PARENTS PACK

MONTHLY UPDATES ABOUT VACCINES ACROSS THE LIFESPAN

FEATURE ARTICLE: RSV AND BABIES — A BIT OF HOPE

October 2023

Does this sound familiar? Fall arrives and with it you find yourself or your school-aged children battling a runny nose and cough, maybe a fever, an ear infection or even some wheezing? Or perhaps, these symptoms occur right in time for holiday visits with your family?

If you can relate, you may have experienced an infection caused by respiratory syncytial virus or RSV. In the United States, RSV is a fall and winter virus that leads to millions of healthcare visits and tens of thousands of hospitalizations each year. Those most seriously affected are children younger than 5 years of age and the elderly.

When we talk to healthcare providers about children and RSV, the conversation often quickly turns to newborns and young infants because RSV can take the form of more than a runny nose and cough for them. Indeed, an RSV infection can cause babies to stop eating, become lethargic, and maybe even have episodes of breathing stoppage (called apnea). Each year in the U.S., as many as 80,000 babies are hospitalized with pneumonia (infection of the lungs) or bronchiolitis (infection of the small breathing tubes) caused by RSV. Sadly, about 100 to 300 young children die each year from this infection, and among those who recover, some experience lingering effects on their lungs, including wheezing and asthma.

Unfortunately, preventing RSV in the youngest among us has been difficult. But in 2023, new tools have poised us to change the story in this long-time battle between human and virus.

TRIVIA CORNER

What vaccine-preventable disease cannot be successfully treated with antibiotics because it is a virus?

A. Influenza

B. Pertussis (Whooping cough)

C. *Haemophilus influenzae* type B

D. Tetanus

A bit of biology

The groups most susceptible to severe RSV are so for different reasons. Among the elderly, RSV can be severe because of a person's aging immune system and other underlying medical conditions that make them more susceptible to this infection. On the other hand, babies are at greater risk because of their small airways and lack of previous exposure to the virus (i.e., no immunologic memory to rely on).

RSV reproduces in the cells that line our airways. When the virus gets into the lower part of the lungs and reproduces, it causes physical damage that interferes with breathing. Physical changes can include damage to the air sacs, fluid leaking from cells, overproduction of mucus, collapse of portions of the airways, and general inflammation of the affected area of the lungs. The end result is difficulty breathing, such as fast breathing, wheezing, or crackles when inhaling. While this type of outcome can happen in people of any age, the small size of an infant's airways compounds the issue, making the infection particularly dangerous.

A bit of history

RSV was identified in 1956 and its danger for young infants was quickly realized. Following the success of Jonas Salk's inactivated polio vaccine in the mid-1950s, an RSV vaccine made in a similar way was tested in the early 1960s. Unfortunately, this vaccine had tragic consequences. Recipients were not only left unprotected, they were also more susceptible to severe disease when subsequently infected. This is a phenomenon known as antibody-dependent enhancement (ADE). Sadly, two children vaccinated during that vaccine trial died when they were later infected with RSV. As soon as the issues with this vaccine were realized, work was halted. Scientists studying the virus and the doomed vaccine were able to learn more about what went wrong and use that knowledge to inform future efforts related to RSV vaccine development.

However, in the more immediate aftermath of the tragedy, efforts turned to not only learning more about what happened but also figuring out alternative ways to protect babies from RSV. Two alternatives that were explored: treatment with antiviral medications and introduction of antibodies.

Treatment with antiviral medications

Unfortunately, the use of antiviral medications to treat RSV in young infants has met with limited success. Only one medication, called ribavirin, has been approved for this use. It has been available since 1985, but it is most often used in combination with other clinical approaches, and its success has been limited. For example, ribavirin is of little value once a patient has been hospitalized.

Introduction of antibodies

While vaccines cause a person to generate their own immunity, called *active immunity*, another approach is to leverage *passive immunity*. In a situation of passive immunity, the individual is protected by antibodies generated by someone else. One common example is the antibodies passed to an infant from their mother either *in utero* (across the placenta) or after birth (in breast milk). Another example is when we give antibodies isolated from the blood of a person who previously survived an infection or poison, such as following a snake bite (antivenin or antivenom) or during an outbreak, such as the famous Iditarod race when diphtheria antibodies were raced from Nenana to Nome, Alaska, or during COVID-19 before we had other treatments or preventions available.

One of the difficulties of giving antibodies from another person is consistency of dosing because people have different levels of antibodies in their blood. So, often today's antibody treatments are made by figuring out which antibodies are most effective and then making large quantities of them in the lab. This type of work does not require biological agents because antibodies are proteins, so they are made with chemical building blocks called amino acids. When a dose is made of a single type of antibody, it is called a monoclonal antibody preparation (because all of the antibodies are the product of one B cell clone). By the late 1990s, two monoclonal antibody preparations against RSV were available. One, called palivizumab (or Synagis®), was found to be 50 times more effective than the other (RSV-IVIG or RespiGam™). By 2003, RespiGam was discontinued and until this year, palivizumab was the best tool in the fight to protect babies against RSV.

Unfortunately, use of palivizumab is not without issues. First, passive immunity of any kind is short-lived, so it will protect the recipient for a period of time, but not forever. In the case of palivizumab, protection lasts for about one month, so babies getting this preparation need to get a dose every month during RSV season, which generally lasts from late fall until early spring in the U.S. Second, palivizumab is expensive, so it is only recommended for use in the highest-risk babies. Because of both the price and the need for monthly dosing, palivizumab could never be a routine option for protecting all babies.

For these reasons, scientists continued working to develop better tools to protect babies against RSV, and in the fall of 2023, that work came to fruition.

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Today: A bit of hope

In 2023, two additional tools for protecting babies have been approved for use. Both are new, so we will continue to learn about them, but they provide hope.

A new monoclonal antibody for babies: Nirsevimab

Like palivizumab, nirsevimab (Beyfortus™) is a monoclonal antibody preparation; however, it solves the two concerns related to palivizumab. First, it is longer lasting with a single dose protecting babies through an entire RSV season. Second, because only one dose is needed, it is significantly less expensive. For these reasons the CDC recently recommended that every baby up to 8 months of age get one dose in the fall before RSV season begins and some 8- to 19-month-old babies get it during their second RSV season if they are at high risk for severe RSV.

Unlike traditional vaccines, which induce active immunity and, therefore, do not rely on weight, this preparation is more like a medication in that the appropriate dose of antibodies must be based on weight. As such, the recommendations for babies in the first year of life are:

- One dose containing 50 milligrams of antibody if they weigh less than 11 pounds
- One dose containing 100 milligrams of antibody if they weigh 11 or more pounds

Babies 8 and 19 months of age who should get nirsevimab during their second RSV season include those with:

- Chronic lung disease resulting from prematurity who needed medical support during the six months prior to the start of their second RSV season
- Severely compromised immune systems
- Cystic fibrosis that includes severe lung disease or who are in the lower tenth percentile for their weight compared with other babies of the same length
- American Indian or Alaskan Native backgrounds

These babies require two doses of 100 milligrams administered at the same time in different locations.

Nirsevimab should be given right before or around the start of RSV season, and babies can get it at the same time that they are getting their recommended childhood vaccines.

This year, as healthcare providers work to include this new option in their practice, they may not all have nirsevimab available or they may not have it available at the same time as other providers. If you have a baby recommended to get this preparation, check with their healthcare provider to see if they will have nirsevimab this season.

A vaccine for pregnant people: Abrysvo™

The second new tool is a vaccine; however, it too relies on passive immunity because the main beneficiary of the immunity is the baby, not the mother. Although pregnant people are at greater risk for severe infection than their nonpregnant counterparts if they get COVID-19 or influenza, the same is not true of RSV. Pregnancy does not increase one's risk for severe RSV. Instead, the pregnant person is recommended to get the RSV vaccine so that the unborn baby can benefit from the antibodies induced through vaccination.

For this reason, like with the Tdap vaccine, Abrysvo is recommended to be given during a specific period of gestation. For Abrysvo that time frame is 32 to 36 weeks gestation.

This vaccine is the same as one of two recently approved to prevent RSV in the elderly; however, importantly, during the clinical trials, pregnant people who got the vaccine were slightly more likely to deliver their babies early compared with those in the control group. The number of occurrences of early delivery during the clinical trials were not sufficient to know for sure if the vaccine induces early labor. However, because of this possibility, the vaccine was recommended to be given only during the four-week period of 32 to 36 weeks gestation, rather than as it was tested (to be given between 24 to 36 weeks gestation). This later and shorter period is meant to decrease the likelihood of preterm birth if it is later found to be causally associated with receipt of the vaccine. This situation will be closely monitored as more doses are given during pregnancy.

Over the next few RSV seasons, we will learn a lot about how effective these new tools are at decreasing the disease and suffering caused by RSV, and we may see even more tools added to the toolbox for prevention of RSV.

Stay tuned!

Resources

- RSV: What Is It?
- Preventing RSV in Babies: A Scientific Milestone
- Respiratory Syncytial Virus (RSV) Vaccine and Monoclonal Antibody
- A New Vaccine ... and It's for Adults! Find Out More About RSV and the Vaccine

For links to resources in the Feature Article, please visit bit.ly/Oct2023FA.

DR. HANDY'S CORNER – WHY HAS MY CHILD BEEN SICK SINCE STARTING DAY CARE?

Are your children in day care? School? Have you felt like when they first started, they were always sick? In this short video, Dr. Handy talks about why your perceptions were probably spot on. Hear what she has to say about children in new social settings, like day care and even college.

Watch the video: *bit.ly/sick-daycare.*

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- Student essay contest winners announced
- Colleges and vaccines
- Questions about COVID-19 vaccine for fall 2023?

Go to bit.ly/Oct2023NN.

TRIVIA ANSWER

The correct answer is A. Because influenza is caused by a virus, it cannot be treated with antibiotics. Antiviral medicines, however, may work.

Go to vaccine.chop.edu/trivia to play Just the Vax, the Vaccine Education Center's trivia game, where you can find this question and others like it.

Children's Hospital of Philadelphia
Vaccine Education Center

Contact us: contactPACK@chop.edu

Learn more: vaccine.chop.edu/parents