COVID-19 Vaccines: What We Know

By Shlomo Maital

In my country Israel, there are more new daily cases per million population than anywhere in the world. Europe too is undergoing a second wave; and many states in the United States are also seeing increasing morbidity. So – everywhere, we await a vaccine.

Over a hundred different efforts are underway to create, produce and administer COVID-19 vaccines. Here is what we know so far, based on a very clear, lucid website sponsored by the Children's Hospital of Philadelphia. This vaccine effort is an amazing global effort, led by the top scientific minds, trying a wide variety of creative approaches, some tried and true, some radical and innovative. One or more of them will save humanity!

What types of vaccine are being tested?

Several.

*** Inactivated vaccine — The whole virus is killed with a chemical and used to make the vaccine. This is the same approach that is used to make the inactivated polio (shot), hepatitis A and rabies vaccines;**

***Subunit vaccine — A piece of the virus that is important for immunity, like the spike protein of COVID-19, is used to make the vaccine. This is the same approach that is used to make the hepatitis and human papillomavirus vaccines.**

*** Weakened, live viral vaccine — The virus is grown in the lab in cells different from those it infects in people. As the virus gets better at growing in the lab, it becomes less capable of reproducing in people. The weakened virus is then used to make the vaccine. When the weakened virus is given to people, it can reproduce enough to generate an immune response, but not enough to make the person sick. This is the same approach that is used to make the measles, mumps, rubella, chickenpox and one of the rotavirus vaccines.**

*** Replicating viral vector vaccine — In this case, scientists take a virus that doesn't cause disease in people (called a vector virus) and add a gene that codes for, in this case, the coronavirus spike protein. Genes are blueprints that tell cells how to make proteins. The spike protein of COVID-19 is important because it attaches the virus to cells. When the vaccine is given, the vector virus reproduces in cells and the immune system makes**

antibodies against its proteins, which now includes the COVID-19 spike protein. As a result, the antibodies directed against the spike protein will prevent COVID-19 from binding to cells, and, therefore, prevent infection. This is the same approach that was used to make the Ebola virus vaccine.

*** Non-replicating viral vector vaccine — Similar to replicating viral vector vaccines, a gene is inserted into a vector virus, but the vector virus does not reproduce in the vaccine recipient. Although the virus can't make all of the proteins it needs to reproduce itself, it can make some proteins, including the COVID-19 spike protein*. No currently licensed vaccines use this approach.***

*** DNA vaccine — The gene that codes for the COVID-19 spike protein is inserted into a small, circular piece of DNA, called a plasmid. The plasmids are then injected as the vaccine. *No currently licensed vaccines use this approach*.**

*** mRNA vaccine — In this approach, the vaccine contains messenger RNA, called mRNA. mRNA is processed in cells to make proteins. Once the proteins are produced, the immune system will make a response against them to create immunity. In this case, the protein produced is the COVID-19 spike protein. *No currently licensed vaccines use this approach*.**

Which type of COVID-19 vaccine is most likely to work?

It is likely that more than one of these approaches will work, but until large clinical trials are completed, we won't know for sure. Likewise, the different approaches may have different strengths and weaknesses. *For example, mRNA or DNA vaccines are much faster to produce*, but neither has been used to successfully make a vaccine that has been used in people. On the other hand, *killed viral vaccines and live, weakened viral vaccines have been used in people safely and effectively for many years, but they take longer to produce.*

In addition to differences in how long it takes to make different types of vaccines, *each type may also cause the immune system to respond differently.* Understanding the immune responses that are generated will be important for determining whether additional (booster) doses will be needed, how long vaccine recipients will be protected, and if one type offers benefits over another.

Is one of the COVID-19 vaccines expected be more effective for the elderly population?

It is likely that COVID-19 vaccines could have different levels of effectiveness in various subgroups of people. Because the elderly generally do not respond as well to vaccines, one or more COVID-19 vaccines may not work well for them, which is concerning given their higher risk of severe disease. The large phase III studies may not include people over a certain age. But, the manufacturers have been encouraged to include older people, so that we have this type of information earlier in the process than may usually occur. We will have to wait and see what the data show to know which vaccine(s) work best in the older population.

How many doses of a COVID-19 vaccine will be needed? Will a booster dose be needed?

The number of doses of a COVID-19 vaccine that will be needed has not yet been determined. The coronavirus vaccines being studied are evaluating one or two doses. When giving two doses, they are usually given one or two months apart. We will need to wait for the results of the clinical trials to have more information about how many doses will be needed.

How long will vaccine immunity last?

Since we do not yet know how long immunity after infection lasts, immunity following vaccination will also have to be determined. Likewise, immunity following vaccination will depend in part on which types of vaccines are licensed, what part of the immune system responds to the vaccine, and the level of immunity that is generated by the vaccine.

If more than one vaccine becomes available, could taking two different vaccines boost the effectiveness?

While it is likely that more than one COVID-19 vaccine will become available, we probably won't have a good answer to this question until vaccines are actually licensed and we know more about them. Three scenarios can occur if a person is vaccinated with two versions of vaccines against the same disease, particularly close in time:

--- They get a stronger immune response. An example of this was when children got inactivated polio vaccine and later got oral polio vaccine.

---- The second vaccine causes immunity that would be similar to receiving a second dose of the original vaccine. Using a different brand of hepatitis B vaccine for one or more doses would be an example of this.

--- The immune response generated by the first vaccine interferes with components of the response to the second vaccine, in some cases causing lower immunity. For example, when people got a pneumococcal polysaccharide vaccine (PPSV) followed by a pneumococcal polysaccharide vaccine with a harmless helper protein attached to it, called pneumococcal conjugate vaccine (PCV), they had lower antibody responses to one part of the PCV vaccine than people who got the two vaccines in the opposite order (PCV followed by PPSV).

For these reasons, studies will need to be done to determine the effects of getting a second type of COVID-19 vaccine shortly after receiving a different one. If, however, we find that COVID-19 vaccines are like influenza vaccines and we need to get vaccinated annually, concerns about switching types from one year to the next are less likely to be an issue.

Will a coronavirus vaccine need to be given annually?

When a vaccine is licensed, we will only have information about length of immunity for as long as we are from the trials. For example, if the first people in the study were vaccinated in July 2020 and the vaccine is licensed in December 2020, we will only have

information about the immune response up to 5 months after vaccination. The vaccine manufacturer will likely continue to monitor vaccine recipients for several months or more, so that over time, we will continue to get a better picture of the durability of immunity. With this information, we will be better able to understand whether vaccines against COVID-19 will require annual dosing like influenza.

Is a coronavirus vaccine necessary?

SARS-CoV-2 infections can be a minor hindrance or lead to severe disease or even death. While hygiene measures such as social distancing, handwashing, and wearing masks offer some help, the best way to stop this virus is to generate SARS-CoV-2-specific immunity. This specific immunity can be achieved in one of two ways — through illness or vaccination. Since illness could lead to severe disease or death, vaccination is a better alternative as long as safe and effective vaccines can be developed.

How long before a coronavirus vaccine takes effect?

Generally speaking, it takes a week or two for immunity to develop following vaccination, but the specific timeline for any coronavirus vaccine will depend to some extent on which type of vaccine is licensed. For example, a live, weakened vaccine requires time to reproduce in the body, whereas an inactivated vaccine is given at a dose that will generate immunity. On the other hand, because the live, weakened vaccine reproduces to generate immunity, it might provide a more robust immune response than an inactivated vaccine