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The race between vaccination and evolution of COVID-19 variants



On Aug 30, 2021, WHO added the SARS-CoV-2 variant B.1.621 to its list of variants of interest. B.1.621, which has been given the label mu, was first identified in Colombia earlier this year. WHO describes it as having a “constellation of mutations that indicate potential properties of immune escape”. Mu has been detected in 50 countries and territories around the world. But it represents less than 0.1% of genetically sequenced cases globally, and its prevalence has fallen in recent weeks, which indicates that for now it is being thoroughly outcompeted by the delta variant (B.1.617.2), at least in those places with the capacity for sequencing.

According to the most recent figures from the GISAID Initiative, which monitors the global distribution of the SARS-CoV-2 variants, mu accounts for 25% of newly sequenced cases in Colombia, and 10% of newly sequenced cases in Ecuador, though neither country does a huge amount of sequencing. As of Sept 23, 2021, 3370 cases of mu have been detected in the USA, with 59 cases in the previous 4 weeks. There have been 1279 confirmed cases in Colombia. The UK, which is by far the biggest contributor to GISAID, has registered 62 cases of mu, with no cases in the previous 4 weeks.

Aside from mu, the variants of interest list is made up of eta (B.1.5250), iota (B.1.526), kappa (B.1.617.1), and lambda (C.37). Variants are added to the list if they harbour genetic changes that look as if they could make the virus more transmissible, more virulent, or more likely to escape the vaccine. There has to be evidence of community transmission in multiple countries. “It is very common for variants to ride an epidemic wave in one particular place—in the case of mu, Colombia—

and to reach a high frequency”, explains Erik Volz, Reader in Population Biology of Infectious Diseases at Imperial College London (London, UK). “It only becomes a serious problem, in terms of transmissibility, if we see the variant reaching a high frequency in a lot of places.”

Variants that demonstrate increased transmissibility, virulence, or likelihood of vaccine escape, as well as widespread transmission, are placed on the variant of concern list. There are currently four variants of concern: alpha (B.1.1.7), beta (B.351), gamma (P.1), and delta. The overwhelming majority of sequenced cases of SARS-CoV-2 involve delta, which has an R0 of nearly 7 in a naive population (the R0 for the original strain of SARS-CoV-2 in a similar population is 2.5).

The process to determine whether a variant warrants monitoring begins with some kind of signal. It could be a genetic alteration. Mu, for example, has the E484K mutation, which is also seen in beta and gamma and is associated with a reduction in neutralising antibodies. Alternatively, the variant might be implicated in high rates of breakthrough infections (this has yet to happen). After the signal comes the investigation, typically involving virological work to assess the variant’s neutralisation capacity against convalescent sera, mathematical modelling to determine whether its patterns of growth are consistent with a transmissibility advantage, and an exploration of how the variant could affect severity of disease and reinfection.

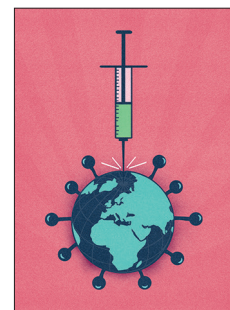
“The variants of interest so far have all had mutations that we have seen before”, noted Martin Hibberd, Professor of Emerging Infectious Diseases at London School of Hygiene & Tropical Medicine (London, UK). “So we can make some predictions

as to how they will behave.” Hibberd worries about the emergence of a new vaccine-resistant variant. He urges policymakers everywhere to give serious thought to recommending a schedule of three doses of the COVID-19 vaccines. “Mild infections in vaccinated people are quite capable of producing variants that might be vaccine-resistant, and the evidence suggests that a third dose boosts the antibody response and reduces the risk of mild infections”, Hibberd told *The Lancet Respiratory Medicine*. “With fewer infections, there is less chance of vaccine-resistant variants arising.”

As things stand, only a handful of mutations are known to be dangerous. A single unknown mutation could still go unheeded and subsequently cause havoc, though Volz believes that this is unlikely. “Something with dramatically different transmissibility or antigenicity would probably require multiple mutations in a combination we have not yet seen”, he said.

The only way to reduce the risk of variants is to cut transmission of SARS-CoV-2 wherever the virus is found. But the rollout of the COVID-19 vaccines continues to favour high-income nations. On Sept 16, 2021, WHO warned that the vaccination drive in Africa is proceeding far too slowly, largely because of a lack of supply. Less than 4% of people on the continent have received two doses of the COVID-19 vaccines. “The staggering inequity and severe lag in shipments of vaccines threatens to turn areas in Africa with low vaccination rates into breeding grounds for vaccine-resistant variants”, stated Matshidiso Moeti, WHO Regional Director for Africa. “This could end up sending the whole world back to square one.”

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