

## Is there light at the end of the Covid-19 tunnel?

The 9 months that have elapsed since the debut of SARS-2 coronavirus in Wuhan, People's Republic of China, have seen widely divergent public health responses: none, though, yet informed by a very profound consideration of what has been the third recognised zoonotic event among coronaviruses in recent years.

In at least one respect, the development of safe and effective vaccines, the advanced economies have acted swiftly, encouraging scientific innovation and funding new approaches to human immunisation. Most of these countries have also sought to contain SARS-2 virus spread through lockdown, but with a variable success that has left the majority of their populations now reliant on early vaccine approval and an adequate product choice as the only escapes from lockdown's associated economic and social harms. A few other developed economies, and many developing ones, have either not chosen or not been in a position to adopt lockdown; but in so far as these countries have a younger demographic profile they have not been overwhelmed by Covid-19 related illnesses. Nonetheless, global Covid-19 mortality is already approaching a million, inviting historical comparison with former years that saw genomic shifts in influenza A.

Both the developed and developing worlds now look forward to seeing the first safe and protective vaccines in 2021, and expect virus near-elimination soon thereafter; but the prospect of this happening depends on the availability of vaccines now in preparation, their cost, their abundant provision and their uptake. There is some background experience of conventionally prepared veterinary coronavirus vaccines and this may be of predictive value as regards immunogenicity.<sup>1</sup> Furthermore, political pressures and financial incentives have since stimulated multinational companies to explore more modern and diverse approaches to vaccine production. Several of these products have now reached the third phase of evaluation,<sup>2</sup> and it is fair to assume that one or two at least of them will meet immunogenic criteria and once they have been shown to be safe begin to be offered to vulnerable populations.<sup>3</sup> However, vaccine-associated morbid enhancement by respiratory virus vaccines was an issue in the early development of a respiratory syncytial virus vaccine, and this phenomenon cannot be ignored as regards SARS-2 virus no matter how strong the political pressures. More especially, safety has to be ensured if Covid-19 vaccines are to be pressed upon younger, healthier cohorts so as to establish herd immunity.

Whether the vaccine uptake will actually ensure a rapid global retreat of SARS-2 virus also remains open to question. In the

medium term (i.e., an interval of a few years rather than just months) the aim must be to establish a population immunity that includes age groups for whom SARS-2 infection constitutes a near negligible risk, and this will involve children whose parents may doubt the value of adding Covid-19 vaccine to an already crowded vaccination schedule. There will be non-compliance: universal immunisation against Covid-19 is not a foregone conclusion.

The long-term prospect is even more uncertain. Continuing human encroachment on natural habitats and further exposure to other species from which virus variants may be acquired are factors that make further zoonotic outbreaks likely even if unpredictable. When they do happen, the public health response to them must be rapid, adept, transparent and trans-national in ways that have until now been lacking.

At the same time, the general vulnerability of the ageing populations of the developed world has to be addressed.<sup>4</sup> The immediate effect of the emergence of SARS-2 virus was ill-controlled morbidity and mortality concentrated in care homes for the elderly,<sup>5</sup> as well as among those with chronic health deficits due to diabetes, obesity and immunological deficits. The immediate anxiety now is that a SARS-2 virus resurgence with a concurrent influenza A genomic drift, if not shift, will create a health crisis this winter. In the future, these vulnerabilities need to be reduced through prophylactic health care backed by continuing financial commitment.

Until very recently, administrative arrangements in advanced economies have mostly lumped the management of emergent infectious diseases in with the wider public health agenda. This has meant marrying unrelated scientific disciplines and overlooking virological detail. So, for example, standardisation of rRT-PCR diagnostic assays for SARS-2 virus has not been insisted upon, and their results have not been interpreted as measures of infectiousness (in terms of cycle threshold values). The future pursuit of mammalian and avian virology and vaccinology needs to be brought under a single umbrella, correcting the misalliance of the infectious and the non-infectious public health agendas; and academic, administrative and financial structures need to be readjusted accordingly. In the era of SARS-2 the voices of virologists have been drowned out by loudly expressed opinions from other quarters, for instance from public health epidemiologists and mathematical modellers who have relied on data too weak to support the statistical weight placed on them. Now is the time for medical virology to assert itself.

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