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#### Learning Objectives

After studying the literature presented in this issue, participants should be able to

- Describe the impact of treatment of premature infants with palivizumab on the occurrence of subsequent wheezing
- Assess the efficacy of dexamethasone in the treatment of pediatric bronchiolitis

#### 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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#### Off-Label Disclosure

Some of the drug treatments discussed in this issue may note uses not approved by the Food and Drug Administration. Articles containing such uses will be noted at the end of the article.

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# PEDIATRIC RESPIRATORY CARE

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## Impact of Palivizumab Prophylaxis on Respiratory Syncytial Virus and Subsequent Recurrent Wheezing in Preterm Infants

**L**ower respiratory tract infection (LRTI) with respiratory syncytial virus (RSV) in early life has been epidemiologically associated with the subsequent development of recurrent wheezing and asthma later in childhood. Additional studies have demonstrated that children who developed LRTI with RSV in early life exhibit airway reactivity 50% to 100% greater when compared with uninfected controls. Furthermore, recurrent wheezing has been observed up to 11 years postinfection suggesting that it may continue even further into early adulthood. Among children at high-risk, preterm infants, regardless of chronic lung disease (CLD) status, may develop serious RSV infections within the first year of life, are at higher risk for developing recurrent wheezing or asthma, and demonstrate persistent abnormal lung function.

In the current report, Simoes and colleagues examined the ability of the humanized monoclonal anti-RSV antibody palivizumab to reduce later recurrent wheezing by ameliorating or preventing early RSV LRTI in preterm infants ( $\leq 36$  weeks gestational age) without CLD or other high risk medical conditions. In this study, a cohort of preterm infants ( $n=191$ ) who had received at least three doses of palivizumab in the first 12 months of life or who had never received palivizumab ( $n=230$ ; 76 who were hospitalized for RSV and 154 who were not) was prospectively followed for 2 years beginning at a mean age of 19 months. Recurrent wheezing was assessed by either a caretaker or recorded in a physician's report.

Treatment with palivizumab resulted in significant decreases in both recurrent wheezing (13% vs 26%,  $P=0.001$ ) and physician-diagnosed recurrent wheezing (16% vs 8%,  $P=0.11$ ) when compared with untreated patients. These data correspond to relative reductions of 49% and 51%, respectively. This decrease was also observed for the 154 nonhospitalized untreated subjects (13% vs 23%,  $P=0.022$  and 13% vs 16%,  $P=0.027$ , respectively). Furthermore, regression models indicated that greater gestational age was associated with a reduced risk of a wheezing event, with an 11% to 21% reduction in the odds of an event per 1 week increase in age. Kaplan-Meier estimates of time to onset of any wheezing event demonstrated palivizumab treatment resulted in significantly longer times to onset of the first episode of either recurrent wheezing (HR=0.46; 95% CI=0.29 to 0.74) or physician-diagnosed recurrent wheezing (HR=0.46; 95% CI=0.25 to 0.83) when compared with the untreated group. Similar results were obtained when treated subjects were compared with untreated non-RSV hospitalized individuals.

The results of this study suggest that prevention of RSV LRTI with palivizumab may protect against subsequent recurrent wheezing in premature infants without CLD.

Simoes EAF et al. Palivizumab prophylaxis, respiratory syncytial virus, and subsequent recurrent wheezing. *J Pediatr.* 2007;151(1):34-42.

*Continued*

#### Disclosures:

\* Dr Piedra is professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine. He has indicated relevant financial relationships as noted: he receives grant/research support from MedImmune, Inc. and Sanofi Pasteur; he is a member of the speakers bureau for MedImmune, Inc.; he is an expert witness for Sanofi Pasteur; he is an ad hoc consultant for MedImmune, Inc., Sanofi Pasteur, GlaxoSmithKline, Novartis, and Roche; and he is part of a collaborative research agreement with NIH and Baylor.

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## COMMENTARY

**ROBERT B. BELSHE, MD, Diane and J. Joseph Adorjan Endowed Professor of Infectious Diseases and Immunology, Professor of Medicine, Pediatrics and Molecular Microbiology, Saint Louis University School of Medicine, St. Louis, Missouri.**

*Acute viral respiratory infection is believed to trigger wheezing events and predispose children to asthma. Furthermore, the prevalence of hospitalization from bronchiolitis and asthma is increasing. Preventive measures that reduce the occurrence of viral respiratory disease may lead to a reduction in wheezing episodes and long-term benefits by reducing asthma. The results of the study by Simoes et al indicate that prevention of RSV leads to long-term benefits such as reducing the occurrence of asthma. In the absence of an RSV vaccine, passive administration of antibodies (palivizumab) has had significant benefits in infants at risk for severe RSV disease. The key to the study conducted by Simoes et al is the selection of controls. Because it would be unethical to conduct a placebo-controlled study in the United States, given the benefit of passive antibodies, the authors turned to statistical methods to select controls who were untreated infants and matched for gestational age. The results were quite spectacular and demonstrate a substantial benefit to the health of the child in preventing RSV infection. While the result is not unexpected, it is dependent on the assumptions of the trial, provided the appropriate controls can be selected using statistical methods. Moving forward with vigor to help prevent RSV infection using currently available therapy (palivizumab), future improved antibodies, and the possibility of future vaccines will be important to reduce the burden of RSV and its complications, including asthma.*

## Are Corticosteroids an Effective Treatment for Bronchiolitis in Infants?

**B**ronchiolitis conveys a significant health and socioeconomic impact. Although numerous pharmacologic therapies, including corticosteroids and bronchodilators, have been used in the treatment of bronchiolitis, to date there has been no demonstrable or consistent benefit from any of these agents. Recently, both experts and reviews have called for an adequately sized trial that is rigorously designed to address the use of corticosteroids as a treatment modality for bronchiolitis. The recent report by Corneli and colleagues describes a double-blind, randomized, controlled trial examining the efficacy of a single oral dose of dexamethasone in the treatment of bronchiolitis.

Infants (n=600), aged 2 to 12 months with a first episode of wheezing diagnosed as moderate-to-severe (Respiratory Distress Assessment Instrument score  $\geq 6$ ) during an emergency department (ED) visit were randomized to receive one dose equaling 1 mg per kilogram of body weight of oral dexamethasone or placebo. Infants were excluded if they were preterm, or

had lung, heart, or immune disorder, received corticosteroids in the previous 14 days, or recent varicella infection. Patients were enrolled at 20 EDs between November and April, over a 3-year period. The primary outcome was hospital admission following a 4-hour ED observation. The secondary outcome was the Respiratory Assessment Change Score (RACS).

Dexamethasone treatment of infants exhibiting moderate-to-severe bronchiolitis did not significantly alter the rate of hospital admission, respiratory status after 4 hours of observation, length of hospital stay, later medical visits, or readmissions. These findings are in agreement with

numerous other studies which demonstrate a lack of efficacy regarding corticosteroids in the treatment of bronchiolitis. The investigators suggest that other treatments and preventive strategies for bronchiolitis be evaluated.

Corneli HM et al. A multicenter, randomized, controlled trial of dexamethasone for bronchiolitis. *N Engl J Med.* 2007;357(4):331-339.



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Post-Test (October 2007)**

1. Palivizumab treatment of preterm infants without chronic lung disease resulted in which of the following outcomes?
  - a. Decreased recurrent wheezing and increased physician-diagnosed recurrent wheezing
  - b. Increased recurrent wheezing and increased physician-diagnosed recurrent wheezing
  - c. Decreased recurrent wheezing of any type
  - d. Increased recurrent wheezing and decreased physician-diagnosed recurrent wheezing
  
2. Which of the following is true with respect to corticosteroid treatment?
  - a. All corticosteroids have been proven effective for the treatment of bronchiolitis
  - b. Dexamethasone is the only corticosteroid proven effective for the treatment of bronchiolitis
  - c. No corticosteroid has been proven effective for bronchiolitis treatment
  - d. All corticosteroids, with the exception of dexamethasone, have proven effective for the treatment of bronchiolitis

1. c. Treatment with palivizumab resulted in significant decreases in both recurrent wheezing and physician-diagnosed recurrent wheezing when compared with untreated patients.  
 2. c. The findings of Cornelli et al are in agreement with numerous other studies which have demonstrated a lack of efficacy with corticosteroids when treating for bronchiolitis.

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