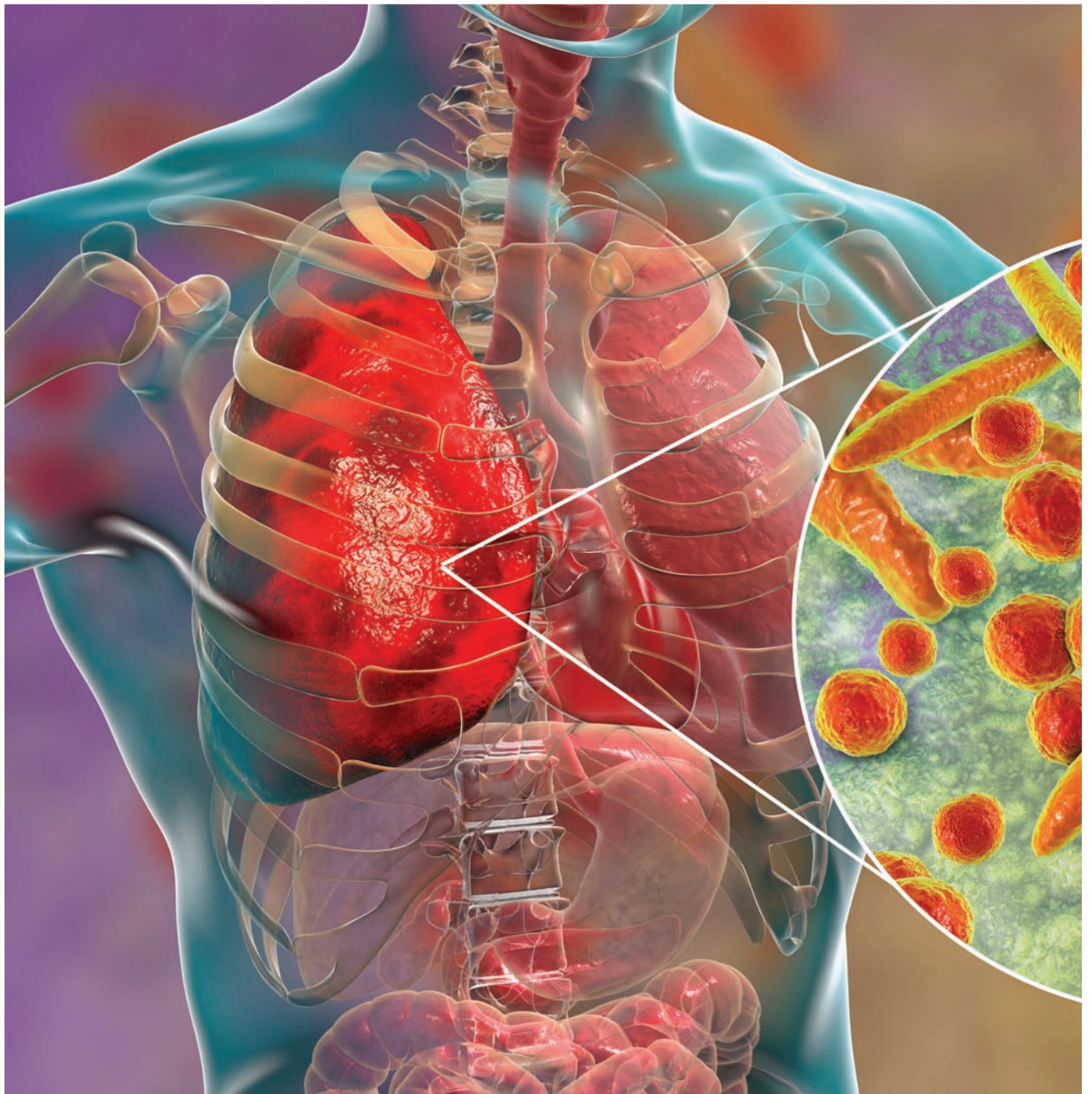




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# Treatment update:



# Outpatient management of community-acquired pneumonia



*Abstract: Pneumonia is a leading cause of morbidity and mortality in the US and a primary cause of hospitalization nationwide. A recent guideline update from the American Thoracic Society and Infectious Diseases Society of America provides evidence-based recommendations for managing adults with community-acquired pneumonia in the outpatient setting.*

By Jana Esden, DNP, APRN, FNP-BC, CNE

**P**neumonia is a leading cause of morbidity and mortality in the US and a primary cause of hospitalization nationwide, particularly for older adults.<sup>1,2</sup> Pneumonia results in 1.7 million ED visits annually.<sup>3</sup> In combination with influenza, pneumonia was the eighth-leading cause of death in the US in 2017 and resulted in over 55,000 deaths that year; 84% of those deaths were in people age 65 and older.<sup>4</sup> Despite this, current estimates indicate that about one-third of patients over age 65 have not been vaccinated for pneumococcal pneumonia, which is the leading pathogenic cause of pneumonia in all age groups.<sup>5</sup>

According to the Infectious Diseases Society of America (IDSA), for a patient to qualify for a community-acquired pneumonia (CAP) diagnosis, he or she must not have been hospitalized nor resided in a long-term-care facility for, at minimum, 14 days prior to the onset of symptoms.<sup>6</sup> The healthcare community has been awaiting the release of an updated CAP guideline for years. The newest clinical practice

**Keywords:** American Thoracic Society, CAP, community-acquired pneumonia, guideline, hospitalization, Infectious Diseases Society of America, outpatient, pneumonia



guideline, approved by the American Thoracic Society (ATS) and the IDSA, was published in October 2019.<sup>7</sup>

The 2019 ATS/IDSA guideline was developed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) technique, which is a method of appraising available studies to make recommendations based both on the quality of evidence and the strength of the recommendation as separate measures.<sup>7</sup> The guideline is an update to the 2007 IDSA/ATS CAP guideline and is written in question/answer format with the answer including 1) the recommendation, 2) a summary of the available evidence, and 3) the rationale for the authors' recommendation.<sup>7</sup> For the treatment of outpatients with CAP, the most significant departure from the 2007 guideline is the antibiotic choice for previously healthy individuals with no risk factors for drug-resistant pathogens.<sup>6,7</sup> Amoxicillin is now the first-line choice, with macrolide therapy falling out of favor due to *Streptococcus pneumoniae* resistance.<sup>7</sup>

### ■ Pathogens

Pneumonia, which causes inflammation and purulent fluid buildup in the alveoli, can be caused by viruses, bacteria, or fungi, with bacteria being the most common pathogens.<sup>8</sup> *S. pneumoniae*, which causes pneumococcal disease, continues to be the most common bacterial pathogen in pneumonia, accounting for approximately 36% of all cases of adult CAP in the US according to the CDC.<sup>8,9</sup> Pneumococcal pneumonia is also a frequent bacterial complication of influenza virus infection.<sup>8,9</sup> Pneumococcal pneumonia contributes to over 400,000 hospitalizations annually,



***Amoxicillin is now the first-line choice of treatment, with macrolide therapy falling out of favor due to *Streptococcus pneumoniae* resistance.***

and more than one quarter of patients with pneumococcal pneumonia go on to have pneumococcal bacteremia.<sup>9</sup> In recent years, the number of cases of pneumococcal pneumonia have declined rapidly, most likely due to increasing rates of pneumococcal vaccination in both adults and children as well as reduced rates of cigarette smoking.<sup>7,10</sup> Although case estimations can vary widely due to the frequency of empiric treatment, particularly in outpatients, this

pathogen definitively remains the most common cause of CAP.<sup>9,11</sup>

Other examples of bacterial pathogens that contribute to CAP include *Haemophilus influenzae*, *Staphylococcus aureus*, *Legionella pneumophila*, which causes Legionnaires disease, and *Mycoplasma pneumoniae*, which is associated with “walking pneumonia.”<sup>8,10,12</sup> The influenza virus is the most common cause of viral pneumonia in adults, and respiratory syncytial virus is the most common cause of viral pneumonia in children.<sup>8</sup> Additionally, it is common to have viral and bacterial coinfection in CAP.<sup>7</sup>

### ■ Pathophysiology and risk factors

Pneumonia is an acute infection of the lung parenchyma.<sup>6</sup> The lung parenchyma includes the alveoli which are responsible for gas exchange and therefore oxygenation of the body's blood supply.<sup>13</sup> The lungs are a sterile environment protected by innate defenses such as the filtering capabilities of the airway; small, flexible bodies called cilia, which move particles up and away from the lungs; and the glottic reflexes, which prevent particles and mucus from descending into the lower airways.<sup>14-16</sup> Although microorganisms colonize the nasopharynx and oropharynx in even healthy individuals, these defenses, along with the human immune system, work to ensure that aspirated pathogenic organisms do not inhabit the lungs.<sup>14</sup>

Pneumonia develops when the body's natural defenses are overwhelmed by a virulent microorganism or microorganisms.<sup>14</sup> Some risk factors for pneumonia relate to inhibition of the body's natural defenses. For example, smoking impairs the function of cilia and is a primary risk factor for pneumonia.<sup>8,17</sup> An altered level of consciousness can impair the gag reflex, so individuals who drink alcohol excessively or who are otherwise overly sedated are at increased risk as well as those who have an

impaired gag reflex due to a medical condition such as a cerebrovascular accident.<sup>8,17</sup> People with compromised immune function are also at increased risk. This includes patients with underlying chronic illnesses and patients who are very young (under age 2 years) and over age 65.<sup>8,17</sup>

A recent systematic review used observational studies to determine risk factors for CAP and discovered robust evidence of risk in several patient

characteristics, lifestyle factors, and clinical factors.<sup>18</sup> Specifically, Almirall and colleagues found the strongest correlations for CAP risk with older age, a previous history of CAP, current tobacco use, environmental irritant exposures, poor oral health or nutritional status, functional impairment, comorbid chronic obstructive pulmonary disease or asthma, immunosuppressive therapy, oral steroid use, and the use of gastric-acid suppressive drugs such as proton pump inhibitors and H2 antagonists.<sup>18</sup> Dang and colleagues had similar findings in systematic review of risk factors for CAP.<sup>17</sup> Additionally, Dang and colleagues found that functional impairment and the use of medications such as corticosteroids and proton pump inhibitors significantly increased risk of recurrent pneumonia in older adults.<sup>17</sup>

### ■ Patient presentation

Transmission of pneumococcal pneumonia results from either person-to-person transfer of respiratory droplets or by autoinoculation in people carrying the *S. pneumoniae* bacteria in the nasopharynx or oropharynx.<sup>8</sup> The incubation period for pneumococcal pneumonia is 1 to 3 days, and patients with pneumococcal pneumonia often present with sudden onset of fever, chills, cough, dyspnea, pleuritic chest pain, weakness, and malaise.<sup>9,19</sup> Although cough is a cardinal symptom, it may be productive or nonproductive.<sup>19</sup> Clinicians may also note vital sign instability such as tachycardia, tachypnea, and hypoxia in patients with pneumococcal pneumonia.<sup>9</sup> Older adults may not present with classic symptoms and instead may be afebrile and can present with confusion and changes in functional status.<sup>19,20</sup> Symptoms in older adults may also be underreported due to underlying cognitive impairment, neurologic impairment, or the presence of chronic respiratory or cardiac conditions.<sup>19</sup>

Although the symptom profile for atypical pathogens such as *M. pneumoniae* varies from typical pathogens such as *S. pneumoniae*, evidence suggests that differentiating between typical and atypical pathogens using patient symptoms and even a chest radiograph is not reliable and should not be used to determine antibiotic choice.<sup>16</sup> Transmission of *M. pneumoniae* results from person-to-person transfer of respiratory droplets, and the incubation period is between 1 and 4 weeks.<sup>21</sup> *M. pneumoniae* starts as a systemic illness with symptoms such as fever, sore throat, headache, and cough.<sup>21</sup> Symptoms tend to

### Lung exam findings and definitions<sup>25</sup>

Finding	Definition
Crackles	Discontinuous, interrupted, explosive sounds that may occur in early or late inspiration
Rhonchi	Continuous, low-pitched sounds in early inspiration that clear or decrease following cough
Wheezes	Continuous, high-pitched hissing sounds that may occur during inspiration or expiration
Tactile fremitus	Unilateral increase in palpable vocal vibrations transmitted through the chest wall as the patient says "ninety-nine"
Bronchophony	An increase in the intensity and clarity of the patient's spoken voice as perceived by the examiner when auscultating transthoracically
Egophony	A nasal or bleating quality of transmitted vocal sounds that is elicited when the patient says the letter "E" and to the examiner, it sounds like the letter "A"

gradually worsen over a period of weeks and then self-resolve.<sup>21</sup> Only 10% of people who contract *M. pneumoniae* illness will go on to have pneumonia, and symptoms are generally considered to be milder in nature which has led to the use of the term "walking pneumonia."<sup>21</sup>

A careful physical exam is helpful in differentiating pneumonia from other acute, upper respiratory tract infections such as acute bronchitis. Although remote studies have indicated that poor interobserver reliability exists and that no single exam finding confirms or excludes a diagnosis of pneumonia, the lung exam is still an important piece of the office visit for patients with symptoms of CAP.<sup>22-25</sup> Within the lung, pneumonia causes a consolidation, which is an area filled with fluid as opposed to air. Some classic lung exam findings that indicate consolidation include dullness to percussion, increased tactile fremitus, crackles, bronchophony (bronchial breath sounds), and egophony<sup>25,26</sup> (See *Lung exam findings and definitions*.) Marchello and colleagues recently determined, through systematic review and meta-analysis, that patients with normal vital signs and no abnormal lung findings are at extremely low risk for CAP.<sup>27</sup> The authors recommend that in these

situations the diagnosis for CAP can be ruled out and no additional diagnostic testing is required.<sup>27</sup>

### ■ Diagnostic testing

**Imaging.** Generally, a diagnosis of pneumonia is made if patients demonstrate symptoms of lower respiratory infection, exhibit clinical signs of pneumonia on the physical exam, and their chest radiograph reveals an acute infiltrate.<sup>6,7</sup> The IDSA and ATS emphasize the need for a new, visible infiltrate on chest radiograph to make a diagnosis of pneumonia due to the imprecision of clinical signs and symptoms.<sup>7,16</sup> To avoid needless adverse medication reactions and the increasing resistance of microorganisms, it is critical to abstain from treating lower respiratory infections empirically with antibiotics without obtaining chest imaging.<sup>7,16</sup> At the same time, concerns exist regarding the low sensitivity of chest radiographs. Up to one-third of initial chest radiographs may be negative in patients with pneumonia, with the identification of new lung infiltrates being less clear in patients with obesity or with underlying chronic lung disease.<sup>10,19</sup> Clinicians can increase the accuracy of chest radiography by ensuring that both posteroanterior and laterolateral images are obtained.<sup>16</sup> Marrie and File recommend repeating the chest radiograph after 24 hours for patients in whom CAP is strongly suspected and who have an initial negative chest radiograph.<sup>19</sup>

Recent research has focused on the use of lung ultrasonography as a viable alternative to chest radiography. Lung ultrasonography has a high sensitivity and specificity for diagnosing pneumonia and can be particularly helpful in older patients and patients who are immobile; however, it is clear that results are dependent on the skill of the operator.<sup>16,19</sup> A meta-analysis by Ye and colleagues documents a pooled sensitivity of lung ultrasonography at 95% with a specificity of 90%.<sup>28</sup> In this meta-analysis, the pooled sensitivity for chest radiography was only 77% with a specificity of 91%.<sup>28</sup> A second meta-analysis by Orso and colleagues found a similar sensitivity and specificity for lung ultrasound in the diagnosis of pneumonia at 92% and 93%, respectively.<sup>29</sup> Although computed tomography is most accurate for the diagnosis of pneumonia, this test is limited by its cost and by concerns of radiation exposure.<sup>16</sup>

**Other testing.** The newest ATS/IDSA guideline continues to recommend against obtaining sputum cultures in the outpatient setting.<sup>7</sup> Reasoning for this

includes challenges in proper collection of sputum samples, limitations in the ability of the sputum Gram stain and culture to detect the causative organism, and a lack of evidence indicating the intervention improves patient outcomes.<sup>7</sup> Collection of blood cultures is also not recommended in the outpatient setting.<sup>7</sup>

Newer diagnostic testing procedures such as urine testing for pneumococcal antigen and the use of procalcitonin are also not recommended as routine tests at this time.<sup>7</sup> Urine antigen testing for *S. pneumoniae* and/or *Legionella* is recommended in hospitalized patients with severe disease as it may reduce mortality in this subset of patients, but there is no clear benefit for routine use.<sup>7</sup> There is a significant amount of new research available on procalcitonin testing with studies focused on determining the sensitivity and specificity of the test in differentiating bacterial versus viral infections as well as concentration cutoff points to assist providers in making the decision of whether or not to treat the patient's pneumonia with antibiotics.<sup>10,16</sup> Although this is an emerging area of research, the ATS/IDSA guideline recommends beginning empiric antibiotic therapy in patients with CAP regardless of the serum procalcitonin level.<sup>7</sup> Concerns with the use of serum procalcitonin level testing include the unknown threshold level that properly differentiates bacterial from viral pathogens, the inconsistent results of studies, and the need for additional studies.<sup>7</sup> In support of this recommendation, a recent systematic review and meta-analysis on the use of procalcitonin to distinguish bacterial from viral pneumonia reported sensitivity and specificity of the test at 55% and 76%, respectively, indicating that antibiotics should not be withheld based on procalcitonin level.<sup>30</sup>

The influenza virus is a common cause of pneumonia and can lead to secondary bacterial infection.<sup>10</sup> It is common to have viral and bacterial coinfection, and a recent meta-analysis reported a significantly increased risk for mortality with coexistent viral and bacterial pathogens.<sup>31</sup> The ATS/IDSA guideline recommends testing patients with CAP for influenza at the time of diagnosis if the virus is active in the community.<sup>7</sup> Rapid influenza molecular assays are preferred over rapid influenza diagnostic tests in the outpatient setting as the sensitivity of the molecular assay method, at 90% to 95%, is significantly better than rapid influenza diagnostic test, which is an antigen test with

a sensitivity of 50% to 70%.<sup>32,33</sup> In adult outpatients who have CAP and a positive influenza molecular assay test, the ATS/IDSA guideline suggests that treatment with antivirals be initiated, regardless of symptom duration.<sup>7</sup> Patients with CAP who test positive for influenza should also receive empiric treatment with antibiotics due to the frequency of bacterial coinfection and risk of delaying antimicrobial treatment.<sup>7</sup>

### ■ Clinical prediction rules for prognosis

The ATS/IDSA guideline recommends that clinicians use a validated clinical prediction rule for prognosis to help guide the plan of care for adults with CAP.<sup>7</sup> Clinical prediction rules assist in clinical decision-making and are used in combination with clinical judgment. A clinical prediction rule is a grouping of clinical findings that statistically demonstrate predictability for aspects of disease such as a specific diagnosis or clinical prognosis.<sup>34</sup>

With regard to CAP, clinical prediction rules for prognosis are used to help clinicians predict a patient's mortality risk to determine whether inpatient care is needed.<sup>7</sup> Two commonly used tools exist: the Pneumonia Severity Index (PSI) and the CURB-65 tool.<sup>35-37</sup> The preferred clinical prediction rule for prognosis of the ATS/IDSA is the PSI.<sup>7,35</sup> (See *PSI*.) The PSI considers age, comorbidities, physical exam findings, and the results of diagnostic testing, including arterial blood gas values and chest X-ray findings.<sup>35,37</sup> In addition to accurately predicting mortality risk in patients with CAP, the PSI is better at identifying patients at low risk for mortality when compared with the CURB-65.<sup>7</sup> The PSI would be the best tool for clinicians to use in an ED setting as there is generally access to all the diagnostic tests needed to accurately calculate risk.

Although the PSI is the most sensitive tool, studies indicate that the CURB-65 tool is still useful and can

accurately predict mortality in patients with CAP.<sup>37-39</sup> The CURB-65 uses confusion, blood urea nitrogen, respiratory rate, BP, and age ( $\geq 65$ ) to calculate mortality risk<sup>36</sup> (see *CURB-65*.) The ATS/IDSA provide a conditional recommendation for the CURB-65 due to its simplicity of use.<sup>7</sup> The CURB-65 is a reasonable tool to use in the outpatient office setting as it does not include values obtained by an arterial blood gas. It is important to note that the CURB-65 becomes a less sensitive tool if the blood urea nitrogen (BUN) is not evaluated and included in the analysis.<sup>37</sup> It is also critical for clinicians to consider that any clinical prediction rule for prognosis must be used in combination with clinical judgment.<sup>37</sup>

PSI		
Criteria	Points	Scoring
<b>Gender</b>		Age $\leq 50$ with no comorbidities and normal physical exam findings (Class I) • 30-day mortality 0.1% • Low risk • Outpatient care
Male	0	
Female	-10	
<b>Demographic factors</b>		
Age (one point per year)	Age (yr)	
Long-term-care facility resident	10	Score of 51–70 (Class II) • 30-day mortality 0.6% • Low risk • Consider outpatient care versus short inpatient observation
<b>Comorbidities</b>		
Malignancy	30	Score of 71–90 (Class III) • 30-day mortality 0.9% • Low risk • Consider outpatient care versus short inpatient observation
Liver disease	20	
Congestive heart failure	10	
Cerebrovascular disease	10	
Renal disease	10	
<b>Physical examination findings</b>		
Altered mental status	20	Score of 91–130 (Class IV) • 30-day mortality 9.3% • Moderate risk • Inpatient care
Respiratory rate $\geq 30$ /minute	20	
Systolic BP $< 90$ mm Hg	20	
Temperature $< 35^\circ\text{C}$ or $\geq 40^\circ\text{C}$	15	
Pulse $\geq 125$ /minute	10	
<b>Laboratory and radiographic findings</b>		
Arterial pH $< 7.35$	30	Score of 131–395 (Class V) • 30-day mortality 27.0% • High risk • Inpatient care
BUN $\geq 30$ mg/dL (11 mmol/L)	20	
Sodium $< 130$ mEq/L	20	
Glucose $\geq 250$ mg/dL (14 mmol/L)	10	
Hematocrit $< 30\%$	10	
Partial pressure of arterial oxygen $< 60$ mm Hg	10	
Pleural effusion on X-ray	10	

Adapted from Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997;336(4):243-250.



## Treatment

**Antibiotic choices.** If the clinician feels that it is reasonable to treat a patient with CAP in the outpatient setting, antibiotic therapy should be initiated as soon as possible.<sup>7</sup> In nearly half of pneumonia cases, the culprit pathogen is not identified, and due to the significant cost of determining the infecting microorganism, patients in the outpatient setting are treated empirically.<sup>10,40</sup> The first-line antibiotic choice for CAP in previously healthy individuals with no risk factors for drug-resistant pathogens is amoxicillin 1g three times daily.<sup>7</sup> (See *ATS/IDSA antibiotic recommendations*.) This is a departure from the previous IDSA/ATS guideline, which placed a macrolide as first-line treatment.<sup>40</sup> The new recommendation of amoxicillin aligns with recommendations from current British and European guidelines.<sup>41,42</sup>

Factors that contributed to this change include the results of several studies indicating that amoxicillin was successful in treating CAP despite lack of coverage for atypical pathogens, the proven safety record of amoxicillin when compared with other options, and increasing resistance to macrolides, particularly in pneumococcal pneumonia.<sup>7</sup> A Cochrane Review published in 2009 and then repeated in 2014 compared various antibiotics and antibiotic groups in treatment of adult outpatients with CAP.<sup>43,44</sup> In both systematic reviews, the authors were unable to recommend one antibiotic regimen over another as they were similarly efficacious.<sup>43,44</sup> A large, recent randomized trial published in the *New England Journal of Medicine* compared the

use of beta-lactam antibiotics with fluoroquinolones and with beta-lactam/macrolide combinations, finding that the use of beta-lactam monotherapy was not inferior to the other antibiotic regimens in noncritical patients admitted with CAP.<sup>45</sup> In this trial, the main outcome studied was 90-day mortality; however, it was also noted that median length of hospital stay was identical between groups.<sup>45</sup>

An alternative choice to the first-line amoxicillin, listed as a conditional recommendation, is doxycycline 100 mg twice daily.<sup>7</sup> The ATS/IDSA guideline includes macrolide treatment as a conditional recommendation as well, only to be used in areas where *S. pneumoniae* resistance to macrolides is under 25%.<sup>7</sup>

In patients with chronic conditions such as chronic heart, lung, liver, or renal disease; diabetes; alcohol use disorder; cancer; or asplenia, a broader-spectrum antibiotic regimen is recommended due to the patients' increased risk of harboring pathogens either resistant to or not well covered by beta-lactam antibiotics (such as *H. influenzae*, *Moraxella catarrhalis*, and *S. aureus*), and the increased risk for poor outcomes if the initial antibiotic regimen is ineffective.<sup>7</sup> In this clinical scenario, antibiotic recommendations from the ATS/IDSA include a combination of a beta-lactam plus a macrolide, or a respiratory fluoroquinolone.<sup>7</sup> When treating with combination therapy, doxycycline is an alternative choice for the macrolide, and this is a conditional recommendation.<sup>7</sup> In this subset of patients, a macrolide as monotherapy would not be appropriate as up to 30% of *S. pneumoniae* strains are resistant to macrolides; however, when used in combination with a beta-lactam, the treatment becomes effective as *S. pneumoniae* continues to be susceptible to beta-lactam antibiotics.<sup>10</sup>

Musher and Thorner report that both regimens have been studied extensively and have been shown efficacious in 90% of patients with mild to moderate CAP.<sup>10</sup> The guideline makes clear that there is no preference between the two options in this patient subset and that clinicians should weigh the risks and benefits of monotherapy versus combination therapy prior to choosing a treatment plan.<sup>7</sup> Several factors to consider include cost, convenience of the regimen, medication allergies, recent usage of one class of antibiotics, and comorbidities or other risk factors that increase the possibility of adverse reactions with particular antibiotic choices.<sup>7</sup>

Although fluoroquinolones continue to carry black box warnings to avoid in patients with myasthenia gravis and for tendon rupture, peripheral neuropathy, and

### CURB-65

Criteria	Scoring
Confusion	Each positive result worth one point: Score of 0 or 1
BUN >19 mg/dL (>7 mmol/L)	• 30-day mortality 1.5%
Respiratory rate ≥30	• Outpatient care reasonable
Systolic BP <90 mm Hg or Diastolic BP ≤60 mm Hg	Score of 2
Age ≥ 65	• 30-day mortality 9.2%
	• Inpatient or observation admission recommended
	Score of ≥3
	• 30-day mortality 22%
	• Inpatient admission needed with possible ICU placement for scores of 4–5

Adapted from Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003;58(5):377-382.

**ATS/IDSA antibiotic recommendations<sup>7</sup>**

Patient group	Strong recommendation	Conditional recommendations
Healthy outpatient adults with no comorbidities	amoxicillin 1g three times daily	doxycycline 100 mg twice daily  A macrolide (only in areas where <i>S. pneumoniae</i> resistance to macrolides is <25%) <ul style="list-style-type: none"> <li>• azithromycin 500 mg on the first day, then 250 mg daily</li> <li>• clarithromycin 500 mg twice daily</li> <li>• clarithromycin ER 1,000 mg daily</li> </ul>
Outpatient adults with comorbidities	<p>Combination therapy*</p> <p>A beta-lactam</p> <ul style="list-style-type: none"> <li>• amoxicillin/clavulanate 500 mg/125 mg three times daily</li> <li>• amoxicillin/clavulanate 875 mg/125 mg twice daily</li> <li>• amoxicillin/clavulanate 2,000 mg/125 mg twice daily</li> <li>• cefpodoxime 200 mg twice daily</li> <li>• cefuroxime 500 mg twice daily</li> </ul> <p><b>and</b></p> <p>A macrolide</p> <ul style="list-style-type: none"> <li>• azithromycin 500 mg on the first day, then 250 mg daily</li> <li>• clarithromycin 500 mg twice daily</li> <li>• clarithromycin ER 1,000 mg daily</li> </ul> <p>Monotherapy with a respiratory fluoroquinolone*</p> <ul style="list-style-type: none"> <li>• levofloxacin 750 mg daily</li> <li>• moxifloxacin 400 mg daily</li> <li>• gemifloxacin 320 mg daily</li> </ul>	For patients who are unable to have a macrolide in combination therapy: doxycycline 100 mg twice daily

Length of treatment for all medication regimens and all patient groups recommended until the patient achieves clinical stability (and for no less than 5 days)

\*In no particular order of preference—assess risk/benefit in each patient case

central nervous system effects, which are particularly a concern in patients over age 60, the ATS/IDSA indicates that their use is still justified in the treatment of CAP due to their efficacy and because serious adverse reactions are relatively rare.<sup>7,46</sup> It is important to note that the US FDA has recently strengthened warnings on fluoroquinolones due to other possible adverse reactions including hypoglycemia, delirium, disorientation, agitation, anxiety, and memory impairment.<sup>47</sup>

In August, 2019, the FDA approved lefamulin for the treatment of CAP.<sup>48</sup> Lefamulin is in the antibiotic subclass of pleuromutilins and works by inhibiting bacterial protein synthesis.<sup>49</sup> Lefamulin is available for oral and I.V. administration.<sup>49</sup> Two important non-inferiority trials recently reported that lefamulin was not inferior to moxifloxacin (a fluoroquinolone).<sup>50,51</sup> File and colleagues found similar rates of adverse reactions among the lefamulin group and the moxifloxacin group; however, Alexander and colleagues

reported an increase in mild-to-moderate adverse reactions in the lefamulin group.<sup>50,51</sup> Although lefamulin, priced at \$275 per day for oral treatment, is significantly more expensive than fluoroquinolones, it is expected to be an important new option for the treatment of CAP.<sup>52,53</sup>

Supportive care for outpatients with CAP includes fluids, antipyretics, and analgesics. Generally, avoiding cough suppressants is considered prudent, and a recent systematic review was not able to find evidence to support the use of mucolytics.<sup>54</sup>

**Length of treatment.** The recommended length of treatment for all antibiotic regimens is no less than 5 days with generally 5 to 7 days of treatment being considered reasonable in outpatients.<sup>7,10,16</sup> Several recent meta-analyses have documented efficacy in antibiotic courses of 7 days or fewer with no differences when compared with longer courses of therapy.<sup>7,10,16</sup> For antibiotic discontinuation, patients must have reached




clinical stability, which is evidenced by normal vital signs, normal mentation, and the ability to eat.<sup>7</sup>

### ■ Follow-up

Frequency of follow-up visits will depend on the patient's individual situation. With proper antibiotic coverage, patients with CAP will generally reach clinical stability in the first 48 to 72 hours, and CAP symptoms will resolve within 5 to 7 days.<sup>7</sup> If patients do not reach clinical stability within a reasonable period of time or if symptoms worsen, a change in antibiotic therapy may be required.<sup>7</sup>

Follow-up chest radiography is not recommended routinely for all patients; however, this is a conditional recommendation with low quality of evidence.<sup>7</sup> The overarching rationale for reevaluating a chest radiograph is to ensure for resolution of a lung infiltrate as an unresolved suspicious area on the radiograph may indicate a previously undiagnosed lung malignancy.<sup>7</sup> Because this is not common, the guideline only recommends repeat chest radiography in patients for whom symptoms have not resolved adequately.<sup>7</sup> In patients with recurrent pneumonia, it is critical that clinicians evaluate for risk factors and consider alternative diagnoses such as lung cancer or tuberculosis.<sup>16</sup>

### ■ Conclusion

In addition to being a common diagnosis in the primary care setting, pneumonia places a heavy burden on the healthcare system and is a common cause of hospitalization, morbidity, and mortality. Using evidence-based recommendations to guide diagnostic testing strategies and to choose antimicrobial therapies will help to reduce the future burden of CAP by expanding antibiotic stewardship to avoid increasing microorganism resistance to available treatments. 

### REFERENCES

- Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project. HCUP fast stats - most common diagnoses for inpatient stays. [www.hcup-us.ahrq.gov/faststats/NationalDiagnosesServlet?year1=2015&characteristic1=0&included1=0&year2=&characteristic2=0&included2=1&expansionInfoState=hide&dataTablesState=hide&definitionsState=hide&exportState=hide](http://www.hcup-us.ahrq.gov/faststats/NationalDiagnosesServlet?year1=2015&characteristic1=0&included1=0&year2=&characteristic2=0&included2=1&expansionInfoState=hide&dataTablesState=hide&definitionsState=hide&exportState=hide).
- Jain S, Self WH, Wunderink RG, et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. *N Engl J Med*. 2015;373(5):415-427.
- Rui P, Kang K, Ashman JJ. National Hospital Ambulatory Medical Care Survey: 2016 emergency department summary tables. 2016. [www.cdc.gov/nchs/data/nhamcs/web\\_tables/2016\\_ed\\_web\\_tables.pdf](http://www.cdc.gov/nchs/data/nhamcs/web_tables/2016_ed_web_tables.pdf).
- Kochanek KD, Murphy SL, Xu S, Arias E. National vital statistics reports. *Natl Vital Stat Rep*. 2019;68(9):1-77.
- National Center for Health Statistics. Early release of selected estimates based on data from the 2018 national health interview survey. [www.cdc.gov/nchs/nhis/releases/released201905.htm#5](http://www.cdc.gov/nchs/nhis/releases/released201905.htm#5).
- Bartlett JG, Dowell SF, Mandell LA, File TM Jr, Musher DM, Fine MJ. Practice guidelines for the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2000;31(2):347-382.
- Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.
- National Heart, Lung, and Blood Institute. Pneumonia. [www.nhlbi.nih.gov/health-topics/pneumonia](http://www.nhlbi.nih.gov/health-topics/pneumonia).
- Centers for Disease Control and Prevention. Pneumococcal disease. [www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html](http://www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html).
- Musher DM, Thorner AR. Community-acquired pneumonia. *N Engl J Med*. 2014;371(17):1619-1628.
- Wunderink RG, Waterer G. Advances in the causes and management of community acquired pneumonia in adults. *BMJ*. 2017;358:j2471.
- Slack MPE. A review of the role of *Haemophilus influenzae* in community-acquired pneumonia. *Pneumonia (Nathan)*. 2015;6:26-43.
- Suki B, Stamenović D, Hubmayr R. Lung parenchymal mechanics. *Compr Physiol*. 2011;1(3):1317-1351.
- Alcón A, Fàbregas N, Torres A. Pathophysiology of pneumonia. *Clin Chest Med*. 2005;26:39-46.
- Eddens T, Kolls JK. Host defenses against bacterial lower respiratory tract infection. *Curr Opin Immunol*. 2012;24(4):424-430.
- Prina E, Ranzani OT, Torres A. Community-acquired pneumonia. *Lancet*. 2015;386(9998):1097-1108.
- Dang TT, Majumdar SR, Marrie TJ, Eurich DT. Recurrent pneumonia: a review with focus on clinical epidemiology and modifiable risk factors in elderly patients. *Drugs Aging*. 2015;32:13-19.
- Almirall J, Serra-Prat M, Bolibar I, Balasso V. Risk factors for community-acquired pneumonia in adults: a systematic review of observational studies. *Respiration*. 2017;94(3):299-311.
- Marrie TJ, File TM Jr. Bacterial pneumonia in older adults. *Clin Geriatr Med*. 2016;32(3):459-477.
- Wyrwich KW, Yu H, Sato R, Strutton D, Powers JH. Community-acquired pneumonia: symptoms and burden of illness at diagnosis among US adults aged 50 years and older. *Patient*. 2013;6(2):125-134.
- Centers for Disease Control and Prevention. *Mycoplasma pneumoniae* infections. [www.cdc.gov/pneumonia/atypical/mycoplasma/index.html](http://www.cdc.gov/pneumonia/atypical/mycoplasma/index.html).
- Benbassat J, Bauml R. Narrative review: should teaching of the respiratory physical examination be restricted only to signs with proven reliability and validity? *J Gen Intern Med*. 2010;25(8):865-872.
- Saldias PF, Cabrera TD, de Solminiach LI, Hernández AP, Gederlini GA, Díaz FA. Predictive value of history and physical examination for the diagnosis of community-acquired pneumonia in adults. *Rev Med Chil*. 2007;135(2):143-152.
- de Jongh TO, Thiadens HA. Physical examination of the lungs in suspected pneumonia. *Ned Tijdschr Geneesk*. 2011;155:A2656.
- Wipf JE, Lipsky BA, Hirschmann JV, et al. Diagnosing pneumonia by physical examination: relevant or relic? *Arch Intern Med*. 1999;159(10):1082-1087.
- Sattar SBA, Sharma S. Bacterial pneumonia. [www.ncbi.nlm.nih.gov/books/NBK513321](http://www.ncbi.nlm.nih.gov/books/NBK513321).
- Marchello CS, Ebell MH, Dale AP, Harvill ET, Shen Y, Whalen CC. Signs and symptoms that rule out community-acquired pneumonia in outpatient adults: a systematic review and meta-analysis. *J Am Board Fam Med*. 2019;32(2):234-247.
- Ye X, Xiao H, Chen B, Zhang S. Accuracy of lung ultrasonography versus chest radiography for the diagnosis of adult community-acquired pneumonia: review of the literature and meta-analysis. *PLoS One*. 2015;10(6):1-9.
- Orso D, Guglielmo N, Copetti R. Lung ultrasound in diagnosing pneumonia in the emergency department: a systematic review and meta-analysis. *Eur J Emerg Med*. 2018;25(5):312-321.
- Kamat IS, Ramachandran V, Eswaran H, Guffey D, Musher DM. Procalcitonin to distinguish viral from bacterial pneumonia: a systematic review and meta-analysis. *Clin Infect Dis*. [e-pub Jun. 25, 2019]
- Burk M, El-Kersh K, Saad M, Wiemken T, Ramirez J, Cavallazzi R. Viral infection in community-acquired pneumonia: a systematic review and meta-analysis. *Eur Respir Rev*. 2016;25(140):178-188.
- Centers for Disease Control and Prevention. Overview of influenza testing methods. [www.cdc.gov/flu/professionals/diagnosis/overview-testing-methods.htm](http://www.cdc.gov/flu/professionals/diagnosis/overview-testing-methods.htm).

33. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical practice guidelines by the Infectious Diseases Society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. *Clin Infect Dis*. 2019;68(6):e1-e47.
34. Cook CE. Potential pitfalls of clinical prediction rules. *J Man Manip Ther*. 2008;16(2):69-71.
35. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med*. 1997;336(4):243-250.
36. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003;58(5):377-382.
37. Long B, Long D, Koyfman A. Emergency medicine evaluation of community-acquired pneumonia: history, examination, imaging and laboratory assessment, and risk scores. *J Emerg Med*. 2017;53(5):642-652.
38. Armiñanzas C, Velasco L, Calvo N, Portilla R, Riancho JA, Valero C. CURB-65 as an initial prognostic score in internal medicine patients. *Eur J Intern Med*. 2013;24(5):416-419.
39. Sharp AL, Jones JP, Wu I, et al. CURB-65 performance among admitted and discharged emergency department patients with community-acquired pneumonia. *Acad Emerg Med*. 2016;23(4):400-405.
40. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44(suppl 2):S27-S72.
41. National Institute for Health and Care Excellence. Pneumonia (community-acquired): antimicrobial prescribing. [www.nice.org.uk/guidance/NG138](http://www.nice.org.uk/guidance/NG138).
42. Woodhead M, Blasi F, Ewig S, et al. Guidelines for the management of adult lower respiratory tract infections—full version. *Clin Microbiol Infect*. 2011;17(suppl 6):E1-E59.
43. Bjerre LM, Verheij TJ, Kochen MM. Antibiotics for community acquired pneumonia in adult outpatients. *Cochrane Database Syst Rev*. 2009;(4):CD002109.
44. Pakhale S, Mulpuru S, Verheij TJ, Kochen MM, Rohde GG, Bjerre LM. Antibiotics for community-acquired pneumonia in adult outpatients. *Cochrane Database Syst Rev*. 2014;(10):CD002109.
45. Postma DF, van Werkhoven CH, van Elden LJ, et al. Antibiotic treatment strategies for community-acquired pneumonia in adults. *N Engl J Med*. 2015;372(14):1312-1323.
46. U.S. Food and Drug Administration. FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. [www.fda.gov/media/99425/download](http://www.fda.gov/media/99425/download).
47. U.S. Food and Drug Administration. FDA updates warnings for fluoroquinolone antibiotics on risks of mental health and low blood sugar adverse reactions. [www.fda.gov/news-events/press-announcements/fda-updates-warnings-fluoroquinolone-antibiotics-risks-mental-health-and-low-blood-sugar-adverse](http://www.fda.gov/news-events/press-announcements/fda-updates-warnings-fluoroquinolone-antibiotics-risks-mental-health-and-low-blood-sugar-adverse).
48. U.S. Food and Drug Administration. FDA approves new antibiotic to treat community-acquired bacterial pneumonia. [www.fda.gov/news-events/press-announcements/fda-approves-new-antibiotic-treat-community-acquired-bacterial-pneumonia](http://www.fda.gov/news-events/press-announcements/fda-approves-new-antibiotic-treat-community-acquired-bacterial-pneumonia).
49. Rodvold KA. Introduction: lefamulin and pharmacokinetic/pharmacodynamic rationale to support the dose selection of lefamulin. *J Antimicrob Chemother*. 2019;74(suppl 3):iii2-iii4.
50. File TM, Goldberg L, Das A, et al. Efficacy and safety of intravenous-to-oral lefamulin, a pleuromutilin antibiotic, for the treatment of community-acquired bacterial pneumonia: the phase III Lefamulin Evaluation Against Pneumonia (LEAP 1) Trial. *Clin Infect Dis*. 2019;69(11):1856-1867.
51. Alexander E, Goldberg L, Das AF, et al. Oral lefamulin vs moxifloxacin for early clinical response among adults with community-acquired bacterial pneumonia: the LEAP 2 randomized clinical trial. *JAMA*. [e-pub Sep. 27, 2019]
52. Nabriva Therapeutics. Nabriva Therapeutics receives U.S. FDA approval of Xenleta™ (lefamulin) to treat community-acquired bacterial pneumonia (CABP). <https://investors.nabriva.com/news-releases/news-release-details/nabriva-therapeutics-receives-us-fda-approval-xenleta>.
53. Malani PN. Lefamulin—a new antibiotic for community-acquired pneumonia. *JAMA*. [e-pub Sep. 27, 2019]
54. Chang CC, Cheng AC, Chang AB. Over-the-counter (OTC) medications to reduce cough as an adjunct to antibiotics for acute pneumonia in children and adults. *Cochrane Database Syst Rev*. 2012;(2):CD006088.

Jana Esden is an associate professor at Frontier Nursing University, Hyden, Ky, and a member of *The Nurse Practitioner* Editorial Advisory Board.

The author and planners have disclosed no potential conflicts of interest, financial or otherwise.

DOI:10.1097/01.NPR.0000653944.99226.25

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