CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., Editor

Community-Acquired Pneumonia

Richard G. Wunderink, M.D., and Grant W. Waterer, M.B., B.S., Ph.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

A 67-year-old woman with mild Alzheimer's disease who has a 2-day history of productive cough, fever, and increased confusion is transferred from a nursing home to the emergency department. According to the transfer records, she has had no recent hospitalizations or recent use of antibiotic agents. Her temperature is 38.4°C (101°F), the blood pressure is 145/85 mm Hg, the respiratory rate is 30 breaths per minute, the heart rate is 120 beats per minute, and the oxygen saturation is 91% while she is breathing ambient air. Crackles are heard in both lower lung fields. She is oriented to person only. The white-cell count is 4000 per cubic millimeter, the serum sodium level is 130 mmol per liter, and the blood urea nitrogen is 25 mg per deciliter (9.0 mmol per liter). A radiograph of the chest shows infiltrates in both lower lobes. How and where should this patient be treated?

THE CLINICAL PROBLEM

Pneumonia is sometimes referred to as the forgotten killer. The World Health Organization estimates that lower respiratory tract infection is the most common infectious cause of death in the world (the third most common cause overall), with almost 3.5 million deaths yearly.¹ Together, pneumonia and influenza constitute the ninth leading cause of death in the United States, resulting in 50,000 estimated deaths in 2010.² This number is probably underestimated, since deaths from sepsis (for which pneumonia is the most common source)³ and deaths attributed to other conditions (e.g., cancer and Alzheimer's disease) for which pneumonia is the terminal event are coded separately.

Community-acquired pneumonia that is severe enough to require hospitalization is associated with excess mortality over the subsequent years among survivors,⁴⁻⁶ even among young people without underlying disease.⁵ Admission to the hospital for community-acquired pneumonia is also costly, especially if care in an intensive care unit (ICU) is required.⁷

Because of the economic cost, associated mortality, and heterogeneity of management, community-acquired pneumonia has been a focus of Centers for Medicare and Medicaid Services (CMS) and the Joint Commission (TJC) quality-improvement efforts, public reporting of outcomes, and possible pay-for-performance initiatives.⁸ This article focuses on management strategies for community-acquired pneumonia, with particular emphasis on interventions to reduce mortality and costs.

STRATEGIES AND EVIDENCE

DIAGNOSIS

The diagnosis of community-acquired pneumonia is not difficult in patients who do not have underlying cardiopulmonary disease. A triad of evidence of infection From the Division of Pulmonary and Critical Care Medicine, Northwestern University Feinberg School of Medicine, Chicago (R.G.W., G.W.W.); and the University of Western Australia, Perth (G.W.W.). Address reprint requests to Dr. Wunderink at r-wunderink@northwestern.edu.

N Engl J Med 2014;370:543-51. DOI: 10.1056/NEJMcp1214869 Copyright © 2014 Massachusetts Medical Society

49

An audio version of this article is available at NEJM.org

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

KEY CLINICAL POINTS				
COMMUNITY-ACQUIRED PNEUMONIA				
• Con wor	nmunity-acquired pneumonia remains a leading cause of death in the United States and around th ld.			
	ough the diagnosis of community-acquired pneumonia is straightforward in most cases, underly- cardiopulmonary disease and atypical presentation in elderly persons can delay recognition.			
	majority of hospitalized patients with community-acquired pneumonia can be treated with er a respiratory fluoroquinolone or a combination of cephalosporin and a macrolide.			
care syne	rnative antibiotic treatment should be based on the presence of multiple risk factors for health —associated pneumonia, specific risks (e.g., structural lung disease), or uniquely characteristic dromes (e.g., the toxin-mediated, community-acquired, methicillin-resistant <i>Staphylococcus aureus</i> drome).			
anti	current criteria for health care–associated pneumonia result in excessive use of broad-spectrum biotic agents. The presence of multiple pneumonia-specific alternative risk factors may allow used diagnostic testing and treatment.			
urea	ents with three or more minor criteria for severe community-acquired pneumonia (e.g., elevated blood n nitrogen, confusion, and a high respiratory rate) should receive extensive intervention in the emer- cy department and be considered for admission to the intensive care unit.			

(fever or chills and leukocytosis), signs or symptoms localized to the respiratory system (cough, increased sputum production, shortness of breath, chest pain, or abnormal pulmonary examination), and a new or changed infiltrate as observed on radiography usually accurately identifies a patient with community-acquired pneumonia. Table 1 reviews the differential diagnosis of community-acquired pneumonia.

In patients with lung cancer, pulmonary fibrosis or other chronic infiltrative lung disease, or congestive heart failure, the diagnosis of community-acquired pneumonia can be very difficult. Atypical presentations also complicate diagnosis. Confusion may be the only presenting symptom in elderly patients, leading to a delay in diagnosis.⁹ Infiltrates on radiographs may also be subtle: an individual radiologist may miss infiltrates in up to 15% of cases, and two radiologists reading the same chest radiograph disagree in 10% of cases.¹⁰

INITIAL MANAGEMENT

Choice of Antibiotic Therapy

Three interrelated decisions must be made almost simultaneously when a patient first presents — the choice of antibiotic therapy, the extent of testing to determine the cause of the pneumonia, and the appropriate location of treatment (home, inpatient floor, or ICU). Numerous antibiotics are approved for the treatment of community-acquired pneumonia by the Food and Drug Administration on the basis of randomized, controlled trials comparing them to other antibiotics previously approved for community-acquired pneumonia. The key to appropriate therapy is adequate coverage of *Streptococcus pneumoniae* and the atypical bacterial pathogens (mycoplasma, chlamydophila, and legionella).

For outpatients, the coverage of atypical bacterial pathogens is most important, especially for young adults, for whom herd immunity from widespread vaccination of infants and children with a conjugate pneumococcal vaccine has decreased the rates of pneumococcal pneumonia.¹¹ The primary factors in the choice of agent for a particular episode among the large number of approved oral antibiotics are recent antibiotic use (which may be associated with a risk of class resistance¹²) and cost. Macrolides, doxycycline, and fluoroquinolones are the most appropriate agents for the atypical bacterial pathogens.

For patients admitted to a regular hospital unit, guidelines from the Infectious Diseases Society of America and the American Thoracic Society (IDSA–ATS) recommend first-line treatment with either a respiratory fluoroquinolone (moxifloxacin at a dose of 400 mg per day or levofloxacin at a dose of 750 mg per day) or the

N ENGLJ MED 370;6 NEJM.ORG FEBRUARY 6, 2014

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

combination of a second-generation or third-generation cephalosporin and a macrolide.¹³ These recommendations are based primarily on large inpatient administrative databases that show reduced mortality with recommended antibiotics as compared with other antibiotics or combinations.^{14,15} Quality-improvement projects also consistently show that as adherence to these recommended antibiotics increases, mortality and length of hospital stay decrease.^{16,17}

Although *S. pneumoniae* remains the most common cause of severe community-acquired pneumonia requiring ICU admission, combination therapy consisting of a cephalosporin with either a fluoroquinolone or a macrolide is recommended.¹³ Observational evidence suggests that the macrolide combination may be associated with better outcomes.^{15,18,19} Since fluoroquinolones have essentially the same antibacterial spectrum as macrolides, the better outcome with macrolides may be explained by nonbactericidal effects, such as immunomodulation.

Timing of Initiation of Therapy

A CMS-TJC quality metric for community-acquired pneumonia is administration of the first antibiotic dose within 6 hours after presentation.8 This cutoff was modified from retrospective analyses of large Medicare databases^{20,21} showing that an interval of more than 4 hours between the initial presentation and the first antibiotic dose was associated with increased in-hospital mortality. However, efforts to decrease the time to the first administration of antibiotic therapy have resulted in an increase in inappropriate antibiotic use in patients who do not have community-acquired pneumonia, with adverse consequences such as Clostridium difficile colitis,²² and have not resulted in corresponding decreases in mortality.23,24 A shorter time to antibiotic administration may simply be a marker of multiple beneficial care patterns (e.g., less crowding in the emergency department, prompt fluid resuscitation, and the recognition of and early intervention for incipient respiratory failure) that are associated with improved patient outcomes.25,26

The current IDSA–ATS guidelines do not recommend a specific time to the administration of the first antibiotic dose but instead encourage treatment as soon as the diagnosis is made.¹³ An exception is made for patients in shock; antibiotics should be given within the

Pneumonia.
Abnormal chest radiograph
Congestive heart failure with associated viral syndrome to explain infectious symptoms
Aspiration pneumonitis
Pulmonary infarction
Acute exacerbation of pulmonary fibrosis
Acute exacerbation of bronchiectasis
Acute eosinophilic pneumonia
Hypersensitivity pneumonitis
Pulmonary vasculitis
Cocaine-induced lung injury ("crack lung")
Normal chest radiograph
Acute exacerbation of chronic obstructive pulmonary disease
Influenza
Acute bronchitis
Pertussis
Asthma with associated viral syndrome to explain infec- tious symptoms

first hour after the onset of hypotension. An observational study involving patients with septic shock showed a decrease in survival rates of 8% for each hour of delay.²⁷

Duration of Antibiotic Treatment

The currently recommended duration of antibiotic therapy for community-acquired pneumonia is 5 to 7 days.¹³ There is no evidence that prolonged courses lead to better outcomes, even in severely ill patients, unless they are immunocompromised.

TREATMENT OF PATIENTS AT RISK FOR RESISTANT ORGANISMS

Although the above recommendations apply to the majority of patients with community-acquired pneumonia, physicians need to identify patients who are at increased risk for bacteria resistant to these empirical antibiotic regimens. Most common among these are patients with risk factors for health care–associated pneumonia (Table 2).²⁸ Health care–associated pneumonia has been categorized as a discrete entity, with the goal of identifying patients with pneumonia that develops outside the hospital yet is caused by pathogens usually associated with hospital-acquired pneumonia or even ventilator-associated pneumonia,

N ENGLJ MED 370;6 NEJM.ORG FEBRUARY 6, 2014

545

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

Table 2. Criteria for Health Care-Associated Pneumonia.	Table 3. Clinical Features Suggesting Community- Acquired MRSA Pneumonia.*
Original criteria [*] Hospitalization for ≥2 days during the previous 90 days Residence in a nursing home or extended-care facility Long-term use of infusion therapy at home, including antibiotics Hemodialysis during the previous 30 days Home wound care Family member with multidrug-resistant pathogen	Cavitary infiltrate or necrosis Rapidly increasing pleural effusion Gross hemoptysis (not just blood-streaked) Concurrent influenza Neutropenia Erythematous rash Skin pustules
Immunosuppressive disease or therapy† Pneumonia-specific criteria;	Young, previously healthy patient Severe pneumonia during summer months
Hospitalization for ≥2 days during the previous 90 days Antibiotic use during the previous 90 days Nonambulatory status	* MRSA denotes methicillin-resistant <i>Staphylococcus aureus</i> .
Tube feedings Immunocompromised status Use of gastric acid suppressive agents	pulmonary disease [COPD]) who have receiv multiple courses of outpatient antibiotics; t frequency of <i>P. aeruginosa</i> infection is particula increased in this population. ¹³

* Original criteria are from the American Thoracic Society and Infectious Diseases Society of America.28

† This criterion was not included in the original criteria but is frequently included in many studies of health careassociated pneumonia.

‡ Pneumonia-specific criteria are from Shindo et al.²⁹

including methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant (MDR) gram-negative pathogens.

In reports of data from tertiary care centers, patients with culture-positive health care-associated pneumonia were more likely than patients who did not meet the definition for health careassociated pneumonia to have these resistant pathogens and to receive initially inappropriate antibiotic therapy, which has been associated with increased mortality among these patients.30,31 Empirical broad-spectrum therapy with dual coverage for Pseudomonas aeruginosa and routine MRSA coverage has therefore been recommended for patients with risk factors for health care-associated pneumonia (Table 2).28 However, there is increasing recognition that using all these risk factors as indications for broad-spectrum therapy may lead to antibiotic overtreatment of many patients. The appropriate criteria for initial broadspectrum therapy remain controversial (see the Areas of Uncertainty section). Another group of patients at risk for pathogens resistant to the usual antibiotics for community-acquired pneumonia are those with structural lung disease (bronchiectasis or severe chronic obstructive

ved the arly increased in this population. Whereas MRSA is commonly identified in

patients with risk factors for health care-associated pneumonia, a community-acquired strain of MRSA that causes community-acquired pneumonia in previously healthy patients without health care-associated pneumonia or other risk factors for MDR pathogens has increasingly been recognized.32,33 Exotoxin production by this strain (as well as by the methicillin-sensitive variant) results in characteristic presenting features (Table 3). Because the clinical presentation of this infection is disproportionately exotoxin-mediated, treatment is recommended with antibiotics that suppress toxin production, such as linezolid or clindamycin (added to vancomycin); these regimens have been associated with reduced mortality.33

DIAGNOSTIC TESTING

The extent of testing that is warranted to identify the causative microorganism in communityacquired pneumonia is controversial. Because the recommended antibiotic regimens are effective for the majority of patients, diagnostic testing will rarely affect therapy. Table 4 reviews conditions in which specific testing may lead to different treatment. Extensive diagnostic testing is most helpful in patients with risk factors for health care-associated pneumonia3 or with severe community-acquired pneumonia requiring ICU admission,¹³ in whom the probability of the presence of bacteria that are resistant to usual therapy is greatest.

N ENGLJ MED 370;6 NEJM.ORG FEBRUARY 6, 2014

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

Influenza testing in the appropriate season is the diagnostic test that is most likely to affect treatment. Depending on current local influenza rates, antiviral treatments may be started empirically and stopped if testing is negative, or they may be started only in response to a positive test.

SITE OF CARE

Hospital Admission

A physician's decision to hospitalize a patient with community-acquired pneumonia is the major determinant of cost. Between 40% and 60% of patients who present to the emergency department with community-acquired pneumonia are admitted.³⁴⁻³⁶ Considerable variation in this decision among patients with similar clinical characteristics emphasizes the opportunity for standardization.

Scoring systems that predict short-term mortality, such as the Pneumonia Severity Index (PSI)³⁵ and the CURB-65 scores,³⁶ were developed specifically to make admission decisions more objective. Use of the PSI results in fewer admissions of patients with mild illness, with no increase in adverse outcomes.34 However, calculating the PSI score is complex, requiring formal scoring or electronic decision support (http:// pda.ahrq.gov/clinic/psi/psicalc.asp). The CURB-65 score (which assigns 1 point each for confusion, uremia [blood urea nitrogen ≥20 mg per deciliter], respiratory rate ≥ 30 breaths per minute, systolic blood pressure <90 mm Hg or diastolic blood pressure $\leq 60 \text{ mm Hg}$, and age $\geq 65 \text{ years}$, with a score \geq 3 indicating the need for hospitalization) is easy to remember and calculate but has not been as well validated as the PSI score. Although both scores are valid for the analysis of groups of admissions for quality improvement or research in community-acquired pneumonia, individual decisions that are inconsistent with the score are often made for legitimate reasons, both objective (e.g., low arterial saturations) and subjective (e.g., unreliable home support and concern regarding adherence to therapy).

ICU Admission

Decisions regarding initial admission to the ICU of patients with community-acquired pneumonia and questionable cardiopulmonary stability probably have the greatest potential effect on mortality. Patients transferred to the ICU within 48 hours

-						
Condition and Response to Test Result	Blood Culture	Respiratory Tract Culture	Influenza Test during Influenza Season	Test for Urinary Pneumococcal Antigen	Test for Urinary Legionella Antigen	Pleural-Fluid Culture
Severe community- acquired pneumonia†	Strongly recommended if the patient is hypotensive or if patient has been trans- ferred from a general medical unit to the ICU	Strongly recommended if there is tracheal aspirate or bronchoalveolar-lavage aspirate in an intubated patient; recommended if there is productive cough in a nonintubated patient	Strongly recommended	Strongly recommended	Strongly recommended	Strongly recommended
Health care–acquired pneumonia	Recommended	Strongly recommended if there is a pro- ductive cough; not recommended if there is no cough	Recommended	Strongly recommended	Recommended if patient resides in a nursing home	Strongly recommended
Other condition or circumstance	Recommended if there is cirrhosis or asplenia	Recommended if the patient has struc- tural lung disease or severe COPD with productive cough	Recommended	No specific recommendation	Recommended if pa- tient has traveled recently	Strongly recommended
Strategy if test result positive	Change to specific therapy	Change to specific therapy	Add or continue oseltamivir	Change to narrow antibiotic therapy	Change to specific ther- apy; public report- ing and potential point-source inves- tigation	Change to specific therapy; perform drainage proce- dure

Severe community-acquired pneumonia is defined as community-acquired pneumonia for which admission to the intensive care unit is being considered

N ENGLJ MED 370;6 NEJM.ORG FEBRUARY 6, 2014

547

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

after initial admission to a general medical service have higher mortality than those with an obvious need for ICU care (mechanical ventilation or hypotension requiring vasopressors) at the time of admission.^{26,37,38} However, no prospective studies have been performed to establish whether initial admission to the ICU of patients without these major criteria for ICU admission would prevent subsequent deterioration better than initial admission to a general unit.

The percentage of hospitalized patients with pneumonia who are admitted to the ICU also varies widely (ranging from 5 to 20%) depending on hospital and health-system characteristics.^{26,39-41} Because the PSI and CURB-65 scores have limited ability to identify patients whose condition is likely to deteriorate if they are admitted to a general ward, the IDSA-ATS guidelines suggest that the presence of three or more of nine minor criteria should warrant consideration of ICU admission (Table 5).13 Other scores for predicting clinical deterioration have also been developed and validated.³⁹⁻⁴¹ For each of these scores, the probability of the need for invasive ventilatory or vasopressor therapy increases with higher numbers of criteria met or points tallied. These scores have many variables in common (Table 5) and use a similar threshold score (approximately 3) to consider ICU admission. If followed rigidly, all result in substantially more ICU admissions of patients who will never need ICU-level interventions.13,26

The most appropriate use of these scores may be to focus attention on patients who have high scores while still in the emergency department. A quality-improvement study showed that increased attention in the emergency department to patients with three or more IDSA-ATS minor criteria resulted in a decrease in mortality (from 23 to 6%) and fewer floor-to-ICU transfers (from 32 to 15%) without substantially increasing direct ICU admissions.²⁶ Potentially useful interventions include aggressive fluid resuscitation,⁴² prompt initiation of appropriate antibiotics, measurement of arterial blood gas in patients with borderline hypoxemia or lactate in those with borderline hypotension, and treatment of coexisting illnesses (e.g., administration of bronchodilators for asthma and COPD); reassessment after such interventions can clarify the trajectory of the patient's illness.26

AREAS OF UNCERTAINTY

Concerns have been raised that the original definition of health care-associated pneumonia, with the associated recommendation for broad-spectrum antibiotic treatment, results in overuse of antibiotics. The group of risk factors included in the original definition of health care-associated pneumonia (Table 2) were extrapolated from studies of health care-associated bacteremia²⁸ and may therefore not be entirely appropriate for pneumonia. As compared with early observational studies of culture-positive cases that suggested benefits of broad-spectrum antibiotic therapy in persons with these risk factors,^{30,31} subsequent prospective studies of patients with health careassociated pneumonia have shown markedly lower rates of antibiotic-resistant pathogens and high rates of culture-negative cases.29,43,44 The use of risk factors for health care-associated pneumonia as the basis for antibiotic choices results in broad-spectrum treatment of almost half the patients with community-acquired pneumonia in some centers.29,30

Of particular concern are findings that suggest increased risks of adverse outcomes among persons who are treated with broad-spectrum antibiotics for health care-associated pneumonia, although selection bias cannot be ruled out as an explanation for these findings.29,45,46 A multicenter quality-improvement project showed increased mortality in association with broadspectrum therapy in such patients.⁴⁵ Similarly, an analysis that included patients with risk factors for health care-associated pneumonia who were treated at Veterans Affairs medical centers showed higher mortality among those who were given broad-spectrum therapy than among those who received standard treatment for communityacquired pneumonia.46

The most appropriate criteria for identifying patients who should receive initial empirical broadspectrum coverage are unclear. A recent prospective, multicenter study identified six risk factors (Table 2) for pneumonia caused by pathogens resistant to the usual inpatient antibiotic regimens recommended by IDSA–ATS guidelines.²⁹ These pneumonia-specific risk factors are consistent with those cited in other reports that indicate that recent antibiotic use or hospitalization and poor functional status are more important

N ENGLJ MED 370;6 NEJM.ORG FEBRUARY 6, 2014

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

Table 5. Criteria for Consideration of ICU Admission for Patients without an Obvious Need.*					
Criterion	Definition	Other Scoring System or Strategy with Similar Criterion			
IDSA-ATS minor criteria					
Confusion	None specified	SMART-COP, ³⁹ CURXO, ⁴¹ and REA-ICU ⁴⁰			
Elevated blood urea nitrogen	Blood urea nitrogen ≥20 mg/dl	CURXO ⁴¹ and REA-ICU ⁴⁰			
Tachypnea	Respiratory rate ≥30 breaths/min	SMART-COP, ³⁹ CURXO, ⁴¹ and REA-ICU ⁴⁰			
Multilobar infiltrates ob- served on radiograph	None specified	SMART-COP, ³⁹ CURXO, ⁴¹ and REA-ICU ⁴⁰			
Hypoxemia	Ratio of partial pressure of oxygen in arterial blood to fraction of inspired oxygen <250 mm Hg	SMART-COP, ³⁹ CURXO, ⁴¹ and REA-ICU ⁴⁰			
Thrombocytopenia	<100,000 platelets/mm ³	—			
Hypotension	Hypotension (systolic pressure <90 mm Hg) requiring aggressive fluid resuscitation	SMART-COP ³⁹ and CURXO ⁴¹			
Hypothermia	Core temperature of <36°C	—			
Leukopenia	White-cell count <4000/mm ³	REA-ICU ^{₄o}			
Other criteria					
Lactic acidosis	Lactic acid level ≥4 mmol/liter	Early goal-directed therapy ⁴²			
Low pH	<7.30–7.35, depending on scoring system†	SMART-COP, ³⁹ CURXO, ⁴¹ and REA-ICU, ⁴⁰ depending on pH†			
Low albumin	<3.5 g/dl	SMART-COP ³⁹			
Hyponatremia	Sodium level <130 mmol/liter	REA-ICU ⁴⁰			
Leukocytosis	Leukocyte count >20,000/mm ³	REA-ICU ⁴⁰			
Tachycardia	Heart rate ≥125 beats/min	SMART-COP ³⁹ and REA-ICU ⁴⁰			
Older age	>80 yr	CURXO ⁴¹ and REA-ICU ⁴⁰			

* A patient without an obvious need was defined as one who did not require endotracheal intubation and mechanical ventilation or as one who did not have hypotension requiring vasopressors while in the emergency department. Risk increases proportionally with the presence of more than three criteria. IDSA-ATS denotes Infectious Diseases Society of America-American Thoracic Society, and REA-ICU Risk of Early Admission to ICU.

The criterion of a pH level of less than 7.30 is used in the calculation of the CURXO⁴¹ score. The criterion of a pH level of less than 7.35 is used in the calculation of the SMART-COP³⁹ and REA-ICU⁴⁰ scores.

home residence alone.47

Available data suggest that the incidence of MDR pathogens generally is not significantly increased unless three or more risk factors are present.²⁹ However, MRSA is an exception: the presence of one MRSA-specific risk factor (prior MRSA infection or colonization, long-term hemodialysis, or heart failure) and another pneumonia-specific risk factor may warrant MRSA coverage (but not dual antipseudomonal antibiotics).29 The importance of distinguishing between health care-associated pneumonia and community-acquired pneumonia depends on the local prevalence of antibiotic-resistant patho-

predictors of resistant pathogens than nursing gens, which varies markedly within the United States, highlighting the value of knowledge of local epidemiologic data.

> Data from randomized trials are lacking to guide treatment in patients with culture-negative health care-associated pneumonia.29,43 Whereas studies indicate that initially inappropriate empirical antibiotic therapy for health care-associated pneumonia is associated with increased mortality among patients with culture-positive cases,^{30,31} observational data suggest that a switch to traditional antibiotic regimens for community-acquired pneumonia is safe when cultures are negative,43 and such treatment may be associated with reduced mortality.29 Targeted diagnostic testing

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

allows the de-escalation of therapy if cultures are negative (or positive for typical communityacquired pneumonia pathogens).

GUIDELINES

The IDSA–ATS guidelines for community-acquired pneumonia were published 7 years ago,¹³ but little has changed regarding antibiotic treatment of community-acquired pneumonia, and the recommendations in this article are generally consistent with these guidelines. Criteria and antibiotic recommendations for health care–associated pneumonia from the older guidelines for hospitalacquired and ventilator-acquired pneumonia²⁸ are outdated. The discussion of health care–associated pneumonia has been removed from the planned update of the guidelines for hospitalacquired and ventilator-acquired pneumonia and will be incorporated in a future guideline by these organizations.

The IDSA–ATS guidelines for communityacquired pneumonia differ only slightly from non-U.S. guidelines. European guidelines keep the option of beta-lactam monotherapy and deemphasize the use of fluoroquinolones in hospitalized patients outside the ICU.⁴⁸

CONCLUSIONS AND RECOMMENDATIONS

The woman described in the vignette has a CURB-65 score of 4, suggesting that she would benefit from inpatient therapy.³⁴ She has at least

four minor criteria for severe community-acquired pneumonia (confusion, respiratory rate \geq 30 breaths per minute, multilobar infiltrates, and uremia). Although ICU admission may be prudent, she would clearly benefit from further evaluation. We would measure the arterial blood gas and lactate levels, given the high respiratory rate and low saturation, and hydrate aggressively.

As a nursing home resident, the patient meets the current criteria for health care–associated pneumonia. However, since she has no pneumonia-specific MDR risk factors but does have risk factors for severe community-acquired pneumonia, we would initiate treatment with ceftriaxone and azithromycin. Influenza testing should be requested if she has presented during the appropriate season, and empirical oseltamivir started if the local influenza rate is high. We would not obtain blood cultures or attempt to obtain sputum cultures because of the low likelihood of the presence of pathogens resistant to usual treatment for community-acquired pneumonia.

Dr. Wunderink reports receiving fees for board membership from Pfizer, AstraZeneca, and Achaogen; consulting fees from Crucell (Johnson & Johnson), Accelerate Diagnostics, Bayer Healthcare, Sanofi, and GlaxoSmithKline; and grant support through his institution from bioMérieux and Pfizer. He was cochair of the last Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) community-acquired pneumonia guidelines committee and participated in the hospital-acquired, ventilator-acquired, and health care–associated pneumonia guidelines committee. Dr. Waterer has been selected as co-chair of the next ATS–IDSA community-acquired pneumonia guidelines committee and is a member of the current IDSA hospital-acquired and ventilator-associated pneumonia guidelines. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

REFERENCES

1. The top 10 causes of death. Geneva: World Health Organization, 2013 (http:// www.who.int/mediacentre/factsheets/ fs310/en/index.html).

2. Murphy SL, Xu J, Kochanek KD. Deaths: preliminary data for 2010. Natl Vital Stat Rep 2012;60:1-51.

3. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29:1303-10.

4. Brancati FL, Chow JW, Wagener MM, Vacarello SJ, Yu VL. Is pneumonia really the old man's friend? Two-year prognosis after community-acquired pneumonia. Lancet 1993;342:30-3.

5. Waterer GW, Kessler LA, Wunderink RG. Medium-term survival after hospitalization with community-acquired pneu-

monia. Am J Respir Crit Care Med 2004; 169:910-4.

Yende S, Angus DC, Ali IS, et al. Influence of comorbid conditions on long-term mortality after pneumonia in older people. J Am Geriatr Soc 2007;55:518-25.
Angus DC, Marrie TJ, Obrosky DS, et al. Severe community-acquired pneumonia: use of intensive care services and evaluation of American and British Thoracic Society diagnostic criteria. Am J Respir Crit Care Med 2002;166:717-23.

8. Wilson KC, Schünemann HJ. An appraisal of the evidence underlying performance measures for community-acquired pneumonia. Am J Respir Crit Care Med 2011;183:1454-62.

9. Waterer GW, Kessler LA, Wunderink RG. Delayed administration of antibiotics and atypical presentation in community-acquired pneumonia. Chest 2006;130:11-5.

10. Albaum MN, Hill LC, Murphy M, et al. Interobserver reliability of the chest radiograph in community-acquired pneumonia. Chest 1996;110:343-50.

11. Griffin MR, Zhu Y, Moore MR, Whitney CG, Grijalva CG. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. N Engl J Med 2013; 369:155-63.

12. Vanderkooi OG, Low DE, Green K, Powis JE, McGeer A. Predicting antimicrobial resistance in invasive pneumococcal infections. Clin Infect Dis 2005;40: 1288-97.

 Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44:Suppl 2:S27-S72.
Gleason PP, Meehan TP, Fine JM, Ga-

N ENGLJ MED 370;6 NEJM.ORG FEBRUARY 6, 2014

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.

lusha DH, Fine MJ. Associations between initial antimicrobial therapy and medical outcomes for hospitalized elderly patients with pneumonia. Arch Intern Med 1999; 159:2562-72.

15. Brown RB, Iannini P, Gross P, Kunkel M. Impact of initial antibiotic choice on clinical outcomes in community-acquired pneumonia: analysis of a hospital claims-made database. Chest 2003;123:1503-11.

16. Capelastegui A, España PP, Quintana JM, et al. Improvement of process-of-care and outcomes after implementing a guideline for the management of community-acquired pneumonia: a controlled before-and-after design study. Clin Infect Dis 2004;39:955-63.

17. Dean NC, Silver MP, Bateman KA, James B, Hadlock CJ, Hale D. Decreased mortality after implementation of a treatment guideline for community-acquired pneumonia. Am J Med 2001;110:451-7.

18. Metersky ML, Ma A, Houck PM, Bratzler DW. Antibiotics for bacteremic pneumonia: improved outcomes with macrolides but not fluoroquinolones. Chest 2007;131:466-73.

19. Sligl WI, Asadi L, Eurich DT, Tjosvold L, Marrie TJ, Majumdar SR. Macrolides and mortality in critically ill patients with community-acquired pneumonia: a systematic review and meta-analysis. Crit Care Med 2013 October 23 (Epub ahead of print).

20. Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Arch Intern Med 2004;164: 637-44.

21. Meehan TP, Fine MJ, Krumholz HM, et al. Quality of care, process, and outcomes in elderly patients with pneumonia. JAMA 1997;278:2080-4.

22. Polgreen PM, Chen YY, Cavanaugh JE, et al. An outbreak of severe Clostridium difficile-associated disease possibly related to inappropriate antimicrobial therapy for community-acquired pneumonia. Infect Control Hosp Epidemiol 2007;28: 212-4.

23. Kanwar M, Brar N, Khatib R, Fakih MG. Misdiagnosis of community-acquired pneumonia and inappropriate utilization of antibiotics: side effects of the 4-h antibiotic administration rule. Chest 2007; 131:1865-9.

24. Barlow G, Nathwani D, Williams F, et al. Reducing door-to-antibiotic time in community-acquired pneumonia: controlled before-and-after evaluation and cost-effectiveness analysis. Thorax 2007;62:67-74.

25. Pines JM, Isserman JA, Hinfey PB. The measurement of time to first antibiotic dose for pneumonia in the emergency de-

partment: a white paper and position statement prepared for the American Academy of Emergency Medicine. J Emerg Med 2009;37:335-40.

26. Lim HF, Phua J, Mukhopadhyay A, et al. IDSA/ATS minor criteria aided pre-ICU resuscitation in severe community-acquired pneumonia. Eur Respir J 2013 October 31 (Epub ahead of print).

27. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006;34:1589-96.

28. American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005; 171:388-416.

29. Shindo Y, Ito R, Kobayashi D, et al. Risk factors for drug-resistant pathogens in community-acquired and healthcareassociated pneumonia. Am J Respir Crit Care Med 2013;188:985-95.

30. Kollef MH, Shorr A, Tabak YP, Gupta V, Liu LZ, Johannes RS. Epidemiology and outcomes of health-care-associated pneumonia: results from a large US database of culture-positive pneumonia. Chest 2005; 128:3854-62. [Erratum, Chest 2006;129: 831.]

31. Micek ST, Kollef KE, Reichley RM, Roubinian N, Kollef MH. Health careassociated pneumonia and communityacquired pneumonia: a single-center experience. Antimicrob Agents Chemother 2007;51:3568-73.

32. Gillet Y, Vanhems P, Lina G, et al. Factors predicting mortality in necrotizing community-acquired pneumonia caused by Staphylococcus aureus containing Panton-Valentine leukocidin. Clin Infect Dis 2007;45:315-21.

33. Sicot N, Khanafer N, Meyssonnier V, et al. Methicillin resistance is not a predictor of severity in community-acquired Staphylococcus aureus necrotizing pneumonia: results of a prospective observational study. Clin Microbiol Infect 2013; 19:E142-E148.

34. Yealy DM, Auble TE, Stone RA, et al. Effect of increasing the intensity of implementing pneumonia guidelines: a randomized, controlled trial. Ann Intern Med 2005;143:881-94.

35. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997;336:243-50.

36. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospi-

tal: an international derivation and validation study. Thorax 2003;58:377-82.

37. Renaud B, Santin A, Coma E, et al. Association between timing of intensive care unit admission and outcomes for emergency department patients with community-acquired pneumonia. Crit Care Med 2009;37:2867-74.

38. Restrepo MI, Mortensen EM, Rello J, Brody J, Anzueto A. Late admission to the ICU in patients with community-acquired pneumonia is associated with higher mortality. Chest 2010;137:552-7.

39. Charles PG, Wolfe R, Whitby M, et al. SMART-COP: a tool for predicting the need for intensive respiratory or vasopressor support in community-acquired pneumonia. Clin Infect Dis 2008;47:375-84.

40. Renaud B, Labarère J, Coma E, et al. Risk stratification of early admission to the intensive care unit of patients with no major criteria of severe community-acquired pneumonia: development of an international prediction rule. Crit Care 2009; 13:R54.

41. España PP, Capelastegui A, Gorordo I, et al. Development and validation of a clinical prediction rule for severe community-acquired pneumonia. Am J Respir Crit Care Med 2006;174:1249-56.

42. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-77.

43. Labelle AJ, Arnold H, Reichley RM, Micek ST, Kollef MH. A comparison of culture-positive and culture-negative health-care-associated pneumonia. Chest 2010;137:1130-7.

44. Chalmers JD, Taylor JK, Singanayagam A, et al. Epidemiology, antibiotic therapy, and clinical outcomes in health care-associated pneumonia: a UK cohort study. Clin Infect Dis 2011;53:107-13.

45. Kett DH, Cano E, Quartin AA, et al. Implementation of guidelines for management of possible multidrug-resistant pneumonia in intensive care: an observational, multicentre cohort study. Lancet Infect Dis 2011;11:181-9.

46. Attridge RT, Frei CR, Restrepo MI, et al. Guideline-concordant therapy and outcomes in healthcare-associated pneumonia. Eur Respir J 2011;38:878-87.

47. El Solh AA, Pietrantoni C, Bhat A, Bhora M, Berbary E. Indicators of potentially drug-resistant bacteria in severe nursing home-acquired pneumonia. Clin Infect Dis 2004;39:474-80.

48. Woodhead M, Blasi F, Ewig S, et al. Guidelines for the management of adult lower respiratory tract infections: summary. Clin Microbiol Infect 2011;17:Suppl 6:1-24.

Copyright © 2014 Massachusetts Medical Society.

N ENGLJ MED 370;6 NEJM.ORG FEBRUARY 6, 2014

551

The New England Journal of Medicine

Downloaded from nejm.org at FLORIDA STATE UNIVERSITY on November 22, 2016. For personal use only. No other uses without permission.