, those in class III may require a brief inpatient stay, and those in class IV or V should be hospitalized.

The 2001 guidelines of the American Thoracic Society,⁵¹ although acknowledging the value of prediction rules like the Pneumonia Severity Index, recommend that patients with "multiple risk factors" for a complicated course be admitted. The guidelines list these prognostic factors (many of which are included in the Pneumonia Severity Index), but it does not specify how these data might be used to inform the decision about admission. Both guidelines indicate that old age alone is not a reason for hospitalization.

The American Thoracic Society recommends that patients be switched to oral antibiotics and discharged on the same day that the patient's clinical condition stabilizes, if other medical and social factors permit. The society uses the following criteria for switching therapy to oral antimicrobial agents (which should also apply to the discharge decision): an improvement in cough and dyspnea, a temperature of 37.8°C (100°F) or less on two occasions eight hours apart, a decreasing white-cell count, and a functioning gastrointestinal tract with adequate oral intake. The Infectious Diseases Society of America does not specify discharge criteria but does recommend timely conversion to treatment with highly bioavailable oral agents when the patient's condition becomes stable and he or she can tolerate oral medicines. Both guidelines imply that the average hospital course can probably be shorter than previously thought appropriate, since most patients have an adequate clinical response to therapy within three days.

AREAS OF UNCERTAINTY

The randomized controlled trials supporting our recommendations largely used a new antipneumococcal fluoroquinolone or an advanced macrolide antibiotic (agents that cover both typical and atypical organisms) to treat outpatients. This strategy has been associated with better outcomes than the use of more narrowly focused initial regimens.^{19,20} We are less confident that oral therapy at home with non-first-line regimens, such as treatment with a penicillin or cephalosporin alone, can achieve equally favorable results. Although many experts suggest that a short period of observation in the hospital is appropriate for “sicker-appearing” low-risk patients, there have been no published trials of this approach. There are no definitive data addressing whether the criteria for discharge should vary depending on the pathogen (if known) or the presence or absence of complications. An extended course of intravenous antibiotics is generally recommended for patients with legionella infection, bacteremia due to high-risk organisms (*S. aureus* or gram-negative rods), or suppurative complications (e.g., empyema). Nearly all the studies we reviewed excluded patients with human immunodeficiency virus (HIV) infection. The discharge criteria we highlight are from studies that defined stability as demonstrated by a 24-hour period in which vital signs were normal.^{29,33,37} Other studies have required just an 8-hour or 16-hour period of stable vital signs.^{25,40,41} There are no good data comparing the alternative definitions.

CONCLUSIONS AND RECOMMENDATIONS

We believe that most low-risk patients with pneumonia (those in class I, II, or III of the Pneumonia Severity Index) can be treated at home in the absence of extenuating circumstances. The condition of low-risk patients who are admitted is likely to stabilize very quickly, and these patients may need to spend just a few days in the hospital. Conversely, moderate-risk and high-risk patients (those in class IV and class V, respectively) should be admitted. Once the condition of patients is clinically stable, they should be switched to oral antibiotic therapy and discharged within 24 hours (unless they have other medical or psychosocial problems requiring inpatient management). Before being discharged from the emergency department or the hospital, all patients should be informed about the length of time it will take them to recover and alerted to the signs of clinical worsening that would require urgent medical attention. Although data are lacking, we believe that most patients who have HIV infection and true community-acquired pneumonia can be treated in the same way as any other patients with pneumonia, unless they have advanced HIV disease.

With respect to the case vignette, the patient's Pneumonia Severity Index score is 65 on the basis of his

age. He has no other major risk factors or serious abnormalities in laboratory data or vital signs that increase his risk of a poor outcome. His Pneumonia Severity Index score corresponds to risk class II and a predicted 30-day mortality rate of less than 1 percent. Because his condition is hemodynamically stable, he has adequate oxygenation while breathing room air, and there are no contraindications to outpatient care, we would recommend that he be treated as an outpatient and receive an oral antibiotic that covers both typical and atypical organisms (an advanced macrolide or antipneumococcal fluoroquinolone). Finally, we would recommend that, in the future, the patient receive the pneumococcal vaccine if he has not previously been immunized.

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