Respiratory Tract Infection Due to Human Metapneumovirus among Elderly Patients

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(See the article by Boivin et al. on pages 1152–8)

After the initial isolation of human metapneumovirus (hMPV) from infants with respiratory tract illnesses (RTIs), a plethora of studies involving the pediatric population have demonstrated that, in this population, hMPV infection accounts for 5%–25% of reported RTIs. Among infants hospitalized for RTI, hMPV is often the second most detected pathogen after human respiratory syncytial virus (hRSV). The clinical signs induced by both infections in patients of all ages are similar and range from mild upper RTI to bronchiolitis and pneumonia. Primary infection with hMPV does not induce lifelong immunity; several studies have shown that reinfection can occur during adult life, possibly because of waning immunity. Studies among adults have shown that clinical signs related to reinfection are usually restricted to the upper respiratory tract, but respiratory viruses, such as hMPV, hRSV, and influenza virus, have been associated with influenza-like illness, bronchitis, pneumonia, and exacerbations of both asthma and chronic obstructive pulmonary disease in the adult population [1]. This was illustrated in a study among patients of all ages, where Boivin et al. [2] detected hMPV not only in young children with RTI but also in immunocompromized individuals, adults, elderly adults, and institutionalized elderly adults. In adults with underlying disease, in particular, it has been demonstrated that hMPV is a major causative agent of RTI and, in some cases, is associated with fatal outcomes.

Only limited studies of hMPV infection, mostly case reports, are available involving elderly adults or institutionalized elderly adults. Honda et al. [3] described the occurrence of hMPV infection in a hospital for older people in Japan. Eight of 23 patients (age range, 65–89 years) in 1 ward who shared the same day care room were infected with hMPV, and all patients recovered. Kaye et al. [4] detected 20 samples that were positive for hMPV out of 373 total samples obtained in an adult hospital (patient age >18 years); 10 of these samples were obtained from patients who were >75 years old. In addition, in the 2 years of this study, hRSV and hMPV were each responsible for as many hospitalized cases of RTI as was influenza virus. Among 741 samples obtained from patients >18 years old, O’Gorman et al. [5] detected 6 hMPV-positive samples. All 6 patients were aged >50 years (range, 51–83 years); 2 were hospitalized inpatients with chronic obstructive pulmonary disease, and 2 of the patients, both of whom died, received immunosuppressive therapy for rheumatologic conditions. In a 2-year study involving young and older adults, including high-risk patients, elderly adults, and residents of a long-term care facility, Falsey et al. [6] identified hMPV infection in 4.1% of patients, with more-severe illness reported in frail elderly individuals.

In this issue, Boivin et al. [7] are the first to report an outbreak of hMPV infection with a high mortality rate in a long-term care facility. Six of 12 samples collected from a subset of patients with severe RTI had results positive for hMPV infection, and 1 patient had results positive for hRSV. Of the 6 patients with laboratory-confirmed cases, 3 died of hMPV infection—an extremely high fatality rate (50%), which has not been previously reported in association with hMPV infection. These data clearly demonstrate that hMPV infection, like hRSV infection and influenza, is a cause of high morbidity and mortality among (frail) elderly individuals.

Boivin et al. [7] presented histopathological findings associated with hMPV-induced fatal pneumonia in an 89-year-old woman. This is unique, because, to date, postmortem samples have only been obtained from patients with hMPV infection who had underlying disease and, in most...
of these patients, other pathogens have also been present in the lungs. The patient described by Boivin et al. [7], who did not have any medical conditions other than increased age, illustrates that hMPV infection can cause severe pneumonia that can possibly lead to death in elderly individuals. The presence of other pathogens could not be excluded here, however, so the question remains to be answered whether hMPV as a sole pathogen is able to cause death.

Although Boivin et al. [7] clearly demonstrate that hMPV infection caused morbidity and mortality in the facility that they describe, the data presented on the magnitude of the outbreak are based on circumstantial evidence. Questionnaires were used to identify patients who had respiratory symptoms; the authors subsequently defined an attack rate of possible and probable cases of hMPV infection and the associated fatality rate (reaching 9% of all patients with RTI). However, because hMPV-related illness in the elderly population is indistinguishable from infection with hRSV or influenza virus, the causative agents of RTI in the other symptomatic patients remain unknown. It is quite possible that, during the study period, other viruses circulating in the community were introduced in the residency, especially because patients circulated between wards, health care workers were not systematically surveyed, and installment of precautionary measures were delayed. The circulation of several viruses was demonstrated by the fact that 1 of the initial 12 samples had results positive for hRSV and that viruses from the 2 different genetic lineages of hMPV were detected. Nevertheless, because 6 of 12 patients tested positive for hMPV, it is likely that more patients than this had hMPV infection—thus, the authors established the role of hMPV as a cause of severe RTI in residents of long-term care facilities. This report supplies sufficient evidence to initiate active hMPV detection during institutional outbreaks of RTI, because a confirmed diagnosis would restrict the use of antibiotics and corticosteroids and may initiate timely implementation of precautionary measures.

It is well established that influenza virus infection and hRSV infection cause high rates of morbidity and mortality in elderly individuals; the fatality rates for hMPV infection reported by Boivin et al. [7] emphasize the need for thorough epidemiologic studies and assessments of the clinical impact of hMPV infection among elderly individuals in the general community and in long-term care facilities. These studies might identify a similar impact for hMPV infection as for hRSV infection or influenza virus infection in this population, which could argue for the development of therapeutic agents and vaccines. Annual influenza vaccination programs are aimed at reducing morbidity and mortality caused by influenza virus infection [8]. A similar approach might be beneficial for hMPV and hRSV infections. Vaccine development for these viruses for infection-naive individuals is hampered by studies with formalin-inactivated hRSV vaccines in infection-naive children. This is not expected to be an issue in individuals who have preexisting immunity, and boosting of the immune response in the elderly population can be safely achieved with, for instance, subunit vaccines (possibly without the use of adjuvant). For both hMPV and hRSV, such subunit vaccines are currently in development [9].

In conclusion, the work of Boivin et al. [7] illustrates that hMPV-associated severe RTI is not restricted to infants. Their data emphasize the need for more extensive epidemiologic studies among elderly individuals.

Acknowledgments

R.A.M. Fouchier and A.D.M.E. Osterhaus provided assistance in preparing and editing this editorial commentary.

Financial support. MedImmune (Gaithersburg, MD) and a Veni grant from the Dutch Science Foundation (NWO), The Netherlands.

Potential conflicts of interest. B.V. has received recent research funding from ViroNovative BV.

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