REVIEW ARTICLE

Impact of Respiratory Syncytial Virus
The Nurse's Perspective

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Abstract

Respiratory syncytial virus (RSV) is a highly contagious virus, and is the major cause of lower respiratory tract infections in infants and toddlers worldwide. RSV infection poses serious health risks to young children during the first 2 years of life. Several infant populations have been classified as high risk, and additional risk factors are known to increase the likelihood of severe RSV infection. Treatment for active RSV infection is limited to the symptoms of infection rather than the underlying cause; therefore, it is critical to reduce the transmission of RSV. As nurses, we highlight the importance of educating healthcare professionals, both in the hospital and community settings, as well as parents and other caregivers about the risks and outcomes associated with RSV infection, and necessary measures to decrease the risk of infection. We also highlight the importance of the successful identification of those children who are at high risk of RSV infection. RSV prophylaxis (RSVP) with palivizumab has been shown to improve clinical outcome in infants who are considered high risk compared with those who have not received RSVP. The failure of healthcare staff and primary caregivers to protect children against an RSV infection can have lasting detrimental effects on the health and lives of affected children and their families.

1. What is Respiratory Syncytial Virus (RSV)?

First identified as a human pathogen in 1956,[1] respiratory syncytial virus (RSV) is a single-stranded, enveloped, RNA pneumovirus that infects respiratory epithelial cells in susceptible infants. The F glycoprotein on the surface of the virus participates in viral attachment and mediates the process of fusion between the virus and cell membranes, as well as between infected cell membranes, resulting in 'syncytia' formation. There are two subtypes of RSV, type A and type B, which differ in the envelope proteins on the viral shell. Both subtypes circulate annually, and both are infectious; however, there is some evidence that type A is the more common cause of RSV infections[2,3] and may lead to more severe disease.[4] The virus is highly contagious and is the major cause of lower respiratory tract infections in infants worldwide. Nearly all children have been infected by RSV by 2 years of age.[5,6] Autoimmunity to infection in infants is often incomplete and, therefore, reinfection by RSV is common;[7] however, symptoms from subsequent infections are typically less severe.[8] The virus is primarily spread through large particle aerosols (due to coughing or sneezing) or by fomites followed by self-inoculation. RSV can survive on non-porous surfaces for 6–7 hours, porous surfaces such as hospital gowns for 2 hours, and the skin for 20–30 minutes.[9-11] These characteristics make transmission quite likely among children and infants in close contact with each other or with infected caregivers if preventive measures are not strictly followed.

2. Burden of RSV Disease

Although RSV infection often manifests as a mild cold in otherwise healthy adults and can be dismissed as an insignificant nuisance, it can seriously affect many children. It is the leading viral cause of infant mortality, and may cause 7- to 9-fold more deaths than influenza.[12] A recent study by Sampalis[13] demonstrated that hospitalization due to RSV infection leads to increased risk of morbidity and mortality, and increased healthcare resource utilization. The rate of respiratory admissions due to RSV for infants aged <6 months is substantially higher than for any other viral cause, including influenza.[14] Hospitalization for bronchiolitis or pneumonia due to RSV infection can result in additional burdens, such as admission to the pediatric intensive care unit, oxygen supplementation, and mechanical ventilation. Apnea, which may be one of the first signs of RSV disease,[15] is present in 16–20% of young infants. Kneyber et al.[16] also demonstrated that the presence of apnea at hospital admission was related to expression of recurrent apnea and subsequent increased likelihood of mechanical ventilation. In addition, infants or children with active RSV infections may require the cancellation of necessary surgical procedures for underlying medical conditions, specifically those with cardiac anomalies requiring urgent surgery, adding to the risk of additional medical complications. Hospitalization can cause significant disruption of the lives of the families of affected infants, and can lead to increased emotional and financial burdens. The financial burden is not limited to the direct hospital costs for in-patient care and cancellation of scheduled procedures, but also reflects indirect costs such as transportation (which can be substantial for isolated groups), lost wages, food, and daycare for other children in the family.

Adding to the potential cost of infection by RSV is that children with severe RSV infections are more likely to develop ongoing medical problems. Infants hospitalized with RSV infection often have difficulties with feeding, which can persist after recovery from the acute infection.[13] Additionally, Stein et al.[17] demonstrated that hospitalized infants diagnosed with RSV-associated lower respiratory tract infections were 3.2- and 4.3-fold more likely to develop infrequent and frequent wheezing, respectively, by 6 years of age.[17] Sigurs et al.[18] also reported that RSV-associated bronchiolitis in childhood (severe enough to cause hospitalization) was a risk factor for the development of asthma or recurrent wheezing at 13 years of age.[18] Infants with RSV infection are also more likely to need re-hospitalization for respiratory conditions (such as bronchiolitis or pneumonia)

and other conditions (such as anemia or anorexia) after recovery from their initial RSV disease.[13] Older children who had been hospitalized with severe RSV infection as infants are often required to make repeat visits to clinics to address the long-term complications (such as recurrent wheezing and asthma) that occur as a consequence of their earlier RSV infection. These potential additional healthcare and emotional costs add to the overall burden of RSV infection.

3. Risk Factors for Severe RSV Infection

All infants are at risk of RSV disease resulting from infection by the virus; however, certain populations of neonates, medically fragile infants and young children are at higher risk of acquiring severe RSV infection. Premature infants, particularly those of less than 34 weeks' gestation, are at especially high risk, owing to their reduced immune system function and underdeveloped respiratory system.[19,20] There is also evidence that late-preterm (near-term) infants (born between 34 weeks' and 36 weeks and 6 days' gestation) are at increased risk.[21-23] This may partially be due to the fact that while pulmonary function is physiologically premature (inadequate surfactant, incomplete alveolar development, impaired gas exchange),[22] outward physical characteristics (e.g. bodyweight) make these infants appear more like full-term infants. Hence, they may be treated more like full-term infants, rather than being treated with some of the necessary precautionary measures given to other premature infants.[22] While severe RSV infection has most often been associated with younger age (<6 months), there is emerging evidence that the prevalence of acute lower respiratory infection caused by RSV is increasing in relatively older, more mature infants (aged 6–11 months).[24]

Infants and toddlers suffering from chronic lung disease and congenital heart disease (CHD) have a higher risk of hospitalization and fatality resulting from RSV infections,[25] as do children with cystic fibrosis and pulmonary hypoplasia,[26,27] Down syndrome,[28] neuromuscular disease, and severe immune system compromise.[29] The presence of these severe underlying co-morbid conditions, including malignancies, is associated with mortality among term and older children with RSV infection.[25] It also appears that boys have a higher risk of having complications associated with RSV infection than girls. This may be due to the narrower and shorter airways relative to lung size in boys, resulting in lower levels of airway conductance, which in turn makes airway obstruction from respiratory tract infection more common.[30] Generally, birthweight contributes to risk, as infants with low birthweight for their gestational age are more likely to have complications associated with RSV infection.[23] While a high percentage of these 'high-risk' children are hospitalized due to complications from severe RSV infection, a higher overall percentage of hospitalized children derive from non-high-risk groups.[31] This highlights the importance of educating all parents and healthcare staff about the transmission of RSV, since it applies to all infants and children, not just to those considered 'high risk.'

There are additional risk factors that increase the susceptibility of newborns to RSV infection (see table I). In northern latitudes, the 'RSV season'

Table I. Factors that contribute to increased risk of severe respiratory syncytial virus (RSV) infection[a]

Premature birth[21-23]
Chronic illness/disease
chronic lung disease[25,32]
hemodynamically significant congenital heart disease[25,32]
cystic fibrosis and/or pulmonary hypoplasia[26,27]
Down syndrome[28]
neuromuscular disease[29]
severe immune compromise[29]
Male sex[30]
Low birthweight for gestational age[23,33]
Young chronologic age (≤12 weeks at start of RSV season)[34-36]
Attendance in daycare centers[36-38]
Presence of pre-school or school-aged sibling(s)[35-37,39]
High number of people in home or multiple people sharing a bedroom[38,40]
Not breastfeeding[37]
Exposure to tobacco smoke[41,42]
Family history without eczema[43,44]

a Specific risk factors may vary in impact depending on geographic region and ethnic population.

typically runs from early winter (November/ December) through late spring (April/May). It is during this time that the rate of hospitalization due to RSV infection is highest,[14] making this a particularly important time for caregiver vigilance and appropriate prevention measures. However, it has been demonstrated that RSV infections can occur at any time of year,[21,45] highlighting the importance of year-round education and infection reduction measures. Other risk factors that may increase an infant's susceptibility to RSV were reviewed by Simoes,[37] and include attendance in daycare and having pre-school or school-aged sibling(s). Also, higher numbers of people sleeping in the same room has been shown to increase the risk of hospitalization due to respiratory tract infection.[38,40] It is generally thought that breastfeeding confers some protection against RSV-associated lower respiratory tract infection,[37] such that children who are not breastfed are at increased risk. The air quality within the home is of importance as well; exposure to tobacco smoke may cause increased respiratory tract reactivity in susceptible infants, leading to exacerbation of respiratory disease.[41,42]

4. Strategies for Reducing the Risk of RSV Infection

4.1 Education

Due to the severity of RSV disease, and the ease with which the virus is transmitted, an education program for all healthcare providers, including parents and other caregivers, should be a priority (see table II). For primary caregivers, the focus needs to include the identification of those children at risk of severe RSV disease, the characteristics of the virus itself, the mode of virus transmission, and the symptoms of infection, regardless of the risk status of children. Education sessions should also include demonstrations of diligent hand washing, as hand hygiene is a crucial element in infection control. Traditionally, hand washing has been performed with soap and water; however, alcohol-based hand rinses and gels have been shown to be effective in removing microorganisms from hands (reviewed by Boyce

Table II. Measures to reduce respiratory syncytial virus (RSV) transmission

In the hospital/clinic
Hand hygiene: wash hands thoroughly with soap and warm water before and after touching children. Hand sanitizer can be used if hands are not soiled
Wear gloves, gowns, masks
Promptly identify all persons (patients, parents, and others) with febrile respiratory illness in outpatient areas
Effectively isolate or cohort any infant(s) or child(ren) with cold symptoms (cough, runny nose) even if not yet diagnosed with RSV
Promptly screen/test for RSV
Routinely disinfect susceptible surfaces, including toys and books, in waiting rooms of offices and clinics
In the home
Hand hygiene: wash hands thoroughly with soap and warm water before and after touching children. Hand sanitizer can be used if hands are not soiled
Frequently wash children's clothes, bedding and toys
Keep children away from crowded areas and from those who are sick
If parents are sick, minimize close contact with children (avoid kissing)
Encourage and support breastfeeding

and Pittet[46]). Additionally, information should be provided on proper disinfecting of susceptible surfaces and other areas where RSV can be found. Because of its potential to reduce the risk of RSV susceptibility (and provide other health benefits), breastfeeding should be encouraged. Education about the potential consequences of severe RSV disease, including its contribution to persisting health problems, is highly important. Education points for reducing the risk of RSV transmission are outlined in table II and specifically addressed in sections 4.2 and 4.3.

4.2 Reducing Community-Acquired Infection

In the community setting, children at risk of RSV infection are typically healthier (not requiring hospitalization), but are being cared for in clinics and doctors' offices where prevention guidelines and practices may be less rigorous or non-existent (such as in waiting rooms). In an outpatient clinic or doctor's office, minor cold symptoms may often be ignored, as RSV may not be as prominent in the minds of those who are tending to children, specifically those children

who do not have the significant risk factors listed above. Additionally, it has been demonstrated that during RSV outbreaks, infection of medical staff is common, and the symptoms of such infections can be dismissed as being caused by mild colds or flu-like illnesses.[47] Indeed, caregivers who have active RSV infections may even be asymptomatic.[47]

The attention to diligent hand washing before and after contact with patients cannot be overstated for reducing the risk of community-acquired RSV infection. In outpatient clinics and doctors' offices, it is important for staff to wear gloves, gowns, and masks, and to make every effort to immediately isolate any patient with cold symptoms in an assessment room. It is also recommended to routinely disinfect susceptible surfaces (including toys and books) in waiting rooms. It may be best to remove toys and books from waiting rooms altogether and encourage families to bring their own toys, if needed. In the home, primary caregivers should be instructed to keep their children away from large crowds, areas where people are sick, and areas where the children may be exposed to tobacco smoke. When parents are sick, they should make every attempt to minimize close contact with the children and avoid kissing.

4.3 Reducing Nosocomial Infection

Another important consideration regarding the risk of infection by RSV is the potential for nosocomial transmission. Welliver et al.[25] recently reviewed the impact of nosocomial infection, noting a study by Langley et al.[48] in which a 10-fold higher mortality rate was found in children with nosocomial infection compared with those with community-acquired infection. The risk of nosocomial transmission may be higher in children who are being cared for in a hospital's neonatal unit or pediatric ward due to the already compromised health of the child (necessitating hospitalization), and the high density of patients and number of staff. RSV transmission may occur even though there may be standard prevention guidelines in place in such settings.[47] This risk may be increased due to a

delay in detecting and diagnosing RSV infection in infants. Symptoms of RSV infection, such as apnea, bradycardia, and changes in ventilation, can often be attributed to causes other than RSV.[49] The ability to quickly identify those infants who may have an RSV infection can decrease the risk of nosocomial transmission. In addition to the increased mortality risk, RSV infection in hospitalized children can severely impact their health status, and subsequently prolong hospital stays.[47]

To reduce the likelihood of nosocomial transmission, it is recommended to have an annually updated, readily available, written policy for hospital and clinic employees to follow, outlining the important preventive steps. Hospital staff should be educated about how to avoid RSV exposure (by wearing gloves, gowns, masks, and, where necessary, protective eyewear), and on the importance of maintenance of hand hygiene by thorough washing immediately before and after contact with all children. It is a good idea to conduct these training sessions just prior to the start of the annual RSV season. Screening protocols for early RSV identification should be in practice in neonatal and pediatric care facilities. Hospitals should have a policy of immediately isolating or cohorting infants who display cold symptoms. In the ideal situation, infants should be isolated and tested for the pathogen causing the cold symptoms. Children should then be grouped by underlying pathogen once it has been identified (to reduce the likelihood of coinfection). However, not all hospital facilities are equipped to quickly diagnose the underlying cause of symptoms, or have the space to isolate each individual child. In these cases, it is best to immediately cohort children based on symptoms. A demonstration of the effectiveness of these measures to control the spread of RSV among hospitalized infants was reported by Isaacs et al.[50] These authors showed that when the prevention protocol was rigorously followed, RSV infection contracted while in the hospital decreased from 4.2% to 1.1% in non-CHD infants, and from 34.8% to 3.3% in infants with CHD. An added benefit of the implementation of these measures is the potential to decrease the transmission of other infective agents. Attention to

these steps can help reduce the number of children who develop severe RSV disease.

5. Outpatient Care for RSV Infection

The responsibility for outpatient care of patients with RSV infection rests with the primary caregivers as well as physicians and nurses in offices and clinics. Therefore, one of the key priorities for outpatient care, in order to minimize the likelihood of RSV infection, is the education of the primary caregiver. This teaching should include information on factors that contribute to increased risk (table I). Additionally, there should be a focus on the steps that can be taken to minimize the risk of RSV transmission (highlighted in sections 4.2 and 4.3, and in table II). The next step in outpatient care is the education of the primary caregivers about the signs and symptoms of RSV infection. Infection will typically present as a mild upper respiratory tract illness with symptoms such as low grade fever, cough, nasal congestion, vomiting, diarrhea, and decreased food intake. Moderate symptoms include apnea (which may be the first symptom in premature and/or very young infants[15]), irritability, tachypnea, increased coughing and wheezing, diaphoresis, and dehydration. The disease can progress to a lower respiratory tract infection with severe symptoms of respiratory distress, including lethargy, apnea, tachypnea, wheezing, nasal flaring, grunting, retractions, and cyanosis. Importantly, not all infected children will necessarily demonstrate the same symptoms, which can make diagnosis difficult. For example, apnea is more common in preterm, younger infants without fever.[51] It is important to educate caregivers about these common symptoms so that they can alert the child's physician promptly upon their appearance. If symptoms are sufficiently severe, or if there are signs of worsening symptoms, the physician may recommend admission to an inpatient facility.

6. Inpatient Care for RSV Infection

Many treatment approaches, as recently succinctly reviewed by Paes et al.,[52] have been utilized in patients with active RSV bronchiolitis. Treatment with corticosteroids, including dexamethasone, prednisone, and inhaled corticosteroids, has not resulted in clear improvements (reviewed by Mitchell[53]) and is therefore not recommended. Additional approaches have included the use of leukotrienes and ribavirin; however, they are also not recommended due to a lack of evidence for improving clinical outcomes.[53,54] Ribavirin, an agent with broad-spectrum antiviral activity, had previously been used to treat active infection, but limited clinical effectiveness and potential risks to patients and staff have led to decreased use.[55] Bronchodilators can be used on an individual basis; however, their use should be continued only if there is evidence for therapeutic benefit.[53] Antibiotics should be used only when there is a strong suspicion of bacterial infection, and should be stopped when cultures are shown to be negative.[53] There is no evidence of positive therapeutic benefit of antibacterial treatment for bronchiolitis. As a result, treatment of RSV bronchiolitis currently focuses on supportive care, including the administration of supplemental oxygen when oxygen saturation is below 90%, maintenance of fluid balance, and nutrition. When necessary, mechanical ventilation with or without extracorporeal membrane oxygenation is used to maintain adequate oxygenation.

7. Immunoprophylaxis

The only currently available pharmacologic prophylactic to decrease the risk of RSV infection is palivizumab, a passively used monoclonal antibody utilizing a humanized monoclonal antibody specific for the F protein of both subtypes of RSV.[56,57] A pivotal clinical trial conducted in children at high risk of RSV infection demonstrated a significant reduction in RSV-related hospitalization rate in those who received RSV prophylaxis (RSVP) with palivizumab, in addition to a decreased length of stay in the hospital, lower incidence of admission to the intensive care unit, fewer days with increased supplemental oxygen, and fewer days with moderate or severe lower respiratory tract illness compared with those who received placebo.[58] Results support-

ing this initial trial have been obtained by other researchers.[59,60] Feltes et al.[61] also demonstrated the ability of RSVP to reduce hospitalization rates in children aged ≤24 months with hemodynamically significant CHD. Primary adverse effects associated with palivizumab therapy are local erythema, pain at the injection site, upper respiratory infection, fever, and rash, with very rare cases of anaphylaxis reported.[56,57] Because of its positive benefit and adverse-effect profile, palivizumab has been approved for the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients at high risk of RSV disease.[32] While it has been shown to be effective as a prophylactic measure, palivizumab does not appear effective in reducing the severity of active RSV infections.[62] However, if infants contract RSV while receiving palivizumab injections, RSVP should continue for the remainder of the RSV season, as RSV infection does not confer complete immunity; thus, continuation of RSVP may help to prevent reinfection in the same year.[43]

One of the difficulties in the use of RSVP to decrease RSV infection is the determination of 'high-risk' infants. Using the risk factors outlined in table I, guidelines have been developed to determine which children qualify for RSVP. These guidelines may vary depending on the specific country and region, and healthcare staff should contact a regional health authority to determine the approved qualifications for RSVP. There may be certain populations who are at particular risk for RSV disease due to their geographic isolation or ethnic susceptibility. For example, in Canada, Inuit populations are highly susceptible to severe RSV infection, and infections are common throughout the year;[63] therefore, each province in Canada has slightly different guidelines for those children who qualify for RSVP.

The approved administration schedule for RSVP is based on the clinically validated regimen reported by the IMpact-RSV Study Group[58] and includes monthly intramuscular injections throughout the RSV season. In many cases, the first injection (and sometimes subsequent injection) is given in the hospital setting, with the completion of the RSVP regimen occurring in outpatient doctors' offices or specialized RSV clinics. Importantly, to date, it appears that palivizumab can be administered along with other scheduled vaccines without affecting their immunogenicity.[64] However, if a reaction were to occur with coadministration, it would be difficult to determine the cause.

When given monthly as recommended, blood concentrations of palivizumab are sufficient to help improve clinical outcome measures in high-risk infants.[58] However, just prior to the second administration, trough serum antibody levels are the lowest that they will be over the course of RSVP.[65] Missing or delaying a dose of palivizumab will cause the antibody level to drop further and potentially increase susceptibility to RSV infection. Therefore, it is essential that subsequent doses of palivizumab be administered at the scheduled time to ensure that antibody titers are maintained at an effective level. Additionally, it has been shown that children requiring cardiopulmonary bypass for cardiac surgery show significant decreases in serum palivizumab concentrations after surgery.[57] It is recommended that these children receive a dose of palivizumab as soon as possible after surgery to promote effective prophylaxis.[43] Achieving and maintaining target serum palivizumab concentrations may not confer protection for all infants; furthermore, it is possible that the diminished trough serum concentration of palivizumab prior to its second administration may increase the susceptibility of infants to RSV infection. Therefore, increased vigilance and adherence to the approved timeline for RSVP and to other prevention measures may improve the clinical outcome of high-risk infants.

In addition to the effectiveness of palivizumab as a means of reducing the occurrence and severity of RSV infection in high-risk infants, RSVP has also been associated with lower rates of recurrent wheezing by the time children have reached 2–5 years of age.[66] In addition to this important effect on the well-being of the infected infants, successful RSVP may also provide benefits for the infants' primary caregivers. The reduction in duration of moderate or severe lower respiratory tract illness and potential hospitalization results in less time off work (and associated

decrease in income), may help reduce transportation and food costs associated with hospital visits, and may also help reduce the need for alternate care for siblings of the affected infant. However, these potential benefits need to be weighed against the costs associated with RSVP. One recent report has shown that the hospitalization rate due to RSV infection for high-risk infants (aged 0–6 months) ranges between 8% and 56%, compared with 4.4% of infants who are considered low risk.[67] Even with this relatively high rate of hospitalization due to RSV infection, economic cost-benefit analyses have yielded conflicting results.[68-70] Recent Canadian studies have reported that the cost effectiveness of RSVP for infants of 33 to <36 weeks' gestation was best achieved when the Canadian risk-scoring tool was used. The risk assessment tool provides the nurse or doctor with a practical and efficient way of identifying infants who are at low risk of acquiring RSV, therefore excluding them from RSVP - a subsequent cost saving.[71,72]

This highlights the need for appropriate determination of true high-risk infants to implement the most cost-effective strategy for passive immunization while maintaining the highest possible rates of effective RSV disease prevention. However, since children who score low on risk-assessment measures may go on to develop severe RSV disease, attention to risk-reduction techniques is also of critical importance.

8. Strategies for Improving Adherence to Immunoprophylaxis and Preventive Measures

We feel that the best way to improve adherence to preventive measures is to educate all those who are in direct contact with susceptible children about the basic characteristics and common modes of RSV transmission and prevention. This education can take the form of in-service education, 'lunch-and-learn' sessions, and/or seminars for doctors and nurses. Posters that demonstrate ways to decrease the risk of infection can be distributed throughout healthcare facilities and doctors' offices. Parents and other caregivers may need individual education and counseling as well

as information pamphlets that reinforce the necessary risk-reduction information. Essential topics for education are the specific ways to decrease risk of transmitting RSV (see table II), and the necessity of adhering to the timelines for RSVP in children who qualify for immunoprophylaxis. An important step is the successful education about the long-term consequences that can arise from the failure to adequately protect children from severe RSV infection. We propose that these education sessions occur just prior to the start of each annual RSV season, reinforcing the benefits of adhering to prevention protocols, in order to maximize adherence throughout the RSV season.

One additional way to improve the adherence of parents and caregivers when the infants leave the hospital is to ensure that there is effective communication of medical and any other pertinent information between the parents and healthcare provider regarding scheduled immunoprophylaxis requirements. Obtaining sufficient and accurate contact information for the parents of discharged infants allows clinic nurses and doctors' offices to initiate calls to remind families of upcoming appointments for subsequent administrations of RSVP. Also, providing families with an appointment card for the next appointment including date, time, and office phone number, as well as encouraging families to call should they have any questions or concerns, improves the likelihood of successful adherence. It is critically important that families understand the impact of RSV disease so that they can better advocate and follow through with the necessary risk-reduction measures.

9. Potential Treatment Options for RSV Infection in the Future

There are currently several treatment approaches being investigated for RSV infection, as recently reviewed by Empey et al.[62] These treatments target different proteins associated with the replication and/or infection processes of the virus. While these novel treatments are promising, they are either in preclinical development or early clinical trials, suggesting that, even if successful,

they will not be clinically available for years to come.

The promise of a vaccine for RSV has been a discussion point for primary care providers for some time. Unfortunately, due to several factors, a safe and effective RSV vaccine has yet to be developed. One primary factor contributing to the unsuccessful development of a vaccine to date is that the targeted population for the RSV vaccine consists of young infants from birth to 6 months of age. These infants may have an inadequate response to vaccination due to their underdeveloped and under-responsive immune systems, and because of the potential for suppression by maternally transmitted antibodies.[73] A vaccination attempt in the 1960s using inactivated RSV resulted in an exaggerated response to the virus, followed by the hospitalization of 80% of the vaccinated infants and two deaths.[74] This result has hampered the development and testing of novel vaccine approaches.

New approaches to vaccine development are exploring the use of live, attenuated viruses, administered to infants intranasally.[75] Administration directly to the nasal mucosa induces local and systemic immunity, and also minimizes suppression by maternally transmitted antibodies. Intranasal administration may also confer greater protection and higher immunogenicity. Ensuring a balance between immunogenicity and successful attenuation of live virus is of critical importance to the successful development of an RSV vaccine. There are currently several early clinical trials that are aimed at examining the safety and immunogenicity of novel vaccines.

10. Conclusions

RSV infection poses a serious health risk to young infants and children, particularly during the first 2 years of life. There are several categories of patients who are considered to be at high risk of developing severe RSV infection, and additional environmental factors may also contribute to the risk of developing severe RSV disease. Severe RSV infection may be associated with persistent and recurring health problems for children, highlighting the need to reduce the rate

and severity of infection. Education of parents, hospital staff, and nurses who are responsible for the direct care of susceptible children is of critical importance to reduce the transmission of RSV. Education should focus on the characteristics of RSV, routes of transmission, and proper techniques for reducing the risk of transmission. While treatment of active RSV infection is limited and restricted to the symptoms of infection, high-risk infants given palivizumab immunoprophylaxis have a decreased rate of hospitalization and fewer days with moderate or severe lower respiratory tract illness compared with those who do not receive therapy. Identification of eligible infants is critical to the successful implementation of immunoprophylaxis. Effective education and risk-reduction techniques are crucial to minimize infection of young children by RSV and to help to reduce the burden of the disease.

Acknowledgments

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