Respiratory Syncytial Virus Infection
An Illness for All Ages

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KEYWORDS

• Respiratory syncytial virus • Bronchiolitis • Chronic obstructive pulmonary disease • Antivirals • Asthma • Vaccines • Adults

KEY POINTS

- Respiratory syncytial virus (RSV) is an important respiratory pathogen at both ends of the age spectrum, with approximately 100,000 hospitalizations in infants and approximately 177,000 in adults. However, general awareness of RSV in adults among internists and general practitioners is lacking.
- The interaction of RSV with pathogenic bacteria, specifically *Streptococcus pneumoniae* and *Hemophilus influenzae*, seem to influence disease severity and contribute to morbidity, especially in the developing world.
- Prophylaxis with Palivizumab provides effective prevention in specific high-risk infants but there are currently no effective specific therapies or vaccines for most susceptible infants and adults.

Respiratory syncytial virus (RSV) was first identified in 1956 by Robert Chanock and is currently recognized as the most important cause of severe respiratory illness in infants and young children, clinically manifesting most often as bronchiolitis.[1] The virus has also more recently been identified as a significant contributor to morbidity and mortality in older adults and severely immunocompromised persons.[2]

VIRUS STRUCTURE AND GENOME

RSV is an enveloped negative-sense, single-strand RNA virus classified in the family *Pneumoviridae* along with human metapneumovirus, another cause of respiratory infections. The RSV genome contains 10 distinct genes that encode 11 individual proteins, each with distinct roles in viral infection and immune evasion (**Fig. 1**).[3] Surface glycoproteins protruding from the envelope include the viral attachment protein (G) and the fusion protein (F) that mediate entry of the viral genome into cells while transitioning from a thermolabile prefusion F to a stable postfusion F. G may play a role in modulation of the immune and inflammatory response to infection through its CX3C chemokine homologue that binds the CX3C receptor on immune cells and primary ciliated respiratory epithelial cells.[4,5] Two nonstructural RSV proteins (NS1 and NS2) inhibit cellular antiviral innate type I interferons, providing defense against the host immune response.

There are 2 major viral groups, designated A and B, each with numerous subgroups, best identified by G gene sequence variation.[6] However, a causal relationship between antigenic variation in G and reinfections has not been firmly established. Antibody to F and the G proteins is considered a primary determinant of immunity.

EPIDEMIOLOGY

In the temperate climates, annual epidemics occur during the winters. In the United States, epidemics

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Clin Chest Med ■ (2016) ■–■
http://dx.doi.org/10.1016/j.ccm.2016.11.010

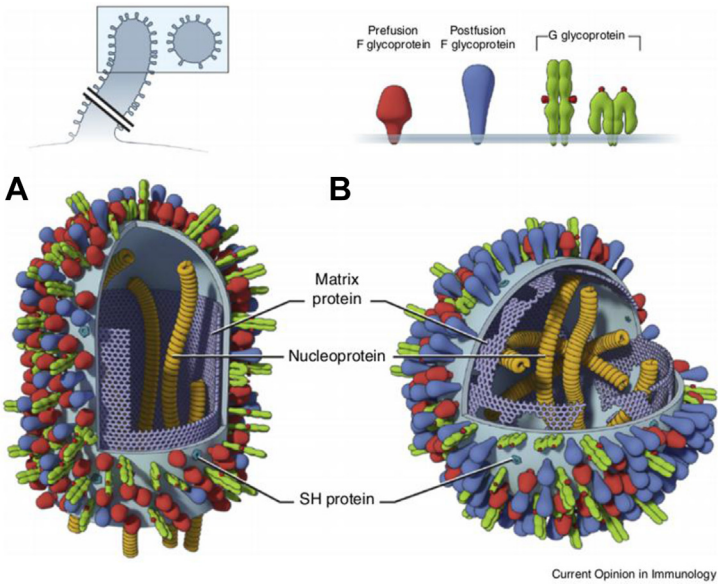

Fig. 1. The filamentous and spherical forms of RSV, indicating the (*A*) prefusion and (*B*) postfusion forms of F and the G glycoprotein. (*From* Graham BS, Modjarrad K, McLellan JS. Novel antigens for RSV vaccines. Curr Opin Immunol 2015;35:30–8; with permission.)

generally begin in the southeast in late summer and spread north and westward reaching a peak in January and February in the northeast and Pacific Northwest.[7] RSV circulation generally persists for 16 to 22 weeks in a community, and overlaps with the more sharply defined 6 to 8 week influenza epidemics. In the tropics, RSV circulation is more variable, frequently being more common during the rainy season and circulating throughout the year.[8] Group A and B RSV viruses cocirculate, with group A viruses tending to be more frequent.

Older children commonly introduce the virus into the family with spread to infants and parents.[9] RSV is most effectively transmitted by large fomites (nasal secretions) whereas aerosol is less important. The virus is stable for several hours on hard surfaces and hands, allowing transmission by direct contact with contaminated objects. The introduction of strict infection control policies in hospital settings (isolation and hand washing) and personal protective equipment (gowns, gloves, and possibly goggles) reduces nosocomial transmission.[10]

PEDIATRIC RESPIRATORY SYNCYTIAL VIRUS INFECTION

The importance of RSV on the health of infants and young children cannot be underestimated. It causes acute illness and, importantly, may be causally related to the development of subsequent wheezing in childhood and asthma later in life. Fifty percent to 70% of newborn infants become infected during their first winter, and virtually all become infected by age 2 years. Reinfections with RSV continue throughout childhood, although their severity diminishes. In the United States, approximately 1% to 2% of infants in their first year of life are hospitalized with RSV infection, whereas another 20% will be seen in pediatric offices or emergency rooms for acute respiratory symptoms.[11] Pediatric mortality from RSV in developed countries is low (~50–100 annually in the United States); however, in the developing world, RSV is estimated to result in 66,000 to 199,000 deaths and more than 3 million hospitalizations in children younger than age 5 years.[12,13]

The course of RSV illness and its manifestations follow a similar pattern in most infants, although disease severity is highly variable. Following an incubation period of 4 to 6 days, nasal congestion with mucus discharge and fever are followed by cough, tachypnea, and respiratory distress with chest retractions and wheezing, the hallmark of bronchiolitis. In young preterm infants, apnea will occasionally be an early manifestation of RSV. The clinical picture of RSV in young infants can change during observation, with hypoxia and physical findings fluctuating even in a matter of several minutes. Radiographs reveal air trapping and infiltrates related to obstructive atelectasis or viral pneumonia. This variability in the clinical appearance of an infant with RSV can make decisions about further observation or whether to hospitalize difficult.

Bacterial coinfection with *Streptococcus pneumoniae* or *Hemophilus influenzae*, either as otitis media or pneumonia, can complicate RSV