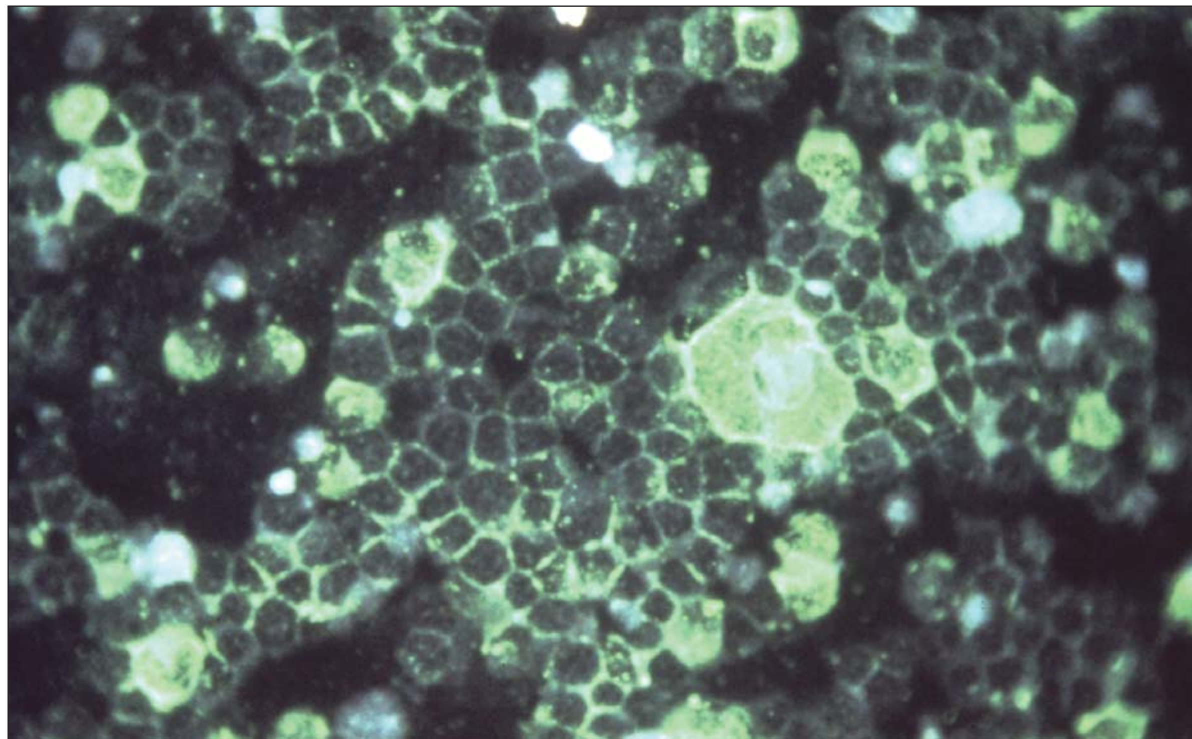
CMPMedica
United Business Media

SUPPLEMENT TO

PEER-REVIEWED / A CLIGGOTT PUBLICATION
DECEMBER 2008
VOL.7 NO.12

Consultant® FOR PEDIATRICIANS

www.ConsultantLive.com



Respiratory Syncytial Virus: From Pathogenesis to Prevention

Proceedings of a Symposium Held September 25, 2008, in Fort Lauderdale, Florida

LEONARD E. WEISMAN, MD
DIANNE S. CHARSHA, RN, MSN, NNP-BC

1 AAFP PRESCRIBED CREDIT HOUR
(accepted as equivalent to
1.0 *AMA PRA Category 1 Credit*™)
1 ACPE CREDIT HOUR
1.0 TOTAL ASNA CREDIT HOUR

Sponsored by **TotalCME, Inc.**
Supported by an educational grant from MedImmune

Contents

Respiratory Syncytial Virus: From Pathogenesis to Prevention

Supported by an educational grant from MedImmune

ACCREDITATION STATEMENT **S2**

RESPIRATORY SYNCYTIAL VIRUS: PATHOGENESIS AND DISEASE BURDEN **S3**
LEONARD E. WEISMAN, MD

RESPIRATORY SYNCYTIAL VIRUS: BEST PRACTICES FOR PREVENTION AND TREATMENT **S10**
DIANNE S. CHARSHA, RN, MSN, NNP-BC

CME POST-TEST & INSTRUCTIONS **S15**

Faculty

LEONARD E. WEISMAN, MD
Professor, Department of Pediatrics, Baylor College of Medicine
Director, Perinatal Center at Texas Children's Hospital
Houston

DIANNE S. CHARSHA, RN, MSN, NNP-BC
Associate Chief Nursing Officer
Cooper University Hospital
Camden, NJ

CONSULTANT FOR PEDIATRICIANS (ISSN 1545-8539) is published 12 times a year by the Cliggott Publishing Group, a division of CMPMedica. It is distributed to over 62,000 physicians, MD and DO, plus nurse practitioners and physician assistants. Subscription rates: $80 a year in the U.S.; $90 a year (U.S. funds only) for Canada and overseas countries (foreign delivery not guaranteed). Periodicals postage paid at Darien, CT 06820-4027 and additional mailing offices. Copyright © 2008 by CMP Healthcare Media LLC, 330 Boston Post Road, Box 4027, Darien, CT 06820-4027, (203) 662-6400. Printed in U.S.A. All rights reserved. No part of this publication may be reproduced or transmitted in any form, by any means, without written permission. CONSULTANT and *What's Your Diagnosis?,* and CONSULTANT FOR PEDIATRICIANS are registered trademarks of CMP Healthcare Media LLC. Postmaster: If undelivered, send form 3579 to CONSULTANT FOR PEDIATRICIANS, 330 Boston Post Road, Box 4027, Darien, CT 06820-4027.

The opinions expressed herein are those of the authors and do not necessarily represent those of CONSULTANT FOR PEDIATRICIANS, TotalCME, Inc, or MedImmune. Any procedures or other courses of diagnosis or treatment discussed or suggested by authors should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use, review of any applicable manufacturer's prescribing information, and comparison with the recommendations of other authorities.

Respiratory Syncytial Virus: From Pathogenesis to Prevention

Supported by an educational grant from MedImmune

Overview

Respiratory syncytial virus (RSV) is the most important cause of viral lower respiratory tract illness in infants and children worldwide. Each year, it is responsible for over 120,000 hospitalizations of infants in the United States alone. The disease spectrum includes a wide array of upper and lower respiratory tract symptoms that can have a significant impact on morbidity and mortality. In addition, RSV infection can be associated with the development of acute, short-term diseases such as otitis media and chronic, long-term conditions such as reactive airway disease and asthma. The costs of caring for patients who experience severe lower respiratory tract infection and their sequelae are substantial and cut across all segments of the neonatal and pediatric health care sector. Currently, pharmacological management of this disease is limited to symptomatic therapy, antiviral therapy, and monoclonal antibody preventive therapy in select patient populations. This supplement will review the pathophysiology and disease burden of RSV infection in the neonatal and pediatric populations as well as highlight proper health care practices that can prevent the development of the disease in the neonatal ICU or its spread beyond the hospital. Finally, the current pharmacological symptomatic treatment and disease prevention options will be reviewed.

Learning Objectives

After completion of this activity, participants should be able to:

- Identify patients at risk for RSV infection.
- Recognize the signs and symptoms of RSV disease presentation.
- Review integrated approaches and action plans for reducing and preventing the spread of RSV in the hospital and at home.
- Compare and contrast existing and emerging pharmacological agents that treat RSV infection.
- Gain an understanding of the risks and benefits of pharmacological options for RSV infection prevention and their impact on the overall health care system.

Release Date: December 2008

Expiration Date: December 2009

Method of Participation

Participants should read the learning objectives and review the articles in their entirety. After reviewing the activity, they should complete and submit the post-test. Upon achieving a passing score of 70% or better on the post-test, a statement of credit will be awarded.

Target Audience

This program is intended for medical health professionals involved in the research or care of patients with RSV infection.

Accreditation and Designation

Physicians

This activity has been reviewed and is acceptable for up to 1 Prescribed credit hour by the American Academy of Family Physicians (AAFP). AAFP Prescribed credit is accepted by the AMA as equivalent to AMA PRA Category 1 Credit™ for The Physician Recognition Award.

Nurses

Educational Review Systems is an approved provider of continuing education in nursing by ASNA, an accredited provider by the ANCC/Commission on Accreditation. Provider # 05-115-08-081. This program is approved for 1 hour of continuing education credit. Educational Review Systems is also approved for nursing continuing education by the state of California and the District of Columbia.

Pharmacists

Educational Review Systems is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmaceutical education. This program is approved for 1 hour (0.1 CEU). ACPE # 761-999-08-118-H01-P

Disclosures

Leonard Weisman, MD
Consultant: MedImmune

Dianne Charsha, RN, MSN, NNP-BC
No real or apparent financial relationships to disclose

Sponsorship and Support

This educational activity is sponsored by TotalCME, Inc. and supported by an educational grant from MedImmune.

LEONARD E. WEISMAN, MD
Baylor College of Medicine

Respiratory Syncytial Virus: Pathogenesis and Disease Burden

Dr Weisman is professor of pediatrics at Baylor College of Medicine and director of the Perinatal Center at Texas Children's Hospital, both in Houston.

ABSTRACT: Although respiratory syncytial virus (RSV) was first described more than 50 years ago, RSV remains a cause of significant disease burden in infants and young children—especially those who are born prematurely or who have certain underlying diagnoses. Lower respiratory tract infections (LRTIs) develop in a significant percentage of patients who become infected with RSV, often resulting in hospitalization. Around 20% of premature infants are hospitalized with RSV-associated illness; in North America, about 1% of children hospitalized with RSV disease die. In addition, infants who have RSV LRTIs may experience pulmonary sequelae, including wheezing and asthma, that can last until adolescence.

Respiratory syncytial virus (RSV) can cause an array of respiratory diseases, such as bronchiolitis and pneumonia, and it has been linked to chronic wheezing and asthma. Each year, infection with RSV causes up to 126,300 hospitalizations of infants in the United States,[1] and the worldwide mortality associated with RSV infection has been estimated as being as high as 1 million per year.[2] Although nearly all children are likely to be infected with RSV at some point within their first 2 years, certain groups of infants are at significantly increased risk for serious infection and associated complications.

In this article, I review the pertinent facts about the virus—its history, structure, mode of transmission, and seasonal nature—as well as the clinical course of RSV infection, including its pathology and pathophysiology, associated morbidity and mortality, hospital course, and costs. I then discuss in depth which patients are at particular risk for RSV infection, the reasons for this heightened risk, and the long-term impact of serious RSV infection.

NATURE OF RSV

RSV was first isolated in 1956,[3] when it was described as a cause of coryza in chimpanzees. RSV infection in children was first diagnosed a year later in hospitalized patients with lower respiratory tract infections (LRTIs).[4] The first documented outbreak of RSV in a neonatal intensive care unit (NICU) occurred in 1964.[5]

Structure of the virus. There are several glycoproteins on the surface of RSV. The 2 most significant of these are the F (fusion) protein and the G (attachment) protein.[6] The F protein, which seems to be the more stable of the two, mediates cell-to-cell fusion of RSV and the formation of syncytia.[7] The G protein is responsible for attachment to respiratory cells.[8] Although both the F and G glycoproteins are major targets of neutralizing antibodies, the F protein elicits a particularly powerful antibody response.[9] Moreover, antibodies against this particular glycoprotein protect against the 2 broad serological subtypes of RSV (A and B). For these reasons, the F protein has been the target of efforts to develop antibodies for the prevention of RSV infection.[7,10] ►

Transmission. RSV is shed in nasopharyngeal secretions; infected patients can shed significant amounts of the virus for up to 21 days.[11] RSV can survive on non-porous surfaces, such as countertops or crib rails, for up to 7 hours; on porous surfaces, such as clothing, for up to 4 hours; and on skin for up to 1 hour.[12] RSV enters the body through the mucosal surfaces of the mouth, nose, and conjunctivae. The ability of the virus to enter via the conjunctivae plays a significant role in its transmission. This stems from the fact that health care personnel typically don gowns, gloves, and masks when working in a nursery in which patients with RSV infection have been isolated; however, they less commonly put on goggles. Thus, if a physician or nurse accidentally rubs his or her eye while working with infected infants then later has contact with an infant who is not infected and rubs the eye again, RSV may be transmitted.

In a study by Hall and colleagues,[12] 3 groups of volunteers were put in rooms with patients infected with RSV. Those in the first group were instructed to simply sit in the room and not touch anything; those in the second group were instructed to touch various surfaces; and those in the third group were asked to hold the infected infants. RSV infection subsequently developed in none of the volunteers in the first group, in 40% of those in the second group, and in 71% of those in the third group (**Figure 1**). This study demonstrated that RSV is not an airborne pathogen.

The transmissibility of RSV in NICUs was historically a significant health care burden: in the 1970s, RSV infection developed in 45% of infants who were hospitalized in the NICU during RSV season for longer than 1 week, and the risk of an RSV infection was even higher among patients who had congenital heart disease; were premature; had chronic lung disease, leukemia, or bone marrow transplants; or were elderly.[13,14] Understanding how RSV is transmitted is the first step to controlling infection; infection rates have been significantly reduced through the imposition of appropriate control measures.

Seasonality. RSV infection is seasonal in nature the world over. Although the timing of the RSV season varies with latitude and climate, it typically occurs at the same time every year. In the United States, the season runs from winter into spring and lasts from 2 to 5 months—usually from November through March (although it can start in October and last as late as April). In more northern parts of the country, the RSV season tends to be shorter than it is further south.

In other countries with a temperate climate, such as the Netherlands, Belgium, and the United Kingdom, RSV season also tends to run from November through March. The season in the southern hemisphere occurs at the opposite time of year. In countries with a tropical climate, such as Indonesia, RSV season typically coincides with the rainy season.

The predictability of the RSV season in the United States is shown in the graph in **Figure 2,** which is based on data collected by the CDC on RSV epidemics.[15] The CDC monitors RSV infections through weekly reports from selected centers (public health laboratories, hospitals, and clinics) on the number of specimens that are tested for RSV and the number of these specimens that test positive. An RSV epidemic is defined as occurring when more than 50% of the reporting centers detect RSV once or more in 2 consecutive weeks or when more than 10% of the specimens tested during the surveillance week are positive for RSV.

The morbidity and mortality that occur during an RSV epidemic are significant and dramatic. During an epidemic, RSV is the principal cause of hospitalizations for LRTIs. Although infections with other viruses (eg, influenza A, influenza B, parainfluenza, adenovirus) also tend to peak during the winter, at the time of an RSV epidemic, the number of hospitalizations for RSV-associated infections typically exceeds those caused by all other

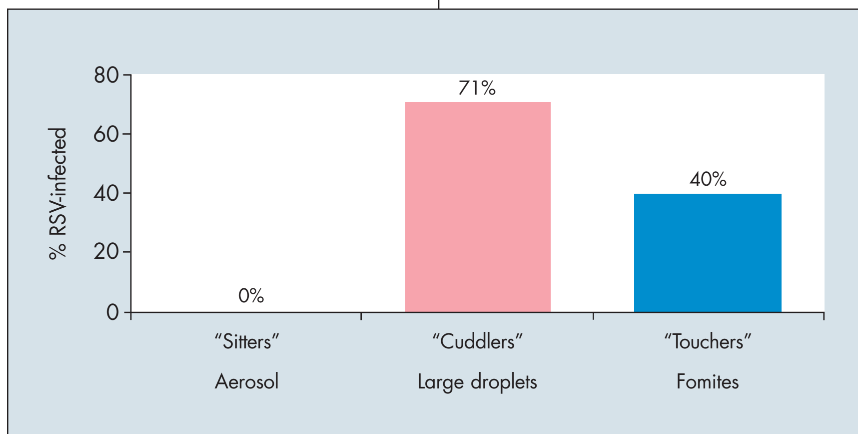


Figure 1 – This graph shows the relative likelihood of infection with respiratory syncytial virus with 3 different types of exposure: sitting in the same room with an infected infant but at a distance from him and without touching anything ("sitters"); sitting in the same room with an infected infant and touching various surfaces ("touchers"); and actually holding an infected infant ("cuddlers"). (Data from Hall et al. *J Infect Dis.* 1980.[12])

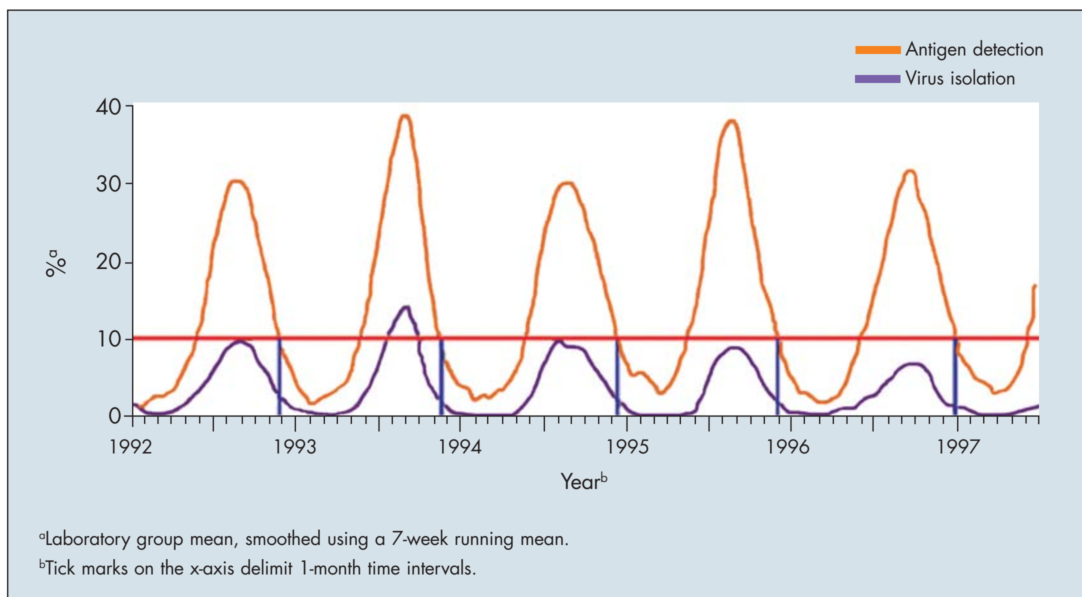


Figure 2 – This graph shows the percentage of specimens that tested positive (using 2 different confirmation methods) for respiratory syncytial virus (RSV) in the United States each week from July 1992 through November 1997; it demonstrates the predictability and consistency of the RSV season.[15]

viruses (**Figure 3**).[16] In addition, infant mortality from LRTIs closely parallels RSV epidemic activity.[17]

CLINICAL COURSE OF RSV INFECTION

Epidemiology. By age 1 year, 50% of children will have had an RSV infection, and by age 2 years, virtually all children will have been infected with RSV. Because infection does not confer long-lasting immunity, as with diphtheria or pertussis, reinfection with RSV is common. By age 2 years, 50% of children will have had 2 or more RSV infections.

RSV causes 40% to 49% of cases of bronchiolitis, up to 44% of cases of outpatient pneumonia, and up to 63% of cases of inpatient pneumonia.

Clinical manifestations. Uncomplicated RSV infection presents with rhinorrhea, cough, and fever. However, a significant number of these infections progress to LRTIs. The clinical presentation of an RSV-associated LRTI includes chest wall retractions, nasal flaring, tachypnea, sometimes cyanosis, and wheezing and rhonchi on auscultation. Neonates, especially those in the NICU, may present with apnea.

Pathology and pathophysiology. RSV infection causes epithelial necrosis of the bronchioles with sloughing of necrotic debris, mononuclear infiltrates in peribronchiolar tissue with edema of the submucosa, and hypersecretion of mucus. These effects produce bronchoconstriction leading to airway obstruction. Turbulent airflow in narrow airways is the cause of the wheezing heard in RSV bronchiolitis. Because the airways in premature and young infants are already relatively narrow, the risk of respiratory symptoms from RSV infection is increased in these populations.

RSV-associated hospitalizations. As many as 126,300 infants in the United States are hospitalized each year for RSV-associated bronchiolitis or pneumonia,[1] and estimates of annual mortality in US infants and children attributed to RSV range from 200[1] to more than 2700.[18] In North America and Europe, RSV-associated hospitalizations involve primarily infants younger than 1 year[19-21]; in developing countries, however, older children are often hospitalized as well.

Among otherwise healthy children, between 0.5% and 2% are hospitalized each year for RSV infection.[22] However, hospitalization rates are significantly increased in various groups of high-risk children. In an analysis of 9 studies of children under age 2 years who had chronic lung disease or bronchopulmonary dysplasia (BPD), the weighted mean hospitalization rate for RSV infection was approximately 17%.[20,23-30] An analysis of studies of infants born at less than 36 weeks' gestation showed a weighted mean hospitalization rate of almost 9%.[24,27,29,31-35]

A study by Boyce and colleagues[26] has shown that, of the risk factors for severe RSV infection, BPD is associated with the highest rate of RSV hospitalization, followed by congenital heart disease and prematurity. Among infants younger than 1 year, the number of RSV-associated hospitalizations per 1000 children-

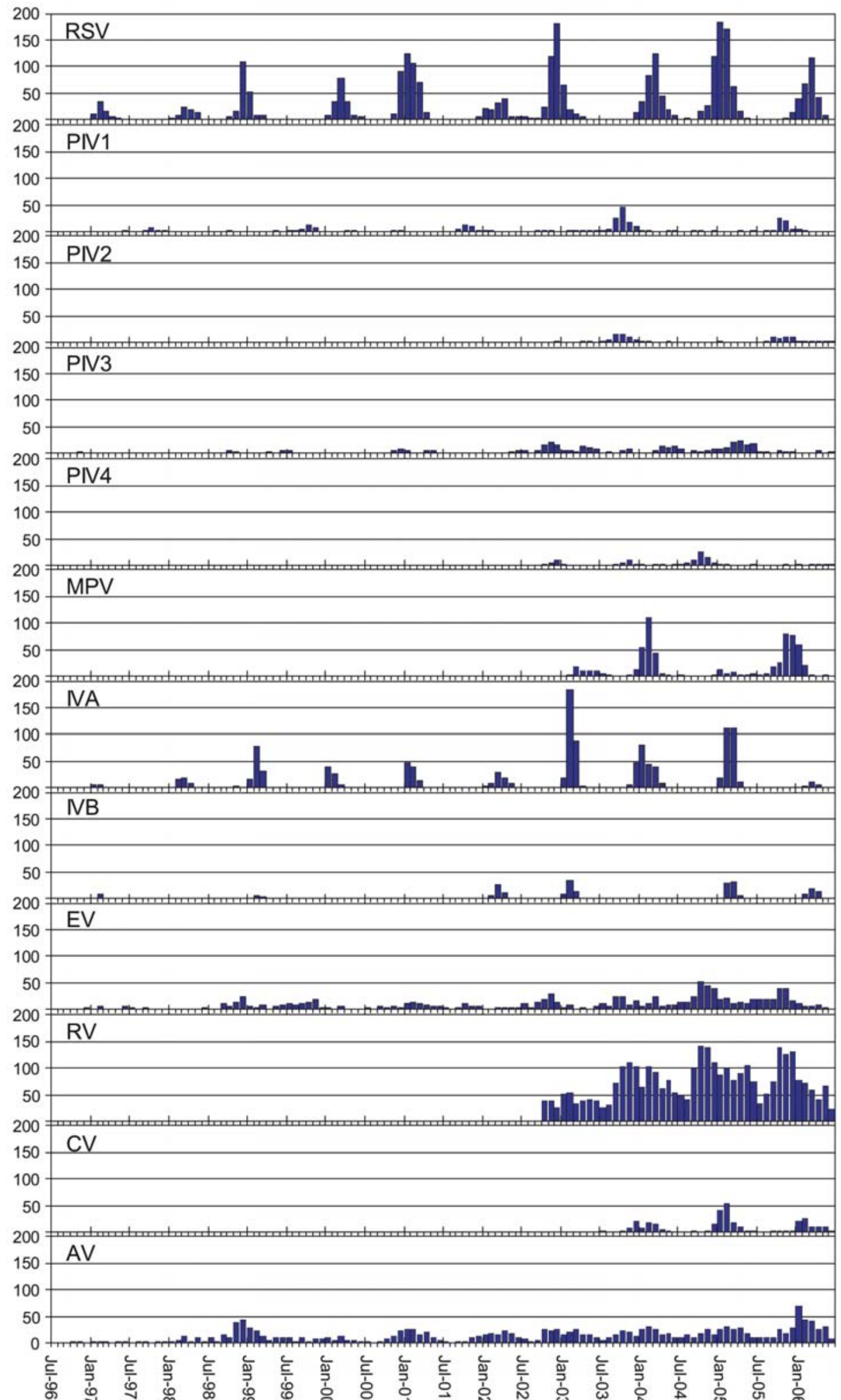


Figure 3 – These graphs show the monthly incidence of 12 common pathogens identified in nasopharyngeal aspirates obtained from German children aged birth to 16 years in whom a lower respiratory infection or complicated acute respiratory infection had been diagnosed (data are shown for the 10-year period July 1996 through June 2006 for all pathogens except rhinoviruses, for which data are shown from October 2002 onwards, and coronaviruses, for which data are shown from April 2003 onwards). At the height of RSV infection epidemics, the number of positive tests for RSV generally surpassed the number of positive results for any other pathogen.

(From Weigl et al. *Eur J Pediatr.* 2007.[16])

years was 388.4 among those with BPD, 92.2 among those with congenital heart disease, and 65.9 among those born between 29 and 32 weeks' gestation. Moreover, by age 2 years, the only children with any substantial persistent risk of hospitalization for RSV infection were those with BPD.

Hospital stays for RSV LRTIs are frequently lengthy. Many factors are involved in determining the duration of such stays, including the presence of an underlying diagnosis (eg, prematurity, congenital heart disease, chronic lung disease) and local practice in the area where the hospital is located. In Canada, the length of an RSV-associated hospital stay ranges from 4.6 to 6.7 days for otherwise healthy patients and from 8.6 to 11.8 days for patients with another diagnosis.[36] In Europe, RSV-associated stays range in length from 4 to 9 days.[37]

In addition, hospitalization for many children who are admitted for an RSV LRTI—especially those with an underlying diagnosis—may involve time in the ICU and/or the need for ventilation. A study by Arnold and colleagues[19] showed that children hospitalized with an RSV LRTI who also had underlying lung disease (eg, cystic fibrosis, chronic lung disease of prematurity, recurrent aspiration) spent between 4 and 11 days in the ICU and between 3.5 and 14 days on ventilation.

Morbidity and mortality. Between 20% and 40% of RSV infections result in LRTI. The vast majority of patients with an RSV LRTI seek medical care, and between 0.5% and 2% of previously healthy patients with an RSV LRTI are hospitalized.[22] In North America, approximately 1% (between 0.1% and 2%) of children hospitalized with RSV infection die; the mortality rate among high-risk children is even greater—3% to 4% of those hospitalized.[38] Worldwide, because of poorer quality health care in many areas, RSV-related mortality is far higher—between 600,000 and 1 million deaths per year of children younger than 5 years.[2]

In the United States, the children at greatest risk for death from RSV infection are those who were infants with very low birth weight (less than 1500 g) or low birth weight (1500 to 2499 g). Their risks of death are, respectively, about 5 times and 2.5 times that of healthy weight infants born at term.[39]

Cost of RSV infection. Data on the costs associated with RSV infection are difficult to come by. The best available data come from Canada and are about 15 years old. However, while the specific numbers may be somewhat out-of-date, the apportionment of costs they show is noteworthy. About 62% of total costs were related to hospital care; nearly 40% of the annual cost of RSV infection was attributable to outpatient care (including physician services, loss of homemaker wages, travel, and so on).[40]

WHICH PATIENTS ARE AT GREATEST RISK—AND WHY

The risk of severe RSV infection is highest in the following 5 groups of infants:

- Those with chronic lung disease.
- Those with cystic fibrosis.
- Those with cardiac disease.
- Those with neuromuscular disorders.
- Those who are immune-deficient.
- Those who were born prematurely.

Of these groups, preterm infants are at greatest risk. In the United States, nearly 300,000 infants are born at less than 36 weeks' gestation each year, and more than 76,000 at less than 32 weeks' gestation.[41] Depending on the study cited, premature infants account for 12%[26] to 27%[42] of all RSV-associated hospitalizations. Thus, approximately 20% of premature infants are hospitalized for RSV infection.

Reasons underlying increased risk. The reasons for the increased risk vary among the different at-risk populations. Infants with chronic lung disease or cystic fibrosis have hyperresponsive airways and reduced lung capacity. Those with cardiac disease often have pulmonary vascular changes that lead to hyperresponsiveness, or increased pulmonary blood flow that could result in pulmonary hypertension, or pulmonary edema. Infants with neuromuscular disorders have decreased respiratory muscle strength and endurance, and those with immune deficiency have a decreased host response and impaired ability to eliminate the virus.

In premature infants, the increased risk can be attributed to underdeveloped lungs, an immature immune system, and incomplete transfer of maternal antibody. Lung volume, lung weight, and alveolar diameters are all substantially reduced in infants born at 30 weeks' gestation compared with those born at full term.[43] When airways are smaller, the risk that a small change—such as that caused by RSV infection—will result in significant respiratory problems is increased. (Of note, the severity of RSV-associated respiratory illness in hospitalized preterm infants born between 32 and 35 weeks' gestation has been shown to be similar to that seen in those born at less than 32 weeks' gestation: length of hospital stay, risk of needing supplemental oxygen and/or ventilation, and risk of transfer to the ICU were roughly the same in both groups.[44])

Although women typically transmit antibody to their babies throughout pregnancy, the majority is transmitted at the end of gestation. Thus, a preterm infant will not receive the "full dose" of maternal antibody. **Figure 4** shows the reduced levels of postnatal IgG seen in infants born at 25 to 28 weeks' gestation and at 29 to 32 weeks' gestation compared with the levels in full-term infants.

Other factors associated with increased risk. In addition to the in-

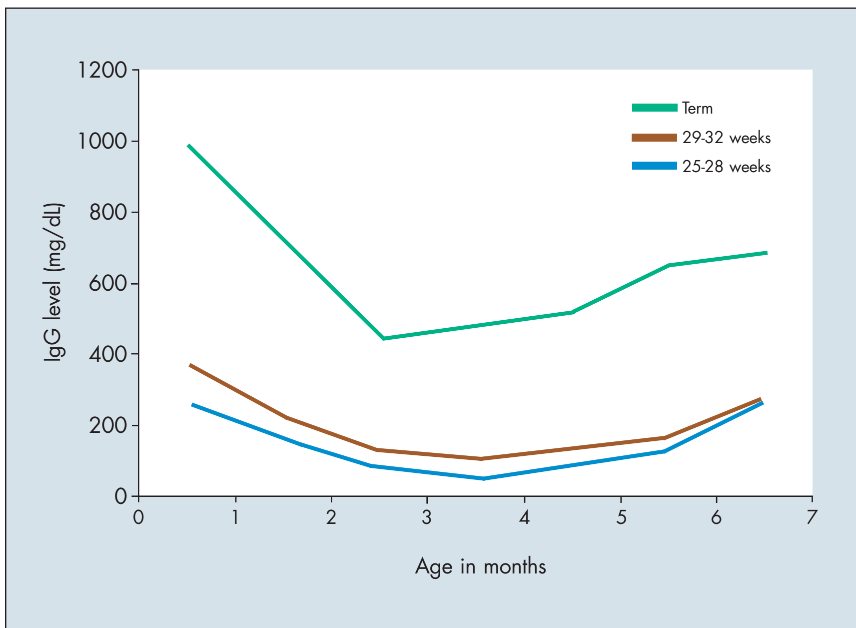


Figure 4 – Postnatal levels of IgG are significantly lower in preterm infants than in full-term infants. (Data from Ballow et al. *Pediatr Res.* 1986.[50])

creased risk of severe RSV infection seen in the 5 groups of infants listed above, a number of other factors can raise the risk still further. These include the following, which have been documented in episodic observational studies:

- Overcrowding.[29,45]
- Use of gas rather than electricity for cooking.[29]
- Day care attendance.[40]
- School-aged siblings.[46]
- Two or more children sharing a bedroom.[23,45]
- Multiple births[45] (although this may be more a result of prematurity).
- Passive smoke exposure[23,46] (although this is currently being debated by the American Academy of Pediatrics).
- Birth in the 6 months before the start of RSV season.[35]

LONG-TERM IMPACT OF RSV INFECTION

RSV infection is a significant cause of morbidity among infants and young children. It also appears to be associated with increased morbidity years after the at-risk period has passed. A 1999 study by Stein and colleagues,[47] published in *The Lancet,* showed that the risk of recurrent wheezing developing later in childhood was significantly greater in children who had LRTIs caused by RSV before age 3 than in children who did not have an early LRTI. In addition, it showed that the risk of wheezing later in childhood was greater in children who had an early LRTI caused by RSV than in those who had an LRTI caused by parainfluenza virus. The increased risk of wheezing was seen at ages 6, 8, 11, and 13 years.

Similar findings are seen in the work of Sigurs and colleagues.[48,49] These researchers compared rates of wheezing and asthma in children who had been hospitalized with RSV infections in the first year of life with rates in those who had not been hospitalized. The children who had been hospitalized with an RSV infection were significantly more likely to have wheezing or asthma than were those who had not been hospitalized—and this was true at ages 3 and 7 years as well as at age 1 year.

CONCLUSION

The disease burden of RSV infection is indeed great. RSV is the cause of significant morbidity and mortality in infants and young children—especially those born prematurely—and of ongoing morbidity in older children who have had early severe infections. However, there are a number of effective strategies physicians can use to help reduce this burden: frequent hand washing; isolation of infected patients from ill contacts; avoidance of second-hand smoke, day care, and crowds during RSV season; the cohorting of hospitalized patients with RSV infection; and passive immunoprophylaxis of high-risk infants. The second article in this supplement will discuss these and other preventive strategies at greater depth. ■

REFERENCES:

1. Shay DK, Holman RC, Roosevelt GE, et al. Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among US children, 1979-1997. *J Infect Dis.* 2001;183:16-22.
2. Simoes EA. Respiratory syncytial virus and subsequent lower respiratory tract infections in developing countries: a new twist to an old virus. *J Pediatr.* 1999;135:657-661.
3. Morris JA, Blount RE Jr, Savage RE. Recovery of cytopathogenic agent from chimpanzees with coryza. *Proc Soc Exper Biol Med.* 1956;92:544-549.
4. Chanock R, Finberg L. Recovery from infants with respiratory illness of a virus related to chimpanzee coryza agent (CCA). II Epdemiologic aspects of infection in infants and young children. *Am J Hyg.* 1957;66:291-300.
5. Berkovich S. Acute respiratory illness in the premature nursery associated with respiratory syncytial virus infections. *Pediatrics.* 1964;34:753-760.
6. Collins PL, Huang YT, Wertz GW. Identification of a tenth mRNA of respiratory syncytial virus and assignment of polypeptides to the 10 viral genes. *J Virol.* 1984;49:572-578.
7. Beeler JA, van Wyke Coelingh K. Neutralization epitopes of the F glycoprotein of respiratory syncytial virus: effect of mutation upon fusion function. *J Virol.* 1989;63:2941-2950.
8. Levine S, Klaiber-Franco R, Paradiso PR. Demonstration that glycoprotein G is the attachment protein of respiratory syncytial virus. *J Gen Virol.* 1987;68:2521-2524.
9. Vainionpaa R, Meurman O, Sarkkinen H. Antibody response to respiratory syncytial virus structural proteins in children with acute respiratory syncytial virus infection. *J Virol.* 1985;53:976-979.
10. Johnson S, Oliver C, Prince GA, et al. Development of a humanized monoclonal antibody (MED–

493) with potent in vitro and in vivo activity against respiratory syncytial virus. *J Infect Dis.* 1997;176: 1215-1224.
11. Hall CB, Douglas RG Jr, Geiman JM. Respiratory syncytial virus infections in infants: quantitation and duration of shedding. *J Pediatr.* 1976;89:11-15.
12. Hall CB, Douglas RG Jr, Geiman JM. Possible transmission by fomites of respiratory syncytial virus. *J Infect Dis.* 1980;141:98-102.
13. Hall CB, Douglas RG Jr, Geiman JM, Messner MK. Nosocomial respiratory syncytial virus infections. *N Engl J Med.* 1975;293:1343-1346.
14. MacDonald NE, Hall CB, Suffin SC, et al. Respiratory syncytial viral infection in infants with congenital heart disease. *N Engl J Med*. 1982;307:397-400.
15. Centers for Disease Control and Prevention (CDC). Update: respiratory syncytial virus activity—United States, 1997-98 season. *MMWR.* 1997;46: 1163-1165.
16. Weigl JA, Puppe W, Meyer CU, et al. Ten years' experience with year-round active surveillance of up to 19 respiratory pathogens in children. *Eur J Pediatr.* 2007;166:957-966.
17. Anderson LJ, Parker RA, Strikas RL. Association between respiratory syncytial virus outbreaks and lower respiratory tract deaths of infants and young children. *J Infect Dis*. 1990;161:640-646.
18. Katz SL. Prospects for immunizing against respiratory syncytial virus. In: Institute of Medicine. *New Vaccine Development: Establishing Priorities.* Vol. 1. Washington, DC: National Academies Press; 1986: 397-409.
19. Arnold SR, Wang EE, Law BJ, et al. Variable morbidity of respiratory syncytial virus infection in patients with underlying lung disease: a review of the PICNIC RSV database. Pediatric Investigators Collaborative Network on Infections in Canada. *Pediatr Infect Dis J.* 1999;18:866-869.
20. Berner R, Schwoerer F, Schumacher RF, et al. Community and nosocomially acquired respiratory syncytial virus infection in a German paediatric hospital from 1988 to 1999. *Eur J Pediatr.* 2001;160: 541-547.
21. Fjaerli HO, Farstad T, Bratlid D. Hospitalisations for respiratory syncytial virus bronchiolitis in Akershus, Norway, 1993-2000: a population-based retrospective study. *BMC Pediatr.* 2004;4:25.
22. Centers for Disease Control and Prevention. About RSV: Infection and Incidence. http://cdc.gov/rsv/about/infection.html. Accessed December 8, 2008.
23. Groothuis JR, Gutierrez KM, Lauer BA. Respiratory syncytial virus infection in children with bronchopulmonary dysplasia. *Pediatrics.* 1988;82:199-203.
24. Cuningham CK, McMillan JA, Gross SJ. Rehospitalization for respiratory illness in infants of less than 32 weeks' gestation. *Pediatrics.* 1991;88:527-532.
25. Wang EE, Law BJ, Robinson JL, et al. PICNIC (Pediatric Investigators Collaborative Network on Infections in Canada) study of the role of age and respiratory syncytial virus neutralizing antibody on respiratory syncytial virus illness in patients with underlying heart or lung disease. *Pediatrics.* 1997; 99:E9.
26. Boyce TG, Mellen BG, Mitchel EF Jr, et al. Rates of hospitalization for respiratory syncytial virus infection among children in Medicaid. *J Pediatr.* 2000; 137:865-870.
27. Stevens TP, Sinkin RA, Hall CB, et al. Respiratory syncytial virus and premature infants born at 32 weeks' gestation or earlier: hospitalization and economic implications of prophylaxis. *Arch Pediatr Adolesc Med.* 2000;154:55-61.
28. Greenough A, Cox S, Alexander J, et al. Health care utilisation of infants with chronic lung disease, related to hospitalisation for RSV infection. *Arch Dis Child.* 2001;85:463-468.
29. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. The IMpact-RSV Study Group. *Pediatrics.* 1998;102:531-537.
30. Reduction of respiratory syncytial virus hospitalization among premature infants and infants with bronchopulmonary dysplasia using respiratory syncytial virus immune globulin prophylaxis. The PREVENT Study Group. *Pediatrics.* 1997;99:93-99.
31. Nachman SA, Navaie-Waliser M, Qureshi MZ. Rehospitalization with respiratory syncytial virus after neonatal intensive care unit discharge: a 3-year follow-up. *Pediatrics.* 1997;100:E8.
32. Emond AM, Howat P, Evans JA, Hunt L. The effects of housing on the health of preterm infants. *Paediatr Perinat Epidemiol.* 1997;11:228-239.
33. Joffe S, Escobar GJ, Black SB, et al. Rehospitalization for respiratory syncytial virus among premature infants. *Pediatrics.* 1999;104(4 Pt 1):894-895.
34. Yüksel B, Greenough A. Birth weight and hospital readmission of infants born prematurely. *Arch Pediatr Adolesc Med.* 1994;148:384-388.
35. Carbonell-Estrany X, Quero J; IRIS Study Group. Hospitalization rates for respiratory syncytial virus infection in premature infants born during two consecutive seasons. *Pediatr Infect Dis J.* 2001;20: 874-879.
36. Wang EE, Law BJ, Boucher FD, et al. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study of admission and management variation in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. *J Pediatr.* 1996;129:390-395.
37. Behrendt CE, Decker MD, Burch DJ, Watson PH. International variation in the management of infants hospitalized with respiratory syncytial virus. International RSV Study Group. *Eur J Pediatr.* 1998; 157:215-220.
38. Navas L, Wang E, de Carvalho V, Robinson J. Improved outcome of respiratory syncytial virus infection in a high-risk hospitalized population of Canadian children. Pediatric Investigators Collaborative Network on Infections in Canada. *J Pediatr.* 1992;121:348-354.
39. Shay et al. Risk factors for bronchiolitis-associated deaths among US children, 1995-1997. Abstract #929; APS/SPR/APA – 2000.
40. Langley JM, LeBlanc JC, Wang EE, et al. Nosocomial respiratory syncytial virus infection in Canadian pediatric hospitals: a Pediatric Investigators Collaborative Network on Infections in Canada Study. *Pediatrics.* 1997;100:943-946.
41. Centers for Disease Control and Prevention. *National Vital Statistics Reports.* April 17, 2001;49(1).
42. Meert K, Heidemann S, Abella B, Sarnaik A. Does prematurity alter the course of respiratory syncytial virus infection? *Crit Care Med.* 1990;18: 1357-1359.
43. Hodson WA. Normal and abnormal development of the lung. In: Polin RA, Fox WW, eds. *Fetal and Neonatal Physiology.* 2nd ed. Philadelphia: W.B. Saunders Co;1998.
44. Imaizumi S, et al. Severity of RSV infection in hospitalized premature infants: the effect of gestational age and immune prophylaxis with palivizumab. Abstract #2311: APS/SPR/APA – 2001.
45. Simoes EA, King SJ, Lehr MV, Groothuis JR. Preterm twins and triplets. A high-risk group for severe respiratory syncytial virus infection. *Am J Dis Child.* 1993;147:303-306.
46. Elder DE, Hagan R, Evans SF, et al. Recurrent wheezing in very preterm infants. *Arch Dis Child Fetal Neonatal Ed.* 1996;74:F165-F171.
47. Stein RT, Sherrill D, Morgan WJ, et al. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. *Lancet.* 1999;354:541-545.
48. Sigurs N, Bjarnason R, Sigurbergsson F, Kjellman B. Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7. *Am J Respir Crit Care Med.* 2000;161: 1501-1507.
49. Sigurs N, Bjarnason R, Sigurbergsson F, et al. Asthma and immunoglobulin E antibodies after respiratory syncytial virus bronchiolitis: a prospective cohort study with matched controls. *Pediatrics.* 1995;95:500-505.
50. Ballow M, Cates KL, Rowe JC, et al. Development of the immune system in very low birth weight (less than 1500 g) premature infants: concentrations of plasma immunoglobulins and patterns of infections. *Pediatr Res.* 1986;20:899-904.

DIANNE S. CHARSHA, RN, MSN, NNP-BC
Cooper University Hospital

Respiratory Syncytial Virus: Best Practices for Prevention and Treatment

Ms Charsha is a neonatal nurse practitioner who currently serves as associate chief nursing officer at Cooper University Hospital in Camden, NJ. She is responsible for the overall operations and strategic plans for the medical-surgical department, the maternal child health department, trauma and respiratory therapy services, and the nursing administrative team.

ABSTRACT: A number of methods may be employed to prevent the spread of respiratory syncytial virus (RSV), including simple hand washing, screening of visitors to neonatal ICUs, and appropriate isolation and cohorting of infected infants. These standards of care must also be transferred to the home. Treatments such as acetaminophen, bronchodilators, and the antiviral agent, ribavirin, are available to treat symptoms of infection. Pharmacological prophylaxis with palivizumab and RSV intravenous immunoglobulin may be used in specific at-risk patients. Research to prevent and treat RSV infection is ongoing; preventive agents in development, such as the monoclonal antibody motavizumab and the vaccine MEDI-534, hold promise for reducing infection-related morbidity and mortality.

Respiratory syncytial virus (RSV) infection can cause significant illness and even death, especially in preterm infants. Therefore, it is important to implement integrated approaches and action plans for preventing the spread of RSV in the hospital and at home.

PREVENTING SPREAD OF RSV IN HOSPITALIZED INFANTS

Hand hygiene. Compliance with standardized hand-washing techniques is very important and should always be a major focus of attention. Hand washing with soap and water inactivates RSV. Research has shown that strict hand-washing control measures can significantly reduce the rate of nosocomial spread of RSV infection from 4.2% to between 0.6% and 1.1%.[1]

Screening visitors. The practice of screening potential visitors to neonatal ICUs (NICUs) and questioning visitors about possible recent exposure to communicable diseases is becoming standard operating procedure in many hospitals. It remains unclear whether this practice substantially reduces RSV infections within the NICU.[2] Despite the lack of controlled trials that measure the impact of such screening, it is imperative to ask NICU visitors about potential recent exposure to infection. Since it is very difficult to obtain this information from families of young children, some hospitals prohibit young siblings from visiting NICUs when RSV is most prevalent in the surrounding community.

NICU design. Single-room (as opposed to pod-designed) NICUs may help minimize the spread of nosocomial infections generally. Research has shown that a single-room design has reduced nosocomial infections both in pediatric ICUs and in hospitalized adults.[3] However, studies of the NICU population are still needed. Such studies should become easier to do as more units are constructed in a single-room design. Single-room design promotes the cohorting of nursing staff as well as the segregation of infected patients; it also reduces the number of potentially infected visitors who come into contact

with the NICU population—which in theory can help prevent the nosocomial spread of RSV.

Isolation of infected patients. The rapid screening and isolation of infected infants has consistently been shown to reduce the spread of RSV infection within the NICU.[4]

Cohorting of infected patients. The practice of assigning screened infants either to a cohort of RSV-infected infants or to one of RSV-uninfected infants (called "cohorting") is very successful in reducing infant-to-infant infections within the NICU. A strict cohorting regimen has been shown to reduce the number of nosocomial RSV infections from 7.17 cases per 1000 patient-days to zero.[5]

Cohorting of staff caring for infected patients. Certain staff should be assigned to RSV-infected infants in the NICU. This practice has not by itself been proved to reduce the spread of RSV infection within the NICU. However, cohorting employed as part of a larger infection reduction strategic plan, including proper hand washing, gowning, and gloving, has been shown to significantly reduce the spread of nosocomial RSV infection.[6]

Unfortunately, hand-washing guidelines are not followed by health care practitioners 100% of the time, despite the overwhelming evidence that this practice decreases the spread of nosocomial viral infections such as RSV.[7,8] Because there are varying degrees of adherence to hand washing and other hygiene measures, the segregation of potentially exposed nursing and support staff is paramount in preventing the spread of RSV infection within the hospital.

Screening of staff. It is imperative that potentially infected nursing staff not enter the NICU during the time when they may be shedding the virus. Adults can shed RSV for up to 5 days, and infants can shed RSV for as long as 21 days.

Appropriate protective equipment. In addition to hand washing, appropriate use of gloves, gowns, and goggles by nursing staff has also been proved to significantly reduce the nosocomial spread of RSV. Proper gowning and gloving has been demonstrated to reduce the spread of RSV within NICUs by 50%, from a rate of 6.4 cases per 1000 patient-days to 3.1 cases per 1000 patient-days.[9]

Other methods that can help prevent the nosocomial spread of RSV include the use of rapid diagnostic tests and the use of prophylaxis in eligible infants. However, no single preventive measure can by itself eliminate the nosocomial spread of RSV infection. Each individual technique must be employed as part of a consistent, staff-wide prevention program and adhered to routinely.

Research has shown that robust preventive strategies, when executed consistently, can reliably prevent the nosocomial spread of RSV. In addition to benefiting patients, this can directly reduce hospital costs. The **Figure** demonstrates the reduction in RSV infection that occurs when a proper preventive strategy is implemented as early as possible.[10]

DECREASING SPREAD OF RSV IN THE HOME

In addition to executing strategies to prevent the spread of RSV in

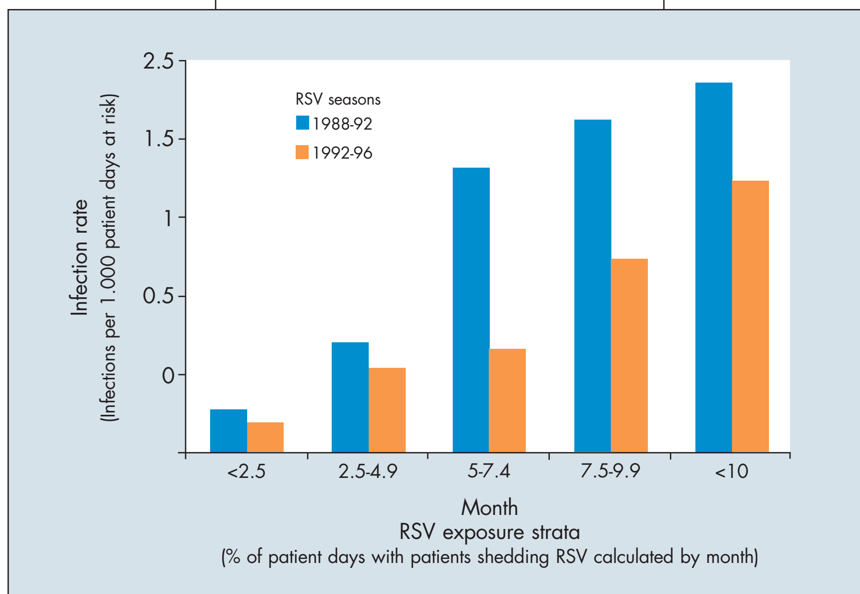


Figure – The pairs of bars on this graph show—for various strata of respiratory syncytial virus (RSV) exposure—the decrease in RSV infections subsequent to implementation of preventive measures. (From Macartney KK et al. *Pediatrics.* 2000.[10])

the hospital, health care practitioners need to educate parents and caregivers regarding the transmission of RSV and the tactics that can be used at home to protect children from infection.

Parent education. Parent education plays a vital role in preventing the spread of RSV. The high standard of care that is maintained in the NICU must—to the degree possible—be transferred to the home. Parents and caregivers need to understand that hand washing is the most important measure they can implement at home to prevent the spread of infection among family members.

Limiting exposure to sick persons and at-risk infants. Although RSV is not an airborne pathogen, it can be acquired simply by being in the same room with an infected person, since it can be spread by contact with contaminated surfaces. Therefore, it is essential that infected people be separated from noninfected people whenever possible, particularly at-risk children.[11]

Smoke-free and clean environments. There is tremendous debate about whether a smoke-free environment can help prevent the spread of RSV infection. Although there is limited research in this area, it is important to remember that a reactive airway can exacerbate an RSV illness. A smoke-free environment certainly is conducive to minimizing the irritants that can exacerbate an RSV lower respiratory tract infection (LRTI).

Ensuring continuity of care from NICU to home. Additional elements that may promote a seamless transition from the hospital to the home include communication of the prophylaxis plan—and the importance of following it—to the patient's primary care provider and the patient's parents. Parents should be provided with a discharge summary, and health care workers should provide confirmation that the parents or caregivers understand the importance of follow-up appointments. A home health care nurse may be beneficial in the coordination of the at-home prevention plan.[12]

PHARMACOLOGICAL TREATMENT OF SYMPTOMS AND PREVENTION OF INFECTION

Pharmacological management of RSV infection falls into 2 major categories: alleviation of symptoms with traditional supportive care medications, and prophylaxis with monoclonal antibodies in at-risk children.

Prophylaxis for which patients? The American Academy of Pediatrics Committee on Infectious Diseases (The Red Book Committee) has issued clear guidelines regarding the patient populations that should be targeted for pharmacological prophylaxis.[13] Acknowledging that administration of prophylaxis for every child susceptible to RSV infection is impractical and not cost-effective, the academy suggests that the following patient groups be targeted:

- Infants and children younger than 24 months with chronic lung disease (CLD) of prematurity who have required therapy (supplemental oxygen, bronchodilator, or corticosteroid therapy) for CLD within the 6 months preceding the start of RSV season: prophylaxis should be considered in such patients. Patients with more severe CLD who continue to require therapy may benefit from prophylaxis during a second RSV season.
- Infants born at 32 weeks' gestation or earlier: these infants may benefit from RSV prophylaxis even if they do not have CLD.

  —In those born at less than 28 weeks' gestation: prophylaxis during the first RSV season that falls within a year of birth.

  —In those born at 29 to 32 weeks' gestation: prophylaxis during RSV season if it occurs during the first 6 months of life.
- Infants born between 32 and 35 weeks' gestation: prophylaxis is usually reserved for those infants at greatest risk for infection who require hospitalization. Risk factors typically include day-care attendance, school-aged siblings, exposure to environmental air pollutants, congenital abnormalities of the airways, and severe neuromuscular disease.
- Children up to 24 months of age with hemodynamically significant cyanotic and acyanotic congenital heart disease: prophylaxis recommended.

  —Those receiving medication to control congestive heart failure.

  —Those with moderate to severe pulmonary hypertension.

  —Those with cyanotic heart disease.[13]

RSV symptom management. Symptom management or supportive care can include any or all of the following:

- Supplemental oxygen.
- Acetaminophen.
- Bronchodilators.
- Antibiotics.
- Ribavirin.

Acetaminophen can be administered for concomitant fever, and bronchodilators (although not recommended) have been used to dilate the airways and reduce airway inflammation, to help reduce wheezing. Antibiotics are often administered for bacterial infections that may co-occur with an RSV LRTI, especially when the infant's respiratory distress is severe enough to require supportive ventilation. Oxygen is also administered when cyanosis or apnea is present in a severely infected infant or child.

Ribavirin, an antiviral agent, can be used to treat acute RSV-induced bronchiolitis; this agent is most commonly used very early in the disease course in patients with severe respiratory distress who require a ventilator. One study suggests that ribavirin

reduces the risk of the development of asthma and recurrent wheezing[14]; however, in another study of 205 patients, no statistically significant difference was observed. Keep in mind that the agents mentioned may appear to improve the status of an infant with an RSV infection simply because resolution occurs with time.

Pharmacological prophylaxis. *RSV intravenous immunoglobulin (RSV-IVIG)* has been used widely to prevent serious LRTIs caused by RSV. It has a 6-fold higher concentration of RSV-neutralizing antibodies than standard IVIG and was one of the first agents that demonstrated predictable utility in combating RSV infection. Clinical trials showed that use of RSV-IVIG decreased the rates of hospitalization for serious LRTIs caused by RSV in certain patient groups. However, this therapy had to be administered as a 3- to 4-hour intravenous infusion, which made the administration impractical and often involved considerable cost and resources. Today, RSV-IVIG has largely been replaced by the humanized monoclonal antibody, palivizumab.[15]

Palivizumab is a monoclonal antibody that is specific for RSV, and it is the only agent that is commercially available for the prevention of RSV infections. Another advantage of palivizumab is that it is given as an intramuscular injection, which makes administration in the NICU much more convenient. The administration of palivizumab in at-risk infants and children has been shown to decrease rates of RSV-associated hospitalizations; in addition, the agent has a favorable safety and tolerability profile.[16]

Palivizumab is currently indicated for the prevention of serious LRTIs caused by RSV in infants with bronchopulmonary dysplasia, infants with a history of premature birth, and children with hemodynamically significant congenital heart disease. In particular, palivizumab has demonstrated greater usefulness than RSV-IVIG in infants with hemodynamically significant congenital heart disease because the administration of RSV-IVIG was contraindicated in this population, in part on account of the substantial amount of fluid administered.[15]

Palivizumab is given in a series of monthly 15 mg/kg intramuscular injections for the duration of the RSV season. This protocol needs to be communicated clearly to parents and caregivers to ensure that at-risk infants and children routinely visit their physician for follow-up doses. The first dose should be administered before the start of the RSV season, which is usually October, and dosing usually continues into April, depending on the length of the RSV epidemic in the local community that year.[17] Common adverse reactions observed with palivizumab are upper respiratory tract infection, rhinitis, otitis media, fever, rash, diarrhea, cough, vomiting, gastroenteritis, and wheezing. Anaphylaxis occurs in 1 in 100,000 patients, and rare acute hypersensitivity reactions have been reported.

Motavizumab. The next-generation monoclonal antibody, which promises to be an improvement over palivizumab, is motavizumab, currently in phase 3 clinical development. Motavizumab demonstrates higher potency and greater affinity for RSV than palivizumab and may reduce the burden of both upper and lower respiratory tract infections caused by RSV. Preliminary studies of more than 6000 patients have suggested that motavizumab may reduce the RSV infection rate to a greater extent than palivizumab. The safety and tolerability profile promises to be equivalent to that of palivizumab.[18]

MEDI-534. The development of an effective RSV vaccine would have a dramatic effect on the morbidity and, potentially, mortality, that is caused globally by this pathogen, and

research in the area of RSV vaccine development is ongoing. At present, one compound, MEDI-534, is in the early stages of clinical development. Phase 1 trials are currently evaluating the usefulness of this compound as a vaccine against RSV and parainfluenza virus 3, two of the most prevalent causes of viral respiratory disease in infants.[19]

Preclinical research in animals has demonstrated that the administration of this vaccine induces an anti-RSV immune response greater than that seen with RSV infection. However, developing a vaccine for RSV entails significant challenges. A vaccine for RSV would need to induce immunity to multiple strains of the virus, and a series of boosters might be required to maintain immunity. Also, because patients at highest risk for RSV infection are younger than 3 months, the continuing presence of maternal antibodies in these young infants might interfere with the antibody stimulation necessary to produce immunity.[19]

CONCLUSION

RSV is a serious health concern for infants. Fortunately, simple prophylactic measures can decrease the spread of RSV infection. Health care professionals can take a number of steps to decrease RSV spread in the hospital setting as well as teach parents how to help prevent infection in the home. Management of RSV illness consists of treating the symptoms in patients already infected and preventing further infection. Patients at greatest risk for infection may receive pharmacological prophylaxis on a monthly basis throughout the RSV season. Research to develop a vaccine for RSV is ongoing. ■

REFERENCES:

1. Isaacs D, Dickson H, O'Callaghan C, et al. Hand washing and cohorting in prevention of hospital acquired infections with respiratory syncytial virus. *Arch Dis Child.* 1991;66:227-231.
2. Hall CB, Geiman JM, Douglas RG Jr, Meagher MP. Control of nosocomial respiratory syncytial viral infections. *Pediatrics.* 1978;62:728-732.
3. National Association of Children's Hospitals and Related Institutions. *Evidence for Innovation: Transforming Children's Health Through the Physical Environment.* Alexandria, VA: NACHRI. 2008:35-37.
4. Doherty JA, Brookfield DS, Gray J, McEwan RA. Cohorting of infants with respiratory syncytial virus. *J Hosp Infect.* 1998;38:203-206.
5. Krasinski K, LaCouture R, Holzman RS, et al. Screening for respiratory syncytial virus and assignment to a cohort at admission to reduce nosocomial transmission. *J Pediatr.* 1990;116:894-898.
6. Madge P, Paton JY, McColl JH, Mackie PL. Prospective controlled study of four infection-control procedures to prevent nosocomial infection with respiratory syncytial virus. *Lancet.* 1992;340:1079-1083.
7. Leclair JM, Freeman J, Sullivan BF, et al. Prevention of nosocomial respiratory syncytial virus infections through compliance with glove and gown isolation precautions. *N Engl J Med.* 1987;317:329-334.
8. Pittet D, Mourouga P, Perneger TV. Compliance with handwashing in a teaching hospital. Infection Control Program. *Ann Intern Med.* 1999;130:126-130.
9. Groothuis J, Bauman J, Malinoski F, Eggleston M. Strategies for prevention of RSV nosocomial infection. *J Perinatol.* 2008;28:319-323.
10. Macartney KK, Gorelick MH, Manning ML, et al. Nosocomial respiratory syncytial virus infections: the cost-effectiveness and cost-benefit of infection control. *Pediatrics.* 2000;106:520-526.
11. Hall CB, Douglas RG Jr, Geiman JM. Possible transmission by fomites of respiratory syncytial virus. *J Infect Dis.* 1980;141:98-102.
12. Austin J. Preventing respiratory syncytial virus in homebound premature infants. *Home Healthc Nurse.* 2007;25:429-432.
13. Pickering LK. *Red Book: 2006 Report of the Committee on Infectious Diseases.* 26th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: 563-565.
14. Chen CH, Lin YT, Yang YH, et al. Ribavirin for respiratory syncytial virus bronchiolitis reduced the risk of asthma and allergen sensitization. *Pediatr Allergy Immunol.* 2008;19:166-172.
15. Wu H, Pfarr DS, Losonsky GA, Kiener PA. Immunoprophylaxis of RSV infection: advancing from RSV-IGIV to palivizumab and motavizumab. *Curr Top Microbiol Immunol.* 2008;317:103-123.
16. Simoes EA. Immunoprophylaxis of respiratory syncytial virus: global experience. *Respir Res.* 2002;3 (suppl 1):S26-S33.
17. Synagis (Palivizumab) package insert. Gaithersburg, MD: MedImmune; 2007.
18. Carbonell X, Losonsky G, Hultquist M, et al. Phase 3 Trial of Motavizumab (MEDI-524), an Enhanced Potency Respiratory Syncytial Virus (RSV) Specific Monoclonal Antibody (Mab) for the Prevention of Serious RSV Disease in High Risk Infants [Abstract]. Presented at: the Pediatric Academic Societies Meeting; May 8, 2007; Toronto. http://www.abstracts2view.com/pasall/view.php?nu=PAS07L1_1310.8220.9. Accessed December 3, 2008.
19. Stevens WW, Falsey AR, Braciale TJ. RSV 2007: recent advances in respiratory syncytial virus research. *Viral Immunol.* 2008;21:133-140.

CME Post-Test

Respiratory Syncytial Virus: From Pathogenesis to Prevention

Post-Test Instructions

1. Read the articles in the *Consultant for Pediatricians* supplement, "Respiratory Syncytial Virus (RSV): From Pathogenesis to Prevention"
2. Go to **http://www.nicuniversity.org** and click on "CME/CE Lecture Series" in the left-hand menu. Course listings will appear on your screen. From this screen you can click on the course title in the list—**Respiratory Syncytial Virus (RSV): From Pathogenesis to Prevention**—to view the lecture detail page (direct course link http://www.nicuniversity.org/lectureDetail.asp?courseid=NICU0006).
3. If you already have an account with NICUniversity.org, log in using your username and password. If you are a first-time user, click on "Register" in the left-hand menu and complete the registration form.
4. From the Lecture Detail screen, click on the "View Post Test" link.
5. After receiving a passing grade (70% or better) on the post-test, follow the online instructions to complete your evaluation and print your CE, CEU, and/or CME certificate. You will have two (2) attempts to achieve a passing score.

To contact a NICUniversity.org Customer Service representative, please e-mail support@nicuniversity.org.

Item Code: NICU0006

1. Which of the following are at greatest risk for developing a respiratory syncytial virus (RSV) infection?

a. Full-term infants
b. Preterm infants
c. Adolescents
d. All of the above
e. None of the above

2. Which of the following is/are the most common presenting symptom(s) of RSV infection?

a. Rhinorrhea
b. Cough
c. Fever
d. All of the above
e. None of the above

3. Which of the following methods is/are useful in preventing the spread of RSV in the home?

a. Routine RSV vaccinations
b. Prophylactic antibiotics
c. Separation of infected and noninfected family members
d. All of the above
e. None of the above

4. Which of the following can be used to manage the symptoms of RSV infection?

a. Ribavirin
b. Sedatives
c. Anticoagulants
d. All of the above
e. None of the above

(Continued) ▶

Respiratory Syncytial Virus: From Pathogenesis to Prevention

5. Which of the following statements about state-of-the-art pharmacological prophylaxis for RSV infection in at-risk infants is/are true?

a. Appropriate prophylaxis can reduce the rate of hospitalizations.
b. Pharmacological prophylaxis must be administered throughout the RSV season.
c. In rare cases, acute hypersensitivity reactions can occur.
d. All of the above
e. None of the above

6. Which of the following is/are pathological feature(s) of RSV infection?

a. Bronchiole epithelial necrosis
b. Hyposecretion of mucus
c. Anemia
d. All of the above
e. None of the above

7. Airway obstruction during RSV infection may be caused by which of the following?

a. Brain stem depression
b. Increased mucus production
c. Increased blood pressure
d. All of the above
e. None of the above

8. Which of the following is/are potential long-term risk(s) associated with RSV infection?

a. Asthma
b. Cystic fibrosis
c. Lung cancer
d. All of the above
e. None of the above

9. Which of the following is/are appropriate agent(s) for pharmacological prophylaxis of RSV in at-risk infants?

a. Palivizumab
b. Corticosteroids
c. Bronchodilators
d. All of the above
e. None of the above

10. Which of the following methods can decrease the spread of RSV infection in the hospital?

a. Hand hygiene
b. Screening of visitors
c. Single-room neonatal ICU design
d. All of the above
e. None of the above