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Learning Objectives

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

- Describe the association between human bocavirus (HBoV) infection and acute respiratory tract infection in children
- Assess the importance of HBoV viral loads as an etiologic factor for respiratory tract disease
- List the most commonly detected pathogens among air travelers with febrile lower respiratory tract symptoms.
- List the most likely source for acquiring the acute respiratory infection in the context of air travel.

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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Off-Label Disclosure

Some of the drug treatments discussed in this issue may note uses not approved by the Food and Drug Administration. Articles containing such uses will be noted at the end of the article.

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PEDRO A. PIEDRA, MD,* EDITOR-IN-CHIEF; H. CODY MEISSNER, MD,[†] REVIEWER; KATHLEEN M. MAJOR,[‡] SENIOR MANAGING EDITOR; MARK PALANGIO,[§] SENIOR MEDICAL WRITER

Human Bocavirus as a Potential Cause of Acute Wheezing in Children

Human bocavirus (HBoV), a newly discovered parvovirus, has been detected mainly in children with acute lower respiratory tract infection. Common clinical findings include respiratory distress and abnormal chest radiography. However, the role of HBoV as a causative agent of respiratory tract disease is unclear. Allander and colleagues investigated the association between HBoV infection and acute respiratory tract infection. In a randomized, placebo-controlled trial evaluating the efficacy of systemic corticosteroids for the treatment of acute expiratory wheezing in children, the prevalence of HBoV and the genome HBoV load in the respiratory tract and blood specimens were determined. Samples were analyzed for 16 respiratory viruses by polymerase chain reaction (PCR), virus culture, antigen detection, and serological assays. This study involved 259 children (median age, 1.6 years) who had been hospitalized for acute expiratory wheezing at Turku University Hospital, Turku, Finland, during the period from September 2000 to May 2002.

These findings suggest that high viral loads can be, potentially, an etiologic factor for respiratory tract disease and may represent primary infection, whereas low viral loads may be indicative of virus persistence after clinical recovery.

At least 1 potential viral pathogen was identified in 95% of children (n=245), and 2 or more agents were detected in 34% of children (n=89). Of note, HBoV was detected in 19% of children (n=49). In this study group, HBoV was the fourth most frequently detected virus, after rhinoviruses (28%, n=73), respiratory syncytial virus (28%, n=72), and enteroviruses (27%, n=69). Most cases of HBoV infection were mixed infections with other viruses. However, HBoV was the sole virus detected in 5% of children (n=12).

HBoV was detected significantly more often among children with acute wheezing than among asymptomatic children (19% vs 0%; $P<0.001$). Additionally, HBoV was more prevalent among children with symptoms of unexplained etiology than among those with other viruses (46% vs 16%; $P<0.001$). High viral loads of HBoV were associated with previously unexplained acute wheezing. Furthermore, HBoV DNA was often detected in serum specimens obtained from patients with acute wheezing, suggesting systemic infection.

This study revealed that HBoV is a common virus in children with acute wheezing and can result in systemic infection. These findings suggest that high viral loads can be, potentially, an

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Disclosures:

- * Dr Piedra is professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine. He has indicated relevant financial relationships as noted: he receives grant/research support from MedImmune, Inc. and Sanofi Pasteur; he is a member of the speakers bureau for MedImmune, Inc.; he is an expert witness for Sanofi Pasteur; he is an ad-hoc consultant for MedImmune, Inc., Sanofi Pasteur, GlaxoSmithKline, Novartis, and Roche; and he is part of a collaborative research agreement with NIH and Baylor.
- † Dr Meissner is chief, Division of Pediatric Infectious Disease at Tufts-New England Medical Center. He has indicated relevant financial relationships as noted: he receives grant/research support from MedImmune, Inc., Merck & Co., Inc., GlaxoSmithKline, Bristol-Myers Squibb, and Wyeth; he is a retained consultant for GlaxoSmithKline, Merck & Co., Inc., Novartis, and MedImmune, Inc.
- ‡ Ms Major is a senior managing editor for Professional Postgraduate Services[®]. She has indicated no relevant financial relationships.
- § Mr Palangio is a senior medical writer for Professional Postgraduate Services[®]. He has indicated no relevant financial relationships. Terri Setteducato is a senior program director for Professional Postgraduate Services[®]. She has indicated no relevant financial relationships. Wade'ah Terry is a CME program manager for Professional Postgraduate Services[®]. She has indicated no relevant financial relationships.



Human Bocavirus as a Potential Cause of Acute Wheezing in Children

(Continued)

etiologic factor for respiratory tract disease and may represent primary infection, whereas low viral loads may be indicative of virus persistence after clinical recovery. As underscored in an accompanying editorial by Anderson, this study does not fully establish a link between HBoV and wheezing because the control specimens were not well-matched by age (median age for control subjects was 4.1 years vs 1.3 years for HBoV

infected children) or method of sample collection (nasal swab specimens for control subjects vs nasopharyngeal aspirate for case subjects). However, this study does add to our understanding of HBoV infection.

Allander T, Jartti T, Gupta S, et al. Human bocavirus and acute wheezing in children. *Clin Infect Dis*. 2007;44:904–910.

COMMENTARY

H. CODY MEISSNER, MD, Chief, Division of Pediatric Infectious Disease, Tufts-New England Medical Center, Boston, Massachusetts.

In recent years, several previously unknown viruses have been isolated from the respiratory tracts of symptomatic children. These viruses include human metapneumovirus, several coronaviruses, and certain influenza viruses. In 2005, a report from Sweden confirmed that a new parvovirus was isolated in nasopharyngeal secretions obtained from hospitalized children with bronchiolitis or recurrent wheezing. The virus was named human bocavirus (HBoV) and subsequent studies have recovered HBoV from approximately 1% to 10% of respiratory tract specimens collected from symptomatic children around the globe. Frequently, HBoV has been isolated concurrently with other known pathogens of the respiratory tract, as reported by Allander et al. Thus, the precise role of HBoV in children with upper- or lower-respiratory tract disease has not been clarified fully. However, taken collectively, available data suggest HBoV will turn out to be yet another viral pathogen causing respiratory tract disease in young children.

Range of Viruses and Atypical Bacteria in Air Travelers With Acute Respiratory Infection

Although respiratory infections frequently occur after intercontinental air travel, epidemiological data for these infections are not complete. As such, Luna and associates evaluated the range of atypical bacteria and respiratory viruses, through the use of sensitive polymerase chain reaction (PCR), in travelers fulfilling the World Health Organization's case definition for suspected or probable severe acute respiratory syndrome (SARS).

This study involved respiratory samples (n=214) from 172 patients. Travel histories were obtained for 164 patients. The majority of these patients (71%) were adults of working age (ie, between 19 and 60 years of age) (mean, 42 years).

At least 1 pathogen was identified in 67 travelers (43.2%). The most commonly detected pathogens were parainfluenza viruses and influenza viruses, present at frequencies of 15.5% and 14.2%, respectively. The frequencies of adenoviruses, human metapneumovirus, coronaviruses, and rhinoviruses ranged from 2.6% to 4.8%. Human bocavirus, respiratory syncytial virus, and *Legionella*, *Mycoplasma*, and *Chlamydomphila* species were either absent or detected

at frequencies of <1%. No association was found between the airport of departure and either the detection of pathogens in general or the detection of any specific pathogen.

This study presents the first specific baseline data for the agents, mentioned in the context of air travel. The primary finding of this study indicates that the range of pathogens in returning air travelers is wide. Almost one-half of these traveling patients with a febrile respiratory illness were infected with a respiratory virus. The study investigators point out that it is unclear how patients acquire viral

respiratory disease in the setting of air travel. Because there was no relationship between the pathogen detected and a particular flight or airport, the investigators surmise the viruses are acquired prior to travel rather than during the flight.

Luna LK, Panning M, Grywna K, Pfeifferle S, Drosten C. Spectrum of viruses and atypical bacteria in intercontinental air travelers with symptoms of acute respiratory infection. *J Infect Dis*. 2007;195:675–679.

*Human bocavirus,
respiratory syncytial virus,
and Legionella, Mycoplasma,
and Chlamydomphila species
were either absent or detected
at frequencies of <1%.*

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1. In the study by Allander T et al, what was the prevalence of HBoV infection in children hospitalized with acute wheezing?
 - a. Approximately 5%
 - b. Approximately 10%
 - c. Approximately 20%
 - d. Approximately 30%

2. In the study by Luna LK et al, which of the following pathogens were most commonly detected in air travelers with acute respiratory infection?
 - a. Adenovirus
 - b. Coronavirus
 - c. Parainfluenza and influenza viruses
 - d. Rhinovirus

1. c. HBoV was detected in 19% of children.
 2. c. The most commonly detected pathogens were parainfluenza and influenza viruses.



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