

# Community-Acquired Pneumonia: A Practical Approach to Management for the Hospitalist

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Community-acquired pneumonia (CAP) is common, and inpatient physicians should be familiar with the most current evidence about and guidelines for CAP management. Our conclusions and recommendations include: *Streptococcus pneumoniae* is the most common identified cause of CAP requiring hospitalization, whereas *Legionella pneumophila* is a common cause of severe CAP. The chest radiograph remains an essential initial test in the diagnosis of CAP and should be supplemented by blood cultures sampled prior to antibiotic therapy and sputum for gram stain and culture if a high-quality specimen can be rapidly processed. Once the diagnosis is made, the Pneumonia Severity Index (PSI) should be used to optimize the location of treatment and to provide prognostic information. Absent other mitigating factors, patients in PSI risk classes I, II, and III can safely be treated as outpatients. Hospitalized patients with CAP should be treated promptly with empiric antibiotics. Nonsevere pneumonia should be treated with a parenteral  $\beta$ -lactam plus either doxycycline or a macrolide. Patients admitted to the intensive care unit should be treated with a  $\beta$ -lactam plus either a macrolide or a fluoroquinolone as well as be evaluated for pseudomonal risk factors. Most patients with nonsevere CAP reach clinical stability in 2-3 days and should be considered for a switch to oral therapy and discharge shortly thereafter. Patients should receive pneumococcal vaccination, influenza vaccination, and tobacco cessation counseling prior to discharge if eligible. Multiple quality indicators are measured and publicly reported in the management of CAP, which provides hospitals with an opportunity to improve care processes and patient outcomes. *Journal of Hospital Medicine* 2006;1:177-190. © 2006 Society of Hospital Medicine.

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*"Pneumonia may well be called the friend of the aged. Taken off by it in an acute, short, not often painful illness, the old man escapes those 'cold gradations of decay' so distressing of himself and to his friends."*

—William Osler, MD, 1898

**C**ommunity-acquired pneumonia (CAP) is commonly defined as an infection of the pulmonary parenchyma that is associated with at least some symptoms and signs of acute infection, accompanied by the presence of an acute infiltrate on chest radiograph, in a patient not hospitalized or residing in a long-term-care facility for 14 days prior to the onset of symptoms.<sup>1</sup> CAP continues to be a common and serious illness, causing substantial morbidity and mortality in the adult population. There are an estimated 5-6 million cases a year in the United States, with greater than 1 million hospitalizations. Community-acquired pneumonia is one of the most common admitting diagnoses

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**TABLE 1**  
Most Common Pathogens in Community-Acquired Pneumonia by Site of Care<sup>5</sup>

Non-ICU inpatients	ICU inpatients (severe)
<i>S. pneumoniae</i>	<i>S. pneumoniae</i>
<i>M. pneumoniae</i>	<i>Legionella</i> spp
<i>C. pneumoniae</i>	<i>H. influenzae</i>
<i>H. influenzae</i>	Gram-negative bacilli
<i>Legionella</i> spp	<i>S. aureus</i>
Aspiration	
Respiratory viruses	

among adults, and with a 30-day mortality between 10% and 14% for patients admitted to the hospital, it is the leading cause of infectious death in the United States.<sup>2</sup> In elderly patients, hospitalization for CAP portends a poor long-term prognosis. In a Medicare database, the 1-year mortality for patients with CAP was nearly 40%, compared to 29% in patients with other diagnoses.<sup>3</sup> Community-acquired pneumonia is a model illness in hospital medicine—it is a common disease that allows for evidence-based and cost-effective management. In addition, many national organizations have proposed multiple quality indicators for community-acquired pneumonia, thus providing an opportunity for institutional quality improvement. This review article outlines the assessment and management of patients admitted to the hospital with community-acquired pneumonia.

### Etiology

Although many pathogens can cause community-acquired pneumonia, the clinical syndromes and microbiology of CAP have traditionally been characterized as either “typical” or “atypical.” The typical organisms include *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, and the atypical organisms include *Chlamydia* spp., *Mycoplasma pneumoniae*, *Legionella* spp., and viruses. This historical distinction has recently come into question. It is now clear that the presenting symptoms, signs, and basic laboratory findings (including the chest radiograph) cannot be reliably used to predict the etiologic pathogen or to distinguish typical from atypical organisms.<sup>4</sup> Rather, the specific causative agent of CAP depends more on the degree of patient illness. Table 1 shows what prospective studies with comprehensive diagnostic

**TABLE 2**  
Common Presenting Symptoms and Signs in Patients with Community-Acquired Pneumonia<sup>7,8</sup>

Symptoms	Signs (exam)
Cough 90%	Fever 80%
Dyspnea 66%	Tachypnea 70%
Sputum 66%	Tachycardia 50%
Pleuritic chest pain 50%	Focal lung exam >90%

strategies determined to be the most common pathogens in patients hospitalized for CAP in ICU and non-ICU settings.<sup>5</sup> *Streptococcus pneumoniae* remains the most common cause of CAP in hospitalized patients and is the most common cause of fatal pneumonia, whereas *Legionella* spp. is a common cause of severe CAP, more often found in patients requiring admission to the intensive care unit. Gram-negative bacilli can cause CAP in elderly patients and those recently treated with broad-spectrum antibiotics or with underlying lung disease. Notably, though, despite improved diagnostic testing, only one quarter of all admitted patients with CAP have the etiologic agent defined, and therefore empiric therapy should be directed broadly at the most likely organisms.<sup>6</sup>

### Clinical Presentation

Patients admitted to the hospital with CAP typically present with a brief history of respiratory complaints, including cough (greater than 90%), dyspnea (66%), sputum production (66%), and pleuritic chest pain (50%); see Table 2.<sup>7,8</sup> In 10%-30% of patients, nonrespiratory complaints predominate, including headache, myalgias, fatigue, and gastrointestinal symptoms.<sup>6</sup> Elderly patients, an increasing percentage of hospitalized patients, are less likely to present with typical CAP symptoms (such as cough) and more likely to have altered mental status as a presenting symptom.<sup>9</sup>

On physical examination, patients with CAP usually have signs of fever (80%), tachypnea (70%), and tachycardia (50%); see Table 2. Most will have a focal lung exam (>90%) with findings ranging from crackles to bronchial breath sounds.<sup>10</sup> No exam finding is specific for the diagnosis of pneumonia, but the *absence* of fever, tachycardia, and tachypnea significantly reduces the probability of CAP in patients with suspected pneumonia.<sup>10</sup> Furthermore, similar to the clinical history, the physi-

cal examination of elderly patients with community-acquired pneumonia is not specific or sensitive for the diagnosis of CAP. For example, up to 40% of elderly patients subsequently determined to have CAP may not have fever.<sup>11</sup>

Leukocytosis is common in patients with CAP; however, its absence does not rule out disease.<sup>12</sup> A number of guidelines recommend laboratory evaluation of electrolytes, urea nitrogen, creatinine, liver enzymes, and bilirubin, although these are used primarily for prognostication and are not specifically useful in the diagnosis of CAP.

## DIAGNOSIS

### Differential Diagnosis

Given the nonspecific nature of the symptoms and signs associated with CAP, there is no single clinical feature or combination of clinical features that adequately rules in or out the diagnosis of CAP. Consequently, the differential diagnosis to be considered in patients with suspected CAP is broad. Noninfectious diseases can often present with similar clinical syndromes; these include congestive heart failure, exacerbation of chronic obstructive pulmonary disease (COPD), asthma, pulmonary embolism, and hypersensitivity pneumonitis. These diseases can often be distinguished with a thorough history and physical examination.

In addition, other upper- and lower-airway infectious diseases can have similar nonspecific signs and symptoms. In particular, pneumonia must often be differentiated from acute bronchitis, which as a diagnosis accounts for up to 40% of patients evaluated for cough (versus 5% for pneumonia).<sup>10</sup> Patients with acute bronchitis frequently do not present with high fevers or hypoxia and in general will not benefit from antibiotic therapy.<sup>13</sup> Patients believed to have community-acquired pneumonia might also be suffering from other “pneumonia syndromes” including aspiration pneumonia, post-obstructive pneumonia, and pneumonia in immunocompromised patients (eg, those with HIV, on steroids, receiving chemotherapy). Determining the correct diagnosis can have implications for therapy and prognosis.

### Diagnostic Studies

The diagnosis of community-acquired pneumonia requires that a patient have both signs and symptoms consistent with pulmonary infection *and* evidence of a new radiographic infiltrate. Therefore, most guidelines recommend that *all* patients with a



**FIGURE 1.** Chest radiograph of right middle lobe infiltrate in a patient with CAP.

possible diagnosis of CAP be evaluated with chest radiography.<sup>1,14,15</sup>

The specific radiographic findings in community-acquired pneumonia range from lobar consolidation to hazy focal infiltrate to diffuse bilateral interstitial opacities (see Figure 1). Although chest radiography has traditionally been considered the gold standard for the diagnosis of CAP, its exact performance characteristics are unknown, and it is clearly not 100% sensitive or 100% specific. The utility of the chest radiograph can be limited by patient body habitus, underlying lung disease, or dehydration. Computed tomography (CT) scanning, although not recommended for routine use, can identify pulmonary consolidation in up to 30% of patients with a normal or equivocal chest radiograph in whom pneumonia is suspected and can also identify complications of pneumonia including an empyema or pulmonary abscess.<sup>16</sup>

Limitations in the performance of the chest radiograph have resulted in an interest in the diagnostic performance of serologic markers of infection such as C-reactive protein (CRP), procalcitonin, and soluble triggering receptor expressed on myeloid cells (s-TREM).<sup>17–19</sup> Preliminary evidence suggests these inflammatory markers may ultimately prove useful in differentiating infectious

**TABLE 3**  
**Independent Predictors of Bacteremia in Patients with Community-Acquired Pneumonia<sup>24</sup>**

Comorbidities
Liver disease
Vital signs
Systolic blood pressure < 90 mm Hg
Temperature < 35°C or ≥ 40°C
Pulse ≥ 125 beats/min
Laboratory and radiographic data
Blood urea nitrogen (BUN) ≥ 30 mg/dL
Sodium < 130 mmol/L
White blood cells < 5000/mm <sup>3</sup> or > 20,000/mm <sup>3</sup>
Prior use of antibiotics (negative predictor)

from noninfectious pulmonary processes, but regular use of these new tests cannot currently be recommended.

Most expert guidelines state that 2 sets of blood cultures should be taken and analyzed *prior to antibiotic administration* in all patients admitted to the hospital with suspected community-acquired pneumonia.<sup>1,14,15</sup> Isolation of bacteria from blood cultures in CAP is a very specific way to identify a causative organism in order to subsequently narrow therapy and also identifies a high-risk group of patients because bacteremia is associated with increased mortality. Obtaining blood cultures within 24 hours of admission has been associated with 10% lower odds of 30-day mortality in patients with CAP,<sup>20</sup> and as a result, drawing blood cultures prior to antibiotic administration is a national quality indicator for CAP.

There are, however, a number of problems with the routine acquisition of blood cultures in all patients admitted with CAP. Practically, the cultures can be difficult to obtain, can potentially delay the initiation of antibiotics, and are often contaminated, which has been shown to increase both cost and length of stay.<sup>21,22</sup> The yield is generally low: the true-positive bacteremia rate for admitted patients with CAP ranges from 6% to 9%, and the culture results rarely change management or outcomes.<sup>23,24</sup> Given these limitations, many have argued that blood cultures should be obtained with a more “targeted” approach. A recent study used a Medicare database to create a decision-support tool to help maximize the value of blood cultures in CAP.<sup>25</sup> The predictors of a positive blood culture are shown in Table 3. Not obtaining cultures on patients who had received prior antibiotics or had no risk factors resulted in about 40% fewer overall cul-

tures while identifying approximately 90% of bacteremias. In their guidelines, the British Thoracic Society (BTS) advocates a similar strategy, recommending blood cultures be omitted in nonsevere pneumonia and in patients without comorbidities.<sup>15,26</sup> Although recommendations vary for nonsevere CAP in hospitalized patients, all professional society guidelines agree that blood cultures should be obtained in critically ill patients, and if cultures are obtained, they should be drawn prior to antibiotics.<sup>1,14,15,26</sup>

Substantial controversy surrounds the utility of routine sputum gram stains and cultures for patients admitted to the hospital with CAP. The Infectious Disease Society of America (IDSA) and the British Thoracic Society (BTS) both recommend that all patients admitted to the hospital with community-acquired pneumonia should have a gram stain and culture of expectorated sputum.<sup>1,15,26</sup> Both organizations argue sputum collection is a simple and inexpensive procedure that can potentially identify pathogenic organisms and can affect both initial and long-term antibiotic therapy. Most notably, they highlight gram stain specificity of greater than 80% for pneumococcal pneumonia. Conversely, the American Thoracic Society (ATS) argues that sputum gram stains and cultures generally have low sensitivity, specificity, and positive predictive value.<sup>14</sup> Furthermore, they argue the utility of sputum testing is also limited practically; in one study 30% of patients could not produce an adequate sputum specimen and up to 30% had received prior antibiotic therapy, substantially reducing the yield.<sup>27</sup> In another study, good-quality sputum with a predominant morphotype could be obtained in only 14% of patients admitted with CAP.<sup>28</sup> However, targeting sputum analysis to patients who have not received prior antibiotics *and* are able to produce an adequate sample improved the yield significantly.<sup>29</sup> In addition, with increasing rates of antibiotic resistance among common community isolates (ie, *S. Pneumoniae*) and the increasing prevalence of infecting organisms not targeted by routine empiric therapy (methicillin-resistant *Staphylococcus Aureus* [MRSA]), isolation of potential causative pathogens is increasingly important. We believe that severely ill patients with CAP (such as patients admitted to the ICU), as well as patients with identifiable risk factors for uncommon or drug-resistant pathogens (eg, *Pseudomonas aeruginosa*, enteric gram-negative rods, MRSA, etc.) should have sputum sent for gram stain and cul-

ture. Ideally, sputum obtained for gram stain and culture should be:

1. Prior to antibiotic therapy,
2. A deep-cough, expectorated specimen,
3. A purulent specimen (>25 polymorphonuclears and less than 10 squamous cells per high-powered field), and
4. Rapidly transported to the laboratory.

Subsequent gram stain and culture results should be interpreted in the specific clinical context and antibiotic choices targeted appropriately.

### Alternative Diagnostic Tests

In recent years, there has been growth in additional diagnostic tests targeting specific organisms. The pneumococcal urinary antigen assay is a relatively sensitive (50%-80%) and highly specific (~90%) test for the detection of pneumococcal pneumonia, when compared with conventional diagnostic methods.<sup>27</sup> The test is simple, convenient, rapid (~15 min), and, with its high specificity, may allow for more focused antimicrobial therapy early in management. Current limitations include the possibility of false-positive tests in patients colonized with *S. pneumoniae* or infected with other streptococcal species, as well as the inability to determine antibiotic sensitivity from positive tests. Updated IDSA and BTS guidelines state pneumococcal urinary antigen testing “is an acceptable” adjunct to other diagnostic tests, but blood and sputum analyses should still be performed.<sup>26,27</sup> For patients with suspected *Legionella* pneumonia (primarily critically ill and immunocompromised patients or in association with regional outbreaks), the urinary *Legionella* antigen assay is the test of choice, which detects 80%-95% of community-acquired cases of Legionnaires’ disease with a specificity of 90%.<sup>27</sup>

During the winter months (typically from October to March), rapid antigen testing for influenza is generally recommended for patients with signs or symptoms consistent with influenza.<sup>27</sup> The sensitivity of these tests is approximately 50%-70%, so negative test results do not exclude the diagnosis, but results can be important epidemiologically and therapeutically (differentiating influenza A and B strains).<sup>27</sup> Diagnostic tests targeting other common CAP pathogens, such as serologic tests for *Mycoplasma pneumoniae* or *Chlamydia* spp, should not be routinely performed. Testing for less common causative pathogens such as *Mycobacterium tuber-*

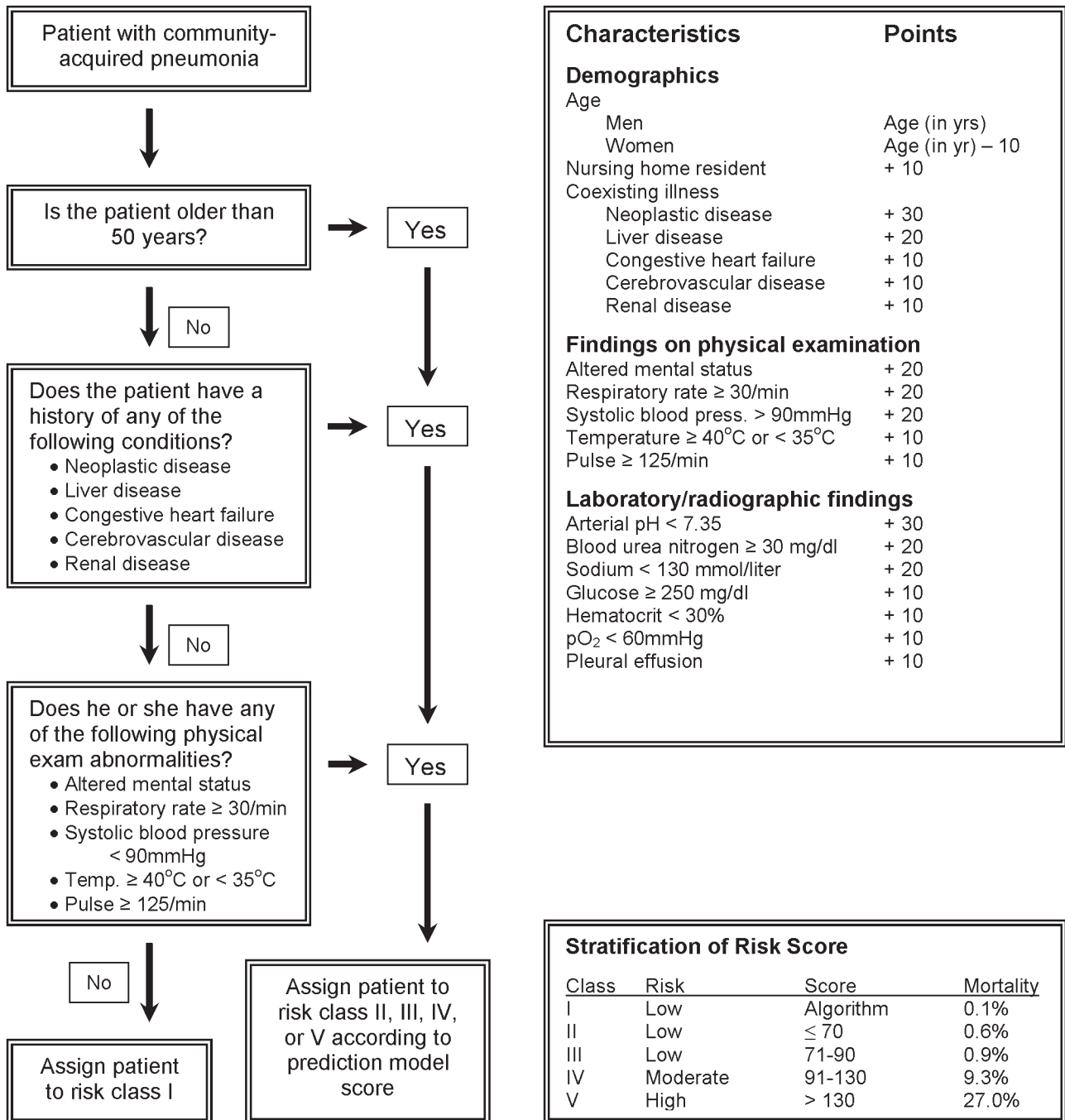
*culosis* should only be employed in the appropriate clinical setting.

### ADMISSION DECISION

Once the diagnosis of CAP has been made, the initial site where treatment will occur, whether the hospital or the home, must be determined. The decision to hospitalize should be based on 3 factors: 1) evaluation of the safety of home treatment, 2) calculation of the Pneumonia Severity Index (PSI), and 3) clinical judgment of the physician.<sup>27</sup> The PSI, or PORT (Pneumonia Outcomes Research Team) score, is a validated prediction rule that quantifies mortality and allows for risk stratification of patients with community-acquired pneumonia.<sup>2</sup> The PSI combines clinical history, physical examination, and laboratory data at the time of admission to divide patients into 5 risk classes and to estimate 30-day mortality (Figure 2), which ranges from 0.1% of patients in risk class I to 27.0% in risk class V.<sup>2</sup>

On the basis of the estimated prognosis and in the absence of concerns about home safety or comorbidities, patients in risk classes I, II, and III should be managed at home. Many prospective trials have shown that implementation of PSI significantly increases the number of low-risk patients managed outside the hospital, with no differences in quality of life, complications, readmissions, or short-term mortality.<sup>30,31</sup> Most recently, a trial randomizing patients in risk classes II and III to treatment in the hospital or at home found no significant differences in clinical outcomes but did find that patients were more satisfied with care at home.<sup>32</sup> Because the number of patients with CAP being treated at home is increasing, the American College of Chest Physicians recently published a consensus statement on the management of community-acquired pneumonia in the home.<sup>33</sup> All national guidelines for the management of community-acquired pneumonia recommend using the PSI to help determine the initial location of treatment, with the caveat that using the prediction rule should never supersede clinical judgment in the decision about whether to admit.<sup>1,14,15,26,27</sup> A practical decision tree for the use of the PSI is shown in Figure 3.

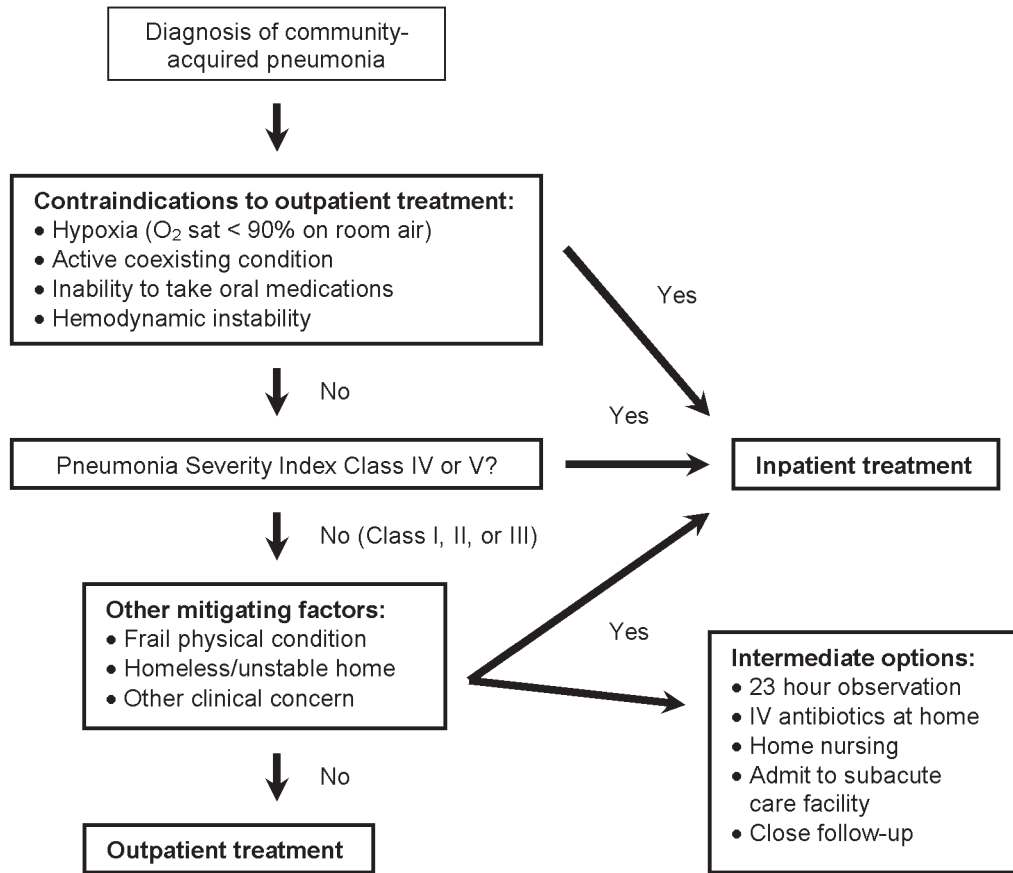
There are no reliable prediction rules for deciding on whether admission to the intensive care unit is necessary. Hemodynamic instability requiring resuscitation and monitoring or respiratory failure requiring ventilatory support are clear indications



**FIGURE 2.** Pneumonia Severity Index (PSI), a validated prediction tool to estimate prognosis and aid in admission decisions for patients with community-acquired pneumonia (CAP). The score was calculated by adding the patient's age (in years for men or in years – 10 for women) plus the points for each applicable characteristic. (Adapted from Halm EA, Teirstein AS. Management of community-acquired pneumonia. *N Engl J Med.* 2002;347(25):2039-2045 with permission. Copyright © 2002. Massachusetts Medical Society. All rights reserved.)

for ICU admission. Additional variables such as tachypnea (respiratory rate  $\geq 30$ ), altered mental status, multilobar disease, and azotemia are asso-

ciated with severe CAP and should prompt consideration of ICU admission, especially when 2 or more variables coexist.<sup>14</sup>



**FIGURE 3.** A practical decision-making tree using the PSI to aid in making the decision to admit. (Adapted from Halm EA, Teirstein AS. Management of community-acquired pneumonia. *N Engl J Med.* 2002;347(25):2039-2045 with permission. Copyright © Massachusetts Medical Society. All rights reserved.)

## TREATMENT

### Initial Treatment

Once the admission decision is made and the initial diagnostic tests are completed (including blood and sputum cultures), patients with presumed community-acquired pneumonia should receive necessary supportive care (O<sub>2</sub>, intravenous fluids, etc.) and prompt antimicrobial therapy. Antibiotics should be administered within 4 hours of arrival to patients with suspected CAP, as such prompt administration may be associated with shorter in-hospital stays and decreased 30-day mortality.<sup>34,35</sup> Regulatory organizations such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the Center for Medicare Services (CMS) have made delivery of antibiotics in less than 4 hours a hospital quality measure.

Despite diagnostic testing, the specific etiologic agent causing the pneumonia of a patient remains unknown in up to 75% of those admitted to the

hospital.<sup>14</sup> Most expert guidelines therefore recommend broad-spectrum empiric therapy targeting both the “typical” and the “atypical” organisms that commonly cause CAP (Table 1).

Recommendations for empiric antibiotics are driven by 2 key factors: antibiotic resistance by *S. pneumoniae* and the results of studies of CAP treatment outcomes. Historically, patients with suspected community-acquired pneumonia were treated with penicillin with generally good outcomes. Recently, the rate of *S. pneumoniae* isolates resistant to penicillin has risen dramatically in the United States, ranging between 20% and 30%, with high-level resistance (MIC ≥ 4 mg/L) as high as 5.7%.<sup>36,37</sup> Concurrently, the rates of resistance of *S. pneumoniae* to many other antibiotics commonly used to treat CAP have also risen.<sup>37</sup> Despite increasing resistance overall, most U.S. pneumococcal isolates have low resistance to third-generation cephalosporins and fluoroquinolones with enhanced

activity against *S. pneumoniae*.<sup>36–38</sup> In addition, despite increasing resistance by pneumococcal isolates to penicillin, several observational studies have shown that regardless of initial therapy, resistance to penicillin as well as third-generation cephalosporins is not associated with higher mortality or worse outcomes when controlled for other risk factors for drug resistance.<sup>39,40</sup> An exception to that rule is pneumococcal isolates that are very highly resistant to PCN (MIC  $\geq$  4 mg/dL). At least one study has shown that patients with such isolates may be at higher risk for adverse outcomes and should probably not be treated with penicillins.<sup>1,14,15,41</sup> However, nationally, fewer than 6% of pneumococcal isolates have this level of resistance.<sup>37</sup>

The rationale for empiric broad-spectrum coverage against both typical and atypical organisms has arisen from many retrospective and observational studies that have suggested that there is clinical benefit and improved outcomes with such regimens. One large retrospective study showed that in elderly patients with CAP, fluoroquinolone monotherapy was associated with lower 30-day mortality when compared to monotherapy with a third-generation cephalosporin.<sup>34</sup> Adding an extended-spectrum macrolide (eg, azithromycin) to an extended-spectrum  $\beta$ -lactam (eg, ceftriaxone) in the treatment of patients hospitalized with nonsevere CAP also appears to be associated with improved outcomes. Adding a macrolide has resulted in shorter lengths of stay (LOS), less treatment failure, and lower mortality.<sup>34,42–44</sup> Similarly, according to unpublished observations, adding doxycycline to a  $\beta$ -lactam as initial therapy was associated with a benefit of decreased mortality.<sup>45</sup> The presumed etiology of the benefit has been the addition of specific coverage of atypical organisms, such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*, which are common causes of CAP (Table 1). Others have proposed that the benefit of therapy with macrolides may be derived from the inherent anti-inflammatory properties of macrolides.<sup>46</sup> Because research has shown a benefit of dual versus monotherapy across a spectrum of antibiotics, others have proposed the benefit is simply a result of receiving “double” antibiotic coverage. In particular, 2 studies found a benefit of reduced mortality from combination therapy over monotherapy in bacterial pneumococcal pneumonia.<sup>47,48</sup>

Yet the accumulated evidence for adding coverage of atypical organisms has been only retro-

spective and observational. Because of this, the recommendation to routinely add antibiotics active against atypical organisms has been questioned by some. Two recent meta-analyses and a systematic review examined all the available data on the need for atypical coverage in the treatment of patients with community-acquired pneumonia.<sup>49–51</sup> Surprisingly, none showed a benefit in clinical efficacy or survival in patients treated with agents active against both atypical and typical organisms when compared to regimens with only typical coverage. In subset analyses, there was a benefit to providing empiric atypical coverage in patients subsequently shown to have *Legionella* spp. as a causative pathogen. However, this organism was uncommon in all 3 studies. Unfortunately, most studies included in the meta-analyses compared fluoroquinolone or macrolide monotherapy with third-generation cephalosporin monotherapy. There have been no high-quality randomized, controlled trials of the treatment of hospitalized patients with CAP assessing combination therapy covering both typical and atypical organisms with monotherapy targeting typical organisms alone. High-quality trials are warranted.

Despite the recent articles questioning the importance of atypical coverage, citing the substantial retrospective data and the general inability to identify causative organisms in most cases of CAP, adding a second agent with atypical coverage to a  $\beta$ -lactam currently appears to be the most efficacious empiric treatment for CAP. Nearly all expert guidelines for the management of community-acquired pneumonia recommend this empiric approach.<sup>1,14,27</sup>

Table 4 displays our recommendations for the treatment of community-acquired pneumonia requiring hospitalization. Before implementation of these guidelines, hospitalists should consult with their infectious disease experts and consider local resistance patterns. In general, a typical adult patient with non-severe CAP without additional risk factors should receive a parenteral extended-spectrum  $\beta$ -lactam plus *either* doxycycline *or* an advanced macrolide (see Table 4). Extended-spectrum  $\beta$ -lactams include cefotaxime, ceftriaxone, ampicillin-sulbactam, and ertapenem. A respiratory fluoroquinolone as a single agent can be used for non-ICU patients with CAP, but some agencies, including the Centers for Disease Control (CDC), discourage routine use of these agents in all patients secondary to concerns about cost and in-



**TABLE 4**  
**Suggested Initial Empiric Antimicrobial Therapy in Immunocompetent Patients with Suspected Community-Acquired Pneumonia**

Patient group	Empiric antibiotic therapy
Inpatient, non-ICU Severe $\beta$ -lactam allergy <sup>c</sup>	$\beta$ -Lactam <sup>a</sup> + either doxycycline or an advanced macrolide <sup>b</sup> Respiratory fluoroquinolone <sup>d</sup>
Inpatient, ICU No risk for <i>Pseudomonas</i> Severe $\beta$ -lactam allergy <i>Pseudomonas</i> risk factors <sup>e</sup> Severe $\beta$ -lactam allergy MRSA risk factors <sup>h</sup>	$\beta$ -Lactam + either an advanced macrolide or a respiratory fluoroquinolone Respiratory fluoroquinolone + clindamycin Antipseudomonal $\beta$ -lactam <sup>f</sup> + an antipseudomonal fluoroquinolone <sup>g</sup> Aztreonam + a respiratory fluoroquinolone Add vancomycin to above regimens
From nursing home Aspiration pneumonia	Should be treated as nosocomial/health-care-associated pneumonia $\beta$ -Lactam or respiratory fluoroquinolone $\pm$ clindamycin <sup>i</sup>

<sup>a</sup>Cefotaxime, ceftriaxone, ampicillin-sulbactam, or ertapenem.

<sup>b</sup>Azithromycin or clarithromycin.

<sup>c</sup>Severe  $\beta$ -lactam allergy, defined as anaphylactic shock, bronchospasm, and hives.

<sup>d</sup>Levofloxacin, moxifloxacin, gatifloxacin.

<sup>e</sup>Risk factors for *Pseudomonas* include severe structural lung disease (eg, bronchiectasis), immunosuppression (eg,  $\geq 10$  mg/day prednisone), or ICU, hospitalization or treatment with broad-spectrum antibiotics in the last 30 days.

<sup>f</sup>Piperacillin, piperacillin-tazobactam, imipenem, meropenem, cefepime.

<sup>g</sup>Ciprofloxacin.

<sup>h</sup>Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia include recent prolonged hospitalization, recent use of broad-spectrum antibiotics, significant underlying lung disease, and, possibly, high institutional prevalence of community MRSA isolates.

<sup>i</sup>Add clindamycin if risk factors for anaerobic infection exist: poor dentition, alcoholism, concern for empyema, or pulmonary abscess.

creasing gram-negative rod fluoroquinolone resistance.<sup>52,53</sup>

Patients hospitalized with severe CAP who require ICU-level care are at increased risk of *Legionella* spp. and drug-resistant *S. pneumoniae*, which must be reflected in their initial antibiotic therapy.<sup>5</sup> Patients with severe pneumonia should receive an intravenous extended-spectrum  $\beta$ -lactam plus either an intravenous macrolide or an intravenous respiratory fluoroquinolone.

All patients with severe CAP who are admitted to the intensive care unit should be routinely screened for risk factors for *Pseudomonas aeruginosa*. The known risk factors for pseudomonal infection are: bronchiectasis, immunosuppression including more than 10 mg/day of prednisone, malnutrition, and treatment with broad-spectrum antibiotics in the last month.<sup>14</sup> Those at risk for *Pseudomonas aeruginosa* or other resistant gram-negative rod infection should be treated with an antipseudomonal  $\beta$ -lactam plus an antipseudomonal fluoroquinolone. Many patients with severe CAP have risk factors for MRSA infection including recent prolonged hospitalization, recent use of broad-spectrum antibiotics, and significant underlying lung disease, which should be considered in choosing initial antibiotic therapy.<sup>54</sup> In addition,

there have been reports of patients without underlying risk factors presenting with severe community-acquired MRSA pneumonia. Many of these patients were younger and the MRSA pneumonia was associated with a necrotizing or cavitary disease requiring prolonged ICU stays.<sup>55-58</sup> In such cases or if an institution's rate of methicillin resistance in *S. aureus* community isolates is high (>15%-20%), it may be appropriate to add initial empiric MRSA coverage for patients admitted to the ICU with CAP.<sup>55</sup>

Some patients will have unique risk factors and clinical presentations, which may require modification of these empiric recommendations. Several studies found 5%-15% of cases of community-acquired pneumonia to be aspiration pneumonia.<sup>57</sup> Risk factors for aspiration events include, among others, dysphagia, history of stroke, altered level of consciousness, poor dentition, and tube feeding. Aspiration pneumonia traditionally was believed to be secondary to oral anaerobes, but recent research suggests gram-positive cocci and gram-negative rods are the predominant organisms.<sup>58</sup> Antibiotic therapy in patients with clear aspiration pneumonia should be directed at these microbes with an extended-spectrum  $\beta$ -lactam (eg, ceftriaxone) or a respiratory fluoroquinolone (eg, levofloxacin or

**TABLE 5**  
**Criteria to Identify Clinically Stable Patients for Potential Switch to Oral Antibiotic Therapy<sup>27</sup>**

Stable vital signs and clinical criteria for $\geq 24$ hours
Temperature $\leq 37.8^{\circ}\text{C}$ ( $100^{\circ}\text{F}$ )
Heart rate $\leq 100$ beats per minute
Respiratory rate $\leq 24$ breaths per minute
Systolic blood pressure $\geq 90$ mm Hg
Oxygen saturation (on room air) $\geq 90\%$
Ability to take oral medications

moxifloxacin). Anaerobic bacterial coverage can be added in patients with severe periodontal disease, alcoholism, concern for empyema, or evidence of aspiration with pulmonary abscess.<sup>58</sup>

Patients residing in long-term care facilities are at high risk of contracting pneumonia. The microbiology of infections acquired in nursing facilities is similar to that in hospital-acquired cases.<sup>59,60</sup> As a result, patients who develop pneumonia in institutional settings such as nursing homes should be treated with broad-spectrum antibiotics, including coverage for MRSA.

### Subsequent Treatment

Initial empiric antibiotic treatment should be modified based on the results of diagnostic testing. Although the specific etiologic agent is determined in only 25% of cases of CAP,<sup>35</sup> when an organism is isolated, antibiotic coverage should be narrowed to cover that particular organism with an antibiotic with adequate lung penetration. Evidence suggests clinicians often do not adjust or narrow antibiotics based on sensitivity results, potentially breeding resistant organisms.<sup>61</sup>

Patients hospitalized with CAP usually improve quickly if they receive early, appropriate antibiotic therapy and supportive care. Excluding patients with severe CAP requiring intensive care unit admission, most patients resolve their tachycardia, tachypnea, and fever by day 2 or 3.<sup>62</sup> Recent practice experience, evidence, and published guidelines<sup>14,27</sup> all indicate that patients can safely be transitioned to oral antibiotic therapy earlier in their hospital course. Table 5 outlines criteria that can be used to identify patients who have had an adequate response to parenteral therapy and can be considered for a switch to oral antibiotics. If these criteria are met, patients have less than a 1% chance of clinical deterioration necessitating admission to an ICU or transitional care unit.<sup>62</sup> When

an etiologic organism is not identified, oral therapy should reflect a spectrum of coverage to that of the initial intravenous therapy. In some cases, this may require use of more than one oral agent. We have had success, however, transitioning non-ICU patients initially treated with intravenous ceftriaxone plus oral doxycycline, typically for 48-72 hours, to oral doxycycline monotherapy at discharge.<sup>45</sup>

There have been a limited number of high-quality randomized trials examining the optimal duration of treatment for community-acquired pneumonia. Most practice guidelines recommend 7-10 days for patients with CAP requiring hospitalization, with 14 days for documented *Mycoplasma pneumoniae* or *Chlamydia pneumoniae*. One recent randomized trial of patients with mild to severe CAP showed a short course of high-dose levofloxacin (750 mg daily  $\times$  5 days) was at least as effective as normal dosing (500 mg daily  $\times$  10 days).<sup>63</sup> Clinical experience with high-dose levofloxacin is limited, but this regimen can be considered because it may reduce costs and exposure to antibiotics. When diagnosed, *Legionella* is usually treated for 10-21 days, but 14 days is adequate with macrolides because of their long half-life.<sup>27</sup> Patients with more virulent pathogens like *Staphylococcus aureus* or *Pseudomonas aeruginosa* or other suppurative complications should be treated for at least 14 days.<sup>1,14,15,27</sup> In determining length of therapy, clinicians should use these durations of treatment as guides, and to individualize therapy, they should always consider patient age and frailty, comorbid conditions, severity of illness, and hospital course.

### Failure to Respond

Although most patients hospitalized for CAP will improve rapidly and reach clinical stability in 2-3 days, some patients fail to respond. Some studies have estimated that failure to improve or clinical deterioration occurs in 5%-10% of patients in the first 2-3 days.<sup>64</sup> The common reasons for clinical decline or nonresponse to treatment, highlighted in Table 6, are:

1. *Incorrect diagnosis:* Illnesses such as congestive heart failure, pulmonary embolism, neoplasms, and hypersensitivity pneumonitis can mimic CAP.
2. *Inadequate antibiotic selection:* The etiologic agent may be resistant to empiric antibiotic selections. Examples would include methicillin-resistant

**TABLE 6**  
Reasons for Clinical Deterioration or Nonresponse to Treatment in CAP

<p>Incorrect diagnosis of CAP.          Inadequate or inappropriate antibiotic selection for CAP.          Unusual pathogen causing CAP.          Pulmonary or extrapulmonary complication of CAP.          Inadequate or poor host response.</p>
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*Staphylococcus aureus* (MRSA) or multiresistant gram-negative bacilli.

3. *Unusual pathogen*: CAP syndromes can be caused by myriad unusual organisms including *Pneumocystis jirovecii*, mycobacterium tuberculosis, endemic fungal infections (eg, coccidioidomycosis), and nocardiosis.
4. *Complications of pneumonia*: Specific complications of CAP include empyema, pulmonary abscess, extrapulmonary spread including meningitis or endocarditis, or other organ dysfunctions such as renal failure or myocardial infarction.
5. *Inadequate host response*: Despite appropriate antibiotic and supportive therapy, patients with CAP often fail to respond.

Progressive pneumonia despite appropriate therapy and empyema were the most common causes of failure to respond in the first 72 hours in a recent study.<sup>64</sup> Risk factors for early failure were older age (>65 years), Pneumonia Severity Index > 90, *Legionella* pneumonia, gram-negative pneumonia, and initial antimicrobial therapy discordant with final culture and susceptibility results. The initial evaluation of the nonresponding patient should address these common causes and is likely to include additional imaging (CT), sampling of potential extrapulmonary infection (thoracentesis), and, in some cases, bronchoscopy.

### DISCHARGE/FOLLOW-UP PLANS

Patients hospitalized for community-acquired pneumonia can be safely discharged when they have reached clinical stability, are able to tolerate oral medications, have no other active comorbid conditions, and have safe, close, appropriate outpatient follow-up (see Table 7). Clinical pathways employing these discharge criteria have been found to be safe and effective in reducing the length of stay for CAP. Most important, patients should have met most if not all of the vital sign and clinical criteria noted in Table 5 in the criteria for switching

**TABLE 7**  
Criteria for Identifying Patients for Possible Discharge

<p>Patients should:          Meet clinical criteria in Table V.          Be able to tolerate oral medications (no need to observe for 24 hours on oral therapy).          Have no evidence of active comorbid conditions (myocardial ischemia, pulmonary edema, etc.).          Have a normal mental status (or have returned to their baseline).          Have safe, appropriate outpatient follow-up.</p>
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to oral therapy. Patients with 2 or more abnormal vital signs (“instabilities”) within 24 hours prior to discharge are at high risk of readmission and mortality, but those with one or no abnormal vital signs generally have good outcomes.<sup>65</sup> Absent other clinical factors or extenuating circumstances (persistent hypoxia, poor functional status, etc.), most patients with CAP should reach clinical stability by day 3 or 4, be considered for a switch to oral therapy, and, if stable, be discharged shortly thereafter.

When patients with CAP are discharged from the hospital, they should be counseled about the expected course of recovery. Most important, patients and families must be informed that many symptoms of CAP may persist well after hospitalization. In one study, up to 80% of patients reported persistent cough and fatigue 1 week after discharge, and up to 50% still had dyspnea and sputum production. In some, the cough can last for 4-6 weeks.<sup>8</sup>

All patients discharged after treatment of community-acquired pneumonia should have follow-up with their outpatient provider. The physician responsible for their inpatient care should communicate directly with the provider and outline the hospital course, the discharge medications, and the duration of antibiotic therapy. There is no specific time frame within which patients must be seen, but follow-up should be dictated by patient age, comorbidities, clinical stability at discharge, and degree of illness. The American Thoracic Society guidelines do recommend patients with a substantial smoking history who are hospitalized with CAP have a follow-up chest radiograph 4-6 weeks after discharge to establish a radiographic baseline and exclude the possibility of underlying malignancy.<sup>14</sup> However, several studies have suggested that radiographic resolution may take 3 or more months in some patients, especially the elderly and those with multilobar disease.<sup>66</sup>

## PREVENTION

Prevention of community-acquired pneumonia and pneumonic syndromes has traditionally relied on vaccination with the polysaccharide pneumococcal pneumonia vaccine and the seasonal influenza vaccine. The vaccine for *S. pneumoniae* used in adults is composed of the 23 serotypes that cause 85%-90% of the invasive pneumococcal infections in the United States. Although in randomized trials the vaccine has not consistently prevented community-acquired pneumonia or death in elderly patients or those with comorbidities, it likely prevents invasive pneumococcal infection.<sup>67</sup> National guidelines and the CDC recommend the pneumococcal vaccine be given to all patients older than 65 years and those with chronic medical conditions.<sup>1,14,15</sup>

The seasonal influenza vaccine has clearly been shown to decrease influenza-related illness in elderly and high-risk patient populations. As well, in a meta-analysis and a large observational study of patients older than 65 years, vaccination against influenza prevented pneumonia, hospitalization, and death.<sup>68,69</sup> Vaccination of health care workers may also confer a benefit to elderly patients of reduced mortality. The CDC recommends the influenza vaccine for all patients more than 50 years old, those with comorbidities, those at high risk for influenza, and health care workers in both inpatient and outpatient settings.

Pneumococcal and influenza vaccination have traditionally been relegated to the outpatient setting. National guidelines and the CDC recommend vaccination of all eligible hospitalized patients. Vaccination is safe and effective with almost any medical illness, and both vaccines can be given simultaneously at discharge.<sup>69</sup> Both JCAHO and CMS have defined administration of the pneumococcal and influenza vaccines to patients hospitalized with CAP as a quality measure. Using "standing orders" is the most effective means of ensuring vaccination.

Some evidence suggests that tobacco smokers are at increased risk of invasive pneumococcal disease or pneumonia.<sup>70</sup> Patients hospitalized (for all illnesses, but for CAP in particular) should be counseled about smoking cessation and offered pharmacotherapy and outpatient follow-up. And, finally, recent observational data suggests that use of acid suppressive therapy, including proton pump inhibitors and H-2 receptor antagonists, may be associated with an increased risk of developing CAP.<sup>71</sup> Patients using these agents who are admitted with

CAP should have their indications for treatment reviewed, especially when the pneumonia has been recurrent and there is no clear indication for continued use of acid suppressive therapy, in which case they should be discontinued in the hospital.

## CONCLUSIONS

Community-acquired pneumonia remains a common cause for hospitalization of adult patients, with significant associated morbidity and mortality. Although there are multiple expert guidelines for the management of community-acquired pneumonia, further research is urgently needed. Clinicians need improved diagnostic tests that enable an earlier and more accurate diagnosis of CAP. In addition, the etiologic agent causing CAP is rarely discovered; improved microbiologic studies might enable antibiotic therapy to be targeted to the organisms responsible. High-quality randomized, controlled trials examining empiric antibiotic therapy in CAP are needed, especially related to the addition of agents covering atypical organisms. Last, the general management of patients hospitalized with CAP is marked by significant heterogeneity, and research and initiatives focusing on improving the quality and process of care of patients with CAP are needed.

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