Human bocavirus was described first in 2005 by Allander and associates. Since then, this virus has been associated with a significant number of respiratory illnesses in children throughout the world.6

HISTORY

Allander and coworkers developed a system for molecular virus screening of clinical nasopharyngeal samples. This system was based on host DNA depletion, random polymerase chain reaction (PCR) amplification, large-scale sequencing, and bioinformatics. Using two pools of nasopharyngeal aspirate samples from patients (mainly children) with respiratory illnesses seen in November and December 2003 and March 2004, they found two agents that had an amino acid sequence that significantly matched bovine parvovirus and canine minute virus. These viruses are members of the Parvoviridae family, subfamily Parvovirinae, genus Bocavirus. These investigators proposed the provisional name human bocavirus for this new virus. During the ensuing years, this virus has been identified in respiratory samples and at other sites from patients throughout the world.1

PROPERTIES

As noted in Chapter 164, members of the family Parvoviridae are small, nonenveloped, single-stranded DNA viruses. The complete genome length of human bocavirus has not been determined, but at least 5299 nucleotides were identified in one of the two reference strains.4

The genome is thought to contain three open-reading frames; two of these frames encode the nonstructural proteins NS1 and NP-1, and the other encodes the two capsid proteins VP1 and VP2.4,6 The function of NS1 in human bocavirus infection is not known. However, in other parvoviruses, NS1 is involved in the binding and hydrolysis of nucleoside triphosphates and has helicase activity. The function of NP-1 is unknown. The virion-associated proteins (VP1, VP2) are more immunogenic than are the capsid proteins VP3 and VP4.4

The cellular site of human bocavirus replication is not known.16 The virus has not been propagated in tissue culture, and, as yet, no animal model of infection has been identified.

EPIDEMIOLOGY

Infection with human bocavirus enjoys worldwide prevalence.16 The virus exists as a single lineage with two genotypes. The virus has been identified in nasopharyngeal samples from children hospitalized with respiratory illnesses in 1.5 to 19 percent of those studied.1 Infection is seen most frequently in children younger than 2 years old, but infection occurs in older children as well. The prevalence of infection in adults with respiratory illness is low. In a seroprevalence study in Japan involving sera from 204 subjects younger than 3 months to older than 20 years in which antibody to the VP1 protein was measured, the following positivity rates were found: younger than 3 months, 90.5 percent; 3 to 5 months, 40.0 percent; 6 to 8 months, 5.6 percent; 9 to 11 months, 33.3 percent; 1 year, 42.3 percent; 2 to 3 years, 83.3 percent.
and older than 20 years, 94.1 percent. Human bocavirus is that males predominated with all viruses except human bocavirus–positive nasopharyngeal samples. In another study, the white blood cell count in children was 3000 to 31,000 cells/mm³ (median, 13,300 cells/mm³). The median differential cell values were neutrophils, 40 percent; band forms, 10 percent; lymphocytes, 39 percent; and monocytes, 10 percent. The C-reactive protein level in six children ranged from 0.4 to 7.3 mg/dL (median, 0.7 mg/dL). In a German study, the white blood cell count ranged from 6700/mm³ to 16,700/mm³, and the median value was 11,500/mm³. The C-reactive protein level ranged from less than 0.3 to 114 mg/L, and the median value was 12.5 mg/L (normal value, <0.3 mg/L). In a Japanese study, the white blood cell count range was 4800 cells/mm³ to 21,980 cells/mm³ (median, 14,000 cells/mm³), and the C-reactive protein level ranged from less than 0.20 to 4.48 mg/dL (median, 0.38 mg/dL).

Upper Respiratory Tract Infections

In one study, 86 percent of 49 human bocavirus infections without coinfection with other agents were classified as upper respiratory illnesses. In contrast, only 42 percent of 50 children in this study who had human bocavirus and a co-infecting agent were classified as having an upper respiratory illness. Pharyngitis was observed in 55 percent of the cases in which human bocavirus was the single agent identified. Of the children with human bocavirus infections without coinfections, 18 percent had acute otitis media and 12 percent had sinusitis. In another study, otitis media was reported in 61 percent of all human bocavirus infections.

In a large study, Arnold and associates noted the following findings at the time of presentation: fever, 68 percent; rhinorrhea, 67 percent; cough, 85 percent; conjunctivitis, 7 percent; vomiting, 30 percent; diarrhea, 21 percent; and rash, 7 percent. Of interest was that the cough was paroxysmal in 19 percent of the human bocavirus–infected children, whereas paroxysmal cough was much less common in adenovirus infections (7%) and human metapneumovirus infections (5%).

In one study in Korea, three of 36 (8.3%) children infected with human bocavirus had croup. In a study in Canada, two of 58 (3%) bocavirus-infected children had croup, and in a study in Japan, one of 18 (6%) had laryngotracheitis.

Lower Respiratory Tract Infections

Longtin and colleagues noted that 42 percent of children with human bocavirus infections had pneumonia and that 82 percent had bronchiolitis. In the large study in San Diego, California, involving 82 children with human bocavirus infections, 76 children with adenoviral infections, and 87 children with human metapneumovirus infections, the investigators were able to compare the rates of various clinical findings. In this study, the following rates of events were noted in bocavirus-infected children: hospitalization, 69 percent; need for oxygen administration, 44 percent; admission to intensive care unit, 11 percent; intubation, 4 percent; clinical lower respiratory tract disease, 61 percent; hypoxia, 41 percent; increased work of breathing, 59 percent; abnormal lung findings, 51 percent; “atelectasis vs. infiltrate,” 11 percent; “infiltrate” or “pneumonia,” 9 percent; and bronchiolitis, 46 percent. Comparatively, adenovirus-infected children had less lower respiratory tract disease, less hypoxia, and less increased work of breathing and were more likely to have normal chest radiographic findings than were children with human bocavirus and human metapneumovirus infections.

In a study in Korea, 53 percent of human bocavirus–infected children had rales noted on chest auscultation and 42 percent had wheezing. The clinical diagnoses in this study were bronchiol-
itis (25%), pneumonia (56%), exacerbation of asthma (11%), and
croup (8%). In a study in Germany, 32 children with lower
respiratory tract disease were studied. The diagnoses were
bronchitis (16%), wheezing bronchitis (14%), bronchiolitis (3%),
and pneumonia (18%). Ten of the 11 patients in this study with
pneumonia had co-infections with other respiratory viruses. In a
study in Canada involving 58 bocavirus infections, 40 percent had
bronchiolitis and 22 percent had pneumonia. In a study of 18
children in Japan, the lower respiratory tract diagnoses were
wheezy bronchitis (33%), pneumonia (33%), bronchiolitis (11%),
bronchitis (11%), and asthmatic attack (6%).

GASTROINTESTINAL ILLNESS
Gastroenteritis is not an uncommon finding in human bocavirus
infections. The virus has been identified in nasopharyngeal
samples and in stool samples of children with diarrhea. In one
study in Hong Kong, diarrhea was noted in 11 percent of 79
patients with respiratory symptoms. In the same study, human
bocavirus was identified in fecal samples of 25 children with gas-
troenteritis. Of these children, 16 percent had blood in the stool,
8 percent had mucus in the stool, 52 percent had vomiting, and
68 percent had fever. The following respiratory findings were
noted in these children with gastroenteritis: coryza (56%), acute
bronchitis (16%), and pneumonia (12%). Co-pathogens were
identified in 56 percent of the children: rotavirus (36%),
Salmonella spp. (8%), Campylobacter spp. (4%), Staphylococcus aureus
(4%), and Chlamydia psittaci (4%).

In a study of 962 stool samples from children with acute gas-
troenteritis in Seoul, Korea, a viral agent was found in 44.4
percent of the specimens. The viral agents included rotavirus
(25.7%), norovirus (13.7%), adenovirus (3.0%), astrovirus (1.1%),
and human bocavirus (0.8%). In another study in Brazil, 2 percent
of 705 diarrhea stool samples were PCR positive for human
bocavirus.

In studies of respiratory illness associated with human boca-
virus infection, diarrhea occurs in 9 to 38 percent.

INFECTIONS IN IMMUNOCOMPROMISED PATIENTS
Koskenvuo and associates described three children with acute
lymphoblastic leukemia who had acute febrile episodes in whom
human bocavirus was detected in their respiratory secretions. In
addition to fever, one of these children had cough, rhinitis, and
otitis media, and another child had vomiting and diarrhea. The
third child had five consecutive febrile episodes during the course
of a 6-month period, and with each of these episodes, human
bocavirus was found in nasal swab samples. Smuts and Hardie noted
eight children with HIV infections and associated human boca-
virus infections but presented no details related to their
illnesses.

OTHER CLINICAL FINDINGS
In addition to respiratory and gastrointestinal signs and symp-
toms, numerous other clinical findings and diagnoses have been
observed in children with human bocavirus infections. Arnold and
colleagues noted four children with maculopapular ery-
thematosus rashes with prominence on the chest and trunk. Two
of these children had involvement of the face. Exanthems have
been noted in other studies. Three studies, the rate of exanthema varied between 5 and 9 percent in the children studied.

REFERENCES
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The human polyomaviruses, JC virus (JCV) and BK virus (BKV), and the simian virus 40 (SV40), which is also able to infect humans, represent a unique group of viruses that cause disease almost exclusively in immunocompromised patients. Polyomaviruses derive their name from poly-, meaning many, and -oma, which refers to their ability to induce tumors in laboratory animals. Their colorful history and critical role in the elucidation of fundamental cellular and molecular pathways have immortalized them as research tools. The finding of polyomaviruses associated with several human cancers and their ability to cause central nervous system and urinary tract disease in immune compromised patients have brought them to the forefront of clinical care and research. The emergence of human polyomavirus disease has highlighted the need to understand the natural history and fundamental host processes that control the persistence of polyomaviruses. The next decade of research undoubtedly will reveal the true nature of these fascinating viruses.

**HISTORY**

The recognition of progressive multifocal leukoencephalopathy (PML) as a clinical entity in 1958 marked the beginning of our knowledge of the human polyomaviruses. Edward P. Richardson, Jr., a neuropathologist at Massachusetts General Hospital in Boston, and his colleagues described three cases of progressive neurologic disease in patients receiving chemotherapy for leukemia. At autopsy, they found many foci of demyelination, includ-