

Editorial

Avoiding Omega

Simon Attard Montalto

The pandemic goes on – smouldering along in developed countries, Malta included, whilst still disseminating widely in other countries. Those countries that have achieved a semblance of control have done so by means of a combination of measures including social distancing, barriers to droplet spread and vaccination. The latter is, undoubtedly, the key measure whereby control of this pandemic can be achieved.¹ Nevertheless, a sizeable minority including otherwise well-informed individuals (doctors included!), continue to scaremonger against vaccination. In a nutshell, COVID 19 vaccines do have adverse effects but, in the vast majority of cases these are minor and no different from those associated with a host of other routine and widely accepted vaccines. More serious adverse events are rare to extremely rare, and no more common or slightly increased compared with naturally occurring events (such as myocarditis, reported in 4.4-12.6 cases/million with the first and second Moderna vaccines, respectively, and resulting in 1 death in every 5 million persons ²; and thrombotic events observed in 417 cases in 24 million doses with the AstraZeneca vaccine, with 72 deaths ³). No country can claim the accolade 'COVID-free'. Those that have achieved a respectable level of control and have relaxed restrictive lock-down measures, usually receive a wake-up call before returning to a semblance of 'normality'. In this regard, Malta was doing well, primarily as lessons from earlier over-zealous premature 'relaxation' were heeded, combined with an aggressive programme of vaccination. Credit is due to all those involved in policy decision, implementation and adherence. Unfortunately, Malta like all other countries, was not immune to Omicron and this latest variant, with its enhanced transmissibility, soon pushed the daily case-load to record figures within a space of a few weeks. Although very rigorous and, at times, draconian measures are required to achieve pandemic 'control', Omicron has highlighted how difficult it is to sustain this. Even if Malta's vaccine coverage continues to improve (it is already one of the best worldwide), this

Cover Picture:

'Early morning in the Doge's palace courtyard'

Pencil

By Alexander Manché

Alexander Manché founded the Cardiothoracic Unit in Malta in 1995, having trained in the UK and the US for almost 20 years.

He also pioneered the transplant programme, mitral valve repair and minimally invasive aortic valve surgery. He was responsible for training the new generation of surgeons.

His interests include art, music, travel and medical history.

Professor Simon Attard Montalto Editor, Malta Medical Journal Head, Department of Paediatrics The Medical School Msida, Malta simon.attard-montalto@gov.mt will still not be sufficient to keep Malta 'off the hook'.

COVID19 like other RNA viruses such as influenza and HIV, has a great propensity to multiply and mutate. Predictably, any mutations that confer a significant biological advantage will rapidly ensure that the newly mutated form will become the dominant virus type in circulation. These have been defined by WHO as Variants of Concern (VOC) and, to-date, there have been 5 major VOCs.^{4,5} Hence, the acquisition of more efficient spike proteins on the B1.1.7 (alpha) variant that emerged in the UK in September 2020 increased its infectiousness by 50%. This variant soon took over in Europe from the originator B.1.17 virus that first emerged in Wuhan at the end of 2019. Similarly, the B.1.359 (beta) variant first reported in May but emerged in October 2020 in South Africa, the P.1 (gamma) variant from Brazil in November 2020, and B.1.617 (*delta*) variant reported in India in October 2020, all went on to become the major players in large parts of their originator country and/or continent. The delta variant was about 60% more transmissible than the original pathogen,⁶ and rapidly spread pan-globally from where it emerged in India. To-date, these four main variants all demonstrate enhanced infectiousness but with variable increases in disease symptomatology, morbidity and mortality and, consequently, have resulted in mild to moderate strain on healthcare resources.⁴ The same is true for the latest VOC, B.1.1.529, Omicron, first reported in South Africa in November 2021 that, with its multiple mutations conveying enhanced spike protein adherence, is far more transmissible.⁷ Luckily, this has not been combined with increased aggressiveness and, on a background of increased population protection (through natural infection and vaccination), has not resulted in the collapse of health services.⁷ However, this status quo can only be sustained provided the new variants remain vaccine-sensitive. This proviso is absolutely paramount and has been the case with,

pe

for example, the Pfizer-BioNTech, Moderna and AstraZeneca (and other) vaccines and the B.1.1.7 (UK/*alpha*) variant, where similar or slightly reduced vaccine effectiveness was reported compared with the original virus.⁸ In contrast, the same cannot be said for the B.1.359/*beta* variant, where vaccine-effectiveness is reduced across the vaccine range and may be as low as 10-60% compared with the original virus.⁹

Many other variants, defined as Variants of Interest (VOIs), have been under investigation by WHO since 2020, and given the sequential Greek letters epsilon (B.1.427/429, USA, June 2020), Eta (B.1.525, Nigeria, December 2020), Iota (B.1.526, USA, November 2020), *Kappa* (B.1.617.1, India, October 2020) Lambda (C.37, Peru, December 2020), and Mu (B1621, Colombia, 2021).^{4,10} (*Nu* and *Xi* were skipped). These variants demonstrate increased viral transmissibility with decreased neutralising antibody titres, although to a lesser degree than the five main variants and, crucially, retain susceptibility to current licensed vaccines.^{4,10} The ultimate concern would be, of course, the emergence of yet another variant that is, this time, immune to current vaccines. This would throw the pandemic crisis into reverse if not free-fall once again, and although vaccine programmes would now have the advantage of pre-existing technology, they would be playing catch-up with all the negative connotations on health, health services, businesses, travel, etc. The economic and health costs of the pandemic have been estimated upwards of \$375 billion per day, so that any 'pandemicreversal' would be disastrous.

The aim must be, therefore, to prevent new strains in the first place and this will only occur if viralreplication is curtailed. Unfortunately, the global reality is just the opposite for the following reasons: some countries are still reporting exceeding low vaccination rates (some below 10% of the population), difficulties producing and distributing vaccines, active misinformation campaigns, and persistence of multiple hot spots where large numbers of people are crowded together in poorly sanitised environments.¹¹⁻¹² This scenario provides for uninhibited viral multiplication and widespread transmission amongst susceptible individuals that, as has already been observed, is rapidly transferred onto the world stage, with the ever-present risk of further mutations. Ultimately, this means that no country is safeguarded regardless of its own level of vaccine-coverage. Upping the protection of the vulnerable, however defined, by, for example administering a third booster dose as opted for by Malta is, in itself, commendable. However, this and all the good work over the past eighteen months will be futile in the face of a new, vaccine resistant VOC. There is, therefore, an urgent need to increase coverage in developing countries without delay. This must be the strongest argument in support of COVAX, and for those countries that have access to vaccines to donate significant numbers to poorer countries.¹³ This needs to happen urgently before health services worldwide will have to deal with a vaccine-resistant strain. Indeed, every effort is required to avoid this eventuality, whether it may be *pi, rho, sigma*... or even *Omega*!

REFERENCES

- C Aschwanden. Five reasons why COVID 19 herd immunity is probably impossible. Nature, March 2021. http://www.nature.com/articles/d41586-021-00728-2
- B Bozkurt, I Kamat, PJ Hotez. Myocarditis with COVID-19 mRNA vaccines. Circulation, Aug 2021. https://pubmed.ncbi.nlm.nih.gov/34281357/
- B Long, R Bridwell, M Gottlieb. Thrombosis and thrombocytopenia syndrome associated with COVID-19 vaccines. Am J Emerg Med. 2021: 49; 58-61. doi: 10.1016/j.ajem.2021.05.054.
- Tracking SARS-CoV-2 variants. WHO, September 2021. http://www.who.int/en/activities/tracking-SARS-CoV-2 variants/
- N Cecil. Indian variant up to 60% more transmissible than Kent variant. https://www.standard.co.uk/news/uk/indian-variantmore-transmissible-kent-variant-prof-neil-fergusonb938729.html
- SE Galloway, P Paul, DR MacCannell, MA Johansson, JT Brooks, A MacNeil, et al. Emergence of SARS-CoV-2 B.1.1.7 lineage – United States, December 29, 2020-January 12, 2021. CDC 24/7; 2021. https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e2 .htm

- M Kozlov. South African SARS-CoV-2 variant alarms scientists. The Scientist, Jan 2021. https://www.thescientist.com/news-opinion/south-african-sars-cov-2variant-alarms-scientists-68317
- C Wilcox. What do we know about Mu, the WHO's latest Variant of Interest. The Scientist. https://www.thescientist.com/news-opinion/what-we-know-about-muthe-who-s-latest-variant-of-interest-69161
- M Khan, SF Adil, HZ Alkhathlan, MN Tahir, S Saif, M Khan, ST Khan. COVID-19: A global challenge with Old History, Epidemiology and Progress so far. Molecules. 2020; 26(1): 39. doi: 10.3390/molecules26010039
- G Forni, A Mantovani. COVID-19 vaccines: where we stand and challenges ahead. Cell Death Differ. 2021; 28(2): 626-639. doi: 10.1038/s41418-020-00720-9. Epub 2021 Jan 21.
- GAVI launches innovative financing mechanism for access to COVID-19 vaccines. https://www.gavi.org/news/media-room/gavi-launchesinnovative-financing-mechanism-access-covid-19vaccines

Corinthia Group Prize in Paediatrics, 2021

The Corinthia Group Prize in Paediatrics for 2021 was awarded to Dr Sara Rapa, who obtained the highest aggregate mark over the combined examinations in Paediatrics in the fourth and final year of the undergraduate course. Whilst offering our congratulations to Dr Rapa, we would also like to congratulate all those who performed admirably during the undergraduate course in Paediatrics. In the accompanying photograph, Dr Rapa is seen receiving her prize from Professor Simon Attard Montalto, Head of Paediatrics, both complying with COVID 19 regulations! Finally, the Academic Department of Paediatrics and Medical School remain indebted and are extremely grateful to the Corinthia Group for their ongoing support.

Professor Simon Attard Montalto

