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5 ways our immune responses to COVID vaccines are unique

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The Oxford vaccine trial at the center of safety concerns this week highlights the idea that people's immune systems respond to vaccines differently.

We don't yet know whether reports of immune complications in one or two trial participants have been linked to the COVID-19 vaccine itself, or if they were given the placebo vaccine.

But it does highlight the importance of phase 3 clinical trials in many thousands of people, across continents. These not only tell us whether a vaccine is safe, but also whether it works for people of different ages or with particular health issues.

So what are some of the immune factors that determine whether any of the 180 or so COVID-19 vaccine candidates being developed around the world actually work?

Our immune responses are all different

An effective vaccine should generate long-lasting protective immunity against SARS-CoV-2, the virus that causes COVID-19.

This can be by generating antibodies to neutralize the virus and likely also by helping the immune system memorize and quickly respond to infection.

We know, from developing vaccines against other viruses, that people's immune response to a vaccine can vary. There's every reason to believe this will also be the case for a COVID-19 vaccine.

1. Vaccine type and how it's delivered

Many COVID-19 vaccine candidates contain parts of the SARS-CoV-2 spike protein to stimulate protective immunity. However, there are many different ways of delivering these proteins to the body, and some may be more effective than others at stimulating your immune system.

For example, the Oxford vaccine combines the spike protein with another virus to mimic the actions of SARS-CoV-2.

Meanwhile, the candidate developed by the University of Queensland contains the spike protein packaged with another compound (an adjuvant) to stimulate the immune system.

Some people will likely need a follow-up booster shot to ensure longer-lasting immunity.

We may also see some vaccines delivered as a nasal spray. This may elicit a more effective immune response to COVID-19 in the upper respiratory tract, including the nostrils, mouth and throat.

2. Our previous infections

Previous infections may prime our immune system to respond differently to vaccination.

For instance, the SARS-CoV-2 virus belongs to a large family of human coronaviruses, four of which are responsible for common colds.

Being exposed to these cold-causing coronaviruses, and developing immune memory cells against them, may mean a stronger or quicker response to a COVID-19 vaccine.

Some people have poor protective immune responses to COVID-19 vaccine candidates. These people may have existing immunity to the adenovirus used in some vaccines to deliver the SARS-CoV-2 spike protein.

In other words, their body mounts an immune response to the wrong part of the vaccine (the delivery mechanism) and not so much to the

characteristic part of the virus (the spike protein).

3. Our genetics

Our genes play a large part in regulating our immune system.

Researchers have already seen sex differences, which are partly governed by genes, in the immune response to the flu vaccine. They have also seen sex differences in the immune response to COVID-19.

So larger clinical trials should help us understand whether men and women respond differently to a COVID-19 vaccine.

People with inherited immune deficiencies may also be unable to generate protective immunity in response to vaccination.

4. Our age

The composition of our immune system changes throughout the course of our lives, and this affects our ability to mount a protective immune response.

Infants' and children's immune systems are still developing. So their immune response may be different to adults'.

Some COVID-19 vaccines may be more effective for children, or recommended for them, as we see already with the flu vaccine.

As we get older, changes in our immune system mean we cannot efficiently maintain long-lasting protective immunity; we are less able to make new antibodies in response to infection.

We already know older people are less likely to mount a protective immune response with the flu vaccine.

So we need the data from large trials to verify whether COVID-19 vaccines work in children and elderly people.

5. Lifestyle factors

Diet, exercise, stress and whether we smoke influence our immune response to vaccination. So we can look after our immune system with a healthy lifestyle where possible.

There is also an emerging hypothesis that our gut microbes may influence our immune response to vaccination. But more research is needed to confirm this could occur during COVID-19 vaccination.

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