

Respiratory Syncytial Virus (RSV) Prevention 2010

Guideline Statement

- I. Issue: While there is a high level of evidence that RSV prophylaxis is effective, some debate remains regarding best strategies for prevention of RSV in neonatal and pediatric patients.¹⁻³
- II. Background: RSV is the leading cause of re-hospitalization in all children less than 12 months of age for the United States.⁴⁻⁶ The majority of these hospitalizations occur in otherwise healthy infants. Certain groups of infants and children have higher rates of re-hospitalization including children with Chronic Lung Disease (CLD)/Bronchopulmonary Dysplasia (BPD), Congenital Heart Disease (CHD), and premature infants.⁷⁻¹⁴ Treatment options for RSV are limited. Supportive care is frequently the only medical therapy available. The best approach to RSV in at risk groups is prevention. In addition to strategies to minimize exposure to RSV, prophylaxis with RSV monoclonal antibody is effective at decreasing hospitalization.^{9,15-19} In patients with CLD/BPD and premature infants born at less than 36 weeks gestational age, prophylaxis decreased hospitalization by 55%; in the subgroup of patients born between 32-35 weeks gestation, hospitalization rates decreased by 80%.¹⁵
- III. Respiratory Syncytial Virus Prophylaxis
 - A. Prophylaxis to prevent RSV is available as intramuscular monoclonal antibody preparation (palivizumab).²⁰⁻²¹
 - B. RSV infection is responsible for significant hospitalizations, morbidity, and mortality in infants less than 24 months of age who have CLD/BPD, Congenital Heart Disease, compromised respiratory or immune systems or who have impaired nutritional status and growth.^{16-17,22}
 - C. Candidates for RSV Prophylaxis: Decisions regarding appropriateness of RSV prophylaxis must be individualized.
 1. Infants or children with CLD/BPD who are less than 24 months of age at the start of RSV season who have required intervention or maintenance therapy for their CLD/BPD within 6 months of the start of the RSV season will benefit from RSV prophylaxis. Other interventions for CLD/BPD may include ongoing use of corticosteroid preparations, methylxanthines, supplemental oxygen, bronchodilators, or diuretics.^{12,23-24}
 2. Infants born at 32 weeks or less without CLD/BPD will also benefit from prophylaxis:²⁵
 - a. Infants born at less than 28 0/7 weeks will benefit from prophylaxis if they are less than 12 months of age at the start of the RSV season. Infants born during RSV season who are less than 12 months of age at the start of the subsequent RSV season are still candidates for prophylaxis.

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- b. Infants born between 28 0/7 and 32 0/7 weeks of gestation will benefit most from prophylaxis if they are less than 6 months of age at the start of RSV season.
3. Birth at a late preterm gestation may merit special consideration.²⁶⁻²⁸ However, prophylaxis for infants born at 32 1/7 to 35 6/7 weeks gestation should be reserved for those infants with additional risk factors that increase risk of RSV exposure or morbidity from RSV disease. An RSV relative risk scale has been proposed and may be useful to the practitioner in identifying at risk patients who may benefit from RSV prophylaxis.²⁹ The cost of prophylaxis should be weighed against the risk of severe RSV disease requiring hospitalization and associated costs to the family as well as perceived long term consequences.³⁰⁻³³ A pediatrician or primary care provider is in the best position to assess and interpret relative risk factors. The most consistently identified factors that are associated with increased risk of RSV disease are child care attendance, school-aged siblings, young chronological age at the start of RSV season and maternal smoking; however, exposure to environmental air pollutants, congenital abnormalities of the airways, or severe neuromuscular disease may also justify concern.^{23,34-38} Correlations exist between air quality and respiratory function.³⁷⁻⁴⁸ Thus, environmental air quality assessment is important for these patients with special consideration given to unique circumstances of unwarranted air pollution such as residence near a bus station or industrial plant, or use of a wood or coal burning stove as a primary heat source. Efforts to reduce risk by isolation of the at risk child, smoking cessation strategies for the parents/caregivers, or relocation to an area with cleaner air may not be practical or workable for the immediate term. Certain risk factors may have greater impact based on the level of exposure (i.e., one school-aged sibling versus three school-aged siblings in three different schools); however, no particular risk factor has been shown to be unique in its predictive value, and frequently many risk factors may exist simultaneously.^{14,46} The greater the number of risk factors, the higher the likelihood of RSV hospitalization.⁴⁹ A history of maternal smoking during pregnancy may be augmented as a risk factor by a history of breastfeeding for less than 2 months.^{41,50-53} These circumstances must be accounted for in the risk assessment. After assessment of an individual patient, if a provider determines that the patient is at high risk for RSV disease complicated by hospitalization, prophylaxis should be provided.⁵⁴
4. Palivizumab has been shown to be of benefit to patients with congenital heart disease.^{16,55-57} The degree and severity of the heart disease may factor into the decision to provide RSV prophylaxis. In order to exclude an infant from receiving palivizumab, the infant must have a documented waiver provided by a board certified pediatric cardiologist that their cardiac defect is hemodynamically insignificant and thereby

poses no additional risk for RSV. Children who are in need of or status post cardiac transplantation are in a particularly high risk group and should be given highest consideration for RSV prophylaxis.^{55,57} During RSV season, post bypass or ECMO management should include a plan for additional dosing as soon as the infant is stable.

5. Infants with severe neuromuscular disease affecting respiratory function may be candidates for palivizumab prophylaxis, including those with neuromuscular maturational disease common in premature infants.⁵⁸ CNS injury prior to, during, or after delivery including but not limited to intraventricular hemorrhage (IVH), hypoxic ischemic encephalopathy (HIE), spinal cord injury, disease of the peripheral nervous system, disease of the neuromuscular junction, and periventricular leukomalacia (PVL) all are considerations for RSV prophylaxis.^{22,24,58} IVH, HIE, and PVL may cause cerebral palsy (CP) at a later time. CP alone may be a qualifier for RSV prophylaxis if there is any association with decreased respiratory function.⁵⁹⁻⁶⁰
6. Patients with congenital abnormalities of the airways that compromise respiratory function should receive prophylaxis.^{8,61-64} This may include persisting wheeze, or disorders of abnormal lung growth. Congenital diaphragmatic hernia is included in this category.
7. Patients with cystic fibrosis and other diseases such as α 1-antitrypsin deficiency where there is a genetic basis for changes in the lung milieu may also benefit from prophylaxis.^{62,65-66}
8. Immune deficiencies are rare disorders and require collaborative management by pediatricians, infectious disease specialists, and immunologists.⁶⁷⁻⁶⁸ Although there is no conclusive evidence for a particular disease category, because of the understood high risk of any infectious process, RSV prophylaxis is indicated unless a waiver can be obtained from a board certified pediatric immunologist or infectious disease specialist.

D. Administration

1. RSV prophylaxis should be initiated prior to the onset of the RSV season and terminated at the end of the RSV season.^{3,69-70} Although there are regional variations in the United States, RSV outbreaks begin as early as October and decrease between March and May. Providers should review local historical RSV surveillance data to assist in the decision-making process. Some locales in the Southern United States, Hawaii, and Alaska may have high enough incidence of RSV to justify initiation in the late summer months and continuation of monthly prophylaxis into the late spring.⁷¹⁻⁷⁴ Although various cost containment models have been proposed to provide relative risk adjustment based on post conceptual age at a specific month during RSV season, there is risk that adequate levels of palivizumab will not be achieved or maintained during months when RSV is widespread.^{15,70} Use of an abbreviated schedule of RSV prophylaxis (e.g., based on post conceptual age mid

season) is contrary to published evidence and FDA approved product indication for palivizumab and is strongly discouraged.⁷⁵ Once a child begins RSV prophylaxis for the RSV season, the child must receive palivizumab monthly through the end of the season.⁷⁶

2. Palivizumab 15 mg/kg IM should be given once a month during the RSV season to increase the likelihood of achieving and maintaining appropriate levels for prophylaxis.²⁰ A dose should be given 24-48 hours prior to discharge from the hospital if the patient meets criteria. The single-dose vial of palivizumab does not contain a preservative. Administration of palivizumab should occur immediately after dose withdrawal from the vial. The vial should not be re-entered.²⁰
3. Patients can be re-infected with RSV multiple times during the same RSV season. Thus, monthly dosing should be continued even if the patient is infected with RSV.²⁰
4. Fever or other illness including viral syndromes are not contraindications to administration of palivizumab.
5. At present, there are no restrictions on concurrent RSV prophylaxis with any immunization.⁷⁷ Immunization with Measles-Mumps-Rubella (MMR) and Varicella vaccines need not be deferred in infants receiving RSV prophylaxis. RSV prophylaxis should not interfere with Hepatitis B vaccine, Diphtheria, Tetanus, Pertussis (DTaP) primary immunization schedule, H. Influenza type B (Hib), seasonal influenza vaccination, Pneumococcal Conjugate Vaccine (PCV), or Inactivated Poliovirus Vaccine (IPV).
6. The safety and efficacy of palivizumab have not been demonstrated for treatment of established RSV disease.
7. Contraindications and Adverse Reactions
 - a. Palivizumab should not be used in pediatric patients with a history of a severe prior reaction to palivizumab or other components of this product.²⁰
 - b. Fever, irritability and injection site reaction are the most commonly reported adverse events.⁷⁸

IV. Nosocomial Infection

- A. RSV is horizontally transmitted in the hospital setting and causes serious disease in high-risk infants and young children.
- B. The best way to prevent RSV disease is strict adherence to infection control practice, including the use of in-hospital screening studies to identify and cohort RSV-infected infants.⁴ Proper hand washing is of paramount importance.
- C. Cohorting of children with *suspected* RSV disease is not recommended.

Indication	Age of Child	Dosing
Chronic Lung Disease requiring medical management	Less than 24 months at start of RSV season	Monthly during RSV season
Born at < 28 0/7 weeks	Less than 12 months at start of RSV season	Monthly during RSV season
Born at 28 0/7-32 0/7 weeks	Less than 6 months at start of RSV season	Monthly during RSV season
Born at 32 1/7-35 6/7 weeks	Less than 6 months at start of RSV season with provider determined significant risk	Monthly during RSV season
Congenital Heart Disease	Less than 24 months at start of RSV season unless cardiology waiver obtained	Monthly during RSV season
Neuromuscular Disease	Less than 24 months at start of RSV season	Monthly during RSV season
Congenital Abnormalities of the Airways	Less than 24 months at start of RSV season	Monthly during RSV season
Immune Disorders	Less than 24 months at start of RSV season unless infectious disease or immunology waiver obtained	Monthly during RSV season

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