



Dear Colleague:

Welcome to *Clinical Insights in Pediatric Respiratory Disease™*, a monthly newsletter containing two relevant reviews of the current literature on focus topics affecting pediatric respiratory disorders. Each month a different topic will be selected to cover the broad spectrum in the field of pediatric respiratory disease. *Clinical Insights in Pediatric Respiratory Disease™* is conducted as a part of the *Pediatric Respiratory Care Initiative®* (PRCI), sponsored by Thomson Professional Postgraduate Services®, Secaucus, NJ. Activities as a part of the PRCI address issues concerning respiratory syncytial virus, interpandemic and pandemic influenza, other viral and bacterial respiratory tract infections, asthma, and other respiratory disorders, and evaluate methods to prevent, control, and treat respiratory illnesses in pediatric patients.

As part of this CME initiative, *Clinical Insights in Pediatric Respiratory Disease™* is designed to be clinically useful in your day-to-day practice by providing the latest summaries of relevant publications in this field. We are confident this newsletter will serve as a valuable resource for pediatricians, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, primary care physicians, and other healthcare professionals involved in the care and management of pediatric respiratory disorders.

Participants will receive a maximum of 2.25 category 1 credits toward the AMA Physician's Recognition Award after completing the 12-part series and post-test, and returning the completed CME Activity Evaluation/Registration Form. For more information about upcoming PRCI CME activities, please see the last page of this issue.

It is our hope that the material you find within these pages will provide you with useful information, positively impact your clinical practice approach, and ultimately provide your pediatric patients with improved health outcomes.

Sincerely,

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**Release Date:** September 2005

**Valid Until:** February 2007

This educational activity is conducted as a part of the *Pediatric Respiratory Care Initiative™* (PRCI™), sponsored by Thomson Professional Postgraduate Services® (PPS), Secaucus, NJ.

Issue No. 1, September 2005, is part of a 12-part CME activity (September 2005 – August 2006).

Physicians who wish to receive CME credit for this educational activity should do the following: (1) read each of the 12 monthly issues in the series and retain them for future reference; (2) review the original articles discussed in their entirety; and (3) complete the post-test that accompanies the last issue in the series (August 2006). The post-test may also be obtained by calling 1 (800) 223-8978. You will receive the post-test and CME Activity Evaluation/Registration Form by fax. To receive CME credit, the participant must complete the 12-part series, post-test, and CME Activity Evaluation/Registration Form and return the completed forms to: Thomson Professional Postgraduate Services®, Attn: CME Dept. T304, PO Box 1505, Secaucus, NJ 07096-1505 (Fax: 1 [201] 430-1441).

Applicants will receive a certificate of participation from PPS by return mail within 6 to 8 weeks of the date of receipt of the completed evaluation/registration form.

#### 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, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, primary care physicians, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

Thomson Professional Postgraduate Services® is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Thomson Professional Postgraduate Services® designates this educational activity for a maximum of 2.25 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

This CME activity is supported by an unrestricted educational grant from MedImmune, Inc.

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*Clinical Insights in*

# PEDIATRIC RESPIRATORY CARE™

VOLUME 1, NUMBER 1 • SEPTEMBER 2005

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## RSV Infection May Predict Development of Future Respiratory Complications but Not Atopy

**R**espiratory syncytial virus (RSV) is an important cause of lower respiratory tract infections in infants and young children, and is believed to predispose these individuals to subsequent development of wheezing disorders and allergic sequelae. Although, recent longitudinal studies appear to confirm an association between RSV infections and development of wheezing and asthma, the data with regard to atopy appears to be more controversial. This is an important consideration given the existence of evidence suggesting an interaction between atopy and RSV in the development of asthma. The recently published, longitudinal, birth cohort study by Henderson et al, based on data from the Avon Longitudinal Study of Parents and Children (ALSPAC), supports the link between early RSV infection and the development of wheezing and asthma, but not to development of atopy.

In ALSPAC, pregnant women were asked to complete questionnaires assessing parental environment and lifestyle, and health of the child during pregnancy, and at approximately annual intervals following birth of the child. Hence, ALSPAC provided a unique, population-based cohort of children for study and Henderson et al utilized the data from ALSPAC to examine the association between proven RSV bronchiolitis

requiring hospital admission during the first year of infancy, and the subsequent development of wheezing, physician-diagnosed asthma, and atopy in later childhood. Specific outcomes were considered in the current study: the presence and frequency of reported wheezing during two 12-month periods (30-42 months and 69-81 months), reported doctor-diagnosed asthma at 91 months, and the presence of

*“Wheezing ... was more prevalent in children who were hospitalized for RSV bronchiolitis compared to children with no history of hospitalization for bronchiolitis ... similar results were observed for doctor-diagnosed asthma...”*

atopy on skin-prick testing at 7 years. Uni- and multivariable regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI) for each outcome.

From a total of 284 infants identified as being admitted to the hospital with bronchiolitis, 150 had confirmed RSV infection on at least one occasion (RSV group), 16 had

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#### Disclosures:

\* Dr Piedra is an associate professor of Molecular Virology and Microbiology, and Pediatrics at Baylor College of Medicine. He has indicated relevant financial relationships as noted: he receives grants/research support from MedImmune, Inc.; speaker for MedImmune, Inc.; is an expert witness for Sanofi-Pasteur; and is an ad hoc consultant for GlaxoSmithKline, MedImmune, Inc., and Sanofi-Pasteur.

† Ms McBride is a senior managing editor for Thomson Professional Postgraduate Services®. She has indicated no relevant financial relationships.

‡ Dr Passador is a medical writer for Thomson Professional Postgraduate Services®. He has indicated no relevant financial relationships.



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another virus identified, 43 had negative specimens, and the remaining 75 had no specimen traced. Wheezing, at 30 to 42 months and 69 to 81 months of age, was more prevalent in children who were hospitalized for RSV bronchiolitis compared to children with no history of hospitalization for bronchiolitis (OR 2.3; 95% CI, 1.3-3.9,  $P=0.002$ ) and (OR 3.5; 95% CI, 1.8-6.6,  $P=0.0001$ ), respectively. Similar results were observed for doctor-diagnosed asthma, with children having had an RSV confirmed hospital admission demonstrating a higher incidence of asthma diagnosis (OR 2.5; 95% CI 1.4-4.3,  $P=0.002$ ). Asthma prevalence was 38.4% in the RSV group and 20.1% in the control group. In contrast to wheezing and asthma, no statistically significant effect on atopy at 7 years of age was observed (OR 0.7, 95% CI 0.2-1.7,  $P=0.4$ ). Prevalence of atopy at 7 years of age was found to be 14.6% in the RSV group compared to 20.7% for the control group. In all cases, OR were adjusted for confounders

including preterm delivery, season of birth, duration of breast feeding, maternal parity, sex of child, maternal age, maternal education status, housing tenure during pregnancy, smoking, and maternal history of asthma.

This study confirms the association between RSV infection and an increased risk for wheezing disorders including doctor-diagnosed asthma. However, no association was seen between RSV infection and subsequent development of atopy. The investigators suggest that long-term follow-up of case intervention studies with effective RSV prophylaxis are needed to more clearly differentiate whether RSV has a causal role in the development of asthma.

Henderson J et al. Hospitalization for RSV bronchiolitis before 12 months of age and subsequent asthma, atopy and wheeze: a longitudinal birth cohort study. *Pediatr Allergy Immunol.* 2005; 16:386-392.

## RSV Is a Significant Cause of Infant Mortality

**R**espiratory syncytial virus (RSV) is known to cause excess winter mortality in children, especially in the first year of life. Influenza, although predominantly associated with excess winter mortality in adults, and particularly in the elderly, is also known to cause occasional deaths in children. Attempts to quantify the mortality attributable to each of these viruses is difficult because they share a common circulation time during winter, a similar symptomology, and a paucity of virological studies of cases. In a recent study, Fleming et al used the national mortality data for England to estimate the number of child deaths that could be attributed to

influenza and RSV over a period of 11 years. The investigators compared death rates from all causes and those certified as being due to respiratory causes, both during and outside of influenza and RSV circulation periods.

Analysis of the data determined that the average winter respiratory deaths attributed to influenza in children (1 month-14 years) was 22 and to RSV, 28. This is in comparison to 78 all-cause deaths for influenza and 79 for RSV. All-cause deaths attributed to RSV in infants (1-12 months) exceeded those for influenza in 10 out of the 11 years studied. For the infants, age-specific estimates of influenza- and RSV-attributed all-cause death rates were 6.7 and 8.4 per

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*“...compared to influenza, RSV appears to be responsible for more deaths in children younger than 1 year, almost equal numbers in children aged 1 to 4 years, and fewer deaths in children older than 5 years.”*

## PRCI™ MISSION STATEMENT

The PRCI™ is a multicomponent educational program on pediatric respiratory disorders designed for pediatricians, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, primary care physicians, and other healthcare professionals involved in the care and management of pediatric respiratory patients. PRCI™ programs address issues concerning asthma, respiratory syncytial virus, viral respiratory tract infections, and other respiratory disorders and evaluate methods to prevent, control, and treat respiratory illnesses.

## RSV Is a Significant Cause of Infant Mortality

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100,000 population, respectively. The rates for children 1 to 4 years of age were much lower: 0.8/100,000 and 0.9/100,000 for influenza and RSV, respectively. In general, rates for all-cause death decreased with age, having rates less than 0.2/100,000 in children 5 to 14 years, except for influenza (0.4/100,000) in children 10 to 14 years. A similar trend was seen for deaths due to respiratory causes, although the rates were much lower (2.0 vs 2.9 per 100,000 for influenza and RSV, respectively [infants]; 0.3/100,000 for both influenza and RSV for children 1-4 years and less than 0.2/100,000 for children 5-14 years regardless of viral infection).

From this data, the authors conclude that RSV and influenza account for similar numbers of deaths in children. However, compared to influenza, RSV appears to be responsible for more deaths in children younger than 1 year, almost equal numbers in children aged 1 to 4 years, and fewer

deaths in children older than 5 years. It should be noted that the numbers of deaths can vary from winter to winter and between age groups. Importantly, the data encompassing all-cause mortality indicate that death rates can be severely underestimated if limited to deaths solely due to respiratory causes. Comparison to a study performed by the Centers for Disease Control in the US suggested similar all-cause mortality rates for children younger than 1 year and also those 1 to 4 years of age, even though there were differences in study methods. These findings emphasize the need for prospective information systems when pediatric deaths are investigated and further underscore the need to have prevention and treatment policies to prevent mortality in infants and young children related to RSV and asthma.

Fleming DM et al. Mortality in children from influenza and respiratory syncytial virus. *J Epidemiol Community Health*. 2005;59:586-590.

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For more information about upcoming PRCI™ CME activities, visit us at [www.ppscme.org](http://www.ppscme.org).

*Clinical Insights in Pediatric Respiratory Care*™ is edited by PRCI™ faculty member Pedro A. Piedra, MD.

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EM-T304-PHYCME-0905-13k