in the clinic

Community-Acquired Pneumonia

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CME Objectives: To review prevention, diagnosis, treatment, and practice improvement for community-acquired pneumonia.

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Community-acquired pneumonia (CAP) can vary from a mild outpatient illness to a more severe disease requiring admission to a hospital or even an intensive care unit (ICU). Along with influenza, CAP is the eighth leading cause of death in persons older than age 65 in the United States and is the leading cause of death from infectious diseases. In contrast to hospital-acquired pneumonia, CAP occurs in the community. This distinction is becoming increasingly blurred because persons in contact with health care environments, such as nursing homes and chronic hemodialysis centers, and those recently discharged from the hospital may be infected with multidrug resistant organisms. These infections have been termed "health care–associated pneumonia." The key management decisions are recognizing and treating CAP in a timely and effective manner, defining the appropriate site of care (home, hospital, or ICU), and ensuring effective prevention.

Prevention

Who is at increased risk for CAP?

Persons with a comorbid illness and elderly persons are at increased risk for pneumonia and for having a more complex illness. In 2005, 1.3 million hospitalizations for pneumonia occurred in the United States, and approximately 60% were in persons older than 65 years (1). Comorbid illnesses that are associated with an increased incidence of CAP include respiratory disease, such as chronic obstructive pulmonary disease (COPD); cardiovascular disease; and diabetes mellitus. In addition, cigarette smoking and alcohol abuse are quite common in those with severe forms of CAP, and cigarette smoking is a risk factor for bacteremic pneumococcal infection (2). Other common illnesses in those with CAP include malignant conditions and any neurologic illness that predisposes to aspiration, including seizures.

Who should receive pneumococcal vaccination and when should they receive it?

All high-risk persons should be vaccinated. The timing of vaccination depends on the indication. All persons older than 65 years should be vaccinated, and risk factors should be reviewed for other persons, with a special effort in those older than 50 years. Vaccination should be offered to immunocompetent patients if they live in special environments, such as long-term care facilities; if they are Alaskan natives or American Indians; or if they have any of the following chronic illnesses: congestive heart failure, other cardiovascular disease, COPD, asthma, diabetes mellitus, alcoholism, chronic liver disease, cerebrospinal fluid leaks, or functional or anatomic asplenia (including sickle cell disease). Although vaccine efficacy may be reduced, immunocompromised patients should be vaccinated, including patients with HIV infection, leukemia, lymphoma, Hodgkin disease, multiple myeloma, generalized malignant conditions, chronic renal disease, nephrotic syndrome, and immunosuppressive therapy (including long-term corticosteroids).

Use the 23-valent polysaccharide vaccine in adults; the 7-valent conjugate vaccine that is used in children has not been approved for adults. In persons older than 65 years, revaccinate once after 5 years anyone who was initially vaccinated before age 65. Revaccinate immunocompromised patients once 5 years after the initial vaccination. Consider vaccinating anyone hospitalized for a medical illness, because they are at increased risk for pneumonia. Do not worry about harm from repeat vaccination, because less than 1% of patients who received at least 3 pneumococcal

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2. Nuorti JP, Butler JC, Farley MM, et al. Cigarette smoking and invasive pneumococcal disease. Active Bacterial Core Surveillance Team. N Engl J Med. 2000;342:681-9. [PMID: 10706897]
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vaccinations had an adverse reaction, and no reaction was severe, even if repeat vaccination was in less than 6 years (3).

Vaccination reduces the frequency of bacteremic pneumonia in healthy, immunocompetent adults. Randomized, controlled trials (RCTs) have not found reductions in the frequency of bacteremic pneumonia in adults with chronic illness, although case–control studies report reductions from 56% to 81%.

Efficacy in nonbacteremic illness is less certain. In 1 study of 47 365 patients older than age 65, pneumococcal vaccine reduced the incidence of pneumococcal bacteremia (odds ratio, 0.56) but had no impact on the frequency of CAP treated in or out of the hospital (4). In another study, pneumococcal vaccination reduced mortality, shortened the length of hospital stay, and decreased the frequency of respiratory failure and other complications (5).

Efficacy has not been established in patients with sickle cell disease, chronic renal failure, immunoglobulin deficiency, Hodgkin disease, lymphoma, leukemia, or multiple myeloma. Although the 7-valent conjugate vaccine may be more immunogenic in patients with sickle cell disease than the 23-valent polysaccharide vaccine, more data are needed, and necrotizing pneumonia caused by nonvaccine strains may be more frequent in children who receive this vaccine (6).

What is the role of influenza vaccination in the prevention of CAP and its complications?

All patients at increased risk for influenza complications and persons who can transmit the infection to high-risk patients, such as health care workers, should be immunized yearly.

In 1 meta-analysis of 20 studies, influenza vaccine was shown to reduce pneumonia by 53%, hospitalization by 50%, and mortality by 68% (7). In addition, observational studies suggest that influenza vaccine can reduce all-cause mortality during influenza season by 27% to 54% and be cost-effective because of its ability to reduce hospitalization rates for congestive heart failure and pneumonia in elderly persons (8). Recent analyses question these benefits, noting that few RCTs have been conducted in this population and that selection bias may lead to vaccination being given to healthier persons (9, 10).

Prevention... Elderly persons and those with a comorbid illness are at increased risk for pneumonia. Identify persons at risk for CAP and its complications and offer them pneumococcal and influenza vaccination. Offer influenza vaccine yearly to persons at risk for the disease, including health care workers. Repeat pneumococcal vaccination once after 5 years in persons who received the first dose before age 65 and in immunocompromised patients. Consider giving both vaccines to patients hospitalized with a medical illness.

CLINICAL BOTTOM LINE

Diagnosis

Which symptoms should lead clinicians to consider the diagnosis of CAP?

Pneumonia usually presents with both respiratory and systemic symptoms, particularly in young patients and in those with an intact immune response. It should be suspected when the patient has cough, purulent sputum, pleuritic chest pain, dyspnea, chills, fever, night sweats, and weight loss. Fever and chills have a sensitivity of 50% to 85%, but may be absent in elderly persons. Dyspnea has a sensitivity of 70% for the diagnosis of CAP, whereas purulent sputum has a sensitivity of only 50%. Hemoptysis suggests necrotizing infection, such as lung abscess, tuberculosis, or gram-negative pneumonia. Many older patients and those with

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chronic illness have a less-intense immune response, and the disease may go unrecognized because the patient has only nonrespiratory symptoms. These include confusion, weakness, lethargy, falling, poor oral intake, and decompensation of a chronic illness (for example, congestive heart failure). Most patients with CAP present with an acute illness of 1 to 2 days' duration, but symptoms may be present for longer in elderly persons.

Which organisms cause CAP?

The most commonly identified bacterial pathogens for CAP are *Streptococcus pneumoniae* (pneumococcus)*; Haemophilus influenzae;* and atypical pathogens, such as *Mycoplasma pneumoniae, Chlamydophila pneumoniae*, and *Legionella.* Drug-resistant pneumococcus (DRSP) is more likely to be the cause in patients older than 65 years and in those with alcoholism, noninvasive disease, antibiotic therapy within 3 months, multiple medical comorbid conditions, exposure to children in a day care center, or immunosuppressive illness (Table 1).

A cohort study of 3339 patients with invasive pneumococcal infection found that if the patient had received penicillin, macrolide, fluoroquinolone, or trimethoprim–sulfamethoxazole in 3 months before the onset of bacteremia, the organism was more likely to be resistant to the antibiotic that the patient had received (11).

Viruses also can cause CAP, and 1 recent study found that they were present in 18% of all patients who had paired serologies. The most common viral organisms were influenza and parainfluenza virus, followed by respiratory syncytial virus and adenovirus. Nearly half of these patients had viral infection as part of a mixed infection, often with bacterial pathogens (12, 13).

Gram-negative bacteria have been found in up to 10% of patients with CAP, particularly in those with a history of chronic cardiopulmonary disease, residence in a nursing home, multiple medical comorbid conditions, recent antibiotic therapy, renal insufficiency, chronic liver disease, diabetes, or active malignant conditions (14). *Pseudomonas aeruginosa* should be considered in persons with bronchiectasis, recent hospitalization, or recent antibiotic

Table 1. Modifying Factors That Increase the Risk for Infection With Specific Pathogens

Organism	Modifying Factor Putting Patient at Risk
Penicillin-resistant and drug-resistant pneumococci	Age >65 years
	β-lactam therapy within the past 3 months
	Alcoholism
	Immune-suppressive illness (including therapy with corticosteroids)
	Multiple medical comorbid conditions
	Exposure to a child in a day care center
Enteric gram-negative bacteria	Residence in a nursing home
	Underlying cardiopulmonary disease
	Multiple medical comorbid conditions
	Recent antibiotic therapy
Pseudomonas aeruginosa	Structural lung disease (bronchiectasis)
	Corticosteroid therapy (prednisone, >10 mg/d)
	Broad-spectrum antibiotic therapy for >7 d in the past month
	Malnutrition

therapy. Although anaerobic organisms should be considered when aspiration is a possibility (for example, in elderly patients with neurologic or swallowing disorders), in 1 study the most common organisms identified in those at risk for aspiration were gram-negative bacteria (15). *Klebsiella pneumoniae* has been reported in patients with alcoholism. Although some studies suggest that health care–associated pneumonia pathogens are more similar to those in hospital-acquired pneumonia than to those in CAP, not all studies confirm these findings. Patients with health care–associated pneumonia who are most at risk for drug-resistant organisms are those with poor functional status, severe illness, recent antibiotic therapy, and recent hospitalization. Methicillin-resistant *S. aureus* can occur in patients with health care–associated pneumonia and also in previously healthy persons after influenza (15, 16).

What is the role of history and physical examination in the diagnosis of CAP?

History and physical examination are valuable for suggesting the presence of pneumonia, for predicting the etiologic pathogen, and for helping to define the severity of illness. The history also should identify risk factors for health care–associated pneumonia, such as hospitalization or antibiotic therapy in the past 90 days, residence in a long-term care facility, chronic dialysis, outpatient wound care, or home infusion therapy. The history should also focus on recent travel to the southwestern United States (endemic fungi), or southeast Asia or China (melioidosis, epidemic viral pneumonia). Exposure to birds, bats, farm animals, and rabbits should also be documented.

Physical examination findings that suggest pneumonia include crackles, bronchial breath sounds, tachypnea, fever, and findings of pleural effusion. Specific findings that are associated with a poor outcome include a respiratory rate greater than 30 breaths/min, diastolic blood pressure less than 60 mm Hg, systolic blood pressure less than 90 mm Hg, heart rate greater than 125 beats/min, and temperature less than 35°C or greater than 40°C.

When should clinicians use chest radiography in the diagnosis of CAP?

Obtain a chest radiograph in any patient with clinical features suggesting CAP. Studies show that the clinical diagnosis of pneumonia is inaccurate; the clinical impression of pneumonia has an overall sensitivity ranging from 70% to 90%, and a specificity ranging from 40% to 70% (17).

When history and physical examination findings were used to predict the presence of radiographic pneumonia in a study of 129 patients with lower respiratory tract infection (26 with pneumonia), no combination of findings was highly accurate. The positive predictive value of each finding varied from 17% to 43% (18).

It is especially important to have a chest radiograph if the diagnosis is uncertain or if pleural effusion, lung abscess, necrotizing pneumonia, or multilobar illness is suspected. If a pleural effusion is present, obtain a decubitus film or computed tomography. Assume pneumonia is present in the absence of a radiographic infiltrate if the patient has a convincing history and focal physical findings. A follow-up radiograph may show an infiltrate. Interobserver variability in chest radiographic interpretation was shown in 1 study that compared the readings of at least 2 radiologists. Positive agreement (59%) was less frequent than negative agreement (94%) (19). Computed tomography may show an infiltrate when the chest radiograph is negative (20).

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What is the role of other laboratory tests in diagnosing CAP?

For outpatients, perform pulse oximetry to assess oxygenation. No other testing is needed.

For inpatients, additional testing is done to define disease severity and to identify pathogens. Measure arterial blood gasses in patients suspected of having carbon dioxide retention. Collect sputum for Gram stain and culture before starting therapy in patients suspected of infection with a drug-resistant or unusual pathogen, but only evaluate sputum if it is of good quality and is processed rapidly. Collect 2 sets of blood cultures, and test the urine for *Legionella* and pneumococcal antigens when patients have severe pneumonia. Limit blood cultures to patients with severe illness; they are positive in only 10% to 20% of all patients with CAP. Culture an endotracheal aspirate in patients who are intubated and mechanically ventilated. The utility of real-time polymerase chain reaction testing of sputum samples has not been demonstrated.

One recent study of 13 043 Medicare patients identified the following predictors of a true-positive blood culture: no previous antibiotics, underlying liver disease, systolic blood pressure less than 90 mm Hg, fever less than 35°C or greater than 40°C, pulse greater than 125/min, blood urea nitrogen greater than 10.71 mmol/L (30 mg/dL), serum sodium less than 130 mmol, and leukocyte count less than 5 or greater than 20×10^9 cells/L. The diagnostic yield of blood cultures increased in patients with 1 or more risk factor and in those who had not received antibiotics before blood was collected (21).

Even with extensive diagnostic testing, a specific etiologic diagnosis is obtained in less than half of all patients with CAP. Do not perform serologic tests for viruses and atypical pathogens, because they require convalescent titers 6 to 8 weeks after the initial test to identify infection. Establishing a specific etiologic diagnosis usually is not necessary, because empirical therapy

is effective. For example, when pathogen-directed treatment was compared with empirical treatment using a broad-spectrum antibiotic, the 2 groups did not significantly differ in the length of hospital stay, 30-day mortality, clinical failure, or resolution of fever (22).

Measurement of serum levels of C-reactive protein or procalcitonin may be helpful, although current guidelines do not recommend their use. C-reactive protein may identify which patients with acute respiratory symptoms have pneumonia; levels are higher in patients who require hospitalization and in patients with pneumococcal and *Legionella* infection. Low levels of procalcitonin identify patients who do not benefit from antibiotic therapy whereas persistently high levels identify patients who have a poor prognosis.

A randomized trial of 302 patients with CAP compared patients managed by usual care with those managed by an algorithm recommending the use of antibiotics and the duration of therapy on the basis of serial measurement of procalcitonin using the highly-sensitive Kryptor assay. Procalcitonin was measured on admission and after 6 to 24 hours, 4 days, 6 days, and 8 days. The procalcitonin-guided group had significantly fewer antibiotic prescriptions on admission and less antibiotic usage, and the duration of therapy was reduced from 12 to 5 days with similar clinical success (23).

What other disorders should clinicians consider in patients suspected of having CAP?

If the patient does not respond to empirical therapy after 48 to 72 hours, consider the possibility of viruses or unusual bacterial pathogens, such as *Mycobacterium tuberculosis*, *Coxiella burnetii* (Q fever), *Burkholderia pseudomalle* (melioidosis), *Chlamydia psittaci* (psittacosis), Paragonimiasis, Endemic fungi (histoplasmosis, coccidioidomycosis, blastomycosis), *Pasteurella multocida*, *Bacillus anthracis*, *Actinomyces Israeli*, *Francisella tularensis* (tularemia), *Leptospira* spp, *Nocardia* spp,

21. Metersky ML, Ma A, Bratzler DW, et al. Predicting bacteremia in patients with community-acquired pneumonia. Am J Respir Crit Care Med. 2004;169:342-7. [PMID: 14630621]
22. van der Eerden MM, Vlaspolder F, de Graaff CS, et al. Comparison between pathogen directed antibiotic treatment and empirical broad spectrum antibiotic treatment in patients with community acquired pneumonia: a prospective randomised study. Thorax. 2005;60:672-8. [PMID: 16061709]

Rhodococcus equi, and *Yersinia pestis* (plague). Also consider noninfectious possibilities, such as bronchiolitis obliterans, organizing pneumonia, pulmonary vasculitis, hypersensitivity pneumonitis, interstitial diseases, lung cancer, lymphangitic carcinoma, lymphoma, and congestive heart failure, particularly if the patient is younger than 55 years, is a nonsmoker, and has a nonfocal lung infiltrate. If the patient starts to respond to therapy and then his condition deteriorates, consider pulmonary embolus, antibiotic-induced colitis, empyema, meningitis, and endocarditis.

When should clinicians consider specialty consultation for the diagnosis of pneumonia, and which types of specialists should they consult?

Consultation is most valuable when patients do not respond to initial therapy. An infectious disease specialist can help identify unusual infections and infectious complications of pneumonia. A pulmonary specialist can help identify inflammatory lung disease and pulmonary embolus, perform a bronchoscopy, and perform a transbronchial biopsy. A surgeon can perform an open-lung biopsy.

Diagnosis... Clinical findings are less dramatic in elderly persons. History is particularly valuable for defining risk factors for specific pathogens, whereas physical findings help define disease severity. Confirm the diagnosis of CAP with a chest radiograph, although this test is not always diagnostic early in the course of illness. Laboratory testing has limited value; its main use is to define pneumonia severity and to identify systemic and respiratory complications. Diagnosing specific pathogens early is less useful because most initial therapy is empirical. If the patient does not respond to initial therapy, consult specialists and consider bronchoscopy and lung biopsy.

CLINICAL BOTTOM LINE

Treatment

How should clinicians determine whether a patient with CAP requires outpatient, inpatient, or ICU care?

Many site-of-care decisions can be facilitated with the Pneumonia Severity Index (PSI) or the British Thoracic Society (BTS) rule. These tools predict the risk for dying; patients with a high risk are generally managed in the hospital, and those with the highest risk are managed in the ICU. The PSI stratifies patients into 5 categories by using a scoring system based on patient age, comorbid illness, physical examination findings, and laboratory data. Patients in classes IV and V are generally admitted to the hospital, those in classes I and II are often treated as outpatients, and those in class III have the site-of-care decision based on careful clinical assessment. The BTS rule has been condensed into the "CURB-65," which is based on the presence of Confusion, blood Urea nitrogen greater than 7.0 mmol/L (19.6 mg/dL), Respiratory rate of 30 breaths/min or greater, systolic Blood pressure less than 90 mm Hg or diastolic blood pressure no greater than 60 mm Hg, and age 65 years or older. Patients meeting at least 2 of these criteria are usually admitted to the hospital, whereas those with at least 3 criteria are considered for ICU admission.

One prospective study of 3181 patients seen in 32 different emergency departments compared the PSI with the CURB and CURB-65 criteria and found that both approaches were successful in identifying low-risk patients. The CURB-65 was better for predicting mortality risk in high-risk patients (24).

23. Christ-Crain M, Stolz D, Bingisser R, et al. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: a randomized trial. Am J Respir Crit Care Med. 2006;174:84-93. [PMID: 16603606]
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27. Liapikou A, Ferrer M, Polverino E, et al. Severe community-acquired pneumonia: validation of the Infectious Diseases Society of America/American Thoracic Society guidelines to predict an intensive care unit admission. Clin Infect Dis. 2009;48:377-85. [PMID: 19140759]

28. Graham WG, Bradley DA. Efficacy of chest physiotherapy and intermittent positive-pressure breathing in the resolution of pneumonia. N Engl J Med. 1978;299:624-7. [PMID: 355879]

29. Li JZ, Winston LG, Moore DH, et al. Efficacy of short-course antibiotic regimens for community-acquired pneumonia: a meta-analysis. Am J Med. 2007;120:783-90. [PMID: 17765048]

In another prospective study of 1651 patients, measurement of serum procalcitonin supplemented the data obtained by prognostic scoring, and patients who had a low value of procalcitonin had a low mortality, regardless of PSI class or number of CURB-65 points (25).

Current guidelines suggest ICU care if the patient needs assisted ventilation or has septic shock requiring vasopressors or if the patient has at least 3 of the following: respiratory rate of 30 breaths/min or greater, PaO_2/FiO_2 ratio no greater than 250, multilobar infiltrates, confusion or disorientation, blood urea nitrogen 7.1 mmol/L (20 mg/dL) or greater, leukocyte count less than 4×10^9 cells/L, platelet count less than 100×10^9 cells/L, temperature less than 36°C, and hypotension requiring aggressive fluid resuscitation (26), although 1 study has questioned the utility of using only minor criteria to define the need for ICU care (27).

What is the role of nondrug therapies in treating CAP?

In outpatients, focus nondrug therapy on encouraging oral hydration. For hospitalized patients, nondrug therapies include intravenous hydration and oxygen for hypoxemia. Chest physiotherapy has not been widely studied, but it has been shown to improve the outcome of patients with pneumonia who have more than 30 mL/d of sputum and impaired clearance of secretions (28).

When using outpatient treatment for CAP, which antibiotics should clinicians prescribe?

For patients with no cardiopulmonary disease and no factors that increase risk for infection with DRSP or enteric gram-negative bacteria (Table 1), prescribe a macrolide (azithromycin, clarithromycin, or erythromycin) or doxycycline (Table 2). For outpatients who have cardiopulmonary disease or factors that increase the risk for infection with DRSP or enteric gram-negative bacteria, prescribe an antipneumococcal quionolone (gemifloxacin, levofloxacin, or moxifloxacin) or a combination of a β-lactam (amoxicillin, 3 g/d; amoxicillin–clavulanate, cefpodoxime, or cufuroxime) with a macrolide or doxycycline. If the patient has received an antibiotic in the past 3 months, avoid using an antibiotic in the same class.

How long should outpatients continue antibiotic treatment?

Base the duration of therapy on the patient's clinical response, severity of illness, and probable pathogen. Treat outpatients with mild-to-moderate CAP for 7 days or fewer if there is a good clinical response, no fever for 48 to 72 hours, and no sign of extrapulmonary infection. Azithromycin has such a long half-life that therapy for 1 or 3 days may be effective.

A meta-analysis of 15 RCTs of mild-to-moderate CAP found that therapy for 7 days or fewer was as effective as longer therapy with regard to clinical failure, mortality, adverse events, and bacteriologic eradication. The trials compared only monotherapies, and 13 of the short-duration trials used azithromycin, fluoroquinolones, or ketolides, which provide coverage for both pneumococcal and atypical pathogens. Only 2 short-duration trials used β-lactam monotherapy (29).

How should clinicians follow patients during outpatient treatment of CAP?

Up to 10% of patients initially managed at home do not respond to outpatient therapy and require hospitalization. To identify these patients early, the physician and patient should agree on a plan to monitor the response to therapy. Ask patients to measure an oral temperature every 8 hours and to report if it increases higher than 38.3°C (101°F) or if it does not decrease below 37.2°C (99°F) after 48 hours. Encourage patients to drink at least 1 to 2 quarts of liquid daily, and ask them to report if they cannot achieve this goal. Instruct patients to report symptoms of

Table 2. Drug Treatment for Community–Acquired Pneumonia

Agent	Mechanism of Action	Dosage	Benefits	Side Effects and Notes
Macrolides Azithromycin Clarithromycin	Bacteriostatic, binds to the 50S ribosomal subunit, and inhibits bacterial protein synthesis.	Azithromycin, 500 mg on day 1 (IV or PO), followed by 500 mg (IV or PO) for 7–10 d for hospitalized patients. 250 mg on d 2–5 for outpatients. Azithromycin in the microspheres oral extended-release formulation, 2 g on day 1 (PO) without follow-up dosing for outpatients. Clarithromycin, 500 mg bid PO, or 1000 mg/d PO (extended-release preparation) for outpatients.	Cover pneumococcus, atypical pathogens, and *Haemophilus influenzae*.	Nausea, vomiting, diarrhea, QT prolongation, dyspepsia (clarithromycin). Use as monotherapy only in patients without cardiopulmonary disease or modifying factors. Otherwise, combine with a β-lactam agent. Erythromycin is less expensive but not recommended because of the need for more frequent dosing, more intestinal upset, and no coverage of *H. influenzae*.
Penicillins Amoxicillin/clavulanate Ampicillin Ampicillin/sulbactam	Bactericidal, interferes with peptidoglycan cross-linking, and prevents formation of the bacterial cell wall.	Amoxicillin/clavulanate, 875 mg bid PO; Ampicillin, 500–1000 mg tid PO; Ampicillin/sulbactam, 1–2 g q6h IV.	Active against pneumococci and β-lactamase-producing *H. influenzae*.	Anaphylaxis, rash, nausea, vomiting, diarrhea, phlebitis, seizures (high doses), hypokalemia (high doses), elevated liver tests, prolonged prothrombin time (especially if on coumadin). Do not use alone in CAP. Combine with a macrolide.
Antipseudomonal β-lactams Piperacillin/tazobactam Cefepime Imipenem Meropenem	Bactericidal, interferes with peptidoglycan cross-linking, and prevents formation of the bacterial cell wall.	Piperacillin/tazobactam, 3.375 mg q4–6h IV; Cefepime, 1–2 g q12h IV; Imipenem, 1 g q8h IV or 500 mg q6h IV; Meropenem, 1 g q8h IV.	Active against pneumococci and *Pseudomonas aeruginosa*.	Anaphylaxis, rash, nausea, vomiting, diarrhea, phlebitis, seizures (high doses), hypokalemia (high doses), elevated liver tests, prolonged prothrombin time (especially if on coumadin). Seizure potential greater with imipenem than meropenem. Only use for patients with pseudomonal risk factors, although generally active against DRSP. Can dose daily if patient has renal insufficiency.
Cephalosporins Cefuroxime Cefpodoxime Ceftriaxone Cefotaxime	Bactericidal, interferes with peptidoglycan cross-linking, and prevents formation of the bacterial cell wall.	Cefuroxime, 500 mg bid PO; Cefpodoxime, 400 mg bid PO; Ceftriaxone, 1–2 g q12–24h (usually q24h); Cefotaxime, 1 g q8h.	Active against pneumococci and *H. influenzae*, including β-lactamase–producing organisms.	Anaphylaxis, rash, nausea, vomiting, diarrhea, elevated liver function test results, interstitial nephritis, altered coagulation, pseudomembranous colitis. Not to be used alone in CAP. Combine with a macrolide. Although cefuroxime can be used as oral therapy, it should not be used IV, because it is not as active against DRSP as other cephalosporins.
Quinolones Ciprofloxacin Gemifloxacin Levofloxacin Moxifloxacin	Bactericidal, interferes with bacterial DNA gyrase. Kills bacteria in a concentration-dependent fashion.	Ciprofloxacin, 400 mg q8-12h IV; Gemifloxacin, 320 mg/d (PO only); Levofloxacin, 750 mg/d (IV or PO); Moxifloxacin, 400 mg/d (IV or PO).	Ciprofloxacin and Levofloxacin are active against *P. aeruginosa*, atypicals, and *H. influenzae*. Levofloxacin and Moxifloxacin are the "respiratory quinolones" with activity against DRSP, *H. influenzae*, and atypical pathogens.	Seizures, hypersensitivity, photosensitivity, tendon rupture, nausea, vomiting, diarrhea, QT prolongation. Ciprofloxacin: only to be used in severe CAP. Not always reliable against pneumococci, and should be combined with other agents if DRSP is possible. If used in severe CAP, do not use as monotherapy.
Tetracyclines Doxycycline	Bacteriostatic, binds to 30S ribosomal subunit, and interferes with bacterial protein synthesis.	Doxycycline, 100 mg bid (IV or PO).	Active against key bacterial and atypical pathogens.	Nausea, vomiting, diarrhea, photosensitivity. Not always fully reliable against pneumococci.

bid = twice daily; CAP = community-acquired pneumonia; DNA = deoxyribonucleic acid; DRSP = drug-resistant Streptococcus pneumonia; IV = intravenous; PO = oral; tid = three times daily.

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chest pain, severe or increasing shortness of breath, or lethargy. Encourage patients to take their antibiotic therapy on schedule and to continue taking antibiotic therapy after they begin feeling better until they have taken all of it.

If the response to therapy is satisfactory, ask the patient to return for a repeat examination within 10 to 14 days. Give pneumococcal and influenza vaccinations if they have not previously been given. Obtain a repeat chest radiograph no sooner than 1 month after starting pneumonia therapy. Exclude lung cancer, immunodeficiency, and other possibilities during follow-up visits.

When patients require hospitalization for CAP, how soon after admission should antibiotics be started, and which antibiotics should patients receive if they do not need ICU care?

Patients should receive initial antibiotic therapy as soon as possible after the diagnosis of pneumonia is established and before the patient leaves the emergency department. A large Medicare study found that antibiotic administration within 4 hours of arrival to the hospital was associated with a lower mortality and a shorter length of stay. As a result, prompt antibiotic administration has become a widely used measure of the quality of pneumonia care (9, 30). However, delayed administration of antibiotics may be only a surrogate for other factors that are the direct causes of increased mortality; for example, immunocompromised patients probably have higher mortality rates and have atypical presentations that probably delay the start of therapy. Too strong a focus on timely antibiotic therapy can result in unnecessary antibiotic use in patients who do not have pneumonia. In 1 study, the final diagnosis of pneumonia in patients suspected of having pneumonia in the emergency department decreased from 75.9% to 58.9% after the initiation of a program to give more patients antibiotics within 4 hours of arrival in the emergency department (31).

Give hospitalized patients who are not in the ICU intravenous azithromycin if they have no cardiopulmonary disease and no factors that increase the risk for DRSP or gram-negative bacteria (26, 32). For hospitalized patients not in the ICU who have cardiopulmonary disease or factors that increase the risk for DRSP or gram-negative bacteria, give an intravenous quinolone (levofloxacin, 750 mg, when renal function is normal or moxifloxacin, 400 mg/d) or the combination of a β-lactam (cefotaxime, ceftriaxone, ampicillin–sulbactam, or high-dose ampicillin, but not cefuroxime) with a macrolide or doxycycline (26). The addition of a macrolide to a β-lactam has been associated with a reduction in mortality and length of hospital stay (33, 34) even for bacteremic pneumococcal pneumonia (35). Specific β-lactams are preferred if DRSP is suspected. Ceftriaxone and cefotaxime are as effective against DRSP with mean inhibitory concentration values up to 2 mg/L as they are against non-resistant organisms (36). Cefuroxime may not be an ideal β-lactam if DRSP is suspected, because 1 study showed increased mortality when this agent was used in patients with bacteremic DRSP (37).

One international study of 4337 hospitalized patients with CAP showed that approximately 20% had evidence of atypical pathogen infection and that therapy directed against these organisms decreased the time to clinical stability, length of stay, total mortality, and CAP-related mortality (38). However, another study of 2209 hospitalized Medicare patients with bacteremic pneumonia found that therapy directed at atypical pathogens led to reduced 30-day mortality and 30-day readmission rate, but the benefits occurred only with macrolides and not with fluoroquinolones (39).

Which antibiotics should be given to patients admitted to an ICU?

No patient in the ICU should receive empirical monotherapy. Assess these patients for risk factors for *P. aeruginosa*. Treat those without risk factors with intravenous ceftriaxone or cefotaxime plus either azithromycin or a quinolone, such as levofloxacin or moxifloxacin. Treat patients who have risk factors with an intravenous, antipseudomonal β-lactam (cefepime, piperacillin–tazobactam, imipenem, meropenem) plus an intravenous quinolone effective against *Pseudomonas* (ciprofloxacin or high-dose levofloxacin). Alternatively, treat patients who have risk factors with an intravenous, antipseudomonal β-lactam (cefepime, piperacillin–tazobactam, imipenem, meropenem) combined with an aminoglycoside (amikacin, gentamicin, or tobramycin) plus either an intravenous macrolide (azithromycin or erythromycin) or intravenous antipneumococcal quinolone (levofloxacin or moxifloxacin). In studies of patients admitted to the ICU with severe CAP, mortality was reduced when combination therapy was used; monotherapy, even with a quinolone, was not as effective. In general, the addition of a macrolide to therapy with a β-lactam (either a cephalosporin or β-lactam or β-lactamase inhibitor) led to the best outcomes (40). In patients with bacteremic pneumococcal pneumonia and critical illness, studies have found that mortality was lower with combination therapy than with monotherapy (41).

If community-acquired methicillin-resistant *S. aureus* is suspected, add either linezolid alone or vancomycin in combination with clindamycin, because both of these regimens are antibacterial and inhibit the production of bacterial toxins. Vancomycin alone is antibacterial but cannot inhibit toxin production (42). These regimens are recommended, even though the organisms are often sensitive in vitro to trimethoprim–sulfamethoxizole and quinolones.

What are the other components of ICU care for CAP?

Consider hydration, supplemental oxygen, and chest physiotherapy, but the major issue is ventilatory support for respiratory failure. Use intubation and mechanical ventilation in patients who have oxygen saturation less than 90% on maximal mask oxygen, inability to clear secretions, inability to protect the airway, or hypercarbia. If the patient has only hypoxemia or hypercarbia and is alert and cooperative, it may be possible to use noninvasive positive pressure ventilation, which may be associated with fewer complications than endotracheal intubation, including ventilator-associated pneumonia.

Consider systemic corticosteroids, especially if relative adrenal insufficiency is suspected. Because many patients with severe CAP also have systemic sepsis, consider using drotrecogin α, aggressive hydration, vasopressors, and measurement of serum lactate. Do not use granulocyte-colony stimulating factor routinely for patients with severe CAP.

In 1 study of 40 patients with severe CAP, when random serum cortisol levels were measured in the first 72 hours, 65% of patients met criteria for adrenal insufficiency, and 63% of the 19 patients with CAP and septic shock also had adrenal insufficiency (43). In 4 studies, including randomized trials, evidence was inconsistent for a benefit from routine corticosteroid therapy, but if the patient required this therapy for another reason (such as underlying COPD), corticosteroid therapy seemed to cause no harm (44).

In a randomized, placebo-controlled trial, drotrecogin α led to reduced mortality for patients with severe sepsis, including the 35.6% of patients who had severe CAP. Patients who were vasopressor-dependent and were treated with the drug had a relative risk reduction in mortality of 28% at 28 days. The survival benefit was most pronounced in patients with severe CAP and S. pneumoniae and in patients with severe CAP at high risk

37. International Pneumococcal Study Group. An international prospective study of pneumococcal bacteremia: correlation with in vitro resistance, antibiotics administered, and clinical outcome. Clin Infect Dis. 2003;37:230-7. [PMID: 12856216]
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for death as indicated by Acute Physiology and Chronic Health Evaluation II score 25 or greater, PSI score IV or greater, or CURB-65 score 3 or greater (45).

When can clinicians switch hospitalized patients from intravenous to oral antibiotics?

Switch from intravenous to oral antibiotics once the symptoms of cough, sputum production, and dyspnea improve; the patient is afebrile on 2 occasions 8 hours apart; and the patient is able to take medications orally. This switch can be made as early as 24 to 48 hours after admission and is made by day 3 in up to half of all patients. The switch to oral therapy can be done safely even if pneumococcal bacteremia has been documented, although these patients may take longer to respond. Longer durations of therapy may be needed for patients infected with *P. aeruginosa* or *S. aureus* or for those with extrapulmonary complications, such as empyema or meningitis. Select an oral regimen that covers all organisms isolated in blood or sputum cultures and reflects the intravenous therapy. For some patients, this will mean a β-lactam–macrolide combination or a quinolone alone. In patients who have responded to a β-lactam–macrolide combination, therapy can be continued on a macrolide alone unless cultures justify dual therapy.

To facilitate the switch to oral therapy, hospitals should consider using a standing order set supplemented by prospective case management. In a cohort study, patients were managed in each of 3 successive time periods with conventional therapy, a guideline-based order set supported by prospective case management that provided feedback to clinicians, and a guideline-based order set alone. In all 3 time periods, the time to clinical stability was similar, but prospective case management led to the greatest reductions in the time to oral antibiotics, time from oral therapy to discharge, and overall length of stay (46).

When should a consultation be requested for hospital patients, and which types of specialists or subspecialists should be consulted?

Ask for an infectious disease or pulmonary consultation if there are questions about the selection of initial antibiotic therapy or when the patient does not respond to initial therapy. Ask for a pulmonary or critical care consultant for patients with severe illness to help select antibiotics, decide about using vasopressors, determine the appropriate site of care, decide about the need for ventilatory support, and aid in managing the mechanical ventilator. Ask for a pulmonary consultant if a pleural effusion is documented and help is needed with a thoracentesis. Ask for a pulmonary or thoracic surgical consultation for placement of a chest tube if a complicated parapneumonic effusion or empyema is found on thoracentesis, because early therapy can reduce hospital stay and avoid complications. A thoracic surgeon can perform surgical decortication for advanced and loculated pleural effusion and empyema. A cardiology consultation may be needed if complications of cardiac ischemia or congestive heart failure occur. In a study of 170 patients with pneumococcal pneumonia, 19.4% had at least 1 major cardiac event, including 12 with acute myocardial infarction, 8 with new-onset atrial fibrillation or ventricular tachycardia, and 13 with newly diagnosed or worsening heart failure without other cardiac complications. The patients with cardiac events had a significantly higher mortality rate (27.3% vs. 8.8%) (47).

When can inpatients be discharged from the hospital?

Discharge patients once the switch to oral therapy is made, because no proven benefit exists for observation in the hospital. In 1 study, two-thirds of clinically stable patients were observed on oral therapy before discharge, and no deterioration occurred during this

44. Salluh JI, Póvoa P, Soares M, et al. The role of corticosteroids in severe community-acquired pneumonia: a systematic review. Crit Care. 2008;12:R76. [PMID: 18547407]
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period (48). Another study compared patients kept in the hospital for 1 day after the switch from intravenous to oral therapy with those who were discharged on the day of the switch. The study excluded patients with complicated pneumonia, those who were not eligible to be switched to oral therapy, and those with lengths of stay less than 3 days or more than 7 days. There were no differences in mortality or 14-day readmission rate (49). Therapy may need to continue after discharge, but usually the total duration of therapy is 5 to 7 days.

What are the indications for follow-up chest radiography?

Patients who are in the hospital for pneumonia management do not need a routine chest radiograph before discharge, but those who do not reach clinical stability and those who deteriorate despite therapy need an aggressive evaluation, including an early follow-up chest radiograph. If the patient has a good clinical response to therapy, a chest radiograph should not be repeated any earlier than 4 to 6 weeks after initial therapy. Radiographic resolution usually lags behind clinical resolution and can take 6 to 8 weeks or longer, but early improvement is usually substantial. In a prospective study of patients aged 70 years or older, 58% had a clear chest radiograph after 3 weeks, but it took 12 weeks until at least 75% had a radiographic resolution of CAP. Predictors of slow resolution included a high comorbidity index, bacteremia, multilobar involvement, and infection with enteric gram-negative bacteria (50).

How can patients prevent recurrent CAP?

Make sure that patients with community-acquired pneumonia have current pneumococcal and influenza vaccinations, avoid cigarette smoking, and receive optimal therapy for comorbid illnesses, such as congestive heart failure and COPD. In addition, carefully evaluate patients for medical conditions that could predispose to recurrent infection. One study found new comorbid conditions in 6% of patients with CAP, including diabetes mellitus, malignant conditions, COPD, and HIV infection (51). Evaluate the patient for aspiration risk factors. If pneumonia recurs in the same location, consider bronchiectasis, aspirated foreign body, or endobronchial obstruction. Consider immune deficiency if the patient has recurrent pneumonia or pneumonia with an unusual pathogen.

Treatment… The important clinical decisions in the treatment of CAP include determining the site of care (outpatient, hospital, or ICU), selecting antibiotic therapy, delivering supportive care (oxygen, hydration), and determining the need for ventilatory support. Antibiotic therapy differs for outpatients, inpatients, and for those in the ICU, but all patients should receive timely empirical therapy directed at pneumococcus, atypical pathogens, and other organisms when they have risk factors for those organisms. The Pneumonia Severity Index and the CURB-65 aid decisions about the site of care. Manage patients in the ICU if they require ventilatory or vasopressor support or close observation. Ask for a consultation when patients have severe disease, do not respond to initial therapy, or have complications. For inpatients, transition to oral antibiotics once the inpatient responds to treatment and is clinically stable, then proceed with discharge and outpatient management. Wait at least 4 to 6 weeks for routine follow-up chest radiography if the patient has a good response to therapy. During follow-up, evaluate patients for undiagnosed or ineffectively managed comorbid illness, make sure they have current pneumococcal and influenza vaccinations, and advise them to avoid cigarette smoking.

CLINICAL BOTTOM LINE

48. Rhew DC, Hackner D, Henderson L, et al. The clinical benefit of in-hospital observation in 'low-risk' pneumonia patients after conversion from parenteral to oral antimicrobial therapy. Chest. 1998;113:142-6. [PMID: 9440581]
49. Nathan RV, Rhew DC, Murray C, et al. In-hospital observation after antibiotic switch in pneumonia: a national evaluation. Am J Med. 2006;119:512.e1-7. [PMID: 16750965]
50. El Solh AA, Aquilina AT, Gunen H, et al. Radiographic resolution of community-acquired bacterial pneumonia in the elderly. J Am Geriatr Soc. 2004;52:224-9. [PMID: 14728631]
51. Falguera M, Martín M, Ruiz-González A, et al. Community-acquired pneumonia as the initial manifestation of serious underlying diseases. Am J Med. 2005;118:378-83. [PMID: 15808135]

What factors do U.S. stakeholders use to evaluate the quality of care for CAP?

The Center for Medicare & Medicaid Services (CMS) and the Joint Commission for the Accreditation of Healthcare Organizations (JCAHO) have endorsed a set of "core measures" for CAP, and CMS makes the data available on a public Web site. The current quality measures reported to CMS include whether or not patients with CAP are vaccinated for pneumococcus and influenza, get their first dose of antibiotics within 6 hours of arrival to the hospital, have appropriate antibiotics, have blood cultures within 24 hours of arrival to the hospital for patients admitted or transferred to the ICU, have blood cultures in the emergency department before initial hospital anti-biotics, and receive smoking cessation advice.

National adherence rates generally exceed 80% (9).

What do professional organizations recommend regarding the care of patients with CAP?

The 2007 guidelines from the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) recommended 4 performance measures: 3 regarding treatment and 1 regarding prevention (26). These performance measures include initial empirical antibiotic therapy consistent with guideline recommendations, delivery of the first dose of antibiotics in the emergency department (but not within a specific time) for patients admitted to the hospital, measurement of mortality, and determination of the percentage of at-risk patients in a physician's practice with influenza and pneumococcal vaccinations.

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in the clinic
Tool Kit

Community–Acquired Pneumonia

PIER Modules

http://pier.acponline.org/physicians/diseases/d104/d104.html

Access information about community-acquired pneumonia. PIER modules provide evidence-based, updated information on current diagnosis, treatment, and management in an electronic format designed for rapid access at the point of care.

Patient Information

www.annals.org/intheclinic/toolkit-cap.html

Acess the Patient Information material that appears on the following page for duplication and distribution to patients.

http://www3.niaid.nih.gov/topics/pneumonia/default.htm (English)
http://www3.niaid.nih.gov/topics/pneumonia/PDF/NeumoniaBacteriana.pdf (Spanish)

Access information written for patients by the National Institute of Allergy and Infectious Diseases.

Quality Measures

www.jointcommission.org/PerformanceMeasurement/PerformanceMeasurement/Pneumonia+Core+Measure+Set.htm

Access information about the Joint Commission's performance measurement initiative for pneumonia.

http://pier.acponline.org/qualitym/index.html

Access information about the quality measures included in the 2009 Physician Quality Reporting Initiative.

Clinical Guidelines

www.cdc.gov/mmwr/PDF/wk/mm5753-Immunization.pdf

Access the CDC's Advisory Committee on Immunization Practices (ACIP) 2009 update for the adult immunization schedule.

http://thorax.bmj.com/cgi/content/full/56/suppl_4/iv1

Access the British Thoracic Society's guidelines for the Management of Community Acquired Pneumonia in Adults.

www.journals.uchicago.edu/doi/pdf/10.1086/511159?cookieSet=1

Access the Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults.

www.acep.org/WorkArea/DownloadAsset.aspx?id=45809

Access the American College of Emergency Physicians' Clinical Policy on Critical Issues in the Management of Adult Patients Presenting to the Emergency Department With Community-Acquired Pneumonia.

in the clinic

WHAT YOU SHOULD KNOW ABOUT PNEUMONIA

What is pneumonia?

Pneumonia is an infection of the lungs.

What causes pneumonia?

Pneumonia can be caused by many viruses, bacteria, and sometimes fungi. The most common cause is a bacterium called pneumococcus.

How is it spread?

Pneumococcus is spread from persons who are ill or who carry the bacteria in their throat. You can get pneumococcal pneumonia from respiratory droplets from the nose or mouth of an infected person. It is common for people, especially children, to carry the bacteria in their throats without being sick.

What are the symptoms?

Pneumococcal pneumonia may begin suddenly. You may first have a severe shaking chill which is usually followed by:

- High fever
- Cough
- Shortness of breath
- Rapid breathing
- Chest pains

Other symptoms may include nausea, vomiting, headache, tiredness, and muscle aches.
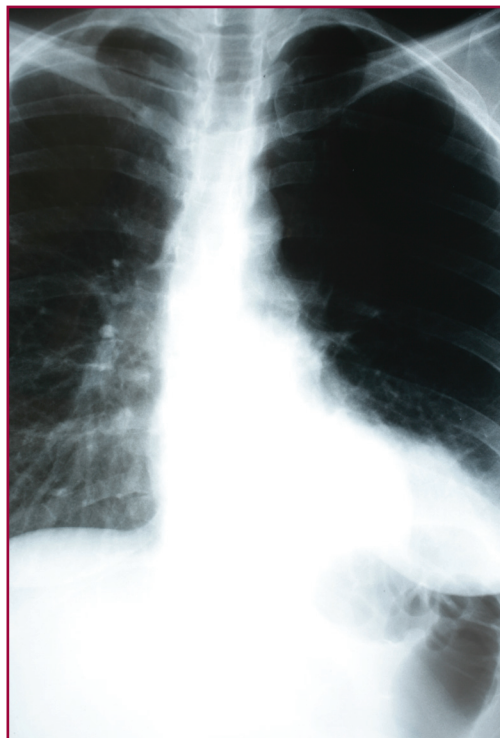
How is it treated?

Your health care provider usually will prescribe antibiotics to treat this disease. The symptoms of pneumococcal pneumonia usually go away within 12 to 36 hours after you start taking medicine.

For More Information

Web Sites With Good Information on Pneumonia

American Lung Association
www.lungusa.org/site/apps/nlnet/content3.aspx?c=dvLUK9O0E&tb=2060321&content_id={71CC3CFD-4B3E-49C8-AA88-D76EAE1FB9F5}&notoc=1

National Institute of Allergy and Infectious Diseases
http://www3.niaid.nih.gov/topics/pneumonia/default.htm (English)
http://www3.niaid.nih.gov/topics/pneumonia/PDF/NeumoniaBacteriana.pdf (Spanish)

Centers for Disease Control and Prevention
www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm (pneumococcal vaccine)
www.cdc.gov/vaccines/vpd-vac/flu/default.htm (influenza vaccine)

National Foundation for Infectious Disease
www.nfid.org/pdf/factsheets/pneuadult.pdf

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Patient Information

CME Questions

1. A 79-year-old woman is hospitalized for treatment of community-acquired pneumonia. The patient is frail but able to live at home. Two months ago, she had a urinary tract infection that was treated with ciprofloxacin. She had an apparent upper respiratory tract infection 7 days ago and developed left-sided pleuritic chest pain and shaking chills 1 day before admission.

   On physical examination, temperature is 38.7°C (101.7°F), pulse rate is 110/min and regular, respiration rate is 24 breaths per minute, and blood pressure is 90/60 mm Hg. Examination of the chest discloses crackles, diminished breath sounds at the left lung base, and egophony. The leukocyte count is 31×10^9 cells/L, with 85% segmented neutrophils and 7% band forms. The patient is unable to produce sputum for examination. A chest radiograph shows a left lower lobe pulmonary infiltrate.

   According to the hospital's antibiogram, local isolates of *Streptococcus pneumoniae* are often multiresistant (that is, 30% of isolates are resistant to penicillin, of which two thirds of these are high-grade resistance) and a similar number are resistant to macrolides.

   Which of the following is the most appropriate therapy for this patient at this time?

   A. Intravenous vancomycin plus ceftriaxone
   B. Intravenous ceftriaxone plus azithromycin
   C. Intravenous levofloxacin
   D. Oral telithromycin

2. A 35-year-old woman has a 3-day history of fever, productive cough, and wheezing. Her 2-year old son recently had a cough and fever to 38.9°C (102°F) that subsequently resolved. The patient has mild asthma that has not required treatment. She has a 10-pack-year smoking history but stopped smoking 3 years ago.

   On physical examination, she coughs frequently and has mildly audible wheezing. Temperature is 38.2°C (100.8°F), pulse rate is 100/min, respiration rate is 16 breaths/min, and blood pressure is 115/75 mm Hg. Examination of the chest reveals bronchial breath sounds and a few crackles in the lateral right lower chest near the mid-axillary line. Arterial oxygen saturation is 94% by pulse oximetry with the patient breathing room air.

   The leukocyte count is 11.9×10^9 cells/L with 80% neutrophils, 2% band forms, 14% lymphocytes, and 4% monocytes. A chest radiograph shows right middle lobe consolidation.

   In addition to starting inhaled bronchodilators, which of the following is most appropriate at this time?

   A. Await results of sputum culture before beginning therapy
   B. Begin trimethoprim–sulfamethoxazole
   C. Begin ciprofloxacin
   D. Begin azithromycin
   E. Begin gentamicin

3. A 72-year-old male smoker with chronic obstructive pulmonary disease was hospitalized 2 days ago because of patchy left lower lobe pneumonia accompanied by fever, cough, and dyspnea. His initial leukocyte count was 14.3×10^9 cells/L. Intravenous levofloxacin and supplemental oxygen, 2 L/min by nasal prongs, were started on admission.

   On hospital day 3, the patient has been afebrile for the past 18 hours. He has good oral intake, his cough has decreased, and he is no longer dyspneic. Arterial oxygen saturation is 92% by pulse oximetry with the patient breathing room air, and his leukocyte count is now 9.6×10^9 cells/L. A repeat chest radiograph shows no change in the size of the left lower lobe infiltrate.

   Which of the following is most appropriate at this time?

   A. Computed tomography of the chest
   B. Consultation for fiberoptic bronchoscopy
   C. Replacement of intravenous levofloxacin with oral levofloxacin
   D. Addition of intravenous ceftriaxone

4. A 73-year-old man has a 1-day history of increasing cough, dyspnea, fever, and chills. He has chronic obstructive pulmonary disease and type 2 diabetes mellitus complicated by mild azotemia. The patient has a 60-pack-year smoking history and continues to smoke. Current medications are inhaled ipratropium bromide, inhaled salmeterol, and glyburide.

   On physical examination, he is obese and in mild respiratory distress. Temperature is 38°C (100.4°F), pulse rate is 100/min, respiration rate is 20 breaths/min, and blood pressure is 135/85 mm Hg. Chest examination discloses decreased breath sounds bilaterally, scattered rhonchi, and a few crackles at the left base posteriorly. Arterial oxygen saturation is 86% by pulse oximetry with the patient breathing room air.

   The leukocyte count is 9.7×10^9 cells/L with 72% neutrophils, 10% band forms, and 18% lymphocytes. Blood urea nitrogen is 14.3 mmol/L (40 mg/dL), and serum creatinine is 112.16 µmol/L (2.4 mg/dL). A chest radiograph shows a patchy infiltrate at the left lung base. The patient is hospitalized.

   Which of the following is the most appropriate intravenous antibiotic therapy at this time?

   A. Ceftriaxone plus azithromycin
   B. Ampicillin–sulbactam
   C. Ticarcillin plus tobramycin
   D. High-dose penicillin
   E. Trimethoprim–sulfamethoxazole