Respiratory Syncytial Virus in Blood and Marrow Transplant Recipients

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Respiratory syncytial virus (RSV) is a common community-acquired respiratory infection characterized by symptoms similar to those of the common cold. Most children have been infected with RSV by age two; as with the common cold, reinfection occurs because immunity is not persistent (Centers for Disease Control and Prevention [CDC], 2000). The significant difference between RSV and a cold is RSV’s propensity to cause lower airway respiratory infections and its considerable morbidity in immunocompromised patients. Scattered documented cases of RSV outbreaks in blood and marrow transplant recipients have reported mortality ranging from 0%–82% (Bowden, 1997; Ghosh et al., 2001; Harrington et al., 1992). These studies have conveyed lessons that can guide creation of clinical practice protocols aimed at preventing exposure and managing infection. This article reviews the clinical risks of RSV, transmission modes, its signs and symptoms, diagnosis, treatment options, and impact on transplant recipients. Nursing care issues are described as well.

What Is Respiratory Syncytial Virus and How Does It Spread?

RSV is an RNA-enveloped virus that incubates from two to eight days and replicates in the nasopharyngeal epithelium. In immunocompromised patients, upper respiratory symptoms alone are relatively uncommon but connote a better prognosis than lower airway disease (Bowden, 1997; Ghosh et al., 2001; Harrington et al., 1992). Infection usually spreads to the lower respiratory tract in one to three days, causing a viral pneumatic process similar to other viral pneumonias. Lower respiratory tract infection with RSV causes airway inflammation, necrosis, and sloughing of the small airway epithelium. Edema and increased mucous production lead to pulmonary congestion and productive cough. Complete healing takes four to six weeks, although transmission risk in immunocompetent individuals usually is limited to 10–16 days (Harrington et al.). Immunocompromised patients have been shown to shed the virus for as long as 17–22 days, producing a prolonged transmission risk for all who come in contact with them (Harrington et al.). Transmission may be shortened to 10 days in those who have limited upper respiratory infection (URI), although studies supporting this conclusion are limited (Harrington et al.). Healthcare providers must recognize this discrepancy in time of contagiousness and consider that blood and marrow transplant recipients with RSV disease may shed the virus longer. Therefore, isolation precautions may be required for longer periods of time. Symptoms of protracted disease include a prolonged cough, wheezing, and altered pulmonary function (Hall & McCarthy, 2000).

RSV primarily is transmitted via respiratory secretion droplets and is considered a contact infection. Contact with contaminated secretions, such as those produced by coughing, sneezing, or tearing, is a potential method of transmission. The viral organism survives only a few hours on inanimate surfaces and is inactivated easily with soap and water or disinfectants (CDC, 2000). Transmission of RSV has been documented in circumstances of close contact with respiratory secretions from infected people or surfaces.
contaminated with their secretions. The spread of this community-acquired infection among immunocompromised people can occur rapidly and persist for prolonged periods of time. RSV most often is introduced into transplantation units by staff or visitors with mild URIs (Hall & McCarthy, 2000). Outbreaks are likely to be seen from November through May (Hall & McCarthy) but also have occurred through June (Bowlden, 1997). Community-acquired RSV infections in blood and marrow transplant recipients reportedly lead to prolonged infection, higher chances of nosocomial acquisition among cohorted patients, and a high incidence of RSV pneumonia with a high mortality (Englund, 2001).

Signs and Symptoms

URI with RSV is characterized by the presence of cough, fever, nasal or sinus congestion, rhinorrhea, sore throat, or hoarseness without an infiltrate on chest radiograph (Harrington et al., 1992). Excess oral, nasal, and upper airway secretions are prevalent in infections involving the upper respiratory tract (Harrington et al.). Otitis media is an unusual but potential clinical finding (Ghosh et al., 2000). Blood and marrow transplant recipients who develop URI often manifest fewer symptoms because of their decreased inflammatory response. RSV pneumonia is a major clinical complication prevalent in immunocompromised patients and confers a poorer prognosis than other infections limited to the upper respiratory tract (Englund, 2001). Studies of this disease in blood and marrow transplant recipients show that pneumonia is more common during the pre-engraftment period (79%–80% of cases) than after engraftment (27%–41% of cases). Mortality rates are similar regardless of when infection occurs (Champlin & Whimbey, 2001; Harrington et al.; Ghosh et al., 2001). Cardinal signs and symptoms of RSV pneumonia in blood and marrow transplant recipients include rapid onset of dyspnea with hypoxia, low-grade fever, wheezing, and crackles (Harrington et al.).

Diagnosis

Several highly sensitive and specific laboratory tests are available to diagnose RSV infection. Rapid antigen-detection kits that use indirect immunofluorescence, direct immunofluorescence, or enzyme-linked immunosorbent assay provide results within hours and are the current state of the art for detecting community-acquired respiratory viruses. The sensitivity of rapid diagnostic tests is reliable for detection and monitoring of RSV outbreaks. The sensitivity for these tests ranges from 53%–96%, making viral cultures with a 95%–98% specificity the gold standard for detecting the presence of RSV antigen (American Academy of Pediatrics, 2000). Viral cultures, although a more accurate form of diagnosis, may require days to yield positive results. To facilitate rapid diagnosis and implementation of treatment, rapid antigen testing most commonly is performed in addition to cultures. Polymerase chain reaction technology and serum testing for RSV-specific immunoglobulin M antibodies still are being evaluated for their clinical utility (Walsh & Graham, 1999). RSV pneumonia is characterized by the presence of an infiltrate on a chest radiograph with a positive RSV antigen test from respiratory secretions (Nichols, Gooley, & Boeckh, 2001).

Accurate RSV diagnosis depends on obtaining an adequate specimen. Nasal washes, nasopharyngeal aspirates, and nasopharyngeal swabs have been used for routine RSV screening (Englund, 2001). See Figure 1 for information about how to obtain nasal washes for viral culture (Johns Hopkins Hospital, 1999). Nasal washes and swabs have shown significantly greater accuracy in studies of RSV among children, but results were less accurate in adults (Englund et al., 1996). Throat swabs are inadequate for detection of RSV infection (Englund). Bronchoalveolar lavage (BAL) specimens have a significantly higher yield for positive RSV results. This discrepancy is thought to be related to enhanced viral loads obtained by BAL, but risks and benefits must be weighed carefully prior to choosing a method for obtaining viral cultures (Englund; Englund et al., 1996; Hall, 2001).

Preventing Infection

No unique recommendations exist for preventing RSV infection; prevention strategies are similar to measures for preventing other communicable diseases. Conscientious avoidance of contact with individuals with upper respiratory symptoms and good hand washing and hygiene are the mainstays of prevention. Despite such general recommendations, several facilities caring for immunocompromised patients have instituted more stringent barrier protection for prevention of community-acquired respiratory viruses in response to the devastating effects that have occurred during RSV outbreaks (Champlin & Whimbey, 2001; Nichols et al., 2001).

More vigilance infection-control practices may include masks, gowns, and gloves for all people who have contact with blood and marrow recipients. This strategy is based on knowledge of a prodromal period during which infected people are asymptomatic or unaware that they have a contagious disease rather than a disorder such as allergy. Some institutions experiencing RSV outbreaks or higher incidence than predicted also have determined that staff education about the disease, its transmission, and the potentially lethal effects on blood and marrow recipients can be instrumental in reducing infection rates. In one blood and marrow transplant setting, a task force reviewed existing and published guidelines for prevention and management of RSV infection, then initiated changes in policies related to barrier protection during high-risk periods of time, strategies for screening at-risk patients, and clinical management of mild and severe disease (Stanford University Medical Center, 2001). Guidelines for the prevention of RSV among blood and marrow recipients are included in Figure 2 (CDC, 2000; Champlin & Whimbey, 2001; Dykewicz, 2001; Garcia et al., 1997; Raad, Abbas, & Whimbey, 1997; Stanford University Medical Center).

Treatment

Because research is limited, no recommendations currently exist for specific antiviral therapy to treat RSV in the blood and marrow.
• Create cohorts or groups of patients to confine them in a limited area to reduce spread of virus (works well for outpatients).
• Create cohorts of nurses caring for patients with respiratory symptoms.
• See outpatients first (i.e., early in the morning) and facilitate prompt appointment times with no waiting in general areas.
• Educate family members and significant others about contact precautions.
• Reinforce proper hand washing and hand hygiene to patients, significant others, and healthcare providers.
• Promptly recognize symptoms of respiratory syncytial virus (RSV) and screen symptomatic patients as well as significant others who have upper respiratory infection symptoms.
• Implement immediate isolation (i.e., contact) precautions for patients with suspicious symptoms until two negative cultures are noted.
• Perform a viral culture and rapid diagnostic test immediately after recognition of suspicious symptoms. If two diagnostic tests taken two days apart do not identify a pathogen despite symptoms, bronchoalveolar lavage and further testing are suggested.
• Healthcare workers should not care for blood and marrow recipients if they have any upper respiratory infections.
• Reinforce sick policy for healthcare providers.
• Provide inpatients with private rooms if possible.
• Post signs on units for screening visitors and employees for upper respiratory symptoms.
• Limit visitors to immediate family members, not allowing children younger than 12.
• Mail or provide educational pamphlets to patients, support members, and employees who have signs and symptoms of RSV to help increase awareness.
• Provide information about RSV and infection-prevention guidelines to staff.
• Consider additional barrier precautions (e.g., masks for patients and caregivers) during periods of high risk or when documented cases of RSV have been noted within the institution.
• Designate stethoscopes, commodes, and thermometers to a single patient or a cohort of patients.
• Keep medical records outside of examination and treatment rooms.
• Practice thorough hand washing to prevent nosocomial spread.

Figure 2. Guidelines for the Prevention of Respiratory Syncytial Virus Infection in Blood and Marrow Transplant Recipients

Note. Based on information from Centers for Disease Control and Prevention, 2000; Campplin & Whimbey, 2001; Dykewicz, 2001; Garcia et al., 1997; Raad et al., 1997; Stanford University Medical Center, 2001.

recipients (CDC, 2000). Of utmost importance for patients with suspected or confirmed RSV infection is immediate implementation of contact isolation precautions as outlined by the CDC. Contact isolation precautions are based on the presumption that infectious organisms are aerosolized through normal encounters and remain communicable for some period of time on all inanimate objects that have been contaminated with respiratory secretions (e.g., saliva, tears, nasal drainage). Because of the high mortality from RSV pneumonia in the blood and marrow recipient population, more stringent isolation precautions often are instituted.

The use of surgical or eye and nose masks remains a controversial and unresolved issue in the prevention of RSV infection (CDC; Garcia et al., 1997). Contact isolation precautions are outlined in Figure 3 (CDC).

Clinical trials of antiviral medications and immunoglobulin currently are being conducted to help determine optimal therapy for isolated URI and pneumonitis (Nichols et al., 2001). Clinical trials aimed at preventing upper respiratory RSV from progressing to pneumonia involve the use of aerosolized ribavirin plus IV immunoglobulin (IVIG) therapy or palivizumab (Nichols et al.). Since 1992, 66 RSV-positive blood and marrow recipients at one major comprehensive cancer center have been treated with aerosolized ribavirin in combination with several different IVIG preparations (Champlin & Whimbey, 2001). Results of the study showed that, with early treatment, mortality rates decreased by 28% from the reported 60%–100% in patients who were not treated, treated late, or not able to tolerate ribavirin (Champlin & Whimbey).

Ribavirin is a synthetic guanosine nucleoside with broad-spectrum antiviral activity and has been licensed since 1986 for treatment of RSV infection in children and patients with underlying immunocompromise. It is administered as a small-particle aerosol from a solution containing the drug via a mist tent, mask, oxygen hood, or ventilator for 8–20 hours each day (Hall & McCarthy, 2000) (see Figure 4). Because ribavirin is potentially mutagenic, tumor-promoting, and gonadal toxic, healthcare workers must take precautions to reduce exposure during administration (Ribavirin Nursing Lexi-Drugs Online, 2002). Data on ribavirin teratogenicity and aerosolized ribavirin exposure in humans are minimal. Until more research is available in these areas, caution should be exercised (Adams, 1994; Gladu & Ecoichinson, 1989; Jury, 1993). Because ribavirin is administered in an aerosolized form, preventing exposure of healthcare providers is a challenging aspect of care for these patients. The small-particle aerosol generator tent allows for aerosolization of the medication and immediate scavenging of particles escaping the enclosed delivery system, thus reducing airborne particles and exposure of healthcare providers and visitors to the toxic medication (Adams). Aerosolized ribavirin provides high levels of the drug in pulmonary secretions without systemic absorption. Therapy can last from 4–14 days in immunocompromised hosts (Englund, Piedra, & Whimbey, 1997). Adverse reactions associated with administration of inhaled ribavirin include fatigue, headache, insomnia, nausea, anorexia, and anemia (Ribavirin Nursing Lexi-Drugs Online). Ghosh et al. (2000) reported that the most common adverse effect of ribavirin in blood and marrow recipients receiving the agent in a scavenger tent was the psychological distress of being isolated. Of special note is that when ribavirin must be administered through a mechanical ventilator, scavenging systems cannot be used. Debate is ongoing about how best to administer the agent and protect healthcare providers. Additionally, ribavirin delivered through a mechanical ventilator circuit can precipitate and potentially occlude the airway tube, requiring intensive respiratory care and ventilator monitoring (Ribavirin Nursing Lexi-Drugs Online). Guidelines and precautions for administration of aerosolized ribavirin are described in Figure 5 (Adams; Jury; Ribavirin Nursing Lexi-Drugs Online).

During the 1980s, IVIG was developed and used with patients with compromised immune systems to protect them from infection. It is derived from pooled plasma of adults and consists of immunoglobulin fraction of IgG and trace amounts of IgA and IgM. Adverse events related to IVIG include fever, chills, systemic reactions, headache, myalgia, anxiety, lightheadedness, nausea, vomiting, flushing, blood pressure changes,
The tubing entering the small-particle aerosol generator tent at face level is delivering aerosolized ribavirin. The tubing at the top of the tent is scavenging and vacuuming particles. The small-particle aerosol generator is to the right of the tent.

**Figure 4. Bone Marrow Transplant Recipient Receiving Aerosolized Ribavirin**

*Note.* Photo courtesy of Stanford University Medical Center.

**Nursing Care**

Blood and marrow recipients who present with upper respiratory symptoms in October through May might need to be screened for RSV. Some transplant centers have advocated screening patients prior to transplants, particularly if they have been in contact with anyone with URI one or two weeks prior to evaluation for transplant (Champlin & Whimbey, 2001). Patients who present with upper respiratory symptoms require private rooms and are placed on contact isolation until antigen testing or cultures are negative twice at least two days apart (CDC, 2000). Patients and visitors should be taught about the disease, its clinical implications, and the rationale for isolation precautions. Diversional activities such as exercise bikes, videos, music, art, or occupational therapy consultation and increased social support can be provided to reduce the negative effects of isolation.

Patients with RSV require frequent physical assessment. Even if symptoms initially are isolated to the upper respiratory system, respiratory assessment should be performed at least every four to eight hours. Assessment includes respiratory rate, rhythm, use of accessory muscles, characteristics of cough, oxygen saturation level, breath sounds, and secretion observation. If symptoms of progression to pneumonia are present, assessment every one to four hours might be necessary. When ribavirin is administered as treatment for RSV infection, nurses must follow institutional policies for safe administration and implement additional patient supportive measures, such as administering antianxiety medication as necessary and appropriate. Because of the necessity of closing doors during ribavirin treatment, rooms monitored by camera might be desirable for patients with unstable respiratory status. Nursing care of patients with RSV infection is extremely challenging intellectually, physically, and emotionally. The high incidence of progression to pneumonia and poor prognosis associated with infection contribute to making management of this patient population one of the most difficult in transplant care. Considering that this high acuity arises from a common community-acquired infection makes vigilant early prevention essential.

**Conclusion**

Nurses caring for blood and marrow recipients must understand the effects that RSV infection can have on transplant recipients, family members, and healthcare providers. With knowledge of the virulence and transmission of this virus, nurses are in a position to educate patients and family, reduce nosocomial spread, and influence clinical practice. Recog-
nizing specific risk factors for infection, nurses can act as gatekeepers who can identify candidates to screen and enhance early detection of infection. Nurses’ knowledge of clinical management strategies and precautions to implement will optimize delivery of appropriate therapy while maintaining a safe environment for all people involved.

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References


Stanford University Medical Center. (2001, October). Infection Control and Epidemiology Department. Meeting of the Respiratory Syncytial Virus/Bone Marrow Transplant Subcommittee, Stanford, CA.


For more information on this topic, visit the following Web sites.

American Lung Association Fact Sheet: Respiratory Syncytial Virus
www.lungusa.org/diseases/rsfvsac.html

Centers for Disease Control and Prevention: Respiratory and Enteric Viruses Branch
www.cdc.gov/nicidod/dvrd/revb

RSV Info Center
www.rsvinfo.com

Links can be found using ONS Online at www.ons.org.

Rapid Recap

Respiratory Syncytial Virus in Blood and Marrow Transplant Recipients

- Respiratory syncytial virus (RSV) infections in blood and marrow transplant recipients lead to prolonged infections, higher chance of nosocomial spread of infection, and a greater incidence of pneumonia, with a mortality rate more than 80%.
- Conscientious avoidance of contact with individuals with upper respiratory symptoms and good hand hygiene are the mainstays of RSV prevention.
- Accurate RSV screening and diagnosis depend on obtaining adequate specimens via nasal washes, nasopharyngeal aspirates, or nasopharyngeal swabs. Throat swabs are inadequate for detection of RSV infection.
- As recommended by the Centers for Disease Control and Prevention, contact isolation precautions are of utmost importance for patients with suspected or confirmed RSV infection.
- Ribavirin often is used to treat RSV. It is potentially mutagenic, tumor-promoting, and gonadal toxic; therefore, preventing exposure during its administration is a challenging aspect of nursing care.