An expert explains viral variants, mutations and strains

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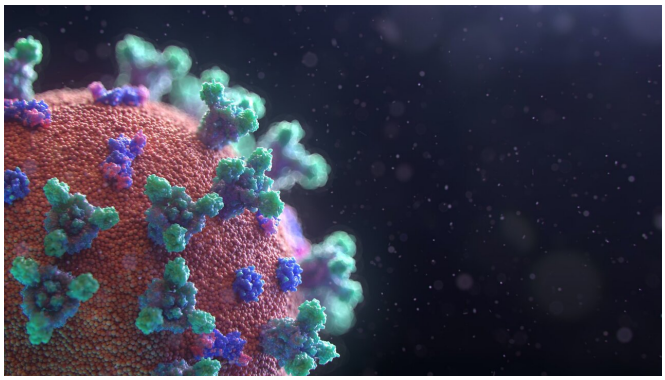

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What are variants? We asked Divya Shah, Epidemics Research Lead, to explain how variants happen, what they mean for treatments and vaccines—including for COVID-19—and how we can prevent them.

What are mutations, variants and strains?

Although the terms viral mutants, variants and strains are often used interchangeably, they generally hold different meanings.

To spread, a virus needs to infect a host, replicate and produce lots of copies of itself.

When a virus replicates it doesn't always manage to produce an exact copy of itself. This means that, over time, the virus may start to differ slightly in terms of its genetic sequence. Any changes to the viral genetic sequence during this process is known as a mutation and viruses with new mutations are sometimes called variants. Variants can differ by one or multiple mutations.

When a new variant has different functional properties to the original virus and becomes established in a population, it is sometimes referred to as a new strain of the virus. In short, all strains are variants, but not all variants are strains.

Are variants more dangerous than the original virus?

All viruses mutate. Most mutations are harmless and do not affect the properties of the virus. However, some mutations give the virus a selective advantage, increasing the likelihood that it will go on to infect another person.

Mutations which have a selective advantage could be ones which result in greater viral shedding—the release of infectious virus particles into the environment, for example when we talk, cough or sneeze—or they enable the virus to evade the body's immune responses.

Potential consequences of new variants include:

- change in transmissibility
- difference in disease severity
- ability to evade detection by viral diagnostic tests
- reduced susceptibility to treatments
- ability to evade natural or vaccine-induced immunity.

Do variants affect current treatments and vaccines?

Variants have the potential to make current treatments and vaccines less effective.

The influenza virus, which causes flu, is known to be a frequently mutating virus. Every flu season, we see several different influenza variants in circulation, which means that existing vaccines need to be updated so they are effective against the new variants.

Some individual mutations may reduce the virus'

sensitivity and vulnerability to human antibodies (part of the immune response) and could therefore make a vaccine or treatment less effective.

So should we be worried about COVID-19 variants?

There have been many mutations of the virus (SARS-CoV-2) that causes COVID-19 since it was first identified in Wuhan.

Currently, there are three variants of concern:

- B.1.1.7 (or 20I/501Y.V1, first identified in the UK)
- Contains many mutations, several of which are on the spike protein (the protein used to enter our bodies cells). This variant is associated with increased transmissibility
- B.1.351 (or 501Y.V2, first identified in South Africa)
- Has the same mutations as B.1.1.7 (increased transmissibility) and also contains two other mutations which seem to make it harder for antibodies to bind to and destroy it
- P1 (First identified in a group of travellers from Brazil, who were tested at an airport in Japan)
- Contains similar mutations to the B.1.351 variant

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Are the variants impacting the effectiveness of existing COVID-19 vaccines and treatments?

Many COVID-19 vaccines target the spike protein. A virus that accumulates numerous mutations in the spike protein may be able to evade natural or vaccine-induced immunity.

There is ongoing research being conducted to test the efficacy of existing vaccine candidates against a range of variants. Vaccine developers may be able to update their candidates to make them more effective against new variants.

Early lab data suggests that the new variants—especially those first identified in South Africa and Brazil—may not respond to the first COVID-19 monoclonal antibodies (mAbs). Designed to bind to the spike protein of the virus, like a key in a lock, the mutations found in the variants mean that the key (mAbs) no longer fits the lock (spike protein). While this would be a disappointing setback, this class of treatments still holds great promise for COVID-19 and work is underway to develop combination and second-generation antibody treatments.

There are suggestions that the variants of concern are more prevalent in peoples' noses and throats. This results in a higher viral load, making it easier for the virus to spread between hosts, continue to replicate, and potentially produce new mutations.

This is why it is important to continue to invest in development of a variety of vaccines and treatments to increase the chance of having tools that are effective against new variants.

How are variants tracked?

Due to the potential for a mutation to change the properties of a virus, we need to monitor variants closely to determine if they pose a greater risk of transmission, severe disease or evasion of current interventions.

Since the 1980s we've been monitoring and sequencing influenza (flu) virus strains through global networks, to enable adaptation of the flu vaccine every year.

This is done through genetic sequencing of a virus, and the collection of epidemiological and clinical data. Scientists monitor any changes to a virus' genome. Any concerning changes are reported and shared broadly so that public health interventions and policies can be adapted to limit the spread of a new variant nationally and worldwide.

What are countries doing to track the spread of the COVID-19 variants?

Genomic surveillance—the way in which we track and monitor viruses—varies internationally. This is a concerning because we know that viruses—such as SARS-CoV-2—do not respect geographical borders

and new variants spread across countries. Lack of international genomic surveillance also leads to gaps in data and poses the risk of new harmful variants emerging and spreading undetected.

The GISAID Initiative promotes global rapid sharing of genetic sequencing and relevant epidemiological data associated with the COVID-19 pandemic. This data enables researchers and health authorities to determine if the new variant poses a greater risk of transmission, severe disease or evasion of current interventions. Collection of this data will also help target vaccines and therapeutics development and help monitor their impact when they are introduced.

On the flip side, if an increase in cases is noticed somewhere that cannot be explained or linked to a super-spreader event (for example, a workplace outbreak), health authorities may review the genetic surveillance data to look for mutations that could have caused the increase.

Can we prevent variants emerging?

The more virus that is in circulation, the more opportunity it has to replicate and mutate, potentially producing new variants of concern. Suppression of the spread of the virus will reduce the number of new variants from emerging, while also protecting populations from spreading existing variants of a virus.

To limit spread, we should:

- follow public health interventions, such as social distancing and handwashing
- increase global capacity to monitor and sequence the virus to track and flag any significant changes
- prioritize equitable distribution of vaccines and treatments worldwide. If only a few countries have access to these, the virus will remain active, continue to spread and increase the risk of new variants emerging that evade current treatments and vaccines.

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