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COVID-19 Tidbits about Vaccines, Antibodies, Contagiousness, Variants and Treatment.

> Ann Gerhardt, MD April 1, 2021

Bottom Line at the Top: Persist in wearing a mask (or two) and maintaining social distance, because vaccinated people can continue to carry infectious virus and the duration of antibody production resulting from vaccination or prior infection is not known.

Vaccine Reactions: Severe reactions remain uncommon, even in highly allergic individuals. Polyethylene glycol (PEG) in the Pfizer vaccine and polysorbate 80 in the Moderna vaccine may cause anaphylaxis. PEG and polysorbate share similar structures but allergy to one does not guarantee allergy to the other. According to CDC guidance, polysorbate allergies do not preclude receiving the Pfizer vaccination, but the CDC recommends a longer observation period after vaccination.

The Johnson & Johnson adenovirus vector vaccine contains polysorbate, not PEG. The CDC recommends it as a replacement for the second dose of an mRNA vaccine for patients who had a reaction to the first dose, waiting at least 28 days between doses.

Contagiousness: Even after vaccination or recovery from infection, SARS-CoV-2 virus particles may enter our nose and multiply for a while before our antibodies kill them. Therefore, we remain infectious even if we are not ill.

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Once sick, the duration of positive testing depends on testing method. There are two standard tests - virus culture and RNA testing. Hospitalized patients in China remained culture positive for up to twelve days, but positive RNA test results persisted for up to five weeks after symptom onset. Therefore it's hard to say how long you are infectious after COVID-19 disease.

Most people with persistent (long-haul) COVID symptoms test negative for virus but a few have re-tested positive after a long hiatus, either from persistent or possibly new infection.

Variants: RNA viruses mutate, creating variants from the original infectious agent. Some will be less infectious, some more. Some will be less lethal, some more. Prior to COVID-19, virologists posited that a more infectious variant would be less lethal, because otherwise it would kill all available hosts, causing it to die out. That may have happened in the first coronavirus epidemics caused by SARS-CoV-1 and MERS.

We do not know how many SARS-CoV-2 variants have emerged because viral RNA in every infected person is not sequenced. So far, three highly infectious variants have appeared. The B.1.1.7 variant found in the UK, the B.1.351 variant discovered in South Africa and the P.1 variant found in Brazil spread more easily. All have been identified in U.S. patients. There is a lot we do not know: 1) how well existing tests identify them; 2) if they cause different spectrums of COVID disease; and 3) how well they respond to existing treatment. Experts in the UK reported that the B.1.1.7 variant is more lethal, but more data is needed.

So far, vaccine-induced antibodies bind all these variants. That may not be the case for the future variants. SARS-CoV-2 may become the next virus, like influenza, that mutates enough from year to year to require yearly vaccination.

Anti-SARS-CoV-2 antibody peak and duration: Initial reports of vaccine success were impressive, but we still do not know the duration of antibody protection after COVID vaccines. Vaccine trials just started last summer, so there isn't one year of data and manufacturers haven't reported six month data.

Since antibodies are naturally degraded after about three weeks, we need to keep making them for persistent immunity. The mRNA vaccines induce some of the cellular machinery capable of perpetuating an immune response, but there is no data yet about how well it succeeds.

Antibodies are specialized proteins that our immune systems make to fend off infection. One end of the antibody binds to a part of the virus (like the SARA-CoV-2 Spike protein that bores its way into human cells). The other end determines the fate of the virus protein-antibody complex. Some vaccine-induced antibodies signal killer cells to neutralize virus and others bind viral protein but do not necessarily kill the virus. Clinical tests for antibody do not distinguish the two types. Vaccines induce the two antibody types to a different extent, but we need more long-term data to assess significance.

Young people make more antibody capable of neutralizing SARS-CoV-2 than do old people. In one study, thirty-one percent of people over age 80 years had no detectable neutralizing antibody after two Pfizer vaccine doses. They must make some antibody, because aged vaccine recipients suffer less severe disease and death from COVID-19 infection than do non-vaccinated elderly. People with disease or an organ transplant who take drugs that suppress their immune systems make less antibody after vaccination, especially after the first dose of an mRNA vaccine.

Those who have had COVID-19 infection make antibody that does not guarantee protection from future infection. Infection-induced antibodies do not persist long, possibly only 60 to 90 days, with duration depending somewhat on type of antibody. Antibody specific for Spike protein fades sooner, while antibodies that bind to a variety of SARS-CoV-2 proteins persist longer. Infected people should be vaccinated about 90 days after recovery to be safe. The good news is that they have a more robust antibody response to vaccines.

Treatment: Convalescent plasma is the liquid part of blood that contains antibodies induced by an infection. Ideally, infusing plasma from people who have had COVID-19 infection into a newly infected person transfers antibodies that may immediately fight off infection in the recipient. The sick person does not have to wait the 10 -14 days necessary to produce their own antibodies.

In general, treatment with convalescent plasma containing anti-SARS-CoV-2 antibodies has been disappointing. One study showed that convalescent plasma given to mildly ill people within three days of symptom onset reduced the risk of severe disease. That doesn't help the majority of people with severe disease or those who pass off their symptoms as allergies for more than three days.

Remdesivir (brand name Veklury) remains the only drug approved for treatment of COVID-19 disease. However, doctors have learned ways to treat patients, e.g. dexamethasone to reduce cytokine storm and prone positioning to improve lung aeration, that improve survival.

In conclusion, the best way to not be infected by COVID-19 as your vaccination antibodies wane or you are exposed to a highly infectious variant is to wear at least one mask and social distance. $\frac{1}{2}$



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