



Community-acquired pneumonia in elderly patients

Michael S. Niederman, MD, FACP, FCCP, FCCM^{a,b,*},
Qanta A.A. Ahmed, MD^c

^a*SUNY at Stony Brook, Stony Brook, NY, USA*

^b*Department of Medicine, Winthrop University Hospital, 222 Station Plaza North,
Suite 509, Mineola, NY 11501, USA*

^c*Department of Pulmonary and Critical Care Medicine, Winthrop University Hospital, Mineola, NY*

Community-acquired pneumonia (CAP) is the leading cause of death from infectious diseases in the United States, the sixth-ranked cause of death overall, and a common and serious illness in elderly patients [1]. As the number of elderly individuals rises in this country, the incidence, mortality, and economic impact of CAP in this population will likely also increase. In 1994, more than 5.6 million people were diagnosed with CAP in the United States and 1.7 million of those were older than 65 years [2]. Most patients with CAP are treated on an outpatient basis; however, most patients treated in hospital are elderly. Elderly patients are hospitalized more often because they frequently have comorbid illness more often than a younger population. Because of increased rates of hospitalization and increased length of stay when they are admitted, elderly patients account for \$4.8 billion of the total \$8.4 billion spent for the care of pneumonia [2]. Thus, they represent only about one third of all patients with CAP, yet are responsible for over half of the dollars spent on this illness. The average hospital stay for an elderly person with CAP is 7.8 days, at a cost of \$7166, compared with an average stay of 5.8 days for a younger patient, costing \$6042.

This article examines some specific aspects of CAP in elderly patients, focusing on risk factors, severity assessment, and prognosis, to try to better understand the increased mortality of this illness in an older population. In addition, elderly patients have different clinical manifestations of illness compared with younger patients, which presents unique diagnostic and therapeutic challenges. Finally, the bacteriology of CAP is different in older compared with

* Corresponding author. Department of Medicine, Winthrop University Hospital, 222 Station Plaza North, Mineola, NY 11550.

E-mail address: mniederman@winthrop.org

younger populations; elderly patients have a greater risk of drug-resistant and gram-negative bacteria, which leads to specific algorithms for therapy in this population. Ultimately, the best way to reduce the burden of CAP in the elderly population is through prevention, with the use of both pneumococcal and influenza vaccines, and these strategies are also reviewed.

Aging and pneumonia

Pneumonia develops when there is an adequate inoculum of a virulent organism in a susceptible host. Although elderly individuals are at an increased risk of developing pneumonia, compared with younger patients, the reasons for this are uncertain; many studies suggest that comorbid illnesses, which are common in elderly patients, rather than aging itself, predispose this population to infection. Aging does confer certain deficiencies in host defense, and aging predisposes an individual to certain physiologic changes in the lung that interfere with bacterial clearance.

The physiologic changes in the lung that occur with aging are associated with reduced ability to expectorate and clear bacteria, and reduced physiologic reserve, making it harder for patients to tolerate and overcome severe infection. With aging, the chest wall becomes more rigid, with an increase in the elastic work of breathing [3] and a reduction in respiratory muscle endurance. Advanced age and impaired forced expiratory volume in 1 second, or FEV₁, have been shown to be significant risk factors for severe pneumonia [4]. Increased work of breathing means that physiologic reserves are reduced when the patient is faced with insults such as surgery or superimposed infection.

Oropharyngeal bacterial colonization is also more common in elderly patients. Organisms such as *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Escherichia coli* transiently colonize the oropharynx of the elderly patient, serving as harbingers of subsequent pneumonia [5]. Mechanisms that predispose elderly patients to colonization are complex, but Valenti et al [6] found increased rates of gram-negative colonization in elderly patients who were immobile, incontinent, had chronic cardiopulmonary comorbidities, and who were clinically deteriorating. Colonization can be associated with pneumonia because patients commonly aspirate their oropharyngeal flora, and these organisms can lead to lower respiratory tract infection. Aspiration (small or large volume) is more common in elderly patients because of impaired swallowing reflexes, especially in those with neurologic illness.

Risk factors for CAP and prognostic factors for poor outcome in elderly patients

The elderly population has an increased incidence of pneumonia and an increased mortality compared with younger populations. In a large community-

based study, Marston et al [7] evaluated 2776 patients with CAP, all the residents of two Ohio counties who were hospitalized with CAP in a given calendar year. They found that both the incidence and mortality of CAP increased with advancing age. The overall incidence of illness was 266.8 cases per 100,000 patients aged 18 to 44 years had an incidence of 92 cases per 100,000, compared with a rate of 1014 cases per 100,000 in patients aged older than 65 years. The mortality of CAP was 8.8% overall, but was only 4.5% in patients aged 18 to 44 years, compared with 12.5% in patients older than 65.

Risk factors for CAP

Elderly patients with CAP frequently have serious comorbid illnesses. In general, these diseases are more common in elderly patients with CAP than in younger patients, and comorbid illnesses, more than age, predispose to an increased risk of CAP [1,2,8]. Riquelme et al [9] evaluated the risk factors for developing pneumonia in patients older than 65 years by comparing patients with pneumonia to age-matched controls. Risk factors for CAP included suspicion of aspiration, swallowing disorders, malnutrition (including low serum albumin), prior antibiotic therapy, poor quality of life, and bedridden status. Poor nutritional status, identified by hypoalbuminemia, in elderly patients has also been found to increase the likelihood of nosocomial pneumonia [10] and of pneumonia in postoperative patients [11]. Elderly patients with severe CAP frequently have serious underlying illnesses, but not more often than in younger patients with severe pneumonia [12]. In patients older than 65 years with severe CAP, however, pre-existing chronic obstructive pulmonary disease (COPD) was present in 48%, heart disease in 16%, diabetes in 18%, and malignancy in 12% of cases.

The role of silent aspiration in elderly patients during sleep was investigated by Kikuchi et al [13]. Using a scanning technique with indium 111 chloride, mixed with a paste applied to the patient's teeth in the evening, the investigators found that those with positive scans over the lungs were more often found to have CAP than those without positive scans. Another common risk factor for CAP in elderly patients is cigarette smoking, a modifiable factor that is commonly present in those with pneumonia.

Risk factors for mortality (Table 1)

Studies that have examined the clinical features that predispose elderly patients to mortality have found that these features sometimes differed from factors found in younger patients. Riquelme et al [9,14] found an increased risk of death in patients with the following predisposing features: at least three lobes affected with CAP, a respiratory rate of more than 30 breaths/minute, shock, bedridden status, diminished physical activity status, afebrile on admission, suspected aspiration, severe hypoxemia, altered mental status, and leukocytosis of more than 14.9×10^9 leukocytes/L. Age alone (> 75 years) was not a factor predicting a worse outcome. Poor prognosis did occur when patients were

Table 1

Prognostic factors portending good outcome in elderly hospitalized patients with CAP

Prognostic factors

Fewer involved lobes *
 Respiratory rate less than 30 breaths/min on admission
 Absence of shock
 Prior normal physical activity levels
 Lack of bedridden status before admission *
 Fever to 37° C or more *
 Lack of cyanosis
 No suspicion of aspiration
 No swallowing disorders *
 Normal serum creatinine (<1.4mg/dL)
 PaO₂/FiO₂ ratio of >200 mm Hg on admission
 Leukocytosis >14.0 × 10⁹
 Normal cough

Abbreviation: CAP, community-acquired pneumonia.

* Statistically significant.

afebrile, a finding suggested in other studies, which reported that nonclassic presentations of pneumonia portend a worse outcome in elderly patients [15]. This may be because the absence of classic findings implies both a poor immune response to infection and a likelihood of delayed recognition of infection, both of which can be associated with increased mortality. One other factor associated with an increased risk of mortality at 30 days after the diagnosis of CAP is the administration of antibiotics to hospitalized patients later than 8 hours after admission [16]. This study finding applied to patients older than 65 years, although its applicability to younger patients was unclear. The finding again stressed the need for a prompt and accurate diagnosis in elderly patients. Rello et al [12] examined prognostic factors in elderly patients with severe CAP, and found an increased chance of dying in those with rapid radiographic spread, shock, immune suppression (including with corticosteroids), acute renal failure, and an Acute Physiology and Chronic Health Evaluation (APACHE II) score of more than 22.

Because elderly patients may have variable presentations of pneumonia, some of the prognostic rules that have been applied to younger patients may not work as well in older patients. For example, the British Thoracic Society (BTS) rule has worked well for predicting CAP mortality by focusing on patients with at least two of the following conditions: a respiratory rate of more than 30 breaths/minute, a diastolic blood pressure of less than 60 mm Hg, blood (serum) urea nitrogen (BUN) of more than 19.6 mg/dL, and confusion [17,18]. When this rule has been applied, it has good sensitivity and specificity for identifying patients with an increased chance of dying of CAP. Recently, Lim et al [19] have shown that this rule does not work as well in elderly, compared with younger patients, again reflecting altered clinical presentations of pneumonia in the elderly population. In one study, the rule had a 66% sensitivity and a 73% specificity for predicting mortality in a population that included 48% aged at least 75 years [19]. In that study, the predictors of

mortality in a multivariate analysis were as follows: patient's age older than 65 years, confusion, fever of less than 37° C, respiratory rate of more than 24 breaths/minute, serum sodium concentration less than 135 mmol/L, BUN concentration more than 19.6 mg/dL, and effusion on chest radiograph. Although the BTS rule was not optimal in an elderly population, and did not work as well as it did in other populations, it had a higher sensitivity for predicting mortality than the Prognostic Scoring Index (PSI), derived from the Pneumonia Outcomes Research Team (PORT) study [19,20]. In a subsequent study, these investigators confirmed many of these findings, adding a pulse of more than 95 beats/minute and bilateral infiltrates as prognostic factors for mortality [21].

The PSI is widely used to predict mortality in CAP patients, and to help guide the admission decision. In the new American Thoracic Society (ATS) guidelines for CAP, some of the limitations of this approach were identified, including the fact that age is a heavily weighted variable for defining mortality risk [1,20]. High risk for mortality is defined as a score greater than 90 points, and men are given one point for each year of age. Thus, an elderly man with any chronic illness will have enough points to fall into a high-risk category, and to possibly be admitted to the hospital, regardless of the severity of his pneumonic process. This observation can explain why the use of the rule is of limited value for decision making about mortality risk and need for hospitalization in an elderly population.

Clinical features of CAP in elderly patients

Elderly patients with CAP often present with different signs and symptoms than are found in younger patients (Table 2). This is a consequence of both age- and disease-associated impairments in host defenses, which interfere with the inflammatory response to infection. Instead of classic pneumonic symptoms, an elderly patient can present with failure to thrive, confusion, falling, or worsening of a chronic illness (eg, congestive heart failure). These nonclassic presentations

Table 2
Clinical features of pneumonia in elderly patients

Feature	Characteristics
Fever	Less commonly seen than in younger patients
Tachypnea	Common and reliable feature of CAP
Mental status	Delirium and confusion more likely than in younger patients
Presentation	Cough and sputum production can be absent. Pleuritic chest pain is less common than in younger patients. Confusion and worsening of underlying illness are more common. May present with falling, incontinence, anorexia, reduction in daily activities. Delay in diagnosis common.
Radiology	Incomplete radiologic signs. Radiograph may worsen with hydration.
Course	Delayed clinical and/or radiologic resolution

Abbreviation: CAP, community-acquired pneumonia.

were well known to Sir William Osler, who observed that “in old age pneumonia may be latent, coming on without a chill; the cough and expectoration are slight, the physical signs ill-defined and changeable, and the constitutional symptoms out of all proportion” [22]. Osler also noted the high frequency of extrapulmonary manifestations, such as confusion, often in the absence of any respiratory findings. Many recent series confirm these findings but document that many elderly CAP patients will have cough, fever, abnormal focal physical findings (rales or consolidation), and a respiratory rate of more than 20 breaths/minute. In addition, many patients will have no fever but rather confusion as a common presentation, and pneumonia can only be suspected when focal physical abnormalities and an elevated respiratory rate are identified.

One consequence of the unusual presentations of CAP is a delay in diagnosis. Metlay et al [23] evaluated 1812 patients with CAP and found that elderly patients reported fewer symptoms and that many symptoms (eg, cough, sputum, dyspnea, fatigue, anorexia, myalgias, and abdominal pain) were present for a longer time in older compared with younger patients. For example, in patients older than 75 years, cough, dyspnea, and sputum production were present for 1 day longer before presentation than in those patients aged 18 to 44 years. In addition, whereas fever and pleuritic chest pain were more common in younger patients, tachypnea was more common with advancing age. For example, fever was present in 85% and tachypnea in 36% of patients aged 18 to 44 years compared with 53% and 65%, respectively, in those patients older than 75 years. In another study of CAP in elderly patients, Marrie and Blanchard [24] found that fever was present in only 71% of 93 patients, productive cough in 61%, anorexia in 58%, chills in 58%, shortness of breath in 46%, confusion in 37%, and pleuritic chest pain in 32%. In addition, patients had symptoms for a mean of 6.1 days before admission, again emphasizing the high frequency of delay in recognizing CAP in this population. The consequence of delayed recognition is often delayed therapy and poorer outcome, including higher mortality [14].

Riquelme et al [9] confirmed many of these findings in a study of 101 patients with CAP aged older than 65 years. Most had comorbid illnesses (cardiac disease, neurologic illness, COPD, or malignancy) and presented at a mean of 6 days after the onset of symptoms. More than 60% of patients presented with a delay of at least 72 hours, and half the time the delay was the fault of the family; the other half of the time, it was the consequence of medical decision making. This group had a mortality of 26%. Overall, 71% had dyspnea, 67% cough, 64% fever, and 52% purulent sputum, but 19 patients had no cough, sputum, or pleuritic chest pain.

Radiologically, features may also be different because underlying comorbid illnesses, such as COPD, may lead to incomplete findings of consolidation. Other diagnoses may coexist, such as congestive heart failure, and obscure the presence of a new infiltrate. With the limited history that may be available and a less-than-classic presentation, diagnosing pneumonia in elderly patients is difficult. Another problem with diagnosis is the frequently held belief that patients who have pneumonia and dehydration may have radiographically absent findings,

even in the presence of pneumonia, and the infiltrate only appears after hydration. Although this idea is difficult to prove, Hash et al [25] have found that the concept may have some merit. In a study of 125 patients, 42 had radiographic worsening within 96 hours. The patients with radiographic progression were initially more dehydrated (as defined by BUN) and received more fluid (mean of > 1 L more) than patients who did not have radiographic progression.

Although elderly patients present with attenuated symptoms, this does not indicate a less acute illness. Mortality is actually increased in patients who present without classic findings. Starczweski et al [15] evaluated 100 patients with CAP, of whom 31 died. Those who died had chills, sweats, and rigors less often, and dementia more often than those who survived. Survivors had a higher fever than nonsurvivors, whereas nonsurvivors had tachycardia, tachypnea, and confusion more often than survivors. Thus, those elderly patients with CAP who have signs of an inadequate immune response (afebrile, low white blood cell count) are more likely to die than those with a more vigorous immune response. This finding may relate to differences not only in immunity but to the fact that nonclassic presentations of CAP are often associated with harmful delays in diagnosis and initiation of appropriate therapy.

Patient assessment: need for hospitalization and ICU admission

Severity assessment is key in determining patient disposition, appropriate therapies, and resource allocation. Much of severity assessment hinges on clinical evaluation, but several algorithms have been proposed to guide this process. Although proper patient disposition is essential for CAP management, the ATS guidelines view the hospitalization decision as an “art of medicine decision,” which cannot be easily replaced by any specific prediction rule [1]. Specifically, there is controversy about the role of the PSI [20].

Need for hospitalization

Hospitalization can be detrimental for elderly persons. Hospitalization delays return to full activities when compared with outpatient-based care. Hospitalization is accompanied by increased bed rest and the attendant complications, including venous thromboembolic disease or catheter-related sepsis and exposure to drug-resistant pathogens. Less severely ill patients with CAP, when asked, preferred to remain outpatients in most instances; however, the site of care management usually is determined by the physician. Furthermore, few patients recalled being asked by their doctor where they would like to be treated [26]. Hospitalization does not always need to be a prolonged stay but simply long enough to allow close observation and to determine when it is safe for therapy to be continued in the outpatient setting. The ATS guidelines suggest that when multiple risk factors for a poor outcome are present, hospitalization should be encouraged, but note that other factors may influence this decision. Caregiver

support at home, including the availability of home nursing and home intravenous therapy, and the availability of an intermediate care site, such as a subacute facility, can enable a patient to be safely managed outside the hospital. Few studies of outpatients have been conducted, but the ATS guidelines list the risk factors shown in Table 3 as being associated with a complicated course.

The PSI approach was developed by Fine et al [20] to predict mortality in patients with CAP. The PSI is derived from an assessment of historical information, physical examination, and laboratory testing, and allows all patients to be classified into one of five mortality risk groups. Although the process works well for predicting mortality, mortality risk also can be used to guide the

Table 3
Factors associated with a complicated course of CAP

Factor	Characteristics
Age	> 65 y
Comorbidities	COPD Bronchiectasis Malignancy DM Chronic renal failure CHF Chronic liver disease Chronic alcohol abuse Malnutrition Cerebrovascular accident Postsplenectomy
Physical findings	RR >30 breaths/min Diastolic blood pressure <60 mm Hg Systolic blood pressure <90 mm Hg Pulse >125 beats-min Fever <35° C, >40° C Decreased level of consciousness Evidence of extrapulmonary infection
Laboratory data	WBC <4 or >30 × 10 ⁹ or/L or absolute neutrophil count <1000/mm ³ PaO ₂ <60 mm Hg and/or PaCO ₂ >50 mm Hg on room air Serum creatinine >1.2 mg/dL, BUN >20 mg/dL Anemia (hematocrit <30%, hemoglobin <9 mg/dL)
Radiologic data	Rapidly progressing infiltrate Pleural effusion Presence of cavitary infiltrates
Systemic sepsis	Coagulopathy, metabolic acidosis pH <7.35 Evidence of disseminated intravascular coagulation
Other	Suspicion of aspiration Need for mechanical ventilation

Abbreviations: BUN, blood urea nitrogen; CAP, community-acquired pneumonia; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DM, Diabetes Mellitus; RR, respiratory rate; WBC, white blood cell count.

admission decision, with hospitalization being reserved for patients in categories IV and V, and for selected patients in category III [27]. This approach may have limited applicability to elderly patients because age and comorbid illness are weighted so heavily in the scoring. In fact, most patients older than 65 years would be recommended for admission, regardless of the severity of the pneumonia itself. In addition, some “low risk” patients could have findings not included in the scoring process that would push physicians to admit them, regardless of their score. For example, in one prospective randomized trial, clinicians were instructed to use the PSI to guide admission, yet they often ignored the actual score and admitted low-risk patients based on clinical evaluation. In this trial, 30% of the patients were designated as low risk by the PSI, yet still admitted by the clinicians who saw them [28]. Thus, the PSI should be viewed as a decision-support tool, and not as an absolute rule to define the need for admission.

Similarly, the BTS rule can be used as a way to recognize patients with an increased risk for death, and these patients can be appropriately triaged to admission to the hospital or ICU. Originally, the rule used three factors to predict mortality: respiratory rate of more than 30 breaths/minute, diastolic blood pressure less than 60 mm Hg, BUN more than 19.6 mg/dL. Patients who had any two of these factors present had a 21-fold increased risk of death [17]. A fourth factor, confusion, has been added to a modified version of the rule, but still this rule may have limitations in an elderly population [18]. In one study, the factors in the modified BTS rule were found to be important predictors of mortality, but not the only important factors, in patients older than 75 years [21]. In that population, the modified rule had a positive predictive value for death of 56%, which suggests that many patients who had these criteria did poorly. The rule only had a 66% negative predictive value, however, meaning that some patients died, even without fulfilling the modified BTS criteria. These findings indicate that elderly patients with CAP need to have multiple factors included in the evaluation of mortality risk and need for hospitalization.

Need for ICU admission

The ATS guidelines report factors predicting a more severe and complicated course in the CAP patient, as shown in Table 3; however, there are no good studies that have prospectively applied a prediction rule to define the need for ICU admission of CAP patients. Ewig et al [29] looked at the sensitivity, specificity, and predictive values of 10 factors used to define severe pneumonia in the 1993 ATS guidelines. In that study, 422 consecutive patients with CAP were evaluated, including 64 who were admitted to the ICU. They found that the need for ICU admission could not be defined by the presence of only one severe pneumonia risk factor, because nearly 70% of patients admitted to the medical floor, and not the ICU, had one such factor present. Consequently, Ewig et al developed a new rule for defining severe pneumonia and need for ICU admission. In general, they found that ICU admission should be considered if

Table 4
Severe CAP criteria for ICU admission

Criteria
Any two of the following:
PaO ₂ /FiO ₂ ratio <250
Multilobar infiltrates
Systolic blood pressure <90 mm Hg
Or any one of the following:
Septic shock
Mechanical ventilation

Abbreviation: CAP, community-acquired pneumonia.

Data from Ewig S, Ruiz M, Mensa J, et al. Severe community-acquired pneumonia. Assessment of severity criteria. Am J Respir Crit Care Med 1998;158:1102–8.

a patient has any two of the following three findings: a PaO₂-to-FiO₂ ratio of less than 250, multilobar infiltrates, and a systolic blood pressure of less than 90 mm Hg; or any one of the following two findings: septic shock or need for mechanical ventilation (Table 4). This rule had a sensitivity of 78%, a specificity of 94%, and a positive predictive value of 75%, but prospective validation is needed [29].

Bacteriology

In studies of CAP, even those with extensive diagnostic testing, no etiologic diagnosis is found in up to half of all patients, and the yield may be even lower in older patients because many of these individuals are unable to provide adequate sputum samples for evaluation. In the elderly and other populations, the most common causative agent is *Streptococcus pneumoniae*, but age older than 65 years has been identified as a risk factor for drug-resistant streptococcal pneumococcus (DRSP) [1,30,31]. Other common pathogens include *Hemophilus influenzae*, especially in cigarette smokers; *Staphylococcus aureus*, after influenza and in those with diabetes or chronic renal failure; anaerobes, in those at risk for aspiration caused by impaired swallowing or neurologic illness; and viruses. Controversy exists about the frequency of enteric gram-negative organisms, which are found in elderly patients with increased frequency compared with younger patients, especially those with comorbid medical illnesses. In one study, the risk for infection with gram-negative bacteria was 4.4 times greater for patients who were at least 60 years old and with any medical comorbidity [32], and when *Pseudomonas aeruginosa* was a CAP pathogen, it occurred almost exclusively in this population. Atypical pathogens are also found in elderly patients, and one study found that the frequency of infection with *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and *Legionella pneumophila* was higher in patients aged 65 to 79 years, than in patients aged 18 to 34 years [7]. Pathogens such as *C pneumoniae* can even occur in nursing home patients, and in an epidemic fashion, spread from one patient to

another [33]. The likely pathogens causing CAP in elderly patients are listed in Table 5.

Riquelme et al [9] evaluated 101 elderly (> 65 years) patients with CAP with extensive diagnostic testing, which included two sets of blood cultures, respiratory tract cultures (sputum in 47, bronchoscopic in 15, and needle aspirate or pleural fluid in 5 patients) and acute and convalescent serum testing to evaluate for influenza and other viruses, such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Coxiella burnetti*, and *L pneumophila*. With this approach, 53 patients had an etiologic diagnosis established, but only 18 of 47 sputum samples were considered valid for evaluation, and most diagnoses were made by blood cultures or serologic testing. The obvious limitation of serologic testing is that results are not available for weeks, so in this population, few pathogen diagnoses were made at the time of admission. Of the 42% of patients who had an etiologic diagnosis established, *S pneumoniae* was the most common organism (36% of all diagnoses, 26% of which were penicillin resistant), followed by *C pneumoniae* (17%), *C burnetti* (11%), *L pneumophila* (6%), and *M pneumoniae* (4%). *P aeruginosa*, *Proteus mirabilis*, *Streptococcus viridans*, and *Moraxella catarrhalis* were each recovered in 2% of all patients with an etiologic diagnosis. Similar data were found by Metlay et al [23] in a group of 583 hospitalized patients older than 65 years. In this population, 427 patients had no etiologic diagnosis established, although 164 patients had no diagnostic testing done. Of the patients with an established diagnosis, *S pneumoniae* was most common, followed by *H influenzae*, gram-negatives, *S aureus*, and atypical pathogens. In addition, some patients had mixed infection, an increasingly recognized pattern, especially involving atypical pathogens such as *C pneumoniae* and bacterial pathogens such as pneumococcus [1,34,35].

With severe forms of CAP, the pathogens are similar, but certain organisms are more common than in patients with less severe illness. Rello et al [12]

Table 5
Likely pathogens causing CAP in elderly patients (in order of decreasing frequency)

Patient status	Pathogen
Outpatient and non-ICU	Pneumococcus (including DRSP)
	<i>H influenzae</i>
	Atypicals
	Influenza and viruses
	Enteric gram-negatives
	Anaerobes (aspiration)
	<i>S aureus</i>
ICU-treated	Pneumococcus (including DRSP)
	Enteric gram-negatives (including <i>P aeruginosa</i>)
	<i>S aureus</i>
	<i>H influenzae</i>
	Atypicals (including <i>Legionella</i>)

Abbreviations: CAP, community-acquired pneumonia; DRSP, drug-resistant streptococcal pneumococcus.

evaluated 95 patients with severe CAP and found that pneumococcus was the most common organism, followed by gram-negatives (including *P aeruginosa*), and *H influenzae*, with some patients being infected with the other pathogens listed in Table 5. El-Solh et al [36] evaluated 104 patients aged 75 and older who were admitted with severe pneumonia from either the community ($n = 57$) or a nursing home ($n = 47$). For the patients coming from their homes, pneumococcus was the most common organism (in 14%), followed by *Legionella* (9%), *S aureus* (7%), and *H influenzae* (7%). Gram-negatives, as a group, occurred in 17% of all patients. In these patients, *E coli* was the most common organism, although some patients had *P aeruginosa* as well. Among patients admitted from the nursing home, *S aureus* was the most common organism, followed by pneumococcus; 18% of patients had enteric gram-negatives. Infection with *P aeruginosa* was associated with residence in a nursing home and bronchiectasis. As patient functional status declined, the frequency of *S aureus* and enteric gram-negatives increased, whereas the frequency of pneumococcus declined.

Drug-resistant S pneumoniae

Penicillin-resistant *Streptococcus pneumoniae* (PRSP) has become common enough to require special consideration in the management of patients with CAP. Up to 40% of pneumococci are penicillin resistant and, of these, 26.5% are intermediately resistant, and 17.5% are highly resistant [37]. Intermediate-level resistance to penicillin is defined as minimum inhibitory concentration (MIC) values ranging from 0.12 mg/L to 1.0 mg/L, whereas high-level resistance is defined as MIC values of more than 2.0 mg/L. PRSP exists in specific clones, mainly of serotypes 6A, 6B, 9A, 14, 19F, and 23F. Resistance to other agents often coexists with penicillin resistance, hence the term drug-resistant *Streptococcus pneumoniae* (DRSP). Cross-resistance has been seen with cephalosporins, macrolides, trimethoprim-sulfamethoxazole, and tetracyclines, but generally not with quinolones and vancomycin.

Infection with DRSP and enteric gram-negatives is a particular problem in elderly patients. In the new ATS guidelines, the presence of cardiopulmonary disease, nursing home residence, and age older than 65 years are referred to as “modifying factors” that make certain pathogens more likely. DRSP is more likely in those patients older than 65 years and in those with multiple medical comorbidities [1]. In addition, recent antibiotic therapy is a risk factor for both DRSP and enteric gram-negatives. Other risk factors for enteric gram-negatives include cardiopulmonary disease, multiple medical comorbidities, and residence in a nursing home. Malnutrition and chronic corticosteroid therapy are risk factors for infection with *P aeruginosa*. The finding that both advanced age and comorbid illness are risk factors for DRSP has implications for empiric therapy for CAP in elderly patients. At current levels of penicillin resistance, mortality is rarely increased in patients who harbor these organisms [38,39]. One study, however, has shown that the presence of DRSP does increase the risk of

suppurative complications such as empyema, and another study has shown that organisms with penicillin MIC values of 4 mg/L or greater are associated with an increased likelihood of death [38].

Therapy

Early diagnosis and appropriate triage are key to achieving a good outcome in CAP. Timing of therapy is as important as using the right antibiotic, particularly in elderly patients. Meehan et al [16] looked at the timing of initial antibiotic therapy in a hospitalized Medicare population with CAP using a retrospective multicenter analysis of approximately 14,000 patients. Approximately 75% of patients received their first dose of antibiotic therapy within 8 hours of arrival in the hospital, and those patients had a significantly lower 30-day mortality than patients who received their first dose of therapy at a later time point. In defining therapy for CAP in elderly patients, patients fall into one of three groups: an outpatient group that has cardiopulmonary disease, modifying factors (including age > 65 years and comorbid illnesses), or both; an inpatient group not requiring ICU care; and a group with severe CAP [1,8]. Each of these groups has a unique set of pathogens, and from this list, follows suggested empiric therapy.

Guidelines have been developed for the therapy for CAP by several organizations, including the ATS, the Infectious Disease Society of America, the Centers for Disease Control and Prevention (CDC), and a combined pulmonary-infectious disease group from Canada [8,40]. Because many different organizations develop guidelines, it is interesting to see what types of physicians actually treat CAP. Dean et al [41] looked at which physicians treated CAP patients in a study of 16,420 episodes of pneumonia. All patients were Medicare beneficiaries and generally older than 65 years; nursing home residents were excluded. Billing records were used to identify the physician managing these patients. A subspecialist was called in for consultation for only 11.7% of all pneumonia episodes. Of all patients, 10.6% were seen by pulmonologists and 0.9% by an infectious disease specialist. Greater frequency of specialty consultation was seen in those patients who needed hospitalization (20.0% versus 8.6%) or who died (20.5% versus 11.2%). The primary care physician, without the advice of a pulmonary or infectious disease specialist, treated most patients with CAP, but each individual rarely saw many patients with this illness, in contrast to the specialists. Overall, 41.7% of primary care physicians saw less than one case of CAP per month.

The ATS guidelines recommend that elderly outpatients and inpatients (not in the ICU) be treated for the most common bacterial pathogens, and that all patients be treated for the possibility of atypical pathogen infection, either as primary infection, or as copathogen infection [1,8]. Among the bacterial pathogens, all elderly patients are treated for DRSP, and those with comorbid illnesses are treated for enteric gram-negatives. The algorithm for therapy in these patients is to use either a selected β -lactam, combined with a macrolide, or to use monotherapy

Table 6

Empiric antibiotic management of CAP: the American Thoracic Society's 2001 guidelines [1]

Patient characteristics	Empiric therapy
Outpatients	
Cardiopulmonary disease and/or “modifying” factors	Oral cefpodoxime, cefuroxime, high-dose amoxicillin, amoxicillin/clavulanate plus new macrolide (azithromycin or clarithromycin) OR doxycycline or antipneumococcal fluoroquinolone (gatifloxacin, levofloxacin, moxifloxacin) alone
Inpatients	
Mild-moderate (non-ICU)	IV β -lactam (ceftriaxone, cefotaxime, ampicillin sulbactam, high-dose ampicillin plus IV or oral macrolide OR IV antipneumococcal fluoroquinolone (gatifloxacin, levofloxacin, moxifloxacin) alone
Severe (ICU)	
No <i>Pseudomonas</i> risks	IV β -lactam (ceftriaxone, cefotaxime) plus either IV macrolide or IV antipneumococcal fluoroquinolone (never used alone)
<i>Pseudomonas</i> risks	Selected anti-pseudomonal β -lactam (cefepime, imipenem, meropenem, piperacillin/tazobactam) plus antipseudomonal fluoroquinolone (ciprofloxacin) OR selected antipseudomonal β -lactam (cefepime, imipenem, meropenem, piperacillin/tazobactam) plus IV aminoglycoside plus either IV macrolide

with a new antipneumococcal quinolone. The acceptable choices are listed in Table 6. For the ICU patient, the algorithm is to use either a macrolide or a quinolone in combination with other agents. The nature and number of other agents is dictated by the presence of risk factors for *P. aeruginosa*, and these therapy choices also are summarized in Table 6.

Special considerations

Elderly outpatients are treated with the regimens described previously. If the patient is living in a nursing home the same choices apply, but it is necessary to know the specific bacteriology of that nursing home, focusing on local patterns of antibiotic resistance in the selection of initial therapy. Some outpatients will be at risk for aspiration and therapy should be selected accordingly. Elderly patients at risk for aspiration, and possibly infection with anaerobes, include the following: those with impaired swallowing, neurologic illness, impaired consciousness, and alcoholism. Although aspiration can involve gram-negatives and anaerobes, the latter are a particular concern in those with poor dentition, or endobronchial obstruction (suspected foreign body, lung cancer). In these patients, agents like amoxicillin/clavulanate or ampicillin can be used in outpatients, whereas ampi-

cillin/sulbactam, piperacillin/tazobactam, and ampicillin can be used in hospitalized patients. In some instances, clindamycin can be added, especially if a quinolone is being used. Documented anaerobic infection and lung abscess should be treated with metronidazole or clindamycin.

The therapy for severe CAP is stratified in relation to *Pseudomonas* risk factors. Therefore, patients in the hospital (both in and out of the ICU) should not receive anti-*Pseudomonas* agents (cefepime, piperacillin/tazobactam, imipenem, meropenem, ciprofloxacin) unless these risk factors are present. Whereas quinolones are useful in the treatment of CAP, their use in the hospital should be mixed with the use of a β -lactam/macrolide combination, so that not all patients in a given hospital receive the same regimen all the time. This approach to antibiotic heterogeneity should reduce the selection pressure for resistance that could occur if one regimen was used for all patients. In the therapy for severe CAP, quinolones should not be used as monotherapy, because there are insufficient data to know about the safety, efficacy, or proper dosing in this clinical setting. When quinolones are used, there may be an advantage, particularly for minimizing selection pressure for further pneumococcal resistance, in using the most active pneumococcal agent possible. Among the currently available quinolones used against pneumococcus, from most to least active (defined by MIC values), are the following: moxifloxacin, gatifloxacin, levofloxacin [8,42].

The recommended therapies are of particular value in elderly patients, and several outcome studies have shown that when the ATS recommendations are followed mortality in CAP is reduced. The addition of a macrolide to a cephalosporin or the use of a quinolone alone are both regimens associated with reduced mortality, compared with cephalosporin monotherapy, in a Medicare population [43]. This finding supports the idea that routine therapy for atypical pathogens is of value; however, one recent study of Medicare patients found that the magnitude of the benefit for covering atypical pathogens may vary from year to year [44].

Clinical resolution and the response to therapy

The clinical response of the patient determines the total duration of therapy and the duration of intravenous therapy in hospitalized patients. The clinical response, in turn, is dependent on host factors, which include the vigor of the immune response, virulence of the pathogen, and appropriateness of empiric therapeutic choices. The hospitalized CAP patient typically responds to appropriate therapy with clinical stabilization and improvement over the first several days, with up to half of patients reaching clinical stability by day 3 of therapy [1,45]. Clinical stability is defined by improvement in symptoms of cough, sputum production, dyspnea and fever; becoming afebrile (for at least two occasions, 8 hours apart); having good oral intake; and having an improving white blood cell count. Once the patient becomes clinically stable, it is possible to switch to oral therapy and discharge the patient, where continued clinical improvement can occur.

Most patients require 4 to 6 weeks for radiographic resolution, so it is usually not helpful to follow the chest film early in the course of illness to define clinical response to therapy. Delays in resolution are common in the elderly patient who has severe illness, alcoholism, COPD, bacteremia, multiple medical comorbidities underlying chronic illness [1]. In general, delayed response to therapy can be the result of inadequate therapy (pathogen not covered by the agent chosen), an unusual and unsuspected pathogen (tuberculosis, fungus, *P carinii*), a pneumonic complication (empyema, endocarditis, meningitis, pulmonary embolus), or the presence of a noninfectious illness presenting like a pneumonia (bronchiolitis obliterans and organizing pneumonia, pulmonary vasculitis) [1]. The evaluation of nonresponse depends on the timing of deterioration and the patient's overall health status. Patients older than 55 years who have smoked and who have a focal pneumonia commonly take a long time to improve and diagnostic evaluation does not often reveal a specific reason for delayed resolution [46]. In the evaluation of the patient who is slow to respond diagnostic testing can include CT scan of the chest, bronchoscopy, serologic testing, and rarely, open lung biopsy.

There are few good studies about the proper duration of therapy, but traditionally 7 to 10 days are considered sufficient; new agents often have longer serum half-lives, which may obviate the need for longer courses of therapy. Coexisting medical illness, increased severity of illness, bacteremia, and slow clinical response to therapy are major factors that promote a longer duration of therapy. Pneumococcal pneumonia, even with bacteremia, can be treated for 7 to 10 days if there is adequate clinical response, and oral therapy can be used once patients meet the previously described criteria, regardless of the finding of a positive blood culture [1,45]. Atypical pathogens such as *M pneumoniae* and *C pneumoniae* may require a course of therapy for 10 to 14 days. Immunocompetent hosts with *Legionella* infection should also receive 10 to 14 days of therapy, but immunosuppressed patients may need longer courses.

Prevention

Prevention of CAP is important for all population groups but especially elderly patients who are at risk for both a higher frequency of infection and a more severe course of illness. Appropriate patients should be vaccinated with both pneumococcal and influenza vaccines and cigarette smoking should be stopped in all elderly at-risk patients.

Pneumococcal vaccine

The pneumococcal capsular polysaccharide vaccine has been shown to prevent pneumonia in otherwise healthy populations, and was initially demonstrated in South African gold miners and US military recruits [47]. The benefits in patients of advanced age or with underlying conditions in nonepidemic environments are less clearly defined. The vaccine efficacy has ranged from 65% to 84%

in patients with the following conditions: diabetes mellitus, coronary artery disease, congestive heart failure, COPD, and anatomic asplenia [1]. In immunocompetent patients older than 65 years effectiveness has been documented to be 75%. In the immunocompromised patient effectiveness has not been proven; this includes patients with sickle cell disease, chronic renal failure, immunoglobulin deficiency, Hodgkin disease, lymphoma, leukemia, and multiple myeloma. A single revaccination is indicated in persons older than 65 years who initially received the vaccine more than 5 years earlier and who were younger than 65 years on first vaccination. If the initial vaccination was given at 65 years or older a repeat vaccination is not indicated unless the patient has anatomic or functional asplenia or has one of the immune-compromising conditions listed previously. In these patients, revaccination is indicated and the second dose is given at least 5 years after the original dose.

The currently available pneumococcal vaccine is widely underutilized and could be a vital tool in reducing the mortality and morbidity seen in elderly patients with CAP. The 23-valent pneumococcal vaccine carries 23 of the 90 known pneumococcal serotypes that cause most clinical infection seen in the United States, including 85% of all pneumococcal infections seen in elderly patients. Hospital-based immunization for most admitted patients could be highly effective because more than 60% of all patients with CAP have been admitted to the hospital for some indication, in the preceding 4 years and hospitalization could be defined as an appropriate time for vaccination [48]. Pneumococcal vaccine can be given simultaneously with other vaccines, such as influenza vaccine, but each should be given at a separate site, and the vaccine can be given prior to discharge in the patient admitted for CAP.

Influenza vaccination

Influenza epidemics contribute to morbidity and mortality both through direct infection and through postinfluenza complications. The influenza vaccine preparations are revised annually to account for changes in the antigenic nature of the virus (antigenic drift) that is present each season. Three strains are represented in each vaccine preparation: two influenza A strains (H3N2 and H1N1) and one influenza B strain. All patients older than 65 years should be vaccinated, in addition to patients with chronic medical illness (including nursing home residents) and persons who provide health care to patients at risk for complicated influenza. Vaccination is given yearly, usually between September and mid-November.

When the vaccine matches the circulating strain it can prevent illness in 70% to 90% of healthy persons younger than 65 years [1]. For elderly persons with chronic illness the efficacy is less, but the vaccine can still attenuate the influenza infection and lead to fewer lower respiratory tract infections and the associated morbidity and mortality that follow influenza. In many studies the vaccine was shown to be cost effective and able to reduce the occurrence of pneumonia, hospitalization, and death.

Summary

CAP in elderly patients carries a significant economic and clinical burden and will be more commonly encountered in the future as the US population ages. Diagnosis may be obscured by a nonclassic presentation in an elderly patient, and the clinician needs to be especially suspicious of pneumonia whenever the clinical status of an elderly patient deteriorates. The single most important clinical decision is the site of care; this determination is not always based on clinical factors but also on social factors. Severity assessment is key to stratifying appropriate therapy and to predicting outcome. Timely and appropriate empiric therapy enhances the likelihood of a good clinical outcome, although clinical resolution may be more delayed than in younger patients. Newly emerging patterns of antibiotic resistance have altered recent guidelines for CAP treatment; DRSP is now a consideration in elderly patients because an age older than 65 years is a well-described risk factor for infection with this organism. Prevention should always be implemented, with a focus on pneumococcal and influenza vaccination.

References

- [1] Niederman MS, Mandell LA, Anzueto A, et al. Guidelines for the management of adults with community-acquired lower respiratory tract infections: diagnosis, assessment of severity, antimicrobial therapy and prevention. *Am J Respir Crit Care Med* 2001;163:1730–54.
- [2] Niederman MS, McCombs JS, Unger AN, et al. The cost of treating community acquired pneumonia. *Clin Ther* 1998;20:820–37.
- [3] Feldman C. Pneumonia in the elderly. *Clin Chest Med* 1999;20:563–73.
- [4] Lange P, Vestbo J, Nyboe J. Risk factors for death and hospitalization from pneumonia: a prospective study of a general population. *Eur Respir J* 1995;8:1694–8.
- [5] Niederman MS. Pathogenesis of airway colonization: lessons learned from studies of bacterial adherence. *Eur Respir J* 1994;7:1737–40.
- [6] Valenti WM, Trudell RG, Bentley DW. Factors predisposing to oropharyngeal colonization with gram negative bacilli in the aged. *N Engl J Med* 1978;298:1108–11.
- [7] Marston BJ, Plouffe JF, File TM, et al. Incidence of community-acquired pneumonia requiring hospitalization. Results of a population-based active surveillance study in Ohio. The Community-based Pneumonia Incidence Study Group. *Arch Int Med* 1997;157:1709–18.
- [8] Niederman MS. Guidelines for the management of community acquired pneumonia: current recommendations and antibiotic selection issues. *Med Clin North Am* 2001;85:1493–509.
- [9] Riquelme R, Torres A, El-Ebiary M, et al. Community-acquired pneumonia in the elderly: a multivariate analysis of risk and prognostic factors. *Am J Respir Crit Care Med* 1996;154:1450–5.
- [10] Hanson LC, Weber DJ, Rutala WA. Risk factors for nosocomial pneumonia in the elderly. *Am J Med* 1992;92:161–6.
- [11] Garibaldi RA. Epidemiology of community acquired respiratory tract infections in adults. Incidence, etiology and impact. *Am J Med* 1985;78:32–7.
- [12] Rello J, Rodriguez R, Jubert P, et al. Severe community-acquired pneumonia in the elderly: epidemiology and prognosis. *Clin Infect Dis* 1996;23:723–8.
- [13] Kikuchi R, Watabe N, Konno T, et al. High incidence of silent aspiration in elderly patients with community acquired pneumonia. *Am J Respir Crit Care Med* 1994;150:251–3.

- [14] Riquelme R, Torres A, El-Ebiary M, et al. Community acquired pneumonia in the elderly. Clinical and nutritional aspects. *Am J Respir Crit Care Med* 1997;156:1908–14.
- [15] Starczewski AR, Allen SC, Vargas E, Lye M. Clinical prognostic indices of fatality in elderly patients admitted to hospital with acute pneumonia. *Age Aging* 1988;17:181–6.
- [16] Meehan TP, Fine MJ, Krumholz HM, et al. Quality of care, process, and outcomes in elderly patients with pneumonia. *JAMA* 1997;278:2080–4.
- [17] Farr BM, Sloman AJ, Fisch MJ. Predicting death in patients hospitalized for community-acquired pneumonia. *Ann Int Med* 1991;115:428–36.
- [18] Neill AM, Martin IR, Weir R, et al. Community-acquired pneumonia: aetiology and usefulness of severity criteria on admission. *Thorax* 1996;51:1010–6.
- [19] Lim WS, Lewis S, Macfarlane JT. Severity prediction rules in community acquired pneumonia: a validation study. *Thorax* 2000;55:219–23.
- [20] Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997;336:243–50.
- [21] Lim WS, Macfarlane JT. Defining prognostic factors in the elderly with community acquired pneumonia: a case controlled study of patients aged >75 years. *Eur Respir J* 2001;17: 200–5.
- [22] Berk SL. Bacterial pneumonia in the elderly: the observations of Sir William Osler in retrospect. *J Am Geriatr Soc* 1984;32:683–5.
- [23] Metlay JP, Schulz R, Li Y-H, et al. Influence of age on symptoms at presentation in patients with community-acquired pneumonia. *Arch Intern Med* 1997;157:1453–9.
- [24] Marrie TJ, Blanchard W. A comparison of nursing home-acquired pneumonia patients with patients with community-acquired pneumonia and nursing home patients without pneumonia. *J Am Geriatr Soc* 1997;45:50–5.
- [25] Hash RB, Stephens JL, Laurens MB, Vogel RL. The relationship between volume status, hydration, and radiographic findings in the diagnosis of community-acquired pneumonia. *J Fam Pract* 2000;49:833–7.
- [26] Dean NC. Use of prognostic scoring and outcome assessment tools in the admission decision for community acquired pneumonia. *Clin Chest Med* 1999;20:521–9.
- [27] Bartlett JG, Dowell SF, Mandell LA, et al. Practice guidelines for the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2000;31:347–82.
- [28] Marrie TJ, Lau CY, Wheeler SL, et al. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. *JAMA* 2000;283:749–55.
- [29] Ewig S, Ruiz M, Mensa J, et al. Severe community-acquired pneumonia. Assessment of severity criteria. *Am J Respir Crit Care Med* 1998;158:1102–8.
- [30] Clavo-Sánchez AJ, Girón-González JA, López-Prieto D, et al. Multivariate analysis of risk factors for infection due to penicillin-resistant and multidrug-resistant *Streptococcus pneumoniae*: a multicenter study. *Clin Infect Dis* 1997;24:1052–9.
- [31] Heffelfinger JD, Dowell SF, Jorgensen JH, et al. Management of community-acquired pneumonia in the era of pneumococcal resistance: a report from the drug-resistant *Streptococcus pneumoniae* therapeutic working group. *Arch Intern Med* 2000;160:1399–408.
- [32] Ruiz M, Ewig S, Marcos MA, et al. Etiology of community-acquired pneumonia: impact of age, comorbidity, and severity. *Am J Respir Crit Care Med* 1999;160:397–405.
- [33] Troy CJ, Peeling RW, Ellis AG, et al. Chlamydia pneumoniae as a new source of infectious outbreaks in nursing homes. *JAMA* 1997;277:1214–8.
- [34] Kauppinen MT, Saikku P, Kujala P, et al. Clinical picture of Chlamydia pneumoniae requiring hospital treatment: a comparison between chlamydial and pneumococcal pneumonia. *Thorax* 1996;51:185–9.
- [35] Lieberman D, Schlaeffer F, Boldur I, et al. Multiple pathogens in adult patients admitted with community-acquired pneumonia: a one year prospective study of 346 consecutive patients. *Thorax* 1996;51:179–84.
- [36] El Solh AA, Sikka P, Ramadan F, Davies J. Etiology of severe pneumonia in the very elderly. *Am J Respir Crit Care Med* 2001;163:645–51.
- [37] Doern GV, Pfaller MA, Kugler K, et al. Prevalence of antimicrobial resistance among respiratory

- tract isolates of *Streptococcus pneumoniae* in North America: 1997 results from the SENTRY antimicrobial surveillance program. *Clin Infect Dis* 1998;27:764–70.
- [38] Feikin DR, Schuchat A, Kolczak M, et al. Mortality from invasive pneumococcal pneumonia in the era of antibiotic resistance, 1995–1997. *Am J Public Health* 2000;90:223–9.
- [39] Metlay JP, Hoffman J, Cetron MS, et al. Impact of penicillin susceptibility on medical outcomes for adult patients with bacteremic pneumococcal pneumonia. *Clin Infect Dis* 2000;30:520–8.
- [40] Mandell LA, Marrie TJ, Grossman RF, et al, and the Canadian CAP Working Group. Canadian guidelines for the initial management of community-acquired pneumonia: an evidence-based update by the Canadian Infectious Diseases Society and the Canadian Thoracic Society. *Clin Infect Dis* 2000;31:383–421.
- [41] Dean NC, Silver MP, Bateman KA. Frequency of subspecialty physician care for elderly patients with community-acquired pneumonia. *Chest* 2000;117:393–7.
- [42] Chen DK, McGeer A, De Azavedo JC, et al. Decreased susceptibility of *Streptococcus pneumoniae* to fluoroquinolones in Canada. *N Engl J Med* 1999;341:233–9.
- [43] Gleason PP, Meehan TP, Fine JM, et al. Associations between initial antimicrobial therapy and medical outcomes for hospitalized elderly patients with pneumonia. *Arch Intern Med* 1999;159:2562–72.
- [44] Houck PM, MacLehose RF, Niederman MS, Lowery JK. Empiric antibiotic therapy and mortality among Medicare pneumonia inpatients in 10 Western states: 1993, 1995, 1997. *Chest* 2001; 119:1420–6.
- [45] Ramirez JA, Vargas S, Ritter GW, et al. Early switch from intravenous to oral antibiotics and early hospital discharge: a prospective observational study of 200 consecutive patients with community-acquired pneumonia. *Arch Intern Med* 1999;159:2449–54.
- [46] Feinsilver SH, Fein AM, Niederman MS, et al. Utility of fiberoptic bronchoscopy in nonresolving pneumonia. *Chest* 1990;98:1322–6.
- [47] Breiman RF, Butler JC, McInnes PM. Vaccines to prevent respiratory infection: opportunities on the near and far horizon. *Curr Opin Infect Dis* 1999;12:145–52.
- [48] Fedson DS, Harward MP, Reid MA, Kaiser DL. Hospital-based pneumococcal immunization: epidemiologic rationale from the Shenandoah study. *JAMA* 1990;24:1117–22.