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Inhaled vaccines aim to fight coronavirus at its point of attack

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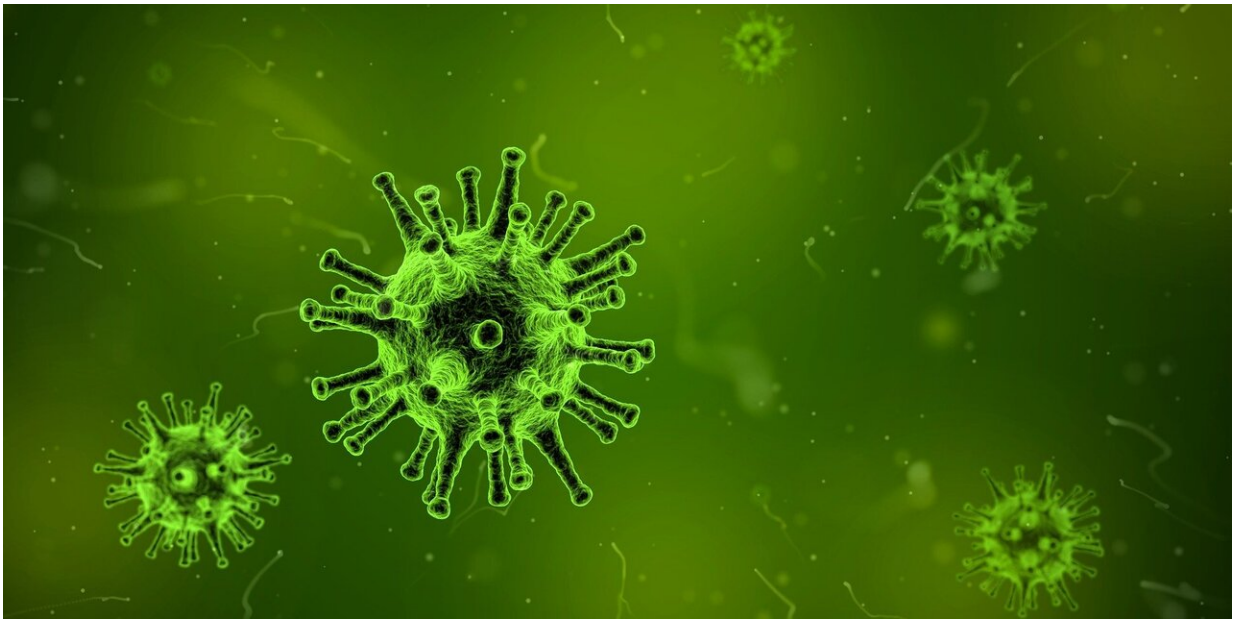

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The COVID-19 vaccines closest to the finish line are designed to be injected into the arm. Researchers are looking at whether they can get better protection from inoculations that fight the virus at its point of attack - the nose and mouth.

Most vaccines in human testing require two shots for effectiveness, and developers still aren't even sure if they'll prevent infections. Scientists

are hoping to generate superior immune responses with inhaled vaccines that directly target the airway cells the virus invades.

An alternative to conventional jabs, sprayed and inhaled immunizations under development in the U.S., Britain and Hong Kong could play an important role in helping society escape restrictions that have upended economies and everyday life. Among their goals is to prevent the pathogen from growing in the nose, a point from which it can spread to the rest of the body, and to other people.

"Local immunity matters," said Frances Lund, a University of Alabama at Birmingham immunologist working with biotech Altimmune Inc. on an early-stage nasal inoculation. "The vaccines that can be delivered to generate that will have some advantages over vaccines that are delivered systemically."

Most early vaccine developers focused on a familiar route - injections - seen as the fastest to protecting the world from disease. Inhaled vaccine makers are counting on some of the unique features of the lungs, nose and throat, which are lined with mucosa. This tissue contains high levels of immune proteins, called IgA, that give better protection against respiratory viruses.

Activating these immune weapons, they theorize, can protect areas deeper in the lungs where the SARS-CoV-2 does the most damage. They also may improve vaccines' chances of blocking transmission.

"The first generation of vaccines are probably going to protect a lot of people," said Michael Diamond, an infectious disease specialist at Washington University in St. Louis. "But I think it's the second- and third-generation vaccines - and maybe intranasal vaccines will be a key component of this - that ultimately are going to be necessary. Otherwise, we'll continue to have community transmission."

In a study of mice in August, Diamond and his team found that delivering an experimental vaccine via the nose created a strong immune response throughout the body; the approach was especially effective in the nose and respiratory tract, preventing infection from taking hold. India's Bharat Biotech and St. Louis-based Precision Virologics last month obtained rights to the single-dose technology.

Vaccines that are sprayed into the nose or inhaled may hold other practical benefits. They don't require needles, may not need to be stored and shipped at low temperatures and can reduce the need for health workers to administer them.

"When you're thinking about trying to deliver that across the world, if you don't need to have an injectable vaccine, your compliance goes up because people don't like getting shots," according to Lund, the Alabama-based researcher. "But secondly, the level of expertise needed to administer that vaccine is significantly different."

Altimmune, based in Gaithersburg, Maryland, plans to enter human testing with a nasal vaccine in the fourth quarter after positive studies in mice. Scientists at the University of Oxford, where a promising shot under development at AstraZeneca Plc was designed, and Imperial College London are also planning studies of slightly different inhaled vaccines.

The experimental immunizations in Britain would be delivered through a mouthpiece in an aerosol, similar to some asthma therapies. Imperial researchers point to evidence that delivering influenza vaccines via a nasal spray can protect people against illness and help reduce transmission; they're keen to explore if that's also the case for SARS-CoV-2. AstraZeneca makes the FluMist nasal spray vaccine.

Data from studies of the inhaled Oxford vaccine could come early in the

new year, followed by Imperial results in the second quarter, according to Robin Shattock, an infectious disease specialist at Imperial College.

"We don't know whether it will work well, but if it does, then it could be very important," he said in an interview.

Imperial College in recent months has been advancing studies of a COVID-19 vaccine using RNA technology that would be delivered via conventional shots and plans to expand its trials to 20,000 people by year-end. Oxford, one of the front-runners in the global quest for an inoculation, is in the final stage of tests for a shot that uses a harmless virus to carry the genetic material of the pathogen into cells to generate an immune response. Both techniques may be conducive to inhalation, Shattock said.

"This is a virus that's transmitted through your respiratory tract, so if you want a vaccine that will really prevent infection and onward transmission you want to have an antibody response in your nose, in your lungs," Shattock said. "The most efficient way to induce that is by inoculating through that route."

Researchers in Hong Kong are aiming for an intranasal vaccine that would simultaneously offer influenza and COVID-19 protection. The first phase of human tests will start next month, said Yuen Kwok-Yung, chair of infectious diseases in the University of Hong Kong's department of microbiology.

The ambition is to come up with the "vaccine of choice," as the world looks to build on the first wave of products, he said.

Questions about the durability of nasal vaccines have yet to be resolved, and they're at an early stage. Despite the advantages, the delivery devices are also more complex, according to Nick Jackson, head of programs

and technology at the Coalition for Epidemic Preparedness Innovations.

"A needle and syringe work very well," he said.

Still, researchers said targeting the airways may pay off down the road. Oslo-based CEPI has provided funding to the Hong Kong project and is open to further investments in vaccines that are taking unconventional approaches as part of an effort to supply billions of doses to every corner of the world, Jackson said.

"Whether it's our vaccine or another one that goes through an intransasal route that actually is successful at disrupting transmission and disrupting the pandemic, I take my hat off," Diamond said. "If we contribute by compelling or nudging these companies to think about an alternative route for what may be a successful platform, then we've done our job."