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OPINION

# Implications of the Emergence of a New Variant of SARS-CoV-2, VUI-202012/01

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Twelve months after the realization that SARS-CoV-2 caused a respiratory syndrome in Wuhan, China, with the constantly worsening COVID-19 pandemic and economic crisis globally, and with international news of vaccine development, a new viral variant, referred to as “SARS-CoV-2 VUI-202012/01” or “B.1.1.7” has been reported in London and southeast England. The variant may have emerged in late September 2020 and carries some 17 mutations. Whether a single or a combination of different mutations would change the viral transmissibility, virulence, clinical and epidemiological presentations, or vaccine efficiency is unknown. Transmission by asymptomatic carriers of the new variant is also unknown. Mutation pressure by antiviral agents or vaccines have not yet been induced; however, additional mutations are expected following global vaccination and, later, after administration of validated treatments. Thus, preparedness for fast emergence of new variants is prudent. One can also expect less virulent but highly transmissible variants, which could facilitate herd immunity. Development of clinical and rapid laboratory tests is required to follow up the vaccinated individuals for a secondary infection potentially by the new variant. Importantly, restrictive countermeasures, personal hygiene, face-masking, spatial distancing, and travel bans remain pertinent in fighting the virus. © 2021 Instituto Mexicano del Seguro Social (IMSS). Published by Elsevier Inc. All rights reserved.

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## SARS-CoV-2

The two viral outbreaks by the coronaviruses responsible for the Middle East respiratory syndrome (MERS) and the severe acute respiratory syndrome (SARS) attracted much international attention twenty years ago. In December 2019, another coronavirus, the 2019-nCoV later called SARS-CoV-2, was reported first in Wuhan, Hubei Province, China, wherefrom it spread and formed an epidemic (1). Rapid spread of SARS-CoV-2 and the severity of COVID-19 led the World Health Organization (WHO) to announce a global pandemic on 11 March 2020 (2,3). In late December 2020, at least 79,153,526 confirmed cases of COVID-19 with 1,739,797 fatalities were documented

globally (4). Studying the COVID-19 timeline (3) shows the complex development of the pandemic that was unanticipated in December 2019, when the initial news of the disease outbreak originated from Wuhan.

## A New Outbreak by the Viral Variant?

From April 2020, the “COVID-19 Genomics UK Consortium” had been sequencing more than hundreds of thousands of the viral samples obtained from positive cases, collected in the UK for documenting the viral movement and genomic alterations. In December 2020, the UK health authorities documented a concerning sharp rise in the number of new COVID-19 cases identified in London and the southeast UK (5,6). The UK’s public health authority, with the help of COVID-19 Genomics UK Consortium, reported on 13 December 2020 that 1,108 cases were found to be infected with a new variant of SARS-CoV-2 (6–8). The variant was identified in late September (6). Some 17 mu-

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tations have been described in this variant, which has been named “the first variant under investigation in December 2020,” that is “VUI-202012/01.”

SARS-CoV-2 is thought to undergo one mutation every two weeks. Such frequency of mutations is naturally expected of any RNA virus during a pandemic or an epidemic. Many such gene mutations likely do not alter the structure of the proteins the genes encode because they translate the same amino acid (i.e., synonymous mutations). Other mutations may alter the protein sequence and structure if they encode a different amino acid compared to the parent strain (i.e., nonsynonymous mutations). Such an amino acid substitution may or may not alter protein function. As reported by the US Centers for Disease Control and Prevention (CDC) (9), the UK variant has 14 nonsynonymous mutations that alter amino acids, six synonymous mutations that do not alter amino acids, and three deletions, including the 69/70 double deletion. This deletion is thought to alter the confirmation of the spike protein (9). The variant strain, which reportedly accounted for 60% of new London cases, harbors a mutation in the spike protein receptor-binding domain at position 501. Here, asparagine has been mutated to tyrosine, that is N501Y, also designated as S:N501Y to specify the mutation in the spike protein (9). The South African government reported on 18 December 2020 that a new strain, which has the S:N501Y mutation has emerged completely independently of the UK strain (9), and this strain has likely spreaded in the UK (10), spurring further travel bans.

The mutations in the new variant have been mostly in the segment of the virus’s genome that codes for the spike protein that coats the virus and allows it to bind to its one confirmed cellular receptor, angiotensin-converting enzyme 2 (11), and thus infiltrate its target cells. The variant also harbors the P681H mutation near the S1/S2 furin-cleavage site, a highly variable site in coronaviruses (9). Neuropilin-1 is known to interact with furin-cleaved substrates, augmenting SARS-CoV-2 infectivity (12,13). Neuropilin-1 is expressed strongly in the respiratory and olfactory epithelia, and the furin-cleaved S1 fragment of the spike protein has been found to bind to cell-surface neuropilin-1, facilitating viral infection. Implications of the viral variant on interactions with the second receptor of SARS-CoV-2, neuropilin-1 (12,13), are also unknown. Changes in the virus–host interactions may reduce or increase the viral transmissibility, infectivity, or disease severity.

#### **VUI-202012/01 and the COVID-19 Vaccines**

WHO reports that some 50 COVID-19 vaccine trials are underway as of December 2020 (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines>). Some candidates expectedly will meet the therapeutic and prophylactic goals of immunization. Different strategies, including inactivated viral particles, adenovirus-

based vectors, and nucleic-acid vaccines (14,15) have been experimental or in trial. The different point mutations or deletions that have occurred in the VUI-202012/01 raise concern about immune evasion and the effectiveness of the presently investigated vaccines. Considering slight target-vaccine modifications to reflect the nonsynonymous viral mutations will help to efficiently control the virus. The US CDC, however, reports that the vaccines authorized by the US Food and Drug Administration would lead to generating polyclonal antibodies that ideally will target different epitopes on the viral spike protein (9). However, when a large proportion of the population is vaccinated, the virus will likely accumulate multiple mutations in the spike protein to potentially evade immunity induced by natural infection during the pandemic. Predicting these mutations is difficult. Given the variant virus has a high chance of spreading beyond the UK borders and considering severity of the pandemic, detailed understanding of the genomic characteristics of the variant will assist decision-makers in better managing the pandemic, likely when the COVID-19 cases surge again. This strategy will help avoid application of such vaccines that may have lost their effectiveness due to viral mutations. Unfortunately, many nations have no data about the sequence of the virus circulating among the infected cases in the past 12 months; therefore, the variant found in the UK or other distinct variants may practically have evolved in other countries, such as that reported in South Africa (9). Such variants may potentially thwart global efforts to control the pandemic. To effectively manage the pandemic by using vaccines, any altered nonsynonymous viral sequence alterations among the COVID-19 cases (potentially by designing new PCR tests or genome sequencing) should be documented, characterized, and followed. Such a strategy will test the effectiveness of the present vaccines. Any new surge of the COVID-19 cases in the vaccinated populations will be a major health-care concern.

#### **VUI-202012/01 and Asymptomatic Carriers of COVID-19**

Deep-sequencing of MERS-CoV and SARS-CoV has shown that they are closely related genetically to SARS-CoV-2 (70.6–74.9% similarity) (16,17). SARS-CoV-2 can easily be transmitted by asymptomatic carriers (18,19), highlighting the importance of tracing the asymptomatic carriers and contact-tracing in various populations. Up to 40–45% of COVID-19 cases are thought to be asymptomatic (20), and such cases can transmit the disease (19–23) such that up to 44% of secondary cases could be infected by presymptomatic cases (18). Asymptomatic carriers of MERS reportedly ranged from 13% to 25% and 42% to 82% in adult and pediatric populations, respectively, and were thought to contribute to the viral transmission (24,25).

Whether the new viral variant causes a more severe disease will become clear. However, the resurgence of cases or fast spread of the disease in some countries in the last few months may suggest involvement of a variant and transmission by asymptomatic carriers. Lack of sophisticated facilities in some countries hampers efforts such as that by the COVID-19 Genomics UK Consortium. Also, only a small fraction of patient samples can be sequenced at a time. However, based on the findings reported in the UK, other nations should be prepared to deal with generation of any new variant before a new surge in cases. Transmission of any new variant by asymptomatic carriers may contribute to the resurgence of cases in the UK and similarly in other countries. This highlights the importance of case-finding and contact-tracing of the international travelers.

### An Idealistic Outcome

While comprehensive data purporting that any new SARS-CoV-2 variant may cause a more severe disease are missing now, the new variant may potentially cause less severe disease with fast transmission. If so, numbers of hospitalizations will likely be reduced, and efficient control of the pandemic may become possible, also likely by generation of herd immunity thanks to a less severe viral variant.

### Conclusion

Appropriate health policies should consider emergence of any new viral variant. The present countermeasures, including travel bans, nation-wide quarantines, strict social distancing especially during festivities, frequent handwashing, and respiratory hygiene, should never be abandoned. Molecular biology experiments, contact-tracing, and COVID-19 testing are necessary to characterize any new viral variant.

### Declaration of Competing Interest

The authors declare no potential conflict of interest.

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