

## How to deal with the pandemic of SARS-CoV-2 variants?

- Geert Vanden Bossche

- i) As a first and most critical measure, I continue to advocate for an immediate stop of the ongoing mass vaccination campaigns as those will only enhance the emergence of new, more infectious variants.

There is increasing evidence that antibody titers in asymptomatically infected people are short-lived and are not responsible for abrogation of infection (see references from the literature: [topic 2, under 'protection of asymptomatic carriers not due to Abs'](#)). On the other hand, there is clear evidence that the affinity of antigen (Ag)-specific Abs for a specific Ag is much higher than the affinity of antigen(Ag)-nonspecific natural Abs (Nabs) for the very same Ag (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5704100/>). It is, therefore, reasonable to assume that S-specific Abs outcompete sIgMs (natural Abs; NABs) for binding to spike (S) protein. Consequently, the capacity of sIgM to reduce S-mediated viral infectiousness may dramatically decrease in the presence of S-specific Abs. This is normally not problematic in case S-specific Abs bind well enough to S to outcompete binding of the ACE2 receptor to the spike protein. However, S-specific Abs that have strongly diminished neutralization capacity as a result of their low binding strength to S (e.g., in case of a mismatch between S used as immunogen and S Ag on the target variant), may still be able to suppress virus binding by NABs.

- ii) It may, therefore, be useful to further investigate whether conservation of a seronegative immune status may enable young and healthy people to resist Covid-19 disease regardless of the variant they get exposed to. Animal models (<https://www.frontiersin.org/articles/10.3389/fimmu.2020.02139/full>) may need to be established to verify NAB-mediated protection against Coronavirus in healthy weaned animals as a function of their maternal, Ag-specific Ab titers. In the meantime, more reliable serodiagnostic fingerprick assays may need to be developed to avoid false negative results.
- iii) Fostering campaigns calling on people to live a healthy life may also need more serious consideration. I am certainly not an expert in this field but there is increasingly compelling scientific evidence showing that a healthy life(style) correlates with a strong innate immune system (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6384419/>; <https://bmccgenomics.biomedcentral.com/articles/10.1186/s12864-020-06994-0>)
- iv) As far as vulnerable people (i.e., especially elderly who are immune suppressed as a result of suppression of their innate immunity or underlying disease) are concerned, it seems paramount to protect them by conventional infection prevention measures, even including avoidance of contact with younger age groups.

- v) Furthermore, data published in peer-reviewed journals provide compelling evidence that treatment of Covid-19 at an early stage of disease can prevent many patients from developing severe illness and ending up in ICUs for prolonged intensive care treatment. I am attaching a link to a seminal paper authored by Prof. McCullough et al.:  
<https://www.amjmed.com/action/showPdf?pii=S0002-9343%2820%2930673-2>
- vi) Also off-label use of approved drugs needs to be given more serious consideration and more financial support is needed to enable clinical studies that document the safety and efficacy of combinatorial use of those in Covid-19-diseased subjects.

A combination of all of the above-proposed actions would allow the scientific community to buy some time for developing a universal strategy aimed at eradicating the steadily growing number of new, more infectious variants. As asymptomatic carriers (whether or not vaccinated) seem to play an important role in sustaining transmission of SARS-CoV-2, I strongly believe that any eradication strategy will need to be implemented as a preventive measure, regardless of whether it is based on a drug- or vaccine-based intervention. However, in terms of immune intervention, it's difficult to imagine how this pandemic could be brought to an end if vaccines are used that do not induce sterilizing immunity. It is not unreasonable to propose that the design of new vaccines capable of inducing sterilizing immunity be inspired by mechanisms underlying abrogation of viral infection in asymptomatically infected subjects.