GUIDELINES FROM THE INFECTIOUS DISEASES SOCIETY OF AMERICA

# Practice Guidelines for the Management of Community-Acquired Pneumonia in Adults

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## Executive Summary

Guidelines for the management of community-acquired pneumonia were issued on behalf of the Infectious Diseases Society of America in April 1998. The present version represents a revision of these guidelines issued in February 2000; updates at 6- to 12-month intervals are anticipated. A summary of these guidelines follows.

*Grading system.* Recommendations are categorized by the letters A–D, according to the strength of the recommendation: A, good evidence to support the recommendation; B, moderate evidence to support the recommendation; C, poor evidence to support the recommendation; and D, evidence against the recommendation. The recommendations are also graded by the quality of the evidence to support the recommendation, on the basis of categories I–III; I, at least 1 randomized controlled trial supports the recommendation; II, evidence from at least 1 well-designed clinical trial without randomization supports the recommendation; and III, "expert opinion."

*Chest radiography.* Chest radiography is considered critical for establishing the diagnosis of pneumonia and for distinguishing this condition from acute bronchitis (AB), which is a common cause of antibiotic abuse.

*Site of care.* Recommendations regarding the decision for hospitalization are based on the methodology used in the clinical prediction rule for short-term mortality, from the publications of the Pneumonia Patient Outcome Research Team (Pneumonia PORT). Patients are stratified into 5 severity classes by means of a 2-step process. Class I indicates an age <50 years, with none of 5 comorbid conditions (neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, or renal disease), normal or only mildly deranged vital signs, and normal mental status. In step 2, patients not assigned to risk class I are stratified in classes II–V on the basis of points assigned for 3 demographic variables (age, sex, and nursing home residency), 5 comorbid conditions (summarized above), 5 physical examination findings, and 7 laboratory and/or radiographic findings.

Patients in risk classes I and II do not usually require hospitalization, those in risk class III may require brief hospitalization, and those in risk classes IV and V usually require hospitalization. It should be noted that social factors, such as outpatient support mechanisms and probability of adherence, are not included in this assessment.

*Laboratory tests.* All patients thought to have pneumonia should undergo chest radiography. The following laboratory values should be determined for patients who are hospitalized: complete blood cell count and differential, serum creatinine, blood urea nitrogen, glucose, electrolytes, and liver function tests. HIV serology with informed consent should be considered, especially for persons aged 15–54 years. Oxygen saturation should be assessed. There should be 2 pretreatment blood cultures, as well as Gram staining and culture of expectorated sputum. Selected patients should have microbiological studies for tuberculosis and legionella infection. The preferred tests for detection of *Legionella* species are the urinary antigen assay for *Legionella pneumophila* serogroup 1 and culture with selective media. The rationale for performing microbiological studies to establish an etiologic diagnosis is based on attempts to improve care of the individual patient with pathogen-specific treatment; to improve care of other patients and to advance knowledge by detecting epidemiologically important organisms (*Legionella*, penicillin-resistant *Streptococcus pneumoniae*, and methicillin-resistant *Staphylococcus aureus*); to implement contact-tracing and antimicrobial prophylaxis in appropriate settings (such as cases of *Neisseria meningitidis* infection, *Haemophilus influenzae* type B infection, and tuberculosis); to prevent antibiotic abuse; and to reduce antibiotic expense.

*Antimicrobial therapy.* Recommendations are provided for pathogen-specific treatment in cases in which an etiologic diagnosis is established or strongly suspected. If this information

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is not available initially but is subsequently reported, changing to the antimicrobial agent that is most cost-effective, least toxic, and most narrow in spectrum is encouraged. Recommendations for treating patients who require empirical antibiotic selection are based on severity of illness, pathogen probabilities, resistance patterns of *S. pneumoniae* (the most commonly implicated etiologic agent), and comorbid conditions.

The recommendation for outpatients is administration of a macrolide, doxycycline, or fluoroquinolone with enhanced activity against *S. pneumoniae*. For patients who are hospitalized, the recommendation is administration of a fluoroquinolone alone or an extended-spectrum cephalosporin (cefotaxime or ceftriaxone) plus a macrolide. Patients hospitalized in the intensive care unit (ICU) should receive ceftriaxone, cefotaxime, ampicillin-sulbactam, or piperacillin-tazobactam in combination with a fluoroquinolone or macrolide. β-lactams, other than those noted, are not recommended. Intravenous antibiotics may be switched to oral agents when the patient is improving clinically, is hemodynamically stable, and is able to ingest drugs. Most patients show a clinical response within 3–5 days. Changes evident on chest radiographs usually lag behind the clinical response, and repeated chest radiography is generally not indicated for patients who respond. The failure to respond usually indicates an incorrect diagnosis; host failure; inappropriate antibiotic; inappropriate dose or route of administration; unusual or unanticipated pathogen; adverse drug reaction; or complication, such as pulmonary superinfection or empyema.

*Prognosis.* The most frequent causes of lethal community-acquired pneumonia are *S. pneumoniae* and *Legionella*. The most frequent reason for failure to respond is progression of pathophysiological changes, despite appropriate antibiotic treatment.

*Pneumococcal pneumonia.* *S. pneumoniae*, the most common identifiable etiologic agent of pneumonia in virtually all studies, accounts for about two-thirds of bacteremic pneumonia cases, and pneumococci are the most frequent cause of lethal community-acquired pneumonia. Management has been complicated in recent years by the evolution of multidrug resistance. β-lactams (amoxicillin, cefotaxime, and ceftriaxone) are generally regarded as the drugs of choice, although pneumonia caused by resistant strains (MIC, ≥2 μg/mL) may not respond as readily as pneumonia caused by more susceptible strains. The activity of macrolides and doxycycline or other β-lactams, including cefuroxime, is good against penicillin-susceptible strains but less predictable with strains that show reduced penicillin-susceptibility. Vancomycin, linezolid, and quinupristin/dalfopristin are the only drugs with predictable in vitro activity. Fluoroquinolones are generally active against strains that are susceptible or resistant to penicillin, but recent reports indicate increasing resistance in selective locations that correlate with excessive fluoroquinolone use.

*Prevention.* The major preventive measures are use of influenza vaccine and use of pneumococcal vaccine, according to guidelines of the Advisory Council on Immunization Practices of the Centers for Disease Control and Prevention (CDC).

*Performance indicators.* Recommendations for performance indicators include the collection of blood culture specimens before antibiotic treatment and the institution of antibiotic treatment within 8 h of hospitalization, since both are supported on the basis of evidence-based trials. Additional performance indicators recommended are laboratory tests for *Legionella* in patients hospitalized in the ICU, demonstration of an infiltrate on chest radiographs of patients with an ICD-9 (International Classification of Diseases, 9th edition) code for pneumonia, and measurement of blood gases or pulse oximetry within 24 h of admission.

## Introduction

Lower respiratory tract infections are the major cause of death in the world and the major cause of death due to infectious diseases in the United States. Recent advances in the field include the identification of new pathogens (*Chlamydia pneumoniae* and hantavirus), new methods of microbial detection (PCR), and new antimicrobial agents (macrolides, β-lactam agents, fluoroquinolones, oxazolidinones, and streptogramins). Despite extensive studies, there are few conditions in medicine that are so controversial in terms of management. Guidelines for management were published in 1993 by the American Thoracic Society [1], the British Thoracic Society [2], and the Canadian Infectious Disease Society [3], as well as the Infectious Diseases Society of America (IDSA) in 1998 [4]. The present guidelines represent revised recommendations of the IDSA. Compared with previous guidelines, these guidelines are intended to reflect updated information, provide more extensive recommendations in selected areas, and indicate an evolution of opinion. These therapeutic guidelines are restricted to community-acquired pneumonia (CAP) in immunocompetent adults.

Recommendations are given alphabetical ranking to reflect their strength and a Roman numeral ranking to reflect the quality of supporting evidence (table 1). This is customary for quality standards from the IDSA [5]. It should be acknowledged that no set of standards can be constructed to deal with the multitude of variables that influence decisions regarding site of care, diagnostic evaluation, and selection of antibiotics. Thus, these standards should not supplant good clinical judgement.

## Epidemiology

### Magnitude

CAP is commonly defined as an acute infection of the pulmonary parenchyma that is associated with at least some symptoms of acute infection, accompanied by the presence of an acute infiltrate on a chest radiograph or auscultatory findings consistent with pneumonia (such as altered breath sounds and/

Table 1. Categories for ranking recommendations in the therapeutic guidelines.

| Category | Description |
|---|---|
| Strength of recommendation | |
| A | Good evidence to support a recommendation for use |
| B | Moderate evidence to support a recommendation for use |
| C | Poor evidence to support a recommendation |
| D | Moderate evidence to support a recommendation against use |
| E | Good evidence to support a recommendation against use |
| Quality of evidence | |
| I | Evidence from at least 1 randomized, controlled trial |
| II | Evidence from at least 1 well-designed clinical trial without randomization |
| III | Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees |

or localized rales), in a patient not hospitalized or residing in a long-term-care facility for ≥14 days before onset of symptoms. Symptoms of acute lower respiratory infection may include several (in most studies, at least 2) of the following: fever or hypothermia, rigors, sweats, new cough with or without sputum production or change in color of respiratory secretions in a patient with chronic cough, chest discomfort, or the onset of dyspnea. Most patients also have nonspecific symptoms, such as fatigue, myalgias, abdominal pain, anorexia, and headache.

Pneumonia is the sixth most common cause of death in the United States. From 1979 through 1994, the overall rates of death due to pneumonia and influenza increased by 59% (on the basis of ICD-9 codes on death certificates) in the United States [6]. Much of this increase is due to a greater proportion of persons aged ≥65 years; however, age-adjusted rates also increased by 22%, which suggests that other factors may have contributed to a changing epidemiology of pneumonia, including a greater proportion of the population with underlying medical conditions at increased risk of respiratory infection.

Annually, 2–3 million cases of CAP result in ~10 million physician visits, 500,000 hospitalizations, and 45,000 deaths in the United States [7, 8]. The incidence of CAP that requires hospitalization is estimated to be 258 persons per 100,000 population and 962 per 100,000 persons aged ≥65 years [8]. Although mortality has ranged from 2% to 30% among hospitalized patients in a variety of studies, the average is ~14% [9]. Mortality is estimated to be <1% for patients not hospitalized [9, 10]. The incidence of CAP is heavily weighted toward the winter months.

### Prognosis, Risk Stratification, and the Initial Site-of-Treatment Decision

Knowledge about the prognosis of a disease allows physicians to inform their patients about the expected natural history of an illness, the likelihood of potential complications, and the probability of successful treatment. Understanding the prognosis of CAP is of particular clinical relevance, since it ranges from rapid recovery from symptoms without functional impairment to serious morbid complications and death. The ability to accurately predict medical outcomes in cases of CAP has a major impact on management. The decision to hospitalize a patient or to treat him or her as an outpatient (figure 1) is perhaps the single most important clinical decision made by physicians during the entire course of illness, which has direct bearing on the location and intensity of laboratory evaluation, antibiotic therapy, and costs. The estimated total treatment cost for an episode of CAP managed in the hospital is $7500 (US dollars) [11], >20-fold higher than the cost of outpatient treatment.

Numerous studies have identified risk factors for death in cases of CAP [9, 10, 12]. These factors were well-defined in the pre–penicillin era; studies of adults showed an increased risk with alcohol consumption, increasing age, the presence of leukopenia, the presence of bacteremia, and radiographic changes [12]. More recent studies have confirmed these findings [2, 13–18]. Independent associations with increased mortality have also been demonstrated for a variety of comorbid illnesses, such as active malignancies [10, 16, 19], immunosuppression [20, 21], neurological disease [19, 22, 23], congestive heart failure [10, 17, 19], coronary artery disease [19], and diabetes mellitus [10, 19, 24]. Signs and symptoms independently associated with increased mortality consist of dyspnea [10], chills [25], altered mental status [10, 19, 23, 26], hypothermia or hyperthermia [10, 16, 17, 20], tachypnea [10, 19, 23, 27], and hypotension (diastolic and systolic) [10, 19, 26–28].

Laboratory and radiographic findings independently associated with increased mortality are hyponatremia [10, 19], hyperglycemia [10, 19], azotemia [10, 19, 27, 28], hypoalbuminemia [16, 19, 22, 25], hypoxemia [10, 19], liver function test abnormalities [19], and pleural effusion [29]. Infections due to gram-negative bacilli or *S. aureus*, postobstructive pneumonia, and aspiration pneumonia are also independently associated with higher mortality [30].

Despite our knowledge regarding the associations of clinical, laboratory, and radiographic factors and patient mortality, there is wide geographic variation in hospital admission rates for CAP [31, 32]. This variation suggests that physicians do not use a uniform strategy to relate the decision to hospitalize to the prognosis. In fact, physicians often overestimate the risk of death for patients with CAP, and the degree of overesti-

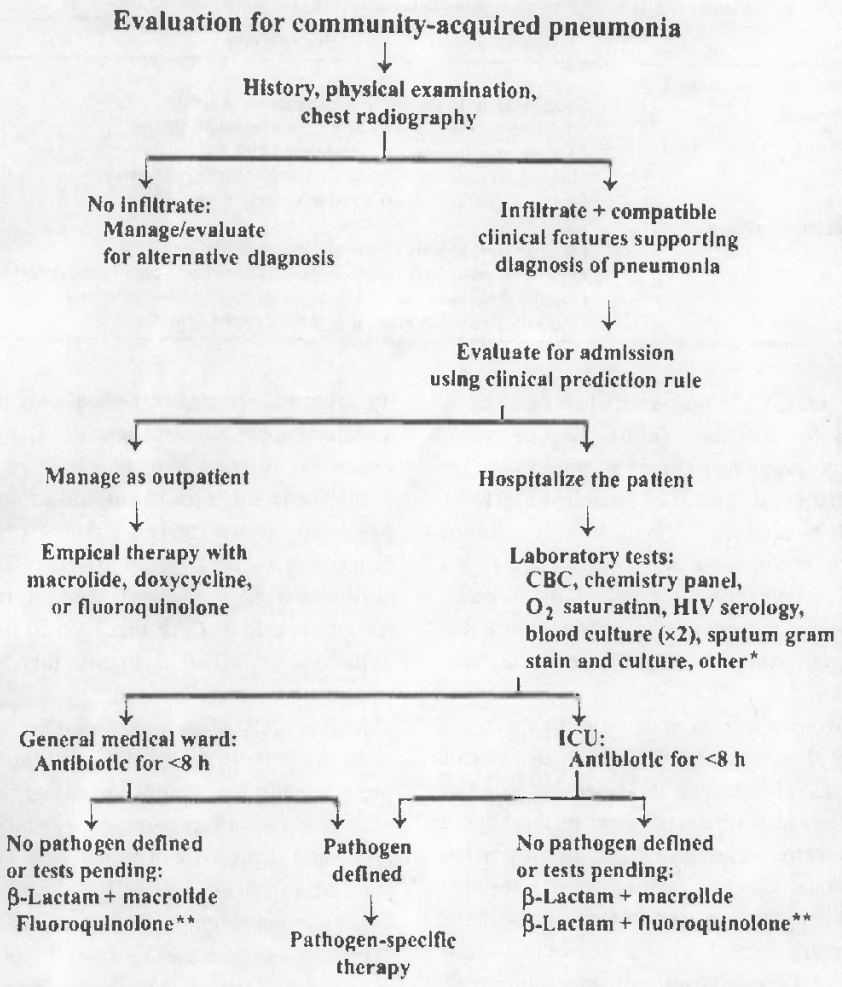


**Figure 1.** Evaluation for diagnosis and management of community-acquired pneumonia, including site, duration, and type of treatment. β-Lactam: cefotaxime, ceftriaxone, or a β-lactam/β-lactamase inhibitor. Fluoroquinolone: levofloxacin, moxifloxacin, or gatifloxacin or another flunroquinolone with enhanced antipneumococcal activity. Macrolide: erythromycin, clarithromycin, or azithromycin. CBC, complete blood cell count; ICU, intensive care unit. *Other tests for selected patients: see text, Diagnostic Evaluation: Etiology. **See table 15 for special considerations.

mation is independently associated with the decision to hospitalize [30].

Over the past 10 years, at least 13 studies have used multivariate analysis to identify predictors of prognosis for patients with CAP [10, 16–20, 25–27, 33–35]. The Pneumonia PORT developed a methodologically sound clinical prediction rule that quantifies short-term mortality for patients with this illness [10]. Used as a guideline, this rule may help physicians make decisions about the initial location and intensity of treatment for patients with this illness (table 2).

The Pneumonia PORT prediction rule was derived with 14,199 inpatients with CAP; it was independently validated with 38,039 inpatients with CAP and 2287 inpatients and outpatients prospectively enrolled in the Pneumonia PORT cohort study. With this rule, patients are stratified into 5 severity classes by means of a 2-step process. In step 1, patients are classified as risk class I (the lowest severity level) if they are aged ≤50 years, have none of 5 important comorbid conditions (neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, or renal disease), and have normal or only mildly deranged vital signs and normal mental status. In step 2, all patients who are not assigned to risk class I on the basis of the initial history and physical examination findings alone are stratified into classes II–V, on the basis of points assigned for 3 demographic variables (age, sex, and nursing home residence), 5 comorbid conditions (listed above), 5 physical examination findings (altered mental status, tachypnea, tachycardia, systolic hypotension, hypothermia, or hyperthermia), and 7 laboratory or radiographic findings (acidemia, elevated blood urea nitrogen, hyponatremia, hyperglycemia, anemia, hypoxemia, or pleural effusion; table 3). Point assignments correspond with the following classes: ≤70, class II; 71–90, class III; 91–130, class IV; and >130, class V.

In the derivation and validation of this rule, mortality was

**Table 2.** Comparison of risk class–specific mortality rates in the derivation and validation cohorts.

| Risk class[a] (total points) | MedisGroups derivation cohort | | MedisGroups validation cohort | | Pneumonia PORT validation cohort | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Inpatients | | Outpatients | | All patients | |
| | *n* | Mortality, % | *n* | Mortality, % | *n* | Mortality, % | *n* | Mortality, % | *n* | Mortality, % |
| I | 1372 | 0.4 | 3034 | 0.1 | 185 | 0.5 | 587 | 0.0 | 772 | 0.1 |
| II (≤70) | 2412 | 0.7 | 5778 | 0.6 | 233 | 0.9 | 244 | 0.4 | 477 | 0.6 |
| III (71–90) | 2632 | 2.8 | 6790 | 2.8 | 254 | 1.2 | 72 | 0.0 | 326 | 0.9 |
| IV (91–130) | 4697 | 8.5 | 13,104 | 8.2 | 446 | 9.0 | 40 | 12.5 | 486 | 9.3 |
| V (>130) | 3086 | 31.1 | 9333 | 29.2 | 225 | 27.1 | 1 | 0.0 | 226 | 27.0 |
| Total | 14,199 | 10.2 | 38,039 | 10.6 | 1343 | 8.0 | 944 | 0.6 | 2287 | 5.2 |

NOTE. No statistically significant differences in overall mortality or mortality within risk class existed among patients in the MedisGroups derivation, MedisGroups validation, and overall Pneumonia Patient Outcome Research Team (PORT) validation cohorts (*n* denotes the no. of patients within each risk class in the derivation and validation cohorts). *P* values for the comparisons of mortality across risk classes are as follows: class I, $P = .22$; class II, $P = .67$; class III, $P = .12$; class IV, $P = .69$; and class V, $P = .09$.

[a] Risk class I was determined by the absence of all predictors identified in step 1 of the prediction rule. Risk classes II–V were determined by a patient's total risk score, which is computed by use of the point scoring system shown in table 3.

low for risk classes I–III (0.1%–2.8%), intermediate for class IV (8.2%–9.3%), and high for class V (27.0%–31.1%). Increases in risk class were also associated with subsequent hospitalization and delayed return to usual activities for outpatients and with rates of admission to the ICU and length of stay for inpatients in the Pneumonia PORT validation cohort. On the basis of these observations, Pneumonia PORT investigators suggest that patients in risk classes I or II generally are candidates for outpatient treatment, risk class III patients are potential candidates for outpatient treatment or brief inpatient observation, and patients in classes IV and V should be hospitalized (table 4). Estimates from the Pneumonia PORT cohort study suggest that these recommendations would reduce the proportion of patients receiving traditional inpatient care by 31% and that there would be a brief observational inpatient stay for an additional 19%.

The effectiveness and safety of applying the Pneumonia PORT prediction rule to the initial site of care for an independent population of patients with CAP have been examined with use of a modified version of the Pneumonia PORT prediction rule [36]. Emergency room physicians were educated about the rule and were encouraged to treat those in risk classes I–III as outpatients, with close, structured follow-up and provision of oral clarithromycin at no cost to the patient, if desired. The outcomes for those treated at home during this intervention phase were compared with the outcomes for historical control subjects from the time period immediately preceding the intervention.

During the intervention period, there were 166 eligible patients classified as "low risk" for short-term mortality (risk classes I–III) for comparison with 147 control subjects. The percentage treated initially as outpatients was higher during the intervention period than during the control period (57% vs. 42%; relative increase of 36%; $P = .01$). When initial plus subsequent hospitalization was used as the outcome measure, there was a trend toward more outpatient care during the intervention period, but the difference was no longer statistically significant (52% vs. 42%; $P = .07$). None of those initially treated in the outpatient setting during the intervention period died within 4 weeks of presentation.

A second multicenter controlled trial subsequently assessed the effectiveness and safety of using the Pneumonia PORT prediction rule for the initial site-of-treatment decision [37]. In this trial, 19 emergency departments were randomly assigned either to continue conventional management of CAP or to implement a critical pathway that included the Pneumonia PORT prediction rule to guide the admission decision. Emergency room physicians were educated about the rule and were encouraged to treat those in risk classes I–III as outpatients with oral levofloxacin. Overall, 1743 patients with CAP were enrolled in this 6-month study. Use of the prediction rule resulted in an 18% reduction in the admission of low-risk patients (31% vs. 49%; $P = .013$). Use of the rule did not result in an increase in mortality or morbidity and did not compromise patients' 30-day functional status. These studies support use of the Pneumonia PORT prediction rule to help physicians identify low-risk patients who can be safely treated in the outpatient setting.

The IDSA panel endorses the findings of the Pneumonia PORT prediction rule, which identifies valid predictors for mortality and provides a rational foundation for the decision regarding hospitalization. However, it should be emphasized that the PORT prediction rule is validated as a mortality prediction model and not as a method to triage patients with CAP. New studies are required to test the basic premise underlying the use of this rule in the initial site-of-treatment decision, so that patients classified as "low risk" and treated in the outpatient setting will have outcomes equivalent to or better than those of similar "low-risk" patients who are hospitalized.

It is important to note that prediction rules are meant to contribute to rather than to supersede physicians' judgment. Another limitation is that factors other than severity of illness must also be considered in determining whether an individual patient is a candidate for outpatient care. Patients designated as "low risk" may have important medical and psychosocial contraindications to outpatient care, including expected compliance problems with medical treatment or poor social support

**Table 3.** Scoring system for step 2 of the prediction rule: assignment to risk classes II–V.

| Patient characteristic | Points assigned[a] |
|---|---|
| Demographic factor | |
| Age | |
| Male | No. of years of age |
| Female | No. of years of age − 10 |
| Nursing home resident | +10 |
| Comorbid illnesses | |
| Neoplastic disease[b] | +30 |
| Liver disease[c] | +20 |
| Congestive heart failure[d] | +10 |
| Cerebrovascular disease[e] | +10 |
| Renal disease[f] | +10 |
| Physical examination finding | |
| Altered mental status[g] | +20 |
| Respiratory rate >30 breaths/min | +20 |
| Systolic blood pressure <90 mm Hg | +20 |
| Temperature <35°C or >40°C | +15 |
| Pulse >125 beats/min | +10 |
| Laboratory or radiographic finding | |
| Arterial pH <7.35 | +30 |
| Blood urea nitrogen >30 mg/dL | +20 |
| Sodium <130 mEq/L | +20 |
| Glucose >250 mg/dL | +10 |
| Hematocrit <30% | +10 |
| Arterial partial pressure of oxygen <60 mm Hg[h] | +10 |
| Pleural effusion | +10 |

[a] A total point score for a given patient is obtained by adding the patient's age in years (age − 10, for females) and the points for each applicable patient characteristic. Points assigned to each predictor variable were based on coefficients obtained from the logistic regression model used in step 2 of the prediction rule.

[b] Any cancer except basal or squamous cell cancer of the skin that was active at the time of presentation or diagnosed within 1 year of presentation.

[c] A clinical or histologic diagnosis of cirrhosis or other form of chronic liver disease such as chronic active hepatitis.

[d] Systolic or diastolic ventricular dysfunction documented by history and physical examination, as well as chest radiography, echocardiography, Muga scanning, or left ventriculography.

[e] A clinical diagnosis of stroke, transient ischemic attack, or stroke documented by MRI or computed axial tomography.

[f] A history of chronic renal disease or abnormal blood urea nitrogen and creatinine values documented in the medical record.

[g] Disorientation (to person, place, or time, not known to be chronic), stupor, or coma.

[h] In the Pneumonia Patient Outcome Research Team cohort study, an oxygen saturation value <90% on pulse oximetry or intubation before admission was also considered abnormal.

at home. Ability to maintain oral intake, history of substance abuse, cognitive impairment, and ability to perform activities of daily living must be considered. In addition, patients may have rare conditions, such as severe neuromuscular disease or immunosuppression, which are not included as predictors in these prediction rules but increase the likelihood of a poor prognosis.

Prediction rules may also oversimplify the way physicians interpret important predictor variables. For example, extreme alterations in any one variable have the same effect on risk stratification as lesser changes, despite obvious differences in clinical import (e.g., a systolic blood pressure of 40 mm Hg vs. one of 88 mm Hg). Furthermore, such rules discount the cumulative importance of multiple simultaneous physiological derangements, especially if each derangement alone does not reach the threshold that defines an abnormal value (e.g., systolic blood pressure of 90/40 mm Hg, respiratory rate of 28 breaths/min, and pulse of 120 beats/min). Finally, prediction rules often neglect the importance of patients' preferences in clinical decision-making. This point is highlighted by the observation that the vast majority of low-risk patients with CAP do not have their preferences for site of care solicited, despite strong preferences for outpatient care [38].

### Role of Specific Pathogens in CAP

Prospective studies evaluating the causes of CAP in adults have failed to identify the cause of 40%–60% of cases of CAP and have detected ≥2 etiologies in 2%–5% [2, 7, 26, 39, 40]. The most common etiologic agent identified in virtually all studies of CAP is *S. pneumoniae*, which accounts for about two-thirds of all cases of bacteremic pneumonia cases [9]. Other pathogens implicated less frequently include *H. influenzae* (most strains of which are nontypeable), *Mycoplasma pneumoniae, C. pneumoniae, S. aureus, Streptococcus pyogenes, N. meningitidis, Moraxella catarrhalis, Klebsiella pneumoniae* and other gram-negative rods, *Legionella* species, influenza virus (depending on the season), respiratory syncytial virus, adenovirus, parainfluenza virus, and other microbes. The frequency of other etiologies is dependent on specific epidemiological factors, as with *Chlamydia psittaci* (psittacosis), *Coxiella burnetii* (Q fever), *Francisella tularensis* (tularemia), and endemic fungi (histoplasmosis, blastomycosis, and coccidioidomycosis).

Comparisons of relative frequency of each of the etiologies of pneumonia are hampered by the varying levels of sensitivity and specificity of the tests used for each of the pathogens that they detect; for example, in some studies, tests used for legionella infections provide a much higher degree of sensitivity and possibly specificity than do tests used for pneumococcal infections. Thus, the relative contribution of many causes to the incidence of CAP is undoubtedly either exaggerated or underestimated, depending on the sensitivity and specificity of tests used in each of the studies.

### Etiology-Specific Diagnoses and the Clinical Setting

No convincing association has been demonstrated between individual symptoms, physical findings, or laboratory test results and specific etiology [39]. Even time-honored beliefs, such

**Table 4.** Risk-class mortality rates.

| Risk class | No. of points | Validation cohort | | Recommended site of care |
|---|---|---|---|---|
| | | No. of patients | Mortality, % | |
| I | —[a] | 3034 | 0.1 | Outpatient |
| II | ≤70 | 5778 | 0.6 | Outpatient |
| III | 71–90 | 6790 | 2.8 | Outpatient or brief inpatient |
| IV | 91–130 | 13,104 | 8.2 | Inpatient |
| V | >130 | 9333 | 29.2 | Inpatient |

NOTE. Table is adapted from [10].

[a] Absence of predictors.

Table 5. Diagnostic studies for evaluation of community-acquired pneumonia.

| |
|---|
| Baseline assessment |
| Chest radiography to substantiate diagnosis of pneumonia, to detect associated lung diseases, to gain insight into causative agent (in some cases), to assess severity, and as baseline to assess response |
| Outpatients |
| Sputum Gram stain and culture for conventional bacteria are optional |
| Inpatients |
| Determination of complete blood cell and differential counts |
| Serum creatinine, urea nitrogen, glucose, electrolyte, bilirubin, and liver enzyme values |
| HIV serological status for persons aged 15–54 years |
| $O_2$ saturation arterial blood gas values for selected patients |
| Blood cultures (×2; before treatment) |
| Gram stain and culture of sputum[a] |
| Test for *Mycobacterium tuberculosis*, with acid-fast bacilli staining and culture for selected patients, especially those with cough for >1 mo, other common symptoms, or suggestive radiographic changes |
| Test for *Legionella* in selected patients, including all seriously ill patients without an alternative diagnosis, especially if aged >40 years, immunocompromised, or nonresponsive to β-lactam antibiotics, if clinical features are suggestive of this diagnosis, or in outbreak settings |
| Thoracentesis with stain, culture, and determination of pH and leukocyte count differential (pleural fluid) |
| Alternative specimens to expectorated sputum |
| Aspirates of intubated patients, tracheostomy aspirates, and nasotracheal aspirates: manage as with expectorated sputum |
| Induced sputum: recommended for detection of *M. tuberculosis* or *Pneumocystis carinii* |
| Bronchoscopy (see text under Special Considerations: Pneumococcal Pneumonia) |
| Transtracheal aspiration: recommended only in cases of enigmatic pneumonia, to be done by persons skilled in the technique, preferably before antibiotic treatment |
| Optional |
| Additional cytological or microbiological tests, as listed in table 8, depending on clinical features, available resources, underlying conditions, and/or epidemiological associations of the patient |
| Serum: to be frozen and saved for serological analysis, if needed[b] |

[a] Should be deep-cough specimen obtained before antibiotic therapy. Gram stain should be interpreted by trained personnel and culture done only if specimen is adequate by cytological criteria, except for *Legionella* and mycobacteria. Consider diagnostic studies for endemic fungi and mycobacteria when clinical features suggest infection with these. For hospitalized patients with severe pneumonia or clinical features that suggest legionnaires' disease, perform culture and urinary antigen testing for *Legionella*. Inability to obtain specimens for diagnostic studies should not delay antibiotic treatment of acutely ill patients.

[b] Serological tests would include those for *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Chlamydia pneumoniae*, or others (i.e., viruses, *Chlamydia psittaci*, or *Coxiella burnetii*), depending on the circumstances.

as the absence of productive cough or inflammatory sputum in pneumonia due to *Mycoplasma*, *Legionella*, or *Chlamydia* species, have not withstood close inspection. On the other hand, most comparisons have involved relatively small numbers of patients and have not evaluated the potential for separating causes by use of constellations of symptoms and physical findings.

In one study, as yet unconfirmed, that compared patients identified in a prospective standardized fashion, a scoring system using 5 symptoms and laboratory abnormalities was able to differentiate most patients with legionnaires' disease from the other patients [41]. A similar type of system has been devised for identifying patients with hantavirus pulmonary syndrome (HPS) [42]. If validated, such scoring systems may be useful for identifying patients who should undergo specific diagnostic tests (which are too expensive to use routinely for all patients with CAP) and be empirically treated with specific antimicrobial drugs while test results are pending.

Certain pathogens cause pneumonia more commonly among persons with specific risk factors. For instance, pneumococcal pneumonia is especially likely to occur in the elderly and in patients with a variety of medical conditions, including alcoholism, chronic cardiovascular disease, chronic obstructed airway disease, immunoglobulin deficiency, hematologic malignancy, and HIV infection. However, outbreaks occur among young adults under conditions of crowding, such as in army camps or prisons. *S. pneumoniae* is second only to *Pneumocystis carinii* as the most common identifiable cause of acute pneumonia in patients with AIDS [43–45]. *Legionella* is an opportunistic pathogen; legionella pneumonia is rarely recognized in healthy young children and young adults. It is an important cause of pneumonia in organ transplant recipients and in patients with renal failure and occurs with increased frequency in patients with chronic lung disease, smokers, and possibly those with AIDS [46]. Although *M. pneumoniae* historically has been thought primarily to involve children and young adults, some evidence suggests that it causes pneumonia in healthy adults of any age [8].

There are seasonal differences in incidence of many of the causes of CAP. Pneumonia due to *S. pneumoniae*, *H. influenzae*, and influenza occurs predominantly in winter months, whereas *C. pneumoniae* appears to cause pneumonia year-round. Although there is a summer prevalence of outbreaks of legionnaires' disease, sporadic cases occur with similar frequency during all seasons [8, 46]. Some studies suggest that there is no seasonal variation in mycoplasma infection; however, other data suggest that its incidence is greatest during the fall and winter months [47].

**Table 6.** Rationale for establishing an etiologic diagnosis.

| |
|---|
| Improve care of the individual patient |
| To permit optimal antibiotic selection specifically directed at the causative agent |
| To allow for a rational basis for change from parenteral to oral therapy and for a change in therapy necessitated by an adverse drug reaction |
| To permit antibiotic selection that limits the consequences of injudicious antibiotic use in terms of cost to the patient, inducible resistance (e.g., inducible β-lactamases), and adverse drug reactions |
| Improve care of other patients and advance knowledge |
| To identify pathogens of potential epidemiological significance, such as *Legionella*, hantavirus, and penicillin-resistant *Streptococcus pneumoniae* |
| To identify newly emergent pathogens (hantavirus) |
| To identify drug-resistant pathogens and monitor trends (drug-resistant *S. pneumoniae*, β-lactamase–producing *Haemophilus influenzae*, or methicillin-resistant *Staphylococcus aureus*) |
| To prompt contact-tracing and antimicrobial prophylaxis (*Neisseria meningitidis*, *H. influenzae* type b, *Mycobacterium tuberculosis*) |
| To permit antibiotic selection that limits the effects of antibiotic overuse on the community |
| Doing so is cost efficient |
| Average cost of standard microbiological studies is <1% of the average hospital bill |
| Narrow-spectrum agents may be less expensive |
| Although many reports indicate that the yield of pathogens in expectorated sputum from patients with CAP is only 30%–40%, this yield may often be increased with improved techniques; furthermore, a negative specimen may enhance the probability of an atypical agent (which may influence the antimicrobial choice), and a specimen of good quality that does not show or yield *S. aureus* or gram-negative bacilli provides good evidence that these organisms are not present; this information may prove useful for patients who do not respond, because conventional cultures of posttreatment specimens are relatively useless |

There are other temporal variations in incidence of some causes of pneumonia. The frequency and severity of influenza vary as a result of antigenic drift and, occasionally, as a result of antigenic shift. For less clear reasons, increases in incidence of mycoplasma infections occur every 3–6 years [47, 48]. Year-to-year variations may also occur with pneumococcal pneumonia [49].

Little is known about geographic differences in the incidence of pneumonia. Surveillance data from the CDC suggest that legionnaires' disease occurs with highest incidence in northeastern states and states in the Great Lakes area [46]; however, differences in ascertainment of disease may be a contributing factor. The incidence of pneumonia due to pathogens that are environmentally related would be expected to vary with changes in relevant environmental conditions. For example, the incidence of legionnaires' disease is dependent on the presence of pathogenic *Legionella* species in water, amplification of the bacteria in reservoirs with the ideal nutritional milieu, use of aerosol-producing devices (which can spread contaminated water via aerosol droplets), ideal meteorological conditions for transporting aerosols to susceptible hosts, and presence of susceptible hosts. Alterations in any of these variables would probably lead to variations in incidence. Likewise, increasing rainfall, with associated increases in the rodent population, was hypothesized to be the basis for the epidemic of HPS in the southwestern United States in 1993 [50].

## Diagnostic Evaluation

Pneumonia should be suspected in patients with newly acquired lower respiratory symptoms (cough, sputum production, and/or dyspnea), especially if accompanied by fever, altered breath sounds, and rales. It is recognized that there must be a balance between reasonable diagnostic testing (table 5) and empirical therapy. The importance of establishing the diagnosis of pneumonia and its cause is heightened with the increasing concern about antibiotic overuse.

### Chest Radiography

The diagnosis of CAP is based on a combination of clinical and laboratory (including microbiological) data. The differential diagnosis of lower respiratory symptoms is extensive and includes upper and lower respiratory tract infections, as well as noninfectious causes (e.g., reactive airways disease, atelectasis, congestive heart failure, bronchiolitis obliterans with organizing pneumonia [BOOP], vasculitis, pulmonary embolism, and pulmonary malignancy). Most cases of upper respiratory tract infection and AB are of viral origin, do not require antimicrobial therapy, and are the source of great antibiotic abuse [51, 52]. By contrast, antimicrobial therapy is usually indicated for pneumonia, and a chest radiography is usually necessary to establish the diagnosis of pneumonia. Physical examination to detect rales or bronchial breath sounds is neither sensitive nor specific for detecting pneumonia [53]. Chest radiography is considered sensitive and, occasionally, is useful for determining the etiologic diagnosis, the prognosis, and alternative diagnoses or associated conditions.

Chest radiographs in patients with *P. carinii* pneumonia (PCP) are false-negative for up to 30% of patients, but this exception is not relevant for the immunocompetent adult host [54]. One study showed spiral CT scans are significantly more sensitive in detecting pulmonary infiltrates [55], but the clinical significance of these results is unclear, and the IDSA panel does

Table 7. Epidemiological conditions related to specific pathogens in patients with selected community-acquired pneumonia.

| Condition | Commonly encountered pathogen(s) |
|---|---|
| Alcoholism | *Streptococcus pneumoniae* and anaerobes |
| COPD and/or smoking | *S. pneumoniae, Haemophilus influenzae, Moraxella catarrhalis,* and *Legionella* species |
| Nursing home residency | *S. pneumoniae,* gram-negative bacilli, *H. influenzae, Staphylococcus aureus,* anaerobes, and *Chlamydia pneumoniae* |
| Poor dental hygiene | Anaerobes |
| Epidemic legionnaires' disease | *Legionella* species |
| Exposure to bats or soil enriched with bird droppings | *Histoplasma capsulatum* |
| Exposure to birds | *Chlamydia psittaci* |
| Exposure to rabbits | *Francisella tularensis* |
| HIV infection (early stage) | *S. pneumoniae, H. influenzae,* and *Mycobacterium tuberculosis* |
| HIV infection (late stage) | Above plus *P. carinii, Cryptococcus,* and *Histoplasma* species |
| Travel to southwestern US | *Coccidioides* species |
| Exposure to farm animals or parturient cats | *Coxiella burnetii* (Q fever) |
| Influenza active in community | Influenza, *S. pneumoniae, S. aureus, Streptococcus pyogenes,* and *H. influenzae* |
| Suspected large-volume aspiration | Anaerobes (chemical pneumonitis, obstruction) |
| Structural disease of lung (bronchiectasis, cystic fibrosis, etc.) | *Pseudonomas aeruginosa, Burkholderia (Pseudomonas) cepacia,* and *S. aureus* |
| Injection drug use | *S. aureus,* anaerobes, *M. tuberculosis,* and *S. pneumoniae* |
| Airway obstruction | Anaerobes, *S. pneumoniae, H. influenzae,* and *S. aureus* |

NOTE. COPD, chronic obstructive pulmonary disease.

not endorse the routine use of this technology because of the preliminary nature of the data and high cost of the procedure.

At times of limited resources, it may seem attractive to treat patients for CAP on the basis of presenting manifestations, without radiographic confirmation. This approach should be discouraged, given the cost and potential dangers of antimicrobial abuse in terms of side effects and resistance. Indeed, the prevalence of pneumonia among adults with respiratory symptoms that suggest pneumonitis ranges from only 3% in a general outpatient setting to 28% in an emergency department [56, 57]. The IDSA panel recommends that chest radiography be included in the routine evaluation of patients for whom pneumonia is considered a likely diagnosis (A-II).

### Etiology

The emphasis on microbiological studies (Gram staining and culture of expectorated sputum) in the IDSA guidelines represents a difference from the guidelines of the American Thoracic Society [1]. Arguments against microbiological studies include the low yield in many reports and the lack of documented benefit in terms of cost or outcome. A concern of the IDSA panel members is our perception that the quality of microbiological technology, as applied to respiratory secretions, has deteriorated substantially, compared with that in an earlier era [12]. Furthermore, it is our perception that regulations of the Clinical Laboratory Improvement Act, which discourage physicians from examining sputum samples microscopically, contributed to this decline. Although no data clearly demonstrate the cost-effectiveness or other advantages of attempts to identify pathogens, studies specifically designed to address this issue have not been reported.

Our rationale for the preservation of microbiological and immunologic testing is summarized in table 6, which classifies advantages with regard to the individual patient, society, and costs. The desire to identify the etiologic agent is heightened by concern about empirical selection of drugs, because of the increasing microbial resistance, unnecessary costs, and avoidable side effects. In addition, the work of prior investigators and their microbiological findings provide the rationale considered essential to the creation of guidelines based on probable etiologic agents.

A detailed history may be helpful for suggesting a diagnosis. Epidemiological clues that may lead to diagnostic considerations are listed in table 7. Certain findings have historically been identified as clues to specific causes of pneumonia, although these have not been confined to controlled studies. Acute onset, a single episode of shaking with chills (rigor), and pleurisy suggest pneumococcal infection. Prodromal fever and myalgia followed by pulmonary edema and hypotension are characteristic of HPS. Underlying COPD is more often seen with pneumonia due to *H. influenzae* or *M. catarrhalis,* separately or together with *S. pneumoniae.* Putrid sputum indicates infection caused by anaerobic bacteria. Although many studies of CAP have found that clinical features often do not distinguish etiologic agents [39, 58, 59], others support the utility of clinical clues for supporting an etiologic diagnosis [41, 60].

Once the clinical diagnosis of CAP has been made, consideration should be given to microbiological diagnosis with bacteriologic studies of sputum and blood [61–66]. Practice standards for collection, transport, and processing of respiratory secretions to detect common bacterial pathogens are summarized in table 8. Many pathogens require specialized tests for their detection, which are summarized in table 9. The rapid

**Table 8.** Recommendations for expectorated sputum collection, transport, and processing.

| |
|---|
| Specimen should be obtained by deep cough and have gross purulence; it should be obtained before treatment with antimicrobial agents and in the presence of a health care provider |
| Specimen should be immediately transported to the laboratory for prompt processing |
| A purulent portion is selected for Gram staining and culture; Quellung staining should be done when available |
| Cytological screening should be done under low-power magnification (×100) to determine the cellular composition (see text, Diagnostic Evaluation: Etiology); cytological assessment is not necessary for screening specimens for detection of respiratory viruses, *Legionella* species, or mycobacteria |
| Culture should be performed with use of standard techniques and results reported with semiquantitative assessment; most pathogens are recovered in 3–4+ growth, indicating >5 colonies, in the second quadrant. |

diagnostic test for routine use is Gram staining of respiratory secretions, usually expectorated sputum; others include direct fluorescent antibody (DFA) staining of sputum or urinary antigen assay for *Legionella,* for use in selected cases, urinary antigen assay for *S. pneumoniae,* acid-fast bacilli (AFB) staining for detection of mycobacterial infections, and several tests for influenza.

Many rapid diagnostic tests, such as PCR, are in early development, not commonly available, or not sufficiently reliable [66]. PCR testing for detection of *Mycobacterium tuberculosis* is the only PCR test for detection of a respiratory tract pathogen that has been cleared by the US Food and Drug Administration (FDA), but it is recommended for use only with specimens that contain AFB on direct smears. Diagnostic procedures that provide identification of a specific etiology within 24–72 h can still be useful for guiding continued therapy.

The etiologic diagnosis can be useful for both prognostic and therapeutic purposes. Once a diagnosis has been established, the failure to respond to treatment can be dealt with in a logical fashion based on the causative organisnt and its documented antibiotic susceptibility, rather than by empiric selection of antimicrobial agents with a broader or different spectrum. Furthermore, if a drug reaction develops, an appropriate substitute can be readily selected.

Performance of blood cultures within 24 h of admission for CAP is associated with a significant reduction in 30-day mortality [67]. With regard to sputum bacteriology, several studies have suggested that mortality associated with CAP in hospitalized patients is the same for those with and without an etiologic diagnosis [68–70]. These studies were not specifically designed to test the hypothesis. Instead, the conclusion is based on retrospective analyses of cases with and without an etiologic diagnosis. Other outcomes also of interest that have not been assessed are length of stay, cost, resource use, and morbidity.

Some studies, although uncontrolled, do suggest benefit of these diagnostic studies [71–76]. For example, Boerner and Zwadyk [64] reported that a positive early diagnosis by sputum Gram staining correlated with more rapid resolution of fever after initiation of antimicrobial therapy. An additional study by Torres et al. [76] showed that inadequate antibiotic treatment was clearly related to poor outcomes, which suggests that the establishment of an etiologic diagnosis is important.

The frequency of microbiological studies for CAP patients is highly variable. A report from the Pneumonia PORT study, with analysis of 1343 hospitalized patients during 1991–1994, showed that the frequencies of sputum Gram staining and sputum culture within 48 h of admission were 53% and 58%, respectively [77]. These studies were done on only 8%–11% of 944 outpatients with CAP. Participating centers in this and most other published studies of CAP are academic institutions at which microbiological studies are probably more frequent than in other health care settings. The finding of a likely pathogen in blood cultures averages 11% in published reports concerning hospitalized patients with CAP [9]. The yield with sputum studies is highly variable, ranging from 29% to 90% for hospitalized patients and usually <20% for outpatients [2, 26, 28, 36, 41, 67, 75–77]. The large variation among studies is presumably explained by variations in the quality of microbiological analyses, epidemiological patterns, and the patient population served.

It is our consensus that establishment of an etiologic diagnosis, with performance of blood cultures before initiation of antimicrobial treatment (A-I) and sputum Gram staining and culture (B-II), has value for patients who require hospitalization. The goal is to establish a specific diagnosis that can be used for more precise and often more cost-effective use of antimicrobial agents. On the other hand, the utility of diagnostic studies for CAP of less severity (not requiring hospitalization) is unclear. More studies are needed to verify the significance of diagnostic studies in these cases.

*Etiologic diagnosis.* Confidence in the accuracy of the diagnosis depends on the pathogen and on the diagnostic test, as follows.

1. Diagnosis definite: a definite etiology is established by a compatible clinical syndrome plus the recovery of a probable etiologic agent from an uncontaminated specimen (blood, pleural fluid, transtracheal aspirate, or transthoracic aspirate) or the recovery from respiratory secretions of a likely pathogen that does not colonize the upper airways (e.g., *M. tuberculosis, Legionella* species, influenza virus, or *P. carinii;* table 10) (A-I). Some serological tests are regarded as diagnostic, although the results are usually not available in a timely manner or the diagnostic criteria are controversial.

2. Diagnosis probable: a probable etiologic diagnosis is established by a compatible clinical syndrome with detection (by staining or culture) of a likely pulmonary pathogen in respiratory secretions (expectorated sputum, bronchoscopic aspirate, or quantitatively cultured bronchoscopic bronchoalveolar lavage [BAL] fluid or brush catheter specimen). With semiquantitative culture, the pathogen should be recovered in moderate to heavy growth (B-II).