New RSV vaccine may prevent illness in infants, seniors

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An RSV vaccine developed by Pfizer provides safe and effective

protection in both seniors and newborns, clinical trial results show.

The vaccine is 86% effective in protecting older adults against RSV infections severe enough to cause three or more symptoms, according to findings published April 5 in the *New England Journal of Medicine*.

And the same vaccine is 82% effective in protecting newborns from hospitalization with a respiratory infection if an expectant mother receives the jab in her second or third trimester, says a companion report in the journal.

The Pfizer vaccine is on track to be approved this year for use in seniors and pregnant women, said Dr. Bill Gruber, senior vice president and head of clinical vaccine research and development for Pfizer in New York City.

"For me personally, this is a dream come true," said Gruber, a co-author of both *NEJM* clinical trial reports. "I've been working in this field looking for a major advance in RSV for probably 40 years. This is a really fantastic advance, I think, for world health."

Respiratory syncytial virus (RSV) typically is a mild respiratory virus that causes the sniffles in most people.

But RSV is the most common cause of bronchiolitis and pneumonia in children under age 1 in the United States, according to the U.S. Centers for Disease Control and Prevention.

Each year, between 58,000 and 80,000 children under age 5 are hospitalized due to an RSV infection, the CDC says.

RSV also poses a risk to older adults, particularly those in poor health. The CDC estimates that 60,000 to 160,000 U.S. seniors are hospitalized

and between 6,000 and 10,000 die from RSV infection annually.

"RSV is the last of the major respiratory viruses for which we don't yet have a licensed vaccine, and we appear to be on the threshold of that," said Dr. William Schaffner, medical director of the National Foundation for Infectious Diseases in Bethesda, Md.

RSV hit the U.S. particularly hard during the last cold and flu season, as pandemic social isolation restrictions were lifted. The virus tore through populations of young children who had never been exposed to it, and, therefore, had weak immunity against it.

A key advisory committee for the U.S. Food and Drug Administration recommended approval of the Pfizer vaccine for seniors last week, based on these clinical trial results. The committee also gave its nod to a competing RSV vaccine developed by GlaxoSmithKline.

Pfizer expects an FDA decision on the RSV vaccine for seniors by May and for pregnant women by August, company officials said.

The Pfizer and GSK vaccines both target RSV's F protein, which the virus uses to attach to and invade human cells.

Failed tries lead to breakthrough

Attempts to create an RSV vaccine in the 1960s failed. That earlier vaccine caused a phenomenon called antibody-dependent enhancement, where the antibodies produced by a vaccine actually make a virus more virulent and harmful. Two children died in the clinical trial.

But in the early 2010s, U.S. National Institutes of Health researchers figured out that the F protein changes shape after it binds with a human cell.

To create a protective immune response, an RSV vaccine would need to target the F protein's pre-infection shape, the researchers reported.

This breakthrough prompted a race among Pfizer, GSK and other pharmaceutical companies to craft a safe and effective RSV vaccine.

For the clinical trial in older adults, researchers randomly assigned more than 34,000 people 60 or older to receive either the Pfizer RSV vaccine or a placebo.

Results show that the vaccine was 86% effective in preventing severe cases of RSV involving three or more symptoms, and 67% effective in stopping an RSV infection involving at least two symptoms.

"They weren't able to show efficacy against hospitalization, which you are most interested in against severe disease, but there was higher efficacy against three symptoms as opposed to two symptoms, which may serve as a proxy for more severe disease," said Dr. Ruth Karron, a professor of epidemiology at Johns Hopkins University's Bloomberg School of Public Health in Baltimore.

Gruber also reflected on its effectiveness in counteracting severe disease.

"The likelihood is if you're protecting against three-plus symptoms—which is on the cusp of putting people into the hospital—your efficacy against severe disease is going to be as good or higher," he said.

The clinical trial in pregnant women involved more than 7,300 females randomly receiving either the Pfizer vaccine or a placebo. Their newborns were then tracked to see if maternal antibodies produced by the vaccine conferred any protection to the babies.

The vaccine provided nearly 82% protection against severe lower respiratory tract infections that required hospitalization within 90 days of birth, results showed.

Gruber said he's hopeful that the vaccine will be approved for use in pregnancy by the end of summer, so that babies born during the next cold and flu season will have some protection against RSV.

"You need to vaccinate the woman while she's still pregnant in order to allow the passive transfer of antibody to provide protection for babies," Gruber said. "The sooner that approval occurs, the more women can be vaccinated and potentially protect their infants."

Safety will continue to be evaluated

The vaccine had acceptable safety and side effect profiles in both seniors and pregnant women, Karron noted in an *NEJM* editorial accompanying the two clinical trials.

However, Gruber said Pfizer will continue to track vaccinated people going forward, both for side effects and to see how long the vaccine's protection lasts.

"We have a study underway and we hope to have results later this year about the potential for protection into a second season," Gruber said. "I think you can envision one of two scenarios—either, yes, there is durability that lasts more than one season or, much like influenza vaccine, individuals need to be vaccinated annually. And so we're looking at both of those."

The next important step will be to convince pregnant women that it's in the best interest of their newborn to get vaccinated, Karron said.

She noted that only around 60% of expectant mothers in the United States get the influenza or the tetanus-diphtheria-pertussis vaccine, even though both vaccines are recommended to protect newborns during their first months of life.

"We have a long way to go in terms of advocacy around vaccination in pregnancy," Karron said.

More information: The U.S. Centers for Disease Control and Prevention has more about respiratory syncytial virus (RSV).

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Ruth A. Karron, RSV Illness in the Young and the Old—The Beginning of the End?, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMe2302646 , www.nejm.org/doi/full/10.1056/NEJMe2302646