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Impact of Respiratory Syncytial Virus Outbreak in a Neonatal Intensive Care Unit

Although respiratory syncytial virus (RSV) is a common cause of nosocomial outbreaks in general pediatric wards, it is a less frequent source of infection in neonatal intensive care units (NICUs). Halasa and colleagues recently evaluated the medical and economic impact of an outbreak of RSV infection in the NICU at Vanderbilt University in Nashville, Tennessee. This study was the first of its kind to determine whether infants were infected with identical RSV subgroups.

After the RSV outbreak, a retrospective chart review was performed where RSV cases were defined as infants with a nasopharyngeal aspirate positive for RSV by viral culture. Day 1 of this 20-day outbreak was defined as the time the first infant developed signs of respiratory disease. To ascertain virus relatedness among cases, nucleotide sequencing of the isolates was performed. Additionally, hospital bills for all RSV culture-positive infants were evaluated.

During the outbreak, 9 infants (mean age, 34 days; mean birth weight, 1757 g; mean estimated gestational age, 31 weeks and 5 days) were infected with genetically identical RSV subgroup B. RSV was first identified in 2 infants on day 9 of the outbreak, prompting immediate infection control measures (eg, screening staff and visitors, hand washing, equipment disinfection). Other cases were identified between day 10 and day 14. All 9 infants were considered to be clinically stable prior to RSV and were in open bassinets. Symptoms ranged in severity from cough and congestion to increased oxygen requirement, apnea, and respiratory failure. None of the infants developed a fever. All infants survived the outbreak.

Intubation was required in 5 of the 9 infants. The mean length of time on the ventilator was 12.2 days (range, 2 to 20 days). Compared with the 4 nonintubated infants, the 5 intubated infants had a significantly lower mean birth weight (1301 g versus 2328 g; P=0.027), mean estimated gestational age (28 weeks and 5 days vs 35 weeks and 2 days; P=0.014), and mean weight at onset of symptoms (2093 g versus 2989 g; P=0.049). All 5 of the intubated infants had been born at less than 31 weeks gestation.

The study investigators suggested that infants in the NICU who develop cough, congestion, or apnea should be tested for RSV and other common respiratory viruses during the winter respiratory season.

In this group, 7 infants tested positive for RSV by antigen detection and viral cultures, whereas 2 infants had positive viral cultures only. Nucleotide sequencing revealed that the isolates were genetically identical; all RSV isolates were subgroup B.

More than $1.15 million in hospital charges were attributable to the RSV outbreak. The 5 intubated infants incurred most of the charges

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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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prci Pediatric Respiratory Care Initiative™

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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.

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Impact of RSV Outbreak *(Continued)*

(94%). Additional expenses included closure of the NICU to incoming admissions and diversion of infants to other regional NICUs; surveillance viral cultures (73 cultures for a total of $20,075) and RSV rapid antigen tests (87 tests for a total of $11,832) that were obtained from all infants in the NICU; and prophylactic palivizumab administration to the other 49 exposed infants in the NICU ($131,609, based on a one-time 15 mg/kg dose per infant). Therefore, total healthcare costs attributable to the RSV outbreak were more than $1.3 million.

Based on this experience, the study investigators suggested that infants in the NICU who develop cough, congestion, or apnea should be tested for RSV and other common respiratory viruses during the winter respiratory season. The investigators also suggested that, once a case of RSV is identified, all infants in the NICU should be screened, all symptomatic and infected infants should be separated from the other infants, and strict infection control methods should be instituted. The findings of this study indicate that nosocomial outbreaks of respiratory viruses can occur in the NICU, negatively impacting healthcare delivery, costs, and outcomes.

Halasa NB, Williams JV, Wilson GJ, et al. Medical and economic impact of a respiratory syncytial virus outbreak in a neonatal intensive care unit. *Pediatr Infect Dis J*. 2005; 24:1040-1044.

COMMENTARY

JAY M. LIEBERMAN, MD, Chief, Pediatric Infectious Diseases, Miller Children's Hospital, Long Beach, California.

Respiratory syncytial virus (RSV) is a very common cause of hospital-acquired infections in general pediatric wards during the winter season. Usually, transmission occurs from direct or close contact with contaminated secretions that may involve droplets or fomites. The virus is hardy and can persist on environmental surfaces for many hours, and on hands for one half hour or more. Outbreaks of RSV infection in neonatal intensive care units (NICUs) are rarely reported, although it is likely they often remain undetected. The source of the outbreak reported in this article was not identified, but the outbreak resulted in significant morbidity and a high economic cost. The 9 infected infants were all clinically stable and thought to be nearing discharge before becoming sick from RSV. Five of the infants required intubations and mechanical ventilation, and the most severely affected infant required extracorporeal membrane oxygenation (ECMO) for 9 days. Because of the outbreak, the NICU was closed to new admissions, except for emergencies, for 21 days. As is emphasized in the article, the key to outbreak control is the early detection of RSV and strict infection control procedures. NICUs should have a low threshold for performing rapid viral diagnostic tests in infants with apnea and/or respiratory tract symptoms during the winter season.

The mean age of onset of symptoms related to RSV infection was 21 days, and all infants with confirmed RSV infection displayed symptoms.

Incidence of Viral Infections in a Neonatal Intensive Care Unit During a 12-Year Period

The incidence of viral infections among infants receiving treatment in the neonatal intensive care unit (NICU) is not well documented. Reasons for this uncertainty include an overlap in signs and symptoms between viral infections and other illnesses, as well as difficulties with laboratory diagnosis.

Verboon-Maciolek and associates determined the incidence of laboratory-confirmed viral infections among infants hospitalized in the NICU at Wilhelmina Children's Hospital in Utrecht, the Netherlands, during the period of 1992 to 2003. In this retrospective analysis, the diagnosis of viral infection was confirmed by positive viral culture and/or polymerase chain reaction from clinical samples.

During the 12-year study period, viral infection was confirmed in 51 of 5,396 infants admitted to the NICU (an overall incidence of 1%). The most common viral illnesses were enterovirus and parechovirus (EV/PEV) infection (20 patients, 39%), respiratory syncytial virus (RSV) infection (15 patients, 29%), rotavirus infection (5 patients,10%), cytomegalovirus (CMV) infection (3 patients, 6%), adenovirus infection (2 patients, 4%), parainfluenza virus infection (2 patients, 4%), herpes simplex virus infection (2 patients, 4%), rhinovirus infection (1 patient, 2%), and rubella virus infection (1 patient, 2%). In this group, 3 of the infants presented at birth with symptomatic rubella virus, CMV, or herpes simplex virus infection.

RSV infection was acquired during hospitalization in the majority of cases (9 of 15 patients, 60%). RSV infection predominately occurred in preterm infants (11 patients, 73%). The mean age of onset of symptoms related to RSV infection was 21 days, and all infants with confirmed RSV infection displayed symptoms. Most infants with RSV infection (12 patients, 80%) required

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Incidence of Viral Infections *(Continued)*

mechanical ventilation. Most RSV infection cases (14 patients, 93%) occurred during the winter (November to March). Mortality with RSV infection was 6% (1 patient).

Manifestations of EV/PEV disease were sepsis-like illness, prolonged seizures in term infants, and apnea or gastrointestinal disease in preterm infants. All patients with EV/PEV infection presented with a sepsis-like illness. RSV, parainfluenza virus, rhinovirus, and CMV resulted in respiratory disease, largely in preterm infants. Gastrointestinal disease was observed only in preterm infants infected with adenovirus, rotavirus, or EV/PEV. Patients infected with EV/PEV had the highest rate of mortality (2 of 20 patients,10%) and serious sequelae (3 of 20 patients,15%). All patients were treated with broad spectrum antibiotics prior to the diagnosis of viral infection. There were no viral infection epidemics during the study period.

This analysis found a 1% incidence of viral infection in the NICU. This incidence may have been underestimated because diagnostic procedures were not consistently performed and collection and transport of specimens were not optimal. The authors of this report speculated that most patients with enteroviral infection and all patients with RSV infection were probably infected by the horizontal route.

Verboon-Maciolek MA, Krediet TG, Gerards LJ, Fleer A, van Loon TM. Clinical and epidemiologic characteristics of viral infections in a neonatal intensive care unit during a 12-year period. *Pediatr Infect Dis J*. 2005;24:901-904.

Clinical Insights® in Pediatric Respiratory Care Post-test

1. A recently conducted retrospective review at the NICU at Vanderbilt University showed that
   a. Intubation was not required in most of the infants infected with RSV.
   b. Low birth weight was associated with the need for intubation in RSV-infected infants.
   c. Nucleotide sequencing revealed that the RSV isolates were genetically dissimilar.
   d. All of the above.

2. In a recently conducted retrospective review of the NICU at Wilhelmina Children's Hospital in Utrecht, the Netherlands
   a. The overall incidence of viral infection was 1%.
   b. The most common viral illnesses were enterovirus and parechovirus.
   c. RSV infection predominately occurred in preterm infants and occurred most often in the winter.
   d. All of the above.

1. *b*. Low birth weight was associated with the need for intubation in RSV-infected infants.
2. *d*. All of the above.

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.

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prci Pediatric Respiratory Care Initiative™

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Overall Program

	Strongly Disagree		Disagree	Agree		Strongly Agree
1. The activity met the stated objectives in such a way that I am better able to:						
a. Identify respiratory disorders in pediatric patients	1	2	3	4	5	6
b. Summarize risk factors for respiratory disorders in pediatric patients	1	2	3	4	5	6
c. Select an appropriate therapeutic regimen for patients with pediatric respiratory disorders	1	2	3	4	5	6

2. Overall, the activity was presented in a fair-balanced manner. ☐ Yes ☐ No*
   * If you checked "No," please explain. _____

3. Overall, the activity was free of commercial bias. ☐ Yes ☐ No*
   * If you checked "No," please explain. _____

4. In reflecting on your practice, what type of impact will this educational activity have?
   ☐ This program has validated my practice in the treatment of respiratory illnesses.
   ☐ Need more information before making a change.
   (*Please specify what information you would require.*) _____

   I will:
   ☐ Test for respiratory syncytial virus and other common respiratory viruses during the winter season in infants in the NICU who develop a cough, congestion, or apnea.
   ☐ Ensure that appropriate hand hygiene measures are undertaken before contact with neonates so that the spread of viral infections in the NICU remains low.

5. What topics should be dealt with in more detail? (*List topics.*)
   _____ _____
   _____ _____

Thank you for your participation.