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COVID Update: Impact of Mutations and Variants

by Ann Gerhardt, MD *December 2021*

Bottom Line at the Top: Failure to respond to the pandemic early in 2020 and failure of many people to be vaccinated gave the COVID virus time to mutate, producing variants that are hard to prevent and treat. If the population doesn't take this virus seriously, by vaccinating while vaccines still work, and masking and social distancing to stop further spread leading to more mutations, we will never control it and millions will die.

In 2020 we hoped that the SARS-CoV-2 virus that causes COVID-19 would not mutate often. The virus and a populace unconcerned about the health of their fellow citizens dashed those hopes. Millions of infections have enabled SARS-CoV-2 to mutate so often that we have 15 variants clinically significant enough to be given a name. With successive mutations, the virus changes enough that vaccines are less effective. We now can dismiss the idea that one vaccine will stop the pandemic.

Mutations, Variants and Immunity briefly explained: Each viral genetic **mutation** changes one tiny part of the RNA genome. That mutation in turn changes one tiny part of a protein's sequence. The effect of a single mutation on a single protein's function ranges from no effect to complete incapacity. That may affect the virus' survival, transmissibility, lethality, or nothing at all.

A virus **variant is a relative of the original virus that is different because it has been mutated one or more times**, changing it significantly from its predecessor. A single mutation doesn't cause or define a variant and some mutations are seen in more than one variant. It is the sum-total of mutations and their effect on viral function that define a variant.

Vaccines available in the U.S. stimulate the immune system to target the spike protein. (Spike protein attaches to and bores a hole into our cells, enabling the virus to enter can cause infection). Vaccine-induced immunity attacks different parts of that protein, which is good because it prevents a single viral mutation from rendering the vaccine useless. As subsequent mutations occur, some of the antibodies' binding sites on the protein may disappear, but ideally there will be enough unmutated spike protein remaining, so that it can be bound and incapacitated by antibody. While our existing vaccines are specific for the original viral strain, multiple mutations over time may make the immunity we mounted to that vaccine increasingly irrelevant as the spike protein changes.

The same is true for natural immunity, that which develops after suffering through an infection. Having been infected by and produced antibodies to a variant doesn't necessarily confer immunity to subsequent variants. **No one can say that their infection earlier in the pandemic will protect them from future infection.** That's why we need everyone to be vaccinated while the vaccine still works.

COVID Variant History: The original SARS-CoV-2 virus was followed through the fall of 2020 by Alpha, Beta and Gamma. Alpha hit Canada, Europe and parts of Asia hard, Gamma slammed Brazil and Argentina, and Beta, found everywhere, dominated nowhere. Each caused infections in the U.S., but Delta, which surged in the summer of 2021, has out-competed the others for susceptible victims and become dominant.

Delta super-surged because of easier transmissibility due to more rapid viral reproduction during infection, but there is no evidence it kills a greater percentage of its victims. That pattern makes sense, since a more lethal virus would kill off

people before they could infect others. Omicron appears to be even more transmissible but we don't yet know if it causes relatively more severe illness – We may see many more deaths, but that may just be because there are more infections.

Public health agencies say that COVID-19 will surge seasonally, but the surge pattern so far seems to be related to new variants and people letting down their guard rather than the weather.

Variants vs. Treatment: The variants currently of major concern are Alpha, Beta, Gamma, Delta and Omicron. All are more infectious than the original strain, but lethality varies. Public health officials worried about Mu and Lambda causing a new surge of infections, but their significance waned as Delta emerged. Omicron, the latest variant, may not only overtake Delta's reach, but may require its own vaccine.

Vaccines: Currently available vaccines induce immunity that protects against Alpha and Gamma, but less so the other variants. It appears that the J&J vaccine may not protect against the Omicron variant. We are likely headed to an influenza-like system, in which we get yearly vaccines to the then-prevalent variant.

Monoclonal antibodies: These medicinal antibodies are lab-manufactured to add to an at-risk person's natural antibody supply. The goal with their use is to prevent progression of mild to severe disease when given soon after symptoms start. Some of the variants (Eta, Iota and Kappa) were mutated enough that treatment with the first of those antibodies (bamlanivimab) was ineffective at preventing disease. Newer monoclonal antibodies and antibody combinations (etesevimab, sotrovimab, casirivimab, imbevimab) are now available, but variant susceptibility to them remains to be seen. A new combination antibody, Evusheld, has been effective for prevention but not treatment. It's not clear how well any of them will work against Omicron or the next variants.

Medication for infection: So far remdesivir, in combination with other intensive care treatment, has been helpful, but far from 100% successful at treating COVID-19. Preliminary data suggest that an experimental new drug, TEMPOL, is at least as helpful, once someone is infected. No available medication is as effective at saving lives as is vaccination.

The fact that scientists across the globe were able sequence the spike protein and create multiple effective vaccines, including one with novel technology, within a year of the pandemic start is just short of miraculous. Though no prevention or treatment is guaranteed for any of the strains, vaccination is still the best way to protect against infection. What's nice about the mRNA vaccines (Pfizer and Moderna) is that it won't be hard to make new, effective vaccines for emerging variants. Regardless of vaccination status, we should also mask and socially distance when in public (including in restaurants and bars when not actually putting food and drink into our mouths), since people with no symptoms can carry the disease and infect others.╣