

# Respiratory Syncytial Virus: Best Practices for Prevention and Treatment

Ms Charsha is a neonatal nurse practitioner who currently serves as associate chief nursing officer at Cooper University Hospital in Camden, NJ. She is responsible for the overall operations and strategic plans for the medical-surgical department, the maternal child health department, trauma and respiratory therapy services, and the nursing administrative team.

**ABSTRACT: A number of methods may be employed to prevent the spread of respiratory syncytial virus (RSV), including simple hand washing, screening of visitors to neonatal ICUs, and appropriate isolation and cohorting of infected infants. These standards of care must also be transferred to the home. Treatments such as acetaminophen, bronchodilators, and the antiviral agent, ribavirin, are available to treat symptoms of infection. Pharmacological prophylaxis with palivizumab and RSV intravenous immunoglobulin may be used in specific at-risk patients. Research to prevent and treat RSV infection is ongoing; preventive agents in development, such as the monoclonal antibody motavizumab and the vaccine MEDI-534, hold promise for reducing infection-related morbidity and mortality.**

Respiratory syncytial virus (RSV) infection can cause significant illness and even death, especially in preterm infants. Therefore, it is important to implement integrated approaches and action plans for preventing the spread of RSV in the hospital and at home.

## **PREVENTING SPREAD OF RSV IN HOSPITALIZED INFANTS**

**Hand hygiene.** Compliance with standardized hand-washing techniques is very important and should always be a major focus of attention. Hand washing with soap and water inactivates RSV. Research has shown

that strict hand-washing control measures can significantly reduce the rate of nosocomial spread of RSV infection from 4.2% to between 0.6% and 1.1%.<sup>1</sup>

**Screening visitors.** The practice of screening potential visitors to neonatal ICUs (NICUs) and questioning visitors about possible recent exposure to communicable diseases is becoming standard operating procedure in many hospitals. It remains unclear whether this practice substantially reduces RSV infections within the NICU.<sup>2</sup> Despite the lack of controlled trials that measure the impact of such screening, it is imperative to ask NICU visitors about potential recent exposure to infection. Since it is very difficult to obtain this information from families of young children, some hospitals prohibit young siblings from visiting NICUs when RSV is most prevalent in the surrounding community.

**NICU design.** Single-room (as opposed to pod-designed) NICUs may help minimize the spread of nosocomial infections generally. Research has shown that a single-room design has reduced nosocomial infections both in pediatric ICUs and in hospitalized adults.<sup>3</sup> However, studies of the NICU population are still needed. Such studies should become easier to do as more units are constructed in a single-room design. Single-room design promotes the cohorting of nursing staff as well as the segregation of infected patients; it also reduces the number of potentially infected visitors who come into contact

with the NICU population—which in theory can help prevent the nosocomial spread of RSV.

**Isolation of infected patients.** The rapid screening and isolation of infected infants has consistently been shown to reduce the spread of RSV infection within the NICU.<sup>4</sup>

**Cohorting of infected patients.** The practice of assigning screened infants either to a cohort of RSV-infected infants or to one of RSV-uninfected infants (called “cohorting”) is very successful in reducing infant-to-infant infections within the NICU. A strict cohorting regimen has been shown to reduce the number of nosocomial RSV infections from 7.17 cases per 1000 patient-days to zero.<sup>5</sup>

**Cohorting of staff caring for infected patients.** Certain staff should be assigned to RSV-infected infants in the NICU. This practice has not by itself been proved to reduce the spread of RSV infection within the NICU. However, cohorting employed as part of a larger infection reduction strategic plan, including proper hand washing, gowning, and gloving, has been shown to significantly

reduce the spread of nosocomial RSV infection.<sup>6</sup>

Unfortunately, hand-washing guidelines are not followed by health care practitioners 100% of the time, despite the overwhelming evidence that this practice decreases the spread of nosocomial viral infections such as RSV.<sup>7,8</sup> Because there are varying degrees of adherence to hand washing and other hygiene measures, the segregation of potentially exposed nursing and support staff is paramount in preventing the spread of RSV infection within the hospital.

**Screening of staff.** It is imperative that potentially infected nursing staff not enter the NICU during the time when they may be shedding the virus. Adults can shed RSV for up to 5 days, and infants can shed RSV for as long as 21 days.

**Appropriate protective equipment.** In addition to hand washing, appropriate use of gloves, gowns, and goggles by nursing staff has also been proved to significantly reduce the nosocomial spread of RSV. Proper gowning and gloving has been demonstrated to reduce the

spread of RSV within NICUs by 50%, from a rate of 6.4 cases per 1000 patient-days to 3.1 cases per 1000 patient-days.<sup>9</sup>

Other methods that can help prevent the nosocomial spread of RSV include the use of rapid diagnostic tests and the use of prophylaxis in eligible infants. However, no single preventive measure can by itself eliminate the nosocomial spread of RSV infection. Each individual technique must be employed as part of a consistent, staff-wide prevention program and adhered to routinely.

Research has shown that robust preventive strategies, when executed consistently, can reliably prevent the nosocomial spread of RSV. In addition to benefiting patients, this can directly reduce hospital costs. The **Figure** demonstrates the reduction in RSV infection that occurs when a proper preventive strategy is implemented as early as possible.<sup>10</sup>

## DECREASING SPREAD OF RSV IN THE HOME

In addition to executing strategies to prevent the spread of RSV in

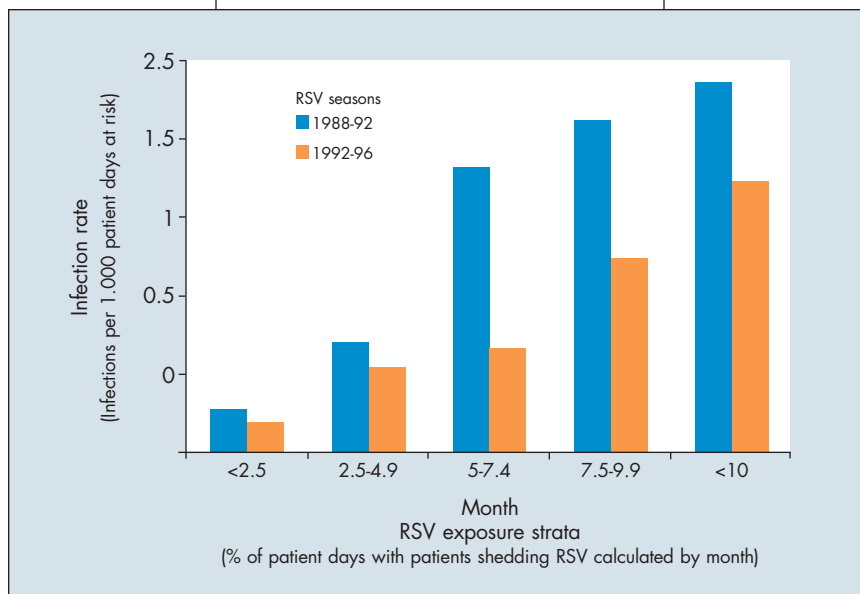


Figure – The pairs of bars on this graph show—for various strata of respiratory syncytial virus (RSV) exposure—the decrease in RSV infections subsequent to implementation of preventive measures. (From Macartney KK et al. *Pediatrics*. 2000.<sup>10</sup>)

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the hospital, health care practitioners need to educate parents and caregivers regarding the transmission of RSV and the tactics that can be used at home to protect children from infection.

**Parent education.** Parent education plays a vital role in preventing the spread of RSV. The high standard of care that is maintained in the NICU must—to the degree possible—be transferred to the home. Parents and caregivers need to understand that hand washing is the most important measure they can implement at home to prevent the spread of infection among family members.

**Limiting exposure to sick persons and at-risk infants.** Although RSV is not an airborne pathogen, it can be acquired simply by being in the same room with an infected person, since it can be spread by contact with contaminated surfaces. Therefore, it is essential that infected people be separated from noninfected people whenever possible, particularly at-risk children.<sup>11</sup>

**Smoke-free and clean environments.** There is tremendous debate about whether a smoke-free environment can help prevent the spread of RSV infection. Although there is limited research in this area, it is important to remember that a reactive airway can exacerbate an RSV illness. A smoke-free environment certainly is conducive to minimizing the irritants that can exacerbate an RSV lower respiratory tract infection (LRTI).

**Ensuring continuity of care from NICU to home.** Additional elements that may promote a seamless transition from the hospital to the home include communication of the prophylaxis plan—and the importance of following it—to the patient's primary care provider and the patient's parents. Parents should be provided with a discharge summary, and health care workers should provide confirmation that the parents or

caregivers understand the importance of follow-up appointments. A home health care nurse may be beneficial in the coordination of the at-home prevention plan.<sup>12</sup>

### PHARMACOLOGICAL TREATMENT OF SYMPTOMS AND PREVENTION OF INFECTION

Pharmacological management of RSV infection falls into 2 major categories: alleviation of symptoms with traditional supportive care medications, and prophylaxis with monoclonal antibodies in at-risk children.

#### Prophylaxis for which patients?

The American Academy of Pediatrics Committee on Infectious Diseases (The Red Book Committee) has issued clear guidelines regarding the patient populations that should be targeted for pharmacological prophylaxis.<sup>13</sup> Acknowledging that administration of prophylaxis for every child susceptible to RSV infection is impractical and not cost-effective, the academy suggests that the following patient groups be targeted:

- Infants and children younger than 24 months with chronic lung disease (CLD) of prematurity who have required therapy (supplemental oxygen, bronchodilator, or corticosteroid therapy) for CLD within the 6 months preceding the start of RSV season: prophylaxis should be considered in such patients. Patients with more severe CLD who continue to require therapy may benefit from prophylaxis during a second RSV season.

- Infants born at 32 weeks' gestation or earlier: these infants may benefit from RSV prophylaxis even if they do not have CLD.

—In those born at less than 28 weeks' gestation: prophylaxis during the first RSV season that falls within a year of birth.

—In those born at 29 to 32 weeks' gestation: prophylaxis during

RSV season if it occurs during the first 6 months of life.

- Infants born between 32 and 35 weeks' gestation: prophylaxis is usually reserved for those infants at greatest risk for infection who require hospitalization. Risk factors typically include day-care attendance, school-aged siblings, exposure to environmental air pollutants, congenital abnormalities of the airways, and severe neuromuscular disease.

- Children up to 24 months of age with hemodynamically significant cyanotic and acyanotic congenital heart disease: prophylaxis recommended.

—Those receiving medication to control congestive heart failure.

—Those with moderate to severe pulmonary hypertension.

—Those with cyanotic heart disease.<sup>13</sup>

#### RSV symptom management.

Symptom management or supportive care can include any or all of the following:

- Supplemental oxygen.
- Acetaminophen.
- Bronchodilators.
- Antibiotics.
- Ribavirin.

Acetaminophen can be administered for concomitant fever, and bronchodilators (although not recommended) have been used to dilate the airways and reduce airway inflammation, to help reduce wheezing. Antibiotics are often administered for bacterial infections that may co-occur with an RSV LRTI, especially when the infant's respiratory distress is severe enough to require supportive ventilation. Oxygen is also administered when cyanosis or apnea is present in a severely infected infant or child.

Ribavirin, an antiviral agent, can be used to treat acute RSV-induced bronchiolitis; this agent is most commonly used very early in the disease course in patients with severe respiratory distress who require a ventilator. One study suggests that ribavirin

reduces the risk of the development of asthma and recurrent wheezing<sup>14</sup>; however, in another study of 205 patients, no statistically significant difference was observed. Keep in mind that the agents mentioned may appear to improve the status of an infant with an RSV infection simply because resolution occurs with time.

#### **Pharmacological prophylaxis.**

*RSV intravenous immunoglobulin (RSV-IVIG)* has been used widely to prevent serious LRTIs caused by RSV. It has a 6-fold higher concentration of RSV-neutralizing antibodies than standard IVIG and was one of the first agents that demonstrated predictable utility in combating RSV infection. Clinical trials showed that use of RSV-IVIG decreased the rates of hospitalization for serious LRTIs caused by RSV in certain patient groups. However, this therapy had to be administered as a 3- to 4-hour intravenous infusion, which made the administration impractical and often involved considerable cost and resources. Today, RSV-IVIG has largely been replaced by the humanized monoclonal antibody, palivizumab.<sup>15</sup>

*Palivizumab* is a monoclonal antibody that is specific for RSV, and it is the only agent that is commercially available for the prevention of RSV infections. Another advantage of palivizumab is that it is given as an intramuscular injection, which makes administration in the NICU much more convenient. The administration of palivizumab in at-risk infants and children has been shown to decrease rates of RSV-associated hospitalizations; in addition, the agent has a favorable safety and tolerability profile.<sup>16</sup>

Palivizumab is currently indicated for the prevention of serious LRTIs caused by RSV in infants with bronchopulmonary dysplasia, infants with a history of premature birth, and children with hemodynamically significant congenital heart disease. In par-

ticular, palivizumab has demonstrated greater usefulness than RSV-IVIG in infants with hemodynamically significant congenital heart disease because the administration of RSV-IVIG was contraindicated in this population, in part on account of the substantial amount of fluid administered.<sup>15</sup>

Palivizumab is given in a series of monthly 15 mg/kg intramuscular injections for the duration of the RSV season. This protocol needs to be communicated clearly to parents and caregivers to ensure that at-risk infants and children routinely visit their physician for follow-up doses. The first dose should be administered before the start of the RSV season, which is usually October, and dosing usually continues into April, depending on the length of the RSV epidemic in the local community that year.<sup>17</sup> Common adverse reactions observed with palivizumab are upper respiratory tract infection, rhinitis, otitis media, fever, rash, diarrhea, cough, vomiting, gastroenteritis, and wheezing. Anaphylaxis occurs in 1 in 100,000 patients, and rare acute hypersensitivity reactions have been reported.

**Motavizumab.** The next-generation monoclonal antibody, which promises to be an improvement over palivizumab, is motavizumab, currently in phase 3 clinical development. Motavizumab demonstrates higher potency and greater affinity for RSV than palivizumab and may reduce the burden of both upper and lower respiratory tract infections caused by RSV. Preliminary studies of more than 6000 patients have suggested that motavizumab may reduce the RSV infection rate to a greater extent than palivizumab. The safety and tolerability profile promises to be equivalent to that of palivizumab.<sup>18</sup>

**MEDI-534.** The development of an effective RSV vaccine would have a dramatic effect on the morbidity and, potentially, mortality, that is caused globally by this pathogen, and

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research in the area of RSV vaccine development is ongoing. At present, one compound, MEDI-534, is in the early stages of clinical development. Phase 1 trials are currently evaluating the usefulness of this compound as a vaccine against RSV and parainfluenza virus 3, two of the most prevalent causes of viral respiratory disease in infants.<sup>19</sup>

Preclinical research in animals has demonstrated that the administration of this vaccine induces an anti-RSV immune response greater than that seen with RSV infection. However, developing a vaccine for RSV entails significant challenges. A vaccine for RSV would need to induce immunity to multiple strains of the virus, and a series of boosters might be required to maintain immunity. Also, because patients at highest risk for RSV infection are younger than 3 months, the continuing presence of maternal antibodies in these young infants might interfere with the antibody stimulation necessary to produce immunity.<sup>19</sup>

### CONCLUSION

RSV is a serious health concern for infants. Fortunately, simple prophylactic measures can decrease the spread of RSV infection. Health care professionals can take a number of steps to decrease RSV spread in the hospital setting as well as teach parents how to help prevent infection in the home. Management of RSV illness consists of treating the symptoms in patients already infected and preventing further infection. Patients at greatest risk for infection may receive pharmacological prophylaxis on a monthly basis throughout the RSV season. Research to develop a vaccine for RSV is ongoing. ■

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