immunocompromised patients, including those with neoplasia, recipients of HSCTs, and children with HIV infection.

DIAGNOSIS

HMPV can be detected in nasal aspirates and respiratory secretions by immunofluorescence, by PCR (the most sensitive technique), or by growth in rhesus monkey kidney (LLC-MK2) tissue cultures. A serologic diagnosis can be made by ELISA, which uses HMPV-infected tissue culture lysates as sources of antigens.

TREATMENT HUMAN METAPNEUMOVIRUS INFECTIONS

Treatment for HMPV infections is primarily supportive and symptom-based. Ribavirin is active against HMPV in vitro, but its efficacy in vivo is unknown.

PREVENTION

Vaccines against HMPV are in the early stages of development.

PARAINFLUENZA VIRUS INFECTIONS

ETIOLOGIC AGENT

Parainfluenza viruses belong to the Paramyxoviridae family (genera *Respirovirus* and *Rubulavirus*). They are 150–200 nm in diameter, are enveloped, and contain a single-stranded RNA genome. The envelope is studded with two glycoproteins: one possesses both hemagglutinin and neuraminidase activity, and the other contains fusion activity. The viral RNA genome is enclosed in a helical nucleocapsid and codes for six structural and several accessory proteins. All types of parainfluenza virus (1, 2, 3, 4A, and 4B) share certain antigens with other members of the Paramyxoviridae family, including mumps and Newcastle disease viruses.

EPIDEMIOLOGY

Parainfluenza viruses are distributed throughout the world; infection with serotypes 4A and 4B has been reported less widely, probably because these types are more difficult than the other three to grow in tissue culture. Infection is acquired in early childhood; by 5 years of age, most children have antibodies to serotypes 1, 2, and 3. Types 1 and 2 cause epidemics during the fall, often occurring in an alternate-year pattern. Type 3 infection has been detected during all seasons, but epidemics have occurred annually in the spring.

The contribution of parainfluenza infections to respiratory disease varies with both the location and the year. In studies conducted in the United States, parainfluenza virus infections have accounted for 4.3–22% of respiratory illnesses in children. The major importance of these viruses is as a cause of lower respiratory illness in young children, in whom they rank second only to HRSV in that regard. Parainfluenza virus type 1 is the most common cause of croup (laryngotracheobronchitis) in children, whereas serotype 2 causes similar, although generally less severe, disease. Type 3 is an important cause of bronchiolitis and pneumonia in infants, whereas illnesses associated with types 4A and 4B have generally been mild. Unlike types 1 and 2, type 3 frequently causes illness during the first month of life, when passively acquired maternal antibody is still present. Parainfluenza viruses are spread through infected respiratory secretions, primarily by person-to-person contact and/or by large droplets, and by contact with fomites contaminated with respiratory secretions. The incubation period has varied from 3 to 6 days in experimental infections but may be somewhat shorter for naturally occurring disease in children.

In adults, parainfluenza virus infections are generally mild and account for fewer than 10% of respiratory illnesses. The advent of contemporary laboratory methods for diagnosis has increased awareness of the impact of parainfluenza infections in adults. In a recent study, parainfluenza virus was the third most common viral isolate from patients 16–64 years old who required hospitalization (0.7 isolate/1000 population). In the 2009 influenza pandemic, parainfluenza virus type 3 was the second most common cause of illness after influenza virus.

PATHOGENESIS

Immunity to parainfluenza viruses is incompletely understood, but evidence suggests that immunity to infections with serotypes 1 and 2 is mediated by local IgA antibodies in the respiratory tract. Passively acquired serum neutralizing antibodies also confer some protection against infection with types 1, 2, and (to a lesser degree) 3. Studies in experimental animal models and in immunosuppressed patients suggest that T cell–mediated immunity may also be important in parainfluenza virus infections. Lack of cellular immune responses is associated with an increased risk of progressive and fatal disease in HSCT recipients.

CLINICAL MANIFESTATIONS

Parainfluenza virus infections occur most frequently among children, in whom initial infection with serotype 1, 2, or 3 is associated with an acute febrile illness in 50–80% of cases. Children may present with coryza, sore throat, hoarseness, and cough that may or may not be croupy. In severe croup, fever persists, with worsening coryza and sore throat. A brassy or barking cough may progress to frank stridor. Most children recover over the next 1 or 2 days, although progressive airway obstruction and hypoxia ensue occasionally. If bronchiolitis or pneumonia develops, progressive cough accompanied by wheezing, tachypnea, and intercostal retractions may occur. In this setting, sputum production increases modestly. Physical examination documents nasopharyngeal discharge and oropharyngeal injection, along with rhonchi, wheezes, or coarse breath sounds. Chest x-rays can show air trapping and occasionally interstitial infiltrates.

In older children and adults, parainfluenza infections tend to be milder, presenting most frequently as a common cold or as hoarseness, with or without cough. Lower respiratory tract involvement in older children and adults is uncommon, although tracheobronchitis and community-acquired pneumonia have been reported in adults.

Parainfluenza viruses, most frequently type 3, are important pathogens in immunosuppressed patients—particularly in HSCT recipients but also in SOT recipients (especially recipients of lung transplants). Patients receiving cancer chemotherapy are also at risk for severe parainfluenza infection. Severe, prolonged, and even fatal parainfluenza-associated respiratory illnesses have been reported in children and adults with severe immunosuppression.

LABORATORY FINDINGS AND DIAGNOSIS

The clinical syndromes caused by parainfluenza viruses (with the possible exception of croup in young children) are not sufficiently distinctive to be diagnosed on clinical grounds alone. A specific diagnosis is established by detection of virus in respiratory tract secretions, throat swabs, or nasopharyngeal washings. Growth of the virus in tissue culture is detected either by hemagglutination or by a cytopathic effect. A rapid diagnosis may be made by identification of parainfluenza antigens in exfoliated cells from the respiratory tract with immunofluorescence or ELISA, although these techniques appear to be less sensitive than tissue culture. Highly specific and sensitive PCR assays have also been developed and have now become the standard for viral diagnosis. Serologic diagnosis can be established by hemagglutination-inhibition, complement-fixation, or neutralization testing of acute- and convalescent-phase specimens. However, because frequent heterotypic responses occur among the parainfluenza serotypes, the serotype causing illness often cannot be identified by serologic techniques alone.

Acute epiglottitis caused by *Haemophilus influenzae* type b must be differentiated from viral croup. Influenza A virus is also a common cause of croup during epidemic periods.

TREATMENT PARAINFLUENZA VIRUS INFECTIONS

For upper respiratory tract illness, symptoms can be treated as discussed for other viral respiratory tract illnesses. If complications such as sinusitis, otitis, or superimposed bacterial bronchitis develop, appropriate antibacterial drugs should be administered. Mild cases of croup should be treated with bed rest and moist air generated by vaporizers. More severe cases require hospitalization