VACCINES AND VARIANTS

With the start of fall many of us are wondering what is on the horizon for COVID-19 and what can we do about it. The first key message is that the pandemic is not over and that the SARS-CoV-2 virus is continuing to evolve and spread throughout the world. Most of the cases at present are the BA.5 Omicron variant. Over the past months the BA.5 variant has outcompeted most other variants to become the dominant variant in many areas. As we have seen several times before, <u>BA.5</u> is both more transmissible and more immune evading then previous variants. That means the virus is easier to spread and catch, and the immunity from either vaccination or previous infection cannot be relied on to prevent infection and COVID-19 disease.

Vaccine boosting (typically a third or fourth dose) has been an effective way to increase protection from COVID-19 disease, especially severe disease. Unfortunately this high level of protective immunity does not last very long (typically less than 6 months), and as the virus continues to evolve the protection offered by the vaccines becomes less. There is still some level of protection offered by the vaccines and boosters, but it cannot be relied on to prevent transmission or disease, including Long Covid. Nearly 50% of the people infected with SARS-CoV-2 develop at least one symptom that persists for 3+ months after resolution of the acute infection, with some symptoms causing long-term disability. Vaccination, including boosting, has been shown to reduce the likelihood of getting Long Covid by 50%. This is helpful but also means that several breakthrough infections may result in long-term disability. This situation is even more concerning with evidence that the severity and likelihood of disease increases with each SARS-CoV-2 infection, even for breakthrough infections.

In an attempt to provide more robust immunity to new variants, several vaccine companies (e.g. Pfizer and Moderna) have developed bivalent vaccines that are now being used in multiple countries. These mRNA vaccines contain mRNA for the Spike protein of the original SARS-CoV-2 strain and for either the BA.1 or BA.5 versions of Omicron. Recent results have shown that these boosters do provide better protection against severe disease for the currently circulating BA.5 variant; however, this protection is still not at the same level we were seeing against variants such as Alpha and we are not sure yet how long this protection will last. In addition, the virus is continuing to evolve, and we are seeing new variants increasing in prevalence (such as BA.2.75). It is not clear how well the new bivalent boosters will protect against BA.2.75 and the subsequent variants, but it is likely that protection will be reduced to some degree.

To an extent this situation is similar to what we see every year with the flu. The virus evolves and each year we need a new vaccine effective against the predicted variant or strain of the flu virus. When this prediction is correct, the vaccine can be quite effective at preventing flu disease, but often the virus evolves such that we have a mis-matched vaccine that is not as effective as hoped. With SARS-CoV-2 the high levels of virus circulation in many areas of the world mean that the virus is evolving very quickly and in ways that we cannot yet predict. Because of this, by the time a new variant vaccine is widely available the virus may have changed, and the new vaccine will no longer be as effective. In addition,

SARS-CoV-2 is a very different virus from the flu and causes disease in different ways, including causing a high prevalence of Long Covid in even mild cases of infection. In addition, with the on-going pandemic the SARS-CoV-2 virus is causing infections all year round, whereas the flu is typically seasonal, with most cases occurring in the winter months. It is unlikely that we will be in a position anytime soon to be able to develop a new variant booster far enough in advance of that variant's spread as is done with the seasonal flu vaccines.

Whilst this situation may seem a little hopeless, it is far from it. The vaccines (and boosters) do provide some level of protection against disease, especially severe disease and for those at high risk of severe acute disease. The new boosters may be very beneficial. We cannot however rely solely on the vaccines to stop the spread of the virus or to completely protect us from acute or Long Covid disease. But the vaccines in conjunction with proven preventative measures can stop virus spread and prevent illness. FFP2/3 (or KN/N95) facemasks and indoor ventilation (including air filtration) are highly effective, and when combined with testing and contact tracing can keep individuals and communities safe, regardless of the next variant that comes our way.

We are grateful to Dr. Jeremy Rossman for providing us with this up-to-date analysis.

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