Commentary on the 1993 American Thoracic Society Guidelines for the Treatment of Community-Acquired Pneumonia*

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Early treatment of community-acquired pneumonia (CAP) is associated with improved outcome. Since extensive diagnostic testing identifies an etiologic agent in only half of the cases and usually requires several hours or even days for results, CAP is most often initially treated empirically. In 1993, the American Thoracic Society (ATS) established guidelines to assist primary care physicians in antibiotic selection for the initial empiric treatment of CAP in immunocompetent adults. Since publication of the guidelines, the incidence of certain bacteria has been redefined, antimicrobial resistance patterns have changed, risk factors for stratifying need for hospitalization have been further defined, and newer antibiotics have been introduced. These changes necessitated a reevaluation of the 1993 ATS guidelines. This article proposes a modification of the ATS guidelines. This modification continues to classify patients into groups, based on specific risk factors, to which a limited number of likely pathogens are identified and for which antibiotic treatment regimens are developed. The modification differs from the original ATS guidelines because of the changes in risk factors. Patient groups are still broadly divided into outpatient and inpatient care, but earlier risk factors of age and coexisting illness have been refined. Risk factors suggested herein as considerations to guide treatment include the presence of cardiopulmonary disease, history of smoking, severity of illness, risk of drug-resistant *Streptococcus pneumoniae* and *Pseudomonas aeruginosa*, and need for ICU admission. (CHEST 1999; 115:14S–18S)

Key words: American Thoracic Society guidelines; antimicrobial resistance; drug-resistant *Streptococcus pneumoniae*; sputum Gram’s stain; treatment regimen

Abbreviations: ATS = American Thoracic Society; CAP = community-acquired pneumonia; DRSP = drug-resistant *Streptococcus pneumoniae*; MIC = minimum inhibitory concentration; SGS = sputum Gram’s stain

Community-acquired pneumonia (CAP) affects 3.3 to 4 million people in the United States each year.1,2 Up to 20% of patients with CAP are admitted to the hospital, resulting in 600,000 to 1 million hospital admissions.3 Mortality ranges from <1%, for younger healthier patients who see a local physician, to almost 50% for ICU patients.4,5

Despite the desire to tailor treatment to the specific pathogen in each case, timely, definitive determination of the etiologic agents is seldom achieved. Clinical criteria do not provide definitive etiologies,6 and chest radiographs, although useful to diagnose pneumonia, rarely provide a specific etiology.7 In a careful analysis of the reliability of the sputum Gram’s stain (SGS), fewer than one third of the patients could have their conditions diagnosed using SGS alone.8 An extensive review of the published data suggests that SGS is particularly prone to error when read by inexperienced personnel, but even infectious-disease or pulmonary specialists often had error rates exceeding 30% in interpretation.9 Also, SGS does not seem to add important information to culture findings. Even when extensive diagnostic testing is employed, an unambiguous etiologic diagnosis is obtained in only about 50% of cases,10 and a diagnosis is often not available for hours or days. Given the evidence of improved outcome with the earliest possible intervention4,11 and the likelihood of inconclusive diagnoses even with extensive (and costly) testing, guidelines are needed to suggest appropriate initial empiric treatment of CAP in the absence of a clinically confirmed etiology.

1993 ATS GUIDELINES

In 1993, the American Thoracic Society (ATS) published guidelines to assist primary care physicians with the initial empiric therapy for CAP in immuno-
Patients presenting with CAP were divided into one of four pneumonia groups based on the need for hospitalization, severity of illness, presence of coexisting disease, and age (Fig 1). This algorithm for patient grouping was not “evidence based” because available data were scarce at that time. Therefore, the guidelines represented the consensus of the ATS Committee of the Scientific Assembly on Microbiology, Tuberculosis, and Pulmonary Infections and pointed to areas in need of clinical research.12

For each of the four ATS pneumonia groups, the most likely etiologic agents were assigned, based on a review of available data. Little data were available on which to base etiologies for otherwise healthy patients; more data were available on etiologies in patients > 60 years of age or those with underlying illness. Each of the four pneumonia groups generally contained four or five common pathogens. The ATS committee ranked those pathogens that were reported to have occurred in at least 5% of infections.

Based on the pathogens considered most likely for each pneumonia group, the ATS recommended antibiotics for initial empiric treatment of CAP. Generally, the recommendations were for broad classes of antibiotics, but in some cases, specific drugs were named. Adherence to the ATS guidelines proved to be associated with improved outcome13 and reduced cost of treatment. The Infectious Diseases Society of America produced their own recommendations for empiric treatment of CAP.14 These differ somewhat from those of the ATS.

**Revisions to the 1993 ATS Guidelines**

The intent of the 1993 ATS guidelines was to classify patients into pneumonia groups to which a limited number of specific pathogens were known to be common and, having done this, to develop an initial empiric antibiotic regimen for immunocompetent adults presenting with CAP. Since the introduction of these guidelines, several changes have occurred that necessitate their revision. These changes include the following:

1. the incidence of specific bacterial pathogens in CAP has been further studied, and antimicrobial resistance has increased—especially for Streptococcus pneumoniae15,16;
2. stratification by risk factor to identify which patients should be hospitalized has become more formalized17; and
3. several new antibiotics (eg, IV azithromycin, fluoroquinolones) have been introduced.

The following is my reinterpretation of the ATS guidelines based on these new results. This reinterpretation is made with an awareness of the potential medical, administrative, and legal problems associated with any guideline. With regard to medical issues, I have attempted to avoid specifying a single antimicrobial agent whenever possible, instead suggesting a class of agents deemed appropriate and leaving the choice of specific antibiotics to the individual physician. Finally, these guidelines are presented only as a template, subject to modification by individual physicians as needed on a case-by-case basis. For example, both the 1993 ATS and this guideline take the position that SGS and/or chest radiograph are not required for all patients, in part because legal and medical problems arise if such guidelines insist on such tests.

There are similarities between these guidelines and the 1993 ATS guidelines. For example, it is generally believed that S pneumoniae is the most common pathogen in CAP, that an etiologic agent is not detected in roughly half of all cases of CAP, and that the incidence of other pathogens is affected by the presence of certain host factors, time of year, and severity of pneumonia. However, differences also arise between these two guidelines, for example, with respect to the significance of drug-resistant S pneumoniae, which was not addressed by the earlier guidelines, and with respect to Gram-negative bacilli in CAP, because more recent studies have shown lower incidence of these pathogens than early studies, leaving the importance of their role in CAP open to question.18

The first change from the 1993 ATS guidelines is a reassessment of the algorithm for patient stratification (Fig 2). Two of the initial criteria for stratification of patients from the 1993 ATS guidelines are retained—the “need for hospitalization” (distinction of inpatients from outpatients) and the “severity of illness” (ward vs ICU hospitalization). The “coexisting illness” criterion is replaced with separation of those with cardiopulmonary disease or smokers from nonsmokers without cardiopulmonary disease. The original grouping according to age (older or younger

**Figure 1. 1993 Algorithm for assigning patients with CAP into ATS pneumonia groups.**

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than 60 years old) was replaced with two separate criteria—distinctions based on the patient’s risk for infection with drug-resistant *S. pneumoniae* (DRSP) or the patient’s risk for infection with *Pseudomonas aeruginosa*.

DRSP risk is emphasized because *S. pneumoniae* is the most common pathogen in CAP. Risk factors for DRSP include antibiotic therapy within the last 3 months, age ≥ 65 years, nursing home patient, immunosuppressive therapy, or history of alcohol abuse. When discussing DRSP, penicillin resistance is most common. Resistance is divided into intermediate levels (minimum inhibitory concentration [MIC], 0.1 to 1.0 µg/mL) and high levels (MIC, ≥ 2.0 µg/mL). These levels were initially chosen for the treatment of meningitis and are appropriate in that setting, but these breakpoints probably are low for treating pneumonia. No studies to date have investigated the efficacy of oral β-lactam agents in the outpatient setting. In the inpatient setting, three large *S. pneumoniae* pneumonia studies, enrolling a total of > 1,100 patients, showed no difference in outcomes among patients infected with *S. pneumoniae* that was sensitive to penicillin, had intermediate resistance to penicillin, and was highly resistant to penicillin, but only a handful of patients had DRSP with a MIC to penicillin of 4.0 µg/mL. This information suggests that high-dose (150,000 to 250,000 mg/kg/d) penicillin, ceftriaxone, or cefotaxime are probably appropriate for therapy in this setting. The effect of resistance to other antimicrobial agents has not been studied as much, but treatment failures in pneumonia patients receiving azithromycin and other macrolides have been reported. Recently, several cases were noted in which bacteremias occurred in patients receiving ongoing azithromycin therapy.

The treating physician still has to identify patients with other risk factors that can alter the spectrum of likely pathogens (eg, aspiration tends to be associated with Gram-negative pneumonias).

Changes have also been made in the recommended treatment for each patient category.

### Recommendations for Group 1

The 1993 ATS guidelines for group 1 (outpatients < 60 years old with no coexisting illness) recommended erythromycin or doxycycline for nonsmokers and clarithromycin or azithromycin (orally) for smokers. Since this patient category is not expected to be at risk for DRSP, current recommendations for the new group 1 (nonsmokers of any age with no cardiopulmonary disease) are macrolides or doxycycline—much the same as the previous recommendations.

### Recommendations for Group 2

In the 1993 ATS guidelines, group 2 patients (outpatients ≥ 60 years old or with coexisting illness) were noted to be at risk for Haemophilus and Staphylococcus infections. The recommended therapy included a second-generation cephalosporin, trimethoprim/sulfamethoxazole, or a β-lactam/β-lactamase inhibitor plus macrolide combination. Outpatients with cardiopulmonary disease or smokers with no DRSP risk) are treated like group 1, with a newer macrolide or doxycycline. For those with DRSP risk, the recommendation is a fluoroquinolone, amoxicillin plus a new macrolide. IV third-generation cephalosporin (either cefotaxime or ceftiraxone) plus a macrolide could be considered in certain situations (eg, nursing homes). IV antibiotics can now be practical options for outpatients; new infusion pump technologies as well as new reimbursement systems for home health care in the United States and Canada make such treatment feasible.

### Recommendations for Group 3

The 1993 ATS guidelines for group 3 patients (hospitalized patients with mild-to-moderate infection) recommended treatment with a second- or third-generation cephalosporin (not necessarily antipseudomonal, since *Pseudomonas* was seldom observed), mainly to cover Gram-negative pathogens.

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**Figure 2. Algorithm for assigning patients with CAP into pneumonia groups.**

```plaintext
Community-Acquired Pneumonia

Outpatient

1. No cardiopulmonary disease & nonsmoker
2. Cardiopulmonary disease or smoker

Inpatient

3. Ward (mild-moderate hospitalized)
4. Intensive care unit
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or a combination of a β-lactam/β-lactamase inhibitor and a macrolide. The new group 3, like the new group 2, is divided based on DRSP risk (or in this case, being a nursing home patient). For hospitalized patients with mild-to-moderate infection without DRSP risk, the recommendation is a β-lactam plus macrolide (or doxycycline) combination, or a fluoroquinolone alone.25 If there is DRSP risk, the recommendation is cefotaxime or ceftiraxone26 combined with a macrolide or a fluoroquinolone alone. Other options are doses of amoxicillin, cefuroxime axetil, and amoxicillin/clavulanate, which have shown equal efficacy in DRSP and non-DRSP infections in a large number of patients with serious pneumococcal pneumonia.27 While higher penicillin-resistant S pneumoniae (eg, higher MICs, ≥ 4 μg/mL) or metastatic infection to the meninges may warrant alternative antibiotic therapies,28 these have not presented a problem at our hospital.

Recommendations for Group 4

For hospitalized patients in the ICU (group 4), the 1993 ATS guidelines suggest a third-generation cephalosporin with antipseudomonal activity or another type of antipseudomonal agent (eg, imipenem, ciprofloxacin) plus a macrolide. These recommendations were based on concerns at the time the 1993 guidelines were drafted about Legionella and S pneumoniae, and also possibly Pseudomonas.2 I recommend that ICU patients without P aeruginosa risk should be treated with either cefotaxime or ceftiraxone. Alternatively, a β-lactam/β-lactamase inhibitor (eg, piperacillin/tazobactam) plus either erythromycin or a fluoroquinolone alone could be used. With P aeruginosa risk, recommendations include a macrolide plus two antipseudomonal agents or ciprofloxacin plus one antipseudomonal agent; these antibiotic combinations should cover S pneumoniae, Legionella, and P aeruginosa. If high-level penicillin-resistant S pneumoniae (MIC, ≥ 4.0 μg/mL) is cultured, strong consideration should be given to initiating vancomycin.

APPENDIX/DISCUSSION

Dr. Bernstein: What about ciprofloxacin resistance? The whole idea of using quinolones against these pathogens is in question.

Dr. Campbell: You need to know local ciprofloxacin resistance levels in your community. At our hospital, we see a high rate of ciprofloxacin resistance, but this is mainly associated with our cystic fibrosis clinic patients. Burn units can also skew the results, giving high levels of ciprofloxacin-resistant Pseudomonas.

Dr. Bernstein: In the Veterans Affairs hospital at which I attend, we do not have any cystic fibrosis patients, and we observe 30% ciprofloxacin resistance vs 10 to 15% resistance at private hospitals. My anxiety level goes up when susceptibility slips below 80%; I would prefer 95% or better. I tell my residents not to rely on ciprofloxacin alone for serious Pseudomonas infections.

Dr. Campbell: I agree. I no longer treat someone at risk for Pseudomonas with a single agent, as we did in 1993.

Dr. Segreti: What are the risk factors for Pseudomonas from the community?

Dr. Campbell: We are still debating those, but structural lung disease, cystic fibrosis, HIV, and bronchiectasis are risk factors.

Dr. Boylen: What about anaerobes? In our hospital, we see a lot of alcoholic patients presenting with community-acquired aspiration pneumonia, to the point where it is the leading cause of CAP.

Dr. Campbell: The incidence of anaerobic lung infection has varied considerably among studies. Most physicians feel reasonably confident in diagnosing CAP caused by anaerobic organisms.

Dr. Levison: There are a limited number of studies. We did a study in the early 1970s in which every CAP patient had a transtracheal tube, and we recovered anaerobes in about 20%.20 A similar study at Temple with community- and hospital-acquired pneumonia got about a third anaerobes for the hospital-acquired infections and about 88% anaerobes for the community-acquired infections, either alone or with other nasty Gram negatives.30

Dr. Bernstein: One question is whether these anaerobes are major pathogens or just “fellow travelers.”

Dr. Campbell: I agree, particularly in the nonintubated patient.

REFERENCES