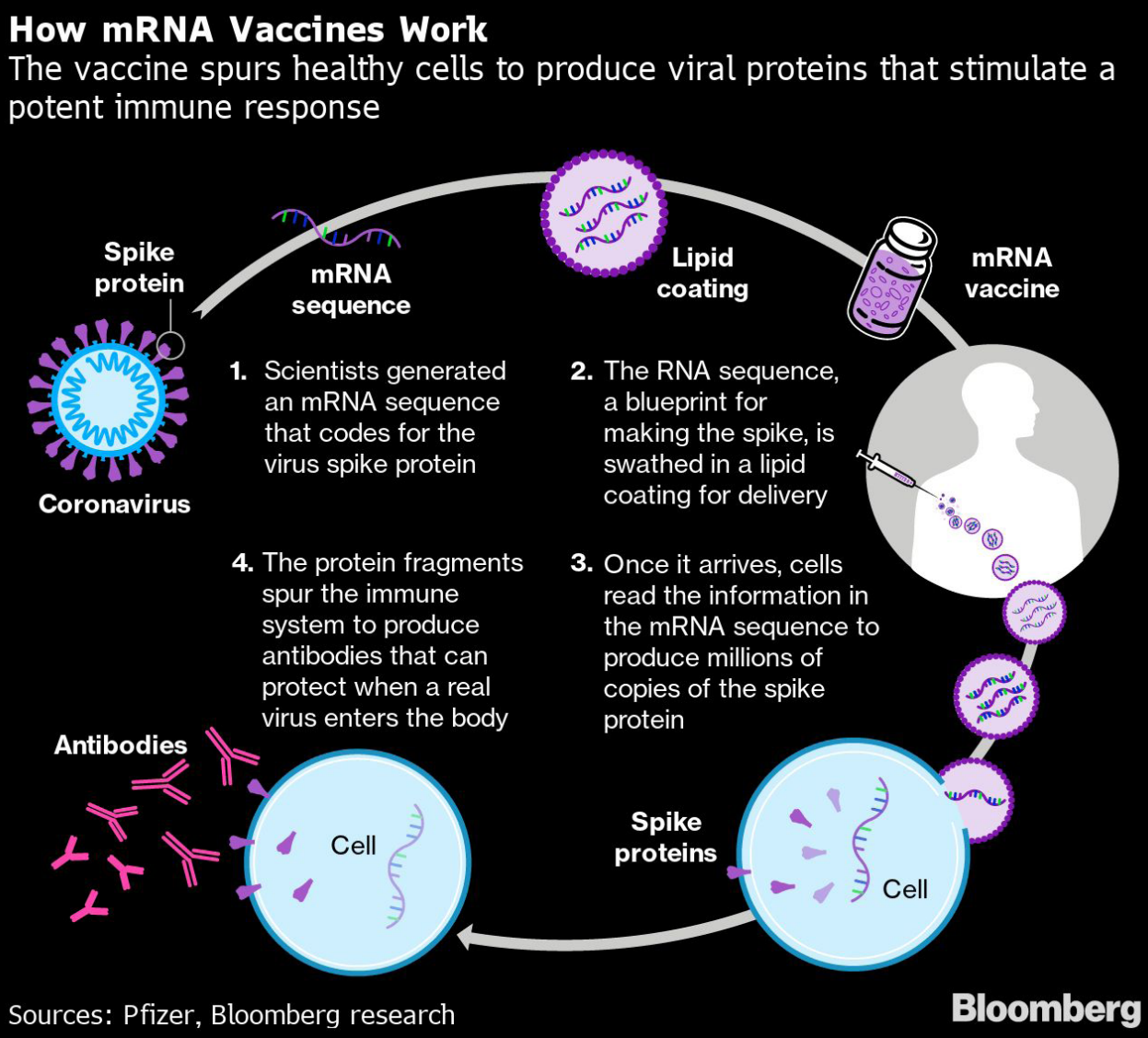


The Science of Vaccines and How They Work

Andrea Marzi, PhD, describes types of vaccines and how they work in the body.

Infectious diseases, such as smallpox, the plague, and influenza virus, have caused millions of deaths over the centuries. Smallpox is a contagious and often deadly disease that has likely killed millions of humans throughout history. In the late 18th century, English physician and scientist Edward Jenner noticed that milkmaids were not getting sick even though others around them were getting sick with smallpox. He hypothesized that the milkmaid's contact with pustules on cows' udders (small blisters on the skin containing pus) might contain the cowpox virus, which could be making them immune to infection with the

Variola virus, the cause of smallpox. Jenner tested his idea by "infecting" people with the cowpox virus. A few weeks later, he repeated the procedure with Variola virus. None of the cowpox virus-infected people developed smallpox and the world had its first vaccine.

Vaccination against smallpox was later implemented globally, and the Variola virus was eradicated in 1980, ridding our planet of a deadly burden. Vaccination against several other infectious diseases like Polio, Measles, Tetanus, Diphtheria, and Hepatitis is still ongoing. The vaccines against the viruses and bacteria causing these diseases follow the same principle – the human body is exposed to a substance that triggers a protective immune response.

HOW DO WE KNOW WHAT WE CAN USE AS A VACCINE?

Scientists have developed a variety of different technologies that can be used as vaccines. A single protein or toxin has been used as well as nucleic acid of a bacterium or virus. In addition, viral vectors as well as the entire bacterium or virus have also been used. The three most used technologies until COVID-19 are the following:

1) Live-attenuated Vaccines:

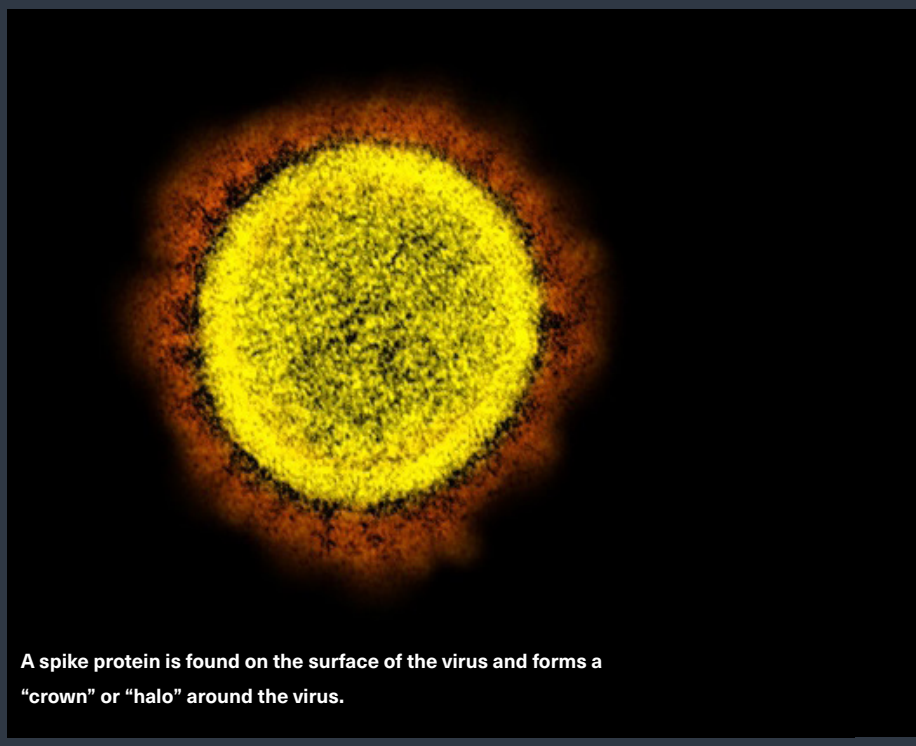
Jenner discovered that with certain viruses there exists a "weaker" version in nature. Following this principle, some of the vaccines we use today are "live-attenuated" (the process of weakening a disease-causing virus or bacterium in a lab so that it cannot cause disease). These types of vaccines infect the human body and grow, but they do not cause disease aside from mild side effects like fever and pain at the vaccination site. Today, we still use this principle for the Measles vaccine, among others.

2) Inactivated Vaccines:

Another common method for vaccine development is called chemical inactivation, which is still used today for the annual flu shot. This process involves a large amount of the virus being grown in a laboratory, and subsequently killed by a chemical treatment and/or heat. After the "killed" vaccine is purified and formulated with an adjuvant (a drug or substance used to increase the efficacy or potency of certain drugs), it can be administered to humans.

3) Subunit Vaccines:

Scientists have established procedures to generate vaccines based on these principles for over 100 years, and these principles have served as a basis to develop newer, safer vaccines that do not involve the entire bacterium or virus. In fact, the hepatitis B vaccine is based on only one protein from the hepatitis B virus. This is called a "subunit vaccine." A formulation of this protein is given in several doses often in combination with vaccines against other diseases like Diphtheria, Tetanus, Pertussis and Polio to children under 10 years.



A spike protein is found on the surface of the virus and forms a "crown" or "halo" around the virus.

Vaccine Development and COVID-19

Vaccines in the U.S. are highly regulated like any other drug and require Food and Drug Administration (FDA) approval before they can be used in humans. Before COVID-19, scientists worked on many ways to make vaccines safer and more effective with only a single dose. The knowledge they gained developing these new strategies was quickly applied to COVID-19 vaccine development at the beginning of 2020 when the disease started to spread. Now, 15 months later, scientists from the U.S. and abroad have developed several vaccines approved for human use to protect individuals from COVID-19 infection.

All approved vaccines for COVID-19 use the spike surface protein of SARS-CoV-2 as the "antigen," the protein triggering an immune response in a vaccinated person's body. Two different vaccine technologies are currently in use for COVID-19 in the U.S. – mRNA (Pfizer, Moderna) and a viral vector vaccine (Johnson & Johnson).

The mRNA-based vaccine has the genetic information for the spike protein as mRNA embedded in a lipid nanoparticle (LNP), or fatty droplet, that is stored at very cold temperatures. Because mRNA is a very unstable molecule and gets degraded quickly, the vaccine must be given to people within hours after a vial is thawed. This mRNA vaccine technology has been successfully developed for Zika virus and influenza virus in the past decade. It is relatively easy to produce as it does not involve production in cell culture and, therefore, could be generated quickly as a COVID-19 vaccine. Once the first vaccine dose (prime) is injected into a person's arm, the LNP fuses with one of their cells and the mRNA is released, causing the spike protein to be produced in the cell. The immune system recognizes the spike protein as a protein foreign to the body and starts to make an immune response against it; during this process, antibodies that protect against SARS-CoV-2 infection are produced. This process can result in fever and pain at the injection site. The second dose (boost) of the mRNA-based vaccine serves as a trial run for the body. After this second dose is injected, the body recognizes the spike protein from the previous injection and ramps up antibody production, resulting in a boosted antibody level.

In the viral vector vaccine, the spike surface protein genetic information is included in the viral vector DNA. During this process, the viral vector only serves as a vehicle to deliver the spike protein DNA into the cell, where then mRNA is produced from the DNA and the same process as with the mRNA vaccine starts. While the mRNA vaccines stay in the cytoplasm of the cell, the DNA in the viral vector vaccine gets into the cell's nucleus and can interact with the cellular DNA.

In case of a COVID-19 infection, the antibodies specific to the spike protein will bind the spike protein on the virus surface and neutralize the infection. Usually, the more antibodies a person has, the more they are protected from disease. However, no vaccine is 100% protective and while vaccinated people have spike antibodies, they can still get infected by SARS-CoV-2 and may even spread the virus to others, albeit at a much lower rate compared to a non-vaccinated person. In fact, two weeks after the vaccination is complete (two doses mRNA vaccine or one dose viral vector), the protection from COVID-19 is 94% (mRNA) and 66% (viral vector), respectively.

Vaccines are also very important for building herd immunity in our communities. Herd immunity is the principle of protecting the vulnerable people in our community. The more people that are vaccinated, the smaller the pool of people is for the virus to infect and make sick (thus reducing the number of people that need hospitalization due to COVID-19 and/or other infectious diseases). In order to slow down the spread of the disease, we need 70% of the people need to be vaccinated.

Curious as to how herd immunity works?
Watch this video: https://imgur.com/gallery/8M7q8

What is a Coronavirus spike surface protein?

The spike protein is found on the surface of the virus and forms a "crown" or "halo" around the virus. In Latin, the word for crown is "corona", which gives this virus family their name - Coronaviruses.

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