Two NIAID Studies Highlight COVID-19 Nasal Vaccine Potential

A single vaccine dose delivered to nose aims to protect children and adults against COVID.

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Roughly two years ago, when people began receiving shots in the arm of mRNA COVID-19 vaccines, scientists said that their work would continue, striving to improve COVID-19 vaccine effectiveness and delivery. Two recent NIAID studies reinforce that mission.

As the SARS-CoV-2 virus has evolved, so has scientists' knowledge of how to manage its spread and severity. Importantly, scientists have learned that the virus first infects the nose and throat before sometimes spreading to the lungs, where severe COVID-19 can develop. But the nose and throat are difficult destinations for the SARS-CoV-2 antibodies that develop in the blood after a vaccine is injected into the arm or leg – making those hard-to-reach areas targets for better vaccines.

The two recent NIAID studies show how one dose of a nasal vaccine against SARS-CoV-2 could protect children and adults. The first study, published June 28 in NPJ Vaccines, used a live vaccine based on a weakened avian paramyxovirus type 3 (APMV3). That vaccine design had been part of research for Ebola and H5N1 influenza viruses when the COVID-19 pandemic began. The scientists, using an updated version of the vaccine designed for SARS-CoV-2, successfully protected hamsters from COVID-19. They next plan to test the vaccine in rhesus macaques.

The second study, published December 8 in Cell, uses a weakened version of a bovine/human parainfluenza virus (B/HPIV3) to deliver the SARS-CoV-2 spike protein into the respiratory tract. In that project, the scientists used the vaccine to protect rhesus macaques from COVID-19. Their vaccine produced a strong immune response to the SARS-CoV-2 spike protein in the respiratory tract, protecting the areas where the virus first infects people. The scientists also noted two additional important findings for protection against severe COVID-19: The vaccine produced strong antibody and white blood cell responses to the spike protein in the blood and lower airways. They plan to proceed to a Phase 1 clinical trial testing the vaccine as a nasal spray in volunteers. Prior to the COVID-19 pandemic, a version of the B/HPIV3 vaccine (without the SARS-CoV-2 spike) had been in studies to prevent respiratory illness caused by human parainfluenza virus type 3 (HPIV3) in young children.

The APMV3 vaccine is being targeted for children and adults, while B/HPIV3 is being targeted for

children. This is because most people of all ages have not been exposed to APMV3 and therefore would not have pre-existing immunity – meaning the vaccine should be broadly effective. For B/HPIV3, most people older than 5 have been exposed to HPIV3 and have likely developed immunity – but most children under age 5 have not – meaning that vaccine design should be ideal for them. In young children, this will be a “two for one” nasal spray: the B/HPIV3/SARS-CoV-2 vaccine is expected to protect young children not only against COVID-19, but also against HPIV3. In the Phase 1 clinical trial, researchers hope to learn if the SARS-CoV-2 S protein delivered by the B/HPIV3 nasal spray vaccine will also work in adults, despite their pre-existing immunity to HPIV3.

There are four types of human parainfluenza viruses, which commonly cause upper and lower respiratory illness in infants, young children, older adults, and people with weakened immune systems. Among the parainfluenza viruses, HPIV3 is responsible for the greatest burden of disease and is more often associated with lower respiratory issues. There is no vaccine or treatment for human parainfluenza viruses; most people recover on their own. In young children disease can progress to serious conditions like bronchiolitis, bronchitis and pneumonia, which also are found in disease caused by respiratory syncytial virus (RSV). These cases sometimes require hospitalization.

Avian paramyxoviruses are found in domestic and wild birds, with 21 types identified. APMV type 1, better known as Newcastle disease virus, is the most common. Newcastle disease is rare in people, mainly found in those who handle birds and usually causing no or mild illness. In the vaccine project, rather than using the Newcastle type – which is a disease threat to poultry – the scientists used a type 3 virus originally identified in parakeets in The Netherlands. Avian paramyxovirus type 3 does not appear to be a significant natural pathogen of poultry.

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