SIDP Breakpoints Episode #143

Tiny Lungs, Big Protection:

RSV Prevention in Infants

Respiratory Syncytial Virus (RSV) is a non-segmented, single stranded negative-sense RNA virus, a member of the Pneumoviridae family. The estimated annual global incidence is 30 million cases in children under the age of 5 years with two-thirds of infants being infected in their first year of life. Infants are especially at risk for severe lower respiratory infections, partly due to differences in immunology and anatomy.

Two Strategies to Reduce RSV Risk in Infants

Vaccine

- Vaccinate the birthing parent at 32-36 weeks gestation, ≥ 14 days before birth of infant
- Stimulate the birthing parent's immune system to produce antibodies and memory cells which then pass through the placenta to the baby before birth

Monoclonal Antibody (mAb)

- Direct administration to the infant
- Lab-made long-acting antibodies to provide immediate passive immunity without need for immune system activation
- Provide protection during the RSV season (~ 5 months) without immune memory

Two recent cohort studies in France compared nirsevimab with maternal vaccination. They showed a relative risk of hospitalization for the nirsevimab group of ~0.75 when compared with maternal vaccination. However, these are small observational studies that assume timely administration of monoclonal antibodies. Accumulated real world data & meta-analyses show ~80% effectiveness of preventing hospitalizations with both interventions making them both effective prevention strategies.

Candidates for RSV Monoclonal Antibody

1. **All infants under 8 months of age** born during or entering their first RSV season UNLESS the infant has documented protection from vaccination of birthing parent

2. **Infants and children 8-19 months of age** who are at high risk of severe disease and entering their second RSV season (see below)

High Risk Criteria for Children 8-19 Months of Age Entering their Second Season (given regardless of maternal vaccination)**:**

- **Preterm** (<32 weeks)
- **Chronic lung disease** attributable to prematurity or to other significant neonatal conditions who required medical support at any time during the 6-month period before the start of the second RSV season
- **Hemodynamically significant congenital heart disease**
- **Anatomic pulmonary abnormalities or neuromuscular disorders**
- **Severe immunocompromising conditions**
- **Down syndrome or other chromosomal differences** associated with increased risk of severe RSV disease
- **Cystic fibrosis** who have either: manifestations of severe lung disease or weight-for-length < 10th percentile
- **American Indian or Alaska Native children**

Are repeat doses of monoclonal antibody necessary?

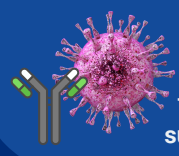
Repeat doses within the same season are generally not recommended UNLESS infant has undergone antibody-depleting treatments or procedures (plasmapheresis, cardiopulmonary bypass, ECMO, exchange transfusion, etc.)

Safety

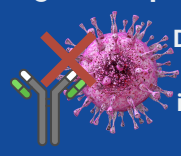
- **Maternal vaccines and mAbs are well tolerated (local injection site reactions)**
- **A numerical imbalance in preterm births observed in patients receiving maternal vaccine led to a restriction of vaccine to 32-36 weeks gestation**

Immune Evasion Through Antigenic Differences

RSV has two subgroups (Type A and B). Distinct amino acid sequences and surface proteins create different antigenic profiles. The antigenic diversity helps RSV evade the host immune response and can drive recurrent infections but cannot undergo significant shifts leading to large scale pandemics



The immune system produces antibodies targeting the specific surface proteins of RSV



Due to antigenic differences, antibodies from the prior infection may bind poorly (if at all) to the other type

Comparing Two Monoclonal Antibodies

Product	Nirsevimab (Beyfortus)	Clesrovimab (Enflonsia)
Mechanism	Binds RSV F protein (site 0 of pre-fusion protein)	Binds RSV F protein (site 4 of pre-fusion protein)
Indication	Infants entering their first RSV season and high-risk children entering their second RSV season	Infants entering their first RSV season only
Dosing	Weight-based (50 mg if <5 kg; 100 mg if ≥5 kg)	Fixed-dose regimen (105 mg)
Product	Prefilled syringe (50 mg and 100 mg)	Prefilled syringe (105 mg)
Approval (U.S.)	2023	2025
Key Data	Pooled trials: ~79% reduction in RSV LRTI requiring medical care, ~80% reduction in hospitalizations	Phase 2b/3: ~60% reduction in medically attended RSV LRTI, ~80% reduction in hospitalizations

RSV immunization may be considered in addition to maternal vaccine in the following scenarios:

Birthing parent may not have mounted an adequate immune response to RSV vaccination

Birthing parent has a medical condition associated with reduced transplacental antibody transfer

Birthing parent has undergone antibody-depleting treatments or procedures (plasmapheresis, cardiopulmonary bypass, ECMO, etc)

The infant has substantial increased risk of severe RSV disease OR timely maternal vaccination (≥14 days before birth) is not clearly documented

Coordinate Visits/Vaccinations

Coordinate administration of mAb with existing well-child visits or at birth hospital whenever possible. RSV mAbs can be safely given with all other routine childhood immunizations.

Stock/Supply

Keep mAbs in stock during RSV season for same visit protection, ideally in both inpatient and outpatient settings.

Building Trust & Vaccine Hesitancy

- **Share real-world efficacy, safety and public health data**
- **Keep the door open for ongoing conversation (reframe a mAb as a protective protein rather than an immunization)**

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Abbreviations: RSV - Respiratory Syncytial Virus, mAb - monoclonal antibody, ECMO - extracorporeal membrane oxygenation, LRTI - lower respiratory tract infection

References: Jabagi et al. JAMA 2026; Valtuille et al. Lancet Child Adolesc Health 2026; AAP RSV Recommendations. Pediatrics 2026; Hammitt et al. NEJM 2022 (MELODY); Drysdale et al. NEJM 2023 (HARMONIE); Simões et al. Lancet Child Adolesc Health 2023; Zar et al. NEJM 2025 (CLEVER).