A Summer Outbreak of Human Metapneumovirus Infection in a Long-Term-Care Facility

Janice K. Louie,1 David P. Schnurr,1 Chao-Yang Pan,1 David Kiang,1 Connie Carter,2 Sandra Tougaw,2 Jean Ventura,2 Agnes Norman,2 Vivian Belmusto,2 Jon Rosenberg,1 and Glennah Trochet2

1California Department of Health Services, Richmond, and 2Sacramento County Public Health, Department of Health and Human Services, Sacramento, California

Human metapneumovirus (hMPV), a recently discovered paramyxovirus, is thought to be primarily a winter-spring pathogen affecting young children with a clinical presentation similar to that of respiratory syncytial virus. In June–July 2006, a respiratory outbreak in a long-term-care facility was reported to the local health department and investigated. Surveillance identified 26 residents and 13 staff with acute respiratory illness; 8 residents (31%) developed radiographically confirmed pneumonia, and 2 (5%) were hospitalized. Five of 14 respiratory specimens were positive by polymerase chain reaction assay for hMPV; sequencing identified genotype A. In institutionalized elderly persons, hMPV may be an important cause of respiratory outbreaks year-round.

Human metapneumovirus (hMPV) is a recently described virus in the Paramyxoviridae family [1]. Since its discovery in 2001, reports in the literature have suggested that hMPV can cause seasonal acute respiratory illnesses in individuals of all ages but predominantly in children [1, 2]. Similar to young children, frail elderly persons are often considered to be especially vulnerable to severe complications and increased morbidity and mortality from a variety of viral infections. To date, the epidemiology and clinical presentation of hMPV in elderly persons has not been well described. In the present report, we describe an outbreak of hMPV infection occurring in the summer months in a long-term-care facility (LTCF).

Subjects, materials, and methods. In June 2006, a respiratory illness outbreak in a 171-bed LTCF was reported to the Sacramento County Department of Health and Human Services and the California Department of Health Services (CDHS). A subsequent outbreak investigation included the initiation of active surveillance for new cases of respiratory illnesses in residents and staff and collection of specimens from ill patients when feasible. Cases were defined by the presence of new respiratory symptoms, including cough, chest congestion, purulent sputum, rhinitis, sore throat, shortness of breath, and/or fever. Epidemiologic and clinical data from ill residents were obtained from a review of medical records and from staff by interview using a standardized questionnaire. Nasopharyngeal swabs were transported on ice to the Sacramento County Public Health Laboratory and the CDHS Viral and Rickettsial Laboratory. Informed consent and approval from an institutional review board were not obtained, because these data were collected as part of a public health investigation.

The nasopharyngeal specimens were cultured for viruses by (1) the R-mix shell vial assay that uses a mixture of A549 and mink lung cells to detect influenza A and B virus, respiratory syncytial virus (RSV), parainfluenza virus types 1–3, and adenovirus (Diagnostic Hybrids) and (2) conventional cultures with primary rhesus monkey kidney (RhMK) cells and human fetal diploid lung cells with gentamicin (10 μg/mL) and fungizone (1 μg/mL) in roller tubes (0.2 mL/tube, 2 tubes each) at 33°C. Cultures were observed daily for 14 days. Hemadsorption with guinea pig red blood cells on RhMK cells was performed at 7 and 14 days. Culture was also performed for Bordatella pertussis and B. parapertussis using Regan Lowe plates and chocolate agar.

Total nucleic acid was extracted using the MasterPure Complete DNA and RNA Purification Kit (Epicentre Technologies). Real-time polymerase chain reaction (PCR) was performed with primers for viruses (influenza A and B virus, RSV, adenovirus, and hMPV) [3] and B. pertussis and B. parapertussis (Cepheid). Primers and probe for the hMPV fusion protein gene were obtained from a protocol developed by the Centers for Disease Control and Prevention and posted on the Association of Public Health Laboratories (APHL) Web site for use by public health laboratories [3]. At present, this hMPV assay is used for the purposes of epidemiologic surveillance and research only. Each specimen that was positive for hMPV by the APHL real-time PCR was also tested with conventional reverse-
transcription PCR for hMPV amplifying a 450-bp fragment of the fusion protein (F) gene. The primers used for the latter assay were as follows: MPVF1 forward, 5'-CTTTGGACTTAATTGACAGATG-3', and MPVF1 reverse, 5'-GTCTTCCCTTGCTA-3' [4]. The genotype was determined by sequencing a (450-bp) region of the F gene, followed by alignment with analogous sequences in GenBank.

**Results.** Twenty-six of 148 residents developed respiratory symptoms, for an attack rate of 18%. Onset of symptoms ranged from 4 June to 8 July 2006. Although residents from all 4 residential units in the facility became ill, 17 resident case patients resided in the same unit as the first case patient to develop symptoms. All resident case patients shared a common dining hall and activity room. The outbreak lasted 5 weeks, peaking at 24 days after onset, when 8 residents and staff persons developed symptoms (figure 1).

The mean and median age of the resident case patients was 70.2 and 72.5 years, respectively. Fifteen (58%) were female. Clinical illnesses in resident case patients were characterized by fever (temperature >38.0°C), nonproductive cough, wheezing, congestion, shortness of breath, and lethargy. All resident case patients had underlying medical conditions, including neurologic disorders (25 in total, including history of cerebrovascular accident [11], dementia or Alzheimer disease [8], Parkinson's disease [4], and status posttraumatic brain injury [2]), diabetes mellitus (12), chronic cardiac disease (11), chronic lung disease (7), and malignancy (1). Twelve resident case patients had a chest x-ray performed, with 8 (31%) showing evidence of unilobar or multilobar pneumonia. Fifteen resident case patients received oral antibiotics. Two resident case patients were hospitalized; none died. Twenty of the resident case patients (77%) had received an influenza vaccination, and 20 (77%) had received pneumococcal vaccination.

In addition to the residents, 13 health care workers, 11 of whom provided direct patient care, became ill during the same time frame (between 23 June and 13 July 2006). All reported symptoms of mild upper respiratory tract infection with dry cough, sore throat, and congestion that resolved over a 2–14-day time course; 1 had a chest x-ray performed that was normal, and none were hospitalized or died.

Fifteen ill resident case patients, including 4 who had radiographically confirmed pneumonia, and 5 staff persons had nasopharyngeal swabs collected within 7 days of symptom onset. All cultures were negative for viruses and for *B. pertussis* and *B. parapertussis*; 2 grew *Haemophilus influenza*, which was felt to be bacterial contamination. Real-time PCR identified hMPV in 5 case patients (all residents), 1 of whom had radiographically confirmed pneumonia. Two had relatively low cy-

---

**Figure 1.** Epidemiologic curve of a respiratory outbreak due to human metapneumovirus in a long-term-care facility (*n* = 39), June–July 2006. Nos. in parentheses indicate the no. of infections confirmed by polymerase chain reaction.
cle-threshold (C) values (<24) and, of these, only 1 was able to be passaged in cell culture. This isolate was amplified by PCR, further characterized by sequencing, and identified as type A2 (GenBank accession number EF422840). Conventional PCR was attempted on the second specimen with a low C value to amplify a fragment for sequencing, but results were negative. No other pathogens, including viruses and *B. pertussis*, were identified by PCR.

**Discussion.** This brief report describes yet another infectious cause of respiratory outbreaks in LTCFs besides the more commonly identified agents influenza virus and RSV. The outbreak described is the second in 2 years to occur in northern California that has been attributed at least in part to hMPV infection; in early May 2005, an LTCF respiratory outbreak attributed to a mixed infection of influenza A virus and hMPV was identified (D.P.S., personal communication).

Since the virus’s discovery, most reports have focused on the burden of hMPV in children [1, 2]. The virus has an epidemiologic and clinical spectrum very similar to that of RSV and appears to be an important cause of winter respiratory illness in young age groups, with almost all children in the Netherlands showing evidence of at least one infection by the age of 5 years [1]. In contrast to the high disease burden in children, hMPV appears to be an infrequent cause of seasonal respiratory illness in young and elderly adults, accounting for <5% of respiratory illnesses in New York [5, 6]. Likewise, studies done in northern California have found that hMPV accounted for few upper respiratory tract infections in young healthy adults presenting to an outpatient clinic at a tertiary-care referral center during the influenza season [7]. The existing number of reports describing hMPV infection in elderly persons is small; in the handful of patients studied, elderly persons were more frequently hospitalized, had longer hospital stays, and often had underlying neurologic or cardiopulmonary disease [5, 6]. Other small case series have suggested a role for hMPV and exacerbation of chronic obstructive pulmonary disease in elderly populations, with detection of hMPV in respiratory secretions in 5%–12% of cases [8, 9]. Although our report is limited to describing only hMPV-infected residents in this outbreak, the high frequency of underlying neurologic illness, diabetes, and cardiopulmonary disease that we observed suggests that further comparative studies are needed to better understand the risk factors for acquisition of hMPV infection in elderly persons.

Although previous reports have described hMPV as a primarily winter-spring pathogen, some studies of predominantly pediatric populations have also identified a low-level frequency of hMPV infection occurring during the summer and fall [2, 10]. To our knowledge, this is the first documentation of an hMPV outbreak occurring during the summer months in a temperate climate. This report underscores the need for continued active surveillance year-round, to better understand the epidemiology of this still relatively newly discovered virus.

Genetic analysis has enabled identification of 2 major groups of hMPV (genotype A and B) in circulation; we identified genotype A as the predominant genotype [11]. Some reports have suggested that the hMPV genotype that circulates in any given season can periodically change and that predominance of one circulating genotype does not correlate with a difference in severity of clinical illnesses [11]. By contrast, others have suggested that genotype A may be associated with greater clinical severity in children, including increased need for hospitalization, oxygen supplementation, and intensive care [12]. The outbreak in an elderly population that we describe was not characterized by substantial morbidity associated with hMPV genotype A infection; although almost one-third of case patients developed radiographically confirmed pneumonia, only 2 were briefly hospitalized for monitoring, and none died. Further study is needed with regard to the influence of hMPV genotype and virulence in different populations and ages.

In conclusion, although hMPV may not be a frequent cause of severe respiratory infection in elderly persons, it may be an important cause of respiratory outbreaks in LTCFs. Other reports of respiratory outbreaks occurring during the winter season in institutionalized elderly persons due to hMPV have recently been described [13, 14]. The findings of hMPV as well as other unusual pathogens reminds us of the vulnerability of the elderly population in LTCFs and the importance of the institution of year-round, comprehensive education and good respiratory hygiene practices [15]. As advances in molecular techniques contribute to the ability to detect new as well as old but previously unrecognized pathogens, it is likely that the spectrum of possible etiologies of respiratory illness that occur in the vulnerable elderly population will continue to grow.

**References**


