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Learning Objectives

After studying the literature presented in this Pediatric Respiratory Care series, participants will be able to:

- Identify respiratory disorders in pediatric patients
- Summarize risk factors for respiratory disorders in pediatric patients
- Select an appropriate therapeutic regimen for patients with pediatric respiratory disorders

Target Audience

This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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Update on RSV Prevention and Treatment

Respiratory syncytial virus (RSV) causes significant mortality and morbidity in children <5 years of age. Severe RSV infection is more likely to occur among premature infants, infants with chronic lung disease, and those with significant congenital heart disease. It is estimated that RSV is responsible for approximately 125,000 hospital admissions and 500 deaths among infants in the United States per year. Venkatesh and Weisman recently reviewed the latest developments in RSV research.

Therapy for RSV infection is limited and generally supportive. Ribavirin, a virustatic agent available in a nebulized form, has been used to treat RSV, but its benefits are unclear. Systemic corticosteroids were not shown to improve clinical status or decrease length of hospitalization. Bronchodilator therapy with beta-agonists has not been found to improve oxygenation or the rate or duration of hospitalization, but may be beneficial in children with bronchiolitis due to RSV. Among intubated and ventilated RSV-positive infants, exogenous surfactant may improve oxygenation and shorten the duration of ventilatory support. Several new compounds are in early clinical development for

treating RSV, including a first-in-class molecule inhibitor, oral small molecule compounds that target the function of the viral F protein, and a small interfering RNA that silences a nucleocapsid gene.

Because of the lack of effective treatments, immunoprophylaxis via passive immunization in high-risk infants is important. Two products are commercially available for RSV prophylaxis: intravenous immune globulin (IGIV) and palivizumab. IGIV may contain variable and inconsistent levels of anti-RSV antibodies and may not be clinically effective for prophylaxis. Palivizumab is a humanized IgG1 monoclonal antibody that targets the F glycoprotein on both the A and B strains of RSV. Palivizumab significantly reduces hospitalization in the first 6 months in premature infants born at <35 weeks, infants <24 months of age with chronic lung disease requiring treatment in the last 6 months, and in children ≤24 months of age with hemodynamically significant heart disease.

The American Academy of Pediatrics (AAP) recommends RSV prophylaxis in infants <2 years of age with chronic lung disease who require therapy (diuretics, oxygen, bronchodilators, or corticosteroids) within 6 months of the start of the RSV season; infants born at ≤28 weeks during

Increased awareness, more potent anti-RSV antibodies, new vaccines, and novel chemical compounds will make RSV more treatable and preventable, especially in high-risk populations.

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Disclosures:

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Update on RSV Prevention and Treatment *(Continued)*

their first RSV season; infants born between 29 and 32 weeks, 0 days during their first 6 months of age; infants born between 32 weeks, 1 day and 35 weeks, 0 days having 2 or more risk factors (eg, childcare attendance, school-aged siblings, exposure to environmental pollutants, congenital abnormalities, or severe neuromuscular disease) for acquiring more severe RSV disease within the first 6 months of life; and children ≤ 12 months of age with hemodynamically significant heart disease. Once a child qualifies for the initiation of prophylaxis at the start of the RSV season, treatment should continue throughout that RSV season. The AAP does not recommend the use of either IGIV or palivizumab in the treatment of RSV infection.

MEDI-524, a humanized recombinant IgG1 monoclonal antibody derived from palivizumab, is currently undergoing evaluation in phase III trials for the prevention of RSV in high-risk infants. MEDI-524 is directed against the RSV F glycoprotein and appears to be more effective in animals than palivizumab, with a 70-fold greater binding affinity.

There is currently no approved RSV vaccine, although significant progress has been made in the area of active immunization. Subunit vaccines, live attenuated and/or recombinant virus vaccines, polypeptide vaccines, and plasmid DNA vaccines (coding for parts of the F and G surface glycoproteins) are currently being investigated. Maternal immunization is another potential method for RSV prevention.

The authors of this review speculate that great strides will be made in the prevention and treatment of RSV over the next 5 years. Increased awareness, more potent anti-RSV antibodies, new vaccines, and novel chemical compounds will make RSV more treatable and preventable, especially in high-risk populations.

Venkatesh MP, Weisman LE. Prevention and treatment of respiratory syncytial virus infection in infants: an update. *Expert Rev Vaccines*. 2006;5:261-268.

COMMENTARY

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The impact of respiratory syncytial virus (RSV) infections continues to be underestimated. Lower respiratory illness caused by RSV infection represents by far the most common cause for hospitalization of infants in the United States. More than 1 million deaths annually worldwide may be attributed to RSV infections, which are increasingly recognized as posing major health threats in the elderly, in those with COPD, and in immunocompromised populations. Whether RSV infection in infancy induces childhood asthma and COPD in adults is an important, unanswered question.

Currently, healthy infants with RSV infections can be managed as outpatients, and even the vast majority of those hospitalized require little more than hydration and supplemental oxygenation. Development of a vaccine for these indications may not be necessary or even possible. An acceptable vaccine would have to have a nearly spotless safety profile and be easily administered to infants within the first few weeks of life. Perhaps effective antivirals that can be administered very early in the course of infection or less expensive anti-RSV antibodies that can be administered to all infants who are born just before or during RSV epidemics show the greatest promise.

Low Birthweight Is an Independent Risk Factor for Severe RSV Infection

Respiratory syncytial virus (RSV) infection is the leading cause of severe acute respiratory infection in infants and young children. Moreover, RSV infection is the major cause of hospitalization in infants in developed countries. Certain underlying conditions, such as prematurity, chronic bronchopulmonary disease, and congenital heart disease, are

associated with higher RSV-related morbidity and mortality.

Recently, Cilla and colleagues evaluated the role of several risk factors for hospitalization due to community-acquired RSV infection in Basque Country, Spain. Inclusion criteria were hospitalization for >24 hours, age <2 years, date of birth in the study period (between July 1996

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Low Birthweight (Continued)

and June 2000), RSV detection in nasopharyngeal aspirate, and a discharge diagnosis of acute respiratory infection. In this retrospective study, risk factors detected in infants hospitalized for RSV infection in the first 24 months of life (n=357) were compared with those in the general infant population (n=13,986).

During the study period, there were 361 episodes of hospitalization for virologically confirmed RSV infection in 357 infants. Most of the RSV episodes causing first hospitalization took place among infants <1 year of age (n=306; 84.8%).

RSV-associated hospitalizations occurred more frequently among premature infants and among those with low birthweight (<2,500 g). The incidence of hospitalization independent of gestational age was 58.4 cases/1,000 infants for those with a birthweight <2,500 g and 19.3 cases/1,000 infants for those with a birthweight ≥2,500 g. Furthermore, the incidence of hospitalization was significantly greater in infants with a birthweight of <2,500 g than in those with higher birthweight and the same gestational age (P<0.001; odds ratio, 2.18; 95% confidence interval, 1.39–3.14).

Multivariate analysis demonstrated an association between RSV-associated hospitalization and birthweight <2,500 g (P<0.001), gestational age <37 weeks (P=0.022), maternal age <25 years (P<0.001), suburban residence (P=0.017), birth in the second half of the year (P<0.001) (in both trimesters), and hemodynamically unstable heart disease (P<0.001). Birthweight of <2,500 g was independently associated with hospitalization for RSV infection and was the most commonly identified medical risk factor.

In this study, 80% of the infants did not present with underlying conditions for severe RSV infection. Furthermore, only 3% were candidates for palivizumab prophylaxis, based on American Academy of Pediatrics criteria.

This study revealed low birthweight to be an independent factor for severe RSV infection. The authors suggested that future studies should examine the effectiveness of palivizumab prophylaxis in low-birthweight infants.

Cilla G, Sarasua A, Montes M, et al. Risk factors for hospitalization due to respiratory syncytial virus infection among infants in the Basque Country, Spain. *Epidemiol Infect.* 2006;134:506–513.

Clinical Insights® in Pediatric Respiratory Care Post-test

1. Which statement is false?
 - a. Therapy for RSV infection is generally supportive.
 - b. Prophylaxis with palivizumab significantly reduces hospitalization in high-risk infants susceptible to RSV.
 - c. MEDI-524 is a humanized recombinant IgG1 monoclonal antibody derived from palivizumab that is being investigated for RSV prophylaxis.
 - d. A RSV vaccine has been recently approved by the FDA.
2. Risk factors for RSV-associated hospitalization in infants are
 - a. Low birthweight
 - b. Prematurity
 - c. Young maternal age
 - d. Birth in the second half of the year
 - e. All of the above.

1. d. There is no approved vaccine for RSV.
2. e. All of the above.

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