

VIEWPOINT

SARS-CoV-2 Variants of Concern in the United States—Challenges and Opportunities

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Multimedia

On January 10, 2020, the first genomic sequence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) isolated from a patient in Wuhan, China, was posted online. As of February 3, 2021, 468 000 sequences of SARS-CoV-2 from COVID-19 cases globally have been uploaded into publicly available databases, including more than 93 000 from individuals in the US. SARS-CoV-2, like other RNA viruses, constantly changes through mutation, with new variants occurring over time. Generally, when new variants become more common, they do so because of some selective advantage to the virus. Among the numerous SARS-CoV-2 variants that have been detected, only a very small proportion are of public health concern because they are more transmissible, cause more severe illness, or can elude the immune response that develops following infection and possibly from vaccination. In the recent months, 3 specific viral lineages reflecting variants of concern have emerged and merit close monitoring: B.1.1.7, B.1.351, and P.1.

The B.1.1.7 lineage (known as 20I/501Y.V1 or variant of concern [VOC] 202012/01) was first detected in the UK in December 2020 with likely emergence during the preceding September; this variant has now been

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identified in at least 80 countries.¹ The first identified US case of the B.1.1.7 variant was detected in Colorado in late December 2020. Since then, B.1.1.7 has been detected in at least 33 US states. Another VOC, the B.1.351 lineage (known as 20H/501Y.V2) was first identified in the Republic of South Africa in December 2020 with likely emergence before October; this variant has been identified in at least 41 countries including the US, where it was first detected in South Carolina and Maryland in late January 2021.¹ The SARS-CoV-2 P.1 lineage (known as 20J/501Y.V3) was identified in December 2020 in travelers from Brazil, with the first case in the US detected in Minnesota in January 2021.²

Preliminary data from the UK suggest that the B.1.1.7 variant is more transmissible than previous variants of SARS-CoV-2 (similar concerns have been raised about the B.1.351 and P.1 variants) and preliminary data suggest the possibility of increased severity of disease

with infection.³ Some data also suggest that people infected with an earlier form of circulating SARS-CoV-2 may have reduced protection from reinfection with the B.1.351 variant.⁴ This observation and a report of an approximately 6-fold reduction in neutralization of B.1.351 variants by sera from vaccinated individuals with a vaccine designed against wild-type virus suggest that currently employed vaccines might be less effective at preventing infection due to this variant.⁵ It should be noted that this type of assessment, neutralizing antibody from vaccinated or previously infected individuals, does not assess other types of potential immunity, such as memory T- and B-cell activity.

Modeling data have illustrated how a more contagious variant, such as B.1.1.7, has the potential to exacerbate the trajectory of the US pandemic and to reverse the present downward trend in new infections and further delay control of the pandemic.^{6,7} A recent report from Minnesota in the *Morbidity and Mortality Weekly Report (MMWR)* on B.1.1.7 variant cases highlighted the risk of domestic and international travel⁸; the Centers for Disease Control and Prevention (CDC) recommends delaying travel to reduce the chance of acquiring and spreading SARS-CoV-2 including emerging VOC. By February 3, 2021, genomic sequencing of circulating viruses from one commercial laboratory suggests that the nationwide prevalence of the B.1.1.7 variant in the US is now approaching 1%, with prevalence in some states exceeding 2%.

There are also signs of concerning increases in cases attributed to the B.1.351 variant in some countries. A recent *MMWR* report shows the substantial increase in the B.1.351 variant that occurred in Zambia, going from none detected by genomic sequencing of a subset of samples from March to early December to 22 of 23 samples (96%) sequenced from a 1-week period in mid-December, corresponding with a more than 16-fold increase in COVID-19 incidence in Zambia from early December to early January 2021.⁹ The possibility of a similar experience in the US is a real threat. However, such an outcome is not inevitable; the US and other countries have the capability to prevent this outcome from occurring with a strong and immediate public health response.

To ensure a proactive rather than reactive response, the Department of Health and Human Services (HHS) established a SARS-CoV-2 Interagency Group (SIG) to improve coordination among CDC, the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Biomedical Advanced

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Research and Development Authority (BARDA), the US Department of Agriculture (USDA), and the Department of Defense (DoD). The SIG focuses on rapid characterization of the emerging VOC and actively monitors their potential influence on critical SARS-CoV-2 countermeasures including diagnostics, therapeutics, and vaccines.

To ensure that diagnostic testing continues to reliably identify infections including those caused by VOC, FDA and CDC are working together with industry to evaluate tests already approved for SARS-CoV-2 detection under Emergency Use Authorization. To address risk of reinfection and ensure vaccine effectiveness, NIH, CDC, and DoD are conducting in vitro neutralization assays to assess the neutralizing activity of human convalescent and postvaccination sera, respectively, against VOC. Similarly, NIH and DoD are assessing the effects of the emerging variants on the efficacy of certain therapeutics by conducting in vitro and in vivo neutralization assays with authorized monoclonal antibody and polyclonal antibody products.

The public health response within the US needs to address not only SARS-CoV-2 variants from other countries, but also be vigilant for the evolution of domestic VOC given the high levels of transmission in much of the nation. A multipronged public health response is needed. First, the level of community transmission must be aggressively decreased by more widespread adoption of demonstrated effective prevention practices, specifically correct and consistent use of face masks, physical distancing, restrictions on high-risk and high-capacity settings, frequent hand washing, delaying travel, and widespread diagnostic testing and screening to swiftly identify and isolate infectious individuals, particularly those who are asymptomatic, and quarantine contacts. Second, increased genome sequence surveillance combined with viral characterization and epidemiological investigation is needed to track recognized VOC and rapidly identify newly emerging variants. Third, in

addition to CDC's partnership with state health departments on national strain surveillance of 750 samples per week, CDC is now contracting with commercial laboratories to significantly increase sequence surveillance to more than 6000 samples per week. Furthermore, state public health laboratories and academic partners have been contributing thousands of viral genome sequences monthly to the US surveillance efforts. Fourth, the US needs to accelerate SARS-CoV-2 vaccination nationally and globally to decrease transmission and thereby viral replication that creates opportunities for VOC to emerge, especially where virus is most rapidly spreading.

Clinical trials have shown that the vaccines authorized for use in the US are highly effective against COVID-19 infection, severe illness, and death. As of February 11, 2021, more than 46 million doses of vaccine have been administered in the US. As the national vaccination program rolls out, CDC is leading a comprehensive suite of studies to assess the actual effectiveness of these vaccines in non-clinical trial settings among the first populations for whom vaccination was recommended, including studies underway now to assess protection in clinicians and other health care personnel. In addition, CDC and NIH are working with state and local health departments to investigate "breakthrough" infections following vaccination, identified through a variety of mechanisms including case-based surveillance. Investigations of vaccine effectiveness, individual breakthrough infections, and the ability of postvaccination serum to neutralize novel variant viruses are important components of monitoring the effectiveness of vaccination in controlling COVID-19 in an arena of evolving viral variants. Finally, a concerted and well-coordinated public health effort, together with rapid and widespread uptake of effective vaccines, is essential to remain ahead of the inevitable evolution of variants that could dangerously accelerate the trajectory of the pandemic.

ARTICLE INFORMATION

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