than at 37°C (the temperature of the lower respiratory tract), whereas HRV-C viruses replicate well at either temperature. Of the 101 initially recognized serotypes of rhinovirus, 88 use intercellular adhesion molecule 1 (ICAM-1) as a cellular receptor and constitute the "major" receptor group, 12 use the low-density lipoprotein receptor (LDLR) and constitute the "minor" receptor group, and 1 uses decay-accelerating factor.

EPIDEMIOLOGY

Rhinovirus infections are worldwide in distribution. They are a prominent cause of the common cold and have been detected in up to 50% of common cold–like illnesses by tissue culture and polymerase chain reaction (PCR) techniques. Overall rates of rhinovirus infection are higher among infants and young children and decrease with increasing age. Rhinovirus infections occur throughout the year, with seasonal peaks in early fall and spring in temperate climates. These infections are most often introduced into families by preschool or grade-school children <6 years old. Of initial illnesses in family settings, 25–70% are followed by secondary cases, with the highest attack rates among the youngest siblings at home. Attack rates also increase with family size.

Rhinoviruses appear to spread through direct contact with infected secretions, usually respiratory droplets. In some studies of volunteers, transmission was most efficient by hand-to-hand contact, with subsequent self-inoculation of the conjunctival or nasal mucosa. Other studies demonstrated transmission by large- or small-particle aerosol. Virus can be recovered from plastic surfaces inoculated 1–3 h previously; this observation suggests that environmental surfaces contribute to transmission. In studies of married couples in which neither partner had detectable serum antibody, transmission was associated with prolonged contact (≥122 h) during a 7-day period. Transmission was infrequent unless (1) virus was recoverable from the donor's hands and nasal mucosa, (2) at least 1000 $TCID_{50}$ (50% tissue culture infectious dose) of virus was present in nasal washes from the donor, and (3) the donor was at least moderately symptomatic with the "cold." Despite anecdotal observations, exposure to cold temperatures, fatigue, and sleep deprivation have not been associated with increased rates of rhinovirus-induced illness in volunteers, although some studies have suggested that psychologically defined "stress" may contribute to development of symptoms.

By adulthood, nearly all individuals have neutralizing antibodies to multiple rhinovirus serotypes, although the prevalence of antibody to any one serotype varies widely. Multiple serotypes circulate simultaneously, and generally no single serotype or group of serotypes has been more prevalent than the others.

PATHOGENESIS

Rhinoviruses infect cells through attachment to specific cellular receptors; as mentioned above, most serotypes attach to ICAM-1, while a few use LDLR. Relatively limited information is available on the histopathology and pathogenesis of acute rhinovirus infections in humans. Examination of biopsy specimens obtained during experimentally induced and naturally occurring illness indicates that the nasal mucosa is edematous, is often hyperemic, and—during acute illness—is covered by a mucoid discharge. There is a mild infiltrate with inflammatory cells, including neutrophils, lymphocytes, plasma cells, and eosinophils. Mucus-secreting glands in the submucosa appear hyperactive; the nasal turbinates are engorged, a condition that may lead to obstruction of nearby openings of sinus cavities. Several mediators—e.g., bradykinin; lysylbradykinin; prostaglandins; histamine; interleukins 1β, 6, and 8; interferon γ–induced protein 10; and tumor necrosis factor α—have been linked to the development of signs and symptoms in rhinovirus-induced colds.

The incubation period for rhinovirus illness is short, generally 1–2 days. Virus shedding coincides with the onset of illness or may begin shortly before symptoms develop. The mechanisms of immunity to rhinovirus infection are not well worked out. In some studies, the presence of homotypic antibody has been associated with significantly reduced rates of subsequent infection and illness, but data conflict regarding the relative importance of serum and local antibody in protection from rhinovirus infection.

CLINICAL MANIFESTATIONS

The most common clinical manifestations of rhinovirus infections are those of the common cold. Illness usually begins with rhinorrhea and sneezing accompanied by nasal congestion. The throat is frequently sore, and in some cases sore throat is the initial complaint. Systemic signs and symptoms, such as malaise and headache, are mild or absent, and fever is unusual in adults but may occur in up to one-third of children. Illness generally lasts for 4–9 days and resolves spontaneously without sequelae. In children, bronchitis, bronchiolitis, and bronchopneumonia have been reported; nevertheless, it appears that rhinoviruses are not major causes of lower respiratory tract disease in children. Rhinoviruses may cause exacerbations of asthma and chronic pulmonary disease in adults. The vast majority of rhinovirus infections resolve without sequelae, but complications related to obstruction of the eustachian tubes or sinus ostia, including otitis media or acute sinusitis, can develop. In immunosuppressed patients, particularly bone marrow transplant recipients, severe and even fatal pneumonias have been associated with rhinovirus infections.

DIAGNOSIS

Although rhinoviruses are the most frequently recognized cause of the common cold, similar illnesses are caused by a variety of other viruses, and a specific viral etiologic diagnosis cannot be made on clinical grounds alone. Rather, rhinovirus infection is diagnosed by isolation of the virus from nasal washes or nasal secretions in tissue culture. In practice, this procedure is rarely undertaken because of the benign, self-limited nature of the illness. In most settings, detection of rhinovirus RNA is more sensitive and easier by PCR than by tissue culture. Accordingly, PCR has generally become the standard for detection of rhinoviruses in clinical specimens. Given the many serotypes of rhinovirus, diagnosis by serum antibody tests is currently impractical. Likewise, common laboratory tests, such as white blood cell count and erythrocyte sedimentation rate, are not helpful.

TREATMENT RHINOVIRUS INFECTIONS

Because rhinovirus infections are generally mild and self-limited, treatment is not usually necessary. Therapy in the form of first-generation antihistamines and nonsteroidal anti-inflammatory drugs may be beneficial in patients with particularly pronounced symptoms, and an oral decongestant may be added if nasal obstruction is particularly troublesome. Reduction of activity is prudent in instances of significant discomfort or fatigability. Antibacterial agents should be used only if bacterial complications such as otitis media or sinusitis develop. Specific antiviral therapy is not available.

PREVENTION

Intranasal application of interferon sprays has been effective in the prophylaxis of rhinovirus infections but is also associated with local irritation of the nasal mucosa. Studies of prevention of rhinovirus infection by blocking of ICAM-1 or by binding of drug (pleconaril) to parts of the viral capsid have yielded mixed results. Experimental vaccines to certain rhinovirus serotypes have been generated, but their usefulness is questionable because of the myriad serotypes involved and the uncertainty about mechanisms of immunity. Thorough hand washing, environmental decontamination, and protection against autoinoculation may help to reduce rates of transmission of infection.

CORONAVIRUS INFECTIONS

ETIOLOGIC AGENT

Coronaviruses are pleomorphic, single-stranded RNA viruses that measure 100–160 nm in diameter. The name derives from the crown-like appearance produced by the club-shaped projections that stud the viral envelope. Coronaviruses infect a wide variety of animal species and have been divided into four genera. Coronaviruses that infect humans (HCoVs) fall into two genera: *Alphacoronavirus*