

# Next generation COVID-19 immunization strategies could deliver vaccine directly to the respiratory tract

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The global COVID-19 vaccination campaign saved an estimated 20 million lives. However, while current COVID-19 vaccines provide

protection against developing severe disease, they do little to prevent infection and transmission.

Findings published in the journal [Nature](#) by physician-scientists at Beth Israel Deaconess Medical Center (BIDMC) and colleagues suggest that it may be possible to improve protection against COVID-19 by delivering the vaccine directly to the [respiratory tract](#)—the primary site of entry in SARS-CoV-2 infection.

"The failure of the current generation of SARS-CoV-2 vaccines delivered by the intramuscular (IM) route to block infection likely relates to their inability to induce robust mucosal immune responses at the portal of entry," said corresponding author Dan H. Barouch, MD, Ph.D., director of the Center for Vaccine and Virology Research at BIDMC.

"In this study, we demonstrated that novel immunization strategies can markedly increase mucosal immunity in non-human primates and improve protective efficacy against a mucosal virus challenge."

Barouch and colleagues primed 40 adult [rhesus macaques](#) with the Ad26 COVID-19 vaccine (Janssen/Johnson & Johnson) administered intramuscularly (IM)—like a shot in the arm adults typically receive. Approximately a year later, the animals received a booster.

Three groups received either a dose of the Ad26 vaccine via the IM route, the intranasal (IN) route (delivered via [nasal spray](#)) or the intratracheal (IT) route (delivered by nebulizer or inhaler). A fourth group received a dose of the bivalent mRNA [vaccine](#) (Pfizer-BioNTech) by the IN route. A sham group received no boosters.

When the macaques were later challenged with a high dose of the virus, the investigators sampled the animals' blood, nasal, and lung fluids to

monitor their immune responses. They found that the Ad26 booster administered via the IT route provided near complete protection against a high-dose SARS-CoV-2 challenge and induced greater mucosal immunity than it did via the IN or IM route.

In contrast, mRNA IN boosting proved ineffective, suggesting that improved formulations will likely be required for effective mucosal delivery of mRNA vaccines.

"Taken together, these data demonstrate that novel immunization strategies can markedly increase mucosal immunity in [non-human primates](#) and improve protective efficacy against a mucosal virus challenge," said Barouch. "These data suggest the feasibility of developing vaccines that block respiratory viral infections."

**More information:** McMahan, K. et al, Mucosal boosting enhances vaccine protection against SARS-CoV-2 in macaques, *Nature* (2023).  
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