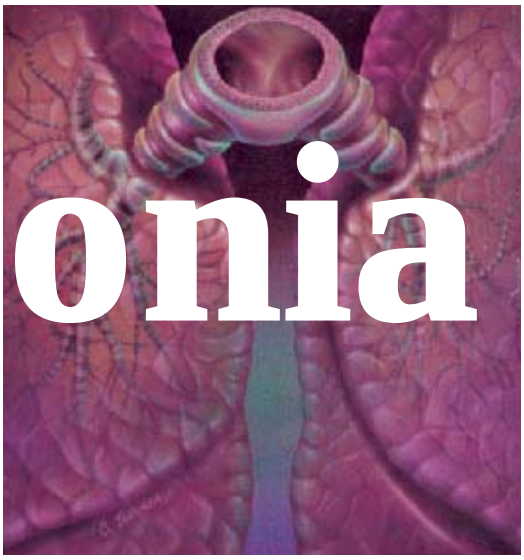
Answering Questions About Community-Acquired Pneumonia



By Thomas J. Marrie, MD

Community-acquired pneumonia (CAP) is a common illness with significant morbidity and mortality.[1,2] There is considerable variation in its management.[3,4] From one hospital to another, there is variation in the admission rate, length of stay and antibiotics used. This article is written in a question and answer format. The questions are those that, as an infectious diseases physician, the author has had to answer most often.

What Are the Most Common Micro-organisms Responsible for CAP?

Over 100 micro-organisms have been implicated in the etiology of CAP, but most cases are caused by *Streptococcus pneumoniae* (Table 1).[5-9] Table 1 also gives data on the micro-organisms that cause pneumonia among people infected with the human immunodeficiency virus (HIV). With the introduction of highly active antiretroviral therapy (HAART) in 1996 and prophylaxis against *Pneumocystis carinii* and *Mycobacterium avium* complex, the rate of pneumonia due to these pathogens has declined. Physicians should not forget, however, that *P. carinii* pneumonia can still be the presenting manifestation of HIV infection.

Clues to the etiology of the pneumonia can be gained from the history (Table 2). Some etiologic diagnoses should trigger other investigations: for example, bacteremic pneumococcal pneumonia in a male under the age of 45 should trigger a discussion regarding testing for HIV infection. In this age group the rate of bacteremic pneumococcal pneumonia is 41 times higher among HIV-infected people

than it is among those who are not infected with HIV. Isolation of *Legionella pneumophila* should result in notification of the public health authorities so they can look for a source of this micro-organism. Of course, once a person is diagnosed as having pulmonary tuberculosis, contact tracing is necessary.

Who Needs To Be Admitted To Hospital for CAP Treatment?

Quick Facts

- There is considerable variation in the management of community-acquired pneumonia (CAP). From one hospital to another, there is variation in the admission rate, length of stay and antibiotics used.
- With the introduction of highly active antiretroviral therapy (HAART) in 1996 and the prophylaxis against *Pneumocystis carinii* and *Mycobacterium avium* complex, the rate of pneumonia due to these pathogens has declined. Physicians should not forget, however, that *P. carinii* pneumonia can still be the presenting manifestation of human immunodeficiency virus (HIV) infection.
- The evaluation of a pneumonia patient consists of an assessment of the severity of the case and using this information to help decide the optimal site of care.

Dr. Marrie is professor and chair, department of medicine, University of Alberta, Edmonton. His area of medical interest is pneumonia.

The evaluation of a pneumonia patient consists of assessing the severity of the case and using this information to help decide the optimal site of care (*i.e.,* Home, hospital [intensive care unit or ward]. For residents of a long-term care facility, the decision must be made whether to treat the patient in the facility or transfer the patient to hospital).

A number of pneumonia-specific severity-of-illness scoring systems have been developed (Tables 3, 4 and 5).[10] The pneumonia-specific severity of illness scoring system developed by Fine *et al* predicts mortality.[11] This system also has been used to guide the admission decision (*i.e.,* all patients in classes I to III can be treated on an ambulatory basis, while those who fall into classes IV and V should be admitted). This scoring system is complex and requires a modest amount of laboratory testing. It should be useful in emergency rooms, where the elements that constitute the score can be maintained on a computer.

The British Thoracic Society rule is the simplest and, while it accurately predicts pneumonia severity, it is only useful for those with the most severe illnesses (Table 4). It is really more of a guide for who to admit to an intensive care unit. More recently, Finnish investigators noted that acute aggravation of a co-existing illness (such as impairment of glucose balance in diabetics or deterioration of congestive heart failure), a respiratory rate of at least 25 breaths per minute (bpm) and a C-reactive protein level of at least 100 were all predictive of mortality. If one or more of these factors was present, the mortality rate was 2.2%, while if all three were present, it was 20%. Table 5 pre-

sents criteria that can be used to decide who should be transferred from a nursing home to a hospital for the treatment of pneumonia.

Although helpful, these scoring systems are never a substitute for a physician's judgment. It is noteworthy that a study designed to elucidate how physicians decided on the site of care for patients with pneumonia found the most common reason given for admitting a patient to hospital was that he/she looked sick. The problem with this approach is it involves a great deal of inter-observer variability. By compiling key features from a number of severity-of-illness scoring systems, the author's recommendations are given in Table 6.

Does Influenza Vaccine Prevent Pneumonia?

The short answer is 'yes.' A systematic review (published in 1995) of the effectiveness of influenza vaccine identified 20 cohort studies.[12] The pooled estimate for preventing pneumonia was an absolute risk reduction of 0.53 (95% confidence interval [CI], 0.35 to 0.66) and for preventing death 0.68 (95% CI, 0.56 to 0.76). Analysis of data from an administrative database of over 25,000 people aged 64 or over suggests that influenza vaccination reduced the rate of admission to hospital for pneumonia and influenza by 48% to 57% ($P < 0.01$).[13]

In Which Patients Should I Use One of the Newer Fluoroquinolones?

The Infectious Diseases Society of America and the Canadian Infectious Diseases Society have recently published guidelines for the treatment of CAP.[14,15] For patients requiring admission to a hospital ward, a respiratory quinolone (*i.e.*, levofloxacin, moxifloxacin, gatifloxacin) alone or a macrolide plus a second- or third-generation cephalosporin is recommended.[14,15] For those who require admission to an intensive care unit, the recommended treatment is

Table 1

The Most Common Micro-organisms That Cause CAP

Micro-organism	United States (% of patients)*	HIV positive (% of patients)**	Susceptibility†
Streptococcus pneumoniae	20 to 60	7	20% resistant to penicillin, 1% to 2% resistant to quinolones
Hemophilus influenzae	3 to 10	4 to 18	30% ampicillin resistant, sensitive to cephalosporins or amoxycillin/clavulanic acid
Staphylococcus aureus	3 to 5	1 to 13	Methicillin-resistant *S. aureus* rare as cause of CAP
Chlamydia pneumoniae	4 to 6	—	Sensitive to macrolides, tetracyclines, quinolones
Mycoplasma pneumoniae	1 to 6	—	Sensitive to macrolides, tetracyclines, quinolones
Legionella pneumophila	2 to 8	2 to 8	Sensitive to macrolides, tetracyclines, quinolones
Gram-negative bacilli	3 to 10	Late in the disease, 6	
Aspiration	6 to 10	3	
Pneumocystis carinii	—	Up to 30	
Viruses	2 to 15	5 (CMV)	
Mycobacterium avium complex	—	5 (less now with prophylaxis)	

**Pooled data from 16 published reports from North America, adapted from:*
Bartlett JG, Mundy LM: Community-acquired pneumonia. N Engl J Med 1995; 333:1618–24; and
Park DR, Sherbin VL, Goodman MS, et al, for the Harborview CAP study group: The etiology of community-acquired pneumonia at an urban public hospital: Influence of human immunodeficiency virus infection and initial severity of illness. J Infect Dis 2001; 184:268-97.
***Information adapted from:*
Park DR, Sherbin VL, Goodman MS, et al, for the Harborview CAP study group: The etiology of community-acquired pneumonia at an urban public hospital: Influence of human immunodeficiency virus infection and initial severity of illness. J Infect Dis 2001; 184:268-97.
Hirschtick RE, Glassroth J, Joradan MC, et al: Bacterial pneumonia in persons infected with the human immunodeficiency virus. N Engl J Med 1995; 333:845-51.
Falco V, deSevilla TF, Alegre, et al: Bacterial pneumonia in HIV-infected patients: A prospective study of 68 patients. Eur Respir J 1994; 7:235-9.
Touchie C, Marrie TJ: Comparison of community-acquired pneumonia requiring admission to hospital in HIV and non-HIV infected patients. Can J Infect Dis 1996; 7:253-8.
†Susceptibility data from recent studies

Table 2

Clues To the Etiology of Pneumonia from the History of Present Illness

Factor	Possible agent(s)
Travel	
Southeast Asia	*Burkholderia pseudomallei* (melioidosis); *Mycobacterium tuberculosis*
Many countries	*M. tuberculosis*
Arizona, parts of California	*Coccidioides immitis*
Occupational history	
Health-care workers	*M. tuberculosis,* acute HIV seroconversion with pneumonia (if recent needlestick injury from an HIV-positive patient)
Veterinarian, farmer, abattoir worker	*Coxiella burnetii*
Host factor	
Diabetic ketoacidosis	*Streptococcus pneumoniae, Staphylococcus aureus*
Alcoholism	*S. pneumoniae, Kelbsiella pneumoniae, S. aureus,* oral anaerobes, *Acinetobacter spp*
Chronic obstructive lung disease	*S. pneumoniae, Hemophilus influenzae, Moraxella catarrhalis*
Solid organ transplant recipient (pneumonia occurring more than three months after transplant)	*S. pneumoniae, H. influenzae, Legionella* species, *Pneumocystis carinii, cytomegalovirus, Strongyloides stercoralis*
Sickle cell disease	*S. pneumoniae*
HIV infection and CD4 cell count of less than 200/µL	*S. pneumoniae, P. carinii, H. influenzae, Cryptococcus neoformans, M. tuberculosis, Rhodococcus equi*
Dementia, stroke, altered level of consciousness	Aspiration pneumonitis
Structural lung disease (bronchiectasis)	*Pseudomonas aeruginosa*
Environmental factor	
Exposure to: contaminated air-conditioning, cooling towers, hot tub, recent travel stay in a hotel, exposure to grocery store mist machine, or visit to/recent stay in a hospital with contaminated (by *Legionellaceae*) drinking water	*Legionella pneumophila* or other *Legionellaceae*
Exposure to mouse droppings in an endemic area	Hantavirus
Pneumonia after windstorm in an area of endemicity	*C. immitis*

cont'd on p.56

Table 2 (cont'd)

Clues To the Etiology of Pneumonia from the History of Present Illness

Factor	Possible agent(s)
Environmental factor	
Outbreak of pneumonia in shelter for homeless men or jail	*S. pneumoniae, M. tuberculosis*
Outbreak of pneumonia occurs in military training camp	*S. pneumoniae, Chlamydia pneumoniae,* Adenovirus
Outbreak of pneumonia in a nursing home	*C. pneumoniae, S. pneumoniae,* Respiratory syncytial virus, Influenza A virus; *M. tuberculosis*
Pneumonia associated with mowing a lawn in an endemic area	*Francisella tularensis*
Exposure to bats, excavation or residence in an endemic area (Ohio and Mississippi River valleys)	*Histoplasma capsulatum*
Exposure to parturient cats in an endemic area	*C. burnetii*
Sleeping in a rose garden	*Sporothrix shenkii*
Camping, cutting down trees in an endemic area	*Blastomyces dermatiditis*

erythromycin or azithromycin, or a fluoroquinolone with enhanced activity against *S. pneumoniae* plus cefotaxime, ceftriaxone or a beta-lactamase inhibitor.[14] Data from two studies (one a retrospective review of 12,945 Medicare inpatients with CAP, the other an observational study of 2,963 patients with CAP) indicate initial treatment with a second-generation cephalosporin plus a macrolide, or a non-pseudomonal third-generation cephalosporin plus a macrolide, or a fluoroquinolone alone, was independently associated with lower 30-day mortality.[16,17] Treatments with a beta-lactam/beta-lactamase inhibitor plus macrolide, or with an aminoglycoside plus another agent, were associated with 30-day mortality. These studies, even though they are retrospective reviews, show for the first time, that the type of initial antibiotic therapy does make a difference.

The respiratory quinolones seem like ideal choices for the treatment of CAP since they are active against most of the microbial causes of pneumonia, including: penicillin-susceptible and penicillin-resistant *S. pneumoniae, H. influenzae, M. catarrhalis, S. aureus, Mycoplasma pneumoniae, Legionella spp* and *Chlamydia pneumoniae.* A study by File *et al* found levofloxacin and, by inference, other respiratory quinolones were superior to ceftriaxone/cefuroxime for the treatment of mild-to-moderately severe CAP.[18] There is concern, however, that the widespread use of the respiratory fluoroquinolones will lead to the emergence of resistance among these respiratory pathogens. Indeed, Chen *et al* found that 2.9% of *S. pneumoniae* isolates from adults were resistant to ciprofloxacin and 4.1% of isolates with high-level penicillin resistance also were ciprofloxacin resistance.[19]

Table 3

Severity of Nursing Home Pneumonia Scoring System

Condition	Points
Respiratory rate greater than 30 bpm	2
Pulse rate higher than 125 bpm	1
Altered mental status	1
Dementia	1

No. of points	Mortality (%)
0	7.4
1	10.3
2	26.1
3	37.5
4	56.3
5	80.0

Adapted from: Fine MJ, Auble TE, Yealy DM, et al: A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997; 336:243-50.

Table 4

British Thoracic Society Rule For Severity of CAP

If two or more of the factors below are present, the pneumonia is severe and the patient is likely to require admission to an intensive care unit:

- Respiratory rate greater than 30 bpm
- Diastolic blood pressure lower than 60 mmHg
- Blood urea nitrogen level higher than 7 mm/L

For this reason, the Centers for Disease Control (CDC) working group on the management of CAP in the era of pneumococcal resistance recommended macrolides or doxycycline as first-line therapies for the management of ambulatory pneumonia. The

CDC also recommended the new fluoroquinolones should be reserved for adults who:

- Have already failed one of the first-line drugs;
- Are allergic to the first-line drugs; or
- Have documented infection with highly drug resistant pneumococci.[20]

The CDC group recommends that, for moderately ill people hospitalized with CAP, first-line treatment should be with a parenteral beta-lactam antibiotic, such as cefuroxime, cefotaxime, ceftriaxone or a combination of ampicillin sodium and sulbactam sodium (not available in Canada) and a macrolide, such as erythromycin, azithromycin or clarithromycin.[20] The author's observations indicate patients with chronic obstructive lung disease, who have had multiple courses of fluoroquinolones (especially ciprofloxacin), are most likely to have *S. pneumoniae* resistance to quinolones when they present with pneumonia. Hence, the author recommends that such patients be treated empirically with a beta lactam antibiotic plus a macrolide.

Currently, there are no clinical trial data that indicate one of the newer fluoroquinolones is superior to another. There are many studies comparing the activity of these agents against common respiratory pathogens and combining these data with pharmacokinetic data to try and predict which agent might be superior.

When Should I Suspect Legionnaires' Disease or Q Fever?

Legionnaires' disease is an acute infectious disease of which the predominant manifestation is pneumonia.[21] The most common cause is *Legionella pneumophila* serogroup 1, however, just under half of the over 40 recognized species in the *Legionellaceae* family can cause Legionnaires' disease.[22] Mulazionoglu and Yu reviewed 14 studies of the etiology of CAP to determine clinical features that would distinguish Legionnaires' disease from other causes of pneumonia.[23] They included only studies that used culture methods to diagnose *Legionella* infection and excluded studies that relied only on serology.

They found that headache, diarrhea, neurologic symptoms (especially confusion), fever higher than 39 C, hyponatremia, elevated creatinine phosphokinase and abnormal liver function tests were the most consistent in distinguishing Legionnaires' disease from other etiologies of CAP. If any of the above are present and there is an appropriate epidemiologic history (*i.e.,* exposure to contaminated water aerosols [cooling towers, decorative fountains, hot tubs, visiting a hospital or a country in which there is an outbreak of Legionella infections]), your suspicion that you are dealing with Legionnaires' disease should be high. Legionnaires' disease frequently causes rapidly progressive pneumonia with a substantial mortality rate.

Q fever is a zoonosis with worldwide distribution.[24] New Zealand is the only country free of the disease. Q fever is due to infection with *Coxiella burnetii.* Due

Table 5

Criteria for Treatment of Pneumonia in a Nursing Home

- Respiratory rate lower than 30 bpm.
- Oxygen saturation of at least 92% while breathing room air.
- Pulse rate lower than 90 bpm.
- Temperature 36.5 C to 38.1 C.
- Systolic and diastolic blood pressure within 10 mmHg of usual readings.
- No feeding tube present.
- Conscious.
- Severity of pneumonia score 2.0 or less (Table 3).
- Availability of medical and nursing care.
- Wishes of patient and family.

Table 6

Criteria for Hospital Admission due to CAP

Admit if any of these are present in an adult with CAP:

- Respiratory rate higher than 28 bpm.
- Systolic blood pressure lower than 90 mmHg or 30 mmHg lower than baseline.
- Confusion or impaired level of consciousness.
- Hypoxemia — $p0_2$ less than 60 torr while breathing room air or an oxygen saturation of less than 90%.
- Unstable comorbid illness (*i.e.,* decompensated congestive heart failure or uncontrolled diabetes mellitus).
- Multilobar pneumonia.
- Pleural effusion.

torr = mmHg pressure

to its nonspecific presentation, *C. burnetii* often goes unrecognized so the true prevalence of disease is unknown. The most common reservoirs for infection in humans are cats and domestic farm animals, such as cattle, goats and sheep. *C. burnetii* localizes in the uterus and mammary glands of infected animals and is shed in the urine, feces and milk. It is found in particularly high concentrations in the placenta and amniotic fluid (10^9 organisms/g of placental tissue). Infection in humans follows inhalation of aerosol containing *C. burnetii.*

The manifestations of infection often are nonspecific and can be asymptomatic or manifest as a self-limiting febrile illness, pneumonia, hepatitis or overlapping clinical syndrome. Patients often present with a severe headache, which is a clinical clue to the diagnosis. Mild elevations of liver transaminases are common. Pneumonia can be rapidly progressive, atypical or present as fever without pulmonary symptoms. In a patient who has had exposure to a parturient cat, goat, sheep or cow within the past three weeks, and presents with pneumonia, Q fever should be suspected. Multiple round nodules may be present on chest radiograph, although segmental, subsegmental or lobar opacities also may be found.[24] CME

References

1. Koivula I, Stenn M, Makela PH: Risk factors for pneumonia in the elderly. Am J Med 1994; 96:313-20.
2. National Centre for Health Statistics: National hospital discharge survey: Annual summary 1990:Vital Health Statistics 1992; 13:1-225.
3. Fine MJ, Hough LJ, Medsger AR, et al: The hospital admission decision for patients with community-acquired pneumonia. Arch Intern Med 1997; 157:36-44.
4. Fine MJ, Medsger AR, Stone RA, et al: The hospital discharge decision for patients with community-acquired pneumonia. Arch Intern Med 1997; 157:47-56.
5. Bartlett JG, Mundy LM: Community-acquired pneumonia. N Engl J Med 1995; 333:1618-24.
6. Park DR, Sherbin VL, Goodman MS, et al, for the Harborview CAP study group: The etiology of community-acquired pneumonia at an urban public hospital: Influence of human immunodeficiency virus infection and initial severity of illness. J Infect Dis 2001; 184:268-97.
7. Hirschtick RE, Glassroth J, Joradan MC, et al: Bacterial pneumonia in persons infected with the human immunodeficiency virus. N Engl J Med 1995; 333:845-51.
8. Falco V, Fernandez de Sevilla T, Alegre J, et al: Bacterial pneumonia in HIV-infected patients: A prospective study of 68 episodes. Eur Respir J 1994; 7(2):235-9.
9. Touchie C, Marrie TJ: Comparison of community-acquired pneumonia requiring admission to hospital in HIV and non-HIV infected patients. Can J Infect Dis 1996; 7:253-8.
10. Fine MJ, Auble TE, Yealy DM, et al: A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997; 336:243-50.
11. Naughton BJ, Mylotte JM, Tayara A: Outcome of nursing home-acquired pneumonia: Derivation and application of a practical model to predict 30 day mortality. J Am Geriatr Soc 2000; 48: 1292-9.
12. Gross PA, Hermogenes AW, Sacks HS, et al: The efficacy of influenza vaccine in elderly persons: A meta-analysis and review of the literature. Ann Intern Med 1995; 123:518–27.
13. Nichol KL, Margolis KL, Wuorenma J, et al: The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. N Engl J Med 1994; 31:778-4.
14. Bartlett JG, Dowell SF, Mandell LA, et al: Practice guidelines for the management of community-acquired pneumonia in adults. Clin Infect Dis 2000; 31:347-82.
15. Mandell LA, Marrie TJ, Grossman RF, et al, and the Canadian Community-Acquired Pneumonia Working Group: Canadian guidelines for the initial management of community-acquired pneumonia: An evidence-based update by the Canadian Infectious Diseases Society and the Canadian Thoracic Society. Clin Infect Dis 2000; 31:383-421.
16. Gleason PP, Meehan TP, Fine JM, et al: Associations between initial antimicrobial therapy and medical outcomes for hospitalized elderly patients with pneumonia. Arch Intern Med 1999; 159:2562-72.
17. Dudas V, Hopefl A, Jacobs R, et al: Antimicrobial selection for hospitalized patients with presumed community-acquired pneumonia: A survey of nonteaching US community hospitals. Ann Pharmacother 2000; 34:446-52.
18. File TM Jr, Serati J, Dunbar L, et al: A multicenter, randomized study comparing the efficacy and safety of intravenous and/or oral levofloxacin versus ceftriaxone and/or cefuroxime axetil in treatment of adults with community-acquired pneumonia. Antimicrobial Agents Chemother 1997; 41:1965-72.
19. Chen DK, McGeer A, De Azavedo JC, et al: Decreased susceptibility of Streptococcus pneumoniae to fluoroquinolones in Canada. N Engl J Med 1999; 341:233-9.
20. Heffelfinger JD, Dowell SF, Jorgensen JH, et al: Management of community-acquired pneumonia in the era of pneumococcal resistance. A report from the drug-resistant Streptococcus pneumoniae therapeutic working group. Arch Intern Med 2000; 160:1399-1408.
21. Edelstein PH: Legionnaires' disease. Clin Infect Dis 1993; 16:741-9.
22. Dedicoat M, Venkatesan P: The treatment of Legionniares' disease. J Antimicrob Agents Chemotherapy 1999; 43:747-52.
23. Mulazimoglu L, Yu VL: Can Legionnaires' disease be diagnosed by clinical criteria. A Critical Review. Chest 2002 [in press].
24. Marrie TJ, Raoult D: Q fever-a review and issues for the next century. Int J Antimicrob Agents 1997; 8:145-61.