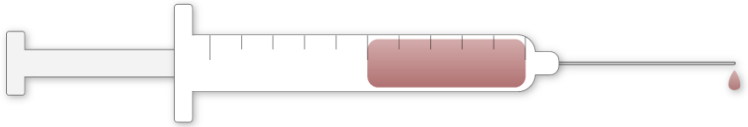
Health

# How the Oxford-AstraZeneca Vaccine Works

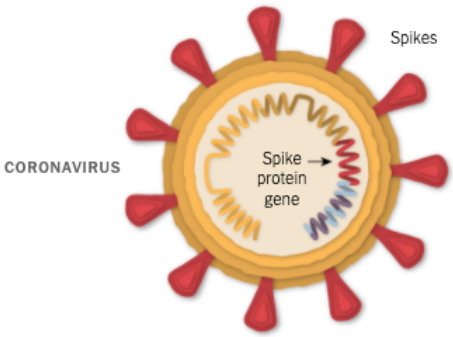
By Jonathan Corum and Carl ZimmerUpdated Jan. 4, 2021



The University of Oxford partnered with the British-Swedish company AstraZeneca to develop and test a coronavirus vaccine known as **ChAdOx1 nCoV-19** or **AZD1222**. A clinical trial revealed the vaccine was up to 90 percent effective, depending on the initial dosage. Despite some uncertainty over trial results, Britain authorized the vaccine for emergency use in December, and India authorized a version of the vaccine called **Covishield** on Jan. 3.

## A Piece of the Coronavirus

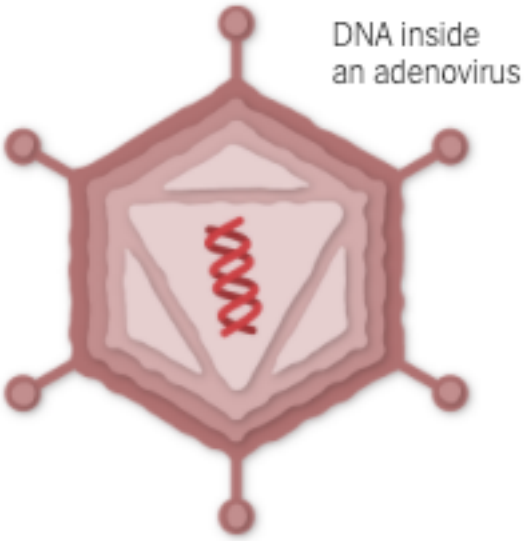
The SARS-CoV-2 virus is studded with proteins that it uses to enter human cells. These so-called spike proteins make a tempting target for potential vaccines and treatments.




The Oxford-AstraZeneca vaccine is based on the virus's genetic instructions for building the spike protein. But unlike the Pfizer-BioNTech and Moderna vaccines, which store the instructions in single-stranded RNA, the Oxford vaccine uses double-stranded DNA.

## DNA Inside an Adenovirus

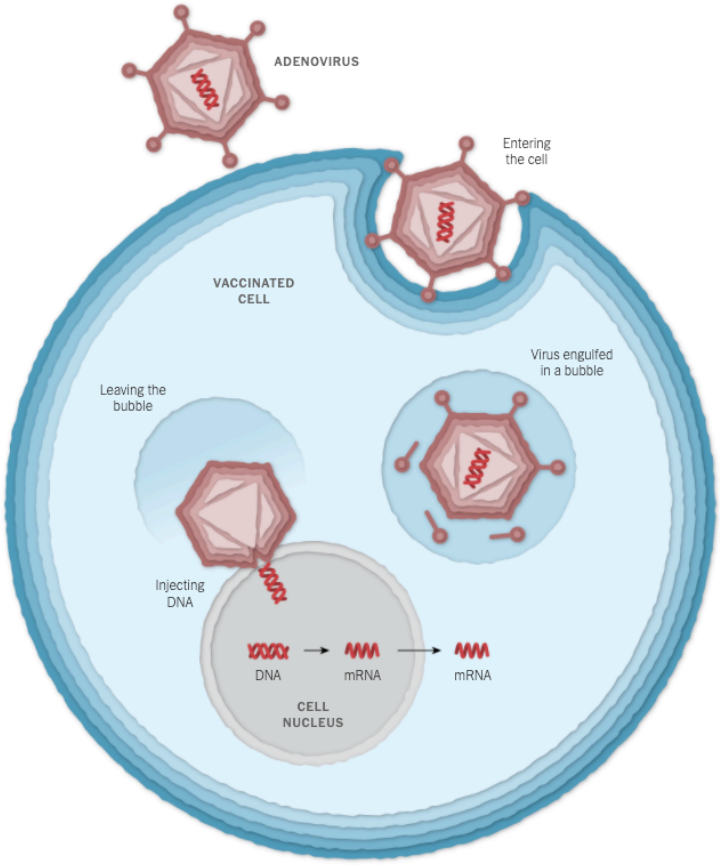
The researchers added the gene for the coronavirus spike protein to another virus called an adenovirus. Adenoviruses are common viruses that typically cause colds or flu-like symptoms. The Oxford-AstraZeneca team used a modified version of a chimpanzee adenovirus, known as ChAdOx1. It can enter cells, but it can't replicate inside them.




AZD1222 comes out of decades of research on adenovirus-based vaccines. In July, the first one was approved for general use — a vaccine for Ebola, made by Johnson & Johnson. Advanced clinical trials are underway for other diseases, including H.I.V. and Zika.

The Oxford-AstraZeneca vaccine for Covid-19 is more rugged than the mRNA vaccines from Pfizer and Moderna. DNA is not as fragile as RNA, and the adenovirus's tough protein coat helps protect the genetic material inside. As a result, the Oxford vaccine doesn't have to stay frozen. The vaccine is expected to last for at least six months when refrigerated at 38–46°F (2–8°C).

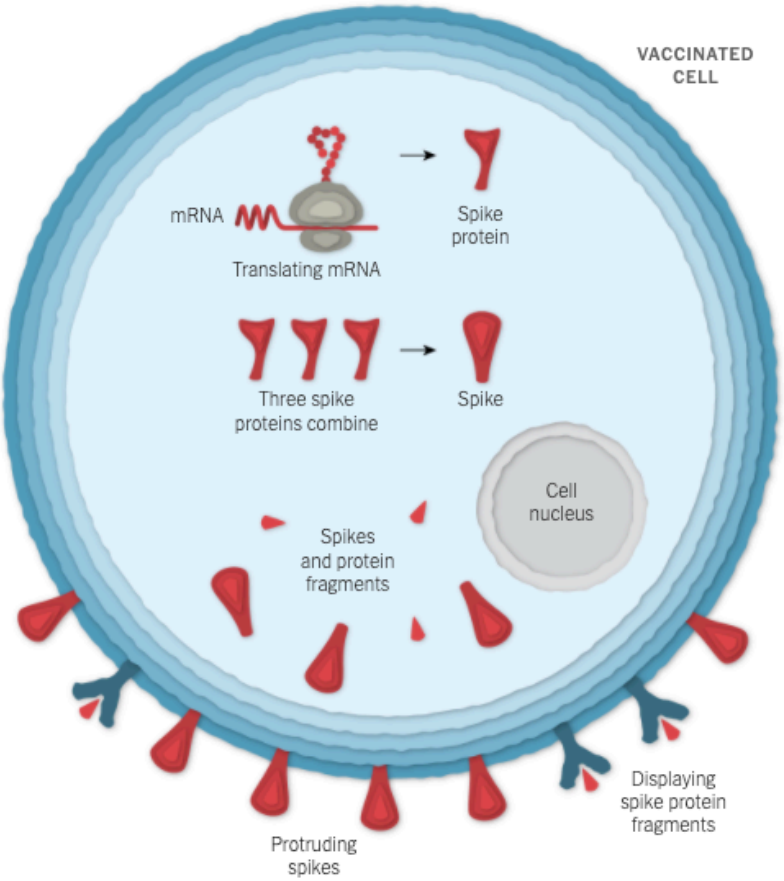
**Entering a Cell**




After the vaccine is injected into a person's arm, the adenoviruses bump into cells and latch onto proteins on their surface. The cell engulfs the virus in a bubble and pulls it inside. Once inside, the adenovirus escapes from the bubble and travels to the nucleus, the chamber where the cell's DNA is stored.

The adenovirus pushes its DNA into the nucleus. The adenovirus is engineered so it can't make copies of itself, but the gene for the coronavirus spike protein can be read by the cell and copied into a molecule called messenger RNA, or mRNA.

## Building Spike Proteins

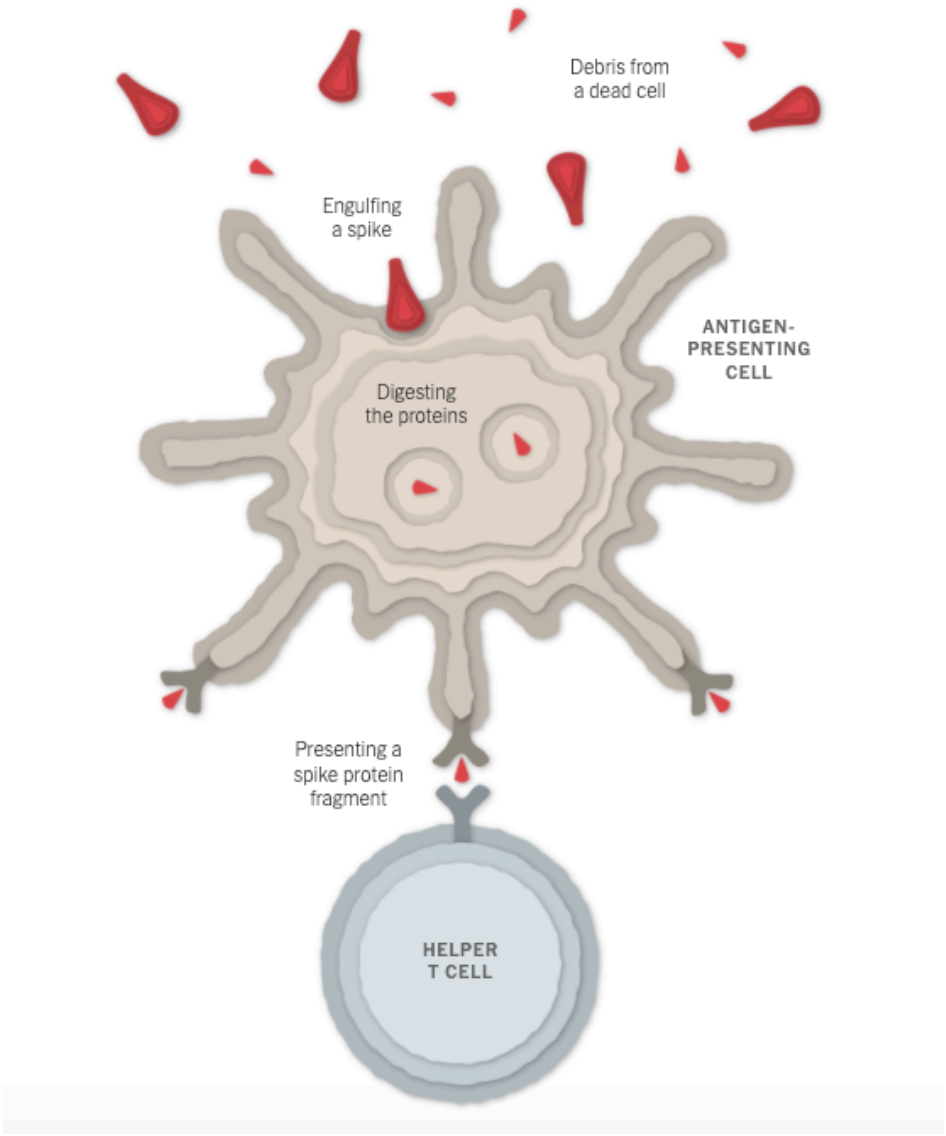



The mRNA leaves the nucleus, and the cell's molecules read its sequence and begin assembling spike proteins.

Some of the spike proteins produced by the cell form spikes that migrate to its surface and stick out their tips. The vaccinated cells also break up some of the proteins into fragments, which they present on their surface. These protruding spikes and spike protein fragments can then be recognized by the immune system.

The adenovirus also provokes the immune system by switching on the cell's alarm systems. The cell sends out warning signals to activate immune cells nearby. By raising this alarm, the Oxford-AstraZeneca vaccine causes the immune system to react more strongly to the spike proteins.

# Spotting the Intruder

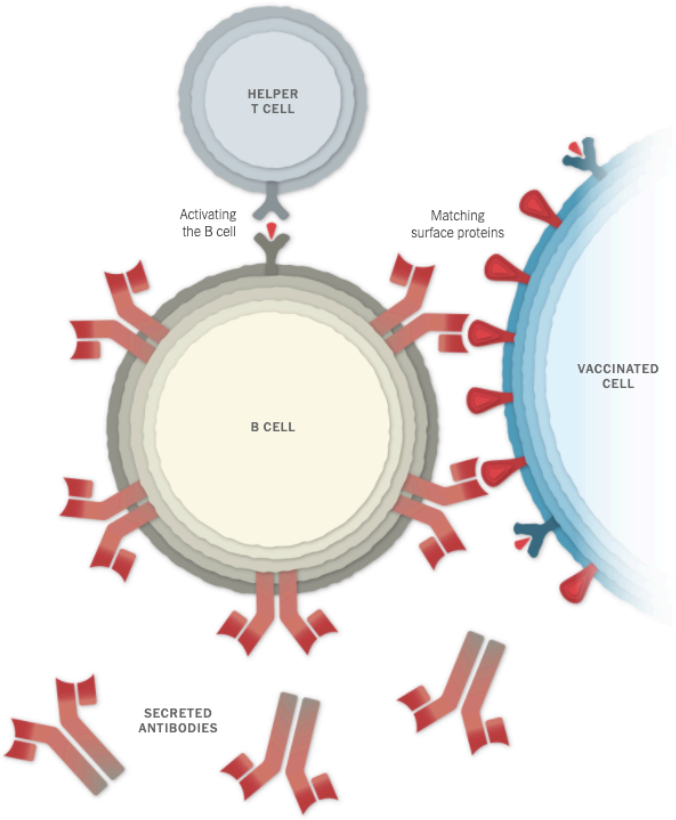



When a vaccinated cell dies, the debris contains spike proteins and protein fragments that can then be taken up by a type of immune cell called an antigen-presenting cell.

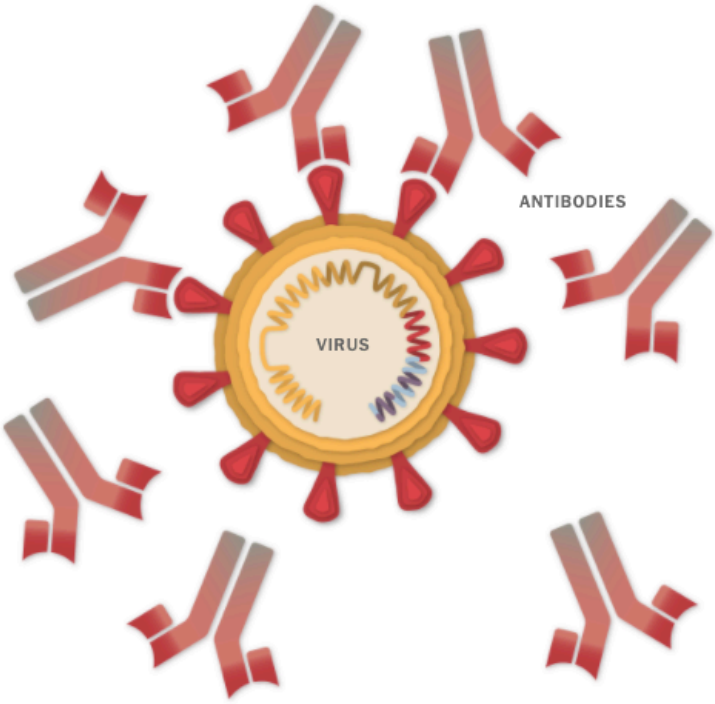
The cell presents fragments of the spike protein on its surface. When other cells called helper T cells detect these fragments, the helper T cells can raise the alarm and help marshal other immune cells to fight the infection.

## Making Antibodies

Other immune cells, called B cells, may bump into the coronavirus spikes on the surface of vaccinated cells, or free-floating spike protein fragments. A few of the B cells may be able to lock onto the spike proteins. If these B cells are then activated by helper T cells, they will start to proliferate and pour out antibodies that target the spike protein.

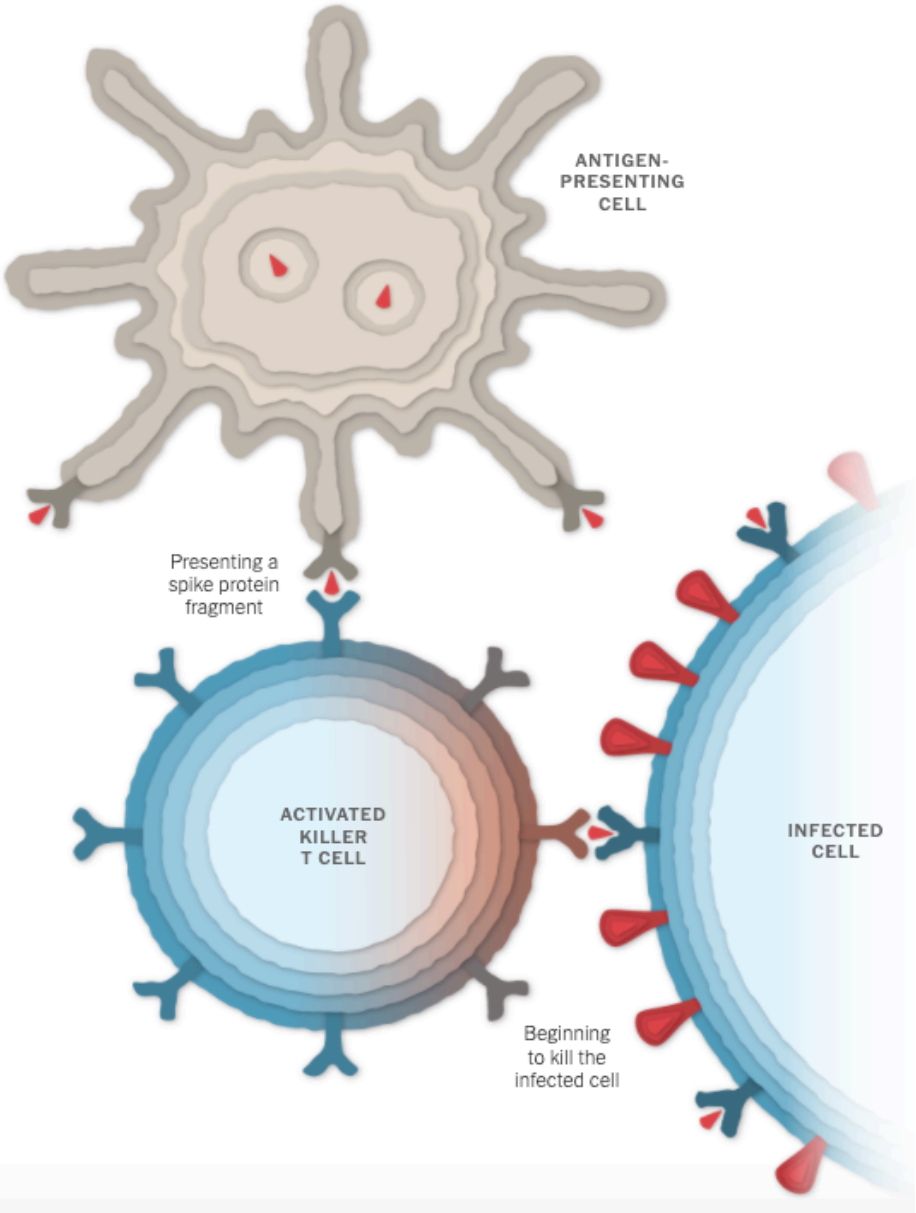



## Stopping the Virus




The antibodies can latch onto coronavirus spikes, mark the virus for destruction and prevent infection by blocking the spikes from attaching to other cells.

## Killing Infected Cells



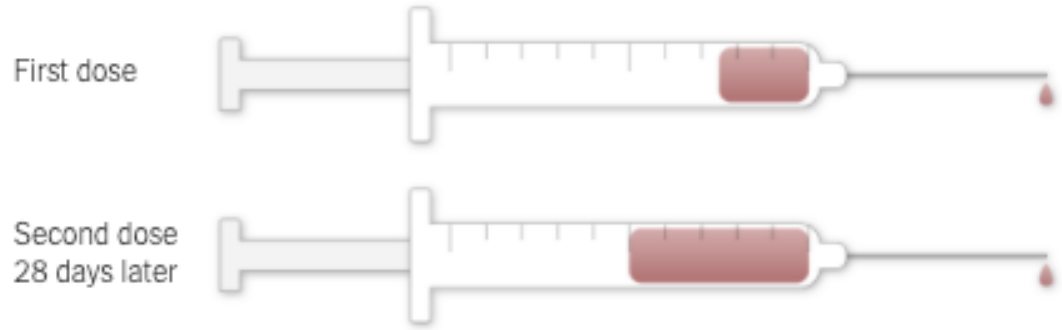

The antigen-presenting cells can also activate another type of immune cell called a killer T cell to seek out and destroy any coronavirus-infected cells that display the spike protein fragments on their surfaces.

## Remembering the Virus

The Oxford-AstraZeneca vaccine requires two doses, given four weeks apart, to prime the immune system to fight off the coronavirus. During the clinical trial of the vaccine, the researchers unwittingly gave some volunteers only half a dose.

Surprisingly, the vaccine combination in which the first dose was only half strength was 90 percent effective at preventing Covid-19 in the clinical trial. In contrast, the combination of two full-dose shots led to just 62 percent

efficacy. The researchers speculate that the lower first dose did a better job of mimicking the experience of an infection, promoting a stronger immune response when the second dose was administered.




Because the vaccine is so new, researchers don't know how long its protection might last. It's possible that in the months after vaccination, the number of antibodies and killer T cells will drop. But the immune system also contains special cells called memory B cells and memory T cells that might retain information about the coronavirus for years or even decades.

For more about the vaccine, see AstraZeneca's Covid Vaccine: What You Need to Know.

## Vaccine Timeline

**January, 2020** Researchers at the University of Oxford's Jenner Institute begin work on a coronavirus vaccine.
**March 27** Oxford researchers begin screening volunteers for a human trial.
**April 23** Oxford begins a Phase 1/2 trial in Britain.


A vial of the Oxford-AstraZeneca vaccine.John Cairns/University of Oxford/Agence France-Presse

**April 30** Oxford partners with AstraZeneca to develop, manufacture and distribute the vaccine.
**May 21** The U.S. government pledges up to $1.2 billion to help fund AstraZeneca's development and manufacturing of the vaccine.
**May 28** A Phase 2/3 trial of the vaccine begins in Britain. Some of the volunteers accidentally receive half of the intended dose.
**June 23** A Phase 3 trial begins in Brazil.
**June 28** A Phase 1/2 study begins in South Africa.
**July 30** A paper in Nature shows the vaccine appears safe in animals and seems to prevent pneumonia.
**Aug. 18** A Phase 3 trial of the vaccine begins in the United States, with 40,000 participants.
**Sept. 6** Human trials are put on hold around the world after a suspected adverse reaction in a British volunteer. Neither AstraZeneca nor Oxford announce the pause.
**Sept. 8** The news about paused trials becomes public.
**Sept. 12** The clinical trial resumes in the U.K. but remains paused in the United States.

A syringe of the vaccine at a trial site in Britain.Andrew Testa for the New York Times

**Oct. 23** After investigation, the Food and Drug Administration allows the Phase 3 clinical trial to continue in the United States.
**Nov. 23** AstraZeneca announces clinical trial data that shows an initial half dose of the vaccine appears more effective than a full dose.
But irregularities and omissions prompt many questions about the results.
**Dec. 7** The Serum Institute of India announces that it has applied to the Indian government for emergency use authorization of the vaccine, known as Covishield in India.
**Dec. 8** Oxford and AstraZeneca publish the first scientific paper on a Phase 3 clinical trial of a coronavirus vaccine.

**Dec. 11** AstraZeneca announces that it will collaborate with the Russian creators of the Sputnik V vaccine, which is also made from adenoviruses.
**Dec. 30** Britain authorizes the vaccine for emergency use.
**Jan. 3, 2021** India authorizes a version of the vaccine called Covishield, made by the Serum Institute of India.
**2021** The company expects to produce up to two billion doses this year. Each vaccinated person will require two doses, at an expected price of $3 to $4 per dose.

Sources: National Center for Biotechnology Information; Nature; Lynda Coughlan, University of Maryland School of Medicine.