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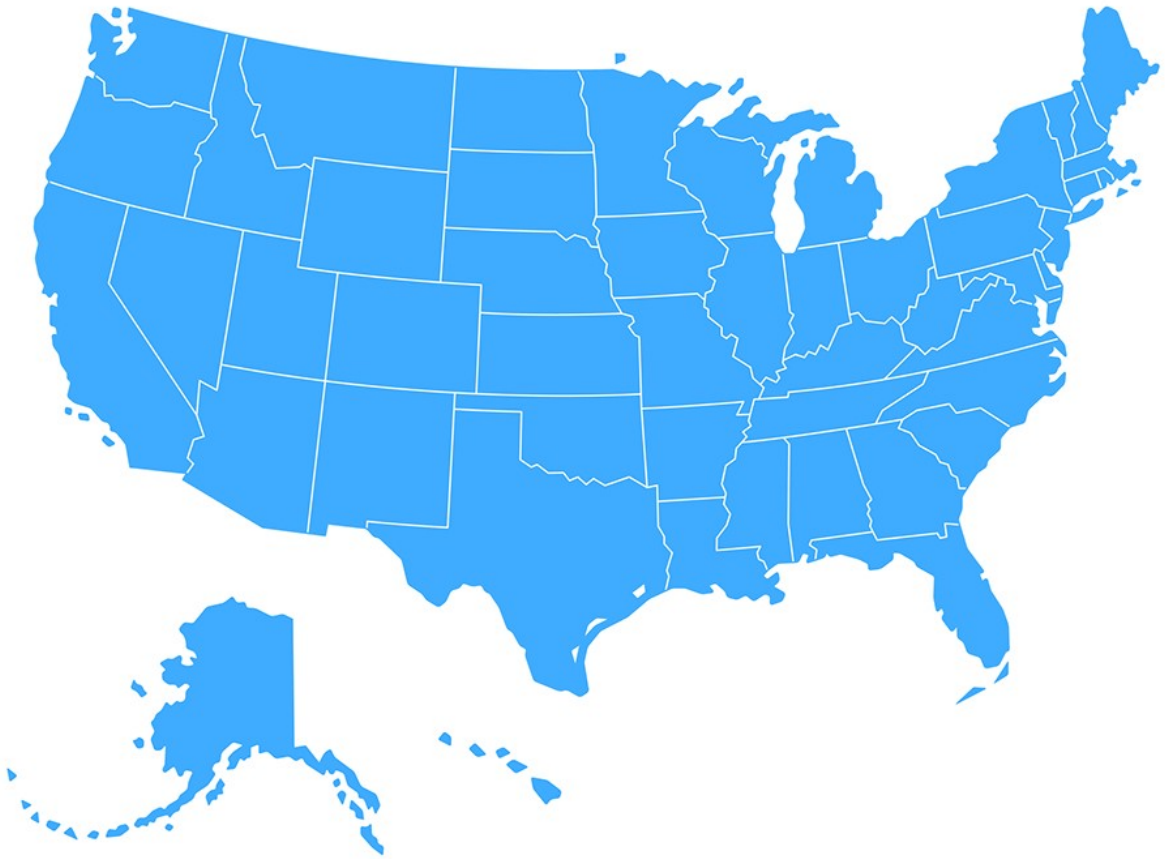
Emerging SARS-CoV-2 Variants

Updated Jan. 15, 2021

Previous update:
Dec. 29, 2020



US COVID-19 Cases Caused by Variants
View a map showing the number of confirmed cases in each state.

Multiple SARS-CoV-2 variants are circulating globally. Several new variants emerged in the fall of 2020, most notably:

- In the United Kingdom (UK), a new variant of SARS-CoV-2 (known as 20I/501Y.V1, VOC 202012/01, or B.1.1.7) emerged with an unusually large number of mutations. This variant has since been detected in numerous countries around the world, including the United States (US) and Canada.
- In South Africa, another variant of SARS-CoV-2 (known as 20H/501Y.V2 or B.1.351) emerged independently of B.1.1.7. This variant shares some mutations with B.1.1.7. Cases attributed to this variant have been detected outside of South Africa.
- In Brazil, a variant of SARS-CoV-2 (known as P.1) emerged and was identified in four travelers from Brazil, who were tested during routine screening at Haneda airport outside Tokyo, Japan. This variant has 17 unique mutations, including three in the receptor binding domain of the spike protein.

Scientists are working to learn more about these variants to better understand how easily they might be transmitted and the effectiveness of currently authorized vaccines against them. At this time, there is no evidence that these variants cause more severe illness or increased risk of death. New information about the virologic, epidemiologic, and clinical characteristics of these variants is rapidly emerging.

CDC, in collaboration with other public health agencies, is monitoring the situation closely. CDC is working to detect and

characterize emerging viral variants. Furthermore, CDC has staff available to provide on-the-ground technical support to investigate the epidemiologic and clinical characteristics of SARS-CoV-2 variant infections. CDC will communicate new information as it becomes available.

Emerging Variants

B.1.1.7 lineage (a.k.a. 20I/501Y.V1 Variant of Concern (VOC) 202012/01)

- This variant has a mutation in the receptor binding domain (RBD) of the spike protein at position 501, where amino acid asparagine (N) has been replaced with tyrosine (Y). The shorthand for this mutation is N501Y. This variant also has several other mutations, including:
  - 69/70 deletion: occurred spontaneously many times and likely leads to a conformational change in the spike protein
  - P681H: near the S1/S2 furin cleavage site, a site with high variability in coronaviruses. This mutation has also emerged spontaneously multiple times.
  - ORF8 stop codon (Q27stop): mutation in ORF8, the function of which is unknown.
- This variant is estimated to have first emerged in the UK during September 2020.
- Since December 20, 2020, several countries have reported cases of the B.1.1.7 lineage, including the United States and Canada.
- This variant is associated with increased transmissibility (i.e., more efficient and rapid transmission).
- Currently there is no evidence to suggest that the variant has any impact on the severity of disease or vaccine efficacy.

B.1.351 lineage (a.k.a. 20H/501Y.V2)

- This variant has multiple mutations in the spike protein, including K417T, E484K, N501Y. Unlike the B.1.1.7 lineage detected in the UK this variant does not contain the deletion at 69/70.
- This variant was first identified in Nelson Mandela Bay, South Africa, in samples dating back to the beginning of October 2020, and cases have since been detected outside of South Africa.
- The variant also was identified in Zambia in late December 2020, at which time it appeared to be the predominant variant in the country.
- Currently there is no evidence to suggest that this variant has any impact on disease severity.
- There is some evidence to indicate that one of the spike protein mutations, E484K, may affect neutralization by some polyclonal and monoclonal antibodies.[1,2]

P.1 lineage (a.k.a. 20J/501Y.V3)

- The P.1 variant is a branch off the B.1.1.28 lineage that was first reported by the National Institute of Infectious Diseases (NIID) in Japan in four travelers from Brazil, sampled during routine screening at Haneda airport outside Tokyo.
- The P.1 lineage contains 17 unique amino acid changes and 3 deletions.
- This variant contains three mutations in the spike protein receptor binding domain: K417T, E484K, and N501Y.
- There is evidence to suggest that some of the mutations in the P.1 variant may affect its transmissibility and antigenic profile, which may affect the ability of antibodies generated through a previous natural infection or through vaccination to recognize and neutralize the virus.
  - A recent study reported on a cluster of cases in Manaus, the largest city in the Amazon region, in which the P.1 variant was identified in 42% of the specimens sequenced from late December.[3] In this region, it is estimated that approximately 75% of the population had been infected with SARS-CoV2 as of October 2020. However, since mid-December the region has observed a surge in cases. The emergence of this variant raises concerns of a potential increase in transmissibility or propensity for SARS-CoV-2 re-infection of individuals.
- This variant has not yet been identified in the United States.

Why Strain Surveillance is Important for Public Health

CDC has been conducting SARS-CoV-2 Strain Surveillance to build a collection of SARS-CoV-2 specimens and sequences to support public health response. Routine analysis of the available genetic sequence data will enable CDC and its public health partners to identify variant viruses for further characterization.

Viruses generally acquire mutations over time, giving rise to new variants. For instance, another strain recently emerged in Nigeria[1]. CDC also is monitoring this strain but, at this time, it has shown no characteristics of greater concern to public health experts.

Some of the potential consequences of emerging variants are the following:

- **Ability to spread more quickly in people.** There is already evidence that one mutation, D614G, confers increased ability to spread more quickly than the wild-type[2] SARS-CoV-2. In the lab, 614G variants propagate more quickly in human respiratory epithelial cells, outcompeting 614D viruses. There also is epidemiologic evidence that the 614G variant spreads more quickly than viruses without the mutation.
- **Ability to cause either milder or more severe disease in people.** There is no evidence that these recently identified SARS-CoV-2 variants cause more severe disease than earlier ones.
- **Ability to evade detection by specific diagnostic tests.** Most commercial polymerase chain reaction (PCR) tests have multiple targets to detect the virus, such that even if a mutation impacts one of the targets, the other PCR targets will still work.
- **Decreased susceptibility to therapeutic agents such as monoclonal antibodies.**
- **Ability to evade natural or vaccine-induced immunity.** Both vaccination against and natural infection with SARS-CoV-2 produce a "polyclonal" response that targets several parts of the spike protein. The virus would likely need to accumulate multiple mutations in the spike protein to evade immunity induced by vaccines or by natural infection.

Among these possibilities, the last—the ability to evade vaccine-induced immunity—would likely be the most concerning because once a large proportion of the population is vaccinated, there will be immune pressure that could favor and accelerate emergence of such variants by selecting for "escape mutants." There is no evidence that this is occurring, and most experts believe escape mutants are unlikely to emerge because of the nature of the virus.

[1] Analysis of sequences from the African Centre of Excellence for Genomics of Infectious Diseases (ACEGID), Redeemer's University, Nigeria, identified two SARS-CoV-2 sequences belonging to the B.1.1.207 lineage. These sequences share one non-synonymous mutation in the spike protein (P681H) in common with the B.1.1.7 lineage but does not share any of the other 22 unique mutations of B.1.1.7 lineage. The P681H residue is near the S1/S2 furin cleavage site, a site with high variability in coronaviruses. At this time, it is unknown when this variant may have first emerged. Currently there is no evidence to indicate this variant has any impact on disease severity or is contributing to increased transmission of SARS-CoV-2 in Nigeria.

[2] "Wild-type" refers to the strain of virus – or background strain – that contains no major mutations.

Strain Surveillance in the US

In the United States, sequence-based strain surveillance has been ramping up with the following components:

- **National SARS-CoV-2 Strain Surveillance ("NS3"):** Since November 2020, state health departments and other public health agencies have been regularly sending CDC SARS-CoV-2 samples for sequencing and further characterization. This system is now being scaled to process 750 samples nationally per week. One strength of this system is that it allows for characterization of viruses beyond what sequencing alone can provide.
- **Surveillance in partnership with national reference laboratories:** CDC is contracting with large national reference labs to provide sequence data from across the United States. As of December 29, CDC has commitments from these laboratories to sequence 1,750 samples per week and anticipates being able to increase this number.
- **Contracts with universities:** CDC has contracts with seven universities to conduct genomic surveillance in collaboration with public health agencies.
- **Sequencing within state and local health departments:** Since 2014, CDC's Advanced Molecular Detection Program

has been integrating next-generation sequencing and bioinformatics into the U.S. public health system. Several state and local health departments have been applying these resources as part of their response to COVID-19. To further support these efforts, CDC released $15 million in funding, with COVID supplemental funds, through the Epidemiology and Laboratory Capacity Program on December 18, 2020.

The SPHERES consortium: Since early in the pandemic, CDC has led a national consortium of laboratories sequencing SARS-CoV-2 (SPHERES) to coordinate U.S sequencing efforts outside of CDC. The SPHERES consortium consists of more than 160 institutions, including academic centers, industry, non-governmental organizations, and public health agencies.

Through these efforts, anonymous genomic data are made available through public databases for use by public health professionals, researchers, and industry.

References

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2. Weisblum Y, Schmidt F, Zhang F, et al. Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants . eLife 2020;9:e61312.
3. Resende PC, Bezerra JF, de Vasconcelos RHT, at al. Spike E484K mutation in the first SARS-CoV-2 reinfection case confirmed in Brazil, 2020 . [Posted on www.virological.org on January 10, 2021]

Last Updated Jan. 15, 2021