

Metapneumovirus and its place in childhood

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Human metapneumovirus (hMPV) was recently identified as a cause of acute upper and lower respiratory tract infection in children and adults. The epidemiology is similar to that exhibited by respiratory syncytial virus, with most episodes occurring during the winter months. The virus likely has a worldwide distribution. Almost all children have been infected by five years of age. The suspicion of hMPV infection should be higher in infants or children presenting with symptoms compatible with a viral etiology and in whom screening tests for other common viral pathogens have been negative. Clinical manifestations may be subtle or severe, including life-threatening bronchiolitis or pneumonia. Fever, rhinorrhea, cough, retractions, tachypnea and wheezing are common findings. Bronchiolitis is perhaps the most common manifestation among hospitalized children. Currently, there is no antiviral treatment or vaccine available and management is simply supportive.

Key Words: *Canada; Human metapneumovirus; Respiratory tract infections*

Viruses are the most common causes of acute respiratory tract infections (RTIs) in children worldwide and are associated with significant morbidity and mortality rates among this age group. Classic common viral etiologies of lower RTIs in children include respiratory syncytial virus (RSV), adenovirus, influenza A and B, and parainfluenza types 1, 2 and 3. However, there is still a considerable percentage of children in whom a viral etiology cannot be proven. Human metapneumovirus (hMPV) has been recently identified as a new cause of upper and lower RTI in children and adults, precisely in patients in whom screening tests for other viral pathogens had been negative (1). Originally described in the Netherlands in 2001, the virus belongs to the Paramyxoviridae family, the Pneumovirinae subfamily, which includes RSV, and is so far the only human pathogen of the Metapneumovirus genus.

EPIDEMIOLOGY

The epidemiology of hMPV infections is similar to that of RSV, with most episodes occurring during the winter months. Infants and young children are the most commonly

Le métapneumovirus et sa place dans l'enfance

Le métapneumovirus humain (MPVh) a récemment été dépisté comme une cause d'infection aiguë des voies respiratoires supérieures et inférieures chez les enfants et les adultes. L'épidémiologie est semblable à celle du virus respiratoire syncytial, la plupart des cas se produisant pendant les mois d'hiver. Le virus a probablement une distribution mondiale. Presque tous les enfants sont infectés avant cinq ans. La présomption d'infection au MPVh devrait être plus élevée chez les nourrissons ou les enfants présentant des symptômes compatibles avec une étiologie virale et chez qui les tests de dépistage d'autres pathogènes viraux communs sont négatifs. Les manifestations cliniques peuvent être subtiles ou graves, incluant une bronchiolite ou une pneumonie mettant la vie en danger. La fièvre, la rhinorrhée, la toux, les rétractions, la tachypnée et le wheezing (respiration sifflante) sont des observations courantes. La bronchiolite est peut-être la manifestation la plus fréquente chez les enfants hospitalisés. Pour l'instant, il n'existe aucun traitement ou vaccin antiviral, et la prise en charge consiste simplement à soutenir le patient.

affected, but the virus has also been documented in adults and the elderly (2).

Since the original report was published in 2001 (1), approximately 15 countries worldwide have documented the circulation of metapneumovirus in their human populations (2-17). However, it seems likely that this emerging pathogen has a global distribution similar to the majority of other respiratory viruses of childhood. Phylogenetic analysis of strains from different countries demonstrate two distinct hMPV genotypes. An individual can be infected with a virus from one subgroup and not be protected by a previous infection with a virus of the other subgroup.

Canada was the third country in the world, after the Netherlands and Australia, to report the circulation of hMPV in its population. Since the original description by investigators in Quebec (2), other reports by this and other groups have been published (5,10,18). The virus has also been detected in patients from Ontario, Saskatchewan, British Columbia, Manitoba and Nova Scotia (18-21).

In a recent paper on hMPV infection in the Canadian population (20), 445 specimens from children and adults of

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all age groups who had acute RTIs during the period from October 2001 to April 2002 were analyzed. Of the specimens tested, 66 (14.8%) were positive for hMPV.

As in Hong Kong (22), hMPV has also been detected in respiratory specimens from a few Canadian adults with severe acute respiratory syndrome (SARS) (18) in which SARS-responsible coronavirus was the main pathogen. To date, there are no convincing data supporting hMPV as the causative agent of SARS; instead, findings suggest that in these individuals, hMPV only acts as a coinfecting pathogen rather than causing the syndrome.

CLINICAL FEATURES

The complete clinical spectrum of hMPV disease needs to be fully determined, but manifestations range from mild upper RTI symptoms to severe bronchiolitis, pneumonia and respiratory failure. Common features include fever, rhinorea, sore throat, sneezing, conjunctivitis, cough, myalgia, tachypnea, retractions, wheezing, croup and acute asthma exacerbations (3-7,10,11). Irritability, pallor, apnea, hypoxia, otitis media and febrile seizures may also occur. Bronchiolitis is probably the most common manifestation of the disease in children requiring hospitalization, and it was found in 62% of the patients described by Freymuth and colleagues (7). Wheezing is a common feature in young infants with hMPV disease (6). There has been no evidence so far of extrapulmonary infections such as hepatitis or encephalitis.

Both immunocompetent children and those with underlying conditions such as congenital heart disease or malignancies may suffer hMPV bronchiolitis or pneumonia, and theoretically, be at greater risk for severe disease or complications. For now, there is inadequate evidence to comment on prematurity as a risk factor for developing severe hMPV bronchiolitis or pneumonia, as occurs in RSV disease. Re-infection or recurrence has been described occasionally in healthy and immunosuppressed individuals, and coinfection with other pathogens such as RSV, cytomegalovirus, influenza, SARS-coronavirus and other viruses has been documented (11). Greensill et al (9) documented that hMPV was found in 70% of infants mechanically ventilated for RSV bronchiolitis.

Radiological manifestations of lower RTI by hMPV are similar to those produced by RSV and other pathogens, and include air trapping, pneumonitis and pneumonia.

DIAGNOSIS

Clinical manifestations produced by hMPV are indistinguishable from those caused by other viral pathogens. The clinical suspicion of hMPV infection must be higher in infants and children with presumed viral respiratory infection in whom studies for other viruses have been inconclusive or negative. Collection of nasopharyngeal specimens for immunofluorescence testing, nucleic acid detection tests or cell cultures have been used as noninvasive diagnostic tools for detecting the presence of hMPV. The virus is difficult to identify by cell culture; therefore, other diagnostic tests have been used. When available, electron

microscopy can reveal the presence of hMPV (2). Nucleic acid detection approaches such as reverse transcriptase polymerase chain reaction are currently used for diagnosis. Real-time reverse transcriptase polymerase chain reaction has shown improved sensitivity and offers rapid confirmatory diagnosis (23).

hMPV has been circulating in humans for at least five decades (1), but it was not until 2001 that Dutch scientists discovered the virus in children and adults. In that first report (1), the authors concluded that by five years of age, virtually all children had been infected with hMPV. Reasons for this delay in discovery include, among others, the use of continuous cell lines for viral isolation in many laboratories (in which hMPV does not appear to have an efficient replication) and slow replication kinetics in vitro. Studies have shown a 52% seroprevalence rate by two years of age in Israel (14), and 100% by 10 years of age in the Netherlands (1) and Japan (12).

MANAGEMENT OF PATIENTS

hMPV has been detected in patients with both community- and hospital-acquired respiratory tract illness, but no nosocomial outbreaks have been reported. Common respiratory transmission precautions and measures are suggested. There are no studies published involving vaccinations against metapneumovirus or treatment with immunoglobulin in humans.

Supportive therapy is recommended as in other viral respiratory infections of childhood. No antiviral treatment is yet available. Mechanical ventilation has been used in severe cases, and recently, extracorporeal membrane oxygenation support was required for the first time for the survival of an infant from British Columbia who had severe hMPV pneumonia (21).

CONCLUSION

hMPV must now be considered in the differential diagnosis of acute upper and lower RTI in children, especially those with bronchiolitis or pneumonia. Canadian physicians must be suspicious of the presence of hMPV in children with suspected viral respiratory infection in whom other screening tests have been negative for common viral pathogens.

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