Epidemiology of community-acquired pneumonia

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Community-acquired pneumonia (CAP) is a common and a serious illness. *Streptococcus pneumoniae* accounts for about half of all cases of CAP. Atypical pneumonia, ie, pneumonia due to *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella* species or viruses, is more common among patients treated on an ambulatory basis where these pathogens can collectively cause up to half of all cases of pneumonia. Changes in patient and microbe populations alter the epidemiology of pneumonia. Aspiration and Gram-negative rod pneumonia tend to be more common in nursing home populations. The emergence of macrolide- and beta-lactam-resistant *S pneumoniae* has major implications for the approach to patients with CAP.

Key Words: Community-acquired pneumonia, Epidemiology

Épidémiologie de la pneumonie extra-hospitalière

La pneumonie extra-hospitalière (PEH) est une maladie fréquente et grave, due à *Streptococcus pneumoniae* pour presque la moitié de l'ensemble des cas. Les pneumonies atypiques, pneumonies causées par *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, des espèces de *Legionella* ou des virus se rencontrent plus fréquemment chez les patients traités sur une base externe. En effet, ces pathogènes peuvent collectivement causer près de la moitié de tous les cas de pneumonie. Les modifications dans les populations de patients et de bactéries modifient l'épidémiologie de la pneumonie. Les pneumonies à bacilles gram-négatifs et celles dues à des aspirations semblent être plus fréquentes dans les populations des centres d'accueil. L'émergence de la résistance de *S. pneumoniae* aux macrolides et aux bêta-lactamines a des implications substantielles pour ce qui est de l'approche du traitement des patients atteints d'une PEH.

There are three to four million cases of community-acquired pneumonia (CAP) per year in the United States, with about 3.5 million patients receiving treatment on an ambulatory basis (1). Pneumonia is the fifth leading cause of death, and the costs associated with the diagnosis and management of pneumonia are estimated to be several billion US dollars per year.

Pneumonia used to be a simple entity diagnostically but was a very difficult problem therapeutically. In 1938, *Streptococcus pneumoniae* accounted for almost all cases of CAP. Unfortunately, there was no specific therapy. In the present decade, the situation is reversed. Specific therapy is available for almost every microbial cause of pneumonia, but it is difficult to make an etiological diagnosis. Many causes of CAP

have been identified, but in 30 % to 40% of cases the etiology remains unknown (2,3). To further complicate matters, the population at risk for CAP has changed. The portion of the population 65 years of age or older is the fastest growing population (4). Among other things, this has led to a new nosological entity – nursing home-acquired pneumonia. The explosion of infection due to human immunodeficiency virus (HIV) (5) and the success of organ transplantation, with its attendant need for ongoing immunosuppression, has led to an increasingly larger number of immunocompromised individuals in the general population. Health care economics (ie, the pressure on the health care system to do more with less) has led to treating more patients at home than in the past. In a recent study (January 1995 to August 1995) in which all pa-

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TABLE 1
Rank order of etiological agents in patients with community-acquired pneumonia

1. *Streptococcus pneumoniae*
2. *Mycoplasma pneumoniae*
3. *Chlamydia pneumoniae*
4. *Haemophilus influenzae*
5. Aerobic Gram-negative bacilli*
6. *Staphylococcus aureus*
7. *Legionella* species
8. *Pneumocystis carinii*
9. *Mycobacterium tuberculosis*
10. *Moraxella catarrhalis*

**Escherichia coli*, *Klebsiella* species, *Serratia* species, *Proteus* species, *Providencia* species, *Enterobacter* species and *Pseudomonas aeruginosa*. Data adapted from reference 30

tients with CAP admitted to Victoria General Hospital for discharge on day 3 were assessed, the author found that only 10% (14/140) fit the definition of medical stability for discharge (unpublished data). Despite the fact that most patients with CAP are treated as out-patients, CAP patients have not been studied frequently. Macfarlane (6) found only 12 studies that considered out-patients with pneumonia in any manner, and most of these studies had deficits in design.

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Incidence: The attack rates for CAP are highest in patients at extreme ages (6-10). Foy et al (7) found that the overall attack rate of pneumonia was 12/1000 persons in a study of 180,000 individuals in the 1960s and 1970s. For those aged four years or younger, it was 12/1000 to 18/1000 persons, while it was 1/1000 to 5/1000 persons for the age group five to 60 years. Macfarlane (6) found that the yearly incidence of pneumonia in adults was one to three cases per 1000 adults in a study carried out in England. Studies focusing on pneumonia due to specific microbial agents suggest that the rate for pneumococcal pneumonia is 37.5 cases per 100,000 individuals per year (8). The hospitalization rate for pneumonia ranges from 17% (11) to 35% (unpublished data) for those patients seen in their physicians' offices and 50% for those seen in an emergency room (12).

Etiology: Patients with CAP requiring admission to hospital have been studied extensively (2,3,8,12-27). The results of two recent studies were remarkably similar (2,3). One-third to almost one-half of the cases were of unknown etiology. From its dominant position six decades ago, *S pneumoniae* now causes a mere 8% to 10% of CAP requiring hospitalization. While a large number of the pneumonia cases of unknown etiology can be attributed to inadequate diagnostic studies (eg, respiratory secretions not available for culture), it is likely that there are still agents that are causing pneumonia that have not been discovered or that new agents will emerge as changes occur in the population at risk. This thesis is substantiated by the findings of Ortqvist et al (28), who were unable to make an etiological

diagnosis in five of 24 (21%) patients with CAP despite bronchoscopy and serological studies in all patients. However, using antibodies to *S pneumoniae* pneumolysin and pneumolysin immune complexes as a diagnostic tool for pneumococcal pneumonia, Kauppinen et al (29) found that *S pneumoniae* accounted for 55% of pneumonia cases. Table 1 summarizes the most common causes of CAP requiring admission to hospital. These data are from studies that examined 5225 cases of CAP (30).

There have been very few studies of the etiology of pneumonia in out-patients (31). In a study of 75 such patients, an etiological diagnosis by serological methods was made in 45% of cases (32). *Mycoplasma pneumoniae* accounted for 65% of the cases of known etiology and 29% of the cases overall. *Chlamydia pneumoniae* caused 5%, and *Legionella pneumophila* 3% of the cases overall. Other agents identified included influenza A (7%), *Coxiella burnetii* (3%) and adenovirus (3%). Thirty-five per cent of the 75 patients were hospitalized. The mortality rate was 4%. Similar results were obtained in a practitioner-based study in Switzerland (33). Fourteen of 161 (8.7%) patients required hospitalization. The overall mortality rate was 1.2%. No etiological diagnosis was made in 47% of cases. Agents implicated included the following: *S pneumoniae* (17 cases), *Haemophilus* species (two cases), *M catarrhalis* (one case), *Streptococcus* species (one case), *Legionella* species (three cases), *Chlamydia* species (nine cases), *M pneumoniae* (28 cases), *C burnetii* (three cases), influenza (19 cases) and other respiratory viruses (seven cases). Marrie TJ et al studied 149 ambulatory patients with CAP using serological methods (34). The authors were able to define an etiological agent in 41.7% of patients. *M pneumoniae* accounted for 22.8% of the cases (Table 2).

Comorbidity: Most patients who are hospitalized with pneumonia have one or more comorbidities. Such comorbidities are often age dependent. The mean number of comorbidities increased from 0.73 for those 30 years of age or younger to 2.75 for those in the age group 71 to 80 years (35). Alcoholism, chronic obstructive pulmonary disease, ischemic heart disease, malignancy, diabetes mellitus and neurological disease are all important in either predisposing to pneumonia (neurological disease resulting in aspiration) or influencing recovery from pneumonia (chronic obstructive pulmonary disease, ischemic heart disease, malignancy). In contrast, 59% of patients with CAP treated on an ambulatory basis had no comorbidity.

Outcome: Pneumonia is a serious illness. The overall mortality rate is 1% to 3%. For patients requiring hospitalization, the mortality varies from 6% to 24% depending on the selection criteria (2,3,12-31,36).

Host factors: There are many immunocompromised persons living in the community including patients with HIV infection and those receiving immunosuppressive medications to prevent transplanted organ rejection or to suppress an aberrant immune response. These individuals may develop pneumonia due to any one of the 100 different microbes that cause pneumonia in the immunocompetent host. In addition, *Pneumocystis carinii* and various fungi are also pathogens in this population. Despite prophylaxis for its prevention, *P carinii* is still an important

pathogen in patients with HIV infection. Furthermore, underlying disease (such as lymphoma recurrence) or pulmonary chemotherapeutic agents can also mimic pneumonia in some immunocompromised patients. Thus, an aggressive approach to diagnosis and therapy is necessary.

Organism factors: Penicillin-resistant *S pneumoniae* is now a world-wide problem. The risk factors for penicillin-resistant *S pneumoniae* infection are previous use of beta-lactam antibiotics, alcoholism and noninvasive disease (36). Clavo-Sanchez et al (36) defined invasive disease to mean isolation of *S pneumoniae* from a normally sterile site, eg, blood, pleural fluid; all other infections were termed noninvasive. In addition to the foregoing factors, age younger than five or older than 65 years is predictive of multidrug-resistant *S pneumoniae* (36).

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TABLE 2

Etiology of community-acquired pneumonia in 149 ambulatory patients

Agent	Number (%) of cases due to agent
Undetermined	72 (48.3)
<i>Mycoplasma pneumoniae</i>	34 (22.8)
<i>Chlamydia pneumoniae</i>	16 (10.7)
<i>M pneumoniae</i> and <i>C pneumoniae</i>	5 (3.4)
Influenza A	4 (2.7)
<i>Coxiella burnetii</i>	4 (2.7)
Adenovirus	3 (2.0)
Influenza B	3 (2.0)
Other*	3 (2.0)
<i>Chlamydia psittaci</i>	2 (1.3)
Adenovirus and influenza A	1 (0.7)
Influenza A and <i>C pneumoniae</i>	1 (0.7)
<i>Legionella</i> species	1 (0.7)

* Included are three patients with bacterial pneumonia caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Streptococcus viridans* plus *Veillonella* species. Data adapted from reference 34