Improving Knowledge and Awareness of Preventive Antibodies for Respiratory Syncytial Virus (RSV) for Infants and Young Children

Editor's Note: The is a transcript of a presentation on January 22, 2026. It has been edited and condensed for clarity. To obtain credit for participation CLICK HERE.

RSV Infection in Infants and Children – Epidemiology, Morbidity and Mortality, Signs and Symptoms

Lisa Saiman, MD: Let's begin by discussing some basics related to respiratory syncytial virus (RSV). RSV is a highly contagious and very common infection of the respiratory tract with very widespread prevalence due to a lack of long-term immunity following infection. While illness is usually mild and self-limiting in most adults—although we're learning that even adults may have severe disease—severity is increased among infants and young children. Obviously, this is the topic that we care about. RSV is one of the most common causes of childhood illness and it is actually the second highest cause of infant mortality worldwide, after malaria, and the most common cause of hospitalization in infants. And I think it would be really useful, Mary, if you would describe the seasonal patterns of RSV.

Mary Koslap-Petraco, DNP: That is such an important point—that it's the most common cause of hospitalizations in infants. We do know that RSV is a seasonal illness, usually, generally beginning in October, peaking in December, and ends in most of the United States (US) in April. This is the wintertime when everybody is stuck in the house and daycare centers aren't sending the children outdoors, so it makes perfect sense. It does usually vary geographically from season to season and there are some regions that are considered to have different RSV seasons, such as Alaska, southern Florida, Guam, Hawaii, Puerto Rico, the US Pacific Islands and the US Virgin Islands. That's due to the seasonal weather patterns in those areas. In those cases, it's really important to discuss with the local health departments when is the best time to give this vaccine or the RSV prophylaxis, when to start those.

Some of the disruptions in seasonality did occur during the years of coronavirus disease 2019 (COVID) and we didn't see a whole lot. We saw those disruptions because of the school closures and the masking. I'm a public health nurse, so I love masking. We did see that cases during the 2021 season were pretty low and there was increased offseason circulation. Some of the data now shows that the seasonal patterns are pretty much returning to what they were before the COVID pandemic and are probably going to continue. Lisa, can you just tell us a little bit more about the mortality rate for RSV in the US?

Lisa Saiman, MD: I think the information you just provided about this disruption is really important, but we just need to pay attention to the data as it emerges season by season. Fortunately, in the US, overall mortality for RSV-related disease in under 5-year-olds is really uncommon. It's estimated that there are about 100 to 300 deaths per year in the US, but studies have identified significantly higher rates of mortality among children with underlying risk factors, and obviously among children who require hospitalization. I really want to make the point that, globally, mortality is much, much higher. RSV represents about 2% of neonatal deaths, 7% of deaths in infants between 28 and 364 days and more deaths occur secondary to RSV than any other pathogen, with the exception of malaria, and it's estimated that 70% of RSV-associated deaths occur outside of healthcare facilities. So, really a very, very different burden globally than we do see in the US and other higher-income countries.

Hospitalization is a different story. In the United States, there is an estimated 58,000 to 80,000 children under 5 years of age who are hospitalized for RSV each year. Those numbers are 0.3% of children less than 5 years of age, but really high—2% to 3% of infants under the age of 3 months of age—are thought to be hospitalized with RSV. And then it's also a burden in nonhospital settings where studies have shown that 20% of infants seen in pediatric offices or emergency departments presenting with acute respiratory infections or fever actually are RSV-positives. So, again, a huge morbidity burden secondary to RSV in young children. I think it would be great, Mary, if you would share the transmission aspects of RSV and the pathogenesis.

Mary Koslap-Petraco, DNP: That is so important to point out that it's the infants under 6 months of age who are most at risk for hospitalization from RSV. This is a coughing/sneezing illness. It spreads from person to person through the respiratory droplets. It also—which a lot of folks don't know—can occur during direct contact or surface contamination. We have to consider the daycare centers, and the play dates, and the other children coming home from school. I'm the public health nurse, so hand-washing, covering coughs and sneezes, cleaning those frequently touched surfaces, washing the toys, mask-wearing during sickness and even during nonsickness, like when you're in a very congested place, is certainly very helpful in preventing the spread of this disease.

I'd like to mention a little bit about the incubation period, because it's relatively short. On average, it's approximately 4 to 6 days, but it can range from 2 to 8 days. I worked in a community where we would see children coming in a day or 2 after the children I had seen that day, with the same symptoms, because the children were all either with the moms, or the babies were all hanging out together because of play dates. We need to keep in mind how contagious this illness actually is. It is spread through the nasopharyngeal or the conjunctival mucosa. It's hand-rubbing and rubbing the eyes, teaching people to keep their hands away from their faces. We can't do that with babies, but all the more reason we have to keep things as clean as we can for the babies. It does spread very quickly into those epithelial cells of the respiratory tract. That intracellular replication triggers the host immune response. It is a small-airway obstruction, and mucus plugging results from this virus. It also may generate alveolar obstruction in the lower respiratory tract. We have to remember this can go way down into the lungs and that's what causes all these problems. It's not a "neck up" illness; it's a "neck down" illness.

You can have bacterial coinfection with *Streptococcus pneumoniae* or *Haemophilus influenzae*, which is very commonly seen. The illness is very contagious, and it stays contagious from 3 to 8 days. Children have these snuffy noses and that plays into with adults too. Adults with snuffy noses have to consider that they might be carrying the RSV virus, as well, and can share it with the most vulnerable, who are young babies and our mature population, the 65-year-old and over crowd. Lisa, can you talk to us a little bit about the upper respiratory symptoms and how these mimic so many other illnesses?

Lisa Saiman, MD: I suspect the audience is quite familiar with the clinical manifestations of RSV. Particularly in infants under 2 years of age, they usually initially have upper respiratory infection (URI) symptoms. As Mary described, the inoculation is into the upper respiratory tract, followed by lower respiratory tract illness. The major upper respiratory symptoms include cough, nasal discharge/congestion, sneezing, but once it goes into the lower respiratory tract, then we see shortness of breath, wheezing, accessory muscle use, rhonchi, prolonged expiration. That occurs usually in 20% to 30% of children. There may be

other manifestations, such as vomiting, diarrhea and fever, which are also quite common. It's really important to recognize that symptoms of RSV can look just like other viruses—influenza, COVID-19, and other respiratory viral pathogens. So, testing is truly the only way to differentiate these different organisms. Next we're going to discuss risk factors and complications associated with RSV.

RSV Infection in Infants and Children –Risk Factors, Acute and Chronic Complications

Lisa Saiman, MD: Most babies who are hospitalized with RSV actually have no known risk factors for severe disease, other than being a baby. Infants who are less than 6 weeks are considered particularly vulnerable, as are babies under 6 months of age and who were born at gestational ages of less than 35 weeks. Babies who were born at the onset of or during RSV season are clearly at higher risk because of their age-related vulnerability during peak circulation of RSV. But Pablo, we know that there are additional groups of children that have underlying conditions. Could you share those with us?

Pablo J. Sanchez, MD: First of all, it is, like you mentioned, really important that every single infant who is experiencing their first RSV infection during the RSV season is at highest risk for hospitalization. But there are certain groups of children who are nonetheless considered at increased risk for more severe disease. Those infants and children with suppressed or weakened immune systems—certainly, as a neonatologist, our babies who develop bronchopulmonary dysplasia (BPD), or so-called chronic lung disease of prematurity, are at risk; those infants and children are also eligible for a second season of prophylaxis. Infants with congenital or chronic heart disease, as well. Neuromuscular disorders or congenital anomalies also pose higher risk for more severe disease, as well as those infants and young children who have difficulty swallowing or clearing mucus secretions—therefore, the neuromuscular disorders. Infants with cystic fibrosis (CF) or Down syndrome have been shown to have worse disease as well. Similar to those children with BPD, Alaska Native and American Indian children are also recommended for prophylaxis in a second season.

Studies have also shown that other children with certain other factors are at increased risk for severe disease. So, the presence of siblings in the home, parental tobacco use, daycare attendance, malnutrition, crowded living conditions, as well as lower socioeconomic status, have been shown to pose a higher risk for more severe RSV disease in these children. Lisa, can you comment, though, on some of the complications that we see in these infants who develop RSV infection?

Lisa Saiman, MD: In terms of major complications—otitis media, bronchiolitis, of course, and pneumonia. RSV accounts for 60% to 80% of cases of infant bronchiolitis. Mary did also mention that bacterial superinfection, with *Streptococcus pneumoniae* or *Haemophilus influenzae,* can occur. One thing that is really important to emphasize is that RSV infections have potential morbidity beyond the acute illness. RSV may impact lung function long term in children and potentially extending into adulthood. Studies have demonstrated a connection between having RSV at a young age and development of recurrent wheezing and asthma during the first decade of life and leading to impairments in lung function. Those impairments of lung function may subsequently increase the risk of other respiratory illnesses, recurrent lower respiratory tract infections, and hospitalization. As a pediatrician, I think I was less familiar with the literature that suggests that long-term lung impairment beginning in childhood may actually be associated with a higher risk of cardiovascular events and premature mortality in adults. So, thinking so hard about how we can prevent RSV infections in young infants can have benefit way beyond childhood, but well into adolescence and adulthood. Pablo, can you educate us about RSV treatment?

Pablo J. Sanchez, MD: Certainly, and just to emphasize what you have said with later lung function and really the importance of preventing RSV infection and disease in these young infants and children, as well as in the elderly. And we today are able to really effectively do that. I know that this is something that we will be discussing, but really it just highlights the importance of prevention and preventive strategies. Unfortunately, we don't have any specific treatment for RSV infection. There is currently no antiviral that we can use to treat RSV infection, whether it's mild or severe, or even those children who require intubation and mechanical ventilation. There are ongoing studies looking at antivirals, and certainly that is the hope for the future among those infants and children who do not receive prophylaxis. What we're left with is supportive care.

Given the limitations in treatment, the focus has to be on prevention. As we will be talking about, there are different products available, both for the mother as well as for the infant and high-risk child. Product selection should be based on parent preference, product availability, as well as the timing relative to the RSV season.

RSV Immunoprophylaxis Strategies in Pregnant Parents

Lisa Saiman, MD: There are several newly approved approaches for preventing RSV infection in young infants during their first RSV season, as Pablo mentioned. The option that we're going to be talking about next is pregnant parent or maternal vaccination. And the available, approved vaccine is the RSVpreF, with F standing for fusion vaccine, also called Abrysvo. That's a recombinant and unadjuvanted vaccine approved by the US Food and Drug Administration (FDA) in 2023. Notably, this is the same vaccine that's approved for adults 75 years of age or older or adults 50 to 74 years of age who have comorbidities, placing them at increased risk of severe disease. There are 2 additional vaccines that have been developed, Arexvy and MRESVIA, that are not approved for use in pregnancy. It's really important to recognize that we only have 1 vaccine that is approved for pregnant individuals.

This vaccine contains antigens against the A and B RSV subtypes of the prefusion configuration of the F protein. That's why I said before, preF. It's important to just spend a moment understanding the pathophysiology of RSV. The F protein is 1 of 11 total glycoproteins within the RSV viral genome. What the F protein does is facilitate fusion of the virus to the respiratory epithelial cell membrane, which is the target that we talked about earlier and that facilitates cell-to-cell spread. What the vaccine does is stimulate the immune system to generate neutralizing antibodies against the prefusion form of the F protein. These antibodies are efficiently transferred 14 days or more after vaccination to provide passive protection against RSV to the vaccinated parent's infant. So, a really unique and important vaccine and approval for pregnant individuals is very, very exciting.

So, now we're going to turn to the phase 3, 18-country MATISSE study of the maternal vaccine. I'm going to start with the efficacy data and then Mary's going to share the safety data with us. Pregnant individuals were randomly assigned 1:1 to a single injection of the RSVpreF vaccine vs placebo at 24 to 36 weeks gestation. I want to make the point that people were excluded if they had a high-risk pregnancy, such as multiple birth or a previous infant with congenital anomalies. In this study, the primary outcome was medically-attended severe RSV lower respiratory tract

infection in their babies. This would be a medical visit and then a whole set of clinical and signs and symptoms—for example, nasal discharge, difficulty breathing or tachypnea, cough, inability to feed, or apnea and tachypnea for age, a low oxygen saturation less than 93%, the use of respiratory support, intensive care unit (ICU) admission, and/or failure to respond or unconscious. What this study demonstrated was an 81.8% efficacy of vaccine at 90 days, and very importantly, also a 69.4% efficacy at 180 days. So that efficacy continued over a long time period.

One of the things that is important to recognize is that RSV-associated hospitalizations were also decreased, but this did not reach the previously-established statistically-significant criterion that were reached. So, Mary, could you describe to us the safety profile of the vaccine?

Mary Koslap-Petraco, DNP: That was a really excellent explanation about how effective this vaccine is. What they noted was there were similar rates of adverse events (AEs) between these 2 groups, including the perinatal AEs of interest, such as prematurity, low birth weight, or developmental delay. Those are always the things that are looked at when they're studying vaccines related to pregnancy. The original publication by Kampmann et al that was published in 2023, published outcomes on over 7,000 pregnant parents through 180 days, covering 85% of scheduled follow-up visits. Which was really, really important because they kept track of these folks to make sure that they could see if there were any adverse events, later on, after the vaccine was administered.

The final data for over 7,000 pregnant people was up to 2 years of follow-up that was published by Simões et al in 2025, was consistent with that original analysis. What it did show was that there was no significant increase in preterm birth. They followed those babies and noted that there were no developmental delays or any other significant adverse events noted during that 24-month period. This tells us that this vaccine is not only efficacious, that it's a safe vaccine to administer as well. Can you continue on and tell us a little bit more about what the obstetricians and gynecologists recommend about these vaccines?

Lisa Saiman, MD: The American College of Obstetricians and Gynecologists (ACOG) recommends vaccination with the RSVpreF vaccine for the following individuals between 32 and prior to 37 weeks of gestation who do not have a planned delivery in the next 2 weeks. I earlier said that it takes about 14 days to have enough of an antibody production that would be neutralizing and effective. They have not received this RSVpreF vaccine during a previous pregnancy. Currently, we only recommend the use of this vaccine once because we don't have safety or efficacy data for subsequent use in subsequent pregnancies. We want to consider the RSV season, again to give enough time to develop neutralizing antibodies. The recommendation is between September 1st through January 31st in the continental US, but, as we said earlier in the program, there may be differences in epidemiology in other jurisdictions, so it's important to keep alert to recommendations that occur locally.

Important considerations are, as I mentioned, that revaccination is not recommended for subsequent pregnancies, currently. If the pregnant parent says that they don't wish to be vaccinated, then we would recommend the RSV monoclonal antibody immunization that we'll be talking about in a few moments. I want to emphasize that ACOG does not have a preferential recommendation for the pregnant parent vaccination vs the infant RSV monoclonal antibody. We will be talking in a little while about some real-world, comparative effectiveness data that might help guide us in the future.

We'll now turn our discussion on RSV prevention from the pregnant parent vaccination to RSV monoclonal antibodies for infants and young children.

RSV Immunoprophylaxis Strategies in Infants and Young Children

Pablo J. Sanchez, MD: As an alternative to maternal vaccination, there are 2 products. They are medications, not vaccines. They are antibodies against the prefusion form of RSV that can be given to all infants less than 8 months of age, as well as young children who are at higher risk for severe RSV infection. It provides a really excellent alternative to vaccination in pregnant women.

Historically, only palivizumab or Synagis, that was approved back in 1998, was available for RSV prevention. It was only approved in very selected infants at very high risk for severe disease. Overall, it was preterm births and was recommended for those infants who are less than 29 weeks of gestation, infants who had bronchopulmonary dysplasia or chronic lung disease of prematurity, as well as hemodynamically significant congenital heart disease and severe cystic fibrosis. Palivizumab had to be administered monthly as intramuscular injections just before and throughout the RSV season. It was given in some select infants in the second year of age as well. As of December 2025, however, palivizumab was discontinued due to market shifts. And the fact is that the newer products are very effective and with much easier administration, as well as the cost is significantly less.

These 2 newer RSV recombinant monoclonal antibodies that are currently available are nirsevimab or Beyfortus that was approved by the FDA in 2023, and clesrovimab or Enflonsia that was approved more recently in 2025 by the FDA. Both have been recommended by the Advisory Committee on Immunization Practice (ACIP) and Centers for Disease Control and Prevention (CDC), as well as the American Academy of Pediatrics (AAP) and other physician and nursing groups. A break that we finally have RSV protection that can be extended to all infants and high-risk children, not just selected high-risk babies. Lisa, why don't you tell us a little bit more about these products?

Lisa Saiman, MD: I totally agree with you. It's so exciting that we have them available. Both of the RSV monoclonal antibody products that you mentioned target that RSV F protein, but they have different antigenic sites. They are both involved in blocking viral entry and on preventing conformational changes that would be required for viral fusion. I want to briefly mention that there have been some cost effectiveness studies and modeling studies showing that both products are indeed cost effective. For example, there's an estimate that 100,000 outpatient visits, 38,000 emergency department visits, and 14,000 hospitalizations could be averted yearly if half of the US birth cohort received monoclonal antibodies. So, let's next discuss, Pablo, some of the clinical trials and real-world evidence for these products.

Pablo J. Sanchez, MD: These monoclonal antibodies provide protection against RSV in a different manner than vaccines. It's very important to note that these monoclonal antibodies are not vaccines, they're medications that effectively prevent severe RSV disease. Vaccines stimulate long-term immunity by their nature, and once a vaccine is administered, it takes up to 14 days for antibodies to be produced by that individual. In the case of the pregnant woman, those antibodies then have to cross through the placenta to get into the fetus. Maternal antibodies in

the baby can last up to 18 months, although there is diminution of the antibody titers—the maternal antibody titers—through the first year of age. On the other hand, antibodies, when administered to the infant,

provide immediate but short-term protection. In both of these products, protection with these antibodies can last for at least 150 days. So, 1 injection with these monoclonal antibody products will protect the infant throughout the RSV season.

Now, the safety and efficacy of nirsevimab. One of these monoclonal antibody products and the first one, was established in a really groundbreaking phase 3 so-called MELODY study. Infants were enrolled who were less than 12 months of age. They were randomly assigned 2:1 to receive nirsevimab vs placebo, intramuscularly, before the start of the RSV season. There was pharmacokinetic data that was obtained and it showed that nirsevimab levels were associated with protection in the preclinical studies that were maintained through at least 150 days across all subgroups. It was groundbreaking to see how we could actually prevent severe and medically-attended lower respiratory tract infection in these high-risk children. Lisa, why don't you tell us now about the MEDLEY trial that looked at this product given to premature infants and other high-risk infants?

Lisa Saiman, MD: This is an important study because it compared nirsevimab to palivizumab. Because, as you mentioned earlier, Pablo, that was the product that we had available when these clinical trials were initiated. They performed this study in high-risk infants across 2 RSV seasons, so there were 615 preterm babies born at 35-week gestation or younger and 310 babies with congenital heart disease or chronic lung disease. Because of the sample size, there was a focus on safety and pharmacokinetics of nirsevimab in this population because these were not the patients that were included in the prior study that was the groundbreaking study. The incidence of 1 or more adverse events was similar across the groups and that included both the preterm cohort and the babies with congenital heart disease or chronic lung disease. Most adverse events were described as mild or moderate. The other important thing was that the nirsevimab neutralizing antibody levels were 10-fold higher compared with palivizumab across both seasons. Remember, I mentioned that this was studied across 2 RSV seasons. I think that this study gives us a lot of important information about babies who are at higher risk for severe RSV.

I also now want to turn to a real-world study of nirsevimab, which is called the pragmatic HARMONIE study. In this study, nirsevimab was given in a 1:1 randomization vs standard of care. This is obviously open label because there was no placebo and the administration of nirsevimab was given during the RSV season, alongside routine childhood vaccinations. The primary endpoint in this study was hospitalization, and there was an efficacy of 83.2%—0.3% of the nirsevimab babies vs 1.5% of those babies that had been randomized to standard of care. A secondary efficacy endpoint was very severe RSV, lower respiratory tract infection which in this study was defined as hospitalization and an oxygen saturation less than 90% with the requirement for supplemental oxygen. And with regard to that endpoint, the efficacy was 75.7%. The other area of interest was safety. The rates of serious adverse events were comparable and most of these serious, adverse events were grade 1 or grade 2.

Pablo, I think that the real-world effectiveness of nirsevimab would be really interesting to discuss in the context of a meta-analysis that was recently performed. Could you describe those real-world studies?

Pablo J. Sanchez, MD: It's just been amazing, amazing data that have come out after the nirsevimab has been administered in many countries. In this meta-analysis, it was 32 cohort and case-control studies from 5 different countries. And the studies showed that, when given in these countries, there was reduced RSV hospitalization, reduced ICU admission, and reduced lower respiratory tract infection, as well secondary to RSV in infants who are less than 1 year of age.

Now, we've spoken about the success story of nirsevimab. Lisa, can you tell us about the newer product clesrovimab? The new baby on the block.

Lisa Saiman, MD: Pun intended, Pablo? I just want to really emphasize that while we're very reliant on clinical trial data with placebo controls and all the wonderful safety measures that are done. I always find it very reassuring to see that real-world data confirms the findings because it's a much more applicable scenario to what we're trying to do and affects a lot more people. Thank you so much for covering that so well.

Clesrovimab is a monoclonal antibody and in this study—I love the title—the CLEVER study, 3,614 infants who were 29 weeks gestational age were randomly assigned 2:1 to the active arm vs placebo, prior to the start of an RSV season. The primary endpoint in this study was medically-attended RSV lower respiratory tract infections, and each of the studies had slightly different case definitions. In this study, that case definition was cough or difficulty breathing and at least 1 of the following: wheezing, chest wall retractions, rales or crackles, hypoxemia, tachypnea, or dehydration. Those were evidence of lower tract disease. And the babies were followed through 150 days.

In this study, the efficacy for the primary endpoint was 60.4%—2.5% of the active arm and 6.2% of the placebo arm had this primary endpoint. And safety through 365 days was covered. Most adverse events were mild or moderate; irritability and somnolence were most common, and injection site reactions were the same between the 2 groups. Pablo, I think a lot of people may be wondering, "Oh, which of these 2 products—nirsevimab or clesrovimab—is better?" We'll make this point again later, but I think it's really important to emphasize at this time that variability in study design, for example, inclusion criteria, diagnostic criteria, even the case definitions for endpoints, are different. That renders direct comparisons of efficacy with 1 another—in this case, between the CLEVER study and MELODY study—to be challenging. People can go back and read if they're interested, in a post hoc analysis, the team that did the HARMONIE study with clesrovimab actually used similar criteria to line up with the MELODY study. They demonstrated an 88% efficacy using those criteria. So again, very reassuring, and goes back to what you've been saying how excited we are by this.

I'll briefly mention the phase 3 SMART trial. This is, again, a study looking at the monoclonal antibody vs palivizumab, in this case clesrovimab vs palivizumab. This was again babies that were born either preterm or had congenital heart disease or chronic lung disease. Like the prior study, they focused on safety and pharmacokinetics. The incidence of adverse events was similar across both groups. Most adverse events were mild or moderate. The incidence of RSV-associated disease was similar across both groups during their first RSV season that was studied. The incidence of medically-attended RSV-associated lower respiratory tract infection was 3.6% in the clesrovimab group and 3% in the palivizumab group. Hospitalizations were 1.3% in clesrovimab vs 1.5% in the palivizumab group.

Pablo, I think it's really the perfect opportunity for a transition for what are the actual clinical recommendations for RSV antibodies in young children.

Clinical Recommendations for RSV Prevention

Pablo J. Sanchez, MD: Guidance on the RSV antibody products and their administration is now available from several organizations. ACOG, AAP, and the American Academy of Family Physicians (AAFP), as well as nursing organizations and other healthcare organizations, have really all been very supportive of either administration of RSV vaccine to pregnant women or the administration of these monoclonal antibodies, nirsevimab or clesrovimab, to all infants and high-risk children. In early 2026, the United States Department of Health and Human Services (HHS) did state that RSV antibodies should be administered and recommended for certain high-risk groups or populations. However, every single infant who is less than 8 months of age during the RSV season is at high risk for severe RSV disease. So, it is a universal recommendation that all young infants and high-risk children should receive it.

For RSV antibodies also, this has been defined as all children whose pregnant mother was not vaccinated for RSV, meaning there's no real change from previously recommended practice. Patient education will be essential to help patients and parents navigate messaging that they may have heard regarding any changes in recommendations. For now, we strongly advise and strongly recommend administration of these products to pregnant women or to all infants. Lisa, what can you tell us about more specific recommendations for the administration of nirsevimab or clesrovimab to infants and high-risk children?

Lisa Saiman, MD: If the vaccination status of the parent is unknown, RSV antibody is recommended. But if the pregnant person has gotten the RSVpreF vaccination, for the most part, the use of a monoclonal antibody product is not recommended, although stay tuned because there are a couple of caveats to that particular recommendation.

In terms of operationalizing the administration, infants born during the RSV season should receive the immunization ideally within a week of birth. We'll hear more about this later given how vulnerable these youngest infants are. Administration can occur during any visit, including well child care visits. Infants who have a prolonged birth hospitalization because of prematurity or other causes should receive RSV monoclonal antibody immunization shortly before or promptly after hospital discharge. It really behooves all of us to think about the population, for example, that Pablo cares for, and about how to operationalize giving a dose of the RSV monoclonal antibody to those babies.

Eligible babies who are less than 8 months of age and who were born before the RSV season should get their RSV monoclonal antibody immunization shortly before or during RSV season. That is really important to focus on pediatricians for that. The monoclonal antibody can be given concomitantly with other routine childhood vaccines. It's not expected to interfere with the immune response to these other vaccines.

As I alluded to, there are some few indications for the use of both RSV antibody after the pregnant individual has been vaccinated. So, bear with me here and I'll try to go through these succinctly. If the baby was born less than 14 days before the pregnant parent was given the vaccine, they should still get the monoclonal antibody. Pablo described to you how it takes 14 days at least to get an adequate level of protective antibodies. So, if they were born before that opportunity, they should get the monoclonal antibody. Babies born prior to 34 weeks gestation– again remember the lower limit of vaccination is 32 weeks, so there wouldn't have been 14 days that would have lapsed. For those of us that deal with complex, hospitalized babies who get cardiac surgery, that have cardiopulmonary bypass, or are on extracorporeal membrane oxygenation (ECMO), should get an additional dose as soon as they're stable postsurgically because they may have lost the maternal antibody because of their treatments with cardiopulmonary bypass or ECMO. There are a couple of instances where the treating clinician may think that RSV antibody would be indicated after the maternal vaccine, but I think these would be few and far between based on the following. If the pregnant parent has an immunocompromising condition and may not mount an adequate immune response, maybe those babies should get the monoclonal antibody to protect them. Similarly, if the pregnant parent has a condition with reduced transplacental antibody transfer—for example HIV infection—the babies could get the monoclonal antibody. If the baby has experienced loss of the transplacental antibodies, and we described a couple of examples of that already—babies who may be substantially at increased risk for severe RSV disease, hemodynamically significant congenital heart disease, babies with an ICU admission who have an oxygen requirement at discharge. These are very nuanced and people should be aware of them, but I'm sure it would require review after the talk. Pablo, do you think that you could now describe for us the use of nirsevimab for babies who are 8 to 19 months of age who are at increased risk, because that's another unique group?

Pablo J. Sanchez, MD: That was a great review and recommendations during the first season. As we described previously, there are certain children who are aged 8 to 19 months who are at high risk for having severe RSV disease. For this age group, 8 to 19 months, only nirsevimab is approved and recommended. The administration of clesrovimab in a second season is under study. It is not that it is not safe; it's just that we don't have the data on efficacy or effectiveness and antibody safety. We anticipate that data will be forthcoming in the future, in which case clesrovimab will be added to the second RSV season recommendation. But at this time, only nirsevimab is recommended for these children.

Who are these children? First of all, they have to be aged 8 to 19 months on the day of nirsevimab administration. The groups are the chronic lung disease of prematurity or bronchopulmonary dysplasia, but only those who are receiving medical support during the 6-month period before the start of the RSV season. Medical support has been defined as chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen, again during the 6-month period before the start of the RSV season. Also, children 8 to 19 months of age who are severely immunocompromised, such as those with severe combined immunodeficiency (SCID), should also receive nirsevimab in a second season. Cystic fibrosis, as we mentioned earlier, is also associated with more severe RSV disease. Those children, 8 to 19 months of age, with cystic fibrosis with severe lung disease, as defined as a previous hospitalization for pulmonary exacerbation in the first year of age, those who have abnormal and persistently abnormal chest imaging, or whose weight for length is less than the 10th percentile should receive nirsevimab at age 8 to 19 months of age. And also, American Indian and Alaska Native children. It's been shown over and over again that these children who are American Indian and Alaska Native are at very high risk for having more severe RSV disease. So, not only should they receive it in the first season, but also in the second season.

Lisa Saiman, MD: Just to really reemphasize again that the timing of RSV antibody administration is important. We have to think about it

because we're providing protection during the RSV season and to expect it to provide protection for approximately 5 months. So, most of the continental US, for babies born April to September, we would want to administer the RSV antibody in October. For babies born from October to March, those babies can get the RSV monoclonal antibodies administered within the first week of life, ideally in the hospital. But if they miss that opportunity, we really need to try to get them the monoclonal antibody product as long as they are eligible. So, Pablo, can you briefly describe to us the mechanics of giving these monoclonal antibodies?

Pablo J. Sanchez, MD: Both RSV antibodies, nirsevimab and clesrovimab, are administered as intramuscular injections in the anterolateral thigh region. Nirsevimab has weight- and age-based dosing. For infants less than 8 months of age who weigh less than 5 kg (or less than 11 lb) they receive a 50 mg dose, which is 0.5 mL. For infants who are less than 8 months who weigh 5 kg or more (that is 11 lb or more), they receive a 1 mL dose, which is 100 mg. Importantly, this is not 2 50 mg injections, but it comes as a 100 mg injection. For children 8 to 19 months of age, the dose is 200 mg, which are 2 100 mg injections, 1 mL each.

On the other hand, clesrovimab is much easier. It has a flat 105 mg dose for all infants who are less than 8 months of age, and that 105 mg dose is 0.7 mL. Again, clesrovimab is not to be administered to children 8 to 19 months of age in a second season. Both nirsevimab and clesrovimab are manufactured as prefilled syringes and, very importantly, they both can be administered at the same time as other routine vaccines. They should be stored refrigerated. Nirsevimab can be kept at room temperature for a maximum of 8 hours. Clesrovimab can be kept at room temperature for a maximum of 48 hours. There are some relevant precautions and contraindications. Lisa, would you like to go over that for us?

Lisa Saiman, MD: Sure, very briefly. Infants and young children who, at the time when you're considering monoclonal antibody administration, have moderate or severe acute illness—it's recommended that administration be delayed until the child is improved. Infants and young children with a history of severe allergic reaction to the components of the monoclonal antibody products—in that case, the monoclonal antibodies are contraindicated. Then just to reemphasize that safety data for RSV antibody infants born at a postmenstrual age of less than 32 weeks or who weigh less than 3.5 lb (or 1.6 kg) are limited, although we did have the safety data from the studies that we discussed comparing the products to palivizumab.

Tools to Facilitate RSV Prevention

Mary Koslap-Petraco, DNP: We've really had an interesting discussion up to this point. I think what we need to talk about now is the tools that we have to assist healthcare providers in improving RSV immunoprophylaxis. Let's talk about a list of clinical resources for both healthcare providers and patients that we have alongside this program. Pablo, can you talk about the AAP and the CDC recommendations for these healthcare providers, please?

Pablo J. Sanchez, MD: The American Academy of Pediatrics has produced an RSV Immunization Administration Visual Guide for all healthcare practitioners. I think it's important that they refer to that. They have frequently asked questions that I have found to be very useful as we implement the administration of these products to all infants and high-risk children. The AAP visual guide includes a useful flow diagram that assesses patient eligibility, as well as administration tips.

The CDC also provides general guidance on talking to parents about vaccines and this is really critical. Again, neither nirsevimab nor clesrovimab is a vaccine. It is passive immunization; when I speak with parents, I tell them this is a medication that is given to their infant in order to prevent severe RSV disease. I think we need to tell them that it is not 100% effective—that their child may still get RSV. We still need to take some precautions in terms of preventing exposures. Regardless, there are some important conversation strategies that CDC has urged us to use. We should assume that the parents will either vaccinate with vaccines, but also that parents will agree to get administration of this medication. So, "Your child is due today for an RSV preventive antibody," as opposed to "Have you thought about RSV prevention?" Certainly, open-ended questions are important in discussions with families. We need to be proactive in our recommendation because, in general, parents want to hear from their healthcare professional what their recommendation is. This really provides a strong recommendation as a healthcare professional, but at the same time, we do need to listen and respond to parent questions. Hopefully, our discussions today will facilitate a lot of them.

One issue that does come up is coordination and messaging between the obstetrician and also the pediatrician or the pediatric healthcare professional. Mary, could you discuss some of those issues that come up and how best to deal with maternal vaccination? We heard from Lisa about the somewhat of an indirect comparison, but how do you speak to obstetricians and the parents and how best to phrase that?

Mary Koslap-Petraco, DNP: I think that's such an important point. My bottom line is whenever we speak to parents or as colleagues amongst ourselves, is kill people with kindness. Smile and listen to the questions that they have. It's one of the most important things that I think we do. That's acknowledging the parents' concerns or even another provider who says, "Well I'm not so sure about this, what's the data saying?" but acknowledging their concerns and really listening to them.

We have to coordinate and be consistent with messaging, so that we're all saying the same thing. That's why I'm so thrilled that AAP, AAFP, and ACOG are all putting out the same message so that no matter which provider you talk to, you're going to get that same message. I think that's what we have to always remember and keep in mind. All clinicians have shared responsibility towards RSV immunoprophylaxis. It really can be difficult to know when and if a pregnant parent has been vaccinated.

We know we need to also emphasize that there are differences between vaccines and the monoclonal antibodies. That's going to be very confusing to parents. I like that we've been using the word "product" throughout this program, whether it's a monoclonal antibody or a vaccine. We have lots of opportunities to discuss passive vs active immunization. We know that we want to get that vaccine into the pregnant person at least 2 weeks before the delivery, so that those antibodies can be passed to the baby. Whereas, when the baby gets the monoclonal antibodies, that's passive immunity and that immunity is on board immediately. It's important to emphasize that neither of these interventions is 100% preventive of infection, but they're very effective in reducing the negative outcomes, like hospitalization and death. I think these things are really important to emphasize with our teaching, so that we, as clinicians, know the difference and can respond to the questions that our patients have regarding the vaccine and regarding the monoclonal antibodies. Pablo, can you talk and summarize about the conversations around the general population alongside these interventions, please?

Pablo J. Sanchez, MD: There's also conversations that are needed around general prevention because, again, we need to prevent exposure. Adults kissing infants, particularly during RSV season. Certainly, no person who has any sort of illness, especially colds or sniffles, should be around a young infant, especially in the first month of life. We really need

to prevent that contact. As we mentioned earlier, there is RSV vaccine for elderly individuals 75 years and older, and those 50 to 74 years who are at increased risk of having more severe RSV disease. Whether that may prevent transmission to young infants and other people remains to be seen, but certainly it will be important for them to ameliorate the disease and, hopefully, have some protection against its transmission to others.