



Release Date: September 2005
CME Credit Valid Until: February 2007
CE Credit Valid Until: January 31, 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. 7, March 2006, is part of a 12-part CME/CE activity (September 2005 – August 2006).

Participants who wish to receive CME/CE 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/CE Activity Evaluation/Registration Form by fax. To receive CME/CE credit, the participant must complete the 12-part series, post-test, and CME/CE 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, 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.

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 *AMA PRA Category 1 Credits*[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This program has been approved for 2.7 contact hours of continuing education by the American Academy of Nurse Practitioners. Program ID 0601034.

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

Clinical Insights, *Pediatric Respiratory Care Initiative*, and PRCI are trademarks used herein under license.

Copyright © 2006 Thomson Professional Postgraduate Services[®]. All rights reserved.

Clinical Insights[®] in

PEDIATRIC RESPIRATORY CARE

VOLUME 1, NUMBER 7 • MARCH 2006

PEDRO A. PIEDRA, MD,* EDITOR-IN-CHIEF; CAROLINE B. HALL, MD,† REVIEWER; GRACE L. MCBRIDE,‡ SENIOR MANAGING EDITOR; MARIANA JORDAN,§ SENIOR EDITOR; LUCIANO PASSADOR, PHD,¶ MEDICAL WRITER

Evidence supports viral infections stimulate airway damage and remodeling

The relevancy of antecedent respiratory syncytial virus (RSV) infection to the development of recurrent wheezing is a topic of long-standing discussion. Ongoing prospective studies have demonstrated that RSV-induced bronchiolitis is a significant risk factor for subsequent frequent wheezing throughout the first decade of life. Furthermore, children with recurrent wheezing episodes in infancy are considered to be at greater risk for chronic childhood asthma. The majority of wheezing episodes during infancy are typically caused by viral infections, suggesting that viral infections may play a fundamental role.

Although a number of viruses, specifically rhinovirus, parainfluenza virus, influenza virus, and metapneumovirus, have been associated with pediatric episodic wheezing, RSV garners the most attention because it is the major cause of bronchiolitis during the winter season and accounts for approximately 70% of infant episodic

wheezing during these months. In a recent paper, Gern and colleagues discuss viral respiratory infections and their potential role in the development of recurrent wheezing and asthma. Though not answering the question of whether there is a causal relationship between RSV infection and recurrent wheezing or whether viral infection is merely a trigger for acute lower airway obstruction in children already predisposed to wheezing, the study presents data to further elucidate the role of viral infections.

Pulmonary development, characterized by alveolar multiplication and airway remodeling to accommodate growth, is ongoing during a child's development, especially during the first 2 years of life. Coincidentally, a child's susceptibility to viral infection involving the lower respiratory tract is also increased during this period. Hence, this may represent a period of increased vulnerability to acute lung injury due to viral infection. The authors suggest that in addition to causing airway injury and obstruction, viral

...viral infection may be an important stimulus for airway injury and remodeling, leading to decreased lung function and ultimately to asthma.

Continued

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 grant/research support from MedImmune, Inc.; is a speaker for MedImmune, Inc.; is an expert witness for Sanofi-Pasteur; and is an ad hoc consultant for GlaxoSmithKline, MedImmune, Inc., and Sanofi-Pasteur.
- † Dr Hall indicated that she receives grant/research support from MedImmune, Inc.
- ‡ Ms McBride is a senior managing editor for Thomson Professional Postgraduate Services[®]. She has indicated no relevant financial relationships.
- § Ms Jordan is a senior 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.



Evidence supports viral infections stimulate airway damage and remodeling

Continued

infection may profoundly affect lung growth and development.

Respiratory viruses can impair lung function by direct damage to lung tissue or indirectly by activation of proinflammatory responses. Epithelial damage in the form of edema or shedding of dead cells, along with mucus production, can lead to airway obstruction and wheezing. This damage could also alter mucosal permeability and facilitate contact between allergens and immune cells, thus promoting inflammation. Furthermore, infection activates the innate antiviral pathways, with a subsequent release of chemical mediators (cytokines and chemokines) that ultimately results in the recruitment of neutrophils and mononuclear cells, secretion of proinflammatory cytokines (eg, interleukin-8 [IL-8]), and an inflammatory response.

In addition, production of elastase by the activated neutrophils can upregulate mucus secretion by goblet cells, and elevated IL-8 levels can increase airway hyperresponsiveness. Increased levels of

neutrophil elastase and inflammatory cytokines may also affect alveolar remodeling.

Furthermore, viral infections induce the synthesis of many factors (eg, nitric oxide, transforming growth factor- β , fibroblast growth factor) involved in regulating airway and alveolar development and remodeling. Animal model studies have supported the proposed role of viral infection and various inflammatory molecules in altering airway development and remodeling.

What is the role of viral infections? Although the authors admit additional studies are needed, they conclude that the current evidence suggests viral infection may be an important stimulus for airway injury and remodeling, leading to decreased lung function and ultimately to asthma.

Gern JE, Rosenthal LA, Sorkness RL, Lemanske RF. Effects of viral respiratory infections on lung development and childhood asthma. *J Allergy Clin Immunol*. 2005;115:668-674.

COMMENTARY

CAROLINE B. HALL, MD, Professor of Pediatrics and Medicine, Pediatric Infectious Diseases, University of Rochester School of Medicine and Dentistry, Rochester, New York.

Gern's article suggests that the pathogenesis of wheezing in early childhood and subsequent asthma arises from a complex triangle of lung growth, innate susceptibility, and viral infections. Recent research has added a fourth dimension of inflammatory mediators, thus producing a diamond of multiple facets, including genetics, gender, and environmental exposures. Which facet is most enticing depends on the beholder. Not all facets are visualized, preventing assessment of their relative importance. Some studies determining clinical outcome have given confounding and conflicting results. This article does not provide the much needed answers to clinical management, but does suggest future preventive strategies must recognize that the concurrence of lung development, viral infections, and wheezing in infancy is not a coincidence.

Asthma as a risk factor for invasive pneumococcal disease

Invasive pneumococcal disease (IPD) is an umbrella term for a range of illnesses caused by infection with the bacterium *Streptococcus pneumoniae*. The illnesses can include pneumonia, bacteremia, and meningitis, which are serious medical concerns and sources of considerable

morbidity and mortality. Thankfully, vaccinations are available that can essentially prevent this disease.

Some populations, including children, are at increased risk for IPD, a risk also found in individuals with chronic obstructive pulmonary disease (COPD). While some

Continued



...discussion regarding the feasibility and cost-effectiveness of vaccination of persons with asthma is warranted.

PRCI MISSION STATEMENT

The PRCI is a multicomponent educational program on pediatric respiratory disorders 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. PRCI programs address issues concerning asthma, respiratory syncytial virus, and other respiratory tract infections and disorders. Methods to prevent, control, and treat respiratory illnesses in children are also evaluated.

Asthma as a risk factor for invasive pneumococcal disease

Continued

COPDs (emphysema, chronic bronchitis) are associated with an increased risk of IPD, the risk is unknown for persons who suffer from asthma. The identification of groups at elevated risk of developing IPD is important in identifying candidate populations for vaccination. Importantly, the most recent Centers for Disease Control and Prevention guidelines for vaccination against *S pneumoniae* include COPD, but exclude individuals with asthma except for some very specific cases. Similarly, current guidelines for asthma management also do not include pneumococcal vaccination as a strategy to prevent infectious complications.

In a recent article, Talbot and colleagues examined the association between asthma and IPD by conducting a nested case-control study utilizing data from two large population-based databases. Individuals 2 to 49 years of age from the Tennessee Medicaid program who were residents in a county participating in Active Bacterial Core (ABC) were enrolled in a prospective, active surveillance program for IPD. Following evaluation of the association between asthma and IPD from the available data, a cohort of individuals enrolled in the Medicaid program was analyzed to ascertain the

incidence of IPD regardless of the presence of asthma.

A total of 635 persons with IPD were identified, of whom 18% had asthma. These data were in contrast to 516 (8.1%) of the control group (n=6,350) diagnosed as having asthma. Individuals who had asthma demonstrated an increased risk (odds ratio=2.4; 95% confidence interval, 1.9-3.1) of IPD. Cohort analysis established that the incidence of IPD per 10,000 persons was 4.2 episodes for those with high-risk asthma. High-risk asthma was defined as asthma requiring hospital admission, a visit to an emergency department, the use of rescue therapy, long-term use of oral corticosteroids, or dispensing of ≥ 3 prescriptions for β -agonists in the year prior to enrollment. In comparison, incidence of IPD in individuals with low-risk asthma or without asthma was 2.3 and 1.2 episodes per 10,000 persons, respectively.

From these data, the authors conclude that asthma is an independent risk factor for IPD and suggest that careful discussion regarding the feasibility and cost-effectiveness of vaccination of persons with asthma is warranted.

Talbot TR, Hartert TV, Mitchel E, et al. Asthma as a risk factor for invasive pneumococcal disease. *N Engl J Med.* 2005;352:2082-2090.

Managing the Treatment of RSV and Pediatric Influenza—Did you miss the recent audioconference series? Now's your chance to access an on-demand CME-CE activity at www.freeCME.com. Earn 2 AMA PRA Category 1 Credits™ and 2.4 contact hours of continuing education by the American Academy of Nurse Practitioners. This double feature provides information on identifying the characteristics of both RSV and Influenza and offers a rationale for current and emerging therapeutic strategies specific to pediatric patients affected by these conditions.

If you have any friends or colleagues who would like to receive this newsletter via email, please fill in their information on the lines below and fax this page to us at 1 (800) 471-7716 so they can be added to our subscriber list.

Name: _____

Specialty: _____

Email Address: _____

You have received this email because we believe it may be of interest to you. If you would like your name to be removed from our mailing list, please reply to prci@pps.thomson.com and place REMOVE in the subject line.

Copyright © 2006 Thomson Professional Postgraduate Services®. All rights reserved.