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# Variants, vaccines, and virology - are we protected?

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News reports on mutated, more virulant, strains of the virus most likely conjures movie-like images of an invisible, indestructible enemy causing massive disruption. The reality is fortunately much less dramatic, as these changes are actually expected. Just to reiterate, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has an RNA genome that codes for all the proteins which the virus produces.

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The exact details of how the virus replicates and produces new progeny, although of interest, are beyond the scope of this article. It is sufficient at this point to merely acknowledge that, during replication, the mechanism employed by viruses with an RNA genome allows for the introduction of mutations in the genes that code for the viral proteins.

This is expected to occur and there is substantial evidence that the SARS-CoV-2 viral genes have evolved and adapted globally. Some mutations are silent, in other words, they do not change the viral proteins. However, in some instances the changes can affect the proteins encoded by the virus. If these changes occur in regions of the protein responsible for binding to the cell receptors that facilitate entry of the virus into the cell, or in regions of the protein that induce an immune response, the virus may show new characteristics, such as more successful transmission or escape from an existing immune response.

South Africa and the United Kingdom are probably the two countries globally that have methodically sequenced the largest number of SARS-CoV-2 viruses isolated from patients. This technique allows the determination of the complete genome of each isolate and subsequent comparison, using bioinformatic software specifically designed to compare and identify changes and mutations in the nucleotide sequences.

As we are all now aware, scientists in these two countries have identified virus variants with an accumulation of mutations and deletions occurring in the gene that encodes for the viral spike protein associated with binding to cell receptors and inducing protective immune responses. These variants have now become the predominant lineages circulating within local communities.

## New strains

In December 2020, scientists in South Africa revealed the presence of a variant of concern (VOC), now referred to as

501Y.V2. Sequence data confirmed that this variant initially emerged in October 2020, and by January 2021 it was present in multiple provinces in the country and is considered to be responsible for a significant number of cases occurring in the second wave of infections in the country.

A second VOC reported by scientists in the United Kingdom in December 2020, likely emerged during September 2020. A third VOC has been reported from Brazil and is simply known as variant P1. To date, variant 501Y.V2 has been reported from at least 23 countries. VOC 202012/01 has been reported in at least 60 countries, and although the cases were initially associated with travellers, there is an increasing number of clusters of cases occurring in people with no history of travel.

The United States, Israel, and India currently have the highest number of cases associated with this variant outside of the UK, keeping in mind that at the rate at which the pandemic unfolds, these statistics quickly become outdated. In contrast, variant P1 has only been reported from Brazil, and outside of Brazil it has been associated with travellers in a small number of countries.

Changes in viral proteins may or may not influence certain characteristics of a viral infection. Current epidemiological data and modelling have all suggested that the VOC circulating in South Africa and the UK are more transmissible than previous lineages of the SARS-CoV-2. Despite the increased transmissibility, to date the severity of illness and the proportion of severe disease in different age groups appear to be unaffected by the changes in the protein. The increased transmissibility has increased the burden on the public and private health systems, emphasising the importance of rolling out a vaccine to healthcare workers and persons at increased risk of severe illness.

## Vaccines

The changes in the spike protein responsible for inducing immune responses have sparked research studies to determine whether the vaccines will be able to protect against the new variants. It must be remembered that there are two arms to the immune response with complex interactions, and that natural protection will likely be a combination of responses. However, the presence of antibodies that neutralise the virus, in other words, block it from entering cells, and the ability of these neutralising antibodies to block new variants from entering the cells, can be investigated in the laboratory.

Although the exact responses required for protection are not fully understood and will require studies that take more time to complete, an indication of neutralising capacity provides some information with regard to the potential efficacy of the vaccine against variants. What we currently know from laboratory research is that there is a reduction in the ability of antibody from people previously infected during the first wave of cases to neutralise the new variant circulating in South Africa.

This reduction varied among the cohort of samples tested, but overall, there was a weaker neutralising capability. Similar results were demonstrated using pseudoviruses representing the variant virus. Studies looking at antibodies in people who have been vaccinated show similar reductions in neutralisation. The answer is unfortunately not clear at this stage, with many pieces of the puzzle still to be determined.

The reduced capacity to neutralise in a laboratory was not what we wanted to hear, but it must be remembered that vaccines induce a broad immune response and not only neutralise antibody, and hence there are other components to the immune response that will likely contribute to protection. Nonetheless, even a reduced immune response will contribute towards vaccine-induced herd immunity and saving lives by preventing severe disease.

In addition to the vaccines currently in use, results were released this week from clinical trials using vaccines from Novavax and Johnson & Johnson. Although a lower efficacy was shown among the South African population compared to results obtained in the UK, the efficacy was still in the region of 57% to 60%, which is certainly encouraging in view of the new variant circulating.


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The differences observed illustrate the importance of conducting vaccine trials in local populations. An efficacy of 60% will still contribute towards herd immunity and the prevention of severe disease, emphasising the importance of a rapid roll-out and hopefully a high uptake of the vaccine. Vaccination will not only protect the vaccinee but should contribute to minimising the risk of further variants emerging.

The roll-out of vaccine, further research on immune responses in vaccinated communities, epidemiological data, and sequence data will all contribute towards monitoring the evolution of the outbreak. Flu vaccines are modified annually and if the Covid-19 vaccine needs to be modified, manufacturers have the capability to do this, and some have already started this process.

Additional waves of infection are predicted to occur until herd immunity can be achieved. Whether the current variants will be responsible for the next wave is not possible to predict, and continued research analysing the gene sequences of future isolates will play an important role in determining how the virus is evolving.

In the interim, until we have sufficient vaccine-induced herd immunity to provide protection, non-pharmaceutical interventions and human behaviour will continue to play the important role of minimising new infections. To quote CS Lewis:

> *You can't go back and change the beginning, but you can start where you are and change the ending.*

## ABOUT THE AUTHOR

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