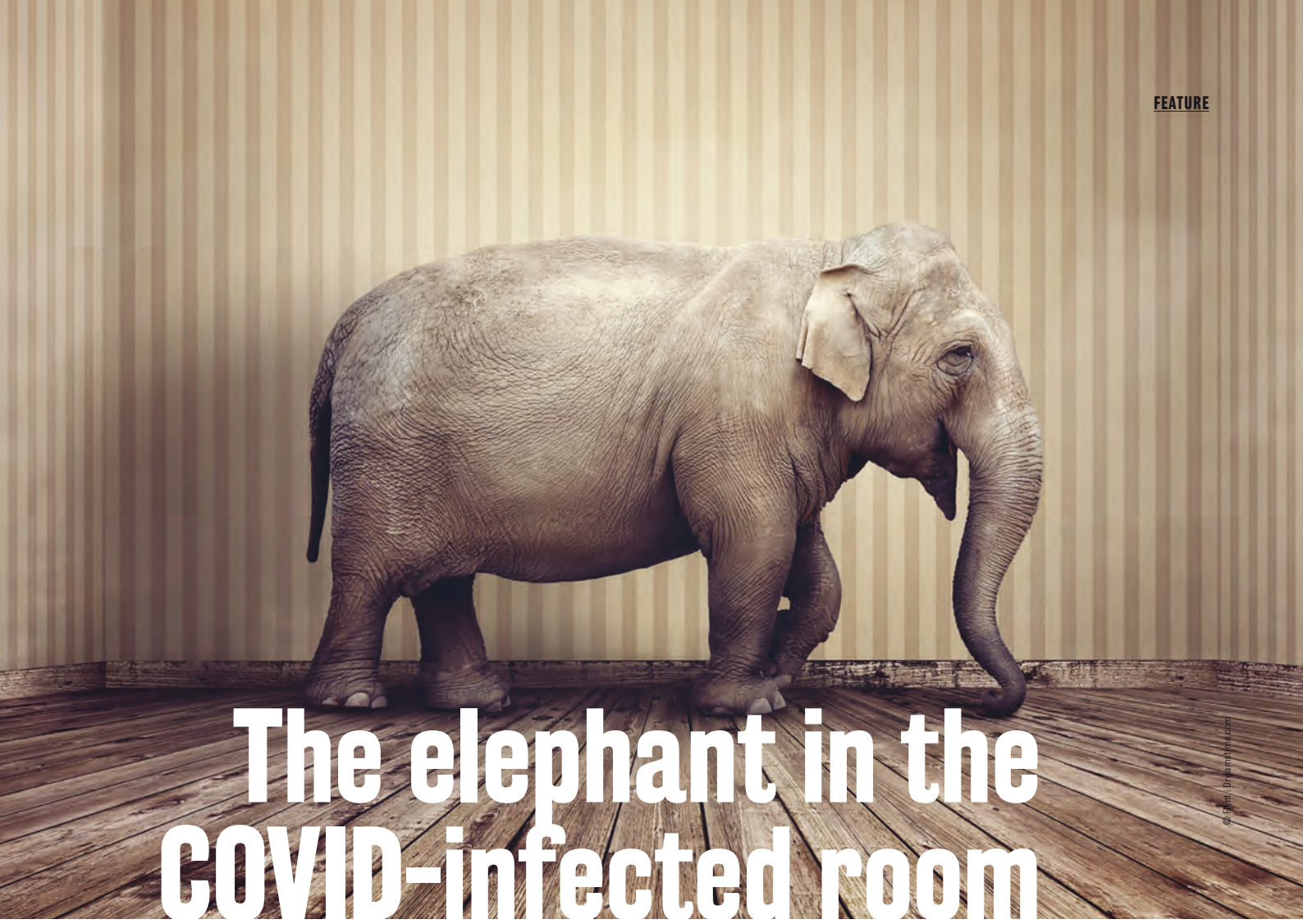

The elephant in the COVID-infected room

How whole system science may facilitate human adaptation to SARS-CoV-2

by Rob Verkerk BSc MSc DIC PhD FACN

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As the scale of social and economic turmoil brought about by national lockdowns continues to escalate, and the possibility of further lockdowns being mandated to blunt expected future waves of infection looks ever more likely, it is a crucial time to reconsider strategies for containment or mitigation of SARS-CoV-2 associated with the newly-described COVID-19 disease.

When investigating options for any novel disease, it is useful to assess the situation from multiple perspectives and scales in order to ensure all possible and potentially viable options are considered adequately. Presently, the primary strategies being enacted for containment or mitigation can be broadly categorised into social distancing and lockdowns, with a view to shifting the emphasis to vaccination as and when safe and effective vaccines are available.

Given that all life forms, including humans, have co-evolved alongside viruses and other elements of the microbiota, it is essential that evolutionary, systems biology and ecological perspectives are maintained in assessments of COVID-19 and the search for

Immune enhancement is the 'elephant in the room'

solutions. Equally, such views cannot be considered without consideration of the political, social and economic responses of humans to the emergence of the pandemic. The purpose of this review is to maintain such perspectives in order to highlight the possibility of more effective pathways towards resolving the current pandemic.

Viruses – the bigger picture

Presently most of the world views viruses, especially SARS-CoV-2, negatively. The problem with viruses, in the minds of most, is that viruses cause disease, from Ebola to Marburg, or measles to HIV. But no virus in living memory has decimated social and economic norms to the extent of the virus associated with COVID-19. Ironically, however, most of this social and economic disruption has been only indirectly caused by SARS-CoV-2, the main culprit being the partially coordinated, global human response to a newly emerged virus of only moderate deadliness and contagiousness.

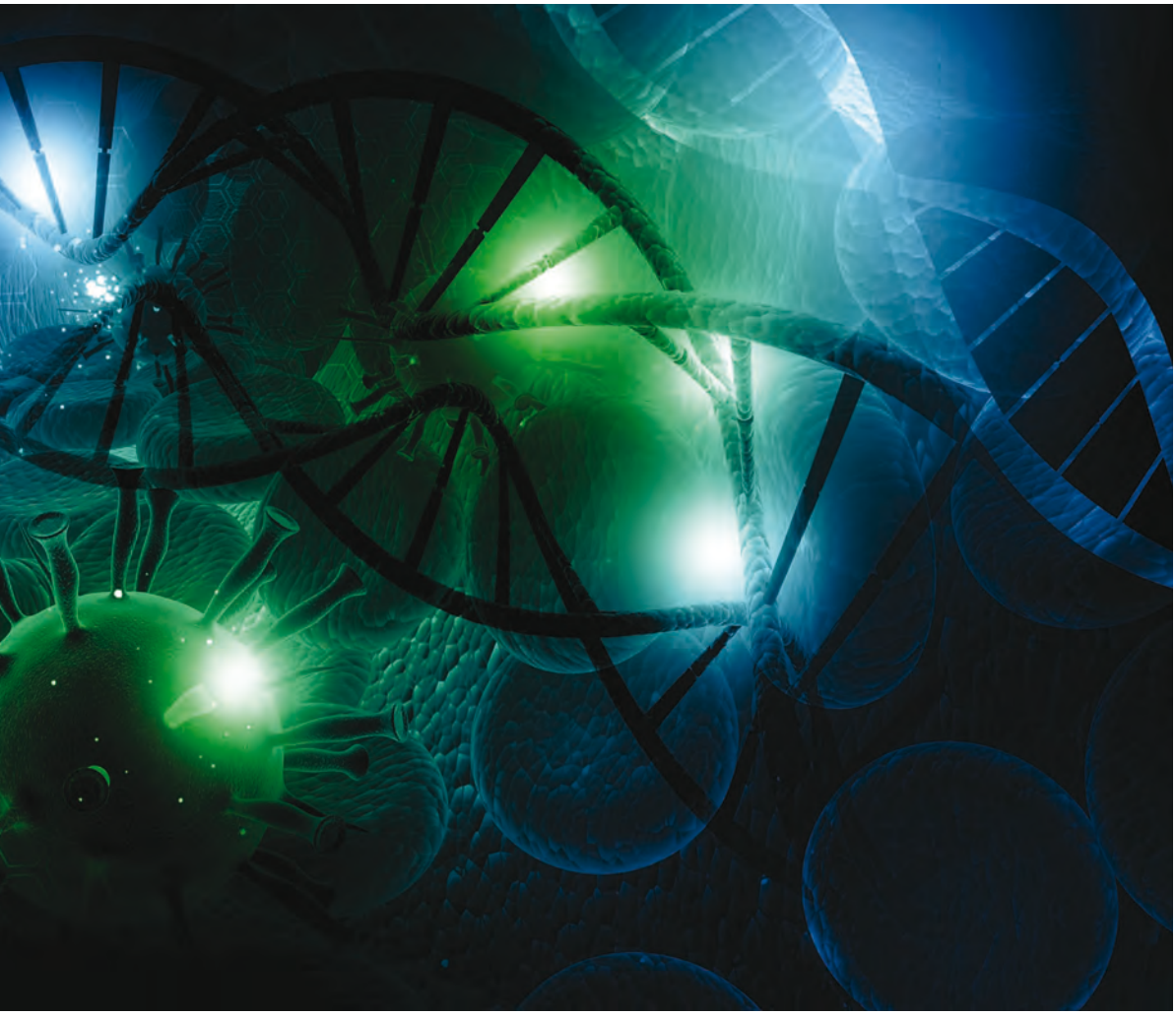
When the public has been so imbued with fear over a new virus, there is very little appetite for the emerging science to inform us that viruses are critical to the evolution of probably all life forms on Earth, humans included. Viruses, of course, are not considered living organisms in their own right because they cannot self-replicate. Accordingly, they are sometimes referred to as pseudo-organisms, a term that has also been applied to bioengineered (genetically modified) organisms. They are simple structures that contain genetic material (either RNA or DNA) in a protein coat (capsid). They lack the ribosomes to synthesise protein or the mitochondria (in animals) or chloroplasts (in plants) to produce energy, so they must use the machinery of their hosts to reproduce. They have the capacity to enter (infect) all life forms, from simple bacteria to fungi, plants and animals, at all levels of complexity. Their method of reproduction, regardless of the type of virus, is essentially similar, going through a number of stages: attachment, penetration, uncoating, replication, assembly, maturation and, finally, virion release. While the virus hijacks the host cells' genetic replication machinery to reproduce and so can be rightly considered a type of non-living obligate parasite, viruses, like bacteria, do not necessarily act as pathogens. Viruses are the most abundant biological entities on Earth and have likely been key drivers of evolution of all life forms since life originated.

The rapidly emerging area of research on the human virome, that has been catalysed both by the availability of affordable, high throughput sequencing technology and interest from the biotechnology sector, suggests that viruses fulfil a wide range of beneficial functions in humans, including maintaining stability of gut microbial communities, host resilience, genetic exchange and turning on or off specific genes. The most abundant forms of viruses are bacteriophages which act on bacteria, hence their extreme importance in the human gut. Prokaryotic phages, as the most populous group of viruses, are thought to outnumber their bacterial hosts by around 10:1 in almost all terrestrial and marine habitats.

Given the pivotal role of viruses in the evolution of humans and other life forms, it is perhaps misleading to regard a new virus that has adapted to entering and

Viruses are critical to the evolution of probably all life forms on Earth, humans included

All life forms have co-evolved alongside viruses



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replicating in human cells as 'the enemy'. That is because today's apparent enemy may, and in fact is likely to, yield benefits for human and other populations in the longer-term. The process in which a new virion is created that in turn adapts to a new host is nothing new or unique, assuming SARS-CoV-2 is of zoonotic origin and not the result of gain-of-function research in a laboratory, a matter that is as yet not entirely decided by scientific consensus.

SARS-CoV-2 is the seventh known coronavirus to have adapted to humans, and is closely related to coronaviruses responsible for SARS and MERS in 2003 and 2012 respectively, both of which have become held by natural processes of adaptation of the virus and its human host without a need for pharmaceutical intervention.

Cause or effect?

If one approaches COVID-19 from what might be described as a Pasteurian perspective, which supports the essential tenet of the germ theory of disease, it is logical to consider SARS-CoV-2 as the cause of our current woes. But science has moved on. Even Louis Pasteur, who picked up Edward Jenner's preliminary work on vaccines a century earlier, has been shown to be mistaken on some fundamental points. One of them is regarding the mechanism of action of the earliest vaccines he developed for chicken cholera and anthrax in sheep. He was convinced that the presence of the microbial pathogen would deplete the host of essential nutrients and was unaware that immunity was developed through an immune response by specialised cells of the host. His work was also driven by a desire to profit from the veterinary community; so it is reasonable to consider Pasteur's efforts as the first example of a biotech company in which the funds were used to support academic research,

Viruses are the most abundant biological entities on Earth

in this case in the Pasteur Institute. This model was deeply influential in creating the current biomedical model of healthcare that continues to be supported largely by investment and support, directly or indirectly, from the pharmaceutical (and vaccine) industry.

The prioritisation of vaccine-based strategies and the relative disinterest in multifactorial strategies that could be used to enhance immune function to protect against a recently emerged virus, reflect the persistence and dominance of this biomedical model that is predicated on faulty principles.

Among these are:

1 *That infectious diseases can be combatted more effectively by targeting the infective agent than by building immune resilience*. This notion is born out of Pasteur's germ theory of disease, furthered by Koch's postulates, and it generally over-emphasises the role of the pathogen, and under-estimates the deficiencies in the human immune system in the manifestation of symptoms of disease. This element of the biomedical model is particularly problematic during the current COVID-19 pandemic, despite clear evidence that those with deficiencies in immune function remain the most vulnerable to severe disease.

2 *That symptomatic treatment is one of the primary functions of healthcare systems*. Accordingly, use of properly prescribed medicine represents the third major cause of death in industrialised countries. This prioritisation of medical interventions that targets symptoms, and not causes, of diseases misrepresents the mission of 'healthcare', which ostensibly is about caring for health, and not disease. The majority of diseases that contribute to healthcare burdens are actually caused by imbalances in physiological, psychological and ecological interactions and any rational approach to healthcare would attempt to correct such imbalances, ideally before they had manifested as disease. Healthcare has yet to fulfil its promise of proactively maintaining or regenerating health (salutogenesis) and existing efforts on disease prevention are deficient in their efforts to correct functional imbalances and have yet to find their rightful place at the heart of healthcare systems.

Resilience as an overriding goal

Resilience requires that multiple systems within the body, particularly those that relate to psycho-neuroimmunoendocrinological (PNIE) function are balanced and optimised. The function of this 'super system', that involves the interconnected psychological, neurological, immunological and endocrine systems, is dependent on multiple factors, including genes, environment and behaviour. There is no 'one-size-fits-all' because each individual has a unique genotype that is, in turn, uniquely marked epigenetically according to the lives and environments of the individual. These epi-marks dictate which genes are silenced and which are expressed – and, if so, by how much. Individual gene expression patterns determine the health and resilience status of an individual at any given point in time, as well as the propensity for particular types of disease.

Pasteur's model was deeply influential in creating the current biomedical model of healthcare

Dietary, lifestyle and environmental changes provide the most potent ways available to humans to change patterns of gene expression and improving resilience – a key imperative when facing adaptation to a virus newly adapted to the human species.

It is not within the scope of this article to detail the extensive and conclusive research data that has emerged since the detection of SARS-CoV-2. However, it demonstrates that defects in immunity, either through immunosenescence in older populations, or through specific risk factors that are associated with morbidities and especially comorbidities (hypertension, diabetes mellitus, drug-induced immunosuppression), are the primary factors contributing to severe disease and SARS-CoV-2-associated mortality.

Given that the level of immune resilience is the primary contributory factor to severe COVID-19 disease, it follows that a rational approach to prevention or mitigation of COVID-19 would involve approaches that seek to regenerate or enhance immune resilience. This

It is perhaps misleading to regard a new virus that has adapted to entering and replicating in human cells as 'the enemy'

remains the 'elephant in the room', and is exemplified by the increasing data showing the value of vitamin D in prevention, and the success of treatment protocols implemented by frontline emergency doctors that target inflammation and immune system modulation.

Barriers to adaptation

The biomedical model that has driven the development of the existing healthcare system has become, ironically, potentially the single greatest stumbling block to increasing the rate of human adaptation to the presence of the newly emerged coronavirus. International cooperative efforts that are directed towards developing prevention, mitigation or treatment efforts are controlled by an astonishingly small number of players, including the World Health Organization, the Coalition for Epidemic Preparedness Innovations (CEPI) and Gavi, the Vaccine Alliance. All these organisations and many of the leading candidate vaccine technologies are supported or funded directly by the Bill and Melinda Gates Foundation. Bill Gates stated the following in his GatesNotes blog on 30 April 2020:

> One of the questions I get asked the most these days is when the world will be able to go back to the way things were in December before the coronavirus pandemic. My answer is always the same: when we have an almost perfect drug to treat COVID-19, or when almost every person on the planet has been vaccinated against coronavirus.
>
> The former is unlikely to happen anytime soon. We'd need a miracle treatment that was at least 95% effective to stop the outbreak. Most of the drug candidates right now are nowhere near that powerful. They could save a lot of lives, but they aren't enough to get us back to normal.
>
> Which leaves us with a vaccine.

Individual gene expression patterns determine the health and resilience status of an individual

Diet is amongst the most potent ways to improve resilience

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Such views do not recognise a knowledge or an understanding of the co-evolutionary relationship between humans, viruses and other microbiota. Instead, they suggest a very strong desire to develop new-to-nature technologies, including genetically engineered, patentable vaccines, as the primary human response to SARS-CoV-2. The unprecedented speed of development of candidate vaccines, including the use of previously untested technologies, brings with it considerable uncertainty over both the safety and the effectiveness of commercialised vaccines.

Those who have the continued capacity to exercise choice in healthcare may do well to help bolster their own innate and adaptive immunity by seeking to improve the function of their PNIE super system. It is this exquisitely adapted system that has helped bring humans this far on our species' evolutionary course, yet public health efforts to help citizens enhance immune function have been conspicuously ignored by governments and health authorities.

An alternative, seemingly higher risk option for both individuals and societies, is to rely on vaccine prophylaxis delivered by non-transparent special interests, likely based on mixtures of genetically engineered antigens and neurotoxic adjuvants (e.g. aluminium) that attempt to mimic the immune response following naturally-acquired infection.

Conclusions

It is likely that the human response to the emergence of SARS-CoV-2 has caused a greater adverse impact on societies than the pathogenic effects of the virus itself. While the virus' origins remain unclear, the relationship remains an ecological one that will likely follow a pattern of increasing host-virus adaptation over time.

Contrary to information presented by governments and health authorities to the public, over-reliance on novel recombinant technologies that have never been used in commercial vaccines, while not prioritising efforts to optimise immune system resilience to naturally-acquired infection, is a high risk strategy. This risk has become even more evident with the publication of preliminary results of Phase 1 and 2 vaccine trials that point to incomplete effectiveness, a need for multiple doses, as well as significant adverse reactions.

Now is the time to establish a new narrative around COVID-19, one based on the ecological relationship between humans, viruses and other elements of the microbiota. Central to this is the notion that every individual has the capacity to optimise his or her ability to tolerate infection by SARS-CoV-2 through enhanced immune function. While immune enhancement remains the 'elephant in the room', its prioritisation is in effect a 'no brainer' given it will yield benefits regardless of the mechanism of induction of the immune response, whether this be through naturally-acquired infection or by exposure to antigens induced following vaccination.

Now is the time to establish a new narrative around COVID-19

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Glossary

- Bacteriophages: viruses that infect and replicate only in bacterial cells
- Epigenetics: the study of changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself
- Epigenetic marks (epi-marks): temporary 'switches' that control how our genes are expressed during gestation and after birth
- Gain-of-function research: experimentation that aims or is expected to (and/or, perhaps, actually does) increase the transmissibility and/or virulence of pathogens
- Genetic exchange: one mechanism by which new genotypes of species are formed
- Genotype: the genetic constitution of an individual organism
- High throughput sequencing (HTS): a plethora of methods to sequence large samples of DNA or RNA or protein
- Immunosenescence: age-associated decline of the immune system that may contribute to the increased incidence and severity of infection and possibly to autoimmune disease and certain cancers in the elderly
- Microbiota: the microorganisms of a particular site, habitat, or geological period
- Prokaryotic: relating to single-cell organisms with no nucleus
- Psychoneuroimmunoendocrinology (PNIE): the study of interactions between the psyche, neural and endocrine functions and immune responses
- Salutogenesis: focusing attention on the study of the origins of health, contra the origins of disease
- Human virome: total collection of viruses in and on the human body
- Zoonotic disease: a disease which can be transmitted from vertebrate animals to humans.

https://www.anhinternational.org/resources/documents/anh-intl-blueprint-for-health-system-sustainability/

https://covid19criticalcare.com (See MATH+ protocol)

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