Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The emergence of the Omicron variant

The recent emergence of the Omicron variant of SARS-CoV-2 with its myriad S gene mutations has caused significant headlines around the world since it was first reported on the 24th November 2021 (WHO, Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern, 2021). This new variant contains 34 mutations in the S protein gene alone; compared to the original Wuhan virus (ECDC, SARS-CoV-2 variants of concern as of 14 December, 2021). The recent dramatic increases in Omicron case numbers in the United Kingdom indicate a significantly increased transmissibility; (UK Health Security Agency, 2021) which may originate from a higher intrinsic intracellular replication rate; (HKUMed finds Omicron SARS-CoV-2) increased ACE receptor binding avidity (CDC, Science Brief: Omicron (B.1.1.529) Variant) as well as enhanced immune escape capability (Pulliam, et al., 2021).

However, questions still remain on the real-life impact of these mutations at large-scale population levels. The current spread of the Omicron variant through the South African population is on a background of relatively low numbers of SARS-CoV-2 infection and low vaccination rates thus far. This raises considerable uncertainty when it comes to assessing the behaviour of Omicron in the more highly vaccinated populations of Western Europe and North America, where COVID-19 cases have been much higher, with recent surges of the still predominant delta variant.

The frequency with which new SARS-CoV-2 variants have arisen during the COVID-19 pandemic has led to additional questions on the mechanisms of this emergence. This may have occurred in previous pandemics but without the now relatively widespread access to viral genome sequencing, timely identification and tracking would not have been possible as it has in this pandemic. With the caveat that sequencing is not conducted on all samples, what information we do have suggests that new variants can arise with multiple novel mutations or novel combination of mutations in a very short space of time. This may come about due to persistent infections in immunosuppressed hosts allowing the evolution of sequential mutations (Choi et al., 2020) which can optimise viral fitness, in terms of host immune escape and/or enhanced intracellular replication rates. This has been seen in previous case reports such as by Chou et al (Pulliam, et al., 2021) and we see it again in the case report in this issue from Stampfer et al, where a patient developed some of the mutations now seen in Omicron. The importance of absent/reduced immune control in virus mutation has been seen experimentally in cell culture (Chen et al., 2021). Other mechanisms such as recombination have occurred in coronaviruses in the past (Graham et al., 2010), particularly when crossing into new host species, and may yet occur in SARS-CoV-2 in the future with an unpredictable effect on the ongoing pandemic (Scientific Advisory Group for Emergencies, 2021).

One aspect of Omicron that has not yet been revealed is how dispersed the infections are, i.e. whether a small proportion of those infected account for most of the transmissions. This property of 'overdispersion' is characterised by a parameter, k, where a low value of k (e.g. 0.1 as for the original Wuhan virus) indicates that a small proportion of infected cases may account for most of the transmission, e.g. for $k = 0.1$, 10% of cases may account for 80% of transmission (Adam et al., 2020; Endo et al., 2020). This effect is likely host immune-mediated and so it is not presently possible to determine who those 10% of cases are, but it is important for modelling the spread and may be an important facet of pandemic control in the future.

However, the key question is whether Omicron will cause milder disease in both unvaccinated (with or without natural immunity) and vaccinated populations, including as noted by Stampfer et al, the subset of immunosuppressed patients who have either not responded to vaccination at all or who exhibit a rapidly waning antibody response. A recent study from South Africa showed more vaccine escape but fewer hospitalisations in Omicron-infected cases, and data from the United Kingdom provides further evidence for this effect (Wolter et al., 2021; Sheikh, et al., 2021; Ferguson, et al., 2021). This might be what we would expect to see for a virus that is adapting better to its new host, with enhanced transmissibility but lower severity – to allow infected but still relatively well individuals to continue mingling in society to spread the viral genes further – which is a measure of viral fitness (Callaway, 2021). Fortunately, there is mounting evidence that boosters with mRNA vaccines do improve effectiveness against the Omicron variant (Garcia-Beltran, et al., 2021), which could also affect how Omicron spreads through populations that have booster programmes under way. Time will tell, and, as always, more real-world data is still required to track Omicron's trajectory, more accurately, across different global populations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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