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**LEARNING OBJECTIVES** After studying the literature presented in this issue, participants will be able to:

- Describe the frequency and source of transmission of rhinovirus within families with children
- Discuss the clinical implications of a recently discovered rhinovirus genotype in children

**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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*Clinical Insights® in*

# PEDIATRIC RESPIRATORY CARE

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## High Incidence of Rhinovirus Transmission Within Families With Children

**R**hinoviruses are the most frequent cause of respiratory tract infections. However, the transmission of these viruses within families has not been investigated using sensitive and specific molecular detection methods such as the reverse transcription-polymerase chain reaction (RT-PCR) assay. Peltola and colleagues analyzed the transmission of rhinovirus infection in families using the RT-PCR assay, along with melting temperature and sequence analysis for virus detection and typing.

In this study, nasal swab samples for rhinovirus screening were obtained from 169 children  $\geq 1$  month of age who were hospitalized for any reason on the pediatric infectious diseases ward of Turku University Hospital, Turku, Finland. Families with only one child were excluded from the study. During a 3-week follow-up period, parents documented respiratory symptoms and fever among family members in a diary. A total of 8 families (consisting of 39 individuals) with a rhinovirus-positive index child and 16 families (consisting of 70 individuals) with a rhinovirus-

negative index child submitted nasal swab samples twice weekly for laboratory analysis and were monitored for 3 weeks. There were 8 rhinovirus-positive index children (median age, 1.3 years) and 16 rhinovirus-negative index children (median age, 4.3 years). The study was performed during months of high rhinovirus activity (September–November).

The rates of any rhinovirus infection (symptomatic or asymptomatic) were 1.00 cases per person among the 17 siblings and 0.50 cases per person among the 14 parents of rhinovirus-positive index patients. Rhinovirus infection was less frequent among families with a rhinovirus-negative index child. The rates were 0.54 cases per person among the 24 siblings and 0.23 cases per person among the 30 parents of rhinovirus-negative index patients. The number of symptomatic infections was associated with young age ( $P=0.0005$ ) but not with a high copy number of rhinovirus genomes. Virus typing revealed that circulation of several virus types could occur simultaneously within families.

*Attesting to frequent transmission from children to other family members, rhinoviruses were detected in all children and in half of adults in families with a rhinovirus-positive index child.*

*Continued*

### Disclosures:

Dr Piedra is professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine, Houston, Texas. He has indicated that he receives grant/research support from Juvaris BioTherapeutics, Inc., MedImmune, Inc., Sanofi Pasteur, and Novartis Pharmaceuticals; is a speaker for MedImmune, Inc.; and is an ad hoc consultant for MedImmune, Inc., Sanofi Pasteur, Novartis Pharmaceuticals, Hoffmann-La Roche Inc., and Merck & Co., Inc.

Dr Belshe has indicated that he receives grant/research support from Merck & Co., Inc.; is a retained consultant for MedImmune, Inc. and Novartis Pharmaceuticals; and is a member of the speakers bureau for MedImmune, Inc., Merck & Co., Inc., and sanofi-aventis.

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### High Incidence of Rhinovirus Transmission Within Families With Children *(Continued)*

This study found a high incidence of rhinovirus infection and high diversity of rhinovirus circulation in families with children during the autumn season. Attesting to frequent transmission from children to other family members, rhinoviruses were detected in all children and in half of adults in families with a rhinovirus-positive index child. Most rhinovirus infections in young children were symptomatic, whereas secondary rhinovirus infections in

adults were mostly asymptomatic. The authors suggested that efforts to prevent rhinovirus transmission should focus on young children with respiratory symptoms.

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Peltola V, Waris M, Österback R, Susi P, Ruuskanen O, Hyypiä T. Rhinovirus transmission within families with children: incidence of symptomatic and asymptomatic infections. *J Infect Dis.* 2008;197(3):382-389.

### COMMENTARY

**ROBERT B. BELSHE, MD, Dianna and J. Joseph Adorjan Endowed Chair of Infectious Diseases and Immunology, Professor of Medicine, Pediatrics, and Molecular Microbiology, Saint Louis University School of Medicine, St. Louis, Missouri.**

*Recent studies of rhinovirus transmission within families with young children, as reported by Peltola et al, contribute substantially to our understanding of rhinovirus epidemiology. Of interest was the large number of serotypes circulating simultaneously in the community and even within individual families. This fascinating study using highly sensitive polymerase chain reaction techniques to identify viral genome—and to distinguish between genotypes—led to the conclusion that young children were the primary sources of rhinoviruses in families. This is not a surprise for any parent. Nearly all of the young children with rhinovirus infections had symptomatic infection; in contrast, about half of the older children and parents had asymptomatic infection.*

*Prior experiences were likely protecting older children and adults from about 50% of symptomatic infections. The quantity of virus shed was high for both symptomatic and asymptomatic infections and not significantly different. The infections were spread primarily from infected symptomatic young children; asymptomatic shedders did not seem to contribute much to the spread of virus. In other words, profuse respiratory secretions from symptomatic children were the vehicle for transmission. This is an important clinical finding, and if this observation holds generally true, then we are provided with a handle to help control rhinovirus infections. By identifying symptomatic individuals in families and instituting simple infection control techniques to reduce the transmission of viruses through hand washing and careful respiratory hygiene, rhinovirus infections may be reduced. To prevent rhinovirus disease, families should focus on preventing spread from symptomatic young children as the primary sources of rhinovirus illness. How to accomplish this will need to be evaluated in clinical trials comparing hand washing, tissues impregnated with acidic compounds to inactivate viruses, or other methods.*

### A Novel Human Rhinovirus Is Implicated in Pediatric Lower Respiratory Tract Infection

**D**espite the use of polymerase chain reaction (PCR) assays and classical diagnostic methods (eg, antigen tests, serology, and culture methods), an infectious agent may not be detected in up to 50% of cases of severe respiratory infection. Human rhinovirus (HRV), a significant cause of morbidity and mortality in children worldwide, has been implicated in common colds as well as lower respiratory tract infection (LRTI). Currently, HRVs are grouped into 2 species, HRV-A and HRV-B, in the genus

*Rhinovirus* of the family Picornaviridae.

Recently, Renwick and colleagues applied MassTag PCR to samples that had tested negative for influenza virus with routine diagnostic techniques from subjects with undiagnosed influenzalike illness in New York State. That study led to the discovery of a novel HRV genotype that diverged from the known genotypes, HRV-A and HRV-B. To characterize the pathogenicity of HRVs, including the recently identified genotype HRV-X, the same group of

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### A Novel Human Rhinovirus Is Implicated in Pediatric Lower Respiratory Tract Infection (Continued)

investigators evaluated nasopharyngeal aspirates collected during the 2003 through 2006 seasons in Bad Kreuznach, Germany, from children hospitalized with acute LRTI.

MassTag PCR was applied to 97 cases from children aged 2 weeks to 5 years (mean age, 5 months) for which no pathogen was identified after testing for influenza virus and respiratory syncytial virus (RSV) by real time, reverse transcription-polymerase chain reaction (RT-PCR). MassTag PCR tested for influenza A and B, RSV A and B, human parainfluenza virus types 1, 2, 3, and 4, human coronavirus 229E and OC43, human metapneumovirus, entero- and rhinoviruses, and adenoviruses. MassTag PCR identified at least 1 respiratory virus in 49 cases (51%). Among the 55 identified viruses, 41 (75%) were rhinoviruses. Coinfection with another virus was found in only 12% (5/41) of cases. HRVs were the viruses that were most often detected in this set of samples, 30 of the 41 rhinoviruses were novel sequences consistent with HRV-X.

The novel genotype HRV-X was associated with a wide range of respiratory diseases. The frequency of fever and cough with HRV (82%) was similar to other respiratory viruses (79%). The frequency of bronchitis, pneumonia, and bronchiolitis occurred in 60%, 36%, and 12% of infections with HRV-X, respectively. In comparison, bronchitis, pneumonia, and bronchiolitis occurred in 67%, 56%, and 11% of infections with HRV-A/B, respectively. There

was no significant relationship between the HRV genotypes and clinical diagnoses. Approximately half of the cases of severe pneumonia associated with HRV-X required supplemental oxygen.

The history of the novel genotype was not clear. The sequence diversity observed with the novel HRV clade in this study was not consistent with a recent introduction. The authors speculated that this discovery may reflect the use of new technologies rather than the emergence of a new agent. This clade may be responsible for previous reports of nontypeable HRVs.

In this cohort of children hospitalized with acute LRTI, HRV was the most commonly identified viral pathogen in specimens that tested negative for influenza and RSV. Of the HRV detected, the novel HRV-X genotype represented the majority of the HRVs. These findings underscore the importance of HRV in pediatric LRTI. The presence of HRV-X in 2 disparate locations (the US and Germany) and its association with serious respiratory infection necessitate further investigation into the pathogenesis of this novel genotype.

Renwick N, Schweiger B, Kapoor V, et al. A recently identified rhinovirus genotype is associated with severe respiratory-tract infection in children in Germany. *J Infect Dis.* 2007;196(12):1754-1760.

### Clinical Insights® in Pediatric Respiratory Care Post-Test

- Which of the following statements is true regarding the study conducted by Peltola et al?
  - Rhinoviruses were detected in half of children in families with a rhinovirus-positive index child.
  - Rhinoviruses were detected in all children in families with a rhinovirus-positive index child.
  - Most rhinovirus infections in young children were asymptomatic.
  - Most secondary rhinovirus infections in adults were symptomatic.
- In the study conducted by Renwick et al, the novel HRV genotype was associated with both upper and lower respiratory tract infections.
  - True
  - False

### ANSWERS

**Question 1 answer:** b. Rhinoviruses were detected in all children in families with a rhinovirus-positive index child.  
**Question 2 answer:** a. The novel HRV genotype was associated with a wide range of respiratory diseases, including upper respiratory tract symptoms and LRTIs (eg, bronchitis, pneumonia, and bronchiolitis).

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