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Bacterial Pneumonia in Older Adults

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KEYWORDS

- Pneumonia Older adults Long-term care facility Multidrug-resistant organisms
- Empiric treatment

KEY POINTS

- The incidence of pneumonia increases with age, and is particularly high in patients who reside in long-term care facilities (LTCFs).
- Despite diagnostic and therapeutic advances, mortality rates for pneumonia in the elderly are high and have not decreased in the last decade.
- Atypical symptoms such as confusion, general clinical deterioration, new onset of recurrent falls, and exacerbation of underlying illness should trigger clinical suspicion and evaluation for pneumonia.
- Decisions regarding the site of care for older adults with pneumonia should take into account scoring systems of pneumonia severity, patient wishes regarding intensity of care, supportive environment, and clinical judgment.
- Empiric treatment of pneumonia should be based on clinical assessment of illness severity and risk factors for multidrug-resistant organisms, which are more common in older adults and LTCF residents.

OVERVIEW AND EPIDEMIOLOGY

Pneumonia is a serious infection that occurs when a pathogen's virulence overcomes a person's host defenses. Aging is associated with general deterioration of organ function in a way that dictates not only an individual's risk of developing pneumonia, but also clinical manifestations and outcomes. In addition to increased complexity of clinical presentation and more rapid progression of disease, older patients are at higher risk to have pneumonia owing to resistant organisms including Gramnegative bacilli, and therefore empiric as well as definitive treatment can be challenging. The incidence of pneumonia increases with age, as does the impact of pneumonia on morbidity and mortality.

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Infect Dis Clin N Am 31 (2017) 689–713 http://dx.doi.org/10.1016/j.idc.2017.07.015 0891-5520/17/© 2017 Elsevier Inc. All rights reserved.

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In the 19th century, before the antimicrobial era, pneumonia was described by Sir William Osler as a fatal disease in older adults. Mortality rates are still high, particularly in elderly patients. Pneumonia, together with influenza, is the eighth leading cause of death in the United States and accounts for 2.3% of all death cases in patients older than 65 years.¹

Risk factors for pneumonia among older adults include underlying comorbid conditions, such as cardiovascular and lung disease, diabetes mellitus, and malignancy, all of which are more prevalent in advanced age. Male gender and smoking have been identified as independent risk factors for community-acquired pneumonia (CAP) in older adults,^{2–4} as has reduced functional capacity, and residence in an institution (long-term care facility [LTCF] or nursing home).^{5–7}

Polypharmacy is a common finding in older patients, and several drugs are associated with higher risk of pneumonia, including antipsychotic and anticholinergic drugs, both used to treat symptoms that are more common in elderly patients. These drugs are used to treat dementia symptoms, urinary incontinence, depression, pain, and insomnia.⁸ Some of the anticholinergic side effects include sedation and altered mental status, which increase the risk of pneumonia, and can also be symptoms of pneumonia.⁹ In addition, inhaled corticosteroids have been associated with recurrent pneumonia.¹⁰

The burden of pneumonia on health care resources is enormous owing to both hospitalization costs and long-term outcomes, particularly in elderly patients.¹¹ With the anticipated growth of the population of older adults, the burden of pneumonia, both community acquired and health care associated, is anticipated to increase.^{11,12}

PATHOGENESIS: WHAT MAKES ELDERLY PATIENTS PRONE TO DEVELOPING PNEUMONIA?

In general, regardless of age, pneumonia occurs when an organism's ability to penetrate and infect the lung parenchyma overcomes the host's defense mechanisms.⁶ Several factors common in the elderly contribute to breaches in their defense systems, making elderly patients not only more vulnerable to infection, but also more vulnerable to severe infection associated with prolonged recovery and poor outcomes.

Structural and functional changes across the respiratory system lead to reduced host defenses. These factors include (1) impaired function of mucociliary clearance, an important defense mechanism against pathogen entrance to the upper airways and respiratory tree. Slower and less efficient clearance of secretions by the mucociliary system in the elderly has been shown to correlate with pneumonia.¹³ (2) Chest wall mobility and compliance decrease with aging owing to costovertebral joint alteration, rib cartilage calcification, loss of muscle strength, and changes in the shape of rib cage such as kyphosis or scoliosis. (3) Lung compliance is reduced owing to changes in lung parenchyma, which affect the lung's elastic recoil.⁶ These alterations in the chest wall and lung compliance lead to increased air trapping, reduced ability to clear secretions, and an increase in the workload of respiratory muscles. In older age, a further increase in the work of breathing, as occurs in cases of pneumonia and particularly in the presence of underlying diseases such as cardiovascular and lung diseases, compromise functionality during infection and may lead to respiratory failure.¹⁴

Neurologic changes predisposing older adults to "silent aspiration" include reduced ability to cough owing to gag reflex dysfunction as well as changes in mental status.¹⁵ In one study, oropharyngeal dysphagia was strongly associated with CAP in the elderly (occurring in 91% of patients with CAP; odds ratio, 16.3; 95% Cl, 4.6–58.2).¹⁶ In addition, pneumonia has been estimated to occur in about 10% to 30% of patients after a

stroke.^{17,18} In a study that followed patients older than 65 years with infarcts, patients with bilateral basal ganglia infarcts had the highest incidence of pneumonia compared with those with no infarct or less extensive lesions.¹⁹ The response to infection is altered in the elderly owing to lower sensitivity of the respiratory centers to hypoxia and hypercapnia. Altered mentation and absence of cough or appropriate ventilator response also modify clinical presentation in the elderly, delay diagnosis and treatment, and consequently impact clinical outcomes.^{20,21} The increased frequency of respiratory tract colonization in older adults^{22–24} leads to an increased likelihood of chemical aspiration developing into aspiration pneumonia.²⁵

The alterations in the immune system that occur with aging are not well-defined. Several animal and human observations have demonstrated immune dysregulation in both innate and adaptive immune components.²⁶ However, some studies demonstrate prolonged low-grade inflammation, and some levels of proinflammatory cyto-kines are higher in patients older than 70 years compared with patients younger than 60 years.^{27–29} Some authors propose that low-grade inflammation, called "inflammaging" may contribute to blunted immune response to respiratory tract infection.^{21,30} Further research is needed to understand the magnitude and the role of alterations in the immune system associated with pneumonia in elderly patients.

Comorbid conditions also contribute to increased risk. Most elderly persons with pneumonia have 1 or more comorbid conditions.³¹ Fry and colleagues⁵ compared 2 cohorts of patients who were hospitalized with CAP and showed that the proportion of patients with 1 or more comorbid conditions increased with age, as well as during the study period (77% in the group of 2000–2002 vs 66% in the group of 1988–1990).

DIFFERENT EPIDEMIOLOGIC CATEGORIES OF PNEUMONIA IN OLDER ADULTS

Pneumonia has traditionally been epidemiologically categorized by the site of onset, for example, CAP, nursing home–acquired pneumonia, and hospital-acquired pneumonia. CAP is defined as pneumonia that occurs in patients who are not hospitalized or who are admitted to the hospital for less than 48 hours.³² Within the spectrum CAP, patients can be categorized to patients who are at risk of acquiring CAP owing to multidrug-resistant organisms (CAP-MDRO), and patients without risk factors of MDROs.

In the 2005 guidelines for hospital-acquired pneumonia the term health care–associated pneumonia (HCAP) was introduced to identify patients who develop pneumonia outside of the hospital but owing to health care exposures were at increased risk for MDRO pathogens. The criteria for HCAP included patients who were hospitalized in an acute care hospital for 2 or more days within the 90 days before infection; had recently resided in a nursing home or a LTCF; had received recent intravenous antibiotic therapy, chemotherapy, or wound care within the 30 days before the current infection; or had recently attended a hospital or hemodialysis clinics.³³

Owing to concerns regarding how effective HCAP was in identifying patients with MDRO pneumonia and concerns that the guidelines in some instances promoted unnecessary broad-spectrum antimicrobial use for HCAP patients,³⁴ recently published 2016 hospital-acquired pneumonia guidelines did not include the category HCAP.³⁵ This issue is pertinent to this article, because between 2005 and 2016, pneumonia acquired in a LTCF was considered to be HCAP, but now would be categorized as CAP, and in many instances CAP with risk factors for MDRO pathogens.

In the current review, we categorize CAP in the unique population of elderly persons into 3 subgroups: CAP in elderly patients who are not at risk for acquiring pneumonia owing to MDRO (referred to as CAP), CAP in elderly patients who are at risk for acquiring pneumonia owing to MDRO (referred to as CAP-MDRO), and CAP among LTCF residents (Fig. 1).^{36,37} Many, but not all persons who fit into the CAP among LTCF residents category also fit into the CAP owing to MDRO category (see Fig. 1). This article does not discuss pneumonia occurring in persons who are ventilator dependent or have hospital-acquired pneumonia.

EPIDEMIOLOGY

CAP is a relatively common infection in older adults, accounting for more than 30% to 40% of the hospitalizations in this age group, and is associated with an increased risk of morbidity and mortality.^{10,38}

In a prospective study that included more than 25,000 men in the United States, the risk of CAP in patients older than 65 years was 4.17 times higher than in patients younger than 45 years of age.³⁹ In another surveillance study in 4 European countries, the incidence of CAP in 2009 was 10.8-fold higher in those aged greater than 85 years compared with adults aged 50 to 64 years.⁴⁰ The incidence of CAP ranges from 8 to 18.2 episodes per 1000 persons who were older than 65 years and remained stable across various studies from different geographic areas between 1981 and 2011.^{2,41–43}

In general, approximately 30% of the patients with CAP (of all ages) require admission to the hospital.⁴⁴ Elderly patients' hospitalization rates are much higher. In the Patient Outcomes Research Team (PORT) study in 1991, of 693 patients with CAP who were older than 65 years, more than 80% of patients were treated as inpatients.⁴⁵ In a large prospective US study (Etiology of Pneumonia in the Community [EPIC]) from 2010 to 2012, the annual incidence of hospitalization for CAP was 24.8 cases per 10,000 adults and increased with age: patients in the age group of 65 to 79 years, and those in the age group of 80 years and older had 9 and 25 times higher incidences of hospitalization, respectively, compared with patients between 18 to 40 years of age.⁴⁶

Fry and colleagues⁵ analyzed data from the National Hospital Discharge Survey (NHDS) to explore the factors that contribute to increased rates of hospitalization among elderly persons with pneumonia from 1988 to 2002. Of 173 million hospitalizations, 9.1% had a pneumonia discharge diagnosis. The rate of hospitalization among patients older than 85 years was 2 to 4 times than the younger groups (65–74, 75–84 years). Underlying diseases (cardiovascular disease, chronic lung disease, and diabetes mellitus) were associated with high rates of hospitalization in this study.

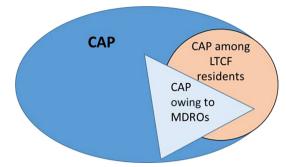


Fig. 1. Distribution of community-acquired pneumonia (CAP) and subsets of CAP, including CAP among long-term care facility residents (LTCF), and CAP owing to multidrug-resistant organisms (MDROs).

Pneumonia Among Lon-term Care Facility Residents

Nursing home–acquired pneumonia constitutes the largest proportion of CAP among LTCF patients.³⁷ In 2014 in the United States, about 1.4 million people were cared for in nursing homes and more than 90% were older than 65 years.^{47,48}

The incidence of pneumonia among residents of LTCFs is higher than among elderly persons who live at home. The median reported annual incidence of pneumonia among LTCF residents is 365 cases per 1000 persons (range, 99–912),⁴⁹ approximately 11 times the incidence reported among patients from the community older than 75 years of age (34 per 1000 persons).^{41,50}

Pneumonia is the most common infectious reason for transfer of a person from the nursing home residence to the hospital, accounting for 21.6% of admissions.⁴⁹ Marrie⁵¹ reported a hospitalization rate among nursing home residents with pneumonia that was nearly 30 times higher than that among elderly patients living at home with CAP (33:1000 persons vs 1.14:1000 persons).

Patients who acquire pneumonia in an LTCF often have multiple comorbid diseases (eg, cardiovascular, respiratory, and neurologic) and poor functional status. In addition, risk factors for aspiration among LTCF residents (eg, nasogastric feeding, difficulty swallowing, receiving sedative agents, and poor functional status) increase risk for the development of pneumonia.^{52–54}

MICROBIOLOGY

In general, despite technological diagnostic improvements, the causative pathogen is not identified in nearly one-half of pneumonia episodes across all ages,^{32,55} and in up to 77% of pneumonia episodes that occur in elderly patients.⁵⁶ Cough reflex dysfunction and altered mentation often preclude the availability of sputum, and only 30% to 40% of patients are able to provide sputum for analysis.^{6,44} In addition, elderly patients tend to receive antibiotic treatment before attempts at diagnostic procedures, particularly in persons residing in LTCFs.⁵⁷

Common Causes of Pneumonia Among Elderly Patients in the Community, Including Long-term Care Facilities

Streptococcus pneumoniae is by far the most common pathogen detected in CAP, and accounts for 20% to 85% of cases in the elderly. *Haemophilus influenza* is the second most common detected pathogen (2.9%–29.4%),^{6,56,58} followed by respiratory viruses, in particular influenza, coronavirus, and rhinovirus (**Table 1**).^{46,56}

Legionella is detected in 1.0% to 17.5%⁵⁷⁻⁵⁹ of cases and in some studies is considered to be the second or third commonest cause of pneumonia in the elderly, particularly in cases of severe CAP.⁶⁰ Other atypical organisms (including *Mycoplasma pneumoniae* and *Chlamydia* spp) are infrequently identified in adults aged over 65 years.^{6,42}

Coinfection with bacterial and viral pathogens has been reported in 3% to 40% of cases of CAP,^{4,44} and detection of coinfection has increased with the use of improved diagnostic tests. Bacterial coinfection complicates approximately 2.5% of influenza cases in older patients and those with comorbid conditions. In the 2009 H1N1 pandemic, bacterial coinfection complicated 18% to 34% of intensive care unit (ICU) cases, and more than one-half of the fatal cases.⁶¹

In 6 studies that evaluated pneumonia among LTCF residents, *S pneumoniae* (12.9%) was identified as the most common cause of pneumonia, followed by *H influenza* (6.4%), *Staphylococcus aureus* (6.4%), and *Moraxella catarrhalis* (4.4%). Enteric Gram-negative bacteria accounted for 4.2% to 14.3% of cases.⁵¹ The role of atypical

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Table 1

Epidemiology of bacterial pathogens causing CAP among elderly patients and residents of LTCF, and risk factors for each organism

	CAP in the Elderly (Range of Prevalence), % ^{36,49,56–58,60,66,81,105,138}	CAP Among LTCF Residents (Range of Prevalence), % ^{45,55,99,133,139}	Risk Factors for Pneumonia Owing to Each Organism ^{65,71,72,75,77,119,140}
Streptococcus pneumonia	20-85	9–55	Risk for pneumonia owing to nonsusceptible <i>S pneumoniae</i> ^a Use of β-lactam, fluoroquinolones or macrolides within the past 90 d COPD Probable expiration
			Probable aspiration Previous episode of pneumonia within the past 12 mo
Staphylococcus aureus	0–7	0–33	Risk for pneumonia owing to MRSA: Hospitalization for ≥2 d within the past 90 d Use of antibiotics within the past 90 d LTCF residence Chronic dialysis during the preceding 30 d Exposure to previous intravenous treatment within the past 30 d Positive MRSA history within the past 90 d Comorbidities: congestive heart failure, diabetes mellitus, dementia, cerebrovascular disease Severe illness at presentation: altered mental status, bilateral or cavitary disease Use of gastric acid suppressive agents
Haemophilus influenza	2.9–29.4	2–22	Risk for pneumonia owing to resistant <i>H influenza^b</i> Use of prior antibiotic within the past 90 d
Legionella	1–17.5	0–6	N/A

Enteric GNB	0–12	4.2-14.3	Risk for pneumonia owing to enteric GNB: LTCF residence Nonambulatory status Probable aspiration Tube feedings Comorbid conditions: pulmonary disease, heart failure, cerebrovascular diseases, dementia Use of gastric acid suppression agents
Pseudomonas aeruginosa	2–17.1	0–6	Risk for pneumonia owing to <i>P aeruginosa</i> Hospitalization for ≥2 d within the past 90 d Use of antibiotics within the previous 90 d Probable aspiration Impaired swallowing Use of gastric acid suppression agents Prior history of severe structural lung disease, either severe COPD or bronchiectasis Prior respiratory culture positive for <i>P aeruginosa</i> within the past 12 mo Severe illness on admission (need for ICU admission or ventilator assistance)
Atypical pathogens: Chlamydia spp, Mycoplasma pneumonia	1–32	0–19	N/A

Abbreviations: CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; GNB, Gram-negative bacilli; ICU, intensive care unit; LTCF, long term care facilities; MRSA, methicillin-resistant S aureus; N/A, not applicable.

^a Nonsusceptible *S pneumoniae* includes resistance to one or more of the following classes of antibiotics: penicillins, cephalosporins, macrolides, and fluoroquinolones.

^b Resistant *H* influenza includes resistance to penicillin, typically owing to β -lactamase production.

pathogens (Chlamydia spp, M pneumoniae, Legionella) as a cause of pneumonia among LTCF patients is less defined. 62

Pneumonia Owing to less Common Pathogens, Including Multidrug-resistant Pathogens, Among Older Adults in the Community and in Long-term Care Facilities

Gram-negative bacilli

Gram-negative bacilli are detected in 2.8% to 14.0% of CAP cases, and may colonize the respiratory tract of elderly patients with oropharyngeal dysphagia,⁶³ particularly those admitted to the hospital from LTCFs.^{50,58} Among LTCF patients with severe aspiration pneumonia, enteric Gram-negative bacilli were detected as the predominant cause in 49% of cases.⁶⁴

In the Competence Network for Community-Acquired Pneumonia (CAPNETZ) study, predictors of CAP owing to *Enterobacteriaceae* included age greater than 65 years, heart failure and cerebrovascular disease.⁶⁵ *Pseudomonas aeruginosa* was reported in 2.0% to 17.1% of patients, and was associated with impaired swallowing, chronic obstructive pulmonary disease, bronchiectasis, severe disease, admission from nursing homes, and presence of a feeding tube.^{36,60,63,65,66} Although there are no data that support empiric anti-*Pseudomonas* treatment in elderly patients, this pathogen should be considered in severe infection in the presence of structural lung disease and known prior colonization.

Resistant Streptococcus pneumoniae

The introduction of pneumococcal conjugated vaccine PCV7 in 2000 (PCV7) and then PCV13 (2010) was followed by a 45% decrease nonsusceptible invasive pneumococcal disease (IPD) in elderly patients.⁶⁷ Data from the Centers for Disease Control and Prevention's active bacterial core surveillance demonstrated a large decrease in the multidrug–nonsusceptible IPD (*S pneumoniae* nonsusceptible to \geq 3 antimicrobial classes), from 4.2 to 1.8 cases per 100,000 adults older than 65 years. Among cases of nonsusceptible IPD, the frequency of nonsusceptibility patterns of *S pneumoniae* strains was as follows: 86.6% nonsusceptible to macrolides, 47.7% to cephalosporins, 43.6% to tetracycline, and 32.1% to penicillin. No fluoroquinolone or glycopeptide resistance was found.⁶⁸ These patterns of resistance should be considered when treating IPD in the post–PCV-13 era.

Staphylococcus aureus including methicillin-resistant Staphylococcus aureus

S aureus has been identified in 1% to 25.5% of CAP cases.^{36,46,60,66,69,70} The AWARE study, a surveillance study that evaluated more than 2000 samples of hospitalized patients from 65 medical centers in the United States, including respiratory tract samples, demonstrated that among patients older than 65 years, 52.6% of *S aureus* were methicillin-resistant *Staphylococcus aureus* (MRSA), and the resistance rates to erythromycin, clindamycin, and levofloxacin were substantially higher in this age group as well.⁷¹ Shorr and colleagues⁷² assessed risk factors for MRSA among patients hospitalized with CAP (cultures were taken within 48 hours of admission). MRSA was the second most common pathogen in the cohort (14%) after *S pneumoniae* (17.5%). In this study, age greater than 79 years was identified as a predictor of MRSA, as were prior health care exposure, severe illness, and comorbidities (dementia, cerebrovascular, and, for females, diabetes mellitus).

Community-acquired MRSA was first described in 1999 in the United States and became a significant pathogen by 2005.⁷³ Community-acquired MRSA pneumonia is a recognized complication of influenza and typically presents as a severe disease. Although MRSA is an important cause of pneumonia in elderly, particularly among

LTCF residents, community-acquired MRSA has not been reported to be a significant cause of pneumonia in elderly patients.⁷⁴

Risk factors for community-acquired pneumonia owing to multidrug-resistant organisms

Several scores were developed in the past decade to evaluate patients who are at risk for CAP owing to MDROs. Table 1 shows risk factors associated with CAP owing to MDRO.^{72,75,76} No consensus exists as to which is the most reliable combination of risk factors predicting the likelihood of patients hospitalized for CAP owing to MDROs. Brito and Niederman⁷⁷ reviewed several studies that evaluated patients with HCAP and proposed an algorithm that combined severity of illness and number of risk factors. In general, most of the studies included patients who were recently hospitalized, or arrived from LTCFs with severe CAP (ie, were admitted to the ICU). The most common resistant pathogens described in these studies were MRSA and P aeruginosa, as well as other gram-negative bacilli. Risk factors included in this algorithm were recent antibiotic therapy in the past 6 months, recent hospitalization in the past 3 months, the presence of immune suppression, and poor functional status as defined by inability to perform activities of daily living.⁷⁷ According to the authors, patients with severe CAP and 1 risk factor should receive empiric broad spectrum antibiotic treatment, whereas patients who have nonsevere CAP needed to have 2 or more risk factors before broad spectrum therapy would be indicated. This algorithm might be useful as a supplement to clinical judgment when managing patients with pneumonia.

CLINICAL PRESENTATION AND DIAGNOSIS

Pneumonia in elderly patients was described by William Osler as a painless and fatal disease. The disease was described as latent, without chills, with mild cough, and sometimes without sputum. Physical examination was marked owing to the lack of classic evidence of consolidation, and mental status changes might be the only signs of pneumonia.²⁵

Not much has changed in our knowledge regarding pneumonia manifestations in the elderly. Fever may be absent in 25% to 55% of pneumonia cases in older adults,^{20,25,78} and a similar proportion of elderly patients present with altered mental status.⁵⁷ Of 48 patients older than 65 years in a veteran's administration medical center who were diagnosed with pneumonia based on new pulmonary infiltrates and symptoms, only 35% presented with fever and cough. The absence of classic symptoms was more common in patients with reduced baseline functional capacity.⁷⁹ A study that evaluated 1812 patients from 4 US hospitals demonstrated that, as patients became older, the number of reported symptoms of pneumonia decreased.²⁰

Among patients who reside in LTCFs, pneumonia-related signs and symptoms were demonstrated to be subtler than in CAP patients from the same age group.⁸⁰ As many as 73% of these LTCF cases present with confusion. Fever and respiratory symptoms were less common than in other CAP patients.⁴⁹ In residents of LTCFs, diagnosis of pneumonia based on symptoms and physical examination has low sensitivity and specificity (47%–69% and 58%–75%, respectively).⁵¹ In addition, owing to the presence of other comorbid conditions, there is often a broad and nonspecific differential diagnosis, which can lead to diagnostic challenges and delays. An association between latent pneumonia and poor outcomes was described by Osler William, who stressed that fever may actually be a positive predictor of outcome, a notion that was later supported by other researchers.^{81–84}

The diagnosis of pneumonia in the elderly depends on a high index of suspicion and should be considered in the presence of one of the following atypical signs and

symptoms: confusion, delirium, disorientation,²⁵ or loss of appetite. Particularly in an older adult with dementia, urinary incontinence may sometimes be an early indicator of debility caused by pneumonia.⁷⁹ These atypical symptoms should not be automatically attributed to a patient's baseline dementia.^{81,85} Unexplained deterioration in general health, weakness, new onset of recurrent falls, and functional decline (ie, general deterioration) may also be important manifestations of pneumonia in older adults, as well as exacerbation of underlying illnesses, such as congestive heart failure, chronic pulmonary lung disease, and impaired diabetic control.²⁵

Simple physical examination findings, including respiratory rate (>25 breathes per minute) and pulse oximetry (oxygen saturation <90%) have a high sensitivity for pneumonia and, if present, indicate the need for further evaluation of pneumonia, potentially including imaging, testing, and referral to an acute care hospital.^{86,87} In 1 study of LTFC subjects with pneumonia, an oxygen saturation of less than 94% was sensitive and specific for the diagnosis of pneumonia (80% and 91%, respectively).⁸⁸

Imaging

Evaluating imaging findings in elderly persons with suspected pneumonia is challenging. The classic pulmonary opacity used as part of the gold standard for diagnosis of pneumonia may not be identified by a regular chest radiograph owing to poor film quality. Poor quality might be owing in part to the patient's poor cognitive status, poor muscle strength, and inability to maintain posture.⁸⁶ In addition, lung disease (chronic obstructive pulmonary disease, malignancies, interstitial lung disease) and chest wall abnormalities, which are more frequent in the elderly, may complicate the interpretation of chest radiographs. In several studies of elderly patients, computed tomography (CT) scan detected pneumonia in up to 47% of cases that were not identified by using chest radiographs.^{89,90} There are also interobserver discrepancies in the interpretation of chest radiographs, which may be particularly problematic when portable chest radiographs are used.⁹¹

Among residents of LTCFs, imaging has an important role in the diagnosis of pneumonia, as well as in identifying other high-risk conditions that warrant the transfer to an acute care facility. Often, LTCFs have contracted services that provide portable chest radiographs; these portable chest radiographs have similar limitations to standard chest radiographs, as described. Further complicating the usefulness of chest radiographs in LTCFs is a lack of previous films for comparison.⁸⁶ Nevertheless, several studies have reported that 75% to 90% of chest radiographs taken for evaluation of suspected pneumonia among LTCF residents showed evidence of pneumonia. Thus, chest radiograph should be conducted as part of the evaluation of pneumonia in LTCF residents.^{86,92}

Although CT scan is the gold standard for diagnosis of pneumonia, limitations such as cost, radiation exposure, availability, and identification of incidental findings, which are particularly common in the elderly,⁹³ limit its usefulness. Chest CT should be limited to cases where chest radiograph findings are inconclusive, pneumonia complications might be present (eg, lung abscess), or when there is suspicion for pathologies that cannot be diagnosed by chest radiograph (eg, pulmonary embolism, tumor, etc).

Lung ultrasound (LUS) imaging was recently evaluated for the diagnosis of CAP in the elderly, when the chest radiograph findings were inconclusive. In a cohort of 169 elderly frail patients, the sensitivity of LUS imaging was 91% and of chest radiograph was 47% (gold standard was considered to be clinical diagnosis, with or without CT scan).⁹⁴ Recent metaanalyses that evaluated LUS imaging for the diagnosis of pneumonia reported a pooled sensitivity of 94% to 95% and specificity of 90% to 96% when LUS imaging findings were compared with diagnosis of pneumonia by

clinical signs and/or chest radiograph or CT findings, and a high correlation between LUS imaging and CT findings was reported (Spearman correlation coefficient of 0.87).^{95,96} Radiographic resolution lags behind clinical resolution of pneumonia, but older age was not found to be associated with delayed resolution compared with younger age groups.⁹⁷

Laboratory Evaluation

As in other age groups, blood tests are indicated to support the diagnosis of pneumonia by evaluating inflammatory markers (white blood cell counts), and to evaluate organ damage and severity of illness (creatinine level, liver enzymes, platelet counts, etc).

In elderly persons, inflammatory responses may be subtle, and white blood cell counts may be normal or low. Several studies of elderly patients who were diagnosed with pneumonia reported that the absence of leukocytosis, as well as leukopenia, was associated with increased mortality (29% vs 4% in patients without vs patients with leukocytosis).^{83,98} Among patients who reside in LTCFs, neutrophil percentage of greater than 90% and left shift (neutrophil band percentage of >6%) were associated with high likelihood of bacterial infection.⁸⁶

Recently, extensive discussion occurred pertaining to the value of inflammatory markers such as C-reactive protein (CRP) and procalcitonin (PCT) in discriminating bacterial pneumonia from other inflammatory and infectious processes. The usefulness of PCT in differentiating bacterial pneumonia from other acute illnesses in the real world is controversial.^{99,100} In addition, the role of PCT in elderly persons is unclear, because this population group is usually excluded from clinical studies. A recent retrospective study in Italy evaluated the role of CRP in elderly patients who presented to the emergency department with respiratory symptoms and were discharged with or without a final diagnosis of pneumonia. This study reported an association between high CRP levels and pneumonia, even after adjusting for confounders, with a cutoff of 61 mg/L providing the best sensitivity and specificity (odds ratio, 3.59; 95% CI, 2.35–5.48). In the same study, PCT levels were not significantly associated with pneumonia.⁹⁰ The use of CRP and PCT was evaluated for severity of pneumonia in elderly patients, and was not found to predict mortality.^{101,102}

Low serum albumin levels are associated with poor prognosis in CAP patients.¹⁰³ In 1 study that compared clinical manifestations of pneumonia among CAP patients and LTCF residents, the albumin level was much lower among LTCF residents with pneumonia than in non-LTCF CAP patients.¹⁰⁴ In another study, low serum albumin levels and lymphocytes (both of which represent poor nutritional status) were associated with mortality.⁸⁰

Microbiologic Diagnosis

The current recommendations are to search for a pathogenic etiology only in patients where the results might lead to a change in management and may reduce treatment failure. These types of patients include high-risk patients, with either severe pneumonia, or who have multiple comorbid conditions.³² In patients who are ill enough to be hospitalized with severe pneumonia, 2 sets of blood cultures should be obtained, in addition to sputum cultures and urinary antigen tests for *Streptococcus pneumonia* and *Legionella pneumophila*. ICU patients with severe pneumonia often require more extensive evaluation, including bronchoalveolar lavage for microbiologic diagnosis of viruses and bacterial pathogens. These recommendations and clinical guidance are not specific for elderly patients. Clinical judgment should be used to consider the yield of a particular test and the impact of its results on clinical management.

Among LTCF residents, the yield from blood cultures is low when patients are treated in the LTCF. However, when an LTCF resident acquires pneumonia severe enough to be transferred to an acute care facility, blood cultures are recommended.⁸⁶ In addition, because of the poor functional capacity of many LTCF residents, sputum examination is often not performed, even when residents are admitted to an acute care facility (<30% of the patients have sputum examined). When sputum is obtained, frequently samples are not adequate for diagnostic evaluation. Thus, sputum sampling is not recommended for initial assessment, except for cases of severe pneumonia.^{86,105} Urine antigen testing may be used to detect *S pneumoniae* or *L pneumophila*. Although the prevalence of Legionella pneumonia in LTCF residents is not greater than in other elderly patients (0.0%–6.5%),^{86,104,106} in outbreak settings, urinary antigen diagnostics might play an important role in diagnosis and infection control. During the appropriate season, rapid antigen and polymerase chain reaction tests for influenza and respiratory syncytial virus are often useful.

MANAGEMENT

Site of Care

Severity assessment and site-of-care decisions are critical when managing elderly patients who present with CAP. Various useful severity of illness scores have been published, aiming to predict risk of mortality and assist in decisions regarding site of care (eg, admission to the hospital vs care as outpatient at home). In both the Pneumonia Severity Index score and CURB-65 score (Confusion, Urea, Respiratory rate, Blood pressure, age >65 years), age is a significant component of severity scoring highlighting the poor outcomes associated with pneumonia in elderly patients.⁴ According to these scores, Pneumonia Severity Index score class of IV or more, or CURB-65 score of 2 or more indicate the need for a patient with pneumonia to be hospitalized.

Parameters that may compromise the success of home care include homelessness, need for oxygen, an impaired ability to take and/or swallow oral medications, poor social support for persons who are frail, and substance abuse. These factors increase the risk of treatment failure, and hence need for hospital admission, and should be part of the clinical decision making regarding need for hospital admission.²¹

Admission to the ICU is appropriate in many patients with severe CAP who require high level of care. The Infectious Diseases Society of America/American Thoracic Society guidelines for CAP management from 2007 proposed criteria for severe CAP. Major criteria include mechanical ventilation and septic shock. There are nine minor criteria, including CURB components, as well as hypothermia, Pao₂:Fio₂ ratio of 250 or less, bilateral or multilobar infiltrates, leukopenia, and thrombocytopenia. One major criteria or 3 minor criteria indicate the need for ICU admission. In addition, a CURB-65 of greater than 3 may indicate severe pneumonia and the potential need for intensive care.³²

For LTCF residents, most mild to moderate pneumonia can be treated in the LTCF, and the decision to transfer the patient to an acute care facility is based on both clinical assessment, LTCF management availability (chest radiograph availability, intravenous treatment, physician availability), and social considerations. Loeb and colleagues¹⁰⁷ demonstrated that an intervention that included initial assessment of patient eligibility to be treated in the LTCF, followed by early imaging, oral antibiotic treatment, as well as intensive maintenance of hydration and oxygenation in, resulted in reduced hospitalization rate (18% compared with 30% in the usual care group) and costs, and did not impact mortality rates. According to expert panel recommendations from the Infectious Diseases Society of America in 2008, LTCF residents who have suspected

pneumonia and an increased respiratory rate (>25/min) as well as hypoxemia (pulse oximetry <90%) should be transferred to the hospital, as should persons with imaging findings that require more intensive management (pleural effusion, heart failure). Residents should also be transferred to an acute care facility when critical diagnostic tests or necessary therapies are not available in the LTCF. In addition to these considerations, when considering site of care for LTCF residents, the patient's desire to be transferred to an acute care facility and intensively treated is another factor to consider.^{51,86}

Antibiotic Treatment

The principles of pneumonia treatment are valid for both CAP in older communitydwelling adults and CAP among LTCF residents and are discussed as a single entity. Treating CAP, including CAP among LTCF residents, is empiric in most cases, and choosing an antibiotic is based on several factors that guide the clinician to the most likely pathogens in different scenarios. These factors include site of care, severity of disease, the patient's risk for resistant organisms, and local epidemiology.

In general, because the most common pathogens causing CAP in the elderly are *S pneumoniae*, *H influenza*, and *Legionella spp*, these organisms need to be routinely covered, regardless of whether the patient is treated as an outpatient, inpatient, or in an ICU. In addition, enteric Gram-negative bacilli and resistant organisms should be treated according to the patient's risk factors to acquire these organisms (see **Table 1**), whether the patient resides at home (CAP) or at an LTCF (CAP among LTCF residents). **Table 2** lists treatment options based on the latest Infectious Diseases Society of America/American Thoracic Society guidelines.³² These guidelines do not specifically address elderly patients.

Considerations in Community-acquired Pneumonia Treatment

The Infectious Diseases Society of America guidelines recommend treating patients admitted to a medical ward (moderate to severe CAP) with either a respiratory fluoroquinolone, or a combination of a β -lactam plus a macrolide. For patients admitted to the ICU, combination of either β -lactam plus a macrolide or fluoroquinolone is recommended, as well as assessing risk factors to determine the need for coverage of *P aeruginosa* and MRSA.

Several studies have reported conflicting results regarding the potential advantage of combination treatment over monotherapy in patients with moderate to severe CAP. The CAP-START study, which evaluated treatment of inpatient, nonsevere CAP patients treated with either monotherapy (a β -lactam or a fluoroquinolone), or combination therapy (a β -lactam plus a macrolide) reported noninferiority of β -lactam monotherapy in terms of 90-day mortality.¹⁰⁸ Another study that evaluated treatment of moderate to severe CAP demonstrated worse outcomes with β-lactam monotherapy (compared with combination therapy with a β -lactam plus a macrolide), with regard to time to clinical stability and readmission within 30 days, particularly in patients older than 65 years.¹⁰⁹ A systematic review of 28 observational studies demonstrated a relative decrease of 18% in mortality when a macrolide-containing regimen was administered in critically ill CAP patients, compared with other nonmacrolide regimens.¹¹⁰ Other studies have reported an advantage of combining a β -lactam with a macrolide as compared with combining a β -lactam with a respiratory fluoroquinolone, in terms of duration of stay¹¹¹ and ICU mortality.¹¹² A potential explanation for these findings relates to the immunomodulatory effects of macrolides.¹¹³

In contrast, in a recent metaanalysis, monotherapy with fluoroquinolones for moderate to severe CAP had an advantage over both the combination of a β -lactam with a

Table 2

Empiric antimicrobial treatment for community-acquired pneumonia among elderly patients, LTCF residence, with or without risk factors for multidrugresistant organisms

	Elderly, Home, No Risk Factors for eGNB, MRSA or <i>P aeruginosa</i>	Elderly, LTCF, No Risk Factors for MRSA or <i>P aeruginosa</i>	Elderly, Home or LTCF, Risk Factors for MRSA or <i>P aeruginosa</i>
Mild pneumonia (outpatient or inpatient owing to other reasons)	Macrolide ^d Alternative: doxycycline Combine β -lactam and macrolide if macrolide resistance is common	β-Lactam ^a + macrolide or Respiratory fluoroquinolone ^e	Consider local susceptibilities for inpatient vs outpatient decision
Moderate pneumonia, in-patient, medical ward	β-Lactam ^b + macrolide or Respiratory fluoroquinolone	β-Lactam ^b + macrolide or Respiratory fluoroquinolone	β-Lactam + macrolide or Respiratory fluoroquinolone <i>P aeruginosa</i> risk: Use antipseudomonal β-lactam ^c MRSA risk: add vancomycin or linezolid or clindamycin
Severe pneumonia, inpatient, ICU	β-Lactam ^c + macrolide or β-Lactam ^c + respiratory fluoroquinolone	β-Lactam ^c + macrolide or β-Lactam ^c + respiratory fluoroquinolone	 β-Lactam^c + macrolide or β-Lactam^c + respiratory fluoroquinolone with or without vancomycin or linezolid

Abbreviations: eGNB, enteric gram-negative bacilli; ICU, intensive care unit; LTCF, long-term care facility; MRSA, methicillin-resistant Staphylococcus aureus; P aeruginosa, Pseudomonas aeruginosa.

^a β-Lactam choices: high-dose amoxicillin, amoxicillin with clavulanate. Alternatives for penicillin allergy: respiratory fluoroquinolone.
 ^b β-Lactam: Ceftriaxone, cefotaxime, Ampicillin/sulbactam. Alternative for penicillin allergy: respiratory fluoroquinolone.

^c β-Lactam with antipseudomonal activity: piperacillin plus tazobactam, cefepime, carbapenems (consider local Paeruginosa susceptibility patterns). Alternative for penicillin allergy: aztreonam plus respiratory fluoroquinolone. ^d Macrolide included: azithromycin, clarithromycin.

^e Respiratory fluoroguinolones include levofloxacin (750 mg), moxifloxacin.

macrolide and the combination of β -lactam with a fluoroquinolone in terms of treatment failure, antimicrobial discontinuation, and adverse events.¹¹⁴ The explanation of these results suggesting an advantage of quinolone monotherapy is unclear, and additional study is needed to further clarify the role of quinolone monotherapy as compared with β -lactam–based combination therapy in moderate to severe CAP.

In summary, there are no solid data to support one guideline-recommended therapy over another. Monotherapy with a β -lactam is not recommended for inpatient treatment. Choosing between the combination of a β -lactam with either a respiratory fluoroquinolones or a macrolide for treatment of severe CAP should be guided in part by local patterns of epidemiology and resistance. For patients treated in the ICU, a β -lactam combined with either a macrolide or fluoroquinolone is recommended.

The duration of treatment for CAP is based on the level of severity at the time of presentation, the presence of infectious complications (empyema, extrapulmonary complications), and the time required to reach clinical stability. In general, for many patients with CAP who become afebrile and reach clinical stability within 3 days, a course of 5 to 7 days of treatment is appropriate. In certain clinical scenarios (such as patients with severe or complicated pneumonia or patients who do not reach clinical stability within 3 days) and for certain pathogens (eg, *Legionella pneumonia, P aeruginosa,* MRSA) longer courses of treatment (7–14 days) are recommended.^{32,115}

Corticosteroids in Community-acquired Pneumonia

Even with appropriate empiric treatment, mortality rates in CAP remain high, particularly in patients with severe CAP, approaching 45% for patients admitted to ICU. This is owing in part to a strong proinflammatory response and dysregulation of the immune system. Antiinflammatory drugs, in particular corticosteroids, have been used in attempts to improve patient outcomes.

A randomized, controlled trial evaluated addition of methylprednisolone (0.5 mg/kg every 12 hours for 5 days started within 36 hours of admission) to standard therapy for patients with severe CAP and a vigorous inflammatory response, defined as a CRP of greater than 150 mg/L. In this study, treatment failure rates (mostly late, defined as progressive pulmonary infiltrates) were higher in the placebo group, whereas no difference in mortality was demonstrated between the groups. Several metaanalyses have been conducted in the last decade and have reported a benefit of using corticosteroids, particularly in severe CAP, including decreased duration of stay in ICU, lower rates of acute respiratory distress syndrome, and a shorter time to clinical stability. Of note, these studies have not demonstrated a clear impact on mortality. Studies have not demonstrated an increased rate of adverse events, including gastrointestinal hemorrhage, in the groups receiving corticosteroids.^{116–118}

Prina and colleagues¹¹⁹ proposed an algorithm for the use of corticosteroids, where patients with severe CAP are evaluated for degree of inflammation based on CRP level. If not contraindicated, the authors recommend that patients with a high degree of inflammation should be treated with methylprednisolone 0.5 mg/kg every 12 hours for 5 days.

Studies that have evaluated corticosteroids in CAP did not specifically study elderly patients or patients in LTCFs. In addition, patients who were at high risk for adverse events (ie, recent gastrointestinal bleeding, immunocompromised patients) were excluded from some of the trials included in the metaanalyses mentioned. Although it may be reasonable to use corticosteroids in some severe cases of CAP, based on currently available data, corticosteroids are not recommended for routine CAP management in elderly patients.

Other Considerations in the Management of Community-acquired Pneumonia in Elderly Patients

Supportive treatment of sepsis has an important role in the management of CAP regardless of age, and is beyond the scope of this review. However, careful monitoring of oxygen saturation and appropriate hydration are extremely important factors to consider in elderly patients, given the considerably high rate of underlying illnesses that might be present and impacted.

Adverse events and drug–drug interactions are more prevalent in older adults and should be considered when choosing an antibiotic as well as in follow-up evaluations. Tendon rupture, in particular Achilles tendon rupture, has been described in association with fluoroquinolone treatment.¹²⁰ Drug–drug interactions (such as those leading to a prolonged QT interval occurring with administration of fluoroquinolones or macrolides) and prolongation of the prothrombin time and International Normalized Ratio (when fluoroquinolones and warfarin are coadministered) are examples of potential adverse events associated with CAP treatment. Renal dose adjustment is important to avoid renal toxicity as well as other adverse reactions.⁶

OUTCOMES

Mortality rates in pneumonia remain high despite effective treatment options, increased vaccination rates, and increased availability of diagnostic tests.¹¹ Rates of mortality range from 4.9% to 48%, increasing with age and severity of illness.^{50,57,121} Age was found as an independent predictor for mortality, even after adjusting for comorbidities.⁵⁹ In a cohort of 173,145 patients who were hospitalized with CAP in 2000 to 2002, the in-hospital mortality rate among patients older than 75 years was twice the mortality rate of patients aged 65 to 74 years (10.6% vs 4.9%, respectively).⁵ Other predictors of mortality in the elderly included residence status (residence in a nursing home or other chronic care institution), cerebrovascular disease, chronic liver disease, treatment failure, immune suppression, malnutrition, and severe pneumonia according to the CURB-65 index.^{7,50,84,122} In addition, admission to the hospital was associated with increased mortality compared with patients who were treated as an outpatient.^{2,11}

A long-term follow-up study reported high rates of 1-year mortality among patients older than 65 years (22.4%–33.6%) and patients older than 90 years (67%).^{31,85,123} Among 428 patients who survived hospitalization for CAP, independent predictors for 1-year mortality included male gender, severe undernutrition (measured as mid arm circumference), recurrent admission for pneumonia, and frailty.¹²³ Studies conducting longer-term follow-up of 5 years or greater reported mortality rates of 30.3% to 53.0%.^{124,125} Other complications in the LTCF population include acute coronary syndrome, congestive heart failure, empyema, nosocomial infection, and venous thromboembolism.^{98,126,127}

The mean duration of stay of elderly patients hospitalized with CAP ranges between 5.6 and 11.2 days.^{3,38,43,50,57} The Centers for Disease Control and Prevention reported a decrease in duration of stay between 1990 and 2009 in patients aged 65 to 74 from 9.8 days to 5.8 days, and from 10.4 to 6.0 days in patients aged 75 to 84 years.¹²⁸

In a systematic review of patients who were discharged after CAP, all-cause 30-day readmission rates ranged from 16.8% to 20.1%, and pneumonia was one of the main reasons for readmissions, accounting for 17.9% to 29.4% of early readmissions.¹²⁹ Risk factors for readmission include age, chronic obstructive pulmonary disease, smoking, increased Pneumonia Severity Index score, and previous ICU admission.¹¹ In addition, nursing miscommunication with patients about their illness and treatment

recommendations at time of discharge was also associated with a higher risk for readmission.¹³⁰ Outpatient visits associate with CAP are also more frequent among patients older than 65 years, reported as annual rate of visits of 45 visits per 1000 patients (compared with an average rate of 12.5–15.7 visits per 1000 patients).¹³¹

In several US studies, the cost of inpatient care for pneumonia ranges between \$3000 and \$18,600 per episode, is higher among patients older than 65 years, and accounts for 80% to 95% of the total cost for pneumonia care in this age group.^{11,132} For patients who have CAP treated as outpatient, the costs of single episode range from \$130 to \$4500.⁹⁸ Most of the costs in the outpatient setting are due to subsequent hospitalization.¹³³ The time to return to usual activities was reported to be up to 8 weeks in patients with CAP who were hospitalized, and may be longer in elderly patients.⁹⁸

Outcomes of Pneumonia Among Residents of Long-term Care Facilities

Pneumonia is the leading cause of death among nursing home residents.⁴⁹ The mortality rate of LTCF residents with pneumonia is close to that of patients with hospitalacquired pneumonia (20% to 40%), and is higher than is seen in elderly persons with CAP. In 1 study that compared 71 hospitalized subjects with pneumonia who were admitted from nursing homes with 93 hospitalized patients with CAP who were admitted from home (median aged, 77 years), the in-hospital mortality rate, as well as the 1-year mortality rate of the hospitalized patients from LTCFs with CAP, was twice the mortality rate CAP patients admitted from home (in-hospital mortality rates of 32% vs 14%, and 1-year mortality rates of 58% vs 33%).⁵¹

Mortality rates are higher for patients who require hospitalization than for patients who are treated in the nursing home (17.6%–53% and 8.8%–28%, respectively). The most important predictor of both in-hospital and long-term mortality in nursing home patients with lower respiratory tract infection is functional status, measured as independence with activities of daily living.^{134,135} A poor activities of daily living score is also more common in patients with recurrent pneumonia,⁵² as well as those who require admission to the hospital for diseases other than pneumonia. Functional deterioration may also be a long term consequence of pneumonia in LTCF patients.¹³⁶

The costs of pneumonia in nursing home patients were prospectively evaluated in 36 nursing homes in Missouri. The estimated mean total cost per episode treated in the hospital was \$10,408, whereas an episode treated in the nursing home cost approximately \$3789.¹³⁷

SUMMARY

Managing elderly patients with pneumonia, in particular LTCF residents, is complex. Recent guidelines do not discuss LTCF residents. Guidelines for management of pneumonia in older adults, and particularly LTCF residents would be very useful to clinicians. Ideally, such guidelines would address not only the challenges in the diagnosis and treatment of elderly, but would address issues that have ethical implications, such where to treat older adults, and in end-of-life situations, how to best manage older adults with pneumonia. Whether pneumonia is the old man's friend or enemy depends on the clinical situation and the patient's perspective.

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