Community-acquired pneumonia

The right clinical information, right where it's needed

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<td>Typically characterized by a new lung infiltrate on chest x-ray, together with one or more of the following: fever, chills, cough, sputum production, dyspnea, myalgia, arthralgia, pleuritic pain.</td>
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<td>Order a chest x-ray in all patients with suspected community-acquired pneumonia (CAP) who are admitted to hospital to confirm or exclude diagnosis.</td>
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<td>Order sputum and blood cultures in all hospitalized patients treated empirically for methicillin-resistant Staphylococcus aureus (MRSA) or Pseudomonas aeruginosa, as well as in patients with severe CAP.</td>
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<td>Use a validated clinical prediction rule for prognosis (e.g., Pneumonia Severity Index), along with clinical judgement, to determine whether the patient should be treated as an inpatient or outpatient.</td>
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<td>Treat with empiric antibiotics. Broader-spectrum regimens are required in patients with comorbidities. Add antibiotic cover for MRSA and P aeruginosa if locally validated risk factors for either pathogen are present.</td>
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Definition

Community-acquired pneumonia (CAP) is defined as pneumonia acquired outside of hospital or healthcare facilities. Clinical diagnosis is based on a group of signs and symptoms related to lower respiratory tract infection with presence of fever >100°F (>38°C), cough, expectoration, chest pain, dyspnea, and signs of invasion of the alveolar space. However, older patients in particular are often afebrile and may present with confusion and worsening of underlying diseases. This topic focuses on the diagnosis and management of CAP in immunocompetent adults.

Epidemiology

The global burden of diseases, injuries, and risk factors (GDB) study showed that lower respiratory tract infections affected over 336 million people all over the world, with an estimated 65.9 million of hospitalizations among all ages and causing 2,377,697 deaths in 2016.[3] In 2017, the GDB study showed that the total deaths from lower respiratory tract infections had fallen by 36% between 2007 and 2017 in children younger than 5 years of age, but had risen by 34% in adults ages 70 years or older.[4]

In the US, the annual incidence of CAP has been estimated at 24.8 cases in 10,000 adults.[5] Pneumonia and influenza, when considered together, were the eighth leading cause of death (13.5 deaths in 100,000 population) and the leading infectious cause in the US in 2016.[6]

Etiology

Streptococcus pneumoniae (the pneumococcus) is the most common causative pathogen of CAP across a range of severities and patient ages.[7] [8] [9] [10] [11] However, other studies have found that influenza virus is the most common cause of CAP in adults.[5] [12] In Europe and the US, S pneumoniae accounts for about 30% to 35% of cases.[8] [13] The overall incidence rates of pneumococcal CAP in Europe were 68-7000 in 100,000.[14] Other bacterial causes include Haemophilus influenzae, Staphylococcus aureus, and Moraxella catarrhalis.

Atypical bacteria are also common causes, although they vary in frequency depending on the year and any epidemics.[11] [15] The incidence of atypical pathogens in CAP is approximately 22% globally, but this varies with location.[16] The most commonly reported atypical bacteria are Mycoplasma pneumoniae, Chlamydophila pneumoniae, and Legionella pneumophila. M pneumoniae accounts for up to 37% of CAP patients treated as outpatients and 10% of patients who are hospitalized.[8] [17] C pneumoniae accounts for 5% to 15% of cases of CAP,[18] and L pneumophila (especially serogroup 1) accounts for 2% to 6% of CAP in immunocompetent patients.[19] A systematic review found that Chlamydia psittaci was the causative organism in 1% of patients.[20] However, a Dutch study identified C psittaci by polymerase chain reaction (PCR) of sputum (when available) as a cause of CAP in 4.8% of cases.[21]

Approximately 6% of cases are due to PES pathogens (Pseudomonas aeruginosa, extended-spectrum beta-lactamase Enterobacteriaceae, and methicillin-resistant S aureus [MRSA]). Of these organisms, P aeruginosa and MRSA are the most frequently reported.[22] [23]

Respiratory viruses are reported in about 10% to 30% of immunocompetent adults hospitalized with CAP.[8] [24] [25] [26] Influenza virus A/B, respiratory syncytial virus, adenovirus, rhinovirus, and parainfluenza virus are the most common viral causes of CAP in immunocompetent adults. Viral sepsis has been reported in 3% of all patients admitted to the emergency department with a diagnosis of CAP, 19% of all patients with CAP.
who are admitted to the intensive care unit, and 61% of those with a diagnosis of viral CAP. Males and older patients (age ≥65 years) are at an increased risk for viral sepsis.[27] Newer pathogens reported to cause CAP include metapneumovirus and coronaviruses.[28] Detection of viral causes is increasing because of the use of PCR.

Polymicrobial etiology in CAP varies from 5.7% to 13.0%, depending on the population and the microbiological diagnostic test used.[8] [25] [29]

Pathophysiology

Pneumonia develops subsequent to the invasion and overgrowth of a pathogenic microorganism in the lung parenchyma, which overpowers host defenses and produces intra-alveolar exudates.[30]

The development and severity of pneumonia is a balance between pathogen factors (virulence, inoculum size) and host factors. The likely microbial causes of CAP differ according to a number of factors, including differences in local epidemiology, the setting (outpatients, hospitalized, or intensive care unit), severity of disease, and patient characteristics (e.g., sex, age, and comorbidities).[8]

Microbes that are present in the upper airways can enter the lower airways by microaspiration. Nevertheless, the defense mechanisms of the lungs (innate and acquired) keep the lower airways sterile. The development of pneumonia indicates a defect in host defenses, exposure to a particularly virulent microorganism, or a large inoculum size.

Impaired immune response (e.g., caused by HIV infection or advanced age) or dysfunction of defense mechanism (e.g., through current or passive smoking, COPD, or aspiration) leads to greater susceptibility to respiratory infections in patients.[31]

Pathogens can reach the lower respiratory tract by 4 mechanisms:

- Inhalation, a common route of entry for viral and atypical pneumonia in younger healthy patients. Infectious aerosols are inhaled into the respiratory tract of a susceptible person to initiate infection
- Aspiration of oropharyngeal secretions into the trachea, the primary route through which pathogens enter the lower airways
- Hematogenous spread from a localized infected site (e.g., right-sided endocarditis)[32]
- Direct extension from adjacent infected foci (e.g., tuberculosis can spread contiguously from the lymph nodes to the pericardium or the lung, albeit rarely).

Pneumonia may result from dysbiosis of the normal lung flora, rather than invasion of pathogenic microorganisms in a sterile environment.[33] Multiple bacterial species (e.g., *Prevotella*, *Veillonella*, *Streptococcus*, *Fusobacterium*, and *Haemophilus*) are present in a healthy lung and are known as the lung microbiome. The upper respiratory tract is the primary source of the lung microbiome. These bacteria are part of a dynamic community where a balance, or equilibrium, is maintained. When disequilibrium (or dysbiosis) occurs, as is the case in acute infections, the microbiome changes. Risk factors for dysbiosis are partially understood, but further study is required.[34] [35]
Primary prevention

Pneumonia prevention is focused on the pathogens that cause disease, through specific vaccination or by managing the risks associated with disease development. The main means of prevention are influenza and pneumococcal vaccination and management of smoking cessation.

Advisory Committee on Immunization Practices (ACIP) vaccination recommendations:[64]

* Adults who are immunocompetent and ages 65 years or older should receive one dose of the 13-valent pneumococcal conjugate vaccine (PCV13) if they have not received PCV13 previously, followed by one dose of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) at least 1 year after PCV13 and at least 5 years after the last dose of PPSV23. Patients who have received PPSV23 previously (but not PCV13), should receive one dose of PCV13 at least one year after PPSV23. Adults ages 19 to 64 years with specific comorbidities, and adults ages 19 years and older with immunocompromising conditions, cerebrospinal fluid leak, or a cochlear implant should also be vaccinated according to the current schedule.
* All patients should receive an annual influenza vaccination with an age-appropriate formulation, provided they do not have a contraindication.
* Further detail on current vaccination schedules and special patient populations can be found in the latest ACIP vaccination schedule.
Case history

Case history #1

A 54-year-old smoker with multiple comorbidities (diabetes, hypertension, coronary artery disease) presents with a 2-day history of a productive cough with yellow sputum, chest tightness, and fever. Physical exam reveals a temperature of 101°F (38.3°C), BP of 150/95 mmHg, heart rate of 85 bpm, and a respiratory rate of 20 breaths per minute. His oxygen saturation is 95% at rest; lung sounds are distant but clear, with crackles at the left base. Chest x-ray reveals a left lower lobe infiltrate.

Other presentations

Pneumonia can occur at any age, but the incidence increases significantly in old age, and pneumonia is a leading cause of illness and death in older patients. The clinical manifestations of pneumonia in elderly persons are often less intense than those in younger patients.[1] Atypical pathogens such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and respiratory viruses can present in a subacute fashion with gradual onset of fever, nonproductive cough, constitutional symptoms, relatively normal white blood cell count, and absent or diffuse findings on lung exam.[2] Patients with severe pneumococcal or *Legionella pneumonia* pneumonia often progress rapidly to respiratory failure.

Step-by-step diagnostic approach

For updates on diagnosis and management of coexisting conditions during the pandemic, see our topic “Management of coexisting conditions in the context of COVID-19”.

Patient history and physical exam are important parts of the diagnosis and may elicit symptoms consistent with CAP, immune defects, and/or potential exposure to specific pathogens. However, a definitive diagnosis of pneumonia requires the presence of a new infiltrate on chest x-ray.

History

The objective of history-taking should be to detect symptoms consistent with CAP, defects of immunity, and possible risk of exposure to specific pathogens.

Risk factors include age >65 years, residence in a healthcare setting, COPD, HIV infection, cigarette smoke exposure, alcohol abuse, poor oral hygiene, contact with children, and use of certain drugs (e.g., acid-reducing drugs, inhaled corticosteroids, antipsychotics, antidiabetic drugs, opioids). Diabetes mellitus and chronic liver or renal disease have also been associated with CAP.

Clinical signs and findings of infection (fever or chills and leukocytosis) and respiratory symptoms (including cough, often with increasing sputum production, expectoration, dyspnea, pleuritic pain, and hemoptysis) are usually present. Nonspecific symptoms such as myalgia and arthralgia may be reported. In patients of advanced age, patients with chronic illness, and immunocompromised patients, the signs and symptoms of pulmonary infection may be less intense and the pneumonia may go unrecognized because of the presence of nonrespiratory symptoms.
Some causes of pneumonia (e.g., legionellosis) may have a specific history. Legionellosis can present with headache, confusion, digestive manifestations such as diarrhea, and clinical manifestations of hyponatremia.

*Mycoplasma pneumoniae* infection is most common in young patients and patients who have been treated with antibiotics before their current presentation with pneumonia. It may present with extrapulmonary manifestations such as myringitis, encephalitis, uveitis, iritis, and myocarditis.[18] [65]

**Physical exam**

Perform a physical exam. The patient may be febrile, tachycardic, and breathless at rest. Auscultation of the chest may reveal crackles, rales, or bronchial breathing, and there may be presence of dullness on percussion or tactile vocal fremitus.

**Imaging**

Order a chest x-ray as soon as possible in all patients admitted to hospital with suspected CAP to confirm or exclude the diagnosis. It is not necessary to perform a chest x-ray in outpatients with suspected CAP unless the diagnosis is in doubt, the patient is not responding to treatment satisfactorily, or the patient is considered to be at risk of an underlying lung pathology.[66] Posteroanterior and latero-lateral projections increase the likelihood of diagnosis of pneumonia and are useful in establishing the severity of the illness.

The primacy of chest x-ray in making the diagnosis of CAP has been challenged by studies using lung ultrasound and computed tomography (CT) scan of the chest. Consider ordering a lung ultrasound if the chest x-ray is negative and the patient is elderly and frail or the clinical suspicion is uncertain. Only consider a chest CT in patients who have an uncertain diagnosis after both a chest x-ray and ultrasound.[67]

Lung ultrasound represents an easy and accessible technique for the diagnosis of CAP. It is radiation-free, and its use is especially valuable when chest x-ray is not available. The diagnosis of CAP via bedside lung ultrasound mainly depends on detecting consolidation. However, consolidation is not always present in CAP, because pneumonia may be interstitial or present as diffuse pulmonary infiltrations.[68] Systematic reviews have found that lung ultrasound can diagnose pneumonia in adults with excellent accuracy, including in the emergency department.[69] [70]

Chest CT may improve the diagnosis of CAP, because chest x-ray may lead to misdiagnosis. Chest CT provides detailed information about the lung parenchyma and the mediastinum. However, the principal limitations include exposure to radiation, high cost, and the impossibility of bedside testing. One study has reported that in patients presenting to the emergency department with suspected CAP, early CT scan findings, when CT is used in addition to chest x-ray, markedly affect both diagnosis and clinical management.[71]

These alternative imaging techniques may be the future of care for the diagnosis of CAP as the availability of CT scanners in emergency departments increases, along with their ability to scan as fast as chest x-ray with an equivalent amount of radiation.[28]

**Microbiology**

The initial antibiotic treatment is empiric in most cases. Determining the microbial etiology reduces inappropriate use of broad-spectrum antibiotics and helps to ensure appropriate antibiotic therapy, which
Community-acquired pneumonia is an important factor in reducing mortality. It also identifies resistant pathogens and pathogens that may have public health implications (e.g., *Legionella*).

**Diagnosis**

Sputum and blood cultures:

- Obtain pretreatment Gram stain and culture of lower respiratory secretions and blood cultures in the following patients in the hospital setting:[17]
  - Patients with severe CAP as defined by American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) criteria for defining severe CAP (see Diagnostic criteria section), especially if they are intubated
  - Patients being empirically treated for methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*
  - Patients who have been previously infected with MRSA or *P. aeruginosa*, especially those with a prior respiratory tract infection
  - Patients who have been hospitalized and received parenteral antibiotics in the past 90 days.

  - These tests are not routinely recommended in other inpatients, and are not recommended in the outpatient setting. Take into account local antimicrobial stewardship protocols, local etiologic factors, and the clinical presentation when deciding whether to obtain these tests.[17]

- Sputum Gram stain is sensitive and highly specific for identifying the causative pathogens in patients with CAP. A meta-analysis found that this test is highly specific for identifying *Streptococcus pneumoniae*, *Haemophilus influenzae*, *S aureus*, and gram-negative bacilli. However, the proportion of false-negative results ranged from 22% (for *H influenzae*) to 44% (for *S pneumoniae*), indicating that a negative result does not conclusively confirm the absence of causative pathogens, and antibiotic therapy should not necessarily be stopped based on a negative sputum Gram stain.[72]

**Pneumococcal and *Legionella* urinary antigen testing:**

- Test urine for pneumococcal antigen in patients with severe CAP. Test urine for *Legionella* antigen in patients with epidemiologic factors (e.g., association with legionella outbreak or recent travel) or patients with severe CAP. Collect lower respiratory tract secretions for *Legionella* culture or nucleic acid amplification in patients with severe CAP at the same time. Urinary antigen testing has been associated with a reduction in mortality in large observational studies, and is important to consider given the increase in *Legionella* infections, especially among severely ill patients.[17]

**Influenza virus testing:**

- Test for influenza virus using a rapid influenza molecular assay (rather than antigen-based detection tests) when influenza viruses are circulating in the community. Testing may also be considered during periods of low influenza activity.[17]

**Laboratory investigations**

Order a complete blood count, blood glucose, serum electrolytes, blood urea nitrogen, and liver function tests in hospitalized patients. An elevated white cell count is suggestive of infection. Chronic renal disease and chronic liver disease are risk factors for mortality and complications in patients hospitalized with CAP.

Measure arterial blood gases in severely ill or hospitalized patients. Oximetry is noninvasive and can be used continually.
Consider ordering biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT). These biomarkers have been found to be useful for predicting inadequate host response. High levels of CRP or PCT at initial presentation represent a risk factor for inadequate host response,[73] whereas low levels are protective. In patients with suspected pneumonia, a CRP level >10 mg/dL makes pneumonia likely.[74] Increased values of PCT are correlated with bacterial pneumonia whereas lower values are correlated with viral and atypical pneumonia. PCT is especially elevated in cases of pneumococcal pneumonia.[75] [76] Initial empiric antibiotic therapy should be started in patients with clinically suspected and radiographically confirmed CAP regardless of the initial serum PCT level.[17]

Consider pleural fluid aspiration and culture in all patients with a pleural effusion. Parapneumonic effusions are exudates; a positive Gram stain of pleural fluid indicates an empyema.

**Bronchoscopy**

Consider bronchoscopy in immunosuppressed patients, in patients with severe CAP, and in cases of treatment failure. The most common sampling techniques are bronchoalveolar lavage (BAL) and protected specimen brushing (PSB). A threshold of $10^4$ colony-forming units (CFU)/mL in BAL samples indicates infection. For PSB, a threshold of $10^3$ CFU/mL has been recommended to distinguish colonization from infection.[77]

**Molecular techniques**

Routine bacterial cultures are too slow to be immediately therapeutically useful. Nucleic acid amplification tests such as polymerase chain reaction have improved diagnostic accuracy in CAP. Molecular techniques provide high sensitivity and specificity in the diagnosis of single or polymicrobial infections, and they can help to determine antimicrobial resistance (as may occur with *Staphylococcus aureus*, nonfermenting gram-negative bacilli, and Enterobacteriaceae) associated with severe CAP.[78]

[VIDEO: Venepuncture and phlebotomy: animated demonstration]

**Risk factors**

### Strong

**age >65 years**

- Incidence increases significantly with age. Very advanced age has been associated with higher mortality from CAP.[36]

**residence in a healthcare setting**

- Approximately 10% to 18% of all patients hospitalized for pneumonia are nursing home residents. Mortality in these patients may reach 55%.[37] [38] Patients in residential homes who develop pneumonia have traditionally been considered to have healthcare-associated pneumonia (HCAP) and not CAP. However, this definition has been criticized because it is not able to distinguish patients at risk for resistant pathogens, and each patient ought to be evaluated individually.
COPD
- Associated with a 2- to 4-fold increased risk of CAP.[31] Data from one study conducted in patients with CAP compared the outcome of patients with and without COPD and found that the presence of COPD was an independent risk factor for mortality.[39]

exposure to cigarette smoke
- Colonization with pathogenic bacteria is frequent in smokers and presents an increased risk of lung infections, especially pneumococcal pneumonia.[40] One study of bacterial pneumonia found that HIV-infected smokers had >80% higher risk of developing pneumonia than those who had never smoked.[41] [42] Another study showed that current smokers with pneumococcal CAP often develop severe sepsis and require hospitalization at a younger age despite having fewer comorbid conditions than older patients.[43] Passive smoking at home is a risk factor for CAP in people aged 65 years or older.[44]

alcohol abuse
- There is clear evidence that alcohol consumption increases the risk for CAP. A meta-analysis of 14 studies found that people who consumed alcohol at all or in higher amounts had an 83% higher risk of CAP compared to people who consumed no alcohol or lower amounts (relative risk of 1.83).[45] Consumption of 24 g, 60 g, and 120 g of pure alcohol daily has been shown to result in a relative risk for incident CAP of 1.12 (95% CI, 1.02 to 1.23), 1.33 (95% CI, 1.06 to 1.67), and 1.76 (95% CI, 1.13 to 2.77), respectively, relative to nondrinkers.[46]

poor oral hygiene
- Oral and respiratory bacteria in dental plaques are shed into the saliva and can then be aspirated into the lower respiratory tract to cause infection. Aspiration pneumonia is one of the most serious problems in older patients. Low-quality evidence suggests that professional oral health care measures (e.g., brushing, swabbing, denture cleaning, mouth rinses) may reduce mortality due to pneumonia in nursing home residents compared to usual care.[47]

use of acid-reducing drugs, inhaled corticosteroids, antipsychotics, antidiabetic drugs
- CAP is one of the most common adverse effects associated with use of proton-pump inhibitors.[48] This is thought to be due to a decrease in gastric acid secretion, which allows pathogens to colonize the upper respiratory tract more easily. Outpatient use of these drugs is associated with a 1.5-fold increased risk of CAP.[49] H2 receptor antagonists may also be associated with an increased risk of CAP.[50]
- Other drugs that have been independently associated with an increased risk for CAP include inhaled corticosteroids (especially at higher doses), antipsychotics (especially atypical antipsychotics and in older people), and antidiabetic medications.[51]

contact with children
- Regular contact with children is associated with an increased risk of CAP.[52] Two studies have reported that having children in the household increases the adjusted odds ratio from 1.00 for households with no children to 3.2,[53] or 3.41[54] for households with 3 or more children.
HIV infection

- Patients with HIV infection are more susceptible to bacterial CAP. Although antiretroviral therapy has improved the immune response and reduced the incidence of CAP, it remains a major cause of morbidity and mortality in these patients, in part because they show altered immunity and because immune activation persists. Mortality in HIV-infected patients with CAP ranges from 6% to 15%.[55]

Weak diabetes mellitus

- Associated with a moderate increase in the risk of CAP. The main reasons are the increased risk of aspiration, hyperglycemia, decreased immunity and impaired lung function, and coexisting morbidity.
- One study found that diabetes (type 1 and type 2) was a risk factor for pneumonia-linked hospitalization. Another study[56] reported that pre-existing diabetes was associated with a higher risk of death after hospitalization for CAP compared with patients hospitalized for noninfectious illnesses.[57] The risk of severe pneumococcal bacteremia is also higher in diabetic patients.[58]

chronic renal disease

- A significant risk factor for mortality in patients with CAP.[59] [60]

chronic liver disease

- It is known that bacterial infections occur in 32% to 34% of hospitalized patients with cirrhosis, and approximately 15% of these infections are pneumonia (the third most common cause of infection in these patients).[61] One study reported that chronic liver disease is a risk factor for pulmonary complications in patients hospitalized with pneumococcal pneumonia.[62]

use of opioids

- A case-control study found that prescribed opioids, especially those with immunosuppressive properties or higher doses, are associated with an increased risk of CAP in people with and without HIV infection.[63]

History & examination factors

**Key diagnostic factors**

**cough with increasing sputum production (common)**
- Usually present. Less common in older patients.

**fever or chills (common)**
- Usually present. Less common in older patients.

**dyspnea (common)**
- Usually present.

**pleuritic pain (common)**
- Associated with bacteremia in outpatients.

**abnormal auscultatory findings (common)**
• Asymmetric breath sounds, pleural rubs, egophony (increased resonance of voice sounds heard on auscultation), and increased fremitus may be heard.

Other diagnostic factors

dullness to percussion (common)
• Suggests consolidations and/or pleural effusion.

myalgia (common)
• Nonspecific symptom that is often reported.

arthralgia (common)
• Nonspecific symptom that is often reported.

confusion (uncommon)
• Not generally common but often seen in older patients.
## Diagnostic tests

### 1st test to order

<table>
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<th>Test</th>
<th>Result</th>
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<tr>
<td><strong>chest x-ray</strong></td>
<td>new infiltrate provides definitive diagnosis of pneumonia</td>
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</table>
| • Order a chest x-ray as soon as possible in all patients admitted to hospital with suspected CAP to confirm or exclude the diagnosis. It is not necessary to perform a chest x-ray in outpatients with suspected CAP unless the diagnosis is in doubt, the patient is not responding to treatment satisfactorily, or the patient is considered to be at risk of an underlying lung pathology. [66]  
  • Posteroanterior and latero-lateral projections increase the likelihood of diagnosis of pneumonia and are useful in establishing the severity of the illness. [Fig-1] |                                                                       |
| **CBC**                           | leukocytosis                                                            |
| • Order in all hospitalized patients. Elevated white cell count is suggestive of infective process. Neutrophil predominance, especially if immature neutrophils, is suggestive of bacterial infection even with a normal or low white cell count. Hematocrit is used as a factor in severity scoring. |                                                                       |
| **serum electrolytes/blood urea nitrogen** | usually normal                                                          |
| • Order in all hospitalized patients. Baseline blood should be taken. Provides information about renal function. Sodium and blood urea nitrogen are used in severity scoring. [79] [80] Chronic renal failure is a significant risk factor for mortality in patients with CAP. [59] [60] |                                                                       |
| **liver function tests**          | usually normal                                                          |
| • Order in all hospitalized patients. Baseline blood should be taken. Provides information about liver function. Pneumonia is common in hospitalized patients with cirrhosis, and chronic liver disease is a risk factor for pulmonary complication in patients hospitalized due to pneumococcal pneumonia. [62] |                                                                       |
| **blood glucose**                 | may be elevated                                                          |
| • Order in all hospitalized patients. Baseline blood should be taken. Blood glucose levels are used in severity scoring. |                                                                       |
| **arterial blood gases/oximetry** | may reveal low arterial oxygen saturation                               |
| • Measure in all severely ill or hospitalized patients. Indicates severity of the pneumonia.  
  • Oximetry is noninvasive and can be used continually. |                                                                       |
| **blood culture**                 | growth of causative bacterial species                                   |
| • Obtain pretreatment blood cultures in the following patients in the hospital setting: [17]  
  • Patients with severe CAP as defined by American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) criteria for defining severe CAP (see Diagnostic criteria section), especially if they are intubated  
  • Patients being empirically treated for methicillin-resistant Staphylococcus aureus (MRSA) or Pseudomonas aeruginosa |                                                                 |
### Test

<table>
<thead>
<tr>
<th>Patients who have been previously infected with MRSA or <em>P. aeruginosa</em>, especially those with a prior respiratory tract infection</th>
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<td>Patients who have been hospitalized and received parenteral antibiotics in the past 90 days.</td>
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### Result

- **sputum culture**
  - Obtain pretreatment Gram stain and culture of lower respiratory secretions in the following patients in the hospital setting:[17]
  - Patients with severe CAP as defined by American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) criteria for defining severe CAP (see Diagnostic criteria section), especially if they are intubated
  - Patients being empirically treated for methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*
  - Patients who have been previously infected with MRSA or *P. aeruginosa*, especially those with a prior respiratory tract infection
  - Patients who have been hospitalized and received parenteral antibiotics in the past 90 days.
  - Sputum Gram stain is sensitive and highly specific for identifying the causative pathogens in patients with CAP. A meta-analysis found that this test is highly specific for identifying *Streptococcus pneumoniae*, *Haemophilus influenzae*, *S. aureus*, and gram-negative bacilli. However, the proportion of false-negative results ranged from 22% (for *H. influenzae*) to 44% (for *S. pneumoniae*), indicating that a negative result does not conclusively confirm the absence of causative pathogens.[72]
## Other tests to consider

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tbody>
<tr>
<td><strong>lung ultrasound</strong></td>
<td>consolidation may be seen</td>
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<tr>
<td>• Consider ordering if the chest x-ray is negative and the patient is older and frail or the clinical suspicion is uncertain.[67]</td>
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<tr>
<td>• Lung ultrasound represents an easy and accessible technique for the diagnosis of CAP. It is radiation-free, and its use is especially valuable when chest x-ray is not available. The diagnosis of CAP via bedside lung ultrasound mainly depends on detecting consolidation. However, consolidation is not always present in CAP, because pneumonia may be interstitial or present as diffuse pulmonary infiltrations.[68] Systematic reviews have found that lung ultrasound can diagnose pneumonia in adults with excellent accuracy, including in the emergency department.[69] [70]</td>
<td></td>
</tr>
<tr>
<td><strong>CT chest</strong></td>
<td>consolidation, cavitation, effusions, neoplasm</td>
</tr>
<tr>
<td>• Consider ordering only in patients who have an uncertain diagnosis after both a chest x-ray and ultrasound.[67]</td>
<td></td>
</tr>
<tr>
<td>• The primacy of chest x-ray in making the diagnosis of CAP has been challenged by studies using CT scanning. Chest CT may improve the diagnosis of CAP, because chest x-ray may lead to misdiagnosis. Chest CT provides detailed information about the lung parenchyma and the mediastinum. However, the principal limitations include exposure to radiation, high cost, and the impossibility of bedside testing. One study has reported that in patients presenting to the emergency department with suspected CAP, early CT scan findings, when CT is used in addition to chest x-ray, markedly affect both diagnosis and clinical management.[71]</td>
<td></td>
</tr>
<tr>
<td><strong>urinary antigen testing for Legionella and pneumococcus</strong></td>
<td>positive for Legionella or pneumococcal antigens</td>
</tr>
<tr>
<td>• Test urine for pneumococcal antigen in patients with severe CAP.[17]</td>
<td></td>
</tr>
<tr>
<td>• Test urine for <em>Legionella</em> antigen in patients with epidemiologic factors (e.g., association with legionella outbreak or recent travel) or patients with severe CAP. Collect lower respiratory tract secretions for <em>Legionella</em> culture or nucleic acid amplification in patients with severe CAP at the same time.[17]</td>
<td></td>
</tr>
<tr>
<td><strong>serum C-reactive protein</strong></td>
<td>may be elevated; level &gt;10 mg/dL makes pneumonia likely</td>
</tr>
<tr>
<td>• Consider ordering. A sensitive marker of progress in pneumonia; should be measured regularly in severely ill patients. High levels at initial presentation represent a risk factor for inadequate response to treatment,[73] whereas low levels are protective.[74]</td>
<td></td>
</tr>
<tr>
<td><strong>serum procalcitonin</strong></td>
<td>may be elevated</td>
</tr>
<tr>
<td>• Consider ordering. A sensitive marker of progress in pneumonia. High levels at initial presentation represent a risk factor for inadequate response to treatment,[73] whereas low levels are protective. Especially elevated in cases of pneumococcal pneumonia.[75] [76]</td>
<td></td>
</tr>
<tr>
<td>• Initial empiric antibiotic therapy should be started in patients with clinically suspected and radiographically confirmed CAP regardless of the initial serum procalcitonin level.[17]</td>
<td></td>
</tr>
<tr>
<td><strong>thoracocentesis and pleural fluid culture</strong></td>
<td>exudate; growth of causative bacterial</td>
</tr>
<tr>
<td>• Consider ordering in all patients with a pleural effusion. Positive Gram stain of pleural fluid indicates an empyema.</td>
<td></td>
</tr>
<tr>
<td>Test</td>
<td>Result</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>bronchoscopy</strong></td>
<td><em>species in case of empyema</em></td>
</tr>
<tr>
<td>• Consider ordering in immunosuppressed patients, in patients with severe CAP, and in cases of treatment failure.</td>
<td></td>
</tr>
<tr>
<td>• The most common techniques are bronchoalveolar lavage (BAL) and protected specimen brushing (PSB).</td>
<td></td>
</tr>
<tr>
<td><strong>tests for respiratory viruses</strong></td>
<td><em>BAL: $10^4$ colony-forming units (CFU)/mL indicates infection; PSB: $10^3$ CFU/mL has been recommended to distinguish colonization from infection</em></td>
</tr>
<tr>
<td>• Test for influenza virus using a rapid influenza molecular assay (rather than antigen-based detection tests) when influenza viruses are circulating in the community. Testing may also be considered during periods of low influenza activity.[17]</td>
<td></td>
</tr>
<tr>
<td>• Rapid antigen testing or direct fluorescent antibody testing can be used to detect other respiratory viruses and can help with decisions regarding antiviral therapy and may reduce the use of antibacterial agents.</td>
<td></td>
</tr>
<tr>
<td><strong>molecular microbiological techniques</strong></td>
<td><em>detection of pathogenic organism</em></td>
</tr>
<tr>
<td>• Includes polymerase chain reaction. Used for bacteria (including atypical pathogens) and respiratory viruses. These tests are rapid and the results may help to guide antimicrobial therapy. Also, new techniques offer antimicrobial resistance patterns and quantified bacteria loads, which may be linked to the degree of infection, as has been shown particularly in pneumococcal infection.</td>
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</tbody>
</table>
# Differential diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
</table>
| Coronavirus disease 2019 (COVID-19)      | • Residence in/travel to a country/area or territory with local transmission, or close contact with a confirmed or probable case of COVID-19, in the 14 days prior to symptom onset.  
  • Signs and symptoms are similar so it may be difficult to differentiate between the conditions clinically.  
  • The situation is evolving rapidly; see our COVID-19 topic for further information. | • Real-time reverse transcription polymerase chain reaction (RT-PCR): positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA.  
  • It is not possible to differentiate COVID-19 from other causes of pneumonia on chest imaging. |
| Acute bronchitis                         | • No dyspnea, no lung crackles, mild presentation. Often related to a viral upper respiratory tract infection.                                                  | • No consolidation on chest x-ray, with frequency related to viral infection.                                                                                                                                             |
| Congestive heart failure                 | • Peripheral edema, cardiomegaly, hypotension.                                                                                                                  | • Bilateral interstitial pattern or pleural effusions seen on chest x-ray.                                                                                                                                                |
| COPD exacerbation                        | • Increased expectoration and cough, and worsening of dyspnea against a background of COPD. Patient is often a smoker.                                          | • Chest x-ray shows hyperinflation.                                                                                                                                                                                       |
| Asthma exacerbation                      | • Symptoms and signs of bronchospasm, with worsening of underlying lung disease.                                                                                | • No consolidation on chest x-ray.                                                                                                                                                                                       |
| Bronchiectasis exacerbation              | • Increased expectoration and cough, and worsening of dyspnea, with worsening of underlying lung disease. Infections are typically recurrent.                  | • No consolidation on chest x-ray.                                                                                                                                                                                       |
| Tuberculosis                             | • Typically a long history, often with constitutional symptoms. Many patients will have lived in an endemic area.                                               | • Cavitation on chest x-ray, enlarged lymph nodes, positive purified protein derivative (PPD) skin testing.                                                                                                                                 |
| Lung cancer or lung metastases           | • Constitutional symptoms are common.                                                                                                                            | • Consolidation on chest x-ray may be multiple, with pleural effusion commonly seen.                                                                                                                                    |
Community-acquired pneumonia

### Diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empyema</td>
<td>• Constitutional symptoms are common, usually associated with a recent respiratory infection.</td>
<td>• Pleural effusion seen on chest x-ray. Microbiology of pleural fluid may reveal infecting organism.</td>
</tr>
</tbody>
</table>

#### Diagnostic criteria

Following a diagnosis of pneumonia, the clinician needs to decide the appropriate location for care (outpatient care, hospital, or the intensive care unit [ICU]) and the appropriate antibiotic treatment. Patients at low risk of complications are candidates for outpatient care, which reduces inappropriate hospitalization and consequent inherent morbidity and costs.[81]

The use of severity assessment tools such as the Pneumonia Severity Index (PSI),[79] CURB-65,[80] severe CAP (SCAP),[82] and SMART-COP[83] can facilitate decision-making and guide the antibiotic choice. The PSI score classifies patients in 5 risk classes associated with the risk of mortality while the CURB-65 score uses 5 variables to calculate severity. However, the decision to admit a patient depends not only on the severity of CAP, but also on the patient’s comorbidities and on social factors. A delay in determining the severity of the illness and where best to treat the patient can have an impact on clinical outcome and costs.[84] PSI is preferred over CURB-65 in the US, as PSI identifies larger proportions of patients as low risk and has a higher discriminative power in predicting mortality.[17]

Management of severe CAP in accordance with guidelines has been associated with decreased mortality.[85] [86] Increasing numbers of risk factors consistently increases the probability of ICU transfer and the need for vasopressors and mechanical ventilation. Probably the best use of these severity scores is to identify at-risk patients who need additional evaluation and monitoring, even if they are not initially admitted to the ICU.

#### Pneumonia Severity Index (PSI)[79]

Recommended by the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA), PSI is a scoring system derived from a retrospective analysis of a cohort of 14,199 patients with CAP and prospectively validated in a separate cohort of 38,039 patients.[79] The PSI score predicts the risk of 30-day mortality; patients with a high risk are managed in the hospital, and those with the highest risk are managed in the ICU. The PSI stratifies patients into 5 categories based on patient age, comorbidities, physical exam, and results of laboratory testing. The principal limitation is the high score accorded to variables such as age and comorbidities.

- Risk class I: 0-50 points: outpatients; 0.1% mortality
- Risk class II: 51-70 points: outpatients; 0.6% mortality
- Risk class III: 71-90 points: short hospital stay for observation; 2.8% mortality
- Risk class IV: 91-130 points: hospital admission; 8.2% mortality
- Risk class V: >130 points: hospital admission; 29.2% mortality.

**Scoring of the PSI for CAP**

- **Demographics**
  - Male: points = age in years
  - Female: points = age in years -10 points
  - Nursing home resident: +10 points
Community-acquired pneumonia

**Diagnosis**

- Liver disease: +20 points
- Neoplastic disease: +30 points
- Congestive heart failure: +10 points
- Cerebrovascular disease: +10 points
- Renal failure: +10 points

* Physical exam findings

  - Altered mental status: +20 points
  - Respiratory rate ≥30 breaths/minute: +20 points
  - Systolic blood pressure <90 mmHg: +20 points
  - Temperature <95°F (<35°C) or ≥104°F (≥40°C): +15 points
  - Pulse rate ≥125 beats/minute: +10 points

* Laboratory and radiographic findings

  - Arterial pH <7.35: +30 points
  - Blood urea nitrogen (BUN) ≥30 mg/dL (≥10.7 mmol/L): +20 points
  - Sodium <130 mEq/L (<130 mmol/L): +20 points
  - Glucose ≥250 mg/dL (≥13.9 mmol/L): +10 points
  - Hematocrit <30%: +10 points
  - PaO₂ <60 mmHg (<90% O₂ saturation): +10 points
  - Pleural effusion: +10 points

[VIDEO: Community-acquired pneumonia severity index (PSI) for adults ]

**CURB-65 score[80]**

Recommended by the British Thoracic Society, CURB-65 stratifies patients on the basis of the presence of confusion, BUN levels >19.6 mg/dL (>7 mmol/L), respiratory rate ≥30 breaths/minute, blood pressure <90/60 mmHg, and age ≥65 years. Mortality at 30 days increases with the number of criteria that are met. The limitation of this score is the low number of variables used.[87] This tool may help physicians in emergency departments to risk-stratify patients, as it has been found to have good accuracy for predicting 30-day mortality among patients who have been discharged.[88]

Scoring of the CURB-65 for CAP

* Prognostic factors

  - Confusion: 1 point
  - BUN >19.6 mg/dL (>7 mmol/L): 1 point
  - Respiratory rate ≥30 breaths/minute: 1 point
  - Blood pressure <90 mmHg systolic or <60 mmHg diastolic: 1 point
  - Age ≥65 years: 1 point

* Score

  - Score 0-1: low risk; recommendation is for outpatient care; 30-day mortality <3%
  - Score 2: moderate risk; recommendation is for hospitalization; 30-day mortality 9%
  - Score 3-5: high risk; recommendation is for ICU admission; 30-day mortality 15% to 40%
Infectious Diseases Society of America/American Thoracic Society criteria for defining severe community-acquired pneumonia[17]

The 2007 IDSA/ATS CAP guidelines recommended a set of two major and nine minor criteria to define severe pneumonia requiring ICU admission. These criteria were revalidated in the 2019 update of this guideline. The presence of either of the major criteria or three or more minor criteria is considered to indicate severe CAP, and ICU admission is recommended.[17]

**Major criteria:**

- Respiratory failure requiring mechanical ventilation
- Septic shock with need for vasopressors.

**Minor criteria:**

- Respiratory rate ≥30 breaths/minute
- Arterial oxygen pressure/fraction of inspired oxygen (PaO₂/FiO₂) ratio ≤250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (BUN ≥20 mg/dL [≥7.14 mmol/L])
- Leukopenia due to infection alone (WBC <4000 cells/mm³ [<4.0 x 10⁹ cells/L])
- Thrombocytopenia (platelet count <100,000 cells/mm³ [<10 x 10⁹ cells/L])
- Hypothermia (core temperature <96.8°F [<36°C])
- Hypotension requiring aggressive fluid resuscitation.

**SMART-COP/SCAP[82] [83]**

SMART-COP or SCAP severity criteria can also be used to predict the need for ICU admission. SMART-COP is the easiest severity assessment tool to use. It shares some of the most common risk factors included in CURB-65 and PSI (systolic blood pressure, multilobar infiltrates, albumin, respiratory rate, tachycardia, confusion, oxygen, and pH). A score >3 identifies 92% of patients who need vasopressor support. It provides a sensitivity of 58% to 85% and specificity of 46% to 75%. [83]
Step-by-step treatment approach

For updates on diagnosis and management of coexisting conditions during the pandemic, see our topic "Management of coexisting conditions in the context of COVID-19".

When a diagnosis of CAP is established, the next step is to determine whether or not the patient requires outpatient care, hospitalization, or admission to the intensive care unit (ICU). Microbial investigation as well as antimicrobial therapy will depend upon the site of care. Decisions about the site of care can vary widely between hospitals and practice sites and may be based on considerations other than severity.

Outpatient selection and management

Use a validated clinical prediction rule for prognosis, preferably the Pneumonia Severity Index (PSI) over CURB-65, in addition to clinical judgement to determine whether the patient should be treated as an outpatient. PSI is preferred over CURB-65, as PSI identifies larger proportions of patients as low risk and has a higher discriminative power in predicting mortality.[17]

Outpatient treatment is recommended for the following patients:[79] [80]

- Patients in PSI risk class I or II, with a PSI score ≤70 (low risk), and a predicted 30-day mortality risk of 0.1% to 2.8%

[VIDEO: Community-acquired pneumonia severity index (PSI) for adults ]

- Patients with a CURB-65 score of 0 to 1 (low severity), and a predicted 30-day mortality risk <3%. Those with a score of 2 [moderate severity] and a mortality risk of 9% should be considered for brief inpatient care or supervised outpatient care.

[VIDEO: CURB-65 pneumonia severity score ]

Be aware of the limitations of severity scores and consider other factors when assessing a patient’s suitability for outpatient management (e.g., contraindications to outpatient therapy such as inability to maintain oral intake, history of substance abuse, severe comorbid illnesses, cognitive impairment, and impaired functional status, or availability of outpatient support resources).

Advise patients not to smoke, to rest, and to stay well hydrated. Also advise them to report any symptoms of chest pain, severe or increasing shortness of breath, or lethargy.

Reassess patients at 48 hours. Symptoms should improve within this time with appropriate treatment. Consider hospital admission in patients who fail to improve within 48 hours. Approximately 10% of outpatients do not respond to antibiotic therapy and require hospitalization.[91]

Perform a repeat examination after 10-14 days if the patient's response to therapy is satisfactory. Routine follow-up chest imaging is not recommended if symptoms resolve within 5-7 days.[17]

Outpatients who recover without hospitalization are able to resume normal activities more quickly than those who are hospitalized. Hospitalization increases the risk of infection with antibiotic-resistant or more virulent bacteria.[92]

Empiric antimicrobial treatment in outpatients

The American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines recommend the following oral empiric treatment options for outpatients:[17]
• Healthy patients without comorbidities or without risk factors for drug-resistant pathogens:
  • Amoxicillin
  • Doxycycline
  • A macrolide (e.g., azithromycin or clarithromycin).
  • Only use a macrolide in areas with pneumococcal resistance to macrolides <25% and when there are contraindications to alternative therapies.
• Patients with comorbidities (e.g., chronic heart, lung, liver, or renal disease; diabetes mellitus; alcohol abuse; malignancy; asplenia):
  • Combination therapy with amoxicillin/clavulanate or a cephalosporin (e.g., cefpodoxime, cefuroxime) plus a macrolide or doxycycline
  • Monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin, gemifloxacin).

Broader-spectrum antibiotic regimens are required in patients with comorbidities as many of these patients have risk factors for drug-resistant pathogens (e.g., prior respiratory isolation of methicillin-resistant *Staphylococcus aureus* [MRSA] or *Pseudomonas aeruginosa*, recent hospitalization and administration of parenteral antibiotics in the past 90 days), and they are more vulnerable to poor outcomes if the empiric regimen is inadequate.[17]

Choice of antibiotic requires a risk-benefit analysis for each patient, weighing up local epidemiologic data, specific patient risk factors and comorbidities, contraindications, and possible adverse effects (e.g., cardiac arrhythmias with macrolides; vascular disease, musculoskeletal/neurologic adverse effects with fluoroquinolones). Despite the safety concerns associated with fluoroquinolones (see below), the ATS/IDSA panel believes that fluoroquinolone use is justified in adults with CAP and comorbidities who are managed in the outpatient setting.[17]

Risk factors for drug resistance

- Risk factors for penicillin-resistant *Streptococcus pneumoniae* include use of a beta-lactam in the previous 3 to 6 months, hospitalization in the previous 3 months, aspiration, previous episodes of pneumonia in the past year, age <5 or >65 years, and COPD.[93] [94] [95] [96] [97]
- Risk factors for macrolide-resistant *S pneumoniae* include use of a macrolide in the previous 3 months, age <5 or >65 years, and recent hospitalization.[93] [94] [95] [96] [97]
- Risk factors for fluoroquinolone-resistant *S pneumoniae* include previous exposure to fluoroquinolones, residence in a nursing home, penicillin resistance, and COPD.[93] [94] [95] [96] [97]

**Hospital admission**

Use a validated clinical prediction rule for prognosis, preferably PSI over CURB-65, in addition to clinical judgement to determine whether the patient should be treated as an inpatient. PSI is preferred over CURB-65, as PSI identifies larger proportions of patients as low risk and has a higher discriminative power in predicting mortality.[17]

Hospital admission is recommended in the following situations:[79] [80]

- Patients with a PSI score of 71-90 (class III), who may benefit from a brief period of hospitalization
[VIDEO: Community-acquired pneumonia severity index (PSI) for adults]

- Patients with PSI class IV or class V pneumonia (who have a 9% and a 27% risk of death, respectively)
- Patients with a CURB-65 score of ≥3, who should be hospitalized, and those with a score of 4 or 5 (with predicted mortality rates of 15% to 40%, respectively), who should be considered for ICU admission.

[VIDEO: CURB-65 pneumonia severity score]

Admit patients with hypotension requiring vasopressor therapy or respiratory failure requiring mechanical ventilation to the ICU. In patients who do not require vasopressor therapy or mechanical ventilation, use the ATS/IDSA criteria for defining severe CAP (see Diagnostic criteria section) and clinical judgement to guide the need for higher levels of treatment intensity. Admit patients with severe CAP (defined as two major criteria or three or more minor criteria) to the ICU.[17]

Administer oxygen therapy as necessary. Monitor oxygen saturation and inspired oxygen concentration with the aim of maintaining SaO₂ above 92%. High concentrations of oxygen can safely be given in uncomplicated pneumonia. Oxygen therapy in patients with COPD that is complicated by ventilatory failure should be guided by repeated arterial blood gas measurements.[66] Patients with respiratory failure, despite appropriate oxygen therapy, require urgent airway management and possible intubation.

Assess patients for volume depletion. Administer intravenous fluids if needed according to local protocols, and give nutritional support in prolonged illness.[66]

Monitor temperature, respiratory rate, pulse, blood pressure, mental status, oxygen saturation, and inspired oxygen concentration at least twice daily and more frequently in patients with severe pneumonia and in those requiring regular oxygen therapy. Monitor C-reactive protein (CRP) levels regularly as they are a sensitive marker of progress in pneumonia. Repeat chest x-rays in patients who are not progressing satisfactorily. Routine follow-up chest imaging is not recommended if symptoms resolve within 5-7 days.[17]

Empiric antimicrobial treatment in hospitalized patients not in ICU

The ATS/IDSA guidelines recommend the following intravenous empiric treatment options in inpatients with nonsevere CAP without risk factors for MRSA or P aeruginosa:[17]

- Combination therapy with a beta-lactam (e.g., ampicillin/sulbactam, cefotaxime, ceftriaxone, ceffaroline) plus a macrolide (e.g., azithromycin, clarithromycin). Note that clarithromycin is only available as an oral formulation in the US, and so can only be used if the oral route is feasible
- Monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin)
- Combination therapy with a beta-lactam plus doxycycline in patients who have contraindications to both macrolides and fluoroquinolones.

Additional empiric antibiotic cover is required in patients with risk factors for MRSA or P aeruginosa if locally validated risk factors for either pathogen are present:[17]

- MRSA: add vancomycin or linezolid
- P aeruginosa: add piperacillin/tazobactam, cefepime, ceftazidime, aztreonam, meropenem, or imipenem/cilastatin.
The strongest risk factors for infection with MRSA or *P. aeruginosa* are prior isolation of these organisms from the respiratory tract, and/or recent hospitalization and exposure to parenteral antibiotics in the past 90 days. Based on this, ATS/IDSA recommend the following:[17]

- If the patient has a prior history of respiratory isolation of MRSA or *P. aeruginosa*: add appropriate antibiotic cover and obtain cultures (or nasal polymerase chain reaction [PCR] for MRSA if available) to guide de-escalation or to confirm the need to continue additional cover.
- If the patient has had a recent hospitalization and parenteral antibiotics in the past 90 days and has been locally validated for risk factors for MRSA: obtain cultures and nasal PCR. If PCR or cultures are negative, withhold additional cover. If PCR or cultures are positive, start additional cover.
- If the patient has had a recent hospitalization and parenteral antibiotics in the past 90 days and has been locally validated for risk factors for *P. aeruginosa*: obtain cultures but only initiate cover if cultures are positive.
- Consider de-escalation to standard antibiotic therapy at 48 hours provided cultures do not reveal a drug-resistant pathogen and the patient is clinically improving.

Additional empiric antibiotic cover is required in patients with risk factors for extended-spectrum beta-lactamase-producing Enterobacteriaceae. Consult an infectious disease specialist for guidance on an appropriate antibiotic regimen. Additional anaerobic cover for patients with suspected aspiration pneumonia is not recommended unless lung abscess or empyema is suspected.[17]

The recommendation to cover atypical pathogens in the empiric antibiotic regimen is debated;[98] [99] [100] however, the recommendation is supported by current data.[101] [102]

**Empiric antimicrobial treatment in ICU patients**

The ATS/IDSA guidelines recommend the following intravenous empiric treatment options in inpatients with severe CAP without risk factors for MRSA or *P. aeruginosa*:[17]

- Combination therapy with a beta-lactam (e.g., ampicillin/subactam, cefotaxime, ceftriaxone, ceftaroline) plus a macrolide (e.g., azithromycin, clarithromycin); there is stronger evidence for this regimen compared with the regimen below. Although ATS/IDSA recommend clarithromycin in these patients, it is only available as an oral formulation in the US so is unlikely to be useful in this setting
- Combination therapy with a beta-lactam plus a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin).

Additional empiric antibiotic cover is required in patients with risk factors for MRSA or *P. aeruginosa* if locally validated risk factors for either pathogen are present:[17]

- MRSA: add vancomycin or linezolid
- *P. aeruginosa*: add piperacillin/tazobactam, cefepime, ceftazidime, aztreonam, meropenem, or imipenem/cilastatin.

Add additional antibiotic cover and obtain cultures (or nasal PCR for MRSA if available) to guide de-escalation of therapy or confirm the need to continue therapy. Consider de-escalation to standard antibiotic therapy at 48 hours provided cultures do not reveal a drug-resistant pathogen and the patient is clinically improving.[17]

Additional empiric antibiotic cover is required in patients with risk factors for extended-spectrum beta-lactamase-producing Enterobacteriaceae. Consult an infectious disease specialist for guidance on
an appropriate antibiotic regimen. Additional anaerobic cover for patients with suspected aspiration pneumonia is not recommended unless lung abscess or empyema is suspected.[17]

**Safety of fluoroquinolone antibiotics**

Consider safety issues before prescribing fluoroquinolones. The Food and Drug Administration (FDA) has issued warnings about the increased risk of aortic dissection, significant hypoglycemia, and mental health adverse effects in patients taking fluoroquinolones.[103][104]

The European Medicines Agency (EMA) completed a review of serious, disabling, and potentially irreversible adverse effects associated with fluoroquinolones in 2018. These adverse effects included tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects. Patients who are older, have renal impairment, or have had a solid organ transplant, and those being treated with a corticosteroid are at a higher risk of tendon damage. Coadministration of a fluoroquinolone and a corticosteroid should be avoided if possible. This review resulted in prescribing restrictions in Europe, limiting the use of fluoroquinolones to severe infections only.[105]

Despite these concerns, ATS/IDSA guidelines recommend fluoroquinolones as a treatment option, including patients with comorbidities who are treated in the outpatient setting, nonsevere CAP in the hospital setting, and severe CAP.[17]

**Route of antibiotic therapy**

Start empiric antibiotic treatment as soon as possible, and give in the emergency department to avoid delay. Delayed administration has been associated with an increased risk in mortality in patients with severe CAP.[106]

The initial route for antibiotic therapy depends on severity, the patient’s condition, and the site of care. Guidelines recommend that oral antibiotics be used for outpatients while intravenous treatment is preferred for hospitalized patients. However, intravenous treatment should always be given in patients with severe CAP (at least within the initial hours following admission), with daily evaluation for switching to oral medication as soon as possible. Consider switching the patient to oral therapy when they are hemodynamically stable and improving clinically, can ingest oral medications, and have a normally functioning gastrointestinal tract. Switch to an oral formulation of the same drug or an oral formulation of a drug within the same drug class.[17]

**Duration of antibiotic therapy**

Treat for a minimum of 5 days. Duration of treatment should be guided by a validated measure of clinical stability (e.g., resolution of vital sign abnormalities, normal cognitive function, ability to eat).[17][107] Consider discontinuing therapy when the patient has been afebrile for 48-72 hours and there are no signs of complications (endocarditis, meningitis). A retrospective cohort study found that two-thirds of hospitalized patients with CAP received excess antibiotic therapy, and each excess day of treatment was associated with a 5% increase in the odds of antibiotic-associated adverse effects after discharge.[108]

Longer treatment courses are recommended in patients with complications and in cases of pneumonia due to less common pathogens. A treatment course of 7 days is recommended in patients with MRSA or *P aeruginosa*. [17] Consult with an infectious diseases expert in these cases.
Microbiologically directed therapy

Consider switching patients to an organism-specific antimicrobial therapy guided by antibiotic sensitivity in patients in whom laboratory tests have revealed a causative organism.

Antiviral treatment in patients with influenza

Add antiviral treatment (e.g., oseltamivir) to antimicrobial treatment in patients with CAP who test positive for influenza in the inpatient setting, independent of duration of illness before diagnosis. Consider antiviral treatment in outpatients who test positive for influenza virus.[17]

Corticosteroid therapy in hospitalized patients

The use of corticosteroids in patients with severe CAP has been a long-debated issue. Current ATS/IDSA guidelines generally recommend against the use of corticosteroids in patients with nonsevere or severe CAP, although acknowledge that they may be considered in patients with refractory septic shock according to Surviving Sepsis Campaign guidelines, and can be used as clinically appropriate for comorbid conditions (e.g., COPD, asthma, autoimmune diseases). This recommendation is based on the fact that there are no data suggesting benefit in patients with nonsevere CAP with respect to mortality or organ failure, and only limited data to support their use in patients with severe CAP.[17]

Meta-analyses of studies of hospitalized adults with CAP found that the use of corticosteroids was associated with reduced need for mechanical ventilation, reduced hospital stay, lower clinical failure rates, fewer complications (including septic shock), decreased CRP levels, and reduced all-cause mortality. However, it appears that the reduction in mortality applies to only patients with severe CAP. In patients with nonsevere disease, adjunctive corticosteroids reduce morbidity, but not mortality.[109] [110] [111] [112] [113] [114] [115]

Patients treated with corticosteroids have an increased risk for hyperglycemia.[111] [112] Other adverse effects include super infection and upper gastrointestinal bleeding.

Nonresponding pneumonia

Nonresponding CAP describes the clinical situation where there is an inadequate response after antibiotic treatment as assessed at day 3 to day 5. The causes of nonresponding pneumonia are classified as infectious, noninfectious, and of unknown origin. Multicenter studies have shown that between 6% and 24% of CAP cases will not respond to antibiotic treatment, and in cases of severe pneumonia, this rate can reach 31%.[18] [116]

One study has described two different clinical patterns of nonresponding pneumonia:[117]

- Progressive pneumonia that follows a course of clinical deterioration with respiratory failure or septic shock
- The situation where clinical stability is not achieved and no other patient characteristics are responsible.

Biomarkers such as CRP and procalcitonin (PCT) have been found to be useful for predicting inadequate host response. High levels of CRP or PCT at initial presentation represent a risk factor for inadequate response,[73] whereas low levels are protective. The use of procalcitonin to guide initiation and duration of antibiotic treatment results in a lower risk of mortality, lower antibiotic consumption, and lower risk for side effects.[118] [119] However, one review found no difference in short-term mortality in critically ill patients specifically,[120] while another study found that PCT-guided therapy did not result in decreased
Consensus algorithms that include PCT cut-off points for deciding when to initiate or discontinue antibiotics may help to facilitate safe and efficient implementation of PCT-guided therapy.[122]

The first response to nonresponse or deterioration should be to re-evaluate the initial microbiology results.[17] Results of cultures and sensitivity testing that were not available at presentation may now make the cause of clinical failure obvious. In addition, a further history of any risk factors for infection with unusual microorganisms, including viruses, should be sought if this has not already been done. Further diagnostic testing may also be warranted.

Bundled interventions

While efficacy of individual interventions may demonstrate efficacy in clinical trials, a bundled intervention, which included adjunct corticosteroids, as well as early mobilization, nutrition screening, and early switch to oral antibiotics, was not found to have a significant effect on hospital stay length, mortality, or complications, but was found to increase the risk of gastrointestinal bleeding when compared with normal care. Therefore, the efficacy of individual interventions may not translate into effectiveness when these interventions are bundled and given in combination, and may even result in net harm.[123]

[VIDEO: Bag-valve-mask ventilation: animated demonstration ]

[VIDEO: Tracheal intubation: animated demonstration ]

[VIDEO: Central venous catheter insertion: animated demonstration ]

[VIDEO: Peripheral venous cannulation: animated demonstration ]

Treatment details overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer
<table>
<thead>
<tr>
<th>Acute</th>
<th>( summary )</th>
</tr>
</thead>
<tbody>
<tr>
<td>outpatient</td>
<td></td>
</tr>
<tr>
<td>- without comorbidities or risk factors for drug-resistant pathogens</td>
<td>1st oral amoxicillin, doxycycline, or a macrolide plus supportive care adjunct influenza antiviral cover</td>
</tr>
<tr>
<td>- with comorbidities or risk factors for drug-resistant pathogens</td>
<td>1st oral combination antibiotic therapy or fluoroquinolone monotherapy plus supportive care adjunct influenza antiviral cover</td>
</tr>
<tr>
<td>inpatient</td>
<td></td>
</tr>
<tr>
<td>- not in intensive care unit (nonsevere)</td>
<td>1st intravenous combination antibiotic therapy or fluoroquinolone monotherapy adjunct MRSA antibiotic cover adjunct Pseudomonas antibiotic cover adjunct Enterobacteriaceae antibiotic cover adjunct influenza antiviral cover plus supportive care</td>
</tr>
<tr>
<td>- in intensive care unit (severe)</td>
<td>1st intravenous combination antibiotic therapy adjunct MRSA antibiotic cover adjunct Pseudomonas antibiotic cover adjunct Enterobacteriaceae antibiotic cover adjunct influenza antiviral cover adjunct corticosteroid plus supportive care</td>
</tr>
</tbody>
</table>
Treatment options

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer.
### Acute outpatient

- **without comorbidities or risk factors for drug-resistant pathogens**  
  1st 
  **oral amoxicillin, doxycycline, or a macrolide**  
  **Primary options**  
  » amoxicillin: 1000 mg orally three times daily  
  OR  
  » doxycycline: 100 mg orally twice daily  
  **Secondary options**  
  » azithromycin: 500 mg orally once daily on the first day, followed by 250 mg once daily thereafter  
  OR  
  » clarithromycin: 500 mg orally (immediate-release) twice daily; 1000 mg orally (extended-release) once daily

> Outpatient treatment is recommended in patients with Pneumonia Severity Index (PSI) risk class I or II with a PSI score ≤70 (low risk), or a CURB-65 score of 0-1 (low severity).[79] [80] PSI is preferred over CURB-65.[17]

» Empiric oral antibiotics are recommended: amoxicillin, doxycycline, or a macrolide (e.g., azithromycin or clarithromycin). Only use a macrolide in areas with pneumococcal resistance to macrolides <25% and when there are contraindications to alternative therapies.[17]

» Treat for a minimum of 5 days. Duration of treatment should be guided by a validated measure of clinical stability (e.g., resolution of vital sign abnormalities, normal cognitive function, ability to eat). Consider discontinuing treatment when the patient has been afebrile for 48-72 hours and there are no signs of complications (endocarditis, meningitis).[17] [107]

» Reassess patients at 48 hours. Symptoms should improve within this time with appropriate treatment. Consider hospital admission in patients who fail to improve within 48 hours.

» Consider switching patients to an organism-specific antimicrobial therapy guided by antibiotic
Community-acquired pneumonia

Treatment

**Acute**

- sensitivity in patients in whom laboratory tests have revealed a causative organism.

  **plus** supportive care

  Treatment recommended for ALL patients in selected patient group

  » Advise patients not to smoke, to rest, and to stay well hydrated.

  **adjunct** influenza antiviral cover

  Treatment recommended for SOME patients in selected patient group

  **Primary options**

  » oseltamivir: 75 mg orally twice daily for 5 days

  » Consider antiviral therapy (e.g., oseltamivir) in outpatients who test positive for influenza virus.[17]

- with comorbidities or risk factors for drug-resistant pathogens

  **1st** oral combination antibiotic therapy or fluoroquinolone monotherapy

  **Primary options**

  » amoxicillin/clavulanate: 500 mg orally (immediate-release) three times daily; 875 mg orally (immediate-release) twice daily; 2000 mg orally (extended-release) twice daily

  Dose refers to amoxicillin component.

  -or-

  » cefpodoxime proxetil: 200 mg orally twice daily

  -or-

  » cefuroxime axetil: 500 mg orally twice daily

  --AND--

  » azithromycin: 500 mg orally once daily on the first day, followed by 250 mg once daily thereafter

  -or-

  » clarithromycin: 500 mg orally (immediate-release) twice daily; 1000 mg orally (extended-release) once daily

  -or-

  » doxycycline: 100 mg orally twice daily

  **OR**

  » levofloxacin: 750 mg orally once daily

  **OR**

  » moxifloxacin: 400 mg orally once daily

  **OR**
Community-acquired pneumonia

**Acute**

- **gemifloxacin**: 320 mg orally once daily

- Outpatient treatment is recommended in patients with Pneumonia Severity Index (PSI) risk class I or II with a PSI score ≤70 (low risk), or a CURB-65 score of 0-1 (low severity).[79][80] PSI is preferred over CURB-65.[17]

- Comorbidities include: chronic heart, lung, liver, or renal disease; diabetes mellitus; alcohol abuse; malignancy; asplenia. Broader-spectrum antibiotic regimens are required in these patients as many will have risk factors for drug-resistant pathogens (e.g., recent hospitalization and administration of parenteral antibiotics in the past 90 days), and they are more vulnerable to poor outcomes if the empiric regimen is inadequate.[17]

- Empiric oral antibiotics are recommended: combination therapy with amoxicillin/clavulanate or a cephalosporin (e.g., cefpodoxime, cefuroxime) plus a macrolide or doxycycline; or monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin, gemifloxacin). These regimens should effectively cover drug-resistant pathogens.[17]

- Consider safety issues before prescribing fluoroquinolones. The Food and Drug Administration (FDA) has warned about the increased risk of aortic dissection, significant hypoglycemia, and mental health adverse effects.[103][104] The European Medicines Agency (EMA) completed a review of serious, disabling, and potentially irreversible adverse effects associated with fluoroquinolones in 2018. These adverse effects included tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[105] Despite these concerns, American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines still recommend fluoroquinolones as an option in patients with low-severity CAP who have comorbidities and are managed in the outpatient setting.[17]

- Treat for a minimum of 5 days. Duration of treatment should be guided by a validated measure of clinical stability (e.g., resolution of vital sign abnormalities, normal cognitive function, ability to eat). Consider discontinuing treatment when the patient has been afebrile for 48-72 hours and there are no signs of
## Community-acquired pneumonia

### Treatment

#### Acute

<table>
<thead>
<tr>
<th>plus support care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for ALL patients in selected patient group</td>
</tr>
<tr>
<td>» Advise patients not to smoke, to rest, and to stay well hydrated.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>adjunct influenza antiviral cover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
</tr>
</tbody>
</table>

**Primary options**

| » oseltamivir: 75 mg orally twice daily for 5 days |
| Consider antiviral therapy (e.g., oseltamivir) in outpatients who test positive for influenza virus. |

#### Inpatient

- **not in intensive care unit**
  - **1st** intravenous combination antibiotic therapy or fluoroquinolone monotherapy

**Primary options**

| » ampicillin/sulbactam: 1.5 to 3 g intravenously every 6 hours |
| Dose consists of 1 g of ampicillin plus 0.5 g sulbactam (1.5 g) or 2 g of ampicillin plus 1 g sulbactam (3 g). |
| -or- |
| » cefotaxime: 1-2 g intravenously every 8 hours |
| -or- |
| » ceftriaxone: 1-2 g intravenously every 24 hours |
| -or- |
| » ceftaroline fosamil: 600 mg intravenously every 12 hours |
| -AND- |
| » azithromycin: 500 mg intravenously every 24 hours |
| -or- |
Community-acquired pneumonia

Treatment

**Acute**

- **clarithromycin**: 500 mg orally (immediate-release) twice daily

  OR

- **levofloxacin**: 750 mg intravenously every 24 hours

  OR

- **moxifloxacin**: 400 mg intravenously every 24 hours

- Hospital admission is recommended in patients with a Pneumonia Severity Index (PSI) risk class III (these patients may benefit from a brief period of hospitalization), PSI risk class IV or V, or a CURB-65 score of 3.[79] [80] PSI is preferred over CURB-65.[17]

- Empiric intravenous antibiotics are recommended: combination therapy with a beta-lactam (e.g., ampicillin/sulbactam, cefotaxime, ceftriaxone, ceftaroline) plus a macrolide (e.g., azithromycin, clarithromycin); or monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin). Consider combination therapy with a beta-lactam plus doxycycline in patients who have contraindications to both macrolides and fluoroquinolones. Note that clarithromycin is only available as an oral formulation in the US, and so can only be used if the oral route is feasible.

- Consider safety issues before prescribing fluoroquinolones. The Food and Drug Administration (FDA) has warned about the increased risk of aortic dissection, significant hypoglycemia, and mental health adverse effects.[103] [104] The European Medicines Agency (EMA) completed a review of serious, disabling, and potentially irreversible adverse effects associated with fluoroquinolones in 2018. These adverse effects included tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[105]

- Treat for a minimum of 5 days. Duration of treatment should be guided by a validated measure of clinical stability (e.g., resolution of vital sign abnormalities, normal cognitive function, ability to eat). Consider discontinuing treatment when the patient has been afebrile for 48-72 hours and there are no signs of complications (endocarditis, meningitis).[17] [107]
<table>
<thead>
<tr>
<th>Acute</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>» Evaluate whether the patient can be switched to oral therapy on a daily basis; the switch should be made as soon as possible. Switch to an oral formulation of the same drug or an oral formulation of a drug within the same drug class.[17]</td>
<td></td>
</tr>
<tr>
<td>» Consider switching patients to an organism-specific antimicrobial therapy guided by antibiotic sensitivity in patients in whom laboratory tests have revealed a causative organism.</td>
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</table>

<table>
<thead>
<tr>
<th>adjunct</th>
<th>MRSA antibiotic cover</th>
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<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary options</th>
</tr>
</thead>
<tbody>
<tr>
<td>» vancomycin: 15 mg/kg intravenously every 12 hours; adjust dose based on serum vancomycin levels</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>» linezolid: 600 mg intravenously every 12 hours</td>
</tr>
</tbody>
</table>

|  » Additional empiric antibiotic cover is required in patients with risk factors for methicillin-resistant Staphylococcus aureus (MRSA) if locally validated risk factors are present.[17] |
|  » If the patient has a prior history of respiratory isolation of MRSA: add vancomycin or linezolid and obtain cultures (or nasal polymerase chain reaction [PCR] if available) to guide de-escalation or to confirm the need to continue additional cover.[17] |
|  » If the patient has had a recent hospitalization and parenteral antibiotics in the past 90 days, and has been locally validated for risk factors for MRSA: obtain cultures and nasal PCR. If PCR or cultures are negative, withhold additional cover. If PCR or cultures are positive, start additional cover.[17] |
|  » Consider de-escalation to standard antibiotic therapy at 48 hours provided cultures do not reveal a drug-resistant pathogen and the patient is clinically improving.[17] |
|  » A longer treatment course of 7 days is recommended in patients with MRSA.[17] |

<table>
<thead>
<tr>
<th>adjunct</th>
<th>Pseudomonas antibiotic cover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
</tbody>
</table>
Community-acquired pneumonia

Treatment

<table>
<thead>
<tr>
<th>Acute</th>
</tr>
</thead>
</table>

**Primary options**

- **piperacillin/tazobactam:** 4.5 g intravenously every 6 hours  
  Dose consists of 4 g of piperacillin plus 0.5 g tazobactam.

  OR

- **cefepime:** 2 g intravenously every 8 hours

  OR

- **ceftazidime sodium:** 2 g intravenously every 8 hours

  OR

- **imipenem/cilastatin:** 500 mg intravenously every 6 hours  
  Dose refers to imipenem component.

  OR

- **meropenem:** 1 g intravenously every 8 hours

  OR

- **aztreonam:** 2 g intravenously every 8 hours

  » Additional empiric antibiotic cover is required in patients with risk factors for *Pseudomonas aeruginosa* if locally validated risk factors are present.[17]

  » If the patient has a prior history of respiratory isolation of *P aeruginosa*: add piperacillin/tazobactam, cefepime, ceftazidime, aztreonam, meropenem, or imipenem/cilastatin, and obtain cultures to guide de-escalation or to confirm the need to continue additional cover.[17]

  » If the patient has had a recent hospitalization and parenteral antibiotics in the past 90 days, and has been locally validated for risk factors for *P aeruginosa*: obtain cultures but only initiate cover for *P aeruginosa* if cultures are positive.[17]

  » Consider de-escalation to standard antibiotic therapy at 48 hours provided cultures do not reveal a drug-resistant pathogen and the patient is clinically improving.[17]
### Acute

» A longer treatment course of 7 days is recommended in patients with *P aeruginosa*.[17]

» Take the initial empiric regimen into account adding *Pseudomonas* cover so that two antibiotics from the same class are not used together.

**adjunct** Enterobacteriaceae antibiotic cover

Treatment recommended for SOME patients in selected patient group

» Additional empiric antibiotic cover is required in patients with risk factors for extended-spectrum beta-lactamase-producing Enterobacteriaceae. Consult an infectious disease specialist for guidance on an appropriate antibiotic regimen.[17]

» A longer treatment course is recommended in patients in cases of pneumonia due to less common pathogens.[17]

**adjunct** influenza antiviral cover

Treatment recommended for SOME patients in selected patient group

**Primary options**

» oseltamivir: 75 mg orally twice daily for 5 days

» Add antiviral treatment (e.g., oseltamivir) to antimicrobial treatment in patients with CAP who test positive for influenza in the inpatient setting, independent of duration of illness before diagnosis.[17]

**plus** supportive care

Treatment recommended for ALL patients in selected patient group

» Administer oxygen therapy as necessary. Monitor oxygen saturation and inspired oxygen concentration with the aim of maintaining SaO₂ above 92%. High concentrations of oxygen can safely be given in uncomplicated pneumonia. Patients with respiratory failure, despite appropriate oxygen therapy, require urgent airway management and possible intubation. Treatment of patients with COPD complicated by ventilatory failure oxygen therapy should be guided by repeated arterial blood gas measurements.[66]

» Assess patients for volume depletion. Administer intravenous fluids if needed
### Community-acquired pneumonia

#### Treatment

**Acute**

- **In intensive care unit (severe)**
  - 1st intravenous combination antibiotic therapy

  **Primary options**
  - ampicillin/sulbactam: 1.5 to 3 g intravenously every 6 hours
    - Dose consists of 1 g of ampicillin plus 0.5 g sulbactam (1.5 g) or 2 g of ampicillin plus 1 g sulbactam (3 g).
    - or-
    - cefotaxime: 1-2 g intravenously every 8 hours
    - or-
    - ceftriaxone: 1-2 g intravenously every 24 hours
    - or-
    - ceftaroline fosamil: 600 mg intravenously every 12 hours
  --AND--
  - azithromycin: 500 mg intravenously every 24 hours

  **Secondary options**
  - ampicillin/sulbactam: 1.5 to 3 g intravenously every 6 hours
    - Dose consists of 1 g of ampicillin plus 0.5 g sulbactam (1.5 g) or 2 g of ampicillin plus 1 g sulbactam (3 g).
    - or-
    - cefotaxime: 1-2 g intravenously every 8 hours
    - or-
    - ceftriaxone: 1-2 g intravenously every 24 hours
    - or-
    - ceftaroline fosamil: 600 mg intravenously every 12 hours
  --AND--
  - levofloxacin: 750 mg intravenously every 24 hours

- according to local protocols, and give nutritional support in prolonged illness.[66]

- Monitor temperature, respiratory rate, pulse, blood pressure, and mental status at least twice daily and more frequently in those with severe pneumonia or requiring regular oxygen therapy. Monitor C-reactive protein (CRP) levels regularly as they are a sensitive marker of progress in pneumonia. Repeat chest x-rays in patients who are not progressing satisfactorily.[66] Routine follow-up chest imaging is not recommended if symptoms resolve within 5-7 days.[17]
### Acute

- **moxifloxacin**: 400 mg intravenously every 24 hours

- Admit patients with hypotension requiring vasopressor therapy or respiratory failure requiring mechanical ventilation to the intensive care unit (ICU). In patients who do not require vasopressor therapy or mechanical ventilation, use the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) criteria for defining severe CAP (see Diagnostic criteria section) and clinical judgement to guide the need for higher levels of treatment intensity. Admit patients with severe CAP (defined as two major criteria or three or more minor criteria) to the ICU.[17]

- Start antibiotic therapy promptly as a delay in administration has been associated with an increased risk in mortality.[106]

- Empiric intravenous antibiotics are recommended: combination therapy with a beta-lactam (e.g., ampicillin/subbactam, cefotaxime, ceftriaxone, ceftaroline) plus a macrolide (e.g., azithromycin, clarithromycin); or combination therapy with a beta-lactam plus a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin). There is stronger evidence for beta-lactam plus macrolide combination.[17] Although ATS/IDSA recommend clarithromycin in these patients, it is only available as an oral formulation in the US so is unlikely to be useful in this setting.

- Consider safety issues before prescribing fluoroquinolones. The Food and Drug Administration (FDA) has warned about the increased risk of aortic dissection, significant hypoglycemia, and mental health adverse effects.[103] [104] The European Medicines Agency (EMA) completed a review of serious, disabling, and potentially irreversible adverse effects associated with fluoroquinolones in 2018. These adverse effects included tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[105]

- Treat for a minimum of 5 days. Duration of treatment should be guided by a validated measure of clinical stability (e.g., resolution of vital sign abnormalities, normal cognitive function, ability to eat). Consider discontinuing treatment when the patient has been afebrile for 48-72 hours and there are no signs of complications (endocarditis, meningitis).[17] [107]
<table>
<thead>
<tr>
<th>Adjunct</th>
<th>MRSA antibiotic cover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» <strong>vancomycin</strong>: 15 mg/kg intravenously every 12 hours; adjust dose based on serum vancomycin levels</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>» <strong>linezolid</strong>: 600 mg intravenously every 12 hours</td>
<td></td>
</tr>
<tr>
<td>» Additional empiric antibiotic cover is required in patients with risk factors for methicillin-resistant <em>Staphylococcus aureus</em> (MRSA) if locally validated risk factors are present.[17]</td>
<td></td>
</tr>
<tr>
<td>» Add appropriate additional antibiotic cover and obtain cultures (or nasal polymerase chain reaction if available) to guide de-escalation of therapy or confirm the need to continue therapy.[17]</td>
<td></td>
</tr>
<tr>
<td>» Consider de-escalation to standard antibiotic therapy at 48 hours provided cultures do not reveal a drug-resistant pathogen and the patient is clinically improving.[17]</td>
<td></td>
</tr>
<tr>
<td>» A longer treatment course of 7 days is recommended in patients with MRSA.[17]</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjunct</th>
<th>Pseudomonas antibiotic cover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
</tbody>
</table>
| » **piperacillin/tazobactam**: 4.5 g intravenously every 6 hours  
  Dose consists of 4 g of piperacillin plus 0.5 g tazobactam. |
| OR |
Community-acquired pneumonia

**Treatment**

### Acute

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>cefepime</strong>:</td>
<td>2 g intravenously every 8 hours</td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td><strong>ceftazidime sodium</strong>:</td>
<td>2 g intravenously every 8 hours</td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
</tbody>
</table>
| **imipenem/cilastatin**: | 500 mg intravenously every 6 hours  
Dose refers to imipenem component. |
| OR | |
| **meropenem**: | 1 g intravenously every 8 hours |
| OR | |
| **aztreonam**: | 2 g intravenously every 8 hours |

Additional empiric antibiotic cover is required in patients with risk factors for *Pseudomonas aeruginosa* if locally validated risk factors are present.[17]

- Add appropriate additional antibiotic cover and obtain cultures to guide de-escalation of therapy or confirm the need to continue therapy.[17]
- Consider de-escalation to standard antibiotic therapy at 48 hours provided cultures do not reveal a drug-resistant pathogen and the patient is clinically improving.[17]
- A longer treatment course of 7 days is recommended in patients with *P aeruginosa*.[17]
- Take the initial empiric regimen into account adding *Pseudomonas* cover so that two antibiotics from the same class are not used together.

### adjunct Enterobacteriaceae antibiotic cover

Treatment recommended for SOME patients in selected patient group

- Additional empiric antibiotic cover is required in patients with risk factors for extended-spectrum beta-lactamase-producing Enterobacteriaceae. Consult an infectious disease specialist for guidance on an appropriate antibiotic regimen.[17]
### Acute

<table>
<thead>
<tr>
<th>Adjunct</th>
<th>Influenza antiviral cover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
</tbody>
</table>

#### Primary options

- **oseltamivir**: 75 mg orally twice daily for 5 days

- Add antiviral treatment (e.g., oseltamivir) to antimicrobial treatment in patients with CAP who test positive for influenza in the inpatient setting, independent of duration of illness before diagnosis.[17]

<table>
<thead>
<tr>
<th>Adjunct</th>
<th>Corticosteroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
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</tbody>
</table>

- **The use of corticosteroids in patients with severe CAP has been a long-debated issue.**

- **Current American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines generally recommend against the use of corticosteroids in patients with nonsevere or severe CAP, although acknowledge that they may be considered in patients with refractory septic shock according to Surviving Sepsis Campaign guidelines, and can be used as clinically appropriate for comorbid conditions (e.g., COPD, asthma, autoimmune diseases). This recommendation is based on the fact that there are no data suggesting benefit in patients with nonsevere CAP with respect to mortality or organ failure, and only limited data to support their use in patients with severe CAP.[17]**

<table>
<thead>
<tr>
<th>Plus</th>
<th>Supportive care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for ALL patients in selected patient group</td>
<td></td>
</tr>
</tbody>
</table>

- **Administer oxygen therapy as necessary. Monitor oxygen saturation and inspired oxygen concentration with the aim of maintaining SaO₂ above 92%. High concentrations of oxygen can safely be given in uncomplicated pneumonia. Patients with respiratory failure, despite appropriate oxygen therapy, require urgent airway management and possible intubation. Treatment of patients with COPD complicated by ventilatory failure oxygen therapy should be guided by repeated arterial blood gas measurements.[66]**
Acute

» Assess patients for volume depletion. Administer intravenous fluids if needed according to local protocols, and give nutritional support in prolonged illness.[66]

» Monitor temperature, respiratory rate, pulse, blood pressure, and mental status at least twice daily and more frequently in those with severe pneumonia or requiring regular oxygen therapy. Monitor C-reactive protein (CRP) levels regularly as they are a sensitive marker of progress in pneumonia. Repeat chest x-rays in patients who are not progressing satisfactorily.[66] Routine follow-up chest imaging is not recommended if symptoms resolve within 5-7 days.[17]
Emerging

Newer antibiotics

Given the concerns over increasing drug resistance and safety issues (e.g., fluoroquinolones) with existing antibiotics, there is a need for further research on new therapeutic agents. Newer antibiotic agents are detailed in this section. Current guidelines do not recommend them yet as they require further validation. Therefore, these agents are still considered to be emerging. Despite this, some of these newer antibiotics are approved by the Food and Drug Administration (FDA) for the treatment of CAP and may be considered under specialist guidance.

Lefamulin

A first-in-class pleuromutilin antibiotic available in oral and intravenous formulations. It inhibits bacterial protein synthesis via interactions with the A- and P- sites of the peptidyl transferase center of the 50S subunit. Lefamulin offers a unique spectrum of activity covering *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Legionella pneumophila*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Staphylococcus aureus* (including methicillin-resistant *S. aureus* [MRSA]), beta-haemolytic streptococci (including *S. pyogenes* and *S. agalactiae*), and *Enterococcus faecium* (including vancomycin-resistant enterococci). It lacks cross-resistance with other antibiotic classes for *S. pneumoniae* and *S. aureus*.\(^1\)\(^2\)\(^3\) The safety and efficacy of lefamulin has been evaluated in two phase 3 clinical trials where it was found to be noninferior to moxifloxacin (with or without linezolid) in terms of primary efficacy endpoints (early clinical response, investigator assessment of clinical response). It was considered safe and well tolerated.\(^4\)\(^5\) However, it has the potential to cause QT interval prolongation and should not be used in patients with known prolongation of the QT interval, ventricular arrhythmias, or who are on other drugs that prolong the QT interval. Lefamulin is approved by the FDA for the treatment of CAP in adults; however, its exact place in management is not clear as yet.

Delafloxacin

A new fluoroquinolone antibiotic approved by the FDA for the treatment of adults with CAP caused by designated susceptible bacteria. The approval is based on results from a phase 3 study that found it was noninferior to moxifloxacin.\(^6\)

Omadacycline

A new modernized tetracycline antibiotic (aminomethylcycline) with broad-spectrum activity, designed to overcome tetracycline resistance. It is available in oral and intravenous formulations. Like other antibiotics in the tetracycline class, omadacycline may cause discoloration of deciduous teeth, and inhibition of fetal bone growth when administered during pregnancy. It has been found to be noninferior to moxifloxacin in terms of efficacy in adults with CAP.\(^7\) Omadacycline is approved by the FDA for the treatment of CAP in adults; however, it was refused approval for this indication in Europe in October 2018.

Ceftobiprole

A broad-spectrum parenteral cephalosporin that has microbiological activity against most typical bacterial pathogens causing CAP, including MRSA. A phase 3 study found that ceftobiprole was noninferior to ceftriaxone with or without linezolid for the treatment of CAP.\(^8\)

Nemonoxacin

A nonfluorinated, broad-spectrum quinolone. It has greater antimicrobial activity than the fluoroquinolones (e.g., levofloxacin) against MRSA, methicillin-sensitive *Staphylococcus epidermidis* (MSSE), methicillin-resistant *S. epidermidis* (MRSE), *S. pneumoniae*, and *Enterobacter faecalis*. A systematic review found that it is as effective and well tolerated as levofloxacin in patients with CAP.\(^9\) Nemonoxacin is approved in Taiwan for the treatment of CAP in adults, but it is not currently approved in the US, UK, or Europe.
Solithromycin

A fluoroketolide with antimicrobial activity against gram-positive and gram-negative bacteria commonly associated with CAP. A completed phase 2 study showed that solithromycin had similar efficacy to that of levofloxacin in adults with bacterial CAP with pneumonia severity index scores of II to IV.[146] It has also been found to be noninferior to moxifloxacin.[147] Solithromycin is currently in phase 3 development for the treatment of bacterial CAP.

Statins

There is evidence to suggest that statins may reduce the risk of CAP and its complications due to their immunomodulatory effects. Data suggest that patients with CAP who are taking a statin on hospital admission have a reduced risk of inpatient mortality.[148] A meta-analysis found that statins may decrease mortality associated with CAP, as well as reduce the need for mechanical ventilation or intensive care unit admission.[149] However, whether statin use can reduce the risk of pneumonia is unclear and further studies are required. It is important to note that statins interact with macrolides, an antibiotic class commonly used for the treatment of CAP. These drugs should not be used in combination as macrolides inhibit the metabolism of statins via the CYP3A4 pathway and therefore increase the risk of myopathy and rhabdomyolysis.
Recommendations

Monitoring

Monitoring parameters for CAP management should include aspects of both antimicrobial therapy and the disease state. A repeat chest x-ray in the weeks after symptoms have resolved may be ordered to confirm that the pneumonia has resolved, and to ensure that the chest x-ray is clear of any abnormalities. Routine follow-up chest imaging is not recommended if symptoms resolve within 5 to 7 days.[17]

Good communication between patient and physician is the most important aspect in follow-up care. Physicians should tell their patients how long to expect the fever to last and when the cough should begin to resolve. The patient should tell the physician if he or she is not improving as predicted.

Patient instructions

Medication adherence is very important in patients with a diagnosis of CAP, even after they experience clinical improvement. Patients should be instructed to contact the physician if their symptoms do not improve within 72 hours.

Adequate hydration and preservation of the cough reflex during convalescence are important. The cough reflex is necessary in order to remove the microorganism from the respiratory tract before it reaches the lung.

In smokers, smoking cessation is an important issue. It should be explained to patients how smoking impairs natural mechanisms for eliminating pathogens and debris.
## Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>septic shock</td>
<td>short term</td>
<td>medium</td>
</tr>
<tr>
<td>Commonly complicates severe CAP. Patients have fever, leukocytosis, tachypnea, tachycardia. Can progress rapidly to multi-organ failure and shock. It is often fatal, and survival is dependent on a high index of suspicion, early recognition, and immediate intervention. The prevalence of sepsis in very old patients (≥80 years) with CAP was 71%. Risk factors included: male sex, chronic renal disease, and diabetes mellitus. Antibiotic therapy before admission was associated with a lower risk of sepsis. In-hospital and 1-year mortality rates were increased in these patients if they developed sepsis.[159]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>acute respiratory distress syndrome (ARDS)</td>
<td>short term</td>
<td>medium</td>
</tr>
<tr>
<td>Pneumonia can be complicated by ARDS, which is a condition of noncardiogenic pulmonary edema and severe lung inflammation. Reported in 2% of CAP patients who are hospitalized, and 13% of CAP patients who are admitted to the intensive care unit. Occurs in 29% of CAP patients who are mechanically ventilated, with a 30-day mortality of 25%.[160] Associated with a 30% to 50% mortality, and treated with low tidal volume plateau pressure limited mechanical ventilation.[31]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>antibiotic-associated Clostridium difficile colitis</td>
<td>short term</td>
<td>medium</td>
</tr>
<tr>
<td>May occur as a result of interruption of the normal bowel flora from antibiotic use. Patients generally have diarrhea, abdominal pain, and leukocytosis. Stool immunoassay for \textit{C difficile} enzymes is diagnostic. Ideally, causative antibiotics should be stopped, and antibiotic treatment started according to current local guidance.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>heart failure</td>
<td>short term</td>
<td>medium</td>
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<tr>
<td>The incidence of heart failure in hospitalized patients with CAP was 14.1% in one study.[161] There is little information about risk factors for the occurrence of cardiac complications in patients with CAP. Older age, pre-existing congestive heart failure, severity of CAP, and the use of insulin by glucose sliding scales in hospitalized patients are possible risk factors.[162] [163] [164] In patients with known cardiovascular disease, use of pneumococcal and influenza vaccine may reduce morbidity and mortality.</td>
<td></td>
<td></td>
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<tr>
<td>acute coronary syndrome</td>
<td>short term</td>
<td>low</td>
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<tr>
<td>The incidence of acute coronary syndrome in hospitalized patients with CAP was 5.3% in one study.[161]</td>
<td></td>
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<tr>
<td>cardiac arrhythmias</td>
<td>short term</td>
<td>low</td>
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<tr>
<td>The incidence of incident cardiac arrhythmia in hospitalized patients with CAP was 4.7% in one study.[161]</td>
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<td></td>
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<tr>
<td>necrotizing pneumonia</td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Regarded as a rare complication of CAP in adults. Associated with pathogens such as \textit{Staphylococcus aureus}, \textit{Streptococcus pyogenes}, \textit{Nocardia} species, \textit{Klebsiella pneumoniae}, and \textit{Streptococcus pneumoniae}.</td>
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### Complications

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<tr>
<td>Smoking, alcoholism, old age, diabetes mellitus, chronic lung diseases, or liver disease are risk factors associated with necrotizing pneumonia.[168]</td>
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#### pleural effusion

- May occur in up to 57% of hospitalized pneumonia patients.\[165\] [166]\n- About 1% to 2% of CAP cases with pleural effusion are complicated with empyema.
- Pleural effusion is considered to be an indicator of pneumonia severity and is clearly associated with an increased risk of treatment failure.\[17\] [167]

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<tr>
<th>lung abscess</th>
<th>variable</th>
<th>low</th>
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<td>A rare complication, frequently requiring prolonged antibiotic therapy and, in some cases, surgical drainage.</td>
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### Prognosis

Prognosis is determined by 3 major factors: age of the patient, general state of health (presence of comorbidities), and the setting where antibiotic treatment is given. In general, the mortality rate in outpatients is <1%, while for hospitalized patients, mortality rate ranges from 5% to 15%, but increases to between 20% and 50% in patients requiring intensive care unit admission.\[31\] [151]

Several risk factors, such as bacteremia, intensive care unit admission, comorbidities (especially neurological disease), and infection with a potentially multidrug-resistant pathogen (e.g., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, Enterobacteriaceae), are associated with increased 30-day mortality.\[36\] [152] [153] [154]

Readmission rates in patients with CAP range from 7% to 12%.\[155\] [156]\n
In most cases, exacerbation of comorbidities (mainly cardiovascular, pulmonary, or neurological disease) is responsible for readmission.

Prognostic biomarkers such as pro-adrenomedullin, prohormone forms of atrial natriuretic peptide, cortisol, procalcitonin, and C-reactive protein are being studied as predictors of mortality; however, further studies are required before these biomarkers are used for this function in clinical practice.\[157\] A new screening tool, the quick Sequential Organ Failure Assessment (qSOFA), has been used to identify patients with infections who are at high risk of death. A meta-analysis found that a qSOFA score of 2 or greater has been strongly associated with mortality in patients with pneumonia; however, this score has poor sensitivity and further studies are required.\[158\]
Diagnostic guidelines

### International

**Diagnosis and treatment of adults with community-acquired pneumonia** [17]

*Published by:* American Thoracic Society; Infectious Diseases Society of America  
*Last published:* 2019

**Community-acquired pneumonia in adults: diagnosis and management** [89]

*Published by:* American Family Physician  
*Last published:* 2016

**Pneumonia in adults: diagnosis and management** [90]

*Published by:* National Institute for Health and Care Excellence (UK)  
*Last published:* 2019

**BTS guidelines for the management of community acquired pneumonia in adults** [66]

*Published by:* British Thoracic Society  
*Last published:* 2009

### Treatment guidelines

#### International

**Diagnosis and treatment of adults with community-acquired pneumonia** [17]

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*Last published:* 2019

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*Last published:* 2016

**Pneumonia in adults: diagnosis and management** [90]

*Published by:* National Institute for Health and Care Excellence (UK)  
*Last published:* 2019

**Pneumonia (community-acquired): antimicrobial prescribing** [150]

*Published by:* National Institute for Health and Care Excellence  
*Last published:* 2019

**BTS guidelines for the management of community acquired pneumonia in adults** [66]

*Published by:* British Thoracic Society  
*Last published:* 2009
Key articles


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    Abstract


    Abstract

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**Images**

*Figure 1*: Posterior-anterior chest radiograph showing right upper lobe consolidation in a patient with community-acquired pneumonia

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