

Pneumonia in Older Persons

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Community-acquired pneumonia (CAP) is an important threat to the health of older adults. *Streptococcus pneumoniae* remains the most important cause of CAP. Risk factors for CAP include alcoholism, asthma, immunosuppression, chronic respiratory or cardiac disease, institutionalization, and increasing age. Residents of long-term care facilities—a distinct subpopulation of elderly people—are at particularly high risk for developing pneumonia. In this setting, swallowing difficulties, witnessed aspiration, and receipt of sedatives are potentially modifiable risk factors. The clinical presentation in elderly patients is characterized by a reduced prevalence of nonrespiratory symptoms. Few randomized, controlled trials of therapy exist for elderly persons living in the community or in a long-term care setting. Good evidence exists to support the annual administration of influenza vaccine to older adults. Although evidence in clinical trials differs from evidence in observational studies that demonstrate clear benefits associated with the polysaccharide pneumococcal vaccine in this population, the vaccine is recommended for adults aged

Community-acquired pneumonia (CAP) is an important threat to the health of older adults. In the United States, it is the fifth leading cause of death in people aged ≥ 65 years, and an estimated 60,000 seniors die annually [1]. The vast majority of the excess deaths and hospitalizations due to lower respiratory infections occur in older adults, as reflected by >44,000 hospitalizations for pneumonia and influenza in people aged ≥ 65 years in 1997 in Canada. On the basis of data from Finland, it is estimated that the age-specific incidence increases from 15.4 to 34.2 cases per 1000 individuals among those aged 60–74 years and ≥ 75 years, respectively [2]. Residents of long-term care facilities—a distinct subpopulation of elderly people—are at particularly high risk for developing nursing home-acquired pneumonia. Health costs for this group are growing at an accelerated rate as the mean age of death increases.

The purpose of this review is to summarize the best evidence associated with the risk factors for and the etiologic agents, clinical presentation, management, and prevention of CAP in persons aged ≥ 65 years. The emphasis is on the clinical char-

acteristics unique to CAP in elderly persons. Pneumonia in residents of long-term care facilities will also be reviewed.

CAP IN OLDER PERSONS

Etiologic agents. Determining the relative importance of the various etiologic agents associated with pneumonia in older adults is challenging (table 1). One reason for this is that it can be difficult for frail elderly persons to produce sputum for microbiological testing. Researchers have attempted to overcome these challenges via serological and urine antigen testing. Jokinen et al. [3] obtained paired serum samples associated with 88% of 345 episodes of CAP in 4 municipalities in Finland where adults met clinical and radiological eligibility criteria. One hundred forty (46%) of these cases were in persons aged ≥ 60 years. *Streptococcus pneumoniae* was the etiologic agent in 48% of patients aged ≥ 60 years, *Chlamydia* species were detected in 12%, *Mycoplasma pneumoniae* in 10%, *Haemophilus influenzae* in 4%, and respiratory viruses (parainfluenza virus, respiratory syncytial virus, adenovirus, and influenza virus) in 10%. The study confirms the importance of *S. pneumoniae* as a cause of CAP in elderly persons.

Although *Chlamydia* or *Mycoplasma* infections occur in elderly persons, such infections are relatively more common in younger populations. This was illustrated in a hospital-based study from Spain in which Ruiz et al. [4] found an increase in the number of *Chlamydia* or *Mycoplasma* infections among

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Table 1. Causative agents of pneumonia in elderly persons who live in the community or in long-term care facilities.

<i>Streptococcus pneumoniae</i>
<i>Chlamydia pneumoniae</i> ^a
<i>Hemophilus influenzae</i>
<i>Mycoplasma pneumoniae</i> ^a
<i>Legionella</i> species ^a
Gram negative agent
<i>Staphylococcus aureus</i>
Respiratory viruses

^a Less frequently documented in older adults who reside in long-term care facilities.

persons <60 years of age (OR, 2.3; 95% CI, 1.2–4.5) but no discernible pattern among persons aged ≥60 years. *Legionella pneumophila* must be considered as a potential cause of CAP in elderly patients because it was detected in 8% of patients in that study. [4].

The exact importance of gram-negative bacteria that cause pneumonia in elderly people living in the community is uncertain. However, evidence does exist that such bacteria are more common etiologic agents of pneumonia in older patients with comorbidities. Ruiz et al. [4] demonstrated that patients aged ≥60 years who had a comorbid condition (cardiopulmonary, renal, hepatic, diabetes, CNS, or neoplasia) had an increased likelihood of acquiring pneumonia due to a gram-negative enteric bacillus (OR, 4.4; 95% CI, 1.2–23.4; *P* = .01) or to *Pseudomonas aeruginosa* (OR, 6.7; 95% CI, 1.0–291; *P* = .04). Additionally, pneumonia caused by gram-negative bacteria, including *P. aeruginosa*, along with pneumonia caused by *S. pneumoniae*, appears to be associated with increased severity. Ruiz et al. [4] reported that pneumonia requiring admission to the intensive care unit was independently associated with presence of pneumococci (OR, 2.5; 95% CI, 1.3–4.7) and gram-negative enteric bacilli and *P. aeruginosa* (OR, 2.5; 95% CI, 0.99–6.5).

Risk factors. Koivula et al. [5] assessed risk factors for CAP in a township in Finland where 4175 individuals were aged ≥60 years. Independent risk factors for pneumonia included alcoholism (relative risk [RR], 9.0; 95% CI, 5.1–16.2), bronchial asthma (RR, 4.2; 95% CI, 3.3–5.4), immunosuppression (RR, 3.1; 95% CI, 1.9–5.1), lung disease (RR, 3.0; 95% CI, 2.3–3.9), heart disease (RR, 1.9; 95% CI, 1.7–2.3), institutionalization (RR, 1.8; 95% CI, 1.4–2.4), and increased age (≥70 years vs. 60–69 years; RR, 1.5; 95% CI, 1.3–1.7). Two hundred seventy-four episodes of pneumonia were documented over the 3-year study period. Because this study included patients from primary care units and hospitals in the

township—a carefully defined population—the results are more likely to be representative of studies of CAP than of studies limited to an acute care setting. In another community-based study in which risk factors for CAP diagnosed by general practitioners were assessed, Farr et al. [6] found that increased age (adjusted OR for a 30-year interval, 2.69; 95% CI, 1.66–4.35) and chronic obstructive pulmonary disease (adjusted OR, 1.99; 95% CI, 1.15–3.45) were risk factors.

Clinical presentation. The clinical presentation of CAP has frequently been described as being more subtle in elderly persons; however, there have been relatively few systematic evaluations to confirm this. Metlay et al. [7] compared the prevalence of symptoms and signs of pneumonia in a cohort of 1812 patients and found that patients aged 65–74 years and ≥75 years had mean numbers 2.9 and 3.3 fewer symptoms, respectively, than those aged 18–44 years. There was a reduced prevalence of symptoms, which included fatigue, fever, chills, anorexia, sweats, headache, myalgia, nausea, sore throat, inability to eat, vomiting, and diarrhea. The reduction was most pronounced for headache, myalgia, and inability to eat (the prevalences were 72%, 67%, 31%, respectively, in patients aged 18–44 years and were 36%, 25%, and 14%, respectively, in patients aged ≥75 years). These findings are consistent with those of Marrie et al. [8] that demonstrated reduced prevalence of fever (26% and 57% among patients ≥65 and <65 years of age, respectively). In a retrospective chart review by Johnson et al. [9], the presence of dementia seemed to account for nonspecific symptoms. Delirium may also be associated with pneumonia, although few studies have documented the prevalence. Evidence, therefore, does exist for a less distinct presentation of nonrespiratory symptoms and signs of pneumonia in elderly persons. Finally, it is important to remember that the presence of pulmonary infiltrates may represent another disease process (e.g., pulmonary emboli) and should not automatically be ascribed to pneumonia. Clinicians also need to remember that tuberculosis can present acutely and should be suspected in older individuals who fail to respond to empirical therapy with antimicrobial agents.

Management. Guidelines for the management of CAP in elderly patients have not been assessed in randomized controlled trials. However, various aspects of management have been addressed in observational studies, including antibiotic use and various processes of care.

Gleason et al. [10] assessed outcomes on the basis of American Thoracic Society antimicrobial therapy guidelines in a cohort of 864 outpatients, of whom 318 were >60 years of age. The study showed that, for outpatients aged >60 years who were treated according to the guidelines current at the time (i.e., administration of a second-generation cephalosporin, sulfamethoxazole-trimethoprim, or β -lactam and β -lactamase inhibitors), antimicrobial costs were higher, and there was a non-

significant trend toward higher mortality and hospitalization rates. The small number of mortality and hospitalization rates may have limited the ability of the study to detect true differences. Gleason et al. [11] also assessed the effect of specific antimicrobial therapy for hospitalized elderly patients with pneumonia. Initial treatment with a second-generation cephalosporin and a macrolide (hazard ratio, 0.71; 95% CI, 0.52–0.96), a nonpseudomonal third-generation cephalosporin and a macrolide (hazard ratio, 0.74; 95% CI, 0.60–0.92), or a fluoroquinolone alone (hazard ratio, 0.64; 95% CI, 0.43–0.94) was associated with lower 30-day mortality than was treatment with a nonpseudomonal cephalosporin alone. This may be because of additive activity against pneumococcus or, perhaps, because of activity against *Legionella* or *Chlamydia* species. Because estimates of effect are generally increased in observational studies, a randomized controlled trial is needed to confirm these findings. In this absence of clinical trial data, antibiotic therapy for CAP in the elderly should follow current guidelines [12].

Several studies have evaluated processes of care for older patients with pneumonia. Meehan et al. [13] evaluated the relationship between processes of care and outcomes in 14,069 hospitalized patients aged ≥ 65 years. Lower 30-day mortality rates were associated with antibiotic administration within 8 h after hospital admission (OR, 0.85; 95% CI, 0.75–0.96) and with performance of blood culture within 24 h after arrival (OR, 0.90; 95% CI, 0.81–1.00). Using a pneumonia-specific severity-of-illness score developed by Fine et al. [14], Marrie et al. [15] conducted a cluster randomized trial in which hospitals were randomized to manage patients with pneumonia according to a clinical pathway or conventional care. The clinical pathway integrated criteria specific to the route of drug administration (based on the pneumonia severity-of-illness score) and hospital discharge. Although the trial was not limited to elderly persons, the mean age of patients was 64 years. Use of the clinical pathway was associated with an 18% decrease in the admission of low-risk patients to the hospital.

Prognosis. A number of studies have assessed the prognosis for elderly persons with CAP. In the pneumonia-specific prognostic score developed by Fine et al. [14], increased age was demonstrated to play an important role in increased mortality [14]. Conte et al. [16] reported that increased age (OR, 1.8; 95% CI, 1.1–3.1), comorbid disease (OR, 4.1; 95% CI, 2.1–8.1), impaired motor response (OR, 2.3; 95% CI, 1.4–3.7), abnormal vital signs (OR, 3.4; 95% CI, 2.1–5.4), and elevated creatinine level (OR, 2.5; 95% CI, 1.5–4.2) were independent predictors of mortality. The authors derived a clinical prediction rule that they validated in a separate cohort. In contrast, Lim et al. [17] compared elderly patients with CAP who died during hospitalization with those who survived and found that, among patients ≥ 75 years of age, advanced age alone was not an important predictor of death. In a long-term follow-up study (median follow-up

period, 9.2 years), Koivula et al. [18] reported that the relative risk of mortality among patients aged ≥ 60 years with CAP was 1.5 (95% CI, 1.2–2.2), compared with that for patients aged ≥ 60 years who did not develop pneumonia. The 1-year mortality rate among older adults hospitalized for CAP has been demonstrated to be twice that of age-matched, hospitalized control patients (11% vs. 5.5%; $P < .001$) [19].

Prevention. Vaccinations against influenza virus and pneumococci are the major preventive strategies for pneumonia in older adults. A systematic review by Gross et al. [20] that included 1 randomized trial and 20 cohort studies showed that, for frail older adults, influenza vaccine had an efficacy of 53% (95% CI, 35%–66%) for preventing pneumonia, 50% (95% CI, 28%–65%) for preventing hospitalization, and 68% (95% CI, 56%–76%) for preventing death. On the basis of this evidence, influenza vaccination is considered to be an important means of preventing pneumonia in elderly people.

In contrast to vaccination against influenza, the efficacy of the pneumococcal vaccine in older adults has been more controversial. In a meta-analysis, Cornu et al. [21] found a significant reduction in the incidence of pneumonia definitely due to pneumococci (OR, 0.29; 95% CI, 0.20–0.42), of mortality due to pneumonia (OR, 0.68; 95% CI, 0.51–0.92), and of pneumonia presumed to be due to pneumococci (OR, 0.60; 95% CI, 0.37–0.96). There was no significant effect on the incidence of pneumonia (OR, 0.78; 95% CI, 0.58–1.07) and on mortality due to any cause (OR, 1.01; 95% CI, 0.91–1.12). In an analysis of clinical trials involving elderly persons, no significant effect of pneumococcal vaccination was noted for pneumonia definitely due to pneumococci (OR, 0.58; 95% CI, 0.18–1.0), mortality due to pneumonia (OR, 0.69; 95% CI, 0.28–1.27), pneumonia due to any cause (OR, 1.10; 95% CI, 0.92–1.32), pneumonia presumed to be due to pneumococci (OR, 1.16; 95% CI, 0.74–1.80), and mortality due to any cause (OR, 1.09; 95% CI, 0.98–1.21) [21]. These findings differ from the results of observational studies in which the vaccine was shown to be effective for reducing the rate of pneumococcal bacteremia among elderly patients [22]. It is important to note that, although the clinical trial data do not show a significant effect in elderly patients, the 95% CIs do not rule out clinically important effects.

PNEUMONIA IN RESIDENTS OF LONG-TERM CARE FACILITIES

Etiologic agents. Establishing the etiology of pneumonia in residents of long-term care facilities is a daunting challenge. Roughly 50%–70% of residents in long-term care facilities cannot produce a sputum specimen that is adequate for analysis. Furthermore, interpreting the results of a Gram stain of a sputum sample is problematic because many residents of long-

term care facilities are chronically colonized with potential bacterial pathogens (table 1). There are no multicenter studies that have used standardized definitions and comprehensive testing (i.e., serological testing, blood culture, Gram staining of sputum samples, and antigen testing) to establish the etiology of pneumonia in residents of long-term care facilities. In his review of published studies of pneumonia in residents of long-term care facilities, Muder [23] found that the proportion of residents in long-term care facilities with pneumonia who had *S. pneumoniae* detected ranged from 0% to 39%. The proportion of pneumonia cases due to gram-negative bacteria ranged from 0% to 55%. Rates of isolation of *Staphylococcus aureus* ranged from 0% to 39%. *Legionella* and *Mycoplasma* species were infrequently detected. Because the number of patients in these studies ranged from 11 to 414 (median, 50 patients), the estimates of the prevalence of pneumonia due these individual pathogens have wide 95% CIs. Although outbreaks of infections due to *Legionella* and *Chlamydia pneumoniae* have been described in long-term care facilities, the exact prevalence of these organisms among residents of long-term care facilities who have pneumonia is uncertain.

Risk factors. In a cohort study to assess risk factors for pneumonia in residents of long-term care facilities, Loeb et al. [24] reported that older age (OR, 1.7; 95% CI, 1.1–2.6 per 10-year interval; $P = .01$), male sex (OR, 1.9; 95% CI, 1.1–3.5; $P = .03$), swallowing difficulty (OR, 2.0; 95% CI, 1.2–3.3; $P = .01$), and the inability to take oral medications (OR, 8.3; 95% CI, 1.4–50.3; $P = .02$) were significant risk factors for pneumonia. Vergis et al. [25] conducted a case-control study and found that risk factors significantly associated with pneumonia included witnessed aspiration (OR, 13.9; 95% CI, 1.7–111.0; $P = .01$), sedative medication (OR, 2.6; 95% CI, 1.2–5.4; $P = .01$), and comorbidity score (OR, 1.2; 95% CI, 1.0–1.4; $P = .05$). Data from patients hospitalized for CAP, as well as data from residents of long-term care facilities with pneumonia, suggest that aspiration is an important cause of infection.

Clinical presentation. Eliciting oral reports of symptoms of pneumonia from residents of long-term care facilities may be challenging, because they often have cognitive impairment or may be aphasic because of strokes. Only approximately two-thirds of residents of long-term care facilities who have pneumonia have cough or fever [23]. There have been few comparisons of CAP to nursing home-acquired pneumonia in elderly patients. Marrie and Blanchard [26] compared residents of long-term care facilities admitted to the hospital with pneumonia with seniors admitted with CAP. The 71 nursing home residents were less likely to experience chills (24% vs. 58% of patients), pleuritic chest pain (14% vs. 32%), headache (5% vs. 32%), anorexia (42% vs. 58%), myalgia (7% vs. 33%), and productive cough (35% vs. 61%) than were the 93 elderly patients with CAP.

Therapy. In contrast to CAP in elderly persons, there have been far fewer studies that have addressed the management of pneumonia in residents of long-term care facilities. Also, studies that have been conducted have been smaller in size. There have been several small, randomized, controlled trials that compared the efficacy of antibiotics (ciprofloxacin or cephalosporins) in long-term care facilities. No differences in efficacy between the agents compared were noted, which was likely because of the small sample sizes of the studies. The Canadian guidelines for initial management of CAP take into consideration the potential for infection with enteric gram-negative bacteria in the long-term care facility population [12]. Empirical therapy with a respiratory fluoroquinolone alone or with amoxicillin-clavulanate and a macrolide are recommended.

Naughton et al. [27] conducted a cluster randomized trial to evaluate strategies for implementing guidelines derived from community practice. Ten facilities were randomized to participate in either an educational program consisting of small group discussion about the guidelines that included nurses and physicians or an educational program geared to physicians alone. No difference in adherence to guideline recommendations was reported between the 2 strategies. When all intervention groups were pooled, there was an increase in adherence to the use of parenteral antibiotics according to guidelines.

Prognosis. In residents of long-term care facilities, poor ability to perform activities of daily living has been shown to be associated with worse outcomes for lower respiratory infections [28]. To gain better discriminative ability in this population, Mehr et al. [28] developed an 8-variable model to predict 30-day mortality. Variables included serum urea nitrogen level, WBC count, body mass index, pulse rate, status of activities associated with daily living, absolute lymphocyte count of <800 lymphocytes/ μL (0.8×10^9 lymphocytes/L), male sex, and deterioration in mood over 90 days [29]. A point score based on the results had discriminative ability. For each variable, a score from 0 to 6 was assigned. After summing scores, the predicted and observed mortality rates were similar, ranging from low rates (2%) for patients with scores of 1–4 to very high rates (60%) for patients with scores of 11–17.

Prevention. In residents of long-term care facilities, vaccination of health care workers with influenza vaccine is an important preventive health measure. Data from 2 cluster randomized clinical trials show the benefit associated with such vaccination [30, 31]. Potter et al. [30] randomized 12 long-term facilities either to offer health care workers vaccination or not to offer vaccination. Vaccination of health care workers was associated with a reduction in total patient mortality from 17% to 10% (OR, 0.56; 95% CI, 0.40–0.80). Carman et al. [31] conducted a randomized trial using cluster randomization in 20 geriatric care hospitals that compared mortality in hospitals where health care workers were vaccinated with mortality in

hospitals where no vaccination was offered. Vaccination of health care workers significantly reduced mortality of elderly people over a period of 6 months in hospitals where influenza vaccine was offered, compared with hospitals where influenza vaccine was not offered (OR, 0.58; 95% CI, 0.40–0.84; $P = .014$).

CONCLUSION

Pneumonia in older adults is a challenge in both community and long-term care settings. There are clear limitations in the literature in this area that clinicians should be aware of.

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An error appeared in an electronic article published in the 15 November 2003 issue of the journal (Barker JH, Luby JP, Dalley AS, Bartek WM, Burns DK, Erdman DD. Fatal type 3 adenoviral pneumonia in immunocompetent adult identical twins. *Clin Infect Dis* 2003; 37:e142–6). In the second paragraph in the Case Report section, the third-to-last sentence should read, “There were positive results of an assay for ade-

novirus by indirect fluorescence antibody in endotracheal secretions and bronchoalveolar lavage (BAL) fluid specimens, and adenovirus was isolated from the endotracheal secretions” (*not* “There were positive results of an assay for indirect fluorescence antibody to adenovirus in endotracheal....”). The authors regret this error.

An error appeared in an article in the 1 December 2003 issue of the journal (Melzer M, Eykyn SJ, Gransden WR, Chinn S. Is methicillin-resistant *Staphylococcus aureus* more virulent than methicillin-susceptible *S. aureus*? A comparative cohort study of British patients with nosocomial infection and bacteremia.

Clin Infect Dis 2003; 37:1453–60). The second affiliation should read “Department of Infection, Guy’s and St. Thomas’ Hospital” (*not* “Department of Infection, Lucy’s and St. Thomas’ Hospital”). The journal regrets this error.

An error appeared in an electronic article in the 15 October 2003 issue of the journal (Myjak P, Nahorski W, Pietkiewicz H, von Nickisch-Rosenegk M, Stolarczyk J, Kacprzak E, Felczak-Korzybska I, Szostakowska B, Lucius R. Molecular confirmation of human alveolar echinococcosis in Poland. *Clin Infect Dis* 2003; 37:e121–5). Reference [12] should appear at the end of the penultimate sentence in the first paragraph of the “Molecular examinations” subsection of Materials and

Methods (p. e121). The sentence should read, “A fragment of mitochondrial 12S rDNA was amplified by PCR (AmpliTaq Gold polymerase; Applied Biosystems) from human genomic DNA using the cestode-specific primers 60 (forward, TTAAGA-TATATGTGGTACAGGATTAGATACCC) and 375 (reverse, 5'-AACCGAGGGTGACGGGCGGTGTGTACC-3') [12].” The journal regrets this error.

An error appeared in an article published in the 15 November 2003 issue of the journal (Loeb M. Pneumonia in older persons. *Clin Infect Dis* 2003; 37:1335–9). The last 2 words in the abstract were inadvertently cut off. The sentence should end

“... the vaccine is recommended for adults aged >65 years” (*not* “... the vaccine is recommended for adults aged”). The journal regrets this error.

In an article in the 1 November 2001 issue of the journal (Ally R, Schürmann D, Kreisel W, Carosi G, Aguirrebengoa K, Dupont B, Hodges M, Troke P, Romero AJ, and the Esophageal Candidiasis Study Group. A randomized, double-blind, double-dummy, multicenter trial of voriconazole and fluconazole in the treatment of esophageal candidiasis in immunocomprom-

ised patients. Clin Infect Dis 2001; 33:1447–54), an error appeared in table 1. In the column labeled “Flu” under the heading “Success,” the value for *C. glabrata* should have been 4 (*not* 14). The corrected table is presented below. The authors regret this error.

Table 1. Primary endoscopic outcome assessments analyzed by mycological findings.

Organism	Total ^a	Success ^b		Failure		Not evaluable	
		Vori	Flu	Vori	Flu	Vori	Flu
<i>Candida albicans</i>	354	132	141	5	9	42	25
<i>C. krusei</i>	4	1	2	0	0	1	0
<i>C. glabrata</i>	12	5	4	0	0	1	2
<i>C. parapsilosis</i>	1	0	1	0	0	0	0
<i>C. tropicalis</i>	1	0	1	0	0	0	0
Unspecified <i>Candida</i> species	20	9	4	0	0	5	2

NOTE. Flu, fluconazole; Vori, voriconazole.

^a >1 isolate per sample; *n* = 392.

^b Defined as “cured + improved.”