Treatment of Nursing Home–Acquired Pneumonia

KYLE MILLS, PharmD, BCPS, and A. CHRISTIE NELSON, PharmD
University of Wyoming School of Pharmacy, Laramie, Wyoming
BRADFORD T. WINSLOW, MD, FAAFP, *Swedish Family Medicine Residency Program, Littleton, Colorado*
KATHRYN LEE SPRINGER, MD, *Greater Denver Infectious Diseases, Denver, Colorado*

Pneumonia is an important cause of morbidity and mortality in nursing home residents, with 30-day mortality rates ranging from 10 to 30 percent. *Streptococcus pneumoniae* is the most common cause of nursing home–acquired pneumonia, although *Staphylococcus aureus* and gram-negative organisms may be more common in severe cases. Antibiotic therapy for nursing home–acquired pneumonia should target a broad range of organisms, and drug-resistant microbes should be considered when making treatment decisions. In the nursing home setting, treatment should consist of an antipneumococcal fluoroquinolone alone *or* either a high-dose beta-lactam/beta-lactamase inhibitor or a second- or third-generation cephalosporin, in combination with azithromycin. Treatment of hospitalized patients with nursing home–acquired pneumonia requires broad-spectrum antibiotics with coverage of many gram-negative and gram-positive organisms, including methicillin-resistant *S. aureus*. Appropriate dosing of antibiotics for nursing home–acquired pneumonia is important to optimize effectiveness and avoid adverse effects. Because many nursing home residents take multiple medications, it is important to consider possible drug interactions. (*Am Fam Physician.* 2009;79(11):976-982.

▶ **See related editorial on page 938.**

Pneumonia is the second most common cause of infection in nursing home residents, and is associated with notable morbidity and mortality.[1] Attributable 30-day mortality rates range from 10 to 30 percent.[2-4] Prompt diagnosis and management are therefore essential. This article reviews the clinical management of nursing home–acquired pneumonia, with an emphasis on antimicrobial therapy.

Etiology

Nursing home–acquired pneumonia is usually bacterial in origin, although the specific microbiologic cause is often not identified.[5-12] Common bacterial etiologies are listed in *Table 1*.[5-12] *Streptococcus pneumoniae* is the most common causative agent. However, in severe cases of nursing home–acquired pneumonia requiring hospitalization and mechanical ventilation, the rates of infection with *Staphylococcus aureus* and enteric gram-negative organisms appear to exceed those of *S. pneumoniae*.[5]

These organisms can be associated with antimicrobial resistance, especially in the nursing home setting. Risk factors for infection with multidrug-resistant pathogens include antibiotic therapy within the preceding 90 days, a high incidence of antibiotic resistance in the community or facility, chronic hemodialysis, and immunosuppression.[7] One study found that recent antibiotic use and the inability to perform activities of daily living were independently associated with antibiotic-resistant nursing home–acquired pneumonia requiring intensive care unit (ICU) admission or mechanical ventilation.[11]

Nursing home–acquired pneumonia can also be caused by viral infection *(Table 1*[5-12]*)*. Influenza and respiratory syncytial virus (RSV) are important causes of respiratory illness and mortality in nursing home residents.[13,14] Physicians should suspect viral etiologies from late fall through early spring, and whenever outbreaks of respiratory infection occur. Influenza predisposes patients to a secondary bacterial pneumonia.[15] In a population-based analysis involving 381 nursing homes over a period of four years, investigators found that each year influenza infection was associated with approximately 28 hospitalizations; 147 courses of antibiotics;

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Physicians should suspect infection with resistant organisms in nursing home patients who received antibiotics within the previous 90 days; when there is a high incidence of antibiotic resistance in the community or facility; and in patients who receive chronic dialysis, are immunosuppressed, or have difficulty performing activities of daily living.	B	7, 11
Nursing home–acquired pneumonia should be suspected in patients with new or progressive infiltrate plus a new-onset fever, leukocytosis, purulent sputum, or hypoxia.	C	7
Nonhospitalized nursing home patients requiring treatment for pneumonia should be treated with an antipneumococcal fluoroquinolone, *or* either a high-dose beta-lactam/beta-lactamase inhibitor or a second- or third-generation cephalosporin, in combination with azithromycin (Zithromax).	C	1, 31, 32
Empiric coverage of methicillin-resistant *Staphylococcus aureus* and double coverage of *Pseudomonal* pneumonia should be prescribed for patients requiring intensive care unit admission.	B	5-7

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

and 15 deaths per 1,000 residents with heart or lung disease, diabetes mellitus, or immunosuppression. Similarly, RSV accounted for approximately 15 hospitalizations, 76 courses of antibiotics, and 17 deaths per 1,000 residents with similar conditions.[13] A recent report described human metapneumovirus as the cause of an outbreak of respiratory infections, including pneumonia, in a Canadian nursing home.[16]

Diagnosis

The clinical manifestations of pneumonia in older adults may be subtle. In one study, investigators found that persons 65 years and older are less likely to complain of fever, chills, myalgia, and pleuritic chest pain than younger persons.[17] One prospective study revealed that 80 percent of nursing home residents with pneumonia exhibit three or fewer respiratory signs or symptoms, but 92 percent have at least one identifiable respiratory manifestation, such as cough, respiratory rate of 30 breaths per minute or more, presence of crackles, or absence of wheezes on auscultation.[18] The 2005 American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guideline recommends that the clinical diagnosis of health care–associated pneumonia, including nursing home–acquired pneumonia, be based on a new or progressive infiltrate on chest radiography plus clinical findings consistent with pneumonia (i.e., new-onset fever [temperature greater than 100.4° F (38° C)], leukocytosis, purulent sputum, or hypoxia).[7]

The 2005 ATS/IDSA guideline also recommends that lower respiratory tract samples be obtained from nursing home residents hospitalized with nursing home–acquired pneumonia, particularly from those who are intubated, to guide treatment.[7] Although respiratory cultures from nonintubated patients, and from those managed in the nursing home, could be considered, it is important to note that these are infrequently obtained, tend to produce a low yield of pathogenic microorganisms, and are commonly contaminated with oropharyngeal microflora, making interpretation difficult.[19,20]

Blood cultures are infrequently positive in patients with pneumonia, but may be considered in those who require intensive care. Rapid antigen tests of respiratory secretions, such as nasal washings, nasopharyngeal swabs, or throat swabs, can assist with the diagnosis of influenza and RSV during the appropriate seasons.[21] Urinary antigen testing for *S. pneumoniae* and *Legionella pneumophila* serotype 1 may be considered, although most studies examining its use have been performed in patients with community-acquired pneumonia (CAP).[22-26] One limitation of urinary antigen testing is the lack of information about antibiotic susceptibility. Therefore, a sputum Gram stain and culture should be considered if patients are able to generate a useful sample and the results can be obtained in time to influence therapeutic decision-making.[21]

Table 1. Common Etiologies of Nursing Home–Acquired Pneumonia

Etiology	*Percentage of isolates*
Gram-negative bacilli	Up to 55
Streptococcus pneumoniae	Up to 48
Staphylococcus aureus	Up to 33
Haemophilus influenzae	Up to 22
Viruses	Up to 10
Pseudomonas aeruginosa	Up to 7
Legionella pneumophila	Up to 6
Mycoplasma pneumoniae	Up to 1

Information from references 5 through 12.

In many nursing home residents with pneumonia, a diagnosis of aspiration pneumonitis or aspiration pneumonia should be considered. Aspiration pneumonitis is an inflammatory syndrome that does not typically require antibiotic therapy,[27] whereas aspiration pneumonia is an infection for which antibiotic therapy should be initiated. Risk factors for these conditions include a history of stroke, dementia, gastroesophageal reflux disease, and tube-feeding requirements. Pathogens isolated from nursing home patients with severe aspiration pneumonia have included enteric gram-negative bacteria, *S. aureus*, and anaerobes.[6] The results of a recent prospective cohort study validated a new algorithm for diagnosis of aspiration pneumonitis versus aspiration pneumonia *(Figure 1)*.[28]

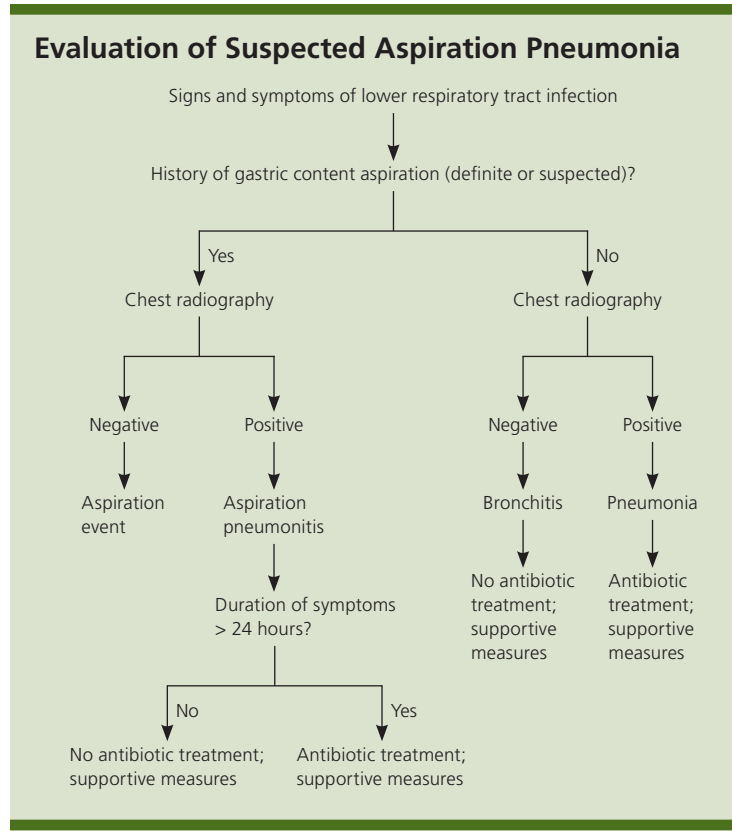

Figure 1. Algorithm for the evaluation of suspected aspiration pneumonia.

Adapted with permission from Mylotte JM, Goodnough S, Gould M. Pneumonia versus aspiration pneumonitis in nursing home residents: prospective application of a clinical algorithm. J Am Geriatr Soc. *2005;53(5):756.*

Treatment

IN THE NURSING HOME SETTING

There is little evidence to suggest the clinical superiority of one antibiotic over another for nursing home–acquired pneumonia, particularly in the nursing home setting. Previous guidelines have recommended antibiotic therapy based primarily on microbiologic data.[7,29,30]

The 2005 ATS/IDSA guideline for the treatment of health care–associated pneumonia does not specifically address treatment of nursing home–acquired pneumonia in the nursing home setting.[7] Guidelines based on limited data and expert opinion recommend the use of an antipneumococcal fluoroquinolone (e.g., levofloxacin [Levaquin] or moxifloxacin [Avelox]) alone *or* either a high-dose beta-lactam/beta-lactamase inhibitor (e.g., amoxicillin/clavulanate [Augmentin]) or a second- or third-generation cephalosporin (e.g., cefuroxime [Ceftin], cefpodoxime [Vantin], ceftriaxone [Rocephin]), in combination with azithromycin (Zithromax). Oral therapy is preferred over parenteral therapy in mild to moderate cases.[29,30] Intramuscular cephalosporins also may be used.[1,31]

A randomized, double-blind trial compared the safety and effectiveness of once-daily intramuscular injections of cefepime (Maxipime) and ceftriaxone for nursing home–acquired pneumonia treated within the nursing home. Sixty-nine residents 60 years and older with radiographically-confirmed pneumonia and creatinine clearances of less than 60 mL per minute were included in the study. Most patients were switched to oral therapy after three days of parenteral therapy. Successful response was documented in 78 percent of patients treated with cefepime and 66 percent of patients treated with ceftriaxone (P = not significant).[32] Each year, the Centers for Disease Control and Prevention (CDC) recommendations for influenza treatment should be consulted for updates on recent resistance patterns and treatment or prevention recommendations.

When a viral etiology of nursing home–acquired pneumonia is diagnosed and there is low suspicion of secondary bacterial infection, antibiotics often can be discontinued. However, it should be noted that older patients with influenza are at high risk of bacterial superinfection. Oseltamivir (Tamiflu) and zanamivir (Relenza) are approved for the treatment of influenza A and B in adults, but therapy should begin within two days of symptom onset to confer the most benefit, and increasing resistance to oseltamivir has recently been reported.[33] These agents may lessen the severity of influenza manifestations and may reduce the incidence of post-influenza bacterial pneumonia.[34]

Influenza vaccination is recommended for the prevention of influenza in nursing home residents, but does not provide complete protection.[34] Similarly, pneumococcal

vaccination is recommended for all nursing home patients in accordance with the latest CDC guidelines for the prevention of pneumococcal pneumonia.[35] Oseltamivir should be used prophylactically when an outbreak of influenza A or B occurs within a nursing home.[34] There are no data to support specific treatments for RSV and human metapneumovirus in nursing home residents.[36]

IN HOSPITALIZED PATIENTS

Intravenous antimicrobial therapy should be initiated for nursing home patients hospitalized with pneumonia, with empiric coverage of methicillin-resistant *S. aureus* (MRSA) and *Pseudomonas aeruginosa*. Antibiotic coverage of atypical organisms is controversial, and there are no data to support such therapy. If an etiologic agent is identified, antibiotic therapy should be narrowed to minimize antibiotic resistance, toxicity, and cost. Hospitalized patients are more likely to have drug-resistant and highly pathogenic organisms.[5-7,11] Antibiotics administered in the past 90 days generally should not be prescribed again, because the risk of infection with resistant pathogens is increased.[37]

Nursing home residency is a major risk factor for MRSA colonization, which can lead to subsequent infection. Rates of MRSA from six nursing homes and one skilled-nursing facility in the United States ranged from 24 to 77 percent.[38-40] Vancomycin (Vancocin; given intravenously) and linezolid (Zyvox; given orally or intravenously) are recommended for the treatment of MRSA pneumonia.[7,41]

Risk factors for pneumonia caused by *P. aeruginosa* were identified in a study of 559 cases of CAP, including 45 cases of nursing home–acquired pneumonia. They include hospitalization within the previous 30 days or pulmonary comorbid illness (e.g., chronic obstructive pulmonary disease, asthma, chronic bronchitis, bronchiectasis, interstitial lung disease).[42] When choosing antipseudomonal agents, the physician should refer to local pseudomonal susceptibility patterns.

One prospective, randomized trial compared the effectiveness of cefepime, with or without metronidazole (Flagyl), versus ertapenem (Invanz) for hospital- or skilled facility–acquired pneumonia in nonventilated, non-ICU patients.[43] The addition of vancomycin was permitted for patients with suspected MRSA infection. *Enterobacteriaceae, S. pneumoniae,* and *S. aureus* comprised 19.5, 12.9, and 11.6 percent of the pathogens recovered, respectively. Forty percent of the *S. aureus* isolates were methicillin-resistant. Outcomes were similar; 87.3 percent of patients who received ertapenem and 86.0 percent of patients who received cefepime improved.

Table 2. Initial Intravenous, Adult Doses of Antibiotics for Empiric Therapy of Hospital-Acquired Pneumonia, Including Ventilator-Associated Pneumonia, and Healthcare–Associated Pneumonia in Patients with Late-Onset Disease or Risk Factors for Multidrug–Resistant Pathogens

Antibiotic	*Dosage**
Antipseudomonal cephalosporin	
Cefepime	1–2 g every 8–12 h
Ceftazidime	2 g every 8 h
Carbapenems	
Imipenem	500 mg every 6 h or 1 g every 8 h
Meropenem	1 g every 8 h
β-lactam/β-lactamase inhibitor	
Piperacillin–tazobactam	4.5 g every 6 h
Aminoglycosides	
Gentamicin	7 mg/kg per d†
Tobramycin	7 mg/kg per d†
Amikacin	20 mg/kg per d†
Antipseudomonal quinolones	
Levofloxacin	750 mg every d
Ciprofloxacin	400 mg every 8 h
Vancomycin	15 mg/kg every 12 h‡
Linezolid	600 mg every 12 h

**—Dosages are based on normal renal and hepatic function.*

†—Trough levels for gentamicin and tobramycin should be less than 1 µg/ml, and for amikacin they should be less than 4–5 µg/ml.

‡—Trough levels for vancomycin should be 15–20 µg/ml.

Reprinted with permission from American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med. *2005;171(4):402.*

For hospitalized patients with nursing home–acquired pneumonia, the 2005 ATS/IDSA guideline[7] recommends a combination antibiotic therapy consisting of the following:

- An antipseudomonal cephalosporin, an antipseudomonal carbapenem, or an extended-spectrum beta-lactam/beta-lactamase inhibitor

plus

- An antipseudomonal fluoroquinolone or an aminoglycoside

plus

- An anti-MRSA agent (vancomycin or linezolid).

The broad empiric therapy includes coverage of MRSA and double-coverage of *P. aeruginosa*. Specific antibiotics and recommended dosages are provided in *(Table 2)*.[7] These recommendations are based on microbiologic data from patients with severe pneumonia. Treatment should be tailored to the local microbiology, resistance patterns,

and specific patient risk factors.[7] Aminoglycoside use increased mortality in a retrospective review.[44] If chosen as therapy, aminoglycosides should be used with caution in patients with impaired renal function. Tigecycline (Tygacil) and doripenem (Doribax) are newer antibiotics being investigated in the treatment of health care–associated pneumonia, but they are not approved by the U.S. Food and Drug Administration for this indication. These medications may play a role in the treatment of hospitalized patients with nursing home–acquired pneumonia in the near future.

Pharmacotherapeutics

TIMING AND DURATION OF ANTIBIOTIC THERAPY

The timing of initiation of antibiotic therapy in hospitalized patients with nursing home–acquired pneumonia may be an important predictor of outcome.[45] Therapy given within four hours of admission was associated with decreased length of stay and decreased mortality in one retrospective study, and is an important outcome measure for the Centers for Medicare and Medicaid Services.[45,46] However, other studies have not demonstrated a survival benefit or a more rapid clinical response.[47,48] The 2007 IDSA/ATS guideline recommends initiation of antibiotic therapy for CAP within the emergency department or as soon as possible after the diagnosis is made, rather than within a specified time period.[21] Although no studies have specifically measured outcomes for nursing home patients, similar recommendations apply to this population.

The IDSA/ATS guideline recommends a seven- to eight-day duration of therapy for health care–associated pneumonia that has been treated with appropriate empiric antibiotics, has clinically improved, and that is not caused by nonfermenting gram-negative bacteria such as *P. aeruginosa*.[7]

DOSING OF ANTIBIOTICS IN THE NURSING HOME PATIENT

Critically ill patients often have altered pharmacokinetics and pharmacodynamics, and antibiotics must be dosed more aggressively than in other patients.[49] Empiric antibiotics in critically ill patients with nursing home–acquired pneumonia should be dosed as outlined in *Table 2*.[7] As renal function declines with age, proper dosing of antibiotic agents must be ensured to avoid adverse effects.[50] The Cockcroft-Gault equation is commonly used to estimate creatinine clearance; manufacturers generally use this equation to estimate creatinine clearance when making recommendations about drug dosing in patients with renal insufficiency. Aminoglycosides, which can cause nephro- and ototoxicity, and imipenem/cilastatin (Primaxin), which can cause seizures, should be avoided in older patients with renal impairment.

Vancomycin dosing should be optimized to maintain trough concentrations in the range of 15 to 20 mcg per mL.[7] However, a retrospective review of patients with MRSA pneumonia did not demonstrate any correlation between serum vancomycin trough concentrations and mortality.[51]

ADVERSE EFFECTS OF ANTIMICROBIAL AGENTS IN OLDER ADULTS

Adverse drug events are more likely to occur in older adults than in other patients.[50] The safest and most effective medication should be prescribed in an appropriate dose for the shortest duration possible to adequately treat the infection. In a study of nursing home patients, use of antibiotics was associated with preventable adverse drug reactions *(Table 3*[50]*)*.[52]

DRUG INTERACTIONS WITH ANTIMICROBIAL AGENTS IN OLDER ADULTS

Increasing age is associated with an increasing number of medications used on a daily or weekly basis.[53] Up to 67 percent of nursing home patients will experience an adverse drug reaction during a six- to 12-month stay, and use of more than eight medications is associated with

Table 3. Adverse Effects of Antibiotics in Older Patients

Antimicrobial class/agent	*Adverse event*
Aminoglycosides	Nephrotoxicity, ototoxicity
Beta-lactams	Diarrhea, *Clostridium difficile*–associated disease, drug-related fever, interstitial nephritis, rash, thrombocytopenia, anemia, neutropenia
Clindamycin (Cleocin)	Diarrhea, *C. difficile*–associated disease
Fluoroquinolones	Nausea, vomiting, central nervous system effects, decreased seizure threshold, QT prolongation
Imipenem/cilastatin (Primaxin)	Seizure
Linezolid (Zyvox)	Thrombocytopenia, anemia
Macrolides	Gastrointestinal intolerance

Adapted with permission from Faulkner CM, Cox HL, Williamson JC. Unique aspects of antimicrobial use in older adults. Clin Infect Dis. *2005;40(7):1002.*

Table 4. Selected Drug Interactions of Common Antibiotics

Antimicrobial class/agent(s)	*Interacting agents*	*Potential clinical effect*
Aminoglycosides	Loop diuretics, nonsteroidal anti-inflammatory drugs, vancomycin (Vancocin)	Additive nephrotoxicity
Azithromycin (Zithromax)	Warfarin (Coumadin)	Increased anticoagulant effect (minor)
Fluoroquinolones	Aluminum, magnesium, iron, zinc, calcium, sucralfate (Carafate)	Decreased absorption
	Class IA and III antiarrhythmics	QT prolongation, arrhythmia
	Warfarin	Increased anticoagulant effect
Linezolid (Zyvox)	Serotonergic agents (selective serotonin reuptake inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors, tramadol [Ultram])	Serotonin syndrome
Metronidazole (Flagyl)	Warfarin	Increased anticoagulant effect (major)
Trimethoprim/sulfamethoxazole (Bactrim, Septra)	Phenytoin (Dilantin)	Increased concentration of phenytoin
	Warfarin	Increased anticoagulant effect (major)

Adapted with permission from Faulkner CM, Cox HL, Williamson JC. Unique aspects of antimicrobial use in older adults. Clin Infect Dis. *2005;40(7):1001.*

increased rates of adverse drug reactions.[54] Because of the large number of medications prescribed in nursing home patients, the potential for drug interactions is very high. *Table 4* lists some common drug interactions with which prescribers should be familiar.[50] Most antibiotics alter the anticoagulant effects of warfarin (Coumadin), primarily by increasing these effects. All patients concurrently taking antibiotics and warfarin should have their International Normalized Ratio monitored closely during antibiotic therapy.

This is one in a series of "Clinical Pharmacology" articles coordinated by Allen F. Shaughnessy, PharmD, Tufts University Family Medicine Residency at Cambridge Health Alliance, Malden, Mass.

The Authors

KYLE MILLS, PharmD, BCPS, is a clinical assistant professor of pharmacy practice at the University of Wyoming School of Pharmacy, Laramie; is on the faculty of the Swedish Family Medicine Residency Program in Littleton, Colo.; and is an assistant clinical professor of family medicine at the University of Colorado–Denver/Health Sciences Center in Aurora. Dr. Mills received his pharmacy degree from the University of Wyoming in Laramie, and completed a pharmacy practice residency at LDS Hospital in Salt Lake City, Utah, and a pharmacy specialty residency in internal medicine and pulmonology at the University of Utah, Salt Lake City.

A. CHRISTIE NELSON, PharmD, is a clinical assistant professor of pharmacy practice at the University of Wyoming School of Pharmacy. Dr. Nelson received her pharmacy degree from the University of New Mexico, Albuquerque, and completed an infectious disease pharmacotherapy specialty residency at the University of New Mexico Hospital, Albuquerque.

BRADFORD T. WINSLOW, MD, FAAFP, is residency director of the Swedish Family Medicine Residency Program, and is assistant professor of family medicine at the University of Colorado–Denver in Aurora. Dr. Winslow received his medical degree from the University of North Carolina at Chapel Hill, and completed a residency in family medicine at the University of Colorado Health Sciences Center, Denver.

KATHRYN LEE SPRINGER, MD, is a consultant in infectious diseases in Denver. She received her medical degree from the University of North Carolina at Chapel Hill, and completed a residency in internal medicine at Dartmouth-Hitchcock Medical Center in Lebanon, N.H., and a fellowship in infectious diseases at the University of Colorado Health Sciences Center, Denver.

Address correspondence to Kyle Mills, PharmD, BCPS, Swedish Medical Center, 501 E. Hampden Ave., #3260, Englewood, CO 80113 (e-mail: kmills1@uwyo.edu). Reprints are not available from the authors.

Author disclosure: Nothing to disclose.

REFERENCES

1. Mylotte JM. Nursing home-acquired pneumonia. *Clin Infect Dis*. 2002; 35(10):1205-1211.
2. Mehr DR, et al. Predicting mortality in nursing home residents with lower respiratory tract infection: the Missouri LRI study. *JAMA*. 2001;286(19):2427-2436.
3. Muder RR, et al. Pneumonia in a long-term care facility. A prospective study of outcome. *Arch Intern Med*. 1996;156(20):2365-2370.
4. Houston MS, et al. Risk factors for 30-day mortality in elderly patients with lower respiratory tract infection. Community-based study. *Arch Intern Med*. 1997;157(19):2190-2195.
5. El-Solh AA, et al. Etiology of severe pneumonia in the very elderly. *Am J Respir Crit Care Med*. 2001;163(3 pt 1):645-651.
6. El-Solh AA, et al. Microbiology of severe aspiration pneumonia in institutionalized elderly. *Am J Respir Crit Care Med*. 2003;167(12):1650-1654.
7. American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171(4):388-416.
8. Loeb M. Pneumonia in older persons. *Clin Infect Dis*. 2003;37(10): 1335-1339.
9. Furman CD, et al. Pneumonia in older residents of long-term care facilities. *Am Fam Physician*. 2004;70(8):1495-1500.
10. Mylotte JM. Nursing home-acquired pneumonia: update on treatment options. *Drugs Aging*. 2006;23(5):377-390.
11. El-Solh AA, et al. Indicators of potentially drug-resistant bacteria in severe nursing home-acquired pneumonia. *Clin Infect Dis*. 2004;39(4):474-480.
12. Muder RR. Pneumonia in residents of long-term care facilities: epidemiology, etiology, management, and prevention. *Am J Med*. 1998; 105(4):319-330.
13. Ellis SE, et al. Influenza- and respiratory syncytial virus-associated morbidity and mortality in the nursing home population. *J Am Geriatr Soc*. 2003;51(6):761-767.

14. Falsey AR, et al. Respiratory syncytial virus infection in elderly adults. *Drugs Aging*. 2005;22(7):577-587.
15. Brundage JF. Interactions between influenza and bacterial respiratory pathogens: implications for pandemic preparedness. *Lancet Infect Dis*. 2006;6(5):303-312.
16. Boivin G, et al. An outbreak of severe respiratory tract infection due to human metapneumovirus in a long-term care facility. *Clin Infect Dis*. 2007;44(9):1152-1158.
17. Marrie TJ, et al. Community-acquired pneumonia requiring hospitalization. Is it different in the elderly? *J Am Geriatr Soc*. 1985;33(10):671-680.
18. Mehr DR, et al. Clinical findings associated with radiographic pneumonia in nursing home residents. *J Fam Pract*. 2001;50(11):931-937.
19. Medina-Walpole AM, et al. Provider practice patterns in nursing home-acquired pneumonia. *J Am Geriatr Soc*. 1998;46(2):187-192.
20. Mylotte JM, et al. Validation and application of the pneumonia prognosis index to nursing home residents with pneumonia. *J Am Geriatr Soc*. 1998;46(12):1538-1544.
21. Mandell LA, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44(suppl 2): S27-S72.
22. Domínguez J, et al. Detection of *Streptococcus pneumoniae* antigen by a rapid immunochromatographic assay in urine samples. *Chest*. 2001;119(1):243-249.
23. Gutíerrez F, et al. Evaluation of the immunochromatographic Binax NOW assay for detection of *Streptococcus pneumoniae* urinary antigen in a prospective study of community-acquired pneumonia in Spain. *Clin Infect Dis*. 2003;36(3):286-292.
24. Murdoch DR, et al. Evaluation of a rapid immunochromatographic test for detection of *Streptococcus pneumoniae* antigen in urine samples from adults with community-acquired pneumonia. *J Clin Microbiol*. 2001;39(10):3495-3498.
25. Benson RF, et al. Evaluation of the Binax and Biotest urinary antigen kits for detection of Legionnaires' disease due to multiple serogroups and species of *Legionella*. *J Clin Microbiol*. 2000;38(7):2763-2765.
26. Murdoch DR. Diagnosis of *Legionella* infection. *Clin Infect Dis*. 2003;36(1):64-69.
27. Marik PE. Aspiration pneumonitis and aspiration pneumonia. *N Engl J Med*. 2001;344(9):665-671.
28. Mylotte JM, et al. Pneumonia versus aspiration pneumonitis in nursing home residents: prospective application of a clinical algorithm. *J Am Geriatr Soc*. 2005;53(5):755-761.
29. Hutt E, et al. Evidence-based guidelines for management of nursing home-acquired pneumonia. *J Fam Pract*. 2002;51(8):709-716.
30. Mandell LA, et al., for the Infectious Diseases Society of America. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. *Clin Infect Dis*. 2003;37(11):1405-1433.
31. Naughton BJ, et al. Treatment guideline for nursing home-acquired pneumonia based on community practice. *J Am Geriatr Soc*. 2000; 48(1):82-88.
32. Paladino JA, et al. Once-daily cefepime versus ceftriaxone for nursing home-acquired pneumonia. *J Am Geriatr Soc*. 2007;55(5):651-657.
33. Centers for Disease Control and Prevention. Summary: interim recommendations for the use of influenza antiviral medications in the setting of oseltamivir resistance among circulating influenza A (H1N1) viruses, 2008-09 influenza season. http://www.cdc.gov/flu/professionals/antivirals/summary.htm. Accessed April 15, 2009.
34. Smith NM, et al. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP) [published correction appears in *MMWR Morb Mortal Wkly Rep*. 2006;55(29):800]. *MMWR Recomm Rep*. 2006;55(RR-10):1-42.
35. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 1997;46(RR-8):1-24.
36. Lee K, et al. Viral & atypical pneumonia. In: Hanley ME, Welsh CH. *Current Diagnosis and Treatment in Pulmonary Medicine*. New York, NY: Lange Medical Books/McGraw-Hill; 2003:372-384.
37. Vanderkooi OG, et al., for the Toronto Invasive Bacterial Disease Network. Predicting antimicrobial resistance in invasive pneumococcal infections. *Clin Infect Dis*. 2005;40(9):1288-1297.
38. Viray M, et al. Longitudinal trends in antimicrobial susceptibilities across long-term-care facilities: emergence of fluoroquinolone resistance. *Infect Control Hosp Epidemiol*. 2005;26(1):56-62.
39. Trick WE, et al. Colonization of skilled-care facility residents with antimicrobial-resistant pathogens. *J Am Geriatr Soc*. 2001;49(3):270-276.
40. Drinka PJ, et al. Antimicrobial use and methicillin-resistant *Staphylococcus aureus* in a large nursing home. *J Am Med Dir Assoc*. 2004; 5(4):256-258.
41. Maclayton DO, et al. Pharmacologic treatment options for nosocomial pneumonia involving methicillin-resistant *Staphylococcus aureus*. *Ann Pharmacother*. 2007;41(2):235-244.
42. Arancibia F, et al. Community-acquired pneumonia due to gram-negative bacteria and *Pseudomonas aeruginosa:* incidence, risk, and prognosis. *Arch Intern Med*. 2002;162(16):1849-1858.
43. Yakovlev SV, et al. Ertapenem versus cefepime for initial empirical treatment of pneumonia acquired in skilled-care facilities or in hospitals outside the intensive care unit. *Eur J Clin Microbiol Infect Dis*. 2006;25(10):633-641.
44. Gleason PP, et al. Associations between initial antimicrobial therapy and medical outcomes for hospitalized elderly patients with pneumonia. *Arch Intern Med*. 1999;159(21):2562-2572.
45. Houck PM, et al. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. *Arch Intern Med*. 2004;164(6):637-644.
46. U.S. Dept. of Health and Human Services. Hospital process of care measures. http://www.hospitalcompare.hhs.gov/Hospital/Static/InformationForProfessionals_tabset.asp?activeTab=1&subtab=3# Pneumonia. Accessed December 10, 2008.
47. Marrie TJ, et al. Factors influencing in-hospital mortality in community-acquired pneumonia: a prospective study of patients not initially admitted to the ICU. *Chest*. 2005;127(4):1260-1270.
48. Benenson R, et al. Effects of a pneumonia clinical pathway on time to antibiotic treatment, length of stay, and mortality. *Acad Emerg Med*. 1999;6(12):1243-1248.
49. Pea F, et al. The antimicrobial therapy puzzle: could pharmacokinetic-pharmacodynamic relationships be helpful in addressing the issue of appropriate pneumonia treatment in critically ill patients? *Clin Infect Dis*. 2006;42(12):1764-1771.
50. Faulkner CM, et al. Unique aspects of antimicrobial use in older adults. *Clin Infect Dis*. 2005;40(7):997-1004.
51. Jeffres MN, et al. Predictors of mortality for methicillin-resistant *Staphylococcus aureus* health-care–associated pneumonia: specific evaluation of vancomycin pharmacokinetic indices. *Chest*. 2006;130(4):947-955.
52. Field TS, et al. Risk factors for adverse drug events among nursing home residents. *Arch Intern Med*. 2001;161(13):1629-1634.
53. Kaufman DW, et al. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. *JAMA*. 2002;287(3):337-344.
54. Nguyen JK, Fouts MM, Kotabe SE, Lo E. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. *Am J Geriatr Pharmacother*. 2006;4(1):36-41.