

# Study indicates vaccines targeting nose, mouth may be key to controlling spread of COVID-19

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The lightning-fast development of COVID-19 vaccines just months after the virus appeared was a triumph of modern science and saved millions

of lives. But for all the good they did in reducing illnesses and deaths, the shots were unable to end the pandemic because of one notable weakness: They couldn't stop the spread of the virus.

A new study by researchers at Washington University School of Medicine in St. Louis indicates that next-generation vaccines that target the virus's points of entry—the nose and mouth—may be able to do what traditional shots cannot: contain the spread of respiratory infections and prevent [transmission](#).

Using a [nasal COVID-19 vaccine](#) based on Washington University technology, approved for use in India and licensed to Ocugen for further development in the U.S., the researchers showed that vaccinated hamsters that developed infections did not pass the virus on to others, breaking the cycle of transmission. In contrast, an approved COVID-19 [vaccine](#) that is injected failed to prevent the spread of the virus.

The findings, [published](#) July 31 in *Science Advances*, provide further evidence that so-called mucosal vaccines sprayed into the nose or dropped into the mouth may be the key to controlling respiratory infections such as influenza and COVID-19 that continue to circulate and cause significant illness and death.

"To prevent transmission, you need to keep the amount of virus in the upper airways low," said senior author Jacco Boon, Ph.D., a professor of medicine, of molecular microbiology and of pathology & immunology.

"The less virus that is there to begin with, the less likely you are to infect someone else if you cough or sneeze or even just breathe on them. This study shows that mucosal vaccines are superior to injected vaccines in terms of limiting viral replication in the upper airways and preventing spread to the next individual. In an epidemic or pandemic situation, this is the kind of vaccine you're going to want."

Developing vaccines that can control virus levels in the nose has proven challenging. Viruses such as [influenza virus](#), SARS-CoV-2 (the virus that causes COVID-19) and respiratory syncytial virus (RSV) multiply rapidly in the nose and spread from person to person within a few days of initial exposure.

Traditional injectable vaccines generate immune responses that can take a week to build to full strength and are much less potent in the nose than in the bloodstream, leaving the nose relatively unprotected against a fast-multiplying, fast-spreading virus.

In principle, a vaccine sprayed or dropped directly into the nose or mouth could limit viral reproduction and thereby reduce transmission by eliciting an [immune response](#) right where it's needed most. But gathering evidence that mucosal vaccines actually do reduce transmission has proven tricky.

Animal models of transmission are not well-established, and tracking person-to-person transmission is fiendishly complicated, given the number and variety of encounters a typical person has on any given day.

For this study, Boon and colleagues developed and validated a model for community transmission using hamsters and then used it to assess the effect of mucosal vaccination on the spread of SARS-CoV-2. (Unlike mice, hamsters are naturally susceptible to infection with SARS-CoV-2, making them the ideal laboratory animals for a transmission study.)

The researchers immunized groups of hamsters with laboratory versions of approved COVID-19 vaccines: the nasal iNCOVACC used in India or the injected Pfizer vaccine.

For comparison, some hamsters were not immunized. After giving the vaccinated hamsters a few weeks for their immune responses to fully

mature, the researchers infected other hamsters with SARS-CoV-2 and then placed the immunized hamsters with the infected hamsters for eight hours. This first step of the experiment mimics the experience of vaccinated people who are exposed to a person with COVID-19.

After spending eight hours rubbing shoulders with infected hamsters, most of the vaccinated animals became infected. Virus was found in the noses and lungs of 12 of 14 (86%) hamsters that had received the nasal vaccine, and 15 of 16 (94%) hamsters that had received the injected vaccine.

Importantly, while most animals in both groups were infected, they weren't infected to the same degree. Hamsters that had been nasally immunized had virus levels in the airways 100 to 100,000 times lower than those that had received the shot or had not been vaccinated.

The study did not assess the animals' health, but previous studies have shown that both vaccines reduce the likelihood of severe illness and death from COVID-19.

The second step of the experiment yielded even more striking results. The researchers took vaccinated hamsters that subsequently developed infections and placed them with healthy vaccinated and unvaccinated hamsters for eight hours to model transmission of virus from a vaccinated person to others.

None of the hamsters that were exposed to nasally vaccinated hamsters became infected, regardless of whether the recipient hamster had been vaccinated or not. In contrast, roughly half of the hamsters that were exposed to [hamsters](#) vaccinated by injection became infected—again, regardless of the recipient's immunization status. In other words, vaccination through the nose—but not by injection—broke the cycle of transmission.

These data, Boon said, could be important as the world prepares for the possibility that [avian influenza](#), currently causing an outbreak in dairy cows, might adapt to humans and trigger a flu epidemic.

An injectable vaccine for avian influenza already exists, and a team of researchers at Washington University is working toward a nasal vaccine for avian influenza. That team includes Boon and co-author Michael S. Diamond, MD, Ph.D., the Herbert S. Gasser Professor of Medicine and one of the inventors of the nasal vaccine technology used in this paper.

"Mucosal vaccines are the future of vaccines for respiratory infections," Boon said.

"Historically, developing such vaccines has been challenging. There's still so much we don't know about the kind of immune response we need and how to elicit it. I think we're going to see a lot of very exciting research in the next few years that could lead to big improvements in vaccines for respiratory infections."

**More information:** Tamarand Darling et al, Mucosal immunization with ChAd-SARS-CoV-2-S prevents sequential transmission of SARS-CoV-2 to unvaccinated hamsters, *Science Advances* (2024). [DOI: 10.1126/sciadv.adp1290](https://doi.org/10.1126/sciadv.adp1290). [www.science.org/doi/10.1126/sciadv.adp1290](https://www.science.org/doi/10.1126/sciadv.adp1290)

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