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Learning Objectives

After studying the literature presented in this Pediatric Respiratory Care series, participants will be able to:

- Identify respiratory disorders in pediatric patients
- Summarize risk factors for respiratory disorders in pediatric patients
- Select an appropriate therapeutic regimen for patients with pediatric respiratory disorders

Target Audience

This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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hMPV Emerges Worldwide as Significant Cause of Childhood Respiratory Disorders

Human metapneumovirus (hMPV) was recently identified as a cause of acute respiratory tract infections (ARTIs) and since its initial description, has been associated with ARTIs in Europe, America, Asia, Australia, and South Africa in individuals of all ages. Recent findings suggest that the incidence of hMPV infection varies from 1.5% to 25%, indicating that hMPV is a ubiquitous virus with a worldwide distribution. Seroprevalence surveys from Europe, Asia, and Israel demonstrate that virtually all children are infected by the age of 5 to 10 years, and primary infection is often acquired in the early years of life.

Evidence suggests that hMPV has been causing infection in humans for a long time. Studies of preserved respiratory samples show hMPV as far back as 1958 in the Netherlands and virus isolation during the past 2 decades in Europe and Canada. hMPV has emerged as a significant cause of acute respiratory disease, especially in childhood, but has been recognized only recently due to the

development of new diagnostic methods that suggest the possibility that additional respiratory pathogens may be identified. Real-time reverse-transcriptase PCR (RT-PCR) has become the method of choice in the diagnosis of acute hMPV, because the virus grows poorly in conventional cell culture.

The epidemiology of this RNA virus and the symptoms of disease appear to be similar to respiratory syncytial virus (RSV) and influenza virus, although the incidence of hMPV infection appears to peak at the end of winter or in early spring, thus peaking later than RSV. The seasonal distribution of hMPV overlaps with outbreaks caused by other winter respiratory viruses, which may result in coinfection with other respiratory viruses like RSV or influenza.

Clinical symptoms in children testing positive for hMPV range from upper respiratory tract disease to severe bronchiolitis and pneumonia, similar to RSV and influenza. One cited study (Greensill et al) found hMPV in 70% of infants with RSV bronchiolitis who required supplemental oxygen and mechanical ventilation, suggesting that hMPV may

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Disclosures:

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influence the severity of RSV disease. However, coinfection with RSV or other viruses does not always result in more severe disease.

Several studies suggest that hMPV may induce airway alterations and may be related to the onset and exacerbation of childhood asthma. The authors' study reported wheezing in 25.7% of children with hMPV and in 23.4% of children with RSV infection. The hMPV-positive children were older on average than the RSV-positive children, which may explain why, when wheezing is diagnosed, asthma exacerbation is more common in the hMPV group and bronchiolitis in the RSV group.

Children infected with hMPV may have a considerable socioeconomic impact on their families. Households with children who tested positive for hMPV had significantly more illnesses, needed more medical visits, received more antipyretics, and missed more work or school days than those of RSV-positive children ($P < 0.05$ for all versus households of RSV-

positive children, except for medical visits, $P < 0.0001$). As a result, hMPV may emerge as a substantial public health problem. At least two circulating serotypes of hMPV have been identified. The authors call for further surveillance studies to define the full spectrum of childhood hMPV and to identify the risk factors associated with severe disease. There are no approved treatment or prevention therapies at this time; however, ribavirin and polyclonal intravenous immunoglobulin preparation have been found to have positive in vitro antiviral effects on hMPV. Prevention with passively administered antibody may prove an option in high-risk populations. Vaccines against hMPV are currently in the early stages of development.

Principi N, Bosis S, Esposito S. Human metapneumovirus in paediatric patients. *Clin Microbiol Infect.* 2006;12:301-308.

In some years, especially during the later months of the respiratory virus season, hMPV was associated with more URIs than either RSV or influenza virus.

hMPV and Upper Respiratory Infections: A Newly Defined Role in Children

Human metapneumovirus (hMPV) is an important cause of lower respiratory tract infection (LRI), accounting for many hospitalizations in the pediatric population of the United States. However, the role hMPV plays in upper respiratory infections (URIs) is less clear. To address this issue, Williams and colleagues examined the frequency, seasonality, and clinical characteristics of hMPV infection in otherwise healthy children presenting with URIs. Such data have not been determined previously, and national estimates of URIs attributable to hMPV are not available.

The study examined frozen nasal wash specimens and medical records gathered between 1982 and 2001 from 1,532 children who were followed for a mean of 2.4 years at a children's clinic in Vanderbilt University. Only specimens that were negative for other viruses were tested for hMPV. Real-

time reverse-transcriptase PCR (RT-PCR) was used to assay the specimens for the presence of hMPV. The primers used could detect four lineages (A1, A2, B1, and B2) with equal sensitivity to estimate the relative contribution of hMPV to URIs in children for whom a routine viral culture had not grown a conventional respiratory virus.

Findings detected hMPV in 118 (5%) of 2,384 specimens from children with URIs who had not received a prior viral diagnosis, with an overall prevalence of 3% in the entire cohort, compared with 6% for RSV and influenza virus, and 7% for parainfluenza virus (PIV). hMPV was detected during every year and its prevalence varied from season to season (ranging from 1% to 5%), as did the prevalence of RSV (3% to 11%), PIV (2% to 14%), and the influenza virus (0.3% to 13%). However, during the peak months, from February to May, hMPV accounted for 16% of all URIs

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hMPV and Upper Respiratory Infections: A Newly Defined Role in Children

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over the 20-year period. In some years, especially during the later months of the respiratory virus season, hMPV was associated with more URIs than either RSV or influenza virus.

Concomitant acute otitis media (AOM) was present in 50% of the children, which did not differ significantly from the rate associated with RSV, PIV, or influenza virus infections. Four genetic lineages of hMPV were present (A1 [11%], A2 [28%], B1 [13%], and B2 [49%]), and often viruses from more than one lineage circulated during a single year. Reinfections with both homologous and heterogeneous strains occurred in the upper respiratory tract.

hMPV-associated URIs occurred mostly among children, mean age 20 months (ranging from 1 to 63 months). This finding is in line with URIs associated with most viral infections, excluding influenza virus (mean age, 27 months). Children with hMPV

infection presented with symptoms typical of other viral respiratory illnesses, but were less likely to be febrile than children with influenza virus infection (54% vs 85%; $P < 0.001$).

The data indicate that the proportion of annual URIs and concomitant AOM associated with pediatric hMPV infection may be greater than previous estimates, the authors conclude. Both major lineages of hMPV are important in clinical disease, which may have important implications for the development of vaccines and prophylactic monoclonal antibodies. Furthermore, the substantial burden of hMPV disease suggests that a vaccine may have significant health and socioeconomic benefits.

Williams JV, Wang CK, Yang C-F, et al. The role of human metapneumovirus in upper respiratory tract infections in children: a 20-year experience. *J Infect Dis.* 2006;193:387-395.

PRCI MISSION STATEMENT

The PRCI is a multicomponent educational program on pediatric respiratory disorders designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients. PRCI programs address issues concerning asthma, respiratory syncytial virus, and other respiratory tract infections and disorders. Methods to prevent, control, and treat respiratory illnesses in children are also evaluated.

COMMENTARY

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Human metapneumovirus (hMPV) was identified as a cause of respiratory tract disease in 2001. hMPV causes upper and lower respiratory tract disease with symptoms that include the common cold, bronchiolitis, pneumonia, croup, and exacerbation of reactive airway disease. Approximately 10% to 15% of all lower respiratory tract disease occurring in the first few years of life is attributable to this viral pathogen. The report by Williams et al confirms the role of hMPV as an important cause of upper respiratory tract disease in children. The many clinical and epidemiologic similarities between hMPV and respiratory syncytial virus suggest that efforts to control hMPV disease will focus on vaccine development, as well as passive immunoprophylaxis with monoclonal antibodies.

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