

# Studies Point to Bocavirus Being Enteric, Seasonal

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CHICAGO — New data suggest the human bocavirus may be an enteric pathogen, and that infection with the parvovirus varies by season, Dr. Jeffrey S. Kahn said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Researchers are beginning to piece together some information about the hu-

man bocavirus since its discovery just 2 years ago (Proc. Natl. Acad. Sci. USA 2005; 102:12891-6).

The virus, which closely resembles the genome of viruses in the *Parvoviridae* family, is common, with a positive infection rate in most studies of 1%-8%, although it exceeds 18% in others.

The majority of positive specimens are from children, said Dr. Kahn, director of the infectious diseases laboratory at Yale University, New Haven, Conn.

The bocavirus is also frequently detected in the presence of other viruses or pathogens.

Three studies published this year support the theory that the human bocavirus (HBoV) is an enteric pathogen, Dr. Kahn said.

In what is believed to be the first report to document HBoV in human feces, Spanish researchers identified HBoV in 48 of 527 (9%) fecal samples collected from children less than 3 years old with acute gastroenteritis without respiratory tract disease (Emerg. Infect. Dis. 2007;13:636-7).

In 28 of 48 (58%) specimens, another enteric pathogen was detected, including salmonella, campylobacter, norovirus, and rotavirus.

A prospective clinical and molecular study in Hong Kong detected HBoV in 30 of 1,435 (2%) fecal samples and in 83 of 1,200 (7%) nasopharyngeal aspirates collected from patients less than 18 years of age (J. Infect. Dis. 2007;196:986-93).

HBoV was codetected with other pathogens in 33% of aspirates and in 56% of fecal samples. There was little difference in genome sequence from isolates detected in each anatomic site, Dr. Kahn said at the meeting, which was sponsored by the American Society for Microbiology.

A third study from Seoul identified HBoV in 0.8% of 962 children hospitalized with gastroenteritis (J. Infect. Dis. 2007;196:994-7). In all, 44% of the study population had a viral agent including rotavirus (26%), norovirus (14%), adenovirus (3%), and astrovirus (1%).

"The spectrum of disease caused by this virus has not yet been defined, though the observation that this virus is frequently

identified with other pathogens suggests that HBoV may not, for some populations, be a major pathogen," Dr. Kahn said in an interview.

A seasonal variation to HBoV infection has also been observed by Yale investigators, which suggests that in the United States the infection starts in the fall and runs into early spring. The study, led by Dr. Deniz Kesebir, identified HBoV in 5% or 22 of 425 respiratory specimens from children less than 2 years of age. Cases began in October (8%), peaked in November (10%) and December (9%), and dropped off in March (3%) and April (6%). No cases were reported from May to September.

None of the 96 asymptomatic children screened for HBoV were positive. Among the 20 children who were positive for HBoV, fever, rhinorrhea, cough, and wheezing were observed in more than 50%, and diarrhea was observed in 25% (J. Infect. Dis. 2006; 194:1276-82).

A recent population-based surveillance study conducted in rural Thailand reported its highest number of cases from January to March and none from August to December, (J. Infect. Dis. 2007; 195:1038-45). In the same study, HBoV infection was detected in 5% of hospitalized patients with pneumonia, of which 83% were children younger than 5 years old.

Although the amount of information collected on HBoV is impressive, further studies are needed on the biology and pathogenesis of the human bocavirus, Dr. Kahn said.

The study of HBoV is limited to the detection of viral DNA because the virus has yet to be successfully propagated in cell culture or animal models. ■



**Among 20 patients positive for HBoV, more than half had rhinorrhea, fever, cough, and wheezing.**

DR. KESEBIR

Gastrointestinal disorders: Nausea, vomiting, diarrhea

Immune system disorders: Hypersensitivity reactions (including anaphylactic reaction, facial edema and urticaria)

Nervous system disorders: Guillain-Barré syndrome, Bell's Palsy

Respiratory, thoracic and mediastinal disorders: Epistaxis

Skin and subcutaneous tissue disorders: Rash

#### DRUG INTERACTIONS

##### Aspirin Therapy

Do not administer FluMist to children or adolescents who are receiving aspirin therapy or aspirin-containing therapy.

##### Antiviral Agents Against Influenza A and/or B

The concurrent use of FluMist with antiviral agents that are active against influenza A and/or B viruses has not been evaluated. However, based upon the potential for antiviral agents to reduce the effectiveness of FluMist, do not administer FluMist until 48 hours after the cessation of antiviral therapy and antiviral agents should not be administered until two weeks after administration of FluMist unless medically indicated. If antiviral agents and FluMist are administered concomitantly, revaccination should be considered when appropriate.

##### Concomitant Inactivated Vaccines

The safety and immunogenicity of FluMist when administered concurrently with inactivated vaccines have not been determined. Studies of FluMist excluded subjects who received any inactivated or subunit vaccine within two weeks of enrollment. Therefore, healthcare providers should consider the risks and benefits of concurrent administration of FluMist with inactivated vaccines.

##### Concomitant Live Vaccines

Concurrent administration of FluMist with the measles, mumps and rubella vaccine and the varicella vaccine was studied in 1245 children 12-15 months of age. Adverse events were similar to those seen in other clinical trials with FluMist. No evidence of interference with immune responses to measles, mumps, rubella, varicella and FluMist vaccines was observed. The safety and immunogenicity in children >15 months of age have not been studied.

##### Intranasal Products

There are no data regarding co-administration of FluMist with other intranasal preparations.

#### USE IN SPECIFIC POPULATIONS

##### Pregnancy

##### Pregnancy Category C

Animal reproduction studies have not been conducted with FluMist. It is not known whether FluMist can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. FluMist should be given to a pregnant woman only if clearly needed.

The effect of the vaccine on embryo-fetal and pre-weaning development was evaluated in a developmental toxicity study using pregnant rats receiving the frozen formulation. Groups of animals were administered the vaccine either once (during the period of organogenesis on gestation day 6) or twice (prior to gestation and during the period of organogenesis on gestation day 6), 250mcL/rat/occasion (approximately 110-140 human dose equivalents based on TCID<sub>50</sub>), by intranasal instillation. No adverse effects on pregnancy, parturition, lactation, embryo-fetal or pre-weaning development were observed. There were no vaccine related fetal malformations or other evidence of teratogenesis noted in this study.

##### Nursing Mothers

It is not known whether FluMist is excreted in human milk. Therefore, as some viruses are excreted in human milk and additionally, because of the possibility of shedding of vaccine virus and the close proximity of a nursing infant and mother, caution should be exercised if FluMist is administered to nursing mothers.

##### Pediatric Use

FluMist is not indicated for use in children <24 months of age. FluMist use in children <24 months has been associated with increased risk of hospitalization and wheezing in clinical trials.

##### Geriatric Use

FluMist is not indicated for use in individuals ≥65 years of age. Subjects with underlying high-risk medical conditions (n=200) were studied for safety. Compared to controls, FluMist recipients had a higher rate of sore throat.

##### Use in Individuals 50-64 Years of Age

FluMist is not indicated for use in individuals 50-64 years of age. In Study AV009, effectiveness was not demonstrated in individuals 50-64 years of age (n=641). Solicited adverse events were similar in type and frequency to those reported in younger adults.

#### PATIENT COUNSELING INFORMATION

Vaccine recipients or their parents/guardians should be informed by the health care provider of the potential benefits and risks of FluMist, and the need for two doses at least 1 month apart in children 2-8 years old who have not previously received influenza vaccine.

##### Asthma and Recurrent Wheezing

Ask the vaccinee or their parent/guardian if the vaccinee has asthma. For children <5 years of age, also ask if the vaccinee has recurrent wheezing since this may be an asthma equivalent in this age group.

##### Vaccination with a Live Virus Vaccine

Vaccine recipients or their parents/guardians should be informed by the health care provider that FluMist is an attenuated live virus vaccine and has the potential for transmission to immunocompromised household contacts.

##### Adverse Event Reporting

The vaccine recipient or the parent/guardian accompanying the vaccine recipient should be told to report any suspected adverse events to the physician or clinic where the vaccine was administered.

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 MedImmune

##### Manufactured by:

MedImmune Vaccines, Inc.

Gaithersburg, MD 20878

For other product information regarding FluMist, call 1-877-FLUMIST (358-6478).

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## Bocavirus Seen in Acute Asthma Cases

The recently identified human bocavirus is present in children hospitalized with asthma, and infects children older than 2 years of age, Dr. Dominique Gendrel and colleagues reported in a poster at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Human bocavirus was detected by real-time polymerase chain reaction in nasopharyngeal aspirate samples from 16 of 136 children (12%), aged 2-16 years, who were hospitalized with severe acute asthma from November 2005 to May 2007 in the St. Vincent de Paul-Cochin Hospital in Paris. All the children had been hospitalized with acute asthma after evaluation in the emergency department.

The infected children had a mean age of 3.2 years; two children were older than 5 years, which suggests that the respiratory tract infection is not limited to young infants.

The bocavirus was associated with *Mycoplasma pneumoniae* in two cases, respiratory syncytial virus (RSV) in one case, and human metapneumovirus in one case.

In all, there were 16 cases of *M. pneumoniae* (12%), 12 cases of RSV (9%), 4 cases of influenza A (3%), 1 case of influenza B, and 1 case of parainfluenza III. Three of 90 children (3%) tested positive for human metapneumovirus, the investigators reported at the meeting, which was sponsored by the American Society for Microbiology.

As was observed in other studies, Dr. Gendrel said in an interview that there was a seasonal variation to the virus, with more cases identified in winter and spring. Dr. Gendrel is with the Pediatric Department, Paris 5 University and Medical School, Hospital St. Vincent de Paul-Cochin, Paris, according to the poster.