CARPHA urges enhanced vigilance in response to COVID-19 UK variant found in the Caribbean.

January 26th, 2020

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of the COVID-19 disease, which was declared a pandemic on March 11, 2020. Since then, at least six (6) variants have emerged. The "UK variant" (B.1.1.7 variant), which emerged in September 2020, has been identified in 60 countries globally and recently, in some Caribbean countries.

The UK variant, based on initial data, has higher transmissibility, which has led it to begin to eclipse and replace other SARS-CoV-2 variants in affected populations. Ongoing studies related to the transmission and severity of the UK variant are underway. This increased ease of transmission is of grave concern for its impact on public health and the fight to contain and end the COVID-19 pandemic. This is further heightened by the fact that, at present, the vaccines have not yet been proven to stop disease transmission but rather to mitigate the severity of infection.

The Caribbean Public Health Agency (CARPHA) thus strongly urges its Member States to enhance community surveillance and public health control measures (including quarantine and isolation, wearing face masks and coverings, physical distancing, hand sanitization, avoiding crowds) in both local and visitor populations. Further, CARPHA reminds its Member States that as most cases will have no or mild symptoms, that COVID-19 cases may quietly increase in the community and result in sudden increases in hospitalizations and deaths. CARPHA also urges enhanced surveillance in residential institutions and face to face educational settings and strict adherence to the requirements of negative COVID-19 results for entry to the ports in the Member States to effectively continue combating COVID-19 spread in the Caribbean.

Background on the Variant

The novel coronavirus, like all other viruses, is susceptible to mutation as it replicates, evolves, and spreads. As a RNA virus, it is apt to have more mutations than a DNA virus. Only mutations that provide an advantage to the virus in transmissibility, replication frequency, viral load, or protection from immunity in the host thrive well in the population. Beginning as a phylogenetic cluster in southern England, the B.1.1.7 variant has 17 lineage-defining mutations. It is now responsible for more than 50% of all COVID-19 cases in the UK and has spread quickly around the globe.

There are eight mutations in the B.1.1.7 variant in the spike glycoprotein, including N501Y in the receptor binding domain (RBD), that could potentially affect viral replication and binding to cells of the body. Focus has been on changes to the spike glycoprotein as the attachment of antibodies and the efficacy of current vaccines could be impacted. The detection of variants may be skewed toward high-income countries, because of the lack of equipment, resources or capacity to perform genomic sequencing

Increased Risk of Infection

As of January 24, 2021, over 60 countries, territories, and areas outside of the UK, in all six WHO Regions, reported community transmission or imported cases of the B.1.1.7 variant. Initial data suggests that the UK variant is more transmissible. Though thorough analysis of the severity of the disease and transmission for this variant are still ongoing, the increased transmissibility of the UK variant is a serious concern regarding its impact on public health and the fight to contain and end this pandemic. There is no reported evidence of a reduction in the efficacy of vaccines approved for SARS-CoV-2 in providing protection from any variants. However, it is important to note that vaccinated persons may still spread COVID-19.

Quarantine

With the discovery and proliferation of multiple COVID-19 mutations and variants, and in light of the infectivity increase posed by the UK variant, mandatory quarantine has become even more important to curb

COVID-19 spread. It continues to be crucial to properly and consistently employ and increase the public's adherence to COVID-19 control measures, which have been shown to reduce the spread of the disease. The first line of defense continues to be isolation of infected persons and quarantine of travellers and any person with known or possible exposure to infected persons. Additionally, individuals must continue practicing the measures of wearing face masks and covering, physical distancing, and hand sanitation in all face-to-face settings. These measures must be practiced by all individuals as asymptomatic persons are known to be able to spread the virus. Adequate testing is critical to surveillance measures for residential institutions, face-to-face schooling, celebratory and religious gatherings, and other potential spreader and super-spreader events and activities.

Some countries have since added quarantine to their negative PCR test requirements for persons entering the country from the UK and mandated state quarantine of persons returning from the UK for 14 days.

Vaccination

Vaccines elicit broad immune responses with various antibodies and cell-mediated immune responses; thus, the current, approved vaccines should be able to provide protection against the variants. Clinical trials to determine the efficacy of COVID-19 vaccines are ongoing, and some vaccines have been shown to be effective in preventing coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). At this time, evidence is still being gathered to determine (i) how well the vaccines prevent infection or prevent the spread of the virus and, (ii) how long immunity would last. In between vaccine doses and immediately after getting all the required doses, persons can still get infected and develop the disease as it will take a couple weeks for the body to build up its immunity.

Persons who have been vaccinated should wait at least 2 weeks to ensure the immune response has been optimised. Thus wait 2 weeks before travelling, and they should continue to follow public health measures of masking, physical distancing and hand hygiene. Herd immunity is estimated to be achieved when 75-95% of the population is immune to an infectious disease, ideally via vaccination. Experts do not yet know what percentage of people would need to get vaccinated to achieve herd immunity against COVID-19. Herd immunity remains an important area of research and will likely vary according to the community, the vaccine, the populations prioritized for vaccination, and other factors. Public health restrictions to prevent the spread of coronavirus 2019 will need to be continually enforced and maintained in order to curb this disease.

PCR tests vs. Rapid Antigen (Ag) detection tests

CARPHA continues to recommend the use of the molecular based polymerase chain reaction (PCR) test for the detection of SARS-CoV-2 as it remains the gold standard due to its high sensitivity and specificity, both of which are greater than 95%. The WHO recommended that, wherever possible, suspected cases with active SARS-CoV-2 infection be tested using molecular methods, such as RT-PCR.

With the experience accumulated using PCR for the diagnosis of SARS-CoV-2 worldwide and by CARPHA Medical Microbiology Laboratory (CMML), the extremely high sensitivity of the test allows obtaining positive results beyond the first week from the onset of symptoms. However, it should be noted that results beyond 14 days from the onset of infection may reflect the presence of RNA fragments, sub-viral particles, or probably non-infectious excretion products.

Rapid Antigen Detection Tests (RADT) detect viral proteins that are excreted during the first 5 days after the onset of symptoms. Although these tests have been effective in some public health settings related to SARS-CoV-2, they are not recommended for use as the first line for diagnosis due to lower sensitivity than that of PCR. According to the PAHO: "a negative result (at any stage of infection) should not be used as a criterion to rule out a case; therefore, additional testing with molecular assays is recommended." Results of a study analysing the sensitivity of RADTs showed sensitivities of 60 to 77% , not yet matching RT-PCR for SARS-CoV-2 detection. The use of these tests on the frontline may have negative implications for the transmission of the virus in our communities. In other studies, conducted by experts at the Public Health Agency of Canada, a review of RADT showed that the sensitivity of the tests decreased for positive samples which had PCR Cycle

Threshold (Ct) values > 26. When examining the number of samples received by the CMML and the proportion in terms of the viral load magnitude, it is observed that 19% of the specimens received have a Ct value < 20, 34% have demonstrated a Ct value between 20 and 30 and almost half of the specimens (47%) have viral loads with a Ct value > 30.This constitutes a serious problem for the use of SARS-CoV-2 rapid antigen detection kits, because a large percentage of the samples received, according to the scientific evidence, will give false-negative results and will have to be referred for confirmation by a PCR test.

For these reasons, CARPHA does not recommend the use of rapid SARS-CoV-2 antigen detection tests as a *first line diagnostic approach* in hospitals and patient care centers. Its use should be restricted only to those situations where the use of the PCR test is not possible (such as in remote areas or difficult-to-access zones), always keeping in mind that negative results do not rule out a positive case of COVID-19 and that all negative results must be reconfirmed by the use of the PCR test. If countries must use rapid test, it is recommended that a test showing a sensitivity and specificity of >90% should be used, CARPHA has develop an assessment tool to guide selection of a rapid test : https://www.carpha.org/Portals/0/Documents/Technical%20Guidance/Guidance%20for%20the%20Evaluation%20and%20Selection%20of%20Diagnostic%20Tests%20for%20the%20COVID-19%20Response.pdf

Identification of COVID-19 variants by Gene Sequencing

The CMML remains committed to delivering prompt COVID-19 results to the Region and is working with its Member States in their submission of positive SARS-CoV-2 to be sequenced. The CMML has been guiding laboratory action through testing protocols based on the latest recommendations by the WHO and PAHO. With the emergence of the UK variant in the Region, it is of critical importance for CARPHA Member States to conduct genomic sequencing to identify this variant.

Currently, COVID-19 isolates received by the CMML from Member States are sent to the University of the West Indies (UWI), St Augustine for genomic sequencing to be performed. Following the sequencing process, the UWI then sends the results to CARPHA. Sequencing is a lengthy process that includes experimental and sequence analysis procedures, and the estimated turnaround time to obtain any relevant conclusions can take up to 2 weeks from the receipt of samples at CARPHA.

Results received from the UWI are sent by CARPHA directly to the Chief Medical Officers at the Ministries of Health, who are responsible for dissemination through nationally established channels of communication.

References

1. Lauring AS, Hodcroft EB. Genetic Variants of SARS-CoV-2—What Do They Mean? JAMA. Published online January 06, 2021. doi: 10.1001/jama.2020.27124.Accessed January 24, 2021: https://jamanetwork.com/journals/jama/fullarticle/2775006.
2. Pan American Health Organization / World Health Organization. Occurrence of variants of SARS-CoV-2 in the Americas. 20 January 2021 : PAHO/WHO; 2021. Accessed January 24, 2021: https://www.paho.org/en/documents/epidemiological-update-occurrence-variants-sars-cov-2-americas-20-january-2021
3. World Health Organization COVID-19 Weekly Epidemiological Update Data. As of 17 January 2021, 10 am CET https://www.who.int/publications/m/item/weekly-epidemiological-update---19-january-2021.
4. World Health Organization. SARS-CoV-2 antigen-detecting rapid diagnostic tests: an implementation guide. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.
5. World Health Organization. Episode #20- COVID-19- Variants & Vaccines. 8 January 2021. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/media-resources/science-in-5/episode-20---covid-19---variants-vaccines
6. Pan American Health Organization. Laboratory Guidelines for the Detection and Diagnosis of COVID-19 Virus Infection. 8 July 2020.
7. Khairat SM, Guindy NE, Motaleb MS, Soliman NS. Evaluation of Two Rapid Antigen Tests for Detection of SARS-CoV-2 Virus. International Journal of Microbiology and Biotechnology Volume 5, Issue 3, September 2020, Pages: 131-134.
8. Scohy A, Anantharajah A, Bodéus M, Kabamba-Mukadi B, Verroken A, Rodriguez-Villalobos H. Low performance of rapid antigen detection test as frontline testing for COVID-19 diagnosis. *J Clin Virol* 2020 129:104455.
9. Mertens P, De Vos N, Martiny D, Jassoy C, Mirazimi A, Cuypers L, Van den Wijngaert S, Monteil V, Melin P, Stoffels K, Yin Development of potential usefulness of the COVID-19 Ag Respi-strip diagnostic assay in a pandemic context. *Fron Med* (Lausanne) 7: 225 doi:10.3389/fmed.2020.00225.