Management of Bronchiolitis and the Use of Palivizumab/Synagis for RSV Prevention

By Keith Perrin, MD, pediatrician at Children’s Hospital. This issue of Pediatric Review is intended for pediatricians, family physicians and all other interested medical professionals. For CME purposes, the author has no relevant financial relationships to disclose.

Objectives
At the end of this activity, the participant should be able to:
1. Identify the populations most at risk for bronchiolitis
2. Describe the current evidence based treatment of bronchiolitis
3. Identify the populations who will benefit most from palivizumab
4. Discuss why patients outside of this population get little benefit from palivizumab prophylaxis at a very high cost

Bronchiolitis Overview
Bronchiolitis is the main cause of hospitalizations due to lower respiratory tract infections in the United States and particularly affects children <1 year of age. Even though the incidence of bronchiolitis has been on the increase, the mortality has remained stable. The main agent causing bronchiolitis is respiratory syncytial virus (RSV), which accounts for 50% to 90% of the cases. Groups of children that have been identified as more frequently and more severely affected by RSV include those of a young age (especially <1 year) or low gestational age (GA; especially <32 weeks) or those who have chronic lung disease (CLD), hemodynamically significant congenital heart disease (HSCHD), or severe immunodeficiency. Specialists have inferred that patients with cystic fibrosis, severe problems with handling secretions and infantile paralysis have more severe problems with bronchiolitis and may benefit from RSV prophylaxis, but to date there is no evidence base confirming this assertion.

In 2006 a study titled Diagnosis and Management of Bronchiolitis, developed evidence-based clinical practice guidelines; these guidelines are incorporated into this review article. Where guidelines have had significant changes due to more recent research, the more recent information is noted. These guidelines with updates are a great foundation for the treatment of bronchiolitis and the prevention of RSV-related disease.

Diagnosis and Assessment of Risk Introduction
The diagnoses of bronchiolitis and assessment of disease severity should be based on history and the physical examination. Clinicians should not routinely order laboratory and radiologic studies for diagnosis. It is important to assess risk factors. Factors that are more likely to have severe disease are: age less than 12 weeks, a history of prematurity, history of chronic lung disease (CLD), hemodynamically significant congenital heart disease (HSCHD), or significant immunodeficiency when making decisions about evaluation and management.

Treatment
Bronchodilators should not be used routinely in the management of bronchiolitis. They can be used when considering other concomitant diagnosis, however, the inhaled bronchodilators should be continued only if there is a documented positive clinical response using an objective means of evaluation. Recently inhalation therapy using hypertonic (3%) saline solution has shown indications that it may be useful. Frequent suctioning of secretions is warranted. Corticosteroid medications should not be used routinely in the management of bronchiolitis. The use of Ribavirin is no longer relevant and is contraindicated. Antibacterial medications should be used only in children with bronchiolitis who have specific indications of the coexistence of a bacterial infection.

Assessment of hydration and appropriate therapy is important. Chest physiotherapy should not be used routinely. Supplemental oxygen is indicated if oxyhemoglobin saturation (SpO2) falls persistently below 90% in previously healthy infants. If the SpO2 does persistently fall below 90%, adequate supplemental oxygen should be used to maintain SpO2 at or above 90%. Oxygen may be discontinued if SpO2 is at or
above 90% and the infant is feeding well and has minimal respiratory distress. As the child’s clinical course improves, continuous measurement of Spo2 is not routinely needed. Infants with a known history of hemodynamically significant heart or lung disease and premature infants require close monitoring as the oxygen is being weaned.

**Prophylaxis**

In 1998, the Impact-RSV study revealed that monthly intramuscular injections of Palivizumab (a monoclonal antibody that binds to the RSV fusion protein and inhibits its entry into the cell) administered to children with CLD or prematurity resulted in a 55% reduction in RSV hospitalization compared with placebo. A similar effect was shown for children with HSCHD. Neither study showed a difference in mortality.

CDC surveillance data has clearly determined that for our region the start of the season is November 1 and the end of the season is usually March 31. It is also clear that giving Palivizumab prophylaxis outside of the indication does not decrease mortality and data indicates it cost much more than the benefit it delivers.

The number of doses recommended for children fitting the criteria in the previous paragraph are: (A) children <32 weeks gestation, with HSCHD or CLD should receive up to five doses monthly of 15 mg/kg per dose administered intramuscularly with the last dose no later than March 31, (B) children gestational age 32 to <35 weeks should receive prophylaxis only until they reach three months of age and should receive a maximum of three monthly doses of 15 mg/kg; many will receive only one or two doses before they reach three months of age. Once an infant 32 to <35 weeks gestational age has passed 90 days of chronologic age, the risk of hospitalization attributable to RSV lower respiratory tract disease is reduced and administration of Palivizumab is not recommended. Again the last dose is to be given no later than March 31.

Although specific recommendations for immunocompromised children cannot be made, infants and young children with severe immunodeficiency (e.g., severe combined immunodeficiency or advanced AIDS) may benefit from prophylaxis. Limited studies suggest that some patients with cystic fibrosis may be at increased risk of RSV infection, however, there is insufficient data to determine the effectiveness of Palivizumab for this patient population.

Hand decontamination remains the most important prophylaxis for RSV. Hands should be decontaminated before and after
direct contact with patients, after contact with inanimate objects in the direct vicinity of the patient, and after removing gloves. Alcohol-based rubs are preferred for hand decontamination with an alternative of hand washing with antimicrobial soap.

Other prophylactic measures that should be considered are: infants should not be exposed to passive smoking, breastfeeding and consideration of complimentary and other alternative medicine.

**Palivizumab Discussion**
Palivizumab administration to well-defined high-risk groups results in reductions of hospital days, but the intervention is costly. Palivizumab, even within indications, does not decrease the mortality rate of bronchiolitis due to RSV. The AAP has recommended which groups should be administered Palivizumab for the best clinical and cost-effective outcomes. Changes in bronchiolitis recommendations are often made in response to new data and should take into account restricting an expensive intervention to those who could benefit the most. The extensive information can cause confusion and complicate appropriate use of the medication.

It is clearly more beneficial to your patients to focus on giving the patients within the AAP guidelines their appropriate doses at the appropriate times. In a recent study physician education was shown to improve the inappropriate use of Palivizumab. However, it is clear that many children receive inappropriate numbers of doses at inappropriate times. It is also clear that following the AAP guidelines will do no harm to your patients and allow you more time to devote to assuring that the appropriate patients are identified and that they receive dosing appropriately in a timely fashion.

**Resource for Educating your Families**
The AAP Bookstore sells a pamphlet: *Bronchiolitis and Your Young Child*

**References**
3) Keith M Perrin, Rodolfo E Bégué. Use of Palivizumab in Primary Practice Pediatrics 2012; 129;55; originally published online December 19, 2011; DOI: 10.1542/peds.2010-2991
4) CDC Morbidity and Mortality Weekly; September 9, 2011/60(35);1203-1206
The Heart Center at Children’s Hospital

The Heart Center at Children’s Hospital is nationally recognized as a leader in the diagnosis and treatment of patients, from fetus to adult, with congenital cardiovascular disorders. Our accomplished and dedicated team of specialists includes physicians and surgeons, nurses and support staff who are trained to care for the unique needs of children whose levels of care range from basic to highly critical.

Each year, nearly 2,000 children and adults from throughout the world visit Children’s Hospital for cardiology services, while our cardiothoracic surgeons perform more than 450 surgical procedures a year. Approximately half of these are performed on children younger than age 1. Additional patients are diagnosed and monitored through the center’s telemedicine program, a service available to physicians practicing at outlying hospitals. The new adult congenital cardiology program provides follow-up and necessary treatment, including therapeutic and interventional options, for adults with congenital heart defects.

Our staff is focused on ensuring the most sophisticated quality of care in a compassionate, comfortable and convenient environment. Our goal is to enhance the quality of life for every child. A full range of congenital heart disease surgeries using the most advanced surgical techniques is performed at Children’s Hospital.

The Heart Center’s partnership with Louisiana State University Health Sciences Center enables residents and medical students from LSU Medical School, as well as nursing students from several local teaching institutions, to receive training in pediatric cardiology and cardiothoracic surgery. Formal lectures and clinical rotations in cardiology and intensive care help ensure that future cardiology specialists and nurses become experts in the field.

Cardiac Catherization
Advanced, invasive diagnostic and interventional procedures are performed in the state-of-the-art, all-digital Solon B. Turman Cardiovascular Biplane Catheterization Laboratory. Our cardiologists specialize in a wide range of diagnostic and interventional procedures. Advanced equipment, such as biplane X-ray, and expert staff ensure the safety of our patients and accuracy of their treatment.

Non-Invasive Imaging
More than 4,000 echocardiograms are performed each year at Children’s Hospital’s state-of-the-art, digital echocardiography lab, complete with the latest 3-D echocardiography technology. Other widely used non-invasive diagnostic services include cardiac MRI 3-D imaging technology and reconstruction, electrocardiograms (EKGs), chest X-rays, stress tests, tilt table tests, Holter and event monitoring.

www.chnola.org/heartcenter
Maternal-Fetal Cardiology

One highlight of our program is the burgeoning Fetal Cardiology Clinic, a program designed to provide the specialized medical care required to treat pregnant women with congenital heart disease and/or women carrying a child with heart disorder. A multi-disciplinary team is composed of perinatologists, cardiologists, neonatologists, congenital heart surgeons and specialized nurses highly skilled in the management and treatment of women and/or their babies with heart conditions. State-of-the-art ultrasound equipment is used to identify fetal cardiac abnormalities as early as 14 weeks gestation. The overall goal of the program is to offer the best possible service to a mother and/or fetus with cardiac abnormality, during pregnancy, labor and following delivery.

Adults with Congenital Heart Disease

This program provides diagnosis with diagnosis and follow-up care, including therapeutic and interventional options, for older patients with congenital heart disorders. Teens and adults with heart disease, both before and following surgery, have unique problems, including residual hemodynamic abnormalities, cardiac rhythm disturbances, and risks for sudden death. A team of highly qualified physicians and surgeons work closely together to treat these patients, as their needs change throughout life.

Cardiothoracic Surgery at Children’s Hospital

One of the most successful cardiac surgical programs in the country is located at Children’s Hospital, where cardiac surgeons perform more than 450 surgical procedures a year to complete repair of complex congenital heart defects. Approximately half of these are performed on children younger than age one.

Our strength stems from the expertise of our surgeons, who in addition to their skilled surgical approach, closely monitor patients long after they leave the operating room. The specially trained team of pediatric anesthesiologists and perfusionists customize aspects of peri-operative care and cardiac bypass to meet the needs of each patient. Cardiac nurses and technicians provide around-the-clock care until patients are able to return home.

ECMO

ECMO (Extra Corporeal Membrane Oxygenation) is a life-sustaining option used to support patients with severe respiratory distress from meconium aspiration, persistent pulmonary hypertension, sepsis or congenital diaphragmatic hernia that have not responded to conventional therapies. ECMO can also be used to support children after cardiac surgery who need more time for cardiopulmonary recovery. Under management by our cardiothoracic surgeons, ECMO is initiated and maintained by our perfusion staff and specially trained respiratory therapists. Children’s Hospital’s ECMO program is the largest and most successful in the region.

Transport/Critical Care

Critical care services at Children’s Hospital offer the highest level of both cardiac and non-cardiac care in the 20-bed cardiac ICU for patients recovering from heart-related illnesses. Transport teams are available 24 hours a day for land or air emergency transports. Approximately 250 to 300 children a year are referred to Children’s Hospital by ground or air for specialty care by pediatric intensivists and staff.

The Heart Team

Cardiology

**Appointments** (504) 896-9751  
**Office Hours** 8 a.m. – 4:30 p.m.  
**Physicians**  
Robert Ascuitto, PhD, MD, Director of Cardiology  
Nancy Ross-Ascuitto, MD,  
Director of Pediatric Cardiology Training Program  
Kelly Gajewski, MD  
Christian Lilje, MD  
Steffan Sernich, MD  
Ernest Siwik, MD  
Aluizio Stopa, MD

Cardiothoracic Surgery

**Appointments** (504) 896-3928  
**Office Hours** 8 a.m. – 4:30 p.m.  
**Physicians**  
Joseph Caspi, MD, Director of Pediatric Cardiothoracic Surgery  
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Please record your responses to the questions on the form below. Please circle the best possible answer. CME offer is good through May 2012.

1. Which of the following groups of children are significantly at higher risk for bronchiolitis:
   a. Children <12 months old
   b. Children with HSCHD or CLD
   c. Children >24 to <36 months old
   d. Children with IgA deficiencies
   e. Only a & b
   f. All of the above

2. The following are evidenced based treatment for bronchiolitis:
   a. Corticosteroids in the routine management of bronchiolitis
   b. Bronchodilators in the routine management of bronchiolitis
   c. Good hydration
   d. Both a & b

3. Which groups of children are recommended to receive palivizumab prophylaxis by AAP guidelines:
   a) Children born gestational age <29 weeks and <12 months of age as of Nov. 1 of the treatment year
   b) Children born gestational age <29 weeks with HSCHD or CLD and > 24 months as of Nov. 1 of the treatment year
   c) Children born gestational age 32 to <35 weeks and age 1 month as of Nov. 1 of the treatment year without a <5 years of age sibling and cared for by mother at home
   d) All of the above

4. Effective prophylaxis measured by outcome and cost for RSV disease is/are:
   a) Good hand washing or use of alcohol-based hand rub
   b) Eliminating as much passive smoking around infants as you can
   c) Breast feeding of infants
   d) Palivizumab prophylaxis given within AAP guidelines
   e) All of the above

5. Following AAP guidelines for palivizumab prophylaxis should any child > 24 months of age receive palivizumab prophylaxis:
   a) Yes
   b) No

To receive CME credit, participants must score 100%.

To receive CME credit, mail, e-mail or fax your completed form to:
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ACC Room 3302

Tumor Board
Wednesdays, 4 – 5 p.m.
Children’s Hospital Auditorium

Weekly Pathology Conference
Thursdays, 8 – 9 a.m.
Research Center, Room 4222

Neonatology Conference
Thursdays, 12:30 – 1:30 p.m.
NICU Conference Room

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