Arkansas Children's
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Respiratory Syncytial Virus

Key Points

- Respiratory syncytial virus (RSV) causes annual seasonal epidemics and is transmitted by contact with contaminated secretions.
- Nirsevimab is a monoclonal antibody recommended for majority of infants in first year of life, and some in second year as well. Palivizumab may still be used in high-risk infants depending on availability.
- Hospitalized infants with RSV infection should be placed in contact precautions and scrupulous adherence to hand hygiene practices should be enforced.
- Parents with signs and symptoms of upper respiratory tract should be excluded from the newborn nursery or intensive care units.

Introduction

Respiratory syncytial virus (RSV) causes acute respiratory tract illness in people of all ages. It is recognized as one of the most common causes of childhood illness and is the most common cause of hospitalization in infants. RSV infection only offers limited protective immunity; therefore, children can be infected repeatedly throughout life.

Epidemiology

- RSV typically causes seasonal outbreaks throughout the world, generally in fall and continuing through early spring.
- RSV is transmitted directly by close contact with contaminated secretions via large droplets or indirectly via RSV-contaminated hands or fomites. Viable RSV can persist on environmental surfaces for several hours and for 30 minutes or more on hands.
- The incubation period ranges from 2 to 8 days. Viral shedding is usually 3 to 8 days but can last as long as 3 to 4 weeks in young infants and immunocompromised individuals.

Clinical Manifestations and Diagnosis

The clinical manifestations vary by age, health status, and whether the infection is primary or secondary. Most RSV-infected infants experience upper respiratory tract symptoms, but 20-30% develop lower respiratory tract disease with the first infection. Signs and symptoms typically begin with rhinitis and cough, which may progress to increased respiratory effort with wheezing and respiratory distress. Fever may occur. Infection with RSV during the first few weeks of life, may present with more general symptoms such as lethargy, irritability, and poor feeding. Infants are at risk of developing apnea, even in the absence of other respiratory symptoms.

In most outpatient settings for children with clinical bronchiolitis, routine specific viral testing has little effect on management and is not recommended. Laboratory diagnosis of RSV should be pursued if identification of RSV will affect clinical management.

- Rapid diagnostic immunoassays for detection of viral antigen in nasopharyngeal specimens. These are commercially available and generally reliable in infants and young children during the annual epidemic. Lower sensitivity is observed in older children and adults.
- Molecular diagnostic tests using polymerase chain reaction (PCR) assays obtained from nasopharyngeal swab have largely replaced culture and antigen detection assays. It is available at Arkansas Children's Hospital. It is designed as multi-plex assays to facilitate testing for multiple respiratory viruses from a single specimen.

Management

Therapy for RSV infection of the lower respiratory tract is primarily supportive. Supportive care includes suction of the upper airway, as necessary, frequent monitoring of clinical status and provision of fluid and respiratory support as necessary.

- Antimicrobial therapy – not indicated unless there is evidence of secondary bacterial infection.
- Corticosteroids and beta-adrenergic agents – not recommended for routine use of wheezing associated with RSV. However, it may be beneficial in RSV-associated bronchial reactivity, particularly those with asthma, in whom RSV may have triggered an exacerbation.
- Ribavirin, IVIG and monoclonal antibodies – not recommended for routine use for RSV infection but may be used in selected patients such as immunocompromised patients.

Prophylaxis/Prevention

- Active immunity: RSVPreF vaccine is an FDA approved vaccine (Pfizer Abrysvo) recommended during weeks 32-36 of pregnancy to protect infants from severe lower respiratory tract disease in the first 6 months of life. There is no vaccine recommend for use in young children.
- Passive immunity:
    - Two monoclonal antibody products are available to protect infants/young children, Nirsevimab (Beyfortus) and Palivizumab (Synagis). Nirsevimab’s long half-life allows for administration of a single dose for the entire season while palivizumab requires monthly administration.
    - Neither nirsevimab nor palivizumab are recommended to prevent hospital-acquired RSV infection. They can be administered to infants who qualify for prophylaxis shortly before hospital discharge (within 48-72 hours prior to discharge from birthing hospital or NICU) or promptly afterwards.
    - Both nirsevimab or palivizumab can be co-administered with other vaccines (live or inactivated).
    - Nirsevimab pooled efficacy in preventing medically attended RSV-associated lower respiratory tract disease was 79.0%, preventing hospitalization was 80.6%, and preventing ICU admission was 90.0%.

The American Academy of Pediatrics (AAP) and the Advisory Committee on Immunization Practicesrecommend nirsevimab for (see attached figure):

- Infants aged <8 months born during or entering their first RSV season whose pregnant parent did not receive RSVpreF vaccine, whose pregnant parent's RSVpreF vaccination status is unknown, or who were born <14 days after the pregnant parent's RSVpreF vaccination.
- Nirsevimab is not needed for most infants aged <8 months whose pregnant parent received RSVpreF vaccine ≥14 days before giving birth. Nirsevimab may be considered for infants born to a vaccinated pregnant parent in rare circumstances when, based on the clinical judgment of the health care provider, the potential incremental benefit of administration is warranted. These situations include, but are not limited to:
    - infants born to pregnant people who might not have mounted an adequate immune response to vaccination (e.g., persons with immunocompromising conditions) or who have conditions associated with reduced transplacental antibody transfer (e.g., persons living with HIV infection).
    - infants who might have experienced loss of trans-placentally acquired antibodies, such as those who have undergone cardiopulmonary bypass or extracorporeal membrane oxygenation; and infants with substantially increased risk for severe RSV disease (e.g., hemodynamically significant congenital heart disease or intensive care admission requiring oxygen at hospital discharge).

- Infants and children 8 through 19 months of age who are at increased risk of severe RSV disease and entering their second RSV season, including those recommended by the AAP to receive palivizumab, regardless of RSV vaccination status of the pregnant parent. This includes the following:
    - Infants and children with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) at any time during the 6-month period before the start of the second RSV season.
    - Infants and children who are severely immunocompromised.
    - Infants and children with cystic fibrosis who have manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable) or have weight-for-length that is less than the 10th percentile.
    - American Indian and Alaska Native children.

- The following are considerations with regard to palivizumab versus nirsevimab administration for high-risk infants during the same RSV season:
    - If nirsevimab is administered, palivizumab should not be administered later that season.
    - If palivizumab was administered initially for the season and <5 doses were administered, the infant should receive 1 dose of nirsevimab. No further palivizumab should be administered. There is no minimum interval between the last dose of palivizumab and the dose of nirsevimab. Because protection from palivizumab wanes after 30 days, nirsevimab should be administered no later than 30 days after the last palivizumab dose, when possible.

- If palivizumab was administered in season 1 and the child is eligible for RSV prophylaxis in season 2, the child should receive nirsevimab in season 2, if available. If nirsevimab is not available, palivizumab should be administered as previously recommended (*palivizumab is dosed at 15 mg/kg intramuscularly (IM) once a month, maximum of 5 doses per season. In Arkansas, administration of palivizumab usually starts on November 1 with the last dose given by March 31*).
- Nirsevimab should be administered for the first (or if high-risk patients, the second) RSV season regardless of whether the infant has already had an RSV infection at any time previously, including during the current season.
- If an infant receiving monthly palivizumab prophylaxis experiences a breakthrough RSV hospitalization, monthly prophylaxis should be discontinued.
- If nirsevimab is not available, then high-risk infants should receive palivizumab. The high-risk infants include:
    - Infants and children with chronic lung disease of prematurity (born at gestational age <32 weeks, and require oxygen >21% for at least the first 28 days of life) in their first RSV season, and who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) at any time during the 6-month period before the start of the second RSV season.
    - Infants with moderate to severe pulmonary hypertension, and acyanotic heart disease who require medication to control congestive heart failure and will require cardiac surgical procedures are included in this category.
    - For infants with cyanotic heart defects, decisions regarding prophylaxis in the first year of life may be made in consultation with a pediatric cardiologist.
    - Infants and children who are severely immunocompromised.
    - Infants and children with cystic fibrosis who have manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable) or have weight-for-length that is less than the 10th percentile.
    - American Indian and Alaska Native children.

Control Measures

- Educate parents/caregivers about RSV.
- Emphasize hand washing.
- Keep high-risk infants away from tobacco smoke. Encourage smoking cessation for family members who are smokers.
- Limiting (where feasible) high-risk infants' exposure to contagious settings (e.g. childcare centers) and anyone who has a respiratory tract infection.
- In the high-risk setting, such as the PICU or NICU, infants with RSV should be identified as soon as possible and isolated with contact precautions careful attention to hand washing. Other methods of control in healthcare settings include cohorting, contact precautions, visitor screening, limiting young children visiting during the RSV season.

Long Term Effects

- Several studies documented that infants hospitalized with viral lower airway disease are more likely to experience recurrent wheezing compared to infants who do not experience severe bronchiolitis.
- The association between RSV infection early in life and subsequent asthma, however, remains incompletely understood. Infants who experience severe lower respiratory tract disease (e.g., bronchiolitis or pneumonia) from RSV have an increased risk of developing asthma later in life. The unresolved question is whether the association between severe infection and airway hyperreactivity is causal, or it reflects a common genotype, indicating the same anatomic or immunologic abnormalities that predispose to asthma also predispose to severe viral lower respiratory tract disease.

Nirsevimab Administration Visual Guide

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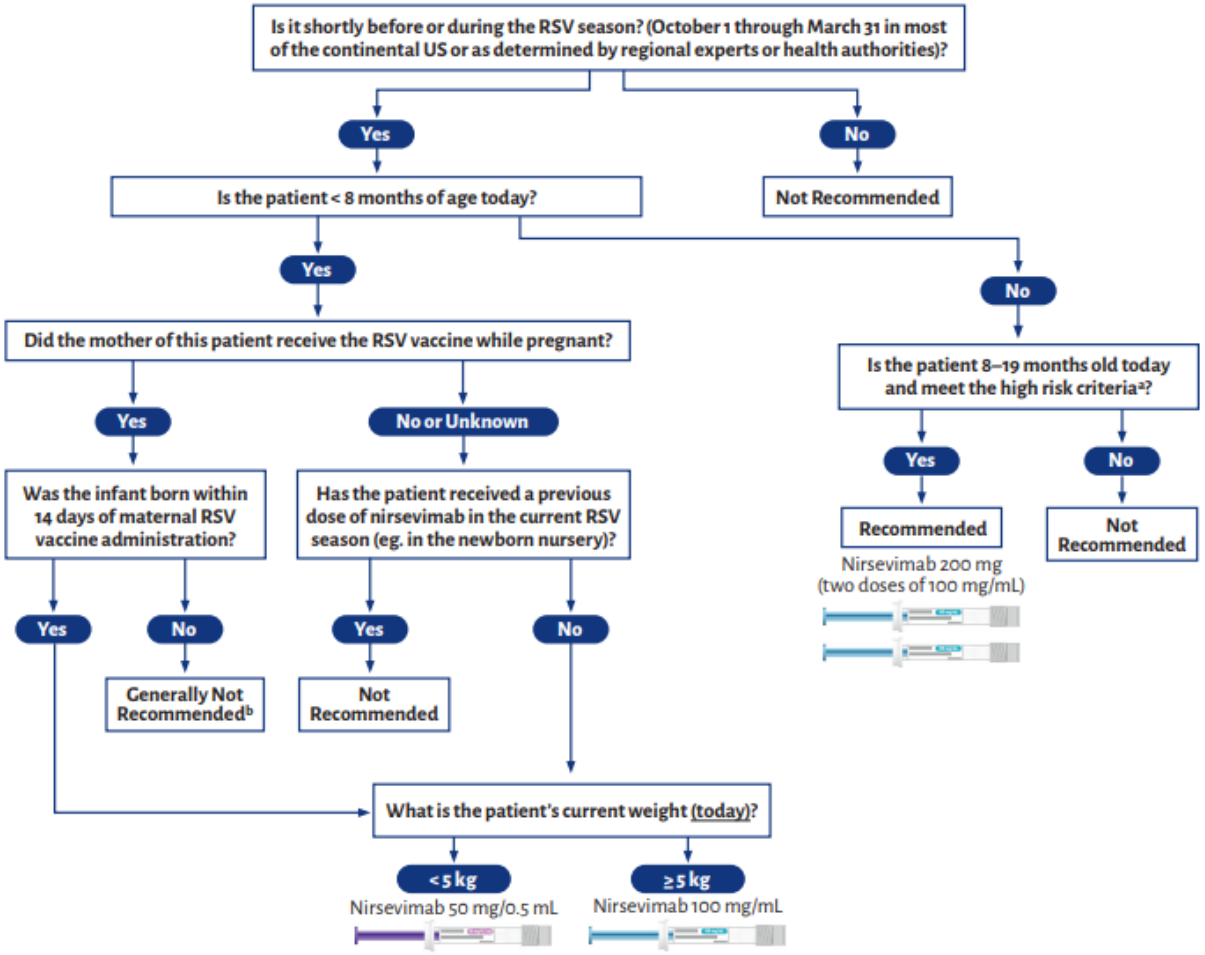

a. Children 8 through 19 months of age who are recommended to receive nirsevimab when entering their second RSV season because of increased risk of severe disease.
- Children with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the 6-month period before the start of the second RSV season.
- Children who are severely immunocompromised.
- Children with cystic fibrosis who have manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable) or have weight-for-length that is <10th percentile.
- American Indian and Alaska Native children (note that this is a new group for whom second-season prophylaxis is recommended in contrast to the current palivizumab recommendations).

b. Nirsevimab can be considered when, per the clinical judgement of the healthcare provider, the potential incremental benefit of administration is warranted, including but not limited to the following rare circumstances:
- Infants born to pregnant people who may not mount an adequate immune response to vaccination or have conditions associated with reduced transplacental antibody transfer.
- Infants who have undergone cardiopulmonary bypass or extracorporeal membrane oxygenation leading to loss of maternal antibodies.
- Infant with substantial increased risk for severe RSV disease (eg, hemodynamically significant congenital heart disease, requiring oxygen at discharge following an intensive care admission).

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

References:

1. Frederick E Barr, M., MBA; Barney S Graham, MD, PhD, *Respiratory syncytial virus infection: Clinical features and diagnosis in infants and children*, in *UpToDate*, C. RF, Editor. 2024, Wolters Kluwer.
2. *Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection.* Pediatrics, 2014. **134**(2): p. 415-20.
3. Committee on Infectious Diseases, A.A.o.P., *Respiratory Syncytial Virus*, in *Red Book: 2024–2027 Report of the Committee on Infectious Diseases*, D.W. Kimberlin, et al., Editors. 2024, American Academy of Pediatrics. p. 0.