Pneumonia in the very old

Jean-Paul Janssens and Karl-Heinz Krause

Pneumonia is a major medical problem in the very old. The increased frequency and severity of pneumonia in the elderly is largely explained by the ageing of organ systems (in particular the respiratory tract, immune system, and digestive tract) and the presence of comorbidities due to age-associated diseases. The most striking characteristic of pneumonia in the very old is its clinical presentation: falls and confusion are frequently encountered, while classic symptoms of pneumonia are often absent. Community-acquired pneumonia (CAP) and nursing-home acquired pneumonia (NHAP) have to be distinguished. Although there are no fundamental differences in pathophysiology and microbiology of the two entities, NHAP tends to be much more severe, because milder cases are not referred to the hospital, and residents of nursing homes often suffer from dementia, multiple comorbidities, and decreased functional status. The immune response decays with age, yet pneumococcal and influenza vaccines have their place for the prevention of pneumonia in the very old. Pneumonia in older individuals without terminal disease has to be distinguished from end-of-life pneumonia. In the latter setting, the attributable mortality of pneumonia is low and antibiotics have little effect on life expectancy and should be used only if they provide the best means to alleviate suffering. In this review, we focus on recent publications relative to CAP and NHAP in the very old, and discuss predisposing factors, microorganisms, diagnostic procedures, specific aspects of treatment, prevention, and ethical issues concerning end-of-life pneumonia.

Physiological changes in the respiratory system associated with ageing

Maximum function of the respiratory system is reached at approximately the age of 20–25 years. Thereafter, ageing is associated with a progressive decrease in lung performance; however, unless affected by disease, the respiratory system remains capable of maintaining adequate gas exchange during the entire life span. Physiological changes associated with ageing have important consequences on the functional reserve of older people, and their ability to cope with the decrease in lung compliance and increase in airway resistance associated with lower-respiratory-tract infection (LRTI).

J-PJ and K-HK are at the Division of Lung Diseases and Department of Geriatrics, respectively, Geneva University Hospitals, Geneva, Switzerland.

Correspondence: Dr Jean-Paul Janssens, Division de Pneumologie, Hôpital Cantonal Universitaire, 1211 Geneva 14, Switzerland. Fax +41 22 372 99 29; email Janssens@prolink.ch
The most important physiological changes associated with ageing are: a decrease in the elastic recoil of the lung, a decrease in compliance of the chest wall, and a decrease in the strength of respiratory muscles. Alterations in lung parenchyma (enlargement of alveoli, or "senile emphysema", decline in small airway diameter) and the associated decline in elastic recoil of the lung cause an increase in functional residual capacity (FRC); older patients thus breathe at higher lung volumes, increasing the workload imposed on respiratory muscles. Calcification and other structural changes within the rib cage and its articulations lead to stiffening of the chest wall (ie, decreased compliance), further increasing the work of breathing. Changes in the shape of the thorax also occur as a result of osteoporosis and vertebral fractures, resulting in dorsal kyphosis and increased anteroposterior diameter ("barrel chest"), which decreases the curvature of the diaphragm and has a negative effect on its force-generating capabilities. Respiratory muscle performance is thus impaired by the age-related increase in FRC, the decrease in chest-wall compliance and the geometric changes in the rib cage.1 Respiratory muscle strength is also affected by nutritional status, often deficient in the elderly, and by age-associated sarcopenia.2-6 Dysfunction of respiratory muscles in situations where an additional load is placed on the respiratory muscles, such as pneumonia, may lead to hypoventilation and hypercapnic respiratory failure. Noteworthy is the fact that normal values for maximum inspiratory pressure in people over 80 are below the threshold defined in an adult population for clinically relevant respiratory dysfunctions.7 Respiratory muscle function also depends on energy availability (ie, blood flow, oxygen content); indeed, decreased respiratory muscle strength has been described in patients with chronic heart failure (CHF), a frequent occurrence in older patients.7 Other frequent clinical situations decreasing respiratory muscle function in the elderly include Parkinson’s disease and sequelae of cerebral vascular disease.8,9

Forced expiratory volumes and peak expiratory flow show an age-related linear decrease, probably indicating structural changes and chronic low-grade inflammation in peripheral airways.11 In the very old, decreased forced expiratory flow rates and lung elastic recoil may compromise the efficacy of clearance of airway secretions by coughing. It has also been suggested that, even in the healthy aged population, mucociliary clearance rates are slowed by comparison with the young.12 Indeed, both smoking and non-smoking elderly people have reduced tracheal mucus velocity compared with younger individuals.1,13

Lower sensitivity of respiratory centres to hypoxia or hypercapnia in older patients results in a diminished ventilatory response in cases of acute disease such as heart failure, infection, or aggravated airway obstruction, and thus delays important clinical symptoms and signs such as dyspnoea and tachypnoea, which are important for diagnosis of pneumonia and appreciation of the severity of the associated respiratory impairment.14

**Effect of ageing on airway defences and pathogenic mechanisms implicated in CAP or NHAP**

**Changes in the immune system**
The ability of antigen-presenting cells (macrophages, dendritic cells) to process and present antigen to T cells is maintained in older individuals. Chemotaxis, adherence, and phagocytosis capacities of monocytes, macrophages, and neutrophils also seem to be unaffected. Conversely, a qualitative decline in humoral immunity, characterised by a loss of high affinity blocking antibodies and an increase in self-reactive antibodies, has been documented in older patients.15-17

There is little or no quantitative decline in circulating T lymphocytes in older individuals. However, the ability to generate a cell-mediated (T lymphocyte) immune response seems diminished.18

**Bronchoaspiration**
Around half of all healthy adults aspirate small amounts of oropharyngeal secretions during sleep. The low burden of virulent bacteria in normal pharyngeal secretions, together with forceful coughing, active ciliary transport, and normal humoral and cellular immune mechanisms, protect the airways from repeated clinical infection.19 However, defence of the airway is impaired in the elderly by decreased mucociliary clearance,20 alteration in respiratory mechanics and, in some cases, concomitant illnesses that predispose to aspiration.

There is a high incidence of silent aspiration in elderly patients who develop pneumonia: 71% of patients with CAP versus 10% of the controls.21 Increased frequency of aspiration is also seen in demented patients22 and patients with stroke.23 Feeding tubes do not protect from bronchoaspiration; this is true for nasogastric, gastrostomy, and postpyloric tubes.11,25 In fact, feeding tubes are associated with an increased rate of pneumonia and death from pneumonia.24 Even normal ageing is associated with impaired oropharyngeal deglutition; this has been attributed to an increased neural processing time and diminished oral control.24

In summary, aspiration is an important pathogenic mechanism for pneumonia in the elderly; in patients with neurological impairment of the glottic barrier, nasogastric tubes or gastrostomy do not seem to reduce the risk of aspiration pneumonia (figure 1).

**Table 1. Range of frequencies reported for common symptoms of pneumonia in patients hospitalised for CAP or NHAP**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>CAP % reported</th>
<th>NHAP % reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>49–81</td>
<td>40–63</td>
</tr>
<tr>
<td>Fever &gt;38°</td>
<td>12–76</td>
<td>64–75</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>38–82</td>
<td>39–79</td>
</tr>
<tr>
<td>Sputum</td>
<td>38–66</td>
<td>37–38</td>
</tr>
<tr>
<td>Chills</td>
<td>8–58</td>
<td>16–24</td>
</tr>
<tr>
<td>Pleural pain</td>
<td>9–43</td>
<td>4–24</td>
</tr>
<tr>
<td>Altered mental state</td>
<td>12–45</td>
<td>53–77</td>
</tr>
<tr>
<td>Focal</td>
<td>64–82</td>
<td>80</td>
</tr>
</tbody>
</table>
Upper airway colonisation

Colonisation of the upper respiratory tract (URT) by both Gram-negative bacteria (enterobacteriaceae, *Pseudomonas aeruginosa*) and Gram-positive bacteria (*Staphylococcus aureus*) is more prevalent in the elderly and is related more to the severity of systemic illness and degree of care than to age itself. Indeed, URT colonisation by Gram-negative bacteria may concern 60–73% of critically ill elderly patients in an acute medical ward and 22–37% of institutionalised older patients. URT colonisation by *S aureus* has been reported in around 12% of institutionalised elderly people. Factors leading to colonisation of the lower respiratory tract (LRT) and URT include antibiotic therapy, endotracheal intubation, smoking, malnutrition, surgery, and any serious medical illness. Decreased salivation such as that induced by antidepressants, antiparkinsonian medications, diuretics, antihypertensives, and antihistamines, also contributes to oropharyngeal Gram-negative bacteria colonisation.

Periodontal disease and antihistamines, also contributes to oropharyngeal Gram-negative bacteria colonisation. Periodontal disease and dental plaque are clearly identified risk factors for the development of nursing-home acquired aspiration pneumonia. The risk of aspiration pneumonia is reduced by appropriate oral care and in edentate people.

Thus there are an increased number of pathogenic bacteria in the URT of sick and institutionalised elderly patients, which increases the risk of pneumonia after bronchospiration.

Comorbidity

Comorbidity is an important determinant of the risk of pulmonary infection and its prognosis: cancer, diabetes, chronic respiratory disorders, chronic renal failure, and chronic heart failure all increase the likelihood of LRTI.

Clinical presentation and microbiology of CAP and NHAP

**Clinical presentation**

Table 1 includes the most common symptoms of CAP and NHAP and their relative frequencies as cited in the most recent studies of elderly patients hospitalised for CAP or NHAP. Cough, sputum, chills, and pleural pain are less frequent in NHAP than in CAP; conversely, elderly patients present more often with altered mental status (delirium) when hospitalised for NHAP than CAP. Fever, which is frequently absent in elderly patients with pneumonia, was more consistently seen in patients with NHAP than in patients with CAP. This finding might be due to a selection bias: only patients with severe NHAP are transferred to the hospital. Tachypnoea (respiratory rate >20/min) and tachycardia (>100/min) were seen in about two-thirds of patients with CAP. This finding might be due to a selection bias: only patients with severe NHAP are transferred to the hospital. Tachypnoea (respiratory rate >20/min) and tachycardia (>100/min) were seen in about two-thirds of patients with CAP. Thus, subtle clinical manifestations of CAP in the very old, such as unexplained falls, incontinence, failure to thrive, or sudden aggravation of a pre-existing comorbidity (eg, diabetes, congestive heart failure, Parkinson’s disease) have to be actively sought.

**Factors associated with morbidity and mortality**

Factors associated with a prolonged hospital stay are age, delirium, NHAP rather than CAP, roentgenograms suggestive of aspiration, cyanosis, leucocytosis, and presence of band forms in blood smears. Pneumonia mortality increases with age, not exclusively due to age itself, but also to associated conditions such as presence of comorbidities and malnutrition.

Fine’s pneumonia predictive index (PPI) for CAP was used in patients aged 65 years or above, and shown to provide an accurate estimate for the length of stay, ICU admission, and mortality. The British Thoracic Society prognostic rules were also used to assess this population and predicted mortality with a sensitivity of 47–65%, a specificity of 73–88%, and an overall accuracy of 72–84%. Thus, these rules cannot be reliably used for the individual patient, but are probably useful for clinical studies.

Other factors associated with increased mortality from pneumonia in this age group include admission from a nursing home, bedridden status, delirium, absence of fever (<37°C), tachypnoea (respiratory rate >30/min), C-reactive protein (CRP) greater than 100 mg/L, hypoalbuminaemia, acute non-respiratory organ dysfunction, affection of several lobes, suspicion of aspiration, and presence of swallowing disorders.

**Microbiology**

Table 2 summarises microbiological findings in recent hospital-based studies of CAP or NHAP.

Streptococcus pneumoniae is by far the predominant pathogen isolated in hospital-based studies of elderly patients with CAP (up to 58%) or NHAP (up to 30%). In older patients treated in the intensive-care unit (ICU),...
S pneumoniae reportedly causes 14% of CAP and 9% of NHAP. Pneumonia caused by S pneumoniae tends to occur more frequently in patients with coexisting lung disease, hepatic disorders, or alcohol abuse. There have been several reports of outbreaks of clusters of pneumococcal pneumonia in unvaccinated residents of long-term care facilities, with a high mortality rate, suggesting a possible protective effect of pneumococcal vaccine in nursing home residents (figure 2).

Haemophilus influenzae is among the most frequently reported pathogens in older patients with CAP or NHAP (up to 14%), and was identified in 7% of elderly patients with severe CAP or NHAP leading to admission to an ICU. Several reports have shown that H influenzae is frequently linked to exacerbations of COPD and bronchiectasis and should thus be considered as a potential pathogen in these patients. (figure 3).

S aureus was documented in up to 7% of patients with CAP and 4% of patients with NHAP. S aureus, particularly species resistant to meticillin (MRSA), are increasingly recognised in the nursing-home population. One study shows an even higher occurrence of S aureus-related pneumonia: of 104 elderly patients with severe CAP or NHAP admitted to an ICU, 17% had S aureus—mostly meticillin-sensitive (MSSA)—as causative agent. In this study, S aureus was identified in 29% of the patients with severe NHAP (78% meticillin-sensitive) versus 7% of those with CAP (all meticillin-sensitive). Because of the increasing rate of MRSA colonisation in the nursing home population, and the relatively high probability of MRSA carriers developing symptomatic infection, MRSA pneumonia is likely to become a more frequently encountered entity. Other pulmonary infections associated with S aureus include lung abscess, empyema, as well as secondary bacterial pneumonia after viral respiratory infection.

Enteric Gram-negative bacteria
Both colonisation by and infection with Gram-negative bacteria is a function of the number and severity of concomitant illnesses (immunosuppression, diabetes, prior cerebrovascular accidents). The likelihood of Gram-negative bacteria pneumonia increases in nursing-home patients and in patients with decreased functional status. In a community setting, Gram-negative bacteria infection occurs primarily in debilitated and chronically ill patients. The presence of Pseudomonas spp suggests bronchiectasis (figure 3).

Agents of “non-typical” pneumonia
Noteworthy is the frequency of “non-typical” microorganisms (Legionella pneumophilia, Chlamydia pneumoniae, Mycoplasma pneumoniae, Coxiella burnetti, table 2) reported in older patients with either CAP or NHAP.

Mycoplasma pneumoniae
Most studies suggest that M pneumoniae is exceedingly rare in the elderly. M pneumoniae was not identified in elderly patients admitted to the ICU for severe CAP.

Legionella pneumophilia
Prevalence of L pneumophilia in CAP shows important geographic variations, being in the range of 1·8–24% in hospital-based studies. In Switzerland, the Federal Agency for Public Health reported 261 cases of definite L pneumophilia infection between 1999 and 2001 (1·7/10 5 inhabitants). Median age of patients infected was 61 years; that of patients dying from the infection was 67 years; 34% of infected people were older than 70.

The incidence of Legionella spp infection may be underestimated in clinical studies because of the low to moderate sensitivity of diagnostic tests. Indeed, sensitivity of serology ranges from 40–60%; that of direct fluorescent antibody staining of sputum is 30–70% (specificity of 94–99%); and sputum culture has a sensitivity of roughly 80%. The most useful test—namely testing for presence of urinary legionella antigen—is highly specific (100%) yet has a sensitivity of 79–83%, increasing to 94% if only L pneumophilia serogroup 1 is considered.

The clinician should also be aware that the urinary-specific antigen for L pneumophilia may persist for several months after resolution of the pneumonia. Thus, a second episode of pneumonia may be incorrectly attributed to L pneumophilia.

In older patients, L pneumophilia was reported by Bentley et al as the most frequent cause of the non-typical pneumonia syndrome (constitutional symptoms, myalgia, diarrhoea, paucity of pulmonary signs). Infection by legionella is frequently heralded by an abrupt onset of...
Viral infection

Viral infections such as adenovirus, respiratory syncitial virus (RSV), influenza, parainfluenza, and rhinoviruses may cause up to 42% of acute LRTI during the winter months in institutionalised elderly people, RSV being the most common viral pathogen in this setting.75,76 Among patients admitted to a hospital for CAP or NHAP, viruses are the causative agents in 2–32% of patients admitted, influenza, RSV, and parainfluenza being the most commonly implicated.2,36,44,77,78

Neither the clinical nor the radiological presentation of acute pulmonary infection in the elderly is sufficiently specific to suggest a specific cause. Thus, the idea of typical and non-typical pneumonia should not be used for therapeutic decisions.2,26

Hospital-acquired pneumonia

Advanced age is associated with an increased risk of nosocomial infection including pneumonia. This risk further increases with length of hospital stay.29 The frequency of colonisation of upper or lower airways, in particular with resistant organisms such as MRSA, enterococci, Stenotrophomonas maltophilia, and P aeruginosa, is also reported to increase with age.22 Yet there are to our knowledge no specific clinical studies of nosocomial pneumonia in the very old. Thus, at this point, recommendations for management of hospital-acquired pneumonia (HAP) are similar to those for nosocomial pneumonia in younger adults (see panel).

The clinical diagnosis of HAP in the very old is difficult because of non-typical and paucisymptomatic presentations (delirium, absence of febrile response or cough, poorly contributive physical examination) and must rely on a high index of suspicion in the presence of unexplained changes in

Chlamydia pneumoniae

C pneumoniae infection in the elderly is generally considered to be a mild disease,28,29 and was reported in only 1% of patients admitted to ICU for CAP.3 However, C pneumoniae outbreaks in nursing homes have been associated with a high attack rate (44–68%) and high mortality (about 35%) of confirmed cases.34 C pneumoniae has no specific clinical presentation but the combination of pharyngitis or hoarseness (laryngitis) and non-productive cough should suggest C pneumoniae infection.24 The infection can be identified by direct fluorescent antibody staining, nasopharyngeal swabs (PCR or culture), or retrospectively by serology.

Figure 3. Elderly woman with diffuse bronchiectasis, predominantly in right lower lobe. The identification of P aeruginosa and, to a lesser degree, H influenzae in sputum should suggest the presence of bronchiectasis. Bronchiectasis is underdiagnosed in older patients. A clinical diagnosis is often difficult because auscultation, although suggestive, is non-specific, and crackles may be absent. When suspected, high resolution computed tomography should be used for definitive diagnosis.
cognitive performance, failure to thrive, worsening of an underlying chronic illness (ie, congestive heart failure, diabetes, Parkinson’s disease), unexplained dyspnoea, tachypnoea, tachycardia, and decreased oxygen saturation in arterial blood.

**Mycobacterial infection**

Incidence of tuberculosis in patients over 65 is higher than in all other age groups, except for HIV-infected patients. The incidence of tuberculosis in nursing-home residents is three to four times higher than that of those living in the community.\(^9\) Comorbidities, immunosenescence, malnutrition, immunosuppressive therapy, and unfavourable socioeconomic conditions all contribute to the higher incidence of tuberculosis in this age group. In Switzerland, the incidence of tuberculosis in patients over 70 (20/105 inhabitants) is 2.5 times that of the general population.\(^8\) Mortality of tuberculosis is much higher than in younger age groups and increases with age.\(^9\)

Advanced age is associated with non-typical clinical presentations of mycobacterial infection,\(^9\)\(^-\)\(^12\) leading to delayed diagnosis and an increased rate of postmortem diagnosis.\(^9\)\(^-\)\(^14\) The differences in clinical presentation in the elderly include: decreased occurrence of cough, fever, haemoptysis, night sweats, and increased incidence of negative tuberculin reactions (32% vs 10% in younger patients). Radiologically, older patients have more frequent lower or middle lobe involvement, miliary tuberculosis, and non-typical presentations (solitary nodules, pseudo-masses, and infiltrates resembling bronchopneumonia),\(^9\) and a lower incidence of cavity lesions.\(^9\)\(^-\)\(^15\) Reluctance to use invasive diagnostic procedures such as bronchoscopy in the very old, and lower sensitivity of sputum examination and cultures contribute to a delay in diagnosis.\(^9\)

In summary, older patients are today the main reservoir of tuberculous infection in the indigenous population of industrialised countries, and clinicians should have a high index of suspicion for mycobacterial infection in the very old even in the presence of apparently non-typical clinical or radiological presentations (figure 4).

**Unusual pulmonary infections in the very old**

Several reports of unusual causes of pulmonary infection in the very old have been published. HIV infection in older patients has been increasingly reported, often discovered by opportunistic infections.\(^9\)\(^-\)\(^13\) Patients without any immunosuppression other than advanced age may also develop opportunistic pulmonary infections with agents such as *Nocardi a asteroidis*.\(^10\)\(^-\)\(^13\) Chronic necrotising pulmonary aspergillosis must be considered in older patients with slowly evolving pulmonary infiltrates, malnutrition, weight loss, immunosuppressive therapy, and pre-existing chronic pulmonary disorders.\(^10\)

Non-typical mycobacteria (mainly *Mycobacterium avium intracellulare* complex) may be responsible for a slowly evolving destructive pulmonary infection, which occurs more frequently in non-smoking women (80%) who present with a chronic cough (86%), fatigue (42%), prolonged fever (10–14%), progressive weight loss leading to cachexia (14–52%), and non-specific pulmonary infiltrates.\(^10\)\(^4\)\(^5\)

**When the pneumonia doesn’t get better**

In patients who are poorly responsive to adequate antibiotic treatment, alternative diagnoses should be considered. Unusual pathogens and mycobacterial infection must be rapidly ruled out, if possible by fibre-optic bronchoscopy. Non-infectious inflammatory or neoplastic disorders must be considered, such as cryptogenic organising pneumonia (previously referred to as idiopathic bronchiolitis obliterans organising pneumonia, or BOOP),\(^10\)\(^6\)\(^17\) vasculitis (Wegener’s granulomatosis),\(^10\)\(^8\) idiopathic acute eosinophilic pneumonia,\(^10\) chronic eosinophilic pneumonia, and bronchoalveolar carcinoma. Cavitary lesions suggestive of pulmonary abscess may in fact be excavated primary pulmonary tumours or vasculitis (Wegener’s granulomatosis).

**Diagnostic procedures**

**Radiology**

Although often difficult to perform in optimum conditions, plain chest radiographs are important for confirming the clinical suspicion of pneumonia, assessing extension of the disease, detecting potential complications such as caviation, parapneumonic effusion, or empyema, and documenting signs of pre-existing pulmonary disorders such as COPD, sequelae of tuberculosis, interstitial lung disease, bronchiectasis, or possible carcinoma. Computed tomography scan is helpful when seeking an underlying cause such as airway obstruction by a proximal tumour,
documenting location and extension of a pleural effusion, or when considering alternative diagnoses (see below).

**Laboratory data**

**Leucocyte count and inflammatory parameters**

Leucocytosis and increase in band forms develop less frequently in elderly patients and are thus less sensitive in the detection of pneumonia. Indeed, the elderly are often too weak to provide an adequate sputum specimen, or too confused to cooperate and the diagnostic yield of sputum analysis is relatively low (table 3). Blood cultures and test for urinary legionella antigen are unanimously recommended in elderly patients hospitalised for CAP or NHAP. PCR testing for *Chlamydia* spp, *M pneumoniae*, and common respiratory viruses are now available, but their clinical usefulness has not yet been established.

Recent studies suggest that a search for urinary *S pneumoniae* capsular antigen (common to all serotypes) may be useful in the diagnosis of pneumococcal pneumonia. For non-bacteraemic pneumonia, reported sensitivity ranges from 64–69%; and from 77–100% for bacteraemic pneumococcal pneumonia. Specificity of urinary *S pneumoniae* capsular antigen is 82–97%. Potential drawbacks of the method are its rather low sensitivity for non-bacteraemic pneumococcal pneumonia, and a high positivity rate 1 month after an acute pneumococcal infection.

**Blood gas analysis**

American Thoracic Society guidelines recommend that arterial blood gases (ABG) be obtained on admission in patients who are hospitalised with severe illness, or in any patient with chronic lung disease, not only for detection of hypoxaemia (for which pulse-oximetry is sufficient), but also for that of hypercapnia, which occurs at a much higher frequency in the very old because of a lesser functional reserve. This recommendation also pertains to HAP. A reasonable limit is to suggest measuring ABG when pulse-oximetry readings for pulse oximetry are below 94%. For patients who are not admitted to an ICU or intermediate-care unit, pulse oximetry is adequate for subsequent monitoring of oxygenation with CAP, NHAP, or HAP.

**Blood chemistry**

Hyponatraemia and elevations of hepatic enzymes (alanine aminotransferase and aspartate aminotransferase) are frequent, non-specific, and are not reported as adverse prognostic factors. Conversely, low serum albumine, and lymphopenia have been described as adverse prognostic factors.

**Microbiology**

Although there is no doubt that a causative diagnosis of pneumonia in the elderly is desirable, the question of whether sputum analysis should be done is controversial (recommended by the Infectious Diseases Society of America, but not by the American Thoracic Society). Indeed, the elderly are often too weak to provide an adequate sputum specimen, or too confused to cooperate and the diagnostic yield of sputum analysis is relatively low (table 3). Moreover, the elderly are often too weak to provide a good-quality sputum sample, or too confused to cooperate and the diagnostic yield of sputum analysis is relatively low (table 3).

**Serological studies**

Serological studies are not recommended initially on a routine basis in available guidelines but may be contributive either in poorly responsive patients, for retrospective confirmation of a suspected diagnosis, or in epidemiological studies.

**Treatment of pulmonary infections of the very old**

Recent guidelines for treatment CAP and HAP are available and will not be covered in detail in this article. We will, however, briefly discuss some questions that specifically concern pneumonia in the elderly.

**Should CAP or NHAP in patients over 65 years be systematically treated with a combination of β-lactam and macrolide?**

In patients aged over 65, British and US guidelines recommend as first-line treatment either the combination of a β-lactam plus a macrolide (or doxycycline), or an “antipneumococcal fluoroquinolone” (orally for outpatients, intravenously for hospitalised patients). A large retrospective study of 12 943 Medicare patients aged over 65 and hospitalised for CAP, showed that patients initially
treated with either a combination of a macrolide with a second-generation cephalosporin or a non-pseudomonal third-generation cephalosporin, or with a fluoroquinolone alone, had lower 30-day mortality than patients treated with a non-pseudomonal third-generation cephalosporin alone (26–36% reduction).120

In spite of these guidelines, such a policy has not been implemented in our institution since we feel that this will lead to an overuse of antibiotics without proven benefit. In general, we initiate a β-lactam treatment and test for legionella urinary antigen. Macrolide treatment is only initiated if the pneumonia is clinically severe, the patient presents defined risk factors for legionella (see above), legionella-antigen test is positive, or the pneumonia responds poorly to β-lactam treatment after 48–72 h.

**Should NHAP be treated as a CAP or HAP?**

Older patients with NHAP are more likely to suffer from dementia or cerebrovascular disease, to present with delirium and malnutrition, to have a lower functional status, or to be bedridden when compared with older patients with CAP.21,22,24,28 Furthermore, comorbidity, delirium, and impaired functional status have all been associated with a higher mortality in the elderly. Indeed, in recent studies of older patients with NHAP and CAP, patients with NHAP have more severe scores by either the British Thoracic Society prediction rule or the PSI,18,19 and accordingly mortality remains higher for NHAP (17·6% vs 10·3% in the largest published study).21

The number of pneumonias due to Gram-negative bacteria as recently reported is not as high as in previous studies: Lim et al27 found no Gram-negative bacteria in 40 patients with NHAP; only two of 71 patients with NHAP had Gram-negative bacteria identified in a study by Marrie et al;61 Kaplan et al19 report a similar rate of Gram-negative bacteria infection in NHAP (10·1%) and CAP (9·6%). Patients admitted from nursing homes are at a higher risk of upper airway colonisation by Gram-negative bacteria because of their impaired functional status, which possibly explains a high rate of Gram-negative bacteria identified in sputum samples in previous studies, and an overestimation of the role of Gram-negative bacteria as pathogens in NHAP. Conversely, *C pneumoniae* has been reported in 18% of NHAP patients.27 *S pneumoniae* remains by far the most frequent microorganism identified (table 2). One study reported a high rate of MSSA and MRSA infection in severe NHAP.27 In summary, functional status, and comorbidities are more relevant than admission from a nursing home in the management of pneumonia. MSSA and MRSA should be considered as possible pathogens in NHAP. Bedridden patients with impaired functional status, and patients at high risk for aspiration should receive adequate antibiotic coverage for Gram-negative bacteria (eg, third generation or antipseudomonal cephalosporin).

**Vaccination for prevention of pneumonia in the very old**

Vaccination of the elderly is generally less accepted than vaccination of children and is consequently underused. In a Spanish study, only 7% of 305 patients aged over 80 and admitted for CAP had received a pneumococcal vaccine in the preceding 5 years.23 A survey among Italian physicians showed that most recommend influenza vaccine (95·2%), but only 47% recommend pneumococcal vaccine (46·9%).23 Thus, there is also a difference in perception of different vaccines for the elderly.

The efficacy of vaccination is decreased in the elderly population.19,122,123 However, it is this part of the population that is most likely to benefit from vaccination. To make this point clear, let us take a population where a vaccination has 100% efficacy, but the disease has a yearly incidence of only 1%. There will be one case of the disease prevented in 100 vaccinations. In a population where the vaccination has a 50% efficacy, but the disease has a yearly incidence of 10%, there will be five cases of the disease prevented in 100 vaccinations. Thus, vaccination in a poorly responding group may be useful if the incidence of the disease is high.

**S pneumoniae** vaccination

Despite appropriate antibiotic therapy and intensive care treatment, there is a considerable case-fatality rate in pneumococcal pneumonia, with the highest rates among the elderly. Thus, prevention through vaccination is an obvious approach. Yet clinical data concerning this issue are limited to such a point that a recent editorial talks about an “embarrassing paucity of data.”124 Basically, our present knowledge on currently available vaccines can be summarised as follows: there is a decreased antibody response to vaccination in the elderly;122,123 the antibody response predicts at least partly the clinically observed protection;123,124 the vaccine prevents invasive (bacteraemic) pneumococcal disease;125,126 the data concerning effect of vaccination on incidence of or death from non-bacteraemic pneumonia in the elderly is contradictory;123,125,126,127 and the best data comes from a study on combined pneumococcal and influenza vaccination: 259 627 individuals were prospectively studied: 39% received influenza and pneumococcal vaccine. Vaccination significantly reduced the incidence of hospitalisation for influenza (–46%), pneumonia in general (–29%), pneumococcal pneumonia (–36%), and invasive pneumococcal disease (–52%), as well as total mortality (–57%).125,127 Importantly, this vaccination protocol was as efficient in those aged over 85 years as it was in the total study group.127

**Influenza vaccination**

Influenza and its complications cause 10 000–40 000 deaths annually in the USA, of which 80% occur among the elderly.131 Although pulmonary infection is not the main presentation of influenza, it is strongly associated with mortality from influenza, either because of viral pneumonia or because of bacterial superinfection.152 Several large studies in community-dwelling elderly people clearly indicate that influenza vaccine is safe and effective, and associated with a significant reduction in morbidity and mortality, including a decrease in pneumonia.153,155–157 Influenza vaccine is also effective in institutionalised elderly
patients, with a significant effect on death rates, and hospital admission rates for respiratory infection.\textsuperscript{136,137} Tolerance to influenza vaccine in the elderly is very good.\textsuperscript{138} Vaccination of health-care workers in nursing homes and hospitals is associated with a substantial decrease in mortality among patients.\textsuperscript{139}

**Recommendations for vaccination in the very old**

At this stage, recommendations cannot be strictly evidence-based. But based on available data, and recommendations by others,\textsuperscript{140} we think that the following approach is reasonable: individuals over 65 years should receive both influenza and pneumococcal vaccine; there is no upper age limit for vaccination; influenza vaccine should be given annually; and pneumococcal vaccine should be given every 5–10 years.

**Pneumonia and end-of-life care in the geriatric setting**

In this section we will use the term “end-of-life pneumonia” to summarise three clinical situations—namely pneumonia in severely demented patients, in terminally ill patients, and in dying patients.

**Does antibiotic treatment affect mortality of end-of-life pneumonia?**

Whether antibiotic treatment of end-of-life pneumonia really affects survival is unclear. In observational studies increased mortality is reported when antibiotic treatment is withheld.\textsuperscript{141–143} However, these studies also show that patients with mild disease and a more favourable prognosis are more likely to receive antibiotic treatment than those with more advanced disease.\textsuperscript{141–143} Thus, patient selection also determines the outcome. To our knowledge there is only one prospective study that addresses this issue.\textsuperscript{144} The authors saw no increase in survival when patients with advanced Alzheimer’s disease were treated with antibiotics, as compared with palliative care only. Importantly, at least two studies show that the severity of dementia critically establishes the outcome of pneumonia.\textsuperscript{145,146} Thus, survival is probably not prolonged by antibiotic treatment of end-of-life pneumonia.

**End-of-life pneumonia and suffering**

Only one study directly addresses the question of pneumonia-related suffering.\textsuperscript{147} Results suggest an increased rate of discomfort in patients in whom antibiotic treatment was withheld. However, these patients also had a higher rate of discomfort before the pneumonia (figure 5). Thus, there was a selection bias towards treating patients with less severe disease and the study therefore does not allow one to conclude that antibiotic treatment is superior to palliation in the end-of-life setting. It does, however, show that the rate of discomfort is higher in patients dying from pneumonia than in patients dying from other causes.\textsuperscript{148}

Death from pneumonia is associated with severe suffering, but presently we do not know whether antibiotics are superior to symptomatic treatment alone for the relief of this suffering.

\textbf{Pneumonia in the very old and admission to the ICU}

Very old patients with CAP are now commonly admitted to the ICU. A recent study from the USA suggests that the fraction of CAP patients admitted to the ICU (and/or subjected to invasive ventilation) is around 20–25% for the 80–89 year age group, and around 15% for those aged over 90.\textsuperscript{139} Mortality approximates 25% for the 80–89 year old, and is close to 30% for those aged over 90.\textsuperscript{139} There is evidence suggesting that quality of life of the very old surviving after treatment in the ICU is comparable to what is seen in younger patients.\textsuperscript{147} Thus, based on currently available evidence, age alone should not be used as a criteria to withhold ICU treatment. However, in our opinion, the decision to admit very old patients with pneumonia to the ICU should be taken very cautiously. Patients with pneumonia and terminal disease certainly should not be admitted. Similarly, generally speaking, patients with significant comorbidities should not be admitted since their likelihood to survive ICU treatment is low.\textsuperscript{147} In very old CAP patients without significant comorbidities, ICU admission may be considered, but only after careful consideration of all aspects, in particular the patient’s autonomy (see below).

**Ethical framework**

Management of end-of-life pneumonia should take into account the four basic principles of bioethics: autonomy, beneficence, non-maleficence, and justice, as described by Beauchamp and Childress and Marcus et al.\textsuperscript{149,150}

**Autonomy**

Autonomy is most difficult to achieve in the terminally ill geriatric patient. Indeed, in the terminally ill geriatric patient with pneumonia, the frequency of dementia and delirium is high. Thus, a substantial portion of patients cannot...
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understand the implication of a decision in favour of or against treatment. A theoretically attractive option is that of advanced directives (also referred to as “living will” or “advance care planning”), issued by the patient at a time when they are still fully mentally aware.\textsuperscript{151,152} Several studies show that the opinion of elderly people concerning end-of-life issues is stable over time.\textsuperscript{153–155} Yet there are several limitations to the use of advance directives.\textsuperscript{151} Thus, in a substantial portion of geriatric patients doctors have to extrapolate the patient’s wishes from indirect information such as discussions with close relatives of the patient; and knowledge about faith and life philosophy of the patient. A recent survey from France suggests that most individuals (90%) would prefer to designate a surrogate (most often the spouse or another family member) authorised to give consent and to participate in medical decisions if the individual were too sick to do so.\textsuperscript{156}

Benefits
In end-of-life pneumonia, life prolongation is not necessarily “benefit”. For most patients, the beneficence of treatment of pneumonia in end-of-life care lies rather in an adequate relief of symptoms. As previously mentioned, abundant bronchial secretions, dyspnoea, or a feeling of suffocation due to pneumonia may lead to substantial suffering for the patient.\textsuperscript{14} Should relief of symptoms rely on antibiotics, or symptomatic means alone (ie, opioids, oxygen, inhibitors of bronchial secretion, aspiration of bronchial secretions)? Since there is no conclusive answer to this question, the non-maleficence principle (see below) becomes crucial.

Non-maleficence
To establish non-maleficence, one should consider very carefully whether antibiotic treatment is really necessary to decrease suffering. Whenever possible, oral antibiotics (ie, a combination of co-trimoxazole and rifampicin rather than vancomycin for MRSA) should be prescribed. If oral antibiotics are not possible, one should consider antibiotics that can be given as a bolus intravenous injection (intramuscular or subcutaneous antibiotic treatment may be considered, but may also cause substantial discomfort). Avoid potentially toxic antibiotics that require therapeutic monitoring (ie, aminoglycosides) and monitor patients carefully for side-effects such as skin rashes, which can increase discomfort.

Intravenous lines frequently cause, in addition to infections, local irritations and after 10 days around half of the patients suffer from phlebitis.\textsuperscript{157} Many of the very old patients under end-of-life care may not be able to communicate the pain caused by phlebitis. It is therefore mandatory that peripheral intravenous lines be inspected daily and immediately removed if there are any signs suggesting phlebitis. Insertion of intravenous lines through specialised “intravenous therapy teams” reduces complications.\textsuperscript{158}

Bronchial and tracheal secretions (“death rattle”) are often a source of discomfort and dyspnoea for the patient in terminal care. Cough is ineffective in clearing secretions in these patients. Cooperation for conventional chest therapy may not be possible. In spite of the use of muscarinic anticholinergics (scopolamine), repeated tracheal aspirations may in some cases be necessary to avoid suffocation and clear the airways, but are themselves uncomfortable and painful if not done with expertise. The effect of antibiotics on production of bronchial secretions in this setting is not clearly established, but may contribute to symptom relief in terminal care. Use of non-invasive techniques (mechanical insufflation-exsufflation via a facial mask) that have been shown to be effective in patients with severe neuromuscular diseases is an interesting option if they can decrease the discomfort related to tracheal aspirations, and have been effective in selected cases in our institution.\textsuperscript{159,160}

Justice
The topic of distributive justice in end-of-life care of a very old patient is a very difficult issue. Do we have the right to consider costs of antibiotic treatment when a terminally ill geriatric patient develops pneumonia? Do we have the right to consider development of antibiotic resistance in this situation? Do we have the right to limit access of terminally ill geriatric patients to the ICU?

Our answer to this question is yes, but with many caveats. Patient age alone cannot, and must not, be a criteria. It is rather the remaining life expectancy and the likelihood of beneficence that should guide our decision. Considerations concerning distributive justice must be carefully integrated with the other elements of the ethical discussion.

Conclusions
Pneumonia in the very old is a challenge for clinicians, because of non-typical symptoms, lower functional reserve, and a high mortality rate. Reluctance to use invasive techniques such as bronchoscopy with BAL should be overcome to improve therapeutic efficacy and identify unusual pathogens or non-infectious disorders. Combined teams of geriatricians together with infectious diseases, and/or pulmonary specialists are likely to improve the quality of care in this situation. Specificities of geriatric infections should be increasingly integrated into the training curriculum of young doctors. More clinical and fundamental research is needed in this specialty to provide answers to the many questions raised in this review.

Conflicts of interest
We have no conflicts of interest regarding this review, for which no funding was received.

Search strategy and selection criteria
Data for this review were identified by searches of Medline, and references from relevant articles. Numerous articles were identified through searches of the extensive files of the authors. English and French language papers from the past 15 years were reviewed. Search terms (using limit: aged over 80) included: “pneumonia, aspiration”, “pneumonia, epidemiology”, “pneumonia, microbiology”, “pneumonia, etiology”, “pneumonia, mortality”, “pneumonia, prevention”, “pneumonia, therapy”, “influenza vaccination”, “pneumococcal vaccination”, and “pneumonia, dementia”.

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