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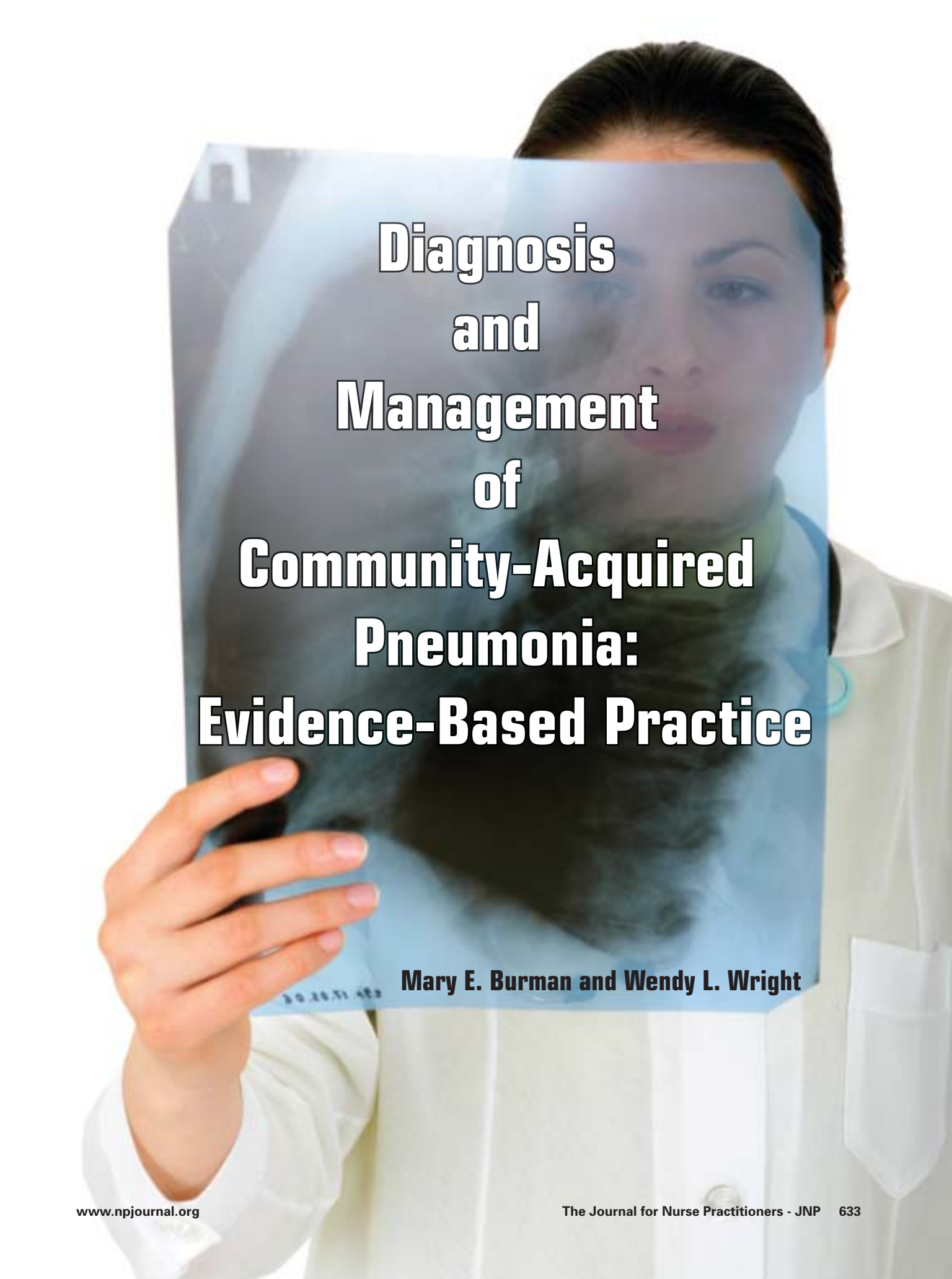

Diagnosis and Management of Community-Acquired Pneumonia: Evidence-Based Practice

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ABSTRACT

The purpose of this article is to evaluate the new Infectious Diseases Society of America and the American Thoracic Society Guideline for Community-Acquired Pneumonia in Adults for nurse practitioner (NP) practice using evidence-based practice principles. The major recommendations for diagnosis, treatment, site of care, and prevention are also summarized. In general, the guideline meets the criteria of evaluation of practice guidelines, although the methods used for the literature search are not adequately described. The guideline was not developed with the input from primary care providers; however, it is appropriate for NPs who work in a variety of settings, including primary care.

Keywords: Adults, community-acquired pneumonia, evidenced-based practice, practice guidelines

IN 1901, Osler proclaimed that the "most widespread and fatal of all acute diseases, pneumonia, is now the Captain of the Men of Death."[1] Today, pneumonia, along with influenza, continues to be a leading cause of death in the United States,[2] despite advances in antimicrobial therapy, vaccines, and critical care. Pneumonia also has a significant effect on morbidity, resulting in more than 10 million outpatient visits, 600,000 hospitalizations, and 64 million days of restricted activity each year.[3] Consequently, nurse practitioners (NPs) in a variety of settings encounter pneumonia on a regular basis, and in order to provide the most optimal care they must review and evaluate the available evidence. Given the growing amount of research on community-acquired pneumonia (CAP), this can be a daunting task for any clinician. Consequently, the purpose of this article is to summarize and evaluate the latest guideline developed by the Infectious Diseases Society of America and the American Thoracic Society (IDSA/ATS) for diagnosis and management of CAP in adults.[4]

OVERVIEW OF CAP

Pneumonia is an infection of the lower respiratory tract caused by bacteria, viruses, fungi, protozoa, or parasites.[5]

Table 1. Most Common Causes of Community-Acquired Pneumonia[4]

Client Type	Cause
Outpatient	*Streptococcus pneumoniae* *Mycoplasma pneumoniae* *Haemophilus influenzae* *Chlamydophila pneumoniae* Respiratory viruses[a]
Inpatient (nonintensive care unit)	*S pneumoniae* *M pneumoniae* *C pneumoniae* *H influenzae* *Legionella* species Respiratory viruses[a]
Inpatient (intensive care unit)	*S pneumoniae* *Staphylococcus aureus* *Legionella species* *Gram-negative bacilli* *H influenzae*

[a] *Influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza.*

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Respiratory pathogens reach the lungs through inhalation of microorganisms, aspiration of oropharyngeal secretions, and hematogenous spread from other bodily sites of infection.[5] CAP refers to pneumonia that is acquired outside health care organizations, including hospitals, nursing homes, and other long-term care facilities. Although antibiotic resistance has increasingly become a recognized problem in pneumonia, older age and underlying disease, not antibiotic resistance, are more important factors in mortality.[1]

Despite advances in diagnostic testing, the causative agent in as many as 50% of clients with CAP is not identified even when extensive testing has been performed.[6] Unfortunately, no diagnostic test exists that can identify all potential pathogens. *Streptococcus pneumoniae, Mycoplasma pneumoniae,* and *Chlamydia pneumoniae* have been the most commonly identified organisms, although their incidence depends on the type of diagnostic testing and criteria used (Table 1). *Legionella* spp and variable infections are also common. Infections by gram-negative bacilli may be increasing in outpatient settings because of the complexity of the clients treated outside of health care settings.[6]

Table 2. Criteria for Severe Community-Acquired Pneumonia[4]

Minor Criteria[a]
Respiratory rate[b] ≥ 30 breaths/min
PaO_2/FiO_2 ratio ≤ 250
Multilobar infiltrates
Confusion or disorientation
Uremia (BUN level ≥ 20 mg/dL)
Leukopenia[c] (WBC count < 4000 cells/mm^3)
Thombocytopenia (platelet count < 100,000 cells/mm^3)
Hypothermia (core temperature < 36°C)
Hypotension requiring aggressive fluid resuscitation
Major Criteria
Invasive mechanical ventilation
Septic shock with the need for vasopressors

BUN, blood urea nitrogen; PaO_2/FiO_2, arterial oxygen pressure/fraction of inspired oxygen; WBC, white blood count.

[a] *Other criteria to consider include hypoglycemia (in nondiabetic patients), acute alcoholism or alcoholic withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia.*

[b] *A need for noninvasive ventilation can substitute for a respiratory rate > 30 breaths/min or a PaO_2/FiO_2 ratio ≤ 250.*

[c] *As a result of infection alone.*

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IDSA/ATS GUIDELINE FOR MANAGEMENT OF CAP

To eliminate some of the confusion arising from multiple national practice guidelines, the IDSA/ATS published a joint clinical practice guideline in 2007.[4] This guideline is geared toward emergency medicine and primary care practitioners and hospitalists, and it is intended primarily for CAP.

Initial diagnosis and treatment decisions are based on assessment of severity. Site-of-care decisions and outpatient treatment versus hospitalization should be based on severity-of-illness scores, such as the CURB-65 criteria (confusion, uremia, respiratory rate, low blood pressure, age 65 years or older), or prognostic models, such as the Pneumonia Severity Index. These objective measures of severity should be supplemented by subjective factors, such as the ability to take medications safely and reliably. Clients with septic shock should be directly admitted to the intensive care unit (ICU) for vasopressors, intubation, and mechanical ventilation. In addition, any clients with three or more of the minor criteria for severe CAP (Table 2) should also be considered for admission to the ICU or high-level monitoring unit.

The diagnosis of CAP is based on presenting signs and symptoms, such as cough, fever, sputum, pleuritic chest pain, and presence of rales or bronchial breath sounds; however, a demonstrable infiltrate by chest X-ray (or other imaging technique) is required to differentiate CAP from other causes of cough and fever (eg, acute bronchitis). Chest radiographs may also be useful in identification of causative agent, prognosis, alternative diagnoses, and associated conditions. In cases when the chest X-ray is not definitive, although the client's toxic condition is suggestive of pneumonia, it may be prudent to treat presumptively for 24 hours and repeat the imaging in 1 to 2 days. It is important to keep in mind that some clients because of age, immune status, and hydration may not present with typical clinical features, radiograph findings, or both.

Routine diagnostic tests (eg, cultures, Gram staining) to identify causative agents are optional in nonhospitalized clients with CAP because studies have shown that that these tests are infrequently done, yet clients do well with empirical antibiotic treatment. Exceptions to this recommendation, such as influenza that can be tested using rapid point-of-care tests, do exist. Specific recommendations for additional diagnostic testing are provided in Table 3. Suspected severe acute respiratory syndrome (SARS), *Mycobacterium tuberculosis* infection, community-acquired Methicillin-resistant *Staphylococcus aureus* (MRSA), fungal infections, avian influenza, and disease caused by agents used in bioterrorism should be verified with further diagnostic testing. Moreover, in situations when antibiotic treatment would likely be altered, investigation for specific causative agents should be undertaken, especially when the presence of specific pathogens is suspected based on the clinical presentation. This allows the clinician to narrow or completely alter antibiotic therapy, improving the likelihood of treatment success. Clearly, extensive diagnostic testing should be indicated for critically ill clients, and the guideline provides additional information about the circumstances in which other testing, such as blood cultures, respiratory tract specimen Gram stain and culture, and antigen tests, should be done.

Table 3. Clinical Indications for More Extensive Diagnostic Testing[4]

Indication	Blood Culture	Sputum Culture	*Legionella* UAT	Pneumococcal UAT	Other
ICU admission	X	X	X	X	X[a]
Failure of outpatient antibiotic therapy		X	X	X	
Cavitary infiltrates	X	X			X[b]
Leukopenia	X			X	
Active alcohol abuse	X	X	X	X	
Chronic severe liver disease	X			X	
Severe obstructive or structural lung disease		X			
Asplenia (anatomic or functional)	X			X	
Recent travel (within 2 wk)			X		X[c]
Positive *Legionella* UAT result		X[d]	NA		
Positive pneumococcal UAT result	X	X		NA	
Pleural effusion	X	X	X	X	X[e]

UAT, urinary antigen test; NA, not applicable.

[a] *Endotracheal aspirate if intubated, possibly bronchoscopy or nonbronchoscopic bronchoalveolar lavage.*

[b] *Fungal and tuberculosis cultures.*

[c] *For travel to or residence in southwestern United States, consider* Coccidioides *species,* Hantavirus*; for travel to Southeast and East Asia, consider* Burkholderia pseudomallei*, avian influenza, SARS.*

[d] *Special media for* Legionella.

[e] *Thoracentesis and pleural fluid cultures.*

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The mainstay of pneumonia treatment is antimicrobial therapy. Appropriate antibiotic selection is based on prediction of most likely causative pathogen (Table 1 and Table 4) and antibiotic susceptibility. For most clients in the outpatient setting, antibiotic selection will be empirical until more rapid and accurate diagnostic tests are developed (Table 5). Other factors to consider in selection include pharmacokinetics and pharmacodynamics, compliance, safety, and cost. Local susceptibility patterns, if available from local or state health departments, should be considered in antibiotic selection. When the specific pathogen(s) is known, antimicrobial therapy should be directed toward that causative agent (Table 6).[1] Clients should be treated with antibiotics for at least 5 days, be afebrile for 48 to 72 hours, and have no more than one sign of clinical instability (heart rate ≤ 100 beats/minute, respiratory rate ≤ 24 breaths/minute, systolic blood pressure ≥ 90 mm Hg, arterial oxygen saturation ≥ 90% or partial pressure of oxygen ≥ 60 mm Hg on room air, ability to maintain oral intake, normal mental status). Clients with persistent clinical instability may need to be hospitalized or treated for a longer duration.

Prevention of pneumonia is also addressed in the IDSA/ATS guideline (Table 7). Vaccination status should be assessed at the time of hospitalization for all persons, and vaccination can be performed at discharge or in the outpatient setting. Smoking cessation is also a critical part of prevention. Respiratory hygiene measures, including hand hygiene and masks and tissue for patients with a cough, should be used in outpatient and inpatient settings.

APPRAISAL OF IDSA/ATS GUIDELINE

A number of criteria have been identified for the evaluation of clinical practice guidelines.[8-11] According to the components in the AGREE (appraisal of guidelines for research and evaluation) instrument, appraisal should address the following: scope and purpose, stakeholder involvement, rigor of development, clarity and presentation, applicability, and editorial independence.

In relation to scope and purpose, the IDSA/ATS guideline has a clear aim: diagnosis and treatment of CAP in adults. Institutionalized and immunocompromised adults are excluded. Relevant clinical questions are addressed, such as antimicrobial selection and determination of site of care.

Table 4. Epidemiologic Conditions and/or Risk Factors Related to Specific Pathogens in Community-Acquired Pneumonia[4]

Condition	Commonly Encountered Pathogen(s)
Alcoholism	*Streptococcus pneumoniae*, oral anaerobes, *Klebsiella pneumoniae, Acinetobacter* species, *Mycobacterium tuberculosis*
Chronic obstructive pulmonary disease, smoking, or both	*Haemophilus influenzae, Pseudomonas aeruginosa, Legionella* species, *S pneumoniae, Moraxella catarrhalis, Chlamydophila pneumoniae*
Aspiration	Gram-negative enteric pathogens, oral anaerobes
Lung abscess	Community-acquired MRSA, oral anaerobes, endemic fungal pneumonia, *M tuberculosis*, atypical mycobacteria
Exposure to bat or bird droppings	*Histoplasma capsulatum*
Exposure to birds	*Chlamydophila psittaci* (if poultry: avian influenza)
Exposure to rabbits	*Francisella tularensis*
Exposure to farm animals or parturient cats	*Coxiella burnetti* (Q fever)
Hotel or cruise ship stay in previous 2 wk	*Legionella* species
HIV infection (early)	*S pneumoniae, H influenzae, M tuberculosis*
HIV infection (late)	Pathogens listed above for early infection plus *Pneumocystis jiroveci, Cryptococcus, Histoplasma, Aspergillus,* atypical mycobacterium (especially *Mycobacterium kansasii*), *P aeruginosa*
Travel or residence in southwestern United States	*Coccidioides* species, *Hantavirus*
Travel or residence in Southeast or East Asia	*Burkholderia pseudomallei*, avian influenza, SARS
Influenza activity in community	Influenza, *S pneumoniae, Staphylococcus aureus, H influenzae*
Cough >2 wk with whoop or posttussive vomiting	*Bordetella pertussis*
Structural lung disease (eg, bronchiectasis)	*P aeruginosa, Burkholderia cepacia, S aureus*
Injection drug use	*S. aureus*, anaerobes, *M. tuberculosis, S. pneumoniae*
Endobronchial obstruction	Anaerobes, *S pneumoniae, H influenzae, S aureus*
In context of bioterrorism	*Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia)

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Stakeholder involvement focuses on how well the guideline represents the views of those who will be using it. The investigators readily acknowledge that, although the guideline is intended for use by primary care, emergency care, and hospitalist physicians, those specialists were not involved in the development. NPs, other primary care providers, and clients were not included either. Finally, no information is available about pretesting of the guideline before dissemination for use.

Rigor refers to the process used to identify, select, and synthesize the evidence used to develop the guideline. The strategy used to search for evidence, including search terms, sources used, and the dates covered, is not provided in the guideline. Information on the inclusion or exclusion of pieces of evidence is also not available. The process for formulation and grading of each recommendation is described. The committee used a three-tier scale to grade the recommendations: high (evidence from well-conducted, randomized controlled trials), moderate (evidence from well-designed, controlled trails without randomization), and low (evidence from case studies and expert opinion). The final grading of

Table 5. Recommended Empirical Antibiotics for Community-Acquired Pneumonia[4]

Client Situation	Treatment Recommendations
Outpatient	1. Previously healthy and no use of antimicrobials within previous 3 mo: a macrolide or doxycycline
	2. Presence of comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions; use of immunosuppressing drugs; or use of antimicrobials within the previous 3 mo (in which case an alternative from a different class should be selected): a respiratory fluoroquinolone moxifloxacin, gemifloxacin, or levofloxacin (750 mg) or a β-lactam **plus** a macrolide
	3. In regions with a high rate (>25%) of infection with high-level (MIC ≥ 16 μg/mL) macrolide-resistant *Streptococcus pneumoniae*, consider use of alternative agents listed above in (2) for patients without comorbidities
Inpatient, Non-ICU	A respiratory fluoroquinolone or a β-lactam **plus** a macrolide
Inpatient, ICU	A β-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) **plus** either azithromycin or a respiratory fluoroquinolone (for penicillin-allergic clients, a respiratory fluoroquinolone and aztreonam are recommended)
Special Considerations	If *Pseudomonas* is a consideration: an antipneumococcal, antipseudomonal β-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750 mg) **or** the above β-lactam plus an aminoglycoside and azithromycin **or** the above β-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for above β-lactam)
	If community-acquired MRSA is a consideration, add vancomycin or linezolid

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each recommendation was a composite of each committee member's evaluation of the evidence and his or her clinical expertise. In the discussion of each recommendation, a clear link is found between the recommendation and evidence on which it is based. It is unclear whether the guideline was externally reviewed. The guideline was reviewed by each of the societies for final approval. The guideline should reflect current research and have a procedure for updating the guideline. The guideline does include 335 references, with publication dates between 1971 and 2006. Approximately 70% were published from 2000 to the present, with 25% of the references published between 2004 and 2006. The references are from the United States, Canada, and Europe, although all the references are in English so it is unknown what effect literature from non-English journals may have on the recommendations. There is no discussion of updating of the guideline.

Clarity and presentation pertains to the language and format of the guideline. The recommendations are concrete with clear descriptions of the diagnosis and management of CAP. Options for diagnosis and treatment are provided. The recommendations are easily identified. The presentation could be enhanced by dissemination of a quick reference guide.

Applicability of the guideline refers to the organizational, behavioral, and cost implications of implementing the guideline. This guideline will potentially require some changes and will have cost implications for some clients and practices; however, these are probably not significant in most situations (see "Summary and Conclusions").

Finally, editorial independence deals with the independence of the recommendations and acknowledgement of any possible conflicts of interest by those developing the guideline. No explicit statement acknowledges the funding source for the guideline development, although presumably it was funded by the two societies. Conflicts of interest, specifically funding by pharmaceutical companies, are acknowledged in the guideline.

SUMMARY AND CONCLUSIONS

The IDSA/ATS guideline for CAP provides a comprehensive overview of diagnosis and treatment, including evaluation of the severity of CAP and determination of site of treatment. The scope and purpose, clarity, and presentation and applicability are strengths of this guideline.

Table 6. Recommended Antimicrobial Therapy for Specific Pathogens[4]

Organism	Preferred Antimicrobial	Alternative Antimicrobial(s)
Streptococcus pneumoniae		
Penicillin nonresistant; MIC < 2 μg/mL	Penicillin G, amoxicillin	Macrolide, cephalosporins [oral (cefpodoxime, cefprozil, cefuroxime, cefdinir, cefditoren) or parenteral (cefuroxime, ceftriaxone, cefotaxime)], clindamycin, doxycycline, respiratory fluoroquinolone[a]
Penicillin resistant; MIC ≥ 2 μg/mL	Agents chosen on basis of susceptibility, including cefotaxime, ceftriaxone, fluoroquinolone	Vancomycin, linezolid, high-dose amoxicillin (3 g/d with penicillin MIC ≤ 4 μg/mL)
Haemophilus influenzae		
Non-β-lactamase producing	Amoxicillin	Fluoroquinolone, doxycycline, azithromycin, clarithromycin[b]
β-Lactamase producing	Second- or third-generation cephalosporin, amoxicillin-clavulanate	Fluoroquinolone, doxycycline, azithromycin, clarithromycin[b]
Mycoplasma pneumoniae/ Chlamydophila pneumoniae	Macrolide, a tetracycline	Fluoroquinolone
***Legionella* species**	Fluoroquinolone, azithromycin	Doxycycline
Chlamydophila psittaci	A tetracycline	Macrolide
Coxiella burnetii	A tetracycline	Macrolide
Francisella tularensis	Doxycycline	Gentamicin, streptomycin
Yersinia pestis	Streptomycin, gentamicin	Doxycycline, fluoroquinolones
***Bacillus anthracis* (inhaled)**	Ciprofloxacin, levofloxacin, doxycycline (usually with second agent)	Other fluoroquinolones, β-lactam, if susceptible; rifampin, clindamycin, chloramphenicol
Enterobacteriaceae	Third-generation cephalosporin, carbapenem[c] (drug of choice if extended-spectrum β-lactamase producer)	β-Lactam/β-lactamase inhibitor,[d] fluoroquinolone
Pseudomonas aeruginosa	Antipseudomonal β-lactam[e] **plus** ciprofloxacin or levofloxacin[f] or aminoglycosides	Aminoglycosides **plus** ciprofloxacin or levofloxacin[f]
Burkholderia pseudomallei	Carbapenem, ceftazidime	Fluoroquinolone, TMP-SMX
***Acinetobacter* species**	Carbapenem	Cephalosporin-aminoglycoside, ampicillin-sulbactam, colistin
Staphylococcus aureus		
Methicillin susceptible	Antistaphylococcal penicillin[g]	Cefazolin, clindamycin
Methicillin resistant	Vancomycin or linezolid	TMP-SMX
Bordetella pertussis	Macrolide	TMP-SMX
Anaerobe (aspiration)	β-Lactam/β-lactamase inhibitor,[d] clindamycin	Carbapenem
Influenza virus	Oseltamivir or zanamivir	
Mycobacterium tuberculosis	Isoniazid plus rifampin plus ethambutol plus pyrazinamide	See TB guidelines[7]
***Coccidioides* species**	For uncomplicated infection in normal host, no therapy generally recommended; for therapy, itraconazole, fluconazole	Amphotericin B
Histoplasmosis	Itraconazole	Amphotericin B
Blastomycosis	Itraconazole	Amphotericin B

Note: Choices should be modified on the basis of susceptibility test results and advice from local specialists. Refer to local references for appropriate doses. TMP-SMX, trimethoprim-sulfamethoxazole; TB, tuberculosis.

[a] *Levofloxacin, moxifloxacin, gemifloxacin (not a first-line choice for penicillin-susceptible strains). Ciprofloxacin is appropriate for* Legionella *and most gram-negative bacilli (including* H influenzae*).*

[b] *Azithromycin is more active in vitro than clarithromycin for H influenzae.*

[c] *Imipenem-cilastatin, meropenem, ertapenem.*

[d] *Piperacillin-tazobactam for gram-negative bacilli, ticarcillin-clavulanate, ampicillin-sulbactam, or amoxicillin-clavulanate.*

[e] *Ticarcillin, piperacillin, ceftazidime, cefepime, aztreonam, imipenem, meropenem.*

[f] *750 mg daily.*

[g] *Nafcillin, oxacillin, flucloxacillin.*

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Table 7. Recommendation for Vaccine Prevention of Community-Acquired Pneumonia[4]

Factor	Pneumococcal Polysaccharide Vaccine	Inactivated influenza vaccine	Live Attenuated Influenza Vaccine
Route of administration	Intramuscular injection	Intramuscular injection	Intranasal spray
Type of vaccine	Bacterial component (polysaccharide capsule)	Killed virus	Live virus
Recommended groups	All persons ≥ 65 y of age High-risk persons 2–64 y of age Current smokers	All persons ≥ 50 y of age High-risk persons 6 mo–49 y of age Household contacts of high-risk persons Health care providers Children 6–23 mo of age	Healthy persons 5–49 y of age,[a] including health care providers and household contacts of high-risk persons
Specific high-risk indications for vaccination	Chronic cardiovascular, pulmonary, renal, or liver disease Diabetes mellitus Cerebrospinal fluid leaks Alcoholism Asplenia Immunocompromising conditions or medications Native Americans and Alaska natives Long-term care facility residents	Chronic cardiovascular or pulmonary disease (including asthma) Chronic metabolic disease (including diabetes mellitus) Renal dysfunction Hemoglobinopathies Immunocompromising conditions or medications Compromised respiratory function or increased aspiration risk Pregnancy Residence in long-term care facility Aspirin therapy in persons ≤ 18 y of age	Avoid in high-risk persons
Revaccination schedule	One-time revaccination after 5 y for (1) adults ≥ 65 y of age, if first dose is received before age 65 y; (2) persons with asplenia, and (3) immunocompromised persons	Annual revaccination	Annual revaccination

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However, several weaknesses do exist. The investigators acknowledge that there was no input from primary care and emergency department physicians and hospitalists in the development of the guideline. In addition, although the approach to grading each recommendation is outlined, the methods for literature review need to be articulated more clearly. The investigators do not provide explicit information about how the articles used in the guideline were identified and selected. This additional information would help practitioners be able to evaluate for any potential biases in the sources used for the guideline.

The next step is for individual NPs to evaluate the guideline to (1) decide whether the strengths outweigh the weaknesses and (2) determine whether the guideline is applicable to their setting and clientele. Straus et al[10] recommend addressing the four "Killer Bs" as a way to evaluate the appropriateness of the guideline for implementation in various settings. Is the *burden* of illness, or the number of clients with this disease, too low to warrant use of the guideline? Are the *beliefs* of the clients served about the type and value of interventions or their potential consequences incompatible with the guideline? Are the opportunity costs associated with guideline implementation a bad *bargain*? In other words, would the resources of the practice or community be better spent elsewhere? Are the *barriers* (geographic, organizational, cultural, legally, etc) so high that it is not worth using the guideline? Implementation of the guideline will be

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problematic in some settings (eg, those in which clients have financial barriers). If clients are being treated in the outpatient setting, inexpensive antibiotics (eg, doxycycline) can be selected; however, the need for chest radiography may be problematic.

In summary, despite some weaknesses, including the acknowledged weakness that no primary care providers were involved in the development of the guideline, the CAP guideline has many strengths and in general is applicable to many NPs who work in primary care and urgent care settings. NPs are encouraged to review the guideline and determine whether it is relevant to their practice setting and clients. JNP

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