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Learning Objectives

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

- Describe the relationship between epidemiologic and socioeconomic factors and RSV disease severity
- Assess the relationship of atopic disposition, wheezing, and atopic disorders with the risk of hospitalizations due to RSV in children younger than 18 months

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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Epidemiologic and Socioeconomic Factors Do Not Predict Severity of Respiratory Syncytial Virus Infection in Previously Healthy Infants

Respiratory syncytial virus (RSV) infection occurs in virtually all children by the age of 2 years. Among those infected, 40% to 50% develop lower respiratory involvement and 1% to 2% require hospitalization. Infants and young children susceptible to severe RSV bronchiolitis include those born prematurely and those with chronic lung disease or congenital heart disease.

Somech and associates prospectively evaluated epidemiologic and socioeconomic factors associated with disease severity in 195 previously healthy infants younger than 1 year, with confirmed RSV infection, and from an inner-city environment. Infants with known risk factors for RSV infection (prematurity, chronic lung disease, congenital heart disease, immunodeficiency, and previous episodes of wheezing) were excluded from the study. A total of 195 infants were enrolled into 3 subgroups according to disease severity: outpatients (n=82), inpatients (n=100), and pediatric intensive care unit (PICU) patients (n=13). The mean age was 3.8±2.3 months, the mean gestational age was 38.9±1.6 weeks, and the mean birth weight was 3,290±1,941 g.

Epidemiologic factors such as gestational age, birth weight, chronologic age at presentation, and gender were not predictive of the severity of RSV illness in the previously healthy infants. Mean gestational ages among

outpatients, inpatients, and PICU patients were 38.8 weeks, 39.1 weeks, and 38.9 weeks, respectively. Respective mean birth weights in these groups were 3,113 g, 3,444 g, and 3,191 g. Mean chronologic ages were 4.0 months, 3.7 months, and 3.5 months among outpatients, inpatients, and PICU patients, respectively. Additionally, 56.1%, 58.0%, and 46.2% of the outpatient, inpatient, and PICU patients, respectively, were male.

Moreover, socioeconomic factors such as ethnic origin, family history of asthma, exposure to cigarette smoke, number of family members, presence of pets at home, breastfeeding, and day-care attendance were not associated with severity of RSV illness. For example, a positive family history of asthma was recognized in 48.8%, 56.0%, and 55.5% of outpatients, inpatients, and PICU patients, respectively.

In contrast, clinical factors were highly predictive of RSV illness severity. Fever was detected in a significantly greater proportion of hospitalized infants than nonhospitalized infants (89.3% vs 34.1%; *P*<0.001). The level of room air oxygen saturation on admission strongly correlated with disease severity in nonhospitalized, hospitalized, and PICU patients (97.9%±1.6%, 92.4%±3.1%, 86.7%±4.1%, respectively; *P*<0.001). Abnormal auscultation findings and abnormal chest

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Disclosures:

- * Dr Piedra is 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.
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Epidemiologic and Socioeconomic Factors Do Not Predict Severity of Respiratory Syncytial Virus *(Continued)*

x-rays were also significantly related with disease severity in the nonhospitalized, hospitalized, and PICU patients, respectively ($P < 0.001$).

The results of this study underscore the complexity of predicting disease severity in previously healthy infants with RSV infection. Clinical factors such as fever, abnormal auscultation findings, low oxygen saturation, and abnormal chest x-ray findings were more predictive of RSV disease severity than socioeconomic and epidemiologic factors. As such, the study authors suggested that host genetic

background might be useful in predicting RSV disease severity. Molecular biology techniques such as DNA microarray and functional genomics analyses might enable identification of groups of infants who are at high risk of severe RSV bronchiolitis.

Somech R, Tal G, Gilad E, et al. Epidemiologic, socioeconomic, and clinical factors associated with severity of respiratory syncytial virus infection in previously healthy infants. *Clin Pediatr*. 2006;45:621-627.

COMMENTARY

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

Somech et al focus on one of the pivotal problems in the conundrum of RSV prevention: which factors place infants most at risk for severe disease? All infants acquire RSV infection within the first 1 to 2 years of life. Immunity is incomplete, not durable, and repetitive infections occur throughout life.¹ Complete prevention of all RSV infections is, therefore unlikely, if not impossible. Thus, control must be prioritized; it currently has been aimed at determining those most at risk based on the infant's history and clinical examination at the time of presentation. The results of numerous studies evaluating such risk factors often have been contrasting. The studies differ in their populations, design, and methods. Most important is the lack of a standardized tool of assessment such as a scoring system, which was used by Somech et al. The results, therefore, cannot necessarily be applied to other populations. Furthermore, the predictability of long-term outcome is even more problematic.

The risk factors that have most frequently been shown to be significant are underlying condition, especially prematurity, compromising cardiopulmonary function. Gestational age generally correlates inversely with the risk of hospitalization. For previously healthy infants, the only factors that appear to be reliable in predicting severe disease are that the infection is the infant's first encounter with RSV and young age (<3 months). Most reports, but not all, indicate that the risk is enhanced by exposure to smoke and lack of breast-feeding.

We may conclude from these studies that an individual child's risk is a collage of viral, environmental, and host factors, most of which are unknown. RSV control, whether by immunization or other means of prophylaxis needs, therefore, to be aimed at all infants with the goal of not eliminating infection but of preventing severe disease and sequelae.

Reference

1. Hall CB. *N Engl J Med*. 2001;344:1917-1928.

Respiratory Syncytial Virus Hospitalization Associated With Atopic Disposition and Prior Wheezing

Respiratory syncytial virus (RSV) is the single most important respiratory pathogen in infancy and early childhood. RSV bronchiolitis in young children has been linked to subsequent wheezing and asthma in later years. Previous work also suggests that a family history of atopy may predispose infants to developing serious RSV lower respiratory tract infections.

Stensballe and colleagues recently examined whether atopic disposition, wheezing, atopic disorders, and other factors increased the risk of hospitalizations due to RSV in children younger than 18 months. Relative risks

for RSV hospitalization were determined in a nested 1:5 case-control design using exposure information obtained from interviews with mothers of 2,564 case and 12,816 control children. As participants in the Danish National Birth Cohort, these children had been followed prospectively from birth and until 18 months of age.

RSV hospitalization occurred in 46.3%, 33.0%, and 20.7% of case children younger than 6 months, between the ages of 6 and 12 months, and older than 12 months, respectively. Demographic facts significantly associated with an increase in RSV hospitalization

Continued



Respiratory Syncytial Virus Hospitalization *(Continued)*

were male gender, nonatopic risk factors, the presence at home of other children younger than 12 years, day care attendance, and maternal smoking. Breast-feeding was associated with a significant decrease in RSV hospitalization.

Asthmatic disposition increased the risk of RSV hospitalization. Physician-diagnosed maternal asthma increased the risk of RSV hospitalization in case children by 72% (95% confidence interval [CI]: 44%-106%), whereas a history of paternal asthma increased the risk by 23% (95% CI: 4%-45%). Infrequent (<3 wheezing episodes) and recurrent wheezing (≥ 3 wheezing episodes) in case children before the RSV hospitalization were significant risk factors. The adjusted relative risks of RSV hospitalization were 5.90 (95% CI: 4.96-7.01) for recurrent wheezing, and 2.98 (95% CI: 2.56-3.48) for infrequent wheezing. Atopic dermatitis in case children was a significant risk factor 1.33 (95% CI: 1.01-1.76) only among children younger than 6 months at the time of hospitalization. Considering family

factors, the adjusted relative risks of RSV hospitalization in case children were 1.73 (95% CI: 1.44-2.06) for physician-diagnosed maternal asthma, and 1.23 (95% CI: 1.04-1.45) for history of paternal asthma. A maternal history of atopic dermatitis was not a significant risk factor 1.11 (95% CI: 0.95-1.29) for RSV hospitalization in children younger than 18 months. Such associations persisted even when infants with medical risk factors were excluded from the analysis.

The results of this study suggest that a combination of host and environmental factors might interact to predispose young children to both hypersensitive airways and RSV lower respiratory tract infection. In this study, a history of infrequent and recurrent wheezing in children were strong determinants of subsequent RSV hospitalization in children younger than 18 months.

Stensballe LG, Kristensen K, Simoes EA, et al. *Pediatrics*. 2006;118:e1360-e1368.

Clinical Insights® in Pediatric Respiratory Care Post-Test

1. Gestational age and birth weight were shown to be predictive of the severity of RSV illness in previously healthy infants from an inner-city environment.
 - a. True
 - b. False
2. Which of the following factors were found to increase the risk of RSV hospitalization in children younger than 18 months? (Choose 1 or more correct answers.)
 - a. Recurrent wheezing in the child
 - b. Maternal history of atopic dermatitis
 - c. Physician-diagnosed maternal asthma
 - d. All of the above

1. *b. False.* Epidemiologic factors such as gestational age and birth weight were not predictive of the severity of RSV illness in the previously healthy infants. Mean gestational ages and birth weights were similar among outpatients, inpatients, and PICU patients.
2. *a and c.* Recurrent wheezing and physician-diagnosed maternal asthma are child and family factors that increase the risk of RSV hospitalization. A history of maternal atopic dermatitis did not significantly increase the risk of RSV hospitalization in children younger than 18 months.

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