

## Guidelines for the Management of Community-Acquired Pneumonia

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### Presentation Summary

Guidelines for the treatment of community-acquired pneumonia (CAP) have been issued by various institutions. These therapeutic recommendations, culled from available medical literature, can be conflicting and confusing. The following factors further complicate clinical management: Accurate diag-

nosis is sometimes challenging, therapeutic options are abundant and aggressively marketed, and drug resistance is an increasing concern. Moreover, costs of care and clinical outcomes can vary significantly with therapeutic approaches. All of these factors point to a critical need for more consistent medical guidelines for treating CAP.

The incidence of community-acquired pneumonia (CAP) has remained relatively static from the prepenicillin era to today. Before penicillin, 3 in 1000 people within the population were reported to have CAP. Today, that number is 2.5 in 1000. As expected, the mortality rate has dropped significantly.

Guidelines for the treatment of CAP have been issued by a number of organizations. The most recent guidelines take an evidence-based approach to the management of this disease. Though organization guidelines vary, all of them attempt to:

- Improve diagnosis
- Optimize treatment and outcomes
- Provide quality measures
- Prevent antibiotic misuse

- Control emergence of drug-resistant bacteria
- Reduce costs

The most widely used guidelines are those issued by the American Thoracic Society (ATS), the Infectious Diseases Society of America (IDSA), and the Centers for Disease Control and Prevention (CDC).

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**ATS Guidelines**

Published in 1993, the ATS guidelines create a framework for the diagnosis and management of CAP.<sup>1</sup> They include recommendations for diagnostic tests, classification of patients, and antimicrobial regimens (Table). The approach is literature based and guided by expert consensus, but it uses no formal system for weighting the literature.

When released, the ATS guidelines were praised by clinicians for their practicality and ease of use. However, they came under fire for their de-emphasis of microbiology in this era of emergent drug resistance. These guidelines do not endorse routine bacterial culture, nor do they promote the Gram stain test of sputum because it is considered neither sensitive nor specific.

ATS therapeutic guidelines list likely organisms and the recommended empiric therapy. The ATS recommends macrolides or tetracyclines for patients younger than 60 years of age with no comorbidity in whom the organisms are likely to be the pneumococcus or mycoplasma (*Chlamydia*

*pneumoniae* or *Haemophilus influenzae*). For patients older than 60 years of age who have a comorbidity, the likely organisms are *Streptococcus pneumoniae*, viruses, *H influenzae*, Gram-negative bacilli, and *Staphylococci*; and the recommended therapies are a second-generation cephalosporin, trimethoprim/sulfamethoxazole (TMP/SMX), or  $\beta$ -lactam with a  $\beta$ -lactamase inhibitor with or without a macrolide. For the patient with severe CAP, recommended therapies include a macrolide plus an antipseudomonal cephalosporin or another antipseudomonal agent such as imipenem or ciprofloxacin.

Revisiting these guidelines today, it is clear that these recommendations do not address the problem of drug resistance in the pneumococcus and the role of the new fluoroquinolones. In addition, serious problems now exist with the use of TMP/SMX and the reliance on antipseudomonal cephalosporins or other antipseudomonal agents in patients with severe CAP. Consequently, these guidelines are now under revision; they should be complete in 2001.

### IDSA Guidelines

Originally published in 1998, the IDSA guidelines have recently been updated.<sup>2</sup> Developed by a committee of pulmonary and infectious diseases experts who used a consensus process, these guidelines provide detailed recommendations for the diagnosis and management of CAP. These include evidence-based prognostic scoring systems for classifying patients in order to take into consideration special circumstances that might influence treatments. The guidelines also make evidence-based recommendations about performance indicators, with recommendations weighted according to the nature of the data and the strength of the recommendation.

**Table.** American Thoracic Society Guidelines

<p><b>ATS diagnostic guidelines recommend:</b></p> <ul style="list-style-type: none"> <li>• Chest X ray for all patients to confirm that the diagnosis is pneumonia rather than bronchitis</li> <li>• Special cultures (eg, for mycobacteria) in certain circumstances</li> <li>• Blood cultures for hospitalized patients</li> <li>• BAL for severely ill patients</li> <li>• Pleural fluid exam, if appropriate</li> </ul> <p><b>ATS guidelines recommend hospitalization be considered in the following circumstances:</b></p> <ul style="list-style-type: none"> <li>• Age over 65 years old</li> <li>• Chronic obstructive pulmonary disease or other lung disease</li> <li>• Diabetes</li> <li>• Renal failure</li> <li>• Congestive heart failure</li> <li>• Liver disease</li> <li>• Prior hospitalization</li> </ul> <p><b>Definition of severe CAP warranting ICU care:</b></p> <ul style="list-style-type: none"> <li>• Respiratory rate greater than 30 breaths per minute</li> <li>• PaO<sub>2</sub>/FiO<sub>2</sub> ratio less than 250 mm Hg</li> <li>• Need for mechanical ventilation</li> <li>• Bilateral or multilobar infiltrates</li> <li>• Shock (systolic blood pressure less than 99 mm Hg or diastolic blood pressure less than 80 mm Hg)</li> <li>• Vasopressors for more than 4 hours</li> <li>• Urine output less than 20 mL/hour</li> </ul>
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ATS = American Thoracic Society; CAP = community-acquired pneumonia; ICU = intensive care unit.

The committee's guideline for attempting to determine an etiologic approach to diagnosis is based on the premise that following this approach will improve care for patients overall by advancing medical knowledge. At the same time, this approach would offer a means of surveillance for drug resistance and emerging pathogens within the community. Finally, such an approach is widely considered to be cost efficient.

IDSA guidelines recommend the following diagnostic approach for CAP, emphasizing the value of well-performed microbiology:

- A chest X ray for all patients to distinguish CAP from bronchitis
- Routine blood work (eg, complete blood count, chemistry panel) for inpatients
- Human immunodeficiency virus serology, especially for patients 15 to 54 years of age
- Oxygen (O<sub>2</sub>) saturation
- Two blood cultures and sputum Gram stain
- Legionella and tuberculosis tests for selected patients

The guidelines also recommend that defined criteria be used to classify patients and assign them to appropriate sites of care. Patients with low mortality risks are generally seen as outpatients; patients with a higher risk of morbidity and mortality are candidates for hospitalization.

IDSA therapeutic guidelines emphasize microbiologic, economic, and adherence issues. In general, IDSA guidelines favor narrow-spectrum, cost-effective, and nontoxic agents. General considerations for therapy are:

- Use narrow-spectrum, nontoxic, cost-effective therapies.
- Drug-resistant pneumococci are a growing problem.
- Resistance to TMP/SMX is increasing.

- Macrolides, doxycycline, and  $\beta$ -lactams are not very active against drug-resistant *Streptococcus pneumoniae* (DRSP).
- Fluoroquinolones are very active, but resistance is a concern.

Agents recommended for treating CAP outpatients include macrolides, fluoroquinolones, or doxycycline; all are weighted equally under the IDSA guidelines. Selection considerations are regional resistance patterns, risk factors for drug resistance, age, and comorbidity.

For inpatients who are not severely ill, therapeutic preferences are also weighted equally. They include an extended-spectrum cephalosporin (cefotaxime or ceftriaxone) with a macrolide, a  $\beta$ -lactam and  $\beta$ -lactamase inhibitor with a macrolide, or a fluoroquinolone alone. For patients in the intensive care unit (ICU), therapeutic recommendations, equally weighted, include an extended-spectrum cephalosporin with a macrolide or a fluoroquinolone, or a  $\beta$ -lactam and  $\beta$ -lactamase inhibitor with a macrolide or a fluoroquinolone.

The guidelines also recommend that the performance of individual physicians and groups of physicians be measured by certain activities. These are:

- Blood cultures before therapy
- Initiation of treatment within 8 hours
- Legionella testing in at least 50% of ICU patients
- A chest X ray with infiltrates for all CAP patients
- Arterial blood gas test or oximetry within 8 hours

The chest X ray is recommended for all patients. The other recommendations apply to inpatients.

It is recommended that therapy be initiated for hospitalized patients within 8 hours, based on the findings of a study conducted by Meehan et al.<sup>3</sup>

Investigators examining the relationship between the start of antibiotic therapy and mortality in patients with CAP found that those treated within 8 to 10 hours of admission had a lower rate of morbidity than those treated later (Figure).

Interestingly, the IDSA decided not to include pneumococcal vaccination as a performance indicator because of the continuing controversy over its efficacy.

### CDC Guidelines

Published in May 2000, the CDC guidelines provide recommendations for surveillance and management of CAP in the DRSP era.<sup>4</sup> These guidelines address the concern that established breakpoints for resistance have not been clinically appropriate. The guidelines also take into consider-

ation the fact that reports of resistance have been influencing physicians to select broader-spectrum antibiotics, even though resistance has been difficult to correlate with clinical treatment failure (See article by Bishai in this supplement).

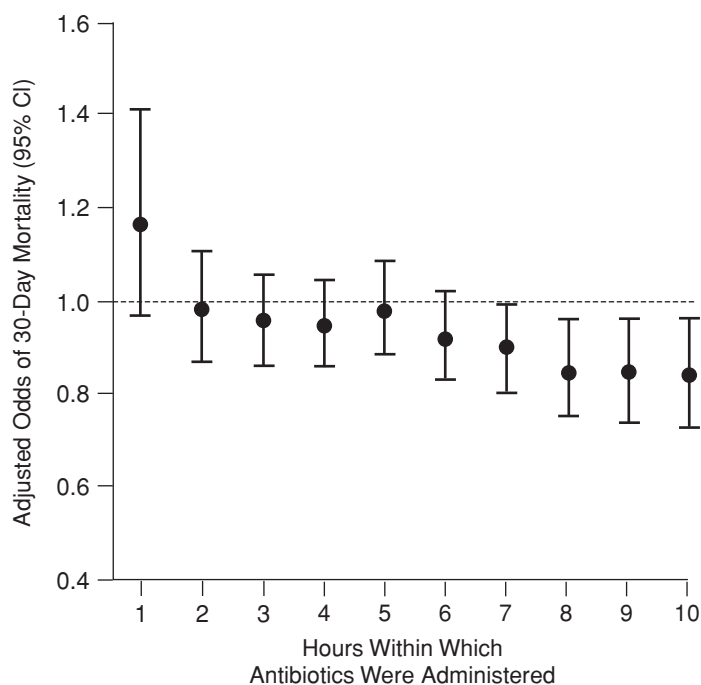
The CDC guidelines, which are based on literature review and a consensus process, respond to specific clinical policy questions.

- Should DRSP influence CAP treatment?
- What empiric regimens should be used to treat CAP in outpatients and inpatients?
- How should laboratories report susceptibility for *S pneumoniae*, and which drugs should be used in surveillance protocols?

CDC guidelines recommend the following diagnostic approach: chest X ray, if possible; sputum Gram stain; culture, if possible; and other diagnostic tests for etiology, as appropriate.

The recommended treatments for CAP in outpatients are macrolide, doxycycline, or an oral  $\beta$ -lactam. Fluoroquinolones are not recommended as first-line treatments; they are reserved for special uses, according to these guidelines. For inpatients who are not in the ICU, a parenteral  $\beta$ -lactam with a macrolide is recommended as first-line therapy; fluoroquinolones are reserved for special uses. For ICU patients, the recommendations are an intravenous (IV)  $\beta$ -lactam with an IV macrolide, an IV  $\beta$ -lactam with a fluoroquinolone, or a fluoroquinolone alone. Although the CDC guidelines recommend the use of a fluoroquinolone in the ICU patient, they recognize that we lack data on the efficacy of these agents in critically ill patients. Other concerns are related to the broad-spectrum activity of the fluoroquinolones, the possibility of resistance, and data from Canada that demonstrate growing

**Figure.** Time to Starting Antibiotics and Mortality



quinolone resistance in pneumococci. Moreover, the CDC has collected unpublished data that suggest an increasing fluoroquinolone resistance in the United States. The CDC, therefore, recommends that the use of fluoroquinolones be reserved for patients who are unresponsive or allergic to other first-line agents or who have an infection documented as a drug-resistant pneumococci. Agents to be generally avoided include first-generation cephalosporins, cefaclor, cefixime, ceftibuten, loracarbef, ceftazidime, ceftizoxime, ticarcillin, TMP/SMX, rifampin, and vancomycin.

Particularly noteworthy is that the CDC is concerned not with pneumococcal resistance to vancomycin, but with the prevention of vancomycin resistance in other organisms. The CDC recommendation is that vancomycin be used only for patients with suspected pneumococcal meningitis and not for patients with possible pneumococcal pneumonia. Despite its efficacy, vancomycin is not considered a good therapeutic choice for CAP.

### Summary

The proliferation of CAP guidelines presents a special challenge to the practicing clinician: Which one should providers use? Clearly, the outdated ATS guidelines should be used only with great caution. Some of the ATS recommendations remain valid today, but others are inappropriate in light of recent scientific findings and are under revision. In contrast, the IDSA guidelines are newly updated, evidence based, and quite com-

prehensive. Clinicians can use them with confidence if close attention is paid to the detailed information therein. Lastly, the CDC guidelines focus especially on DRSP. These guidelines are largely consistent with those issued by the IDSA. The most notable difference is in the use of quinolones: The CDC warns against the outpatient use of quinolones in CAP patients; the IDSA assumes a more liberal position. The practicing physician would welcome the prospect of a single, comprehensive, joint document with recommendations for CAP management. Unfortunately, it seems unlikely that such a joint document will be issued soon.

### ... REFERENCES ...

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