Community-acquired pneumonia in the elderly
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A common cause for admission to the hospital, community-acquired pneumonia (CAP), is a serious and growing health problem in the United States and other developed countries. The elderly account for the majority of CAP-related hospital admissions, have longer lengths of stay than younger patients, suffer from more severe disease that often requires intensive care unit (ICU) admission, and consume the majority of expenses related to CAP. Mortality rates are high particularly among those with most severe disease, the majority of who are in the geriatric age group. Recent data indicate that in the elderly both the incidence and mortality of CAP are rising [1].

Definition

Guidelines from the Infectious Disease Society of America define CAP as an acute infection of the pulmonary parenchyma, accompanied by the presence of an acute infiltrate on a chest radiograph (or altered auscultatory findings consistent with pneumonia) in a patient not hospitalized or residing in a long-term care facility for \( \geq 14 \) days before onset of symptoms [2]. However, this definition is not consistent with the guidelines on CAP from the American Thoracic Society (ATS), which do not exclude the nursing home population from the statement [3]. Both the inconsistent definition and the diagnostic difficulties contribute to the wide variation of reported incidence, comorbidity, and mortality in different studies of CAP.
Incidence

Prospective population based studies from the United States [4] and the UK [5] have reported an annual incidence of CAP between 5 and 11 per 1000 adult population. The incidence varied markedly with age being much higher in the very young and the elderly population [6].

The proportion of adults with CAP who required hospital admission varied also widely with a reported percentage between 22% and 42% [5,7,8], presumably depending on the structure of the population and the structure of the health care system. Population-based studies on the incidence of CAP requiring hospitalization have reported an overall incidence of 1.1 per 1000 adult population in Canada [7] to 4 per 1000 adult population in Pennsylvanian hospitals in the United States [7,9]. However, the incidence of hospitalized CAP is much higher among elderly patients. During the year 1997 there were 623,718 hospital admissions for CAP among US Medicare recipients ≥ 65 years, accounting for an incidence of 18.3 per 1000 elderly [10]. The incidence rose more than fivefold from 8.4 per 1000 in those aged 65 to 69 years to 48.5 per 1000 in those aged 90 years and older (Fig. 1). The absolute number of cases fell beyond the age of 80 years because of the age distribution of the underlying population. Assuming the US census projected population estimates and a constant age-specific incidence of hospitalized CAP, the annual number of cases of hospitalized CAP in the elderly is expected to rise to 750,000 and 1 million in

![Figure 1](image-url)
the years 2010 and 2020, due to the disproportionate growth of the elderly population [10].

Severe CAP is defined as pneumonia requiring ICU admission. The exact criteria behind the decision to admit a patient to the ICU remain, however, undetermined. Data about the proportion of severe CAP among patients hospitalized with CAP are limited, and reported rates vary between 5% [11] and 18% [12]. The proportion of severe CAP defined as ICU admission and/or mechanical ventilation among the 623,718 elderly Medicare recipients hospitalized with CAP was 22.5% (N = 140,226), accounting for an incidence of 4 per 1000 elderly [10]. The proportion decreased with age from 26.7% in those aged 65 to 69 years to 14.7% in those aged ≥90 years (Fig. 2). This observation was not due to decreased severity of CAP because mortality increased with age but rather due to the greater use of advanced directives or limitations of care in the oldest old patients. Among those 140,226 cases with severe CAP, 95,589 (68.2%) received ICU care alone, 41,355 (29.5%) received ICU care and mechanical ventilation, and 3282 (2.3%) received mechanical ventilation outside the ICU, presumably in intermediate care facilities.

Mortality

The reported mortality in adults with CAP managed in an outpatient setting is low at less than 1% [5,13,14]. However, mortality rises sharply in patients

Fig. 2. Age-specific number, occurrence rate, and hospital mortality for complex cases in hospitalized community-acquired pneumonia. Complex pneumonia was defined as one involving ICU care or mechanical ventilation. The proportion of complex cases decreased (squares) and hospital mortality increased (triangles) for each age group (P < 0.001). (Adapted from Kaplan V, Angus DC, Griffin MF, et al. Hospitalized community-acquired pneumonia in the elderly. Am J Respir Crit Care Med 2002;165:766–72; with permission.)
admitted to hospital. Studies from the United Kingdom have reported mortality rates from 8% to 15% [15–17]. Mortality rates from US hospitals tend to be even higher, ranging from 14% to 30%, probably because most of the care in the United States is provided in an outpatient setting, and only high-risk patients with severe disease or underlying illness are admitted to hospitals [2,3,18]. The mortality rates of patients with severe CAP requiring admission to an ICU are particularly high, ranging from 21% to 54% [19–21]. The highest mortality rates of over 50% were reported from the UK [11,21,22]. This is presumably a reflection of the limited number of ICU beds per population in the UK [23], leading to ICU admission for patients with highest severity of illness.

The mortality from pneumonia is increased in the elderly compared with younger population [24]. Bacteremic pneumococcal infections are also more common in the elderly and reach mortality rates close to 40% in those aged 85 years or older [25]. The mortality is also higher in nursing home residents as was shown for age- and sex-matched elderly admitted from nursing homes (mortality rate 40.5%) or from the community (mortality rate 28%) [26]. The mortality of elderly patients with severe CAP who need ICU admission is extremely high. Severe CAP in the elderly has mortality rates above 40%, the risk of death being higher in those with progressive spread of radiographic infiltrates, shock, previous steroid treatment, immunosupression, or Acute Physiology and Chronic Health Evaluation (APACHE) II score greater than 22 on admission [27].

In 1997, hospital mortality was 10.6% among 623,718 hospital admissions for CAP in Medicare recipients ≥ 65 years [10]. Hospital mortality doubled with age from 7.8% in those aged 65 to 69 years to 15.4% in those aged ≥ 90 years (Fig. 1), and was higher in nursing home residents (17.6 versus 10.3%). Mortality was also higher in patients with an underlying illness (11.9% versus 7.6%). Increasing age, residence in a nursing home, and comorbid illness were independent predictors of death. Adjusted odds for death were also increased for men, although this effect was small (odds ratio: 1.15). Patients with severe CAP defined as need for intensive care or mechanical ventilation had a much higher mortality compared with controls (22.5% versus 7.1%). Mortality for patients ≥ 90 years was 15.4% overall, 30.2% for those admitted to the ICU, and 55.4% for those receiving mechanical ventilation.

Resource use and cost of care

In the United States, the annual incidence of 2 to 3 million cases of CAP results in about 10 million physician visits and close to 1 million of hospital admissions [28]. An estimate of the direct health care costs of treating CAP based on 1994 and 1995 data arrived at total costs of $8.4 billion [29]. Most of these costs were spent on inpatient care ($7.5 billion), mainly for patients ≥ 65 years ($4.4 billion) [29]. Outpatient costs were less than 5% of the total costs [29]. Similar estimates from the UK incurred a direct health care cost for CAP of £441 million. The average costs for managing pneumonia in the community were
at £100 per episode, compared with £1,700 to 5,100 for hospitalized patients. Hospitalization accounted for 87% of the total annual costs of CAP [30]. A more current and detailed analysis of Medicare claims data (Center for Medicare & Medicaid Services) found that CAP accounted for 623,718 or 6.2% of all acute care hospital admissions, 4.8 million or 7% of all hospital days, and 633,232 or 7.4% of all ICU days among Medicare recipients ≥ 65 years [10]. Hospitalized CAP incurred $4.4 billion, or 6.3% of total Medicare inpatient expenses ($70 billion). Half of the hospital costs ($2.1 billion) were accounted by patients requiring ICU admission or mechanical ventilation. Expenses for nonsurvivors totaled $779 million, of which 73.8% were spent in nonsurvivors of ICU care. Mean length of stay (LOS) and cost per hospital admission were 7.6 days and $6,949. Patients admitted to the ICU had much higher LOS and costs (11.3 days and $14,294), especially when receiving mechanical ventilation (15.7 days and $23,961). There was a small decrease in LOS and a large decrease in costs with age (7.7 days and $7,768 for those aged 65 to 69 years versus 7.4 days and $5,683 for those aged ≥ 90 years), presumable due to limitation of care in the oldest old population [10].

Long-term outcome

Little is known about the long-term survival of elderly patients discharged from hospital following an episode of CAP. Brancati et al followed a cohort of 119 patients and reported that one in four hospital survivors died in the year following hospital discharge [31]. They found that underlying disease was the major risk factor for long-term mortality while age was not an independent predictor, and concluded that old age should not be a sole criterion for withholding aggressive treatment in elderly with severe CAP. A Finnish population-based study followed for up to 9 years 122 elderly patients who survived a hospitalization for CAP [32]. Mortality was 19% at 1 year, 32% at 2 years, and 54% at 5 years after hospital discharge. The risk of death remained elevated for the entire follow-up period compared with other elderly inhabitants from the same region. The authors concluded that elderly patients treated for CAP are at high risk of subsequent mortality for several years, and that there is a clear need for prevention. However, both studies were of small sample size and from select patient population, potentially limiting their generalizability [31,32].

A recent population-based study analyzed long-term survival in a cohort of 139,768 Medicare recipients ≥ 65 years discharged from hospital following an episode of CAP [33]. Mortality was 9.4%, 18.0%, 25.0%, and 33.6% at 1, 3, 6, and 12 months after hospital discharge, respectively. The risk of death decreased during each consecutive month after hospital discharge. However, 1 year after hospital discharge the risk of death for CAP patients remained elevated compared with that of an age-, sex-, and race-matched general US population (standardized mortality ratio 2.69 [95% CI 2.47–2.93]). One-year mortality doubled with age for subjects ≥ 90 years compared with subjects 65 to 69 years old, was twice as
high for subjects with $\geq 3$ comorbid illnesses compared with subjects with no comorbidity, and was more than 50% in CAP survivors with malignancies, renal disease, liver disease, and neuropsychiatric disorders. Age remained an independent predictor of postdischarge mortality after adjusting for comorbid illnesses. CAP caused more deaths after hospital discharge than during the hospitalization period [33]. Therefore, future efforts in the management of CAP need to address the postdischarge period in addition to the hospitalization to modify the dismal outcome of this common disease in the elderly.

**Etiology**

Despite extensive diagnostic testing prospective studies evaluating the causes of CAP in adults have failed to identify a specific etiology in 40% to 60% of patients [5,34–37]. This seems particularly true in the elderly, who may not be able to produce adequate sputum specimens or undergo other diagnostic procedures [38,39]. Comparisons of relative frequencies of etiologies in different study populations are hampered by the varying level of sensitivity and specificity of the diagnostic test used. No single test is presently available that can identify all potential pathogens, and each diagnostic test has limitations. In addition, several studies have reported that some patients with CAP might have mixed infection, involving more than one pathogen [40]. Thus, the frequency of many causes of CAP is either exaggerated or underestimated.

It appears that the distribution of pathogens in the elderly is different from that in younger adults [38,41]. *Streptococcus pneumoniae* still appears to be the most common isolate, causing close to 50% of infections in the elderly, but infections with *Haemophilus influenzae*, Gram-negative bacilli, *Staphylococcus aureus* and anaerobes are increasingly common [39,42–45]. Enteric Gram-negative infections are common primarily in those with comorbid illness (particularly chronic obstructive pulmonary disease—COPD), recent use of antibiotics, and in those residing in nursing homes [20,46]. Most studies performed in the elderly have not commonly identified infections with *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*, both found commonly in younger patients [47]. However, recent studies have documented that chlamydial infections may account for up to 25% of CAP in patients over the age of 65 years [41,48]. Some of these discrepancies might be explained by the different diagnostic tests used. The frequency of other etiologies such as *C psittaci*, *Coxiella burnetti*, *Fracisella tularensis*, and endemic fungi (histoplasmosis, blastomycosis, and coccidioidomycosis) is dependent on specific epidemiologic factors.

El-Solh et al recently reported the etiology of severe CAP in 104 patients who were 75 years of age and older who acquired the infection outside the confines of a hospital. The predominant organisms were *S pneumoniae* (14%), Gram-negative enteric bacilli (14%), *Legionella* (9%), *H influenzae* (7%), and *S aureus* (7%). In patients with nursing-home acquired pneumonia, the predominant organisms were *S aureus* (29%), Gram-negative enteric bacilli (15%),
*S. pneumoniae* (9%), and *Pseudomonas aeruginosa* (4%). The authors concluded that pathogens responsible for severe CAP in elderly patients differ whether the patient comes from the community or from a nursing home.

**Clinical presentation**

CAP in the elderly has a different clinical presentation than CAP in other age groups. The clinical picture in the elderly is incomplete. This presentation with a concomitant delay in antibacterial treatment may contribute to the greater mortality of CAP in the elderly compared with younger patients. Riquelme et al [49] found that the classic triad of fever, cough, and dyspnea was present in only 31 of 101 elderly patients admitted to a 1000-bed teaching hospital with the diagnosis of CAP [49]. Altered mental status was found in 45 patients, and was more frequent in the pneumonia cohort compared with matched controls. Only 16 patients with pneumonia were considered to be well nourished, as assessed by triceps skin fold thickness, midarm perimeter, and serum albumin. There was no association between the type of isolated microorganism and the clinical presentation of CAP, except for pleuritic chest pain, which was more common in pneumonia episodes caused by classical bacterial microorganism [49]. Other classical physical signs of pneumonia may be also absent on examination. However, tachypnea appears to be a sensitive indicator of the presence of lower respiratory tract infection in the elderly [50]. A high index of suspicion for CAP is important in all elderly patients who manifest with nonspecific deterioration of their condition such as confusion, incontinence, episodes of falling, lethargy, and weakness.

**Severity assessment**

CAP presents as a wide spectrum of illness from a mild and self-limiting process to a life-threatening and occasionally fatal disease. Decisions regarding the level of care, including the hospital and ICU admission decision, the extent of microbiologic investigation, the choice and route of administration of antibiotics, the duration of treatment, and the level of nursing care have consequences for both the level of treatment received and the overall costs of treatment. These decisions are best based on an accurate assessment of the severity of illness at presentation and the likely progression of the disease. Identification of patients at low risk of complications who are suitable for outpatient management has the potential for reducing inappropriate hospitalization and consequent costs. Identification of patients at high risk of death allows early initiation of appropriate antibiotics and admission to an ICU where ventilatory support is readily available.

**Criteria for hospital admission**

The Pneumonia Severity Index (PSI), which is based on work performed by the Pneumonia Patient Outcome Research Team, was developed in a cohort of
14,199 inpatients and independently validated in 38,039 inpatients and in 2287 in- and outpatients enrolled prospectively in the Pneumonia PORT cohort study [18]. The index relies on the identification of preexisting patient characteristics, adverse physical findings, and laboratory and radiographic data (Table 1) to stratify patients into five risk groups with low mortality rates for risk classes I–III (0.1%–2.8%), intermediate for risk class IV (8.2%–9.3%), and high for risk class V (27.0%–31.1%) [18]. This stratification has been extrapolated into defining the need for hospital admission. Patients in risk class I (age ≤ 50 years, no coexisting illness, no adverse clinical findings) and risk class II (PSI score ≤ 70) are considered for outpatient treatment, patients in risk class III (PSI score 71–90) are candidates for outpatient treatment or brief inpatient observation, and patients in risk class IV (PSI score 91–130) and V (PSI score > 130) should receive traditional inpatient care.

The index heavily weights age assigning men over the age of 70 and women over the age of 80 years in risk Class III (even when no other risk factors are identified) and neglects aspects of patients preferences and social circumstances, both of which are important regarding the admission decision in the elderly. In

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Pneumonia severity Index scoring system for assignment to risk class II–IV</th>
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<tbody>
<tr>
<td>Characteristic</td>
<td>Points</td>
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<tr>
<td>Age</td>
<td>Age (years)</td>
</tr>
<tr>
<td>Men</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>Age (years − 10)</td>
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<tr>
<td>Nursing home resident</td>
<td>10</td>
</tr>
<tr>
<td>Coexisting illness</td>
<td></td>
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<tr>
<td>Neoplastic disease</td>
<td>30</td>
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<tr>
<td>Liver disease</td>
<td>20</td>
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<tr>
<td>Congestive heart failure</td>
<td>10</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>10</td>
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<tr>
<td>Renal disease</td>
<td>10</td>
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<tr>
<td>Physical examination findings</td>
<td></td>
</tr>
<tr>
<td>Altered mental status</td>
<td>20</td>
</tr>
<tr>
<td>Respiratory rate ≥ 30/minute</td>
<td>20</td>
</tr>
<tr>
<td>Systolic blood pressure &lt; 90 mm Hg</td>
<td>20</td>
</tr>
<tr>
<td>Temperature &lt; 35°C or ≥ 40°C</td>
<td>15</td>
</tr>
<tr>
<td>Pulse ≥ 125/minute</td>
<td>10</td>
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<tr>
<td>Laboratory and radiographic findings</td>
<td></td>
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<tr>
<td>Arterial pH &lt; 7.35</td>
<td>30</td>
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<tr>
<td>Blood urea nitrogen ≥ 30 mg/dL</td>
<td>20</td>
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<tr>
<td>Serum sodium &lt; 130 mmol/L</td>
<td>20</td>
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<tr>
<td>Serum glucose ≥ 250 mg/dL</td>
<td>10</td>
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<tr>
<td>Hematocrit &lt; 30%</td>
<td>10</td>
</tr>
<tr>
<td>Partial pressure of oxygen &lt; 60 mm Hg</td>
<td>10</td>
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<tr>
<td>Pleural effusion</td>
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addition, the index was never prospectively tested for the purpose of defining the need for hospitalization. Therefore, although prediction rules are important to identify low risk patients that can be managed in an outpatient setting, determination of the initial site of care remains an “art of medicine” because other factors than severity of illness need to be considered.

Criteria for ICU admission

Admission to the ICU defines severe CAP. Early recognition and prompt initiation of treatment in severe CAP is associated with reduced mortality [51,52]. More than a decade ago a study found that among 60 patients with severe CAP eight were admitted to the ICU only after suffering from cardiopulmonary arrest on the general medical ward [34]. Other studies found also evidence of suboptimal care of patients with severe CAP, including lack of appreciation of disease severity and lack of suitable investigations including arterial blood gas analysis [53]. Correct management of severe CAP requires early recognition. Repeated regular assessment at the initial stage of the illness is necessary. Increasing FiO2, altered mental state, and the onset of respiratory or metabolic acidosis are all signs of disease progression and the need for further intervention.

In 1987, the British Thoracic Society Research Committee developed a rule, which was aimed at identification of high-risk patients who not only require hospitalization, but who often require ICU admission [54]. Patients were found to have a 21-fold increased risk of death if they had two or more of the following “core” adverse prognostic features: respiratory rate ≥ 30 per min, diastolic blood pressure ≤ 60 mm Hg, and BUN >19.1 mg/dL This rule has been validated by other research groups, and was found to have a sensitivity and specificity of approximately 80% to predict the need for ICU admission [55].

The original ATS guidelines identified nine criteria for severe illness, and the presence of any one was used to define severe CAP. However, several validation studies have shown that the original definition was overly sensitive [56]. A more recent modification of the ATS rule requires the presence of either one of two major criteria (need for mechanical ventilation, or septic shock) or two of three minor criteria (systolic BP ≤ 90 mm Hg, multilobar disease, PaO2/FiO2 ratio < 250) to predicted the need for ICU admission. The rule was validated in 422 consecutive and nonselected patients hospitalized with CAP and had a sensitivity of 78%, a specificity of 94%, a positive predictive value of 75%, and a negative predictive value of 95% [56]. Other findings that may also have utility to identify severe CAP are confusion and BUN > 19.6 mg/dL; however, these adverse prognostic features have not been formally tested [17]. Most prediction rules have been developed for all age groups, and only a few have been validated specifically in the elderly [57]. However, based on current evidence, there is no support for the use of other predictors for the need of ICU admission in the elderly population [58].
Diagnostic evaluation

Appropriate diagnostic evaluations in patients with suspected CAP have been articulated by different professional societies [2,3,59,60]. Pneumonia should be suspected in all elderly patients with fever, independent of lower respiratory tract symptoms such as cough, sputum production, and dyspnea, especially if accompanied by altered mental status and malnutrition. Because the physical examination to detect bronchial breath sounds or rales is neither sensitive nor specific for pneumonia [61], the ATS guidelines suggest that all patients with suspected CAP should have a chest radiograph taken to confirm the diagnosis, and to search for complications such as the presence of pleural effusion, abscess formation, or multilobar disease [3]. All patients should have a careful assessment of disease severity, and those admitted to hospital should have a blood count and routine blood chemistry, a collection of two sets of blood cultures (which has been associated with reduced 30-day mortality [62]), and an assessment of gas exchange (blood gases). According to the ATS guidelines, Gram’s stain and sputum culture are not required because of low yield and the lack of documented benefit in terms of cost and outcome [3]. In contrast, the Infectious Disease Society of America guidelines emphasize microbiologic studies, driven by the desire to identify the etiologic agent and permit optimal antibiotic selection, to identify newly emerging pathogens or those of potential epidemiologic significance, to recognize drug resistance, and to permit antibiotic selection that limits the effect of antibiotic overuse in the community [2]. ATS guidelines suggest that sputum cultures and Gram’s stain and sputum culture are not required because of low yield and the lack of documented benefit in terms of cost and outcome [3]. In contrast, the Infectious Disease Society of America guidelines emphasize microbiologic studies, driven by the desire to identify the etiologic agent and permit optimal antibiotic selection, to identify newly emerging pathogens or those of potential epidemiologic significance, to recognize drug resistance, and to permit antibiotic selection that limits the effect of antibiotic overuse in the community [2]. ATS guidelines suggest that sputum cultures and Gram’s stain should be obtained only if a drug-resistant pathogen or an organism not covered by the usual empiric therapy is suspected, and that initial empiric treatment can be broadened to include the organisms found on Gram’s stain [3]. Routine serologic testing is not recommended by either society, but for patients with severe CAP, Legionella pneumophila urine antigen, which is sensitive (> 80%) and highly specific (> 95%) for Legionella infections, should be measured. Although it seems reasonable that aggressive efforts to establish an etiologic diagnosis, such as bronchoscopic sampling of lower respiratory tract secretions, can be considered in select patients, the benefits of such an approach have not been shown. If there is a relevant effusion, a thoracentesis should be performed with stain, culture, and determination of pH, and leukocyte count [63]. In complicated parapneumonic effusions (pH ≤ 7.2) or frank empyema, pleural fluid drainage is required [64].

Treatment

Supportive measures include maintenance of adequate oxygenation and attention to hydration and nutrition. One study suggested that nutritional supplementation may help the elderly to recover from chest infections [65].
Empiric antimicrobial treatment

The timely use of appropriate antibiotics abbreviates illness duration, reduces the risk of complications, and lowers mortality in CAP. CAP is rarely defined microbiologically at presentation, and hence, antibiotic prescription is empirical. Clinical, epidemiologic, and radiologic information is not predictive of microbiologic etiology. In recent years, dramatic changes in health care delivery have shifted much of the care of sick individuals from hospitals to the community. Consequently, the traditional classification of infections as community acquired or hospital acquired is increasingly difficult. Patients admitted from the community might have been recently discharged from a hospital, undergone an invasive procedure on an outpatient basis, or might be residents of nursing homes. These groups have distinct epidemiologic, clinical, and bacterial characteristics, as well as distinct antimicrobial susceptibility profiles [66]. These considerations have to be taken into account when choosing an initial antibiotic treatment. Empiric therapy is primarily directed at *S. pneumoniae*, which remains the leading cause of CAP in the elderly [3,24]. However, infections with pathogens such as *Legionella* and *Mycoplasma* that need an additional coverage with erythromycin or the newer macrolide/azalide agents should be considered. In cases with serious underlying illness, additional coverage may be needed for more resistant Gram-negative rods, *Staphylococcus aureus*, and anaerobes.

Numerous guidelines on CAP articulated by various professional societies give specific recommendations for empiric antibiotic treatment [2,3,59,60]. All guidelines organize their approach to the initial treatment of CAP based on the clinical setting (outpatient, hospital ward, ICU). The ATS guidelines further consider coexisting cardiopulmonary disease (chronic obstructive pulmonary disease, congestive heart failure) and the presence of “modifying factors” (risk factors for drug-resistant pneumococcus [DRSP], Gram-negative infection, and *P. aeruginosa*) for risk stratification (Box 1) [3]. Age is not used as a major discriminating factor in defining initial empiric therapy. This concept has been corroborated by studies that have shown that age alone has little impact on the bacterial etiology in the absence of comorbid illness [27,49]. However, one pathogen whose presence may be impacted by age alone is drug-resistant *S. pneumoniae* (DRSP), with several studies showing that age > 65 years is an independent risk factor for CAP due to this organism [67,68]. The clinical relevance of DRSP has been debated, but in the absence of meningitis, clinical failure with high-dose β-lactam therapy is currently unlikely [69].

All guidelines recommend a macrolide or doxycycline for empiric treatment of outpatients with CAP. The recommendation of the ATS guidelines applies only in the absence of cardiopulmonary disease and “modifying factors.” If either is present, a β-lactam (amoxicillin-clavulanate or a second-generation cephalosporin) should be added. An antipneumococcal fluoroquinolone can be substituted for the combination therapy. For patients on general hospital wards, a third-generation cephalosporin plus a macrolide is the first choice. The guidelines issued by the Canadian Infectious Diseases Society and the Canadian Thoracic Society favor
monotherapy with an antipneumococcal fluoroquinolone, because of simpler administration and switching from intravenous to oral forms. For patients who are critically ill, all guidelines recommend combination therapy. In the absence of “modifying factors,” the ATS guidelines suggest combining a β-lactam with a macrolide or intravenous fluoroquinolone. The role of antipneumococcal fluoroquinolone monotherapy in severe CAP is currently uncertain. For critically ill patients at risk for \textit{P} aeruginosa infection, combining an antipseudomonal β-lactam with an antipseudomonal fluoroquinolone (preferably parenteral ciprofloxacin) appears to be best. Antimicrobial treatment should be tailored to the microbiologic results, changing to the antimicrobial agent that is most cost-effective, least toxic, and most narrow in spectrum.

\textit{Respiratory management}

All patients with severe CAP except those with a background of chronic respiratory failure require high-flow oxygen therapy, which can be rapidly titrated against oximetry and arterial blood gases to check calibration. Hypercapnia indicates the need for a more intensive ventilatory support, usually intubation and mechanical ventilation. Noninvasive positive pressure ventilation (NPPV), which is the primary treatment for exacerbation of COPD [70], is a further treatment option for patients with severe CAP. However, a small randomized study of NPPV given in the emergency room showed a higher mortality in the intervention group compared with controls [71]. One explanation for the higher mortality in the NPPV group was delay in intubation in most severely ill patients. Therefore,
enthusiasm for noninvasive ventilatory support should not delay intubation in patients with severe CAP, particularly in those without COPD.

Many patients with severe CAP who require intubation and mechanical ventilation will develop diffuse lung injury, and should be managed in accordance with low tidal volumes as per the recent NHLBI acute respiratory distress syndrome (ARDS) Network trial [72]. Although the ventilatory strategy of limiting tidal volumes has not been examined in patients with severe CAP without ARDS, it still may be prudent to initiate a low tidal volume protocol in all patients with CAP who require intubation and ventilatory support. Patients with severe CAP have sepsis from a respiratory source, and most die from the complication of multiorgan failure, rather than from respiratory failure alone [73]. These patients usually require invasive circulatory monitoring, the use of vasopressors and inotropes, and hemofiltration for renal replacement therapy. Survivors have a prolonged ICU stay and life-threatening complications are frequent during the course of disease.

The nonresponding patient

Most patients with CAP will have an adequate clinical response within 3 days, although improvement in the elderly may take longer. Lack of clinical improvement at 72 hours is usually considered a treatment failure. If a treatment failure is considered, the diagnosis should be reviewed, and alternative conditions such as cardiac failure and pulmonary infarction should be excluded. Pulmonary and extrapulmonary complications of CAP, such as lung abscess and necrosis, empyema, endocarditis, and nosocomial superinfection, should be sought. At this stage, culture results are available, and antibiotic treatment should be modified according to the microbial resistance pattern. Pathogens that are unusual in the United States but common in other countries such as tuberculosis and melioidosis should be considered [74]. A bronchoscopy with bronchoalveolar lavage might be useful at this stage as has been shown for ventilator associated pneumonia [75].

Limitation of care

With the aging process there is a steadily increasing susceptibility to fatal diseases. Respiratory tract infections are diseases to which humans often ultimately succumb and which do not greatly alter the predetermined life span. Pneumonia in the elderly should not be treated in the ICU if it merely represents the expected terminal event of a chronic disabling illness. Age per se, however, does not justify restriction of care, because several studies have shown that advanced age alone is not an independent predictor of death in CAP [27,76].

Limitation of care already occurs on a national level. A population-based US study showed that in the oldest-old patients with CAP the proportion of those managed aggressively (ICU admission or mechanical ventilation) was lower than
in younger elderly counterparts (Fig. 2) [56]. Because mortality increased steadily with each age group, the above-mentioned observation could not be explained by less severe disease but rather reflected limitations of care. The decision to provide intensive care in the elderly patient with CAP varied widely in different reports, raising the possibility that provision of intensive care or life support may be strongly influenced by local practice patterns [58,77,78]. Therefore, as prior efforts have sought to standardize and improve the hospital admission decision [18,79,80], new efforts are required to standardize and improve decisions regarding intensive care and life support in the elderly with CAP. Such decisions should be based on the patient preferences, functional status, underlying illness, social support, and consideration about long-term survival and quality of life after critical care.

**Prevention**

Despite progress in antimicrobial treatment and supportive care, CAP remains a deadly disease. Prevention remains important especially for those at high risk for CAP. Programs to reduce smoking and exposure to environmental tobacco have the potential to reduce the incidence of pneumococcal disease [81]. Vaccines against influenza and *S pneumoniae* are available. Antiviral agents are effective for chemoprophylaxis.

**Pneumococcal vaccine**

Pneumococcal vaccine contains the purified capsular polysaccharide from 23 serotypes that cause 85% to 90% of invasive pneumococcal disease [82]. A single vaccination is applied. It should not be given during acute infection but can be given safely at the same time as the influenza vaccine using a different site for vaccination [83]. In a large meta-analysis the vaccine was shown to be effective in preventing invasive illness caused by the targeted serotypes in two thirds of low-risk adults [84]. This effect could not be confirmed for high-risk patients and for those aged 60 to 70 years [84]. However, a recent retrospective cohort study in subjects > 65 years with chronic lung disease found that pneumococcal vaccination was associated with fewer hospital admissions, fewer deaths, and direct medical cost savings [85]. Another report confirmed that pneumococcal vaccination was at least cost-effective and potentially cost-saving among elderly ≥ 65 years [86]. The vaccination is recommended for all immune-competent patients ≥ 65 years, and all younger persons with chronic illnesses such as cardiovascular disease, chronic pulmonary disease, diabetes mellitus, alcoholism, chronic liver disease, cerebrospinal fluid leak, and functional or anatomic asplenia [82]. For those living in special environments or social settings (Alaskan natives, American Indian, and those in long-term care facilities) the vaccination is also recommended [82].
Influenza vaccine and other prevention strategies

Influenza vaccine prevents or attenuates illness in 70% to 90% of healthy persons younger than 65 years with the efficacy depending on the match between the vaccine and the circulating strain [87]. Current vaccines are trivalent containing two types A and one type B virus. Reported side effects include fever, myalgia, and local and systemic reactions. However, in a large randomized trial, only discomfort at the injection site was more common in the vaccinated group [88]. In the elderly with chronic illness the vaccine is less effective but can still attenuate the disease progression, leading to less frequent lower respiratory tract infections with decrease in the associated morbidity and mortality. A meta-analysis of 20 studies of patients with CAP older than 65 years showed that the vaccine reduced the occurrence of pneumonia by 53%, the hospitalization rate by 50%, and the mortality rate by 68% [89]. A large randomized controlled trial from The Netherlands found that the incidence of serologically proven influenza could also be reduced in the elderly by 50% [90]. In addition, the vaccine has been shown to be cost-effective [91]. The vaccination is recommended to be given annually to individuals at high-risk for influenza complications (persons ≥ 65 years, residents of nursing homes or chronic care facilities, patients with chronic pulmonary or cardiovascular disease, those who required regular medical care or hospital admission in the preceding year, and pregnant women in the second or third trimester during influenza season), to those who can transmit influenza to high-risk patients (health care workers), and to others who wish to reduce the chance of becoming infected with influenza [92].

Older antiviral agents such as amantadine and rimantadine (active against influenza A virus [92]) and the newer neuramidase inhibitors, zanamivir and oseltamivir (active against influenza A and B virus [93–96]), can reduce the severity and duration of influenza if given within 48 hours of the onset of symptoms. These agents can be given during institutional outbreaks of influenza to treat infected individuals or to serve as prophylaxis for unvaccinated persons. Treatment is continued for 1 week after the end of the outbreak. However, their impact on preventing influenza related complications is uncertain. It is likely that neuramidase inhibitors will soon replace the older agents, because the emergence of resistance to these newer agents is slower, the frequency of resistance is lower, and the mutant virus has reduced virulence [93,95].

Summary

CAP is traditionally considered a medical disease, and is managed with intravenous fluids and antibiotics on medical floors. Recent cost-containment efforts have shifted the provision of care to the outpatient settings, and only those with most severe disease and multiple comorbid illnesses are admitted to hospitals. Therefore, the proportion of hospitalized patients with severe CAP that need intensive care and life support is increasing. Furthermore, the
incidence of severe CAP is also rising due to disproportionate growth of the elderly population that is most vulnerable to this deadly disease. Many of these elderly patients have advanced underlying diseases, and CAP might often be a terminal event superimposed on an underlying chronic debilitating illness. As ICU physicians, we need to be familiar with this disease, its complications, and its prognosis to provide intensive care in a timely and rational fashion in some patients, and refrain from life support in others. Just as prior efforts have sought to improve and standardize criteria for hospital admission, future efforts should aim to improve and standardize decisions regarding intensive care and life support in these very sick elderly patients. Future efforts in the management of CAP need to consider the postdischarge period where most deaths occur. Prevention is an important issue especially for those at high risk for CAP.

References


