# SARS-CoV-2 Variants

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# SARS-CoV-2 Variants

- As the virus that causes COVID-19 spreads and replicates during an infection, some of these newly synthesized viruses pick up different mutations at different sites in the genetic code.
  - This process is natural because the biological machinery that the virus utilizes to make more copies of itself isn't perfect.
  - This occurs for all viruses over the course of replications; it just happens at different rates for different viruses due to a multitude of factors.
- Some of these mutations can provide benefits or detriments to the virus's ability to be transmitted or cause disease, so new variants may pop up and then die off without us even noticing.

# SARS-CoV-2 Variants

- Since its first appearance, the virus that causes COVID-19 has developed into ***many*** different variants because of the sheer magnitude of community transmission we have experienced during the pandemic. The more the virus spreads, the greater likelihood there is that a newer variant emerges.
  - By May 2020, 5,775 distinct variants of SARS-CoV-2 had already been identified among samples that had been submitted for genomic analysis.
- Recently, however, a few new variants have become more widespread and there have been a few that have caught global attention for their increased transmissibility and potential severity. These are:
  - 20I/501Y.V1 or **B.1.1.7 or Alpha**
  - 20H/501Y.V2 or **B.1.351 or Beta**
  - 20J/501Y.V3 or **P.1 or Gamma**
  - 20A/S:478K or **B.1.617.2 or Delta**

# Variant B.1.1.7 (Alpha)

- Variant B.1.1.7 was first identified in the United Kingdom in December 2020 but is estimated to have first emerged in September 2020. Since then, more than 30 countries have detected this variant among their populations.
- B.1.1.7 contains 14 defining mutations; however, the most notable are N501Y which alters the receptor binding domain of the spike protein (the area of the spike protein that interacts with ACE2 receptors on our cells), and two deletions at positions 69 and 70 (del69-70).
- While current research has indicated that these mutations do not result in a more severe COVID-19 disease if contracted, **research has indicated that these result in this variant being more transmissible.**
    - This has significant implications. If proper mitigation measures are not followed, this variant could result in greater mortality and burden our healthcare systems without causing increased severity of COVID-19.

# Variant B.1.351 (Beta)

- B.1.351 was first identified in South Africa during a rapid increase in COVID-19 cases in the region after a period of low case counts in October 2020. This variant has recently been detected in the US in January 2021.
- Similar to variant B.1.1.7, B.1.351 also contains the N501Y mutation in the receptor binding domain. In addition to N501Y, this variant contains two other mutations in key residues of the receptor binding domain, E484K and K417N.
- Current research indicates that COVID-19 patients infected with this variant might be associated with increased viral loads and increased transmissibility. More importantly though, **this variant contains the mutation E484K that could increase antibody escape.**
    - The emergence and rapid increase in prevalence of this variant could have implications for both infection-acquired and vaccine-acquired immunity.
    - **Just like with variant B.1.1.7, continued adherence to mitigation measures will be crucial to curbing excess mortality associated with the increased transmissibility of B.1.351.**

# Variant P.1 (Gamma)

- P.1 was first identified in Japan among recent travelers from Brazil, and the variant has been detected among 42% of COVID-19 cases in Manaus in late December.
- Similar to the B.1.1.7 and B.1.351 variants, P.1 has acquired the mutations E484K and N501Y in the receptor binding domain of the spike protein that is responsible for cell entry during infection. However, this variant appears to have acquired an usually large number of mutations, which could be due to the unmitigated spread of COVID-19 in the region.
- This variant appears to be more transmissible like B.1.1.7 and B.1.351 based on current research. More strikingly, **this variant may be associated with reinfection**, meaning those who previously had COVID-19 caused by another strain may be susceptible to developing COVID-19 again if they acquire an infection with this variant.
    - While there is limited research currently, **this variant could also have implications to infection-acquired and vaccine-acquired immunity due to the common E484K mutation it shares with B.1.351.**

# Variant B.1.617.2 (Delta)

- This new variant, which has become dominant in India since first being detected there in December, may be responsible in part for a grievous wave of infections across South Asia, including Nepal.
  - It is now present in 49 countries, including the USA
- That earlier variant, known as B.1.1.7, behind Britain's devastating wintertime surge was considerably more contagious than the one that first emerged last year in Wuhan, China. The India origin variant  appears to be more transmissible than that variant.
- A public Health England Report  suggested that
  - The new  variant was roughly 50 percent more likely than B.1.1.7 to be transmitted to the close contacts of an infected person.
  - It could be anywhere from a few percentage points to 50 percent more contagious than B.1.1.7.
- It is not yet clear if the variant from India is any deadlier than B.1.1.7.

# CAL.20C

- Another variant that is becoming more prevalent in Southern California is CAL.20C. It was first identified via genomic surveillance in July 2020; however, it has recently been detected among 44% of samples collected in Southern California in January 2021.
- This variant has diverged from a common variant that was already circulating in the United States. During its spread, it has accumulated three mutations in the spike protein: S131I, W152C, and L452R
- Researchers currently do not know whether this strain has increased transmissibility or results in more severe COVID-19 disease. **The L452R mutation is, however, located within a region of the receptor binding domain that has been associated with antibody escape**. Mutations within this region have been identified to confer increased resistance to certain monoclonal antibodies.
    - More research will need to be conducted to determine whether this variant will have any impact on current vaccinations with Emergency Use Authorization.

# Commonalities

- Variants B.1.1.7, B.1.351, and P.1 all contain mutations that appear to increase the transmissibility of the virus through various mechanisms including potentially higher viral loads and potentially enhanced cell entry.
    - Furthermore, the P.1 variant seems like it may have the ability to reinfect individuals who have already had, and recovered from, COVID-19.
- While more research still needs to be conducted to definitively determine whether some of these variants result in a more severe COVID-19 disease, all of these are of concern because they can still result in increased healthcare utilization and excess mortality from the increased number of cases of COVID-19 that would require medical intervention.

# Impact on vaccinations

- Some of these variants have been identified to have potentially increased fitness to current antibody treatments and vaccinations.
  - E.g. the Johnson & Johnson and Novavax vaccines, which were trialed in parallel in multiple countries, seem less effective in South Africa—falling from 72 to 57 percent efficacy and 89 to 49 percent efficacy, respectively.
  - The two mRNA vaccines still appear to maintain higher efficacy against these strains.
- This does not mean that the vaccines are ineffective. **You should still receive the vaccination when you are eligible to receive it.** Current research still supports the conclusion that the protection you gain from vaccine-acquired immunity is much more robust than that conferred from infection-acquired immunity, and the likelihood that you would experience severe COVID-19 disease given you happen to develop the disease after vaccination is significantly lower than if you were not vaccinated.

# Impact on vaccinations

- Our current vaccines we have given Emergency Use Authorization to elicit what is called a **polyclonal antibody response**.
  - After vaccination, our bodies produce multiple antibodies that bind to different regions of the spike protein that SARS-CoV-2 uses to enter our cells. For a variant of SARS-CoV-2 to completely evade immune responses elicited by our vaccines, it would need to acquire mutations across all regions of its spike protein.
  - Your immune system's response to the vaccinations has been observed to be much more effective at combatting the virus that causes COVID-19 than the response elicited by acquiring the infection and COVID-19 disease.

# Variant B.1.617.2 (Delta) and vaccinations

- The Pfizer-BioNTech vaccine offered 88 percent protection against the variant first sampled in India, only a slight drop from the 93 percent protection given against the variant from Britain
- The AstraZeneca-Oxford vaccine was 60 percent effective against the variant from India, compared to 66 percent effective against the one first seen in Britain
- Notably, a first dose of either the Pfizer or AstraZeneca vaccines provides only about 34 percent protection against the variant first seen in India
    - This is a relatively steep drop from the roughly 51 percent protection a single dose of either of those vaccines offer against the earlier variant from Britain.

# Preventing the Emergence and Spread of Current/New Variants

- Remember, mutations are more likely to accumulate to produce new variants when there is unrestricted or high levels of transmission.
    - I.e. as the virus replicates more and more, the probability that mutations are passed on is greater.
- In order to slow the spread of the new variants and to prevent the emergence of new potentially more transmissible, more severe variants, we need to continue to follow public health recommendations like wearing masks, avoiding large crowds, and becoming vaccinated once you are eligible (even if you have already had COVID-19).
    - Assume that the variants are already circulating in your community and act accordingly.
- If everyone follows these recommendations, the impact that variants may have on your community can be significantly reduced.

# Why should we care about SARS-CoV-2 variants?

- As has already been observed with some of the new variants currently circulating, other future variants could end up being more transmissible.
    - Even without an increase in severity, an increase in transmissibility could significantly impact our healthcare systems, communities, and lead to even greater deaths.
- Variants that have acquired specific variants could lead to re-infection among persons who have already recovered from COVID-19.
- Variants that have acquired mutations associated with antibody escape could impact vaccine efficacy. Some variants already in circulation are already better able to evade the immune protection gained from current vaccines.
- New variants, with their potential changes in transmissibility and antibody escape could ultimately prolong the pandemic.

# If you have been vaccinated against COVID-19, can you still acquire an infection with a variant?

- **POSSIBLY.** No vaccine is perfect, so there is always a small chance that you could acquire an infection with the virus that causes COVID-19.
- However, whether you would acquire the infection depends on a host of different factors.
    - Depending on which variants are currently circulating in your community, some may be better at evading the protection garnered from your vaccination than others.
    - It also depends on what the level of transmission is in your community, and how well you adhere to mitigation recommendations.
- Its best to just assume that there are variants in your community that could still cause COVID-19 for the time being and continue to limit contacts with larger groups (>10 people) who are unvaccinated, wear masks around those at high risk, and physically distance.

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# If you have recovered from COVID-19, can you still acquire an infection with a variant?

- **POSSIBLY.** Current research suggests that some of the new circulating variants may be able to infect those who have already had COVID-19 and recovered. The chance that you will be reinfected with a new variant is likely greater if you have not yet been vaccinated.
    - Similar to acquiring the infection if you have been vaccinated, it depends on which variants are currently circulating in your community as some appear to be better at evading the immunity you would have gained from your previous COVID-19 illness.
    - This is because the protection garnered from a previous infection with the virus that causes COVID-19 may be more specific to the variant you previously had.
- Getting vaccinated can reduce your chances of being infected with a new variant if you have already had COVID-19 because our current vaccines elicit a **polyclonal response (one that targets multiple regions of the spike protein)** which makes it difficult for the virus to evade your immune system.

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