Viral Infection in Adults Hospitalized With Community-Acquired Pneumonia*

Prevalence, Pathogens, and Presentation

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Background: **The potential role of respiratory viruses in the natural history of community-acquired pneumonia (CAP) in adults has not been well described since the advent of nucleic amplification tests (NATs).**

Methods: **From 2004 to 2006, adults with CAP who were admitted to five hospitals were prospectively enrolled in the study, and clinical data, cultures, serology, and nasopharyngeal swabs were obtained. NATs from swabs were tested for influenza, human metapneumovirus (hMPV), respiratory syncytial virus (RSV), rhinovirus, parainfluenza virus 1–4, coronaviruses (OC43, 229E, and NL63), and adenovirus.**

Results: **A total of 193 patients were included; the median age was 71 years, 51% of patients were male, and 47% of patients had severe CAP. Overall, 75 patients (39%) had a pathogen identified. Of these pathogens, 29 were viruses (15%), 38 were bacteria (20%), 8 were mixed (4%), and the rest were "unknown." Influenza (n = 7), hMPV (n = 7), and RSV (n = 5) accounted for most viral infections; other infections included rhinovirus (n = 4), parainfluenza (n = 3), coronavirus (n = 4), and adenovirus (n = 2). *Streptococcus pneumoniae* was the most common bacterial infection (37%). Compared with bacterial infection, patients with viral infection were older (76 vs 64 years, respectively; p = 0.01), were more likely to have cardiac disease (66% vs 32%, respectively; p = 0.006), and were more frail (*eg*, 48% with limited ambulation vs 21% of bacterial infections; p = 0.02). There were few clinically meaningful differences in presentation and no differences in outcomes according to the presence or absence of viral infection.**

Conclusions: **Viral infections are common in adults with pneumonia. Easily transmissible viruses such as influenza, hMPV, and RSV were the most common, raising concerns about infection control. Routine testing for respiratory viruses may be warranted for adults who have been hospitalized with pneumonia.** ***(CHEST 2008; 134:1141–1148)***

Key words: community-acquired pneumonia; respiratory viruses

Abbreviations: CAP = community-acquired pneumonia; DFA = direct fluorescent antigen test; hMPV = human metapneumovirus; IQR = interquartile range; NAT = nucleic acid amplification test; NP = nasopharyngeal swab; PSI = pneumonia severity index; RSV = respiratory syncytial virus

Community-acquired pneumonia (CAP) is one of the most clinically important diseases in adults, affecting 5 to 20 per 1,000 adults per year.[1] Of these, at least 20 to 40% will require hospitalization for the treatment of their pneumonia.[2] CAP management guidelines[3] have been influenced by older CAP etiology studies,[4] which helped to direct empiric therapeutic antimicrobial choices for therapy against bacterial pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and "atypical" bacteria, including *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*, and *Legionella pneumophila*. Although CAP guidelines[3] acknowledge respiratory viruses as a "cause" of pneumonia, few recommendations are made regarding management, largely due to the paucity of data regarding prevalence, clinical presentation, and outcomes. Furthermore, viral etiology studies in pneumonia are difficult to interpret as noninvasive viral detection methods are often considered to be only markers of infection rather

than the cause of pneumonia.[5] Clearly, much better knowledge of the potential role of respiratory viruses present in patients with pneumonia is needed.

Most published studies[6,7] of respiratory viruses have relied on tests with relatively poor sensitivity such as serology and direct fluorescent antigen (DFA) tests. Such tests are limited in the sample type to which they can be applied and are not suitable for a broad range of respiratory viruses. More recently, the introduction of highly sensitive nucleic acid amplification tests (NATs) has dramatically improved our ability to detect multiple viral pathogens such as influenza, respiratory syncytial virus (RSV), rhinovirus, parainfluenza, and adenovirus. Such tests can be undertaken using a small single sample of respiratory secretions with results available with rapid turnaround times.[7–12] In addition, these tests have allowed us to detect emerging respiratory viruses such as human metapneumovirus (hMPV) and coronaviruses, viruses that are difficult to grow in cell culture.[13–15] To date, there have been few studies[5,7,9–11,16,17] reported in patients with pneumonia using NATs to detect viral infection, and these studies have either not included clinical data[7,9,11] or have not tested for all potentially important respiratory viruses in a comprehensive manner.[10,17]

Better knowledge of the role of infection with respiratory viruses in adults with pneumonia may lead to better management. Thus, we performed a prospective study in consecutive adults who had been admitted to the hospital with CAP, and sought to describe their pathogens, clinical presentation, and outcomes.

Materials and Methods

From January 2004 to January 2006, consecutive adults (≥ 18 years of age) who had been admitted to five hospitals in Edmonton, AB, Canada, with CAP were enrolled in a prospective study of pneumonia. Patients were excluded from the study if they had received antibiotics or been hospitalized within the prior 2 weeks, were unable or unwilling to provide informed consent, or had the following conditions: immunocompromised (*ie*, had received > 10 mg of prednisone per day for > 1 month, other immunosuppressives, had cancer with recent chemotherapy, or had HIV with a CD4 count of < 250 cells/μL); tuberculosis; bronchiectasis; cystic fibrosis; or pregnancy. All patients gave written informed consent, and the Health Research Ethics Board of the University of Alberta approved the study. We did not record data on patients who were unable to provide consent or who did not meet the enrollment criteria.

Data Collection

Pneumonia was defined as an acute lower respiratory tract illness with two or more of the following symptoms or signs: cough; productive cough; fever; chills; dyspnea; pleuritic chest pain; crackles; and bronchial breathing plus an opacity or infiltrate seen on a chest radiograph that was interpreted as pneumonia by the treating physician. To characterize the severity of the pneumonia itself, we calculated the pneumonia severity index (PSI) using the methods of Fine et al.[18]

Clinical, radiographic, and laboratory data and short-term outcomes were collected by a trained research nurse; the nurse was masked to microbiology results at the time of data collection. Patients were followed up throughout their hospital stay until discharge.

Diagnostic Tests Undertaken

Routine blood culture, sputum specimens, nasopharyngeal (NP) swabs, and serum samples were processed for each patient according to the study protocol. NP swabs that were submitted for the detection of viral pathogens first underwent DFA testing for influenza A and B, RSV, and parainfluenza virus 1–3 (Imagen; Dakocytomation Ltd; Ely, UK). In addition, expanded testing of NP samples was undertaken for a range of respiratory pathogens by NATs using extraction and amplification methods that have been described previously.[11] Briefly, NATs were designed to amplify and detect influenza A and B, hMPV, RSV, rhinovirus, parainfluenza 1–4, coronaviruses (OC43, 229E, and NL63), and adenoviruses. All the NATs utilized in this study have been published, and the assay parameters evaluated.[11,12,19,20] Laboratory validation of these assays confirmed a limit of detection of ≤ 100 copies (cloned target or synthetic RNA) or one or fewer tissue culture infectious dose of 50% (for culturable viruses). The specificity of all assays was confirmed using samples and spiked materials containing high loads of alternative respiratory pathogens. (Further details on viral NATs are available from J.D.F. on request [also see references 11, 12, 19, and 20].)

Bacterial infections were identified using standard laboratory protocols. Acute and convalescent serum samples were collected on the day of hospital admission and were repeated 4 to 6 weeks later. Serum samples were tested for the presence of *C pneu-*

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Dr. Majumdar was supported by the Alberta Heritage Foundation for Medical Research (Health Scholar) and the Canadian Institutes of Health Research (New Investigator). This project was funded in part by an establishment grant (to Dr. Marrie) from the Alberta Heritage Foundation for Medical Research.
Funding sources had no role in study design, data collection, data analysis or interpretation, or writing of the report. All authors participated in the study conception, design, analysis, interpretation of results, and revision of the manuscript, and approved the final version of the manuscript. Dr. Johnstone drafted the initial manuscript. Dr. Marrie acquired the data, obtained funding for the study, and will act as guarantor.
The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
Manuscript received April 1, 2008; revision accepted June 18, 2008.
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DOI: 10.1378/chest.08-0888

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