

# Community-Acquired Pneumonia

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## Epidemiology

Bacterial respiratory diseases, including sinusitis, bronchitis, otitis, and pneumonia, are among the most common infectious complications in people with HIV, occurring with increased frequency at all CD4 T lymphocyte cell (CD4) counts.<sup>1</sup> This chapter will focus on the diagnosis, prevention, and management of bacterial community-acquired pneumonia (CAP) in people with HIV. While viral pneumonias are a frequent cause of CAP, particularly influenza and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the management of coronavirus-19 (COVID-19) disease is outside the scope of these guidelines (refer to [NIH COVID-19 Treatment Guidelines](#) for updated treatment recommendations). These guidelines also do not consider hospital acquired pneumonia and ventilator-associated pneumonia; limited data suggest that these do not differ in terms of microbiology, clinical course, treatment, or prevention in people with HIV as compared to in people without HIV with similar HIV-unrelated comorbidities.

Bacterial pneumonia is a common cause of HIV-associated morbidity. Recurrent pneumonia, considered two or more episodes within a 1-year period, is an AIDS-defining condition. The incidence of bacterial pneumonia in individuals with HIV has decreased progressively with the advent of combination antiretroviral therapy (ART).<sup>2-7</sup> In one study, the incidence of bacterial pneumonia declined from 22.7 episodes per 100 person-years before the introduction of ART to 9.1 episodes per 100 person-years by 1997 after ART was introduced. Since then, the incidence of bacterial pneumonia among people with HIV in developed countries has continued to drop. In the Strategic Timing of AntiRetroviral Treatment (START) study, the incidence rate of serious bacterial infections overall was 0.87 per 100 person-years, and approximately 40% of these infections were due to bacterial pneumonia.<sup>4</sup> Recurrent bacterial pneumonia as an AIDS-defining illness is also less frequently encountered in individuals on ART; however, its exact incidence is hard to evaluate because surveillance data for it are not collected systematically as for other opportunistic infections (OIs).<sup>8</sup>

## ***Risk Factors***

Yet despite ART, bacterial pneumonia remains more common in people with HIV than in those who do not have HIV.<sup>9-11</sup> Bacterial pneumonia may be the first manifestation of underlying HIV infection and can occur at any stage of HIV disease and at any CD4 count. Bacterial pneumonia in individuals with HIV results from multiple risk factors, particularly immune defects. A CD4 count decrease, especially when below 100 cells/mm<sup>3</sup>, continues to be a major risk factor for pneumonia due to routine bacterial pathogens. Other immune defects include quantitative and qualitative B-cell abnormalities that result in impaired pathogen-specific antibody production, abnormalities in neutrophil function or numbers, and abnormalities in alveolar macrophage function.<sup>12,13</sup> Lack of ART or intermittent use of ART increases the risk for pneumonia, likely due to uncontrolled HIV viremia.<sup>14</sup>

Additional risk factors that contribute to the continued risk for bacterial pneumonia in individuals with HIV include chronic viral hepatitis, tobacco, alcohol, injection drug use and prescribed opioid

use, particularly higher doses and opioids with immunosuppressive properties.<sup>3,10,15,16,17</sup> Chronic obstructive pulmonary disease (COPD), malignancy, renal insufficiency, and congestive heart failure (CHF) are emerging as risk factors for pneumonia, particularly in the population of older adults with HIV.<sup>18</sup> Risk for CAP can also increase with obesity<sup>4</sup>, an emerging health problem in people living with HIV.

## Microbiology

In individuals with HIV, *Streptococcus pneumoniae* (*S. pneumoniae*) and *Haemophilus* species are the most frequently identified causes of community-acquired bacterial pneumonia, the same as in individuals without HIV.<sup>19-25</sup> *Staphylococcus aureus* (*S. aureus*) and *S. pneumoniae* are among the most common etiologies of pneumonia in association with influenza infection.<sup>26,27</sup> Atypical bacterial pathogens such as *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila* species have been reported as infrequent causes of CAP in individuals with HIV.<sup>22,28</sup> However, when more extensive testing such as serology to detect IgM antibodies (IgM) antibodies and/or positive polymerase chain reaction (PCR) of respiratory secretions was performed, additional infections due to *Mycoplasma* and *Chlamydia* were detected.<sup>29</sup>

Additional microbial etiologies of CAP that should be considered in people with HIV include *Mycobacterium tuberculosis*, *Pneumocystis*, other opportunistic infections, and respiratory viruses. The incidence of these different organisms will vary depending on geographic region and patient risk factors including degree of immunocompromise when considering opportunistic infections. For example, in a recent prospective study from South Africa of 284 patients with HIV and suspected pneumonia, sputum real-time multiplex PCR testing found that tuberculosis was more common than bacterial causes of CAP in this setting; viruses were detected in 203 patients, with the most common being human metapneumovirus, although the pathogenic significance of the viral pathogens was uncertain.<sup>30</sup> As noted, respiratory viruses, influenza and SARS-CoV-2 are also common causes of CAP in people with HIV. While influenza and COVID-19 generally present similarly in people with and without HIV, some studies suggest mortality may be increased among people with HIV for these viral infections, particularly in low-and-middle income country settings.<sup>31-36</sup>

## ***Risk Factors for Pseudomonas aeruginosa and Methicillin-Resistant Staphylococcus aureus***

The frequency of *Pseudomonas aeruginosa* (*P. aeruginosa*) and *S. aureus* as community-acquired pathogens is higher in individuals with HIV than in those without HIV based on studies in the early combination ART era.<sup>23,37</sup> Many of these patients often had poorly controlled HIV or the presence of other concomitant risk factors that contributed to risk for *P. aeruginosa* or *S. aureus*. Patients with advanced HIV disease (CD4 count  $\leq 50$  cells/mm<sup>3</sup>) or underlying neutropenia, as well as pre-existing lung disease such as bronchiectasis or severe COPD have an increased risk of infection with *P. aeruginosa*. Other risk factors for infection include the use of corticosteroids, severe malnutrition, hospitalization within the past 90 days, residence in a health care facility or nursing home, and chronic hemodialysis.<sup>38</sup>

*S. aureus* should be considered in patients with recent viral infection (particularly influenza), a history of injection drug use, or severe, bilateral, necrotizing pneumonia. Risk factors for *S. aureus* pneumonia in patients with HIV include receipt of antibiotics prior to hospital admission, comorbid illnesses, and recent healthcare contact.<sup>39</sup> Community outbreaks of methicillin-resistant *S. aureus* (MRSA) infection have also been seen among men who have sex with men.<sup>40</sup> Studies of patients

without HIV have identified hemodialysis, known prior colonization or infection with MRSA, as well as recurrent skin infections to be risk factors for MRSA pneumonia.<sup>38</sup> Notably, nasal carriage and colonization of skin sites with MRSA is more common in individuals with HIV than in those without HIV, and is more likely in patients recently incarcerated and/or hospitalized.<sup>41,42</sup>

## Clinical Manifestations

### ***Clinical and Radiographic Presentation***

The clinical and radiographic presentation of bacterial pneumonia in individuals with HIV, particularly in those with higher CD4 count and HIV viral suppression, is similar to that in individuals without HIV.<sup>43</sup> Patients with pneumonia caused by bacteria such as *S. pneumoniae* or *Haemophilus* species characteristically have acute onset (3 to 5 days) of symptoms, including fevers, chills, rigors, chest pain or pleurisy, cough productive of purulent sputum, and dyspnea.<sup>44</sup> The presence of fever, tachycardia, and/or hypotension can be indicators of sepsis. Tachypnea and decreased arterial oxygen saturation indicate moderate-to-severe pneumonia, and in such cases, clinicians should strongly consider hospitalizing the patient.

Patients with bacterial pneumonia typically have signs of focal consolidation, such as egophony, and/or pleural effusion on lung examination. In contrast, lung examination often is normal in those with *Pneumocystis* pneumonia (PCP), and if abnormal, reveals inspiratory crackles. In patients with bacterial pneumonia, the white blood cell (WBC) count usually is elevated. The elevation may be relative to baseline WBC count in those with advanced HIV. Neutrophilia or a left shift in WBC differential may be present.

Individuals with bacterial pneumonia characteristically exhibit unilateral, focal, segmental, or lobar consolidation on chest radiograph. The frequency of these typical radiographic findings, however, may depend on the underlying bacterial pathogen. Those with pneumonia due to *S. pneumoniae* or *Haemophilus* typically present with consolidation, whereas cavitation may be a feature more suggestive of *P. aeruginosa* or *S. aureus*.

### ***Risk Factors for Bacteremia***

In individuals with HIV the incidence of bacteremia accompanying pneumonia is greater than in individuals without HIV, especially when infection is due to *S. pneumoniae*.<sup>45</sup> In data from the CDC, the incidence of invasive pneumococcal disease, inclusive of bacteremia, was significantly higher in individuals with HIV: rates were 173 cases per 100,000 in those with HIV infection, compared to 3.8 per 100,000 in younger adults aged 18–34 years and 36.4 per 100,000 among those aged ≥65 years in the general population.<sup>46</sup> Similarly, in a study from Kenya, the rate of pneumococcal bacteremia was significantly higher in individuals with HIV infection (rate ratio of HIV-infected versus HIV-negative adults, 19.7, 95% CI 12.4–31.1).<sup>47</sup> With the introduction of ART and pneumococcal conjugate vaccines for both the general pediatric population and individuals living with HIV, this disparity in incidence rates of bacteremia between people with and without HIV has narrowed but has not been eliminated.<sup>48–52</sup> In one recent study of invasive pneumococcal disease (IPD), which includes bacteremia, IPD was more common in people with HIV who had CD4 counts < 500 cells/mm<sup>3</sup>, but even those with counts > 500 cells/mm<sup>3</sup>, had a higher incidence than in the general population.<sup>53</sup> Risk factors associated with bacteremia include lack of ART, low CD4 count (particularly <100 cells/mm<sup>3</sup>), as well as alcohol abuse, current smoking, and comorbidities, particularly liver disease.<sup>49</sup>

## ***Severity of Illness***

Disease severity and arterial oxygenation should be assessed in all patients with pneumonia. Noninvasive measurement of arterial oxygen saturation by pulse oximetry is an appropriate screening test. Arterial blood gas analysis is indicated for patients with evidence of hypoxemia suggested by noninvasive assessment and for patients who have tachypnea and/or respiratory distress. Assessment of additional clinical features and the use of severity scoring systems for pneumonia such as the Pneumonia Severity Index (PSI) and CURB-65 and their application to patients with HIV are discussed in the Treating Disease section.

## ***Outcomes***

Although some studies suggest that bacterial pneumonia is associated with increased mortality in individuals with HIV,<sup>23,54,55</sup> others do not.<sup>43,56-58</sup> Independent predictors of increased mortality in a prospective, multicenter study of individuals with HIV with community-acquired bacterial pneumonia were CD4 count <100 cells/mm<sup>3</sup>, radiographic progression of disease, and presence of shock.<sup>59</sup> In that study, multilobar infiltrates, cavitory infiltrates, and pleural effusion on baseline imaging were all independent predictors of radiographic progression of disease. However, in patients on ART with controlled HIV viremia, and high CD4 counts (>350 cells/mm<sup>3</sup>), the clinical courses and outcomes of pneumonia appear to be similar to those in patients without HIV.<sup>43</sup>

As in patients without HIV, pneumonia may have an impact on longer term outcomes of patients with HIV. This includes greater long-term mortality, as hospitalization for pneumonia has been associated with increased mortality up to one year later.<sup>60</sup> One factor that may add to this long-term mortality is cardiovascular disease associated with CAP, which occurs at a similar rate in those with HIV infection, as those without, even though in one retrospective cohort study of 4,384 patients, people with HIV were younger, had less severe CAP and fewer traditional cardiovascular risk factors than those without HIV infection.<sup>61</sup> Pneumonia has also been associated with impaired lung function and risk of subsequent lung cancer in individuals with HIV.<sup>62-64</sup>

## **Diagnosis**

### ***General Approach***

Patients with clinical symptoms and signs suggestive of CAP should have posteroanterior and lateral chest radiographs; evidence of pneumonia can also be found on chest computed tomography (CT) scan, but routine use of chest CT scan for this purpose is not recommended. Lung ultrasound can also be used to aid in the diagnosis pneumonia. If previous radiographs are available, they should be reviewed to assess for new findings. The clinical diagnosis of bacterial pneumonia requires a demonstrable infiltrate by chest radiograph or other imaging technique in conjunction with compatible clinical symptoms and signs.

The differential diagnosis of pneumonia in individuals with HIV is broad and a confirmed microbiologic diagnosis should be pursued. Microbial identification can allow clinicians to target the specific pathogen(s) and discontinue broad spectrum antibiotic therapy and/or empiric therapy that targets non-bacterial pathogens. Microbiologic testing should include evaluation of the upper respiratory tract for SARS-CoV-2, influenza in the appropriate season, and may include testing other respiratory viruses.<sup>65</sup> Given the increased incidence of *Mycobacterium tuberculosis* (*M. tuberculosis*) in individuals with HIV, a tuberculosis (TB) diagnosis should always be considered in patients with

HIV who have pneumonia, particularly in high incidence areas. Those with clinical and radiographic findings suggestive of TB should be managed as potentially having TB (i.e., airborne precautions for hospitalized patients), and two to three sputum specimens should be obtained for acid fast bacilli evaluation (including TB PCR; see [Mycobacterium tuberculosis Infection and Disease section](#)). Bronchoscopy with bronchoalveolar lavage should be considered, especially if the differential diagnosis includes opportunistic pathogens such as *Pneumocystis jirovecii*.

Procalcitonin (PCT) testing has been proposed as a tool to distinguish between bacterial and viral respiratory infections. One study from Africa specifically evaluated the usefulness of PCT testing to distinguish CAP due to bacteria (non-TB), *M. tuberculosis*, and PCP in people with HIV. In general, PCT levels associated with bacterial pneumonia are higher than those associated with viral or fungal pneumonias, but levels can also be elevated in non-bacterial pulmonary infections.<sup>66</sup> Specific PCT thresholds have not been established or validated in HIV-associated bacterial pneumonia. Thus, given the lack of data, the use of PCT to guide decisions regarding etiology of pneumonia, initiation of anti-bacterial treatment, or duration of treatment in patients with HIV is not recommended.

### ***Recommended Diagnostic Evaluation in CAP***

American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) guidelines for microbiologic testing for diagnosis of CAP in individuals without HIV generally also apply to people with HIV.<sup>67</sup>

- In patients with HIV with CAP who are well enough to be treated as outpatients, routine diagnostic tests to identify a bacterial etiologic diagnosis are optional, especially if the microbiologic studies cannot be performed promptly.
- In patients with HIV hospitalized for CAP, a Gram stain of expectorated sputum and two blood cultures are recommended, particularly in those with severe pneumonia, in those who are not on ART; or in those who are known to have a CD4 count <350 cells/mm<sup>3</sup> (and especially if <100 cells/mm<sup>3</sup>) prior to hospitalization. Specimens should ideally be obtained before initiation of antibiotics, or within 12 hours to 18 hours of such initiation.
- Urinary antigen tests for *L. pneumophila* and *S. pneumoniae* are recommended in hospitalized patients, particularly those with severe CAP. In addition, lower respiratory tract secretions should be cultured for *Legionella* on selective media or undergo *Legionella* nucleic acid amplification testing in adults with severe CAP. Legionella testing should also be done in people with HIV with non-severe CAP when indicated by epidemiological factors, such as association with a *Legionella* outbreak or recent travel.
- Microbiologic diagnostic testing is indicated whenever epidemiologic, clinical, or radiologic clues prompt suspicion of specific pathogens that could alter standard empirical management decisions.
- If available, rapid MRSA nasal testing should be performed, particularly in patients with risk factors for MRSA or in a high prevalence setting, as results can direct empiric antibiotic therapy.<sup>68</sup>

Gram stain and culture of sputum is recommended in all hospitalized patients meeting the criteria stated above, and is optional in people with HIV with CAP not meeting these criteria. In general, Gram stain and culture of expectorated sputum should be performed only if a good-quality specimen can be obtained prior to—or not more than 12 hours to 18 hours after—initiation of antibiotics, and



quality performance measures for collection, transport, and processing of samples can be met. Sputum cultures in people with HIV have been shown to identify a bacterial etiology in up to 30-40% of good quality specimens<sup>55,69</sup> although yield is less in other studies.<sup>14,29</sup> Correlation of sputum culture with Gram stain can help in interpretation of sputum culture data. For intubated patients, an endotracheal aspirate sample should be obtained promptly after intubation, or bronchoscopy may be indicated.

Blood cultures are more likely to be positive in people with HIV than in those without HIV. Patients with HIV, particularly those with lower CD4 counts, are at increased risk of invasive infection with *S. pneumoniae*. Given concerns for drug-resistant *S. pneumoniae*<sup>70,71</sup>, as well as *S. aureus* and/or other drug-resistant pathogens, blood cultures are recommended for patients with HIV who meet the criteria as noted above, and are optional for those who do not meet the criteria listed.

Diagnostic thoracentesis should be performed in all patients with pleural effusion if concern exists for accompanying empyema, and pleural fluid should be sent for microbiologic studies. Therapeutic thoracentesis should be performed to relieve respiratory distress secondary to a moderate-to-large-sized pleural effusion. Given the increased risk of invasive pneumococcal disease in patients with HIV, clinicians should be vigilant for evidence of extra-pulmonary complications of infection.

## Preventing Exposure

No effective means exist to reduce exposure to *S. pneumoniae* and *Haemophilus influenzae*, which are common in the community. General precautions to maintain health, such as adhering to hand hygiene and cough etiquette and refraining from close contact with individuals who have respiratory infections, should be emphasized for patients with HIV as for other patient populations.

## Preventing Disease

### *Pneumococcal Vaccine*

Vaccination against *S. pneumoniae* is an important measure in preventing bacterial pneumonia. Some observational studies have reported benefits of pneumococcal polysaccharide vaccine (PPSV) use in people with HIV against IPD (e.g., bacteremia, meningitis)<sup>49,72</sup>, and all-cause pneumonia,<sup>73-75</sup> however, results have been variable.<sup>72,76-78</sup> One randomized placebo-controlled trial of PPSV in Africa paradoxically found that vaccination was associated with an increased risk of pneumonia, and there was no evidence of reduced risk of IPD among vaccinated participants.<sup>79</sup> Follow-up of this cohort not only confirmed the increase in pneumonia in vaccinated participants, but also showed a decrease in all-cause mortality, although participants in this study were not treated with ART.<sup>80</sup> A recent study<sup>81</sup> evaluating the impact of the 13-valent pneumococcal conjugate vaccine (PCV13) vaccination on the rates of IPD in adults with HIV between 2008 and 2018 found that IPD rates remained high despite reductions with the introduction of PCV13. PCV20/non-PCV15 serotypes comprised 16.5% of cases of IPD, suggesting that the use of higher valent conjugate pneumococcal vaccines may reduce IPD.

In 2021, two PCVs, 15-valent (PCV15) and 20-valent (PCV20), were licensed by the FDA for use in U.S. adults.<sup>82</sup> PCV15 and PCV20 were licensed based on safety and immunogenicity data compared with the 13-valent PCV or 23-valent pneumococcal polysaccharide vaccine (PPSV23). Effectiveness data of these vaccine against pneumococcal disease in adults with HIV infection are currently not available. One phase 3 clinical trial of PCV15 followed by PPSV23 8 weeks later in people with HIV

demonstrated safety and immunogenicity of this approach.<sup>83</sup> No clinical data exist for the use of PCV20 in people with HIV. To date, one randomized, double-blind, placebo-controlled trial has assessed the efficacy of PCV against pneumococcal disease in adults with HIV. This was a trial on 7-valent PCV (PCV7) among adults with HIV in Malawi, which demonstrated 74% efficacy against vaccine-type IPD, with clear evidence of efficacy in those with CD4 counts <200 cells/mm<sup>3</sup>.<sup>84</sup> However, study participants were those who had recovered from IPD, and received two doses of PCV7 four weeks apart. Therefore, findings may not be directly applicable to adults with HIV infection.

Patients with CD4 counts  $\geq 200$  cells/mm<sup>3</sup> should receive a dose of PPSV23 at least 8 weeks later **(AI)**.<sup>72-75,85-89</sup> While individuals with HIV with CD4 counts <200 cells/mm<sup>3</sup> can also be offered PPSV23 at least 8 weeks after receiving PCV15 **(CIII)** (such as if there are concerns with retention in care), PPSV23 should preferably be deferred until after an individual's CD4 count increases to >200 cells/mm<sup>3</sup> while on ART **(BIII)**. Clinical evidence supporting use of PPSV23 in persons with CD4 counts <200 cells/mm<sup>3</sup> appears strongest in patients who also have HIV RNA <100,000 copies/mL;<sup>75,89</sup> evidence also suggests benefit for those who start ART before receiving PPSV vaccination.<sup>72,90</sup>

People with HIV who have received PCV13 but have not completed their recommended pneumococcal vaccine series with PPSV23, one dose of PCV20 may be used if PPSV23 is not available. If PCV20 is used, their pneumococcal vaccinations are complete **(CIII)**.

## ***Influenza Vaccine***

Influenza vaccination is pertinent to prevention of CAP from influenza or influenza-associated bacterial pneumonia, which can occur as a complication of influenza. Influenza and pneumococcal vaccines can be administered during the same visit. Use of high-dose inactivated influenza vaccine is associated with decreased incidence of influenza and greater antibody response in adults without HIV age  $\geq 65$  years compared with standard-dose inactivated vaccine.<sup>91,92</sup> One trial found greater immunogenicity in people with HIV age  $\geq 18$  years who were given high-dose influenza vaccine compared with standard-dose inactivated vaccine.<sup>93</sup> See the “Influenza Vaccine” section in the [Immunization section](#) of the Adult and Adolescent Opportunistic Infections Guidelines for a detailed evidence summary.

All people with HIV infection during influenza season **(AI)** should be immunized against influenza with inactivated, standard dose or recombinant influenza vaccine per recommendation of the season **(AI)**. High-dose inactivated influenza vaccine may be given to individuals age >65 years **(AIII)**. For pregnant people with HIV, administer inactivated influenza or recombinant vaccine at any time during pregnancy **(AI)**.

## ***Additional Vaccines***

The incidence of *H. influenzae* type b infection in adults with HIV is low. Therefore, *H. influenzae* type vaccine is not usually recommended for adult use **(BIII)**<sup>90</sup> unless a patient also has anatomic or functional asplenia.

Recommendations for COVID-19 vaccination are provided in the [Immunization section](#) of the Adult and Adolescent Opportunistic Infections Guidelines.

## ***Prophylaxis and Risk Reduction***

Several factors are associated with a decreased risk of bacterial pneumonia in HIV, including use of ART and trimethoprim-sulfamethoxazole (TMP-SMX) for PCP prophylaxis.<sup>55</sup> In many studies, daily administration of TMP-SMX for PCP prophylaxis reduced the frequency of bacterial respiratory infections.<sup>9,94,95</sup> This point should be considered when selecting an agent for PCP prophylaxis; however, indiscriminate use of TMP-SMX (when not indicated for PCP prophylaxis or other specific reasons) may promote development of TMP-SMX-resistant organisms. Thus, in the United States, TMP-SMX should not be prescribed solely to prevent bacterial respiratory infection (**AIII**). Similarly, clarithromycin or azithromycin should not be prescribed solely for preventing bacterial respiratory infection (**AIII**).

A decreased absolute neutrophil count (e.g., <500 cells/mm<sup>3</sup>) is associated with an increased risk of bacterial infections, including pneumonia, although this risk has been demonstrated primarily in persons with malignant neoplasms. To reduce the risk of such bacterial infections, clinicians should take steps to reverse neutropenia, such as by stopping myelosuppressive drugs (**CIII**). Studies of granulocyte-colony stimulating factor (G-CSF) in people with HIV have failed to document benefit.<sup>96,97</sup>

Modifiable factors associated with an increased risk of bacterial pneumonia include smoking cigarettes, using injection drugs, and consuming alcohol.<sup>9,74,98-100</sup> Clinicians should encourage cessation of these behaviors, refer patients to appropriate services, and/or prescribe medications to support quitting. Data demonstrate that smoking cessation can decrease the risk of bacterial pneumonia.<sup>15</sup>

## **Treating Disease**

### ***General Approach to Treatment***

The basic principles of antibiotic treatment of CAP are the same for patients with HIV as for those who do not have HIV.<sup>67</sup> As discussed in the Diagnosis section, if specimens are to be collected for diagnosis, they should preferably be collected before antibiotic therapy is initiated or within 12 hours to 18 hours of antibiotic initiation. However, antibiotic therapy should be administered promptly, without waiting for the results of diagnostic testing. Empiric therapy varies based on geographic region and common pathogens in these regions, and should take into account local resistance patterns, results of MRSA rapid swab testing if done, and individual patient risk factors, including severity of immunocompromise (recent CD4 cell count, HIV viral load) and use of ART.

In patients with HIV, providers must also consider the risk of opportunistic lung infections, such as PCP, that would alter empiric treatment. In settings where the prevalence of TB is high, initiation of empiric therapy for both bacterial pneumonia and TB may be appropriate for patients in whom both diagnoses are strong considerations and after diagnostic studies are undertaken. Because respiratory fluoroquinolones are also active against *M. tuberculosis*, they should be used with caution in patients with suspected TB who are not being treated with concurrent standard four-drug TB therapy. Thus, patients with TB who are treated with fluoroquinolones in the absence of standard four-drug TB therapy may have an initial, but misleading response, that could delay diagnosis of TB and initiation of appropriate multidrug TB therapy, increasing the risk of drug-resistant TB and TB transmission.



## ***Assessing Severity of Disease and Treatment Location***

Whether patients should be treated on an outpatient basis or admitted to the hospital depends on several factors. In addition to considerations regarding ability to take oral medications, adherence, and other confounding factors (housing, comorbid diseases, etc.), severity of illness is a key factor that helps to guide decisions regarding treatment location for CAP—outpatient versus inpatient, including intensive care unit (ICU). Notably, no prospective randomized clinical trials have assessed the performance of the [Pneumonia Severity Index \(PSI\) for CAP](#) or other severity scores (e.g., the ATS/IDSA severity criteria<sup>67</sup> or [CURB-65 Score for Pneumonia Severity](#), to guide decisions regarding inpatient or outpatient treatment location for people with HIV. However, the PSI, CURB-65, the ATS/IDSA severity criteria, and other scoring systems appear to be valid for predicting mortality in patients with HIV with CAP, especially when used in combination with CD4 count.<sup>59,101,102</sup>

Whether the performance of severity indices is improved by including HIV-related variables is uncertain. One study suggested that the site of care decision be dictated by considering the PSI score and CD4 count together.<sup>101</sup> Mortality was increased in patients with higher PSI risk class; however, even in those without an increased mortality risk by PSI, a CD4 count  $<200$  cells/mm<sup>3</sup> was associated with an increased risk of death.<sup>101</sup> This led to the suggestion to hospitalize CAP patients with CD4 counts  $<200$  cells/mm<sup>3</sup> and to use the PSI to help guide decision-making in those with higher CD4 counts.<sup>103</sup>

However, other studies have found the PSI was predictive of outcomes independent of CD4 count.<sup>104</sup> Furthermore, CD4 count or HIV RNA level are not clearly associated with short-term outcomes of CAP.<sup>105</sup> Other HIV-specific scoring systems such as the [Veterans Aging Cohort Study \(VACS\) Index](#), although originally designed to predict overall mortality, may also be useful in predicting ICU admission and mortality. In a study of older patients with and without HIV with CAP, a higher VACS Index was associated with greater 30-day mortality, readmission, and length of stay.<sup>106</sup> Another possible tool is the SWAT-Bp tool developed in Malawi.<sup>107</sup> This tool measures male [S]ex, muscle [W]asting, non-[A]mbulatory, [T]emperature ( $>38^{\circ}\text{C}$  or  $<35^{\circ}\text{C}$ ), and [B]lood [p]ressure (systolic $<100$  and/or diastolic $<60$ ). In a retrospective study of 216 patients (84% with HIV), demonstrated moderate discriminatory power, while the CURB-65 was less accurate.

Thus in general, validated clinical prediction scores for prognosis can be used in patients with HIV in conjunction with clinical judgement to guide treatment location for CAP. Low risk patients for whom there are no other concerns regarding adherence or complicating factors can be treated as outpatients. Patients with severe CAP, including those presenting with shock or respiratory failure, usually require a higher level of care, typically ICU admission. Additionally, severe CAP criteria can include PSI risk class of III or IV or CURB-65 scores  $\geq 3$ . Patients with  $\geq 3$  of the ATS/IDSA minor severity criteria for CAP<sup>67</sup> often require ICU or higher level of care, as well.

## ***Empiric Antibiotic Therapy by Treatment Setting and Severity of Diseases***

There is a general paucity of clinical trials evaluating different antibiotic regimens for treating CAP in populations with HIV and a lack of evidence that treatment response to antibiotics is different in individuals with HIV than in those without HIV. Therefore, treatment recommendations for CAP in individuals with HIV are generally consistent with the ATS/IDSA guidelines for people without HIV.<sup>67</sup>

## ***Outpatient CAP Treatment***

Individuals with HIV who are being treated as outpatients should receive an oral beta-lactam plus a macrolide (**AI**), or a respiratory fluoroquinolone (**AI**). Preferred beta-lactams are high-dose amoxicillin or amoxicillin-clavulanate; alternatives are cefpodoxime or cefuroxime. Preferred macrolides are azithromycin or clarithromycin. Preferred respiratory fluoroquinolones are moxifloxacin or levofloxacin. A respiratory fluoroquinolone (moxifloxacin or levofloxacin) should be used as an alternative to a beta lactam in patients who are allergic to penicillin. If a patient has contraindications to a macrolide or a fluoroquinolone, then doxycycline should be given as an alternative (**BIII**) in addition to a beta-lactam.

Empirical monotherapy with a macrolide for outpatient CAP is not routinely recommended in patients with HIV for two reasons (**BIII**). First, increasing rates of pneumococcal resistance have been reported with erythromycin-resistant rates up to 30%,<sup>108</sup> prompting concerns for possible treatment failure. In this regard, local drug resistance patterns, if available, can help inform treatment decisions. Additionally, patients who are already receiving a macrolide for MAC prophylaxis may have resistance due to chronic exposure, and should also not receive macrolide monotherapy for empiric treatment of bacterial pneumonia. However, macrolides can be used as part of a combination CAP regimen.

## ***Non-Severe CAP Inpatient Treatment***

Individuals with HIV who are being treated as inpatients should receive an intravenous (IV) beta-lactam plus a macrolide (**AI**) or a respiratory fluoroquinolone (**AI**). Monotherapy with a macrolide is not recommended in the inpatient setting. The role for dual therapy with a macrolide is somewhat controversial based on prior observational studies and two prospective clinical trials in patients without HIV with CAP that evaluated outcomes in those treated with beta-lactam monotherapy and those treated with dual-therapy including a macrolide.<sup>109,110</sup> In one study, beta-lactam monotherapy was not found to be non-inferior to beta-lactam/macrolide combination therapy. Notably, in the monotherapy arm, patients who had more severe CAP, as indicated by a PSI  $\geq$  IV, or who had atypical pathogens were less likely to reach clinical stability. There were also more 30-day readmissions among the patients on monotherapy.<sup>109</sup> While there was a trend towards improved outcomes in those on dual therapy, the difference between arms was not statistically significant. In a pragmatic, cluster-randomized, cross-over trial of non-ICU hospitalized patients with CAP, beta-lactam monotherapy was found to be non-inferior to beta-lactam/macrolide combination therapy or fluoroquinolone monotherapy.<sup>110</sup> However in this study, the diagnosis of CAP did not require radiographic confirmation, illness was mild, and there were cross-overs between groups.

Only one study thus far has compared a cephalosporin (ceftriaxone) to dual therapy with a cephalosporin (ceftriaxone) plus macrolide in 225 people with HIV with CAP, finding no difference between in-hospital or 14-day mortality between the groups; most patients had lower severity of disease, with only 7% of the cohort having a CURB-65 score  $>2$  and 17% with a PSI risk class  $>III$ .<sup>111</sup> Given the heterogeneity and limitations of recent studies and scarce data in patients with HIV, the recommendation for patients with HIV who are hospitalized with non-severe CAP remains that same as in people without HIV: to administer either beta-lactam/macrolide combination therapy, or a single drug regimen of a respiratory fluoroquinolone (**AI**).

Preferred beta-lactams are ceftriaxone, cefotaxime, or ampicillin-sulbactam. Preferred macrolides are azithromycin and clarithromycin. Preferred respiratory fluoroquinolones are moxifloxacin or

levofloxacin. If a patient has contraindications to a macrolide or a fluoroquinolone, then doxycycline should be given as an alternative (**BIII**) in addition to a beta-lactam. Clinical and Laboratory Standards Institute and U. S. Food and Drug Administration (FDA) changes in the penicillin breakpoints for treatment of non-meningitis pneumococcal disease imply IV penicillin is an acceptable option for treatment of pneumococcal disease in patients with HIV (**BIII**).<sup>112</sup> In patients who are allergic to penicillin, a respiratory fluoroquinolone (moxifloxacin or levofloxacin [750 mg/day]) alone should be used (**AI**). As noted, fluoroquinolone monotherapy should be used with caution in patients in whom TB is suspected but who are not being treated with concurrent standard four-drug TB therapy.

### ***Severe CAP Treatment***

Patients with severe CAP should not receive empiric monotherapy, even with a fluoroquinolone, because of the range of potential pathogens and the desirability of prompt and microbiologically active therapy (**AI**). In one study, the use of dual therapy (usually with a beta-lactam plus a macrolide) was associated with reduced mortality in patients with bacteremic pneumococcal pneumonia, including those admitted to the ICU.<sup>113</sup> Patients with severe pneumonia should be treated with an IV beta-lactam plus either azithromycin (**AI**) or a respiratory fluoroquinolone (moxifloxacin or levofloxacin [750 mg/day]) (**AI**). Both have a strong recommendation. Weak observational data, in the absence of prospective randomized controlled data, suggest that beta-lactam plus macrolide may be associated with decreased mortality.<sup>77,114,115</sup> Preferred beta-lactams are ceftriaxone, cefotaxime, or ampicillin-sulbactam. In patients who are allergic to penicillin, aztreonam plus a respiratory fluoroquinolone (moxifloxacin or levofloxacin [750 mg/day]) should be used (**BIII**).

The majority of CAP pathogens can be treated adequately with recommended empiric regimens. The increased incidence of *P. aeruginosa* and *S. aureus* (including community-acquired MRSA) as causes of CAP are exceptions. Both of these pathogens occur in specific epidemiologic patterns with distinct clinical presentations for which empiric antibiotic coverage may be warranted. Diagnostic tests (sputum Gram stain and culture) are likely to be of high yield for these pathogens, allowing early discontinuation of empiric treatment if results are negative. In the most recent ATS/IDSA CAP guidelines, empiric therapy for *P. aeruginosa* or MRSA is recommended in those with severe CAP, who have had these organisms previously isolated from sputum cultures, with de-escalation if these organisms are not isolated from current cultures.<sup>67</sup>

The addition of corticosteroids for treating CAP has not been studied in people with HIV. Data from studies in people without HIV with CAP suggest that corticosteroids may decrease a composite outcome of mortality, time to clinical stability, and length of hospital stay.<sup>116</sup> Importantly, effects of corticosteroids appear variable according to etiology and severity of pneumonia, however, as corticosteroids may increase mortality in influenza pneumonia,<sup>117</sup> but decrease mortality in patients with COVID-19 who require higher levels of respiratory support.<sup>118</sup> The optimal regimen including dose, duration, and formulation of corticosteroid, and the patient population with bacterial non-viral related CAP most likely to benefit from the additional use of corticosteroids remain uncertain. Selecting HIV-uninfected patients with severe CAP and increased inflammation as defined by C-reactive protein levels >150 mg/mL is one strategy for treatment of CAP that has been shown to be beneficial.<sup>119</sup>

ATS/IDSA guidelines recommend not using corticosteroids routinely in non-severe (**AI**) or severe CAP (**BII**) but endorse use in CAP with refractory shock<sup>67</sup> Similarly, the use of corticosteroids in HIV-infected patients with severe CAP is not routinely recommended (**BII**) given the lack of data

specifically in HIV-infected population. If providers administer corticosteroids to HIV-infected patients with severe CAP, they must ensure that no other contraindications to steroids exist; in patients who have no contraindications and have persistent shock despite fluid resuscitation, Surviving Sepsis Guidelines<sup>120</sup> provide a weak recommendation for administering hydrocortisone 200 mg IV daily for 5 to 7 days or tapering once vasopressors are no longer needed.

### ***Empiric Pseudomonas aeruginosa Treatment***

If risk factors for *Pseudomonas* infection are present, an antipneumococcal, antipseudomonal beta-lactam plus either ciprofloxacin or levofloxacin (750-mg dose) should be used (**AI**). Preferred beta-lactams are piperacillin-tazobactam, cefepime, imipenem, or meropenem. Alternative therapeutic agents that are recommended are an antipneumococcal, antipseudomonal beta-lactam plus an aminoglycoside and azithromycin (**BII**) or an antipneumococcal, antipseudomonal beta-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (**BII**). In patients who are allergic to penicillin, aztreonam is recommended to be used in place of the beta-lactam (**BII**).

### ***Empiric Staphylococcus aureus Treatment***

A nasal swab for MRSA can help inform decision-making whether initial empiric coverage should include MRSA. In studies of patients without HIV, negative test results have a high negative predictive value for pneumonia due to MRSA. If the nasal swab is negative for MRSA and the pneumonia is not severe and no other risk factors or features suggestive of MRSA pneumonia are present, empiric coverage for MRSA may be withheld (**BII**).<sup>68</sup>

However, in patients who have risk factors for *S. aureus* infection, vancomycin or linezolid should be added to the antibiotic regimen (**AII**). Empiric coverage for MRSA should also be added if a rapid nasal swab is positive for MRSA, although the positive predictive value for pneumonia is only moderate, and therapy should be de-escalated if cultures are negative (**BIII**). Although not routinely recommended, the addition of clindamycin to vancomycin (but not to linezolid) or the use of linezolid alone, is recommended by many experts if severe necrotizing pneumonia is present to minimize bacterial toxin production (**CII**).

Telavancin is an alternative agent that can be used for *S. aureus* pneumonia (**BIII**); it is currently FDA-approved for treatment of hospital-acquired and ventilator-associated (rather than community-acquired) pneumonia based on studies in people without HIV infection.<sup>121</sup> While ceftaroline has activity against MRSA, and data suggest it can be effective for MRSA pneumonia, it has been FDA approved for treatment of bacterial CAP based on two studies that did not include any MRSA isolates.<sup>122</sup> Neither telavancin or ceftaroline have been specifically studied in patients with HIV with bacterial pneumonia. Daptomycin should not be used to treat pneumonia as it is not active in the lung (**AI**).

### ***Pathogen-Directed Therapy***

When the etiology of the pneumonia has been identified based on reliable microbiological methods, antimicrobial therapy should be modified and directed at the identified pathogen (**BIII**).

## ***Switch From Intravenous to Oral Therapy***

A switch to oral therapy should be considered in patients with CAP on IV antibiotic therapy who have improved clinically, can swallow and tolerate oral medications, and have intact gastrointestinal function.<sup>67</sup> A longer duration of IV and overall antibiotic therapy is often necessary in patients who have severe CAP or who have bacteremia, particularly if due to *S. pneumoniae* or *S. aureus* and complicated infection is present.

## ***Special Considerations Regarding When to Start Antiretroviral Therapy***

In patients with bacterial pneumonia who are not already on ART, ART should be initiated promptly (i.e., within 2 weeks of initiating therapy for the pneumonia) unless comorbidities make ART unwise (AI).

## ***Monitoring of Response to Therapy and Adverse Events (Including IRIS)***

The clinical response to appropriate antimicrobial therapy for CAP is similar in patients with and without HIV.<sup>43,58</sup> A clinical response (i.e., reduction in fever and improvement in respiratory symptoms, physical findings, and laboratory studies) typically is observed within 48 to 72 hours after initiation of appropriate antimicrobial therapy. A review of patients with CAP found that advanced HIV infection and CD4 count <100 cells/mm<sup>3</sup> were predictors for longer time to clinical stability (i.e., >7 days) and that patients who received ART tended to become clinically stable sooner and had better outcomes.<sup>103,106</sup> The presence of bacteremia is a significant factor that impacts outcomes. Among those with pneumococcal pneumonia, longer time to clinical stability is more often seen in the setting of bacteremia. As in patients without HIV, radiographic improvement usually lags behind clinical improvement.

Immune reconstitution inflammatory syndrome (IRIS) has been rarely described in association with bacterial CAP and initiation of treatment with ART in patients with HIV. This could be secondary to a number of reasons: 1) patients with recurrent pneumonia have not been included in the study population; 2) IRIS among participants with bacterial pneumonia has not been specified or 3) this complication has truly not been observed.<sup>2,123</sup> Only case reports describe IRIS with pneumonia due to *Rhodococcus equii*. More commonly IRIS occurs with pneumonia due to *Pneumocystis* and mycobacterial infections.

## ***Managing Treatment Failure***

Patients who do not respond to appropriate antimicrobial therapy should undergo further evaluation to search for complications secondary to pneumonia (empyema, abscess formation, metastatic infection), other infectious process, the presence of a drug-resistant pathogen, and/or noninfectious causes of pulmonary dysfunction (pulmonary embolus, COPD).

## **Preventing Recurrence**

Patients with HIV should receive pneumococcal (AI) and influenza vaccines (AI) as recommended. Antibiotic chemoprophylaxis generally is not recommended specifically to prevent recurrences of bacterial respiratory infections because of the potential for development of drug-resistant microorganisms and drug toxicity (AI). Smoking cessation reduces the risk of bacterial pneumonia (by approximately 27%),<sup>124</sup> and patients who smoke tobacco should be encouraged to quit and



provided with the appropriate tools and referrals whenever possible (**AI**). Likewise, patients with substance use disorders (alcohol, injection or non-injection drugs) should be referred for appropriate counseling and services (**AI**). However, likely the most important intervention for prevention of bacterial pneumonia (first episode or recurrence) is initiation and adherence to ART, which is beneficial even among those with high CD4 count at time of ART initiation.<sup>4</sup> Thus prompt initiation or re-initiation of ART is recommended for all patients with HIV with bacterial pneumonia (**AI**).

## Special Considerations During Pregnancy

The diagnosis of bacterial respiratory tract infections in pregnant women is the same as in those who are not pregnant, with appropriate shielding of the abdomen during radiographic procedures. Bacterial respiratory tract infections should be managed in pregnant women as in women who are not pregnant, with certain exceptions. Among macrolides, clarithromycin is not recommended because of an increased risk of birth defects seen in some animal studies. Two studies, each involving at least 100 women with first-trimester exposure to clarithromycin, did not document a clear increase in or specific pattern of birth defects, although an increased risk of spontaneous abortion was noted in one study.<sup>125,126</sup> Azithromycin did not produce birth defects in animal studies, but experience with human use in the first trimester is limited. Azithromycin is recommended when a macrolide is indicated in pregnancy (**BIII**). Arthropathy has been noted in immature animals with *in utero* exposure to quinolones. Studies evaluating quinolone use in pregnant women did not find an increased risk of birth defects or musculoskeletal abnormalities.<sup>127,128</sup> When indicated, quinolones can be used in pregnancy for serious respiratory infections only when a safer alternative is not available (**CIII**).<sup>129</sup>

Doxycycline is not recommended for use during pregnancy because of increased hepatotoxicity and staining of fetal teeth and bones. Beta-lactam antibiotics have not been associated with teratogenicity or increased toxicity in pregnancy. Clindamycin use in pregnancy has not been associated with an increased risk of birth defects or adverse outcomes.<sup>130</sup> Aminoglycosides can be used as needed. A theoretical risk of fetal renal or eighth nerve damage exists with aminoglycoside exposure during pregnancy, but this finding has not been documented in humans, except with streptomycin (10% risk) and kanamycin (2% risk). Animal reproductive toxicity studies in rats and rabbits were negative for vancomycin, but data on first trimester exposure in humans are limited.<sup>131</sup> A study of neonates after *in utero* exposure did not find evidence of renal or ototoxicity.<sup>132</sup> Reproductive toxicity studies of telavancin in animals have shown increased rates of limb malformations in rats, rabbits, and mini pigs at doses similar to human exposure; no human data are available.<sup>131</sup> Use of telavancin should be avoided in the first trimester if alternate agents with more experience in use in pregnancy are available. Cases of exposure to telavancin in pregnancy should be reported to the Telavancin Pregnancy Registry at 1-855-633-8479. Experience with linezolid in human pregnancy has been limited, but it was not teratogenic in mice, rats, and rabbits.

Pneumonia during pregnancy is associated with increased rates of preterm labor and delivery. Pregnant women with pneumonia after 20 weeks' gestation should be monitored for evidence of contractions (**BII**). Pneumococcal vaccine can be administered during pregnancy (**AIII**). A study comparing administration of PCV10, PPSV23, or control (1:1:1) among 347 women during weeks 13–34 of pregnancy found that PCV10 and PPSV23 were equally safe and immunogenic in pregnant women with HIV and conferred similar levels of seroprotection to their infants.<sup>133</sup> No adverse consequences have been reported among newborns whose mothers were vaccinated during pregnancy. Women who did not receive vaccines during pregnancy were vaccinated post-partum; these data demonstrated higher antibody responses compared to women vaccinated ante-partum, suggesting that postpartum booster doses may be beneficial and require further study.<sup>134</sup>

Inactivated influenza vaccine is recommended for all pregnant women during influenza season (**AI**). Live attenuated influenza vaccine should not be used in people with HIV (**AIII**). Because administration of vaccines can be associated with a transient rise in plasma HIV RNA levels, vaccination of pregnant women is recommended after ART has been initiated to minimize increases in plasma HIV RNA levels that might increase the risk of perinatal transmission of HIV.

## Recommendations for Preventing and Treating Community-Acquired Pneumonia

### Preventing *Streptococcus pneumoniae* Infections

#### Indications for Pneumococcal Vaccination

- All people with HIV regardless of CD4 count **(AI)**

#### Vaccination Recommendations

- For all people with HIV without history of pneumococcal vaccination or unknown vaccine history:
  - Administer either 15-valent pneumococcal conjugate vaccine (PCV15) or 20-valent pneumococcal conjugate vaccine (PCV20) **(AII)**. If PCV20 is used, their pneumococcal vaccination is complete.
  - If PCV15 is used, a dose of PPSV23 should be administered at least 8 weeks later **(AII)**.<sup>\*</sup> No additional pneumococcal vaccine doses are recommended.
- For people with HIV who previously started or completed a pneumococcal vaccination series, there is no need to restart the series.<sup>\*\*</sup>
  - People with HIV who received PCV13 and were 65 or older when they received a dose of PPSV23 do not require further doses of PPSV23; for those who received PPSV23 younger than age 65, additional doses of PPSV23 are recommended as indicated below **(BIII)**.
    - People with HIV who have received PCV13 and PPSV23 at age <65 should receive a second dose of PPSV23 at least 5 years after the first dose. If they are age 65 or older at the time of their second dose, they do not require additional doses of PPSV23.
    - If they were <65 at the time of the second dose, they should receive a third and final dose at or after age 65, at least 5 years after the second PPSV23 dose.
  - People with HIV who have only received PPSV23 may receive a PCV (either PCV20 or PCV15) ≥1 year after their last PPSV23 dose. When PCV15 is used in those with history of PPSV23 receipt, it need not be followed by another dose of PPSV23 at any age **(BIII)**.

#### Footnotes

<sup>\*</sup> Patients with CD4 counts ≥200 cells/mm<sup>3</sup> should receive a dose of PPSV23 at least 8 weeks later **(AI)**. While individuals with HIV with CD4 counts <200 cells/mm<sup>3</sup> can also be offered PPSV23 at least 8 weeks after receiving PCV15 **(CIII)** (such as if there are concerns with retention in care), PPSV23 should preferably be deferred until after an individual's CD4 count increases to >200 cells/mm<sup>3</sup> while on ART **(BIII)**. Clinical evidence supporting use of PPSV23 in persons with CD4 counts <200 cells/mm<sup>3</sup> appears strongest in patients who also have HIV RNA <100,000 copies/mL; evidence also suggests benefit for those who start ART before receiving PPSV vaccination.

<sup>\*\*</sup> People with HIV who have received PCV13 but have not completed their recommended pneumococcal vaccine series with PPSV23, one dose of PCV20 may be used if PPSV23 is not available. If PCV20 is used, their pneumococcal vaccinations are complete **(CIII)**.

### Preventing Influenza and Bacterial Pneumonia as a Complication of Influenza

#### Indication for Influenza Vaccination

- All people with HIV infection during influenza season **(AI)**

#### Vaccination

- Adults age ≥65 years are recommended to receive high-dose IIV (Fluzone® High-Dose) or adjuvanted IIV (FLUAD®) over standard-dose unadjuvanted vaccine **(AII)**.
- People age ≥18 years also may use RIV (Flublok® Quadrivalent).

## Recommendations for Preventing and Treating Community-Acquired Pneumonia

- For people with egg allergy, use IIV or RIV appropriate for age (if the allergic reaction is more severe than hives, give the vaccine in a medical setting appropriate to manage severe allergic reaction).
- For pregnant people with HIV, administer inactivated influenza or recombinant vaccine at any time during pregnancy **(AI)**.
- Influenza vaccines are quadrivalent, with formulations that change from season to season.

**Note:** Live attenuated influenza vaccine is contraindicated in people with HIV **(AIII)**.

### Treating Community-Acquired Bacterial Pneumonia

**Note:** Empiric antimicrobial therapy should be initiated promptly for patients presenting with clinical and radiographic evidence consistent with bacterial pneumonia. The recommendations listed below are suggested empiric therapy. The regimen should be modified as needed once microbiologic and drug susceptibility results are available. Providers must also consider the risk of opportunistic lung infections such as PCP or TB, which may alter the empiric therapy as needed.

#### Empiric Outpatient Therapy (Oral)

##### *Preferred Therapy*

- An oral beta-lactam + a macrolide (azithromycin or clarithromycin) **(AI)**
  - *Preferred beta-lactams:* high-dose amoxicillin or amoxicillin/clavulanate
  - *Alternative beta-lactams:* cefpodoxime or cefuroxime

*or*

- A respiratory fluoroquinolone (levofloxacin or moxifloxacin)<sup>a</sup> **(AI)**, especially for patients with penicillin allergies.

##### *Alternative Therapy*

- A beta-lactam + doxycycline **(BIII)**

#### Empiric Therapy for Hospitalized Patients with Non-Severe CAP

##### *Preferred Therapy*

- An IV beta-lactam + a macrolide (azithromycin or clarithromycin) **(AI)**
  - *Preferred beta-lactams:* ceftriaxone, cefotaxime, or ampicillin-sulbactam

*or*

- A respiratory fluoroquinolone (levofloxacin or moxifloxacin)<sup>a</sup> **(AI)**, especially for patients with penicillin allergies.

##### *Alternative Therapy*

- An IV beta-lactam + doxycycline **(BIII)**
- IV penicillin may be used for confirmed pneumococcal pneumonia **(BIII)**

#### Empiric Therapy for Patients with Severe CAP

##### *Preferred Therapy*

- An IV beta-lactam + azithromycin **(AI)**, *or*
- An IV beta-lactam + a respiratory fluoroquinolone (levofloxacin or moxifloxacin)<sup>a</sup> **(AI)**
  - *Preferred beta-lactams:* ceftriaxone, cefotaxime, or ampicillin-sulbactam

##### *Alternative Therapy*

##### *For Penicillin-Allergic Patients*

- Aztreonam (IV) + a respiratory fluoroquinolone (moxifloxacin or levofloxacin)<sup>a</sup> **(BIII)**

#### Empiric Therapy for Patients at Risk of Pseudomonas Pneumonia

## Recommendations for Preventing and Treating Community-Acquired Pneumonia

### Preferred Therapy

- An IV antipneumococcal, antipseudomonal beta-lactam + (ciprofloxacin IV or levofloxacin IV 750 mg/day) **(AI)**
  - Preferred beta-lactams: piperacillin-tazobactam, cefepime, imipenem, or meropenem

### Alternative Therapy

- An IV antipneumococcal, antipseudomonal beta-lactam + an IV aminoglycoside + IV azithromycin **(BII)**, or
- An IV antipneumococcal, antipseudomonal beta-lactam + an IV aminoglycoside + an antipneumococcal fluoroquinolone (moxifloxacin or levofloxacin) **(BII)**

### For Penicillin-Allergic Patients

- Replace the beta-lactam with aztreonam **(BII)**.

### Empiric Therapy for Patients at Risk of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Pneumonia

#### Preferred Therapy

- A nasal swab for MRSA can help inform decision of initial coverage for MRSA (see text for discussion)
- Vancomycin IV or linezolid (IV or PO) should be added to the baseline regimen **(AII)**.
- Although not routinely recommended, the addition of clindamycin to vancomycin (but not to linezolid) may be considered for severe necrotizing pneumonia to minimize bacterial toxin production **(CII)**.

### Duration of Therapy

- For most patients: 5–7 days. The patient should be afebrile for 48–72 hours, and should be clinically stable before discontinuation of therapy.
- Longer duration of antibiotics is often required if severe CAP or bacteremia is present, and particularly if due to *S. pneumoniae* or complicated *S. aureus* infection.

### Switch from IV to PO Therapy

- A switch should be considered for patients who have improved clinically, can swallow and tolerate oral medications, and have intact gastrointestinal function **(BIII)**.

### Other Considerations

- Empiric therapy with a macrolide alone is not routinely recommended because of increasing pneumococcal resistance (up to 30%) **(BIII)**, and patients receiving a macrolide for MAC prophylaxis may have resistance due to chronic exposure **(BIII)**.
- Fluoroquinolones should be used with caution in patients in whom TB is suspected but who are not being treated with concurrent standard four-drug TB therapy **(BIII)**.
- Once the pathogen has been identified by reliable microbiologic methods, antibiotic therapy should be modified to target the pathogen **(BIII)**.
- If drug-resistant pathogens have not been identified by reliable microbiologic methods, antibiotic therapy can be de-escalated to cover routine causes of CAP **(BIII)**.
- Antibiotics chemoprophylaxis is generally not recommended because of the potential for development of drug resistance microorganisms and drug toxicities **(AI)**.

<sup>a</sup> Respiratory fluoroquinolones such as levofloxacin or moxifloxacin are also active against *Mycobacterium tuberculosis*. In patients with undiagnosed TB, fluoroquinolones may alter response to therapy, delay TB diagnosis, and increase the risk of drug resistance. These drugs should be used with caution in patients in whom TB is suspected but who are not receiving a standard 4-drug TB regimen.

**Key:** ART = antiretroviral therapy; CD4 = CD4 T lymphocyte cell; IM = intramuscularly; IV = intravenously; MAC = *Mycobacterium avium* complex; MRSA = methicillin-resistant *Staphylococcus aureus*; PCV13 = 13-Valent Pneumococcal Conjugate Vaccine; PO = orally; PPSV23 = 23-Valent Pneumococcal Polysaccharide Vaccine; TB = tuberculosis



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