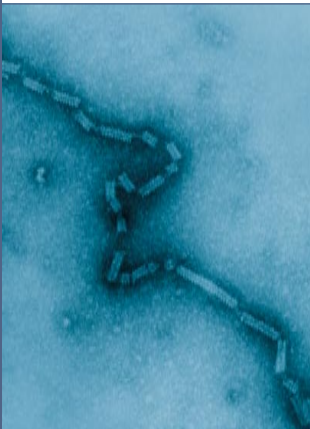


Human Metapneumovirus Overview

ABOUT THE VIRUS

The human metapneumovirus (hMPV) is a negative-sense, single-stranded RNA virus of the Paramyxoviridae family. The virus was first discovered in 2001 from children in the Netherlands with respiratory tract illness similar to respiratory syncytial virus (RSV) infection. Serological evidence dating back more than four decades confirms that hMPV is newly identified rather than newly emerged. Poor growth in cell culture is the main factor for the virus' delayed discovery. RSV is the closest human pathogen related to hMPV; both are members of the Pneumovirinae subfamily. Though still controversial, hMPV appears to be a single serotype with two subgroups, A and B, rather than two distinct serotypes. Data suggests that cross-protective immunity occurs after infection with one subgroup, which is equivalent to the case with RSV subgroups A and B. hMPV is distributed worldwide and is the causative agent of respiratory tract illness, particularly in young children and immunocompromised patients. Approximately 90% of children are seropositive for hMPV infection by the age of 5 years and nearly 100% by adulthood. The presence of maternally derived hMPV antibodies is indicated by a seroprevalence of greater than 90% in infants less than 3 months of age, however, the level of protection these antibodies provide is unknown.



Electron micrograph of a virus member from the Paramyxoviridae family.
Courtesy of CDC/Dr. Fred Murphy.

CLINICAL MANIFESTATIONS

The clinical manifestations of hMPV infections in children are similar to RSV and range from mild upper-airway disease to severe pneumonia and respiratory failure. Symptoms include cough, fever, myalgia, rhinorrhea, nasal congestion, pharyngeal erythema, otitis media, wheeze, dysphonia, stridor, bronchitis and pneumonia. Chest radiograph findings include infiltrates, hyperinflation and peribronchial cuffing. Apnea in preterm infants has been reported. Children less than 2 years of age are most likely to be hospitalized due to complicated lower respiratory tract infections. hMPV is a leading cause of bronchiolitis in early childhood. The role of hMPV in the initiation and progression of asthma remains unclear and controversial. Asymptomatic infection in children is rare. In adults, though to a lesser extent than children, hMPV has been associated with bronchitis, pneumonia and exacerbations of asthma and chronic obstructive pulmonary disease (COPD). Dyspnea is more common in the elderly.

hMPV has been associated with prolonged and serious infections in the immunocompromised patient population. The infection rate of hMPV seems comparable to the observed rates for RSV, parainfluenza and influenza. One study in hematopoietic stem cell transplant (HSCT) recipients noted that hMPV infection was initially characterized by fever, nasal congestion and cough. Pneumonia quickly developed and patients experienced rapidly progressive pulmonary infiltrates accompanied by hypotension and/or septic shock. Diffuse alveolar hemorrhage was also common. Another study in HSCT recipients detected hMPV in nasal specimens without clinical disease. A study of hMPV infection in lung transplant recipients showed clinical symptoms varied from no symptoms to severe pneumonia or acute graft rejection to death. Replication of hMPV significantly correlated with rejection symptoms in this study, suggesting that hMPV is associated with allograft rejection. Additional studies must be performed to determine an accurate frequency of complications, morbidity and mortality rates and distinct clinical characteristics of infection in the immunocompromised patient population.

LABORATORY DIAGNOSIS

hMPV predominately circulates in the United States from January to April; while later than RSV's peak season, the existing overlap and common clinical characteristics make distinction between the two viruses and identification of coinfection unfeasible without laboratory confirmation. Culture is not used in the diagnosis

of hMPV, due to the virus' poor growth in cell culture. hMPV-specific antibodies have been developed for immunofluorescence assays, though the lack of sensitivity is a significant limitation of this method. The most common technique for diagnosis is PCR, which has been shown to be a rapid, sensitive and specific method for detecting hMPV.

TREATMENT

Studies have shown that hMPV cases are clustered in an epidemic manner, in which community acquired infection and nosocomial infection are both believed to contribute. The incubation period, duration of viral shedding and modes of transmission, have not been well defined for hMPV but are likely to be similar to RSV. Thus, preventative actions, such as hand hygiene practices and isolation measures, will help prevent the spread of infection.

Similar to RSV, antiviral therapy for hMPV is limited and controversial. Ribavirin has been shown to have effectiveness in inhibiting replication of hMPV comparable to that of RSV. Limited data on the pathogenesis of hMPV in the natural host impedes treatment strategies.

Selected References

- Dare R, Sanghavi S, Bullotta A, et al. Diagnosis of human metapneumovirus infection in immunosuppressed lung transplant recipients and children evaluated for pertussis. *J Clin Microbiol.* 2007;45(2):548-552.
- Englund J, Boeckh M, Kuypers J, et al. Brief communication: fatal human metapneumovirus infection in stem-cell transplant recipients. *Ann Intern Med.* 2006;(144):344-349.
- Kahn JS. Epidemiology of human metapneumovirus. *Clin Microbiol Rev.* 2006;19(3):546-557.
- Knipe D, Howley P. *Fields Virology*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.
- Larcher C, Geltner C, Fisher H, et al. Human metapneumovirus infection in lung transplant recipients: clinical presentation and epidemiology. *J Heart Lung Transplant.* 2005;24(11):1891-1901.
- Lee I, Barton TD. Viral respiratory tract infections in transplant patients: epidemiology, recognition and management. *Drugs.* 2007;67(10):1411-1427.
- Mahoney J, Chong S, Merante F, et al. Development of a respiratory virus panel (RVP) test for the detection of twenty human respiratory viruses using multiplex PCR and a fluid microbead-based assay. *J Clin Microbiol.* 2007;45(9):2965-2970.
- Ordas J, Boga J, et al. Role of metapneumovirus in viral respiratory infections in young children. *J Clin Microbiol.* 2006;44(8):2739-2742.

