Epidemiologic ramifications and global health consequences of the C-19 mass vaccination experiment

Synopsis

The following predictions are distilled from an in-depth analysis of how the precipitated evolutionary dynamics of SARS-CoV-2 (SC-2) in highly vaccinated populations enable the virus to bypass the cell-based innate immune system (CBIIS) and exhaust the adaptive immune capacity in vaccinees while providing 'power training' to the CBIIS of the unvaccinated. Understanding the immunological consequences of this complex phenomenon provides new insights as to why sidelining of the CBIIS dramatically enhances the susceptibility of vaccinees to re-infection with more infectious variants. Furthermore, it explains how these individuals are now forming an asymptomatic reservoir of 'more virulent' SC-2 variants (BA.4 and BA.5), and some other glycosylated viruses causing acute self-limiting viral infection (ASLVI) or acute self-limiting viral disease (ASLVD). Highly vaccinated populations are now igniting new viral pandemics (e.g., the ongoing pandemic of 'more virulent' SC-2 variants [i.e., BA.4 and BA.5]; a pending pandemic of avian influenza; the ongoing pandemic of monkeypox virus). Due to these asymptomatic reservoirs, several viruses may now also begin to spill over into animal populations. This is especially true for highly infectious viruses in animals with close proximity to humans (e.g., livestock, zoo animals).

Understanding the evolutionary viral dynamics and the corresponding shift in the host's immune response also provides a compelling explanation as to how the infection-enhancing antibodies (IEABs) in vaccinees enable the latter's enhanced susceptibility to SC-2 re-infection while paradoxically protecting them from severe C-19 disease. An analysis of the continuous interplay between viral infection and the subsequent immune response of the host also elucidates how high infectious pressure exerted by more infectious SC-2 variants temporarily increases the risk of enhanced viral infectiousness and severe disease in a minority of young unvaccinated children. Understanding this phenomenon is key as it is likely responsible for the limited but unfortunate increase in

the incidence rate of severe C-19 disease in young unvaccinated children and the irrational incentive for driving parents to get their children C-19 vaccinated.

Sidelining of the CBIIS (due to enhanced viral infectiousness) and exhaustion of the adaptive immune system [AIS] (due to the latter's S(pike)-mediated activation) are now igniting epidemics of other acute (i.e., other than ASLVIs or ASLVDs) and chronic microbial infections or immune-mediated diseases (e.g., cancer and immunopathologies) that are now affecting more and more vaccinees. This will be especially problematic in young, vaccinated children whose CBIIS is untrained and whose AIS is antigen(Ag)-inexperienced, leaving them vulnerable to developing severe disease from other acute or chronic microbial infections or from immunopathology (e.g., autoimmune hepatitis).

Due to strong immune activation of the CBIIS (in the majority of the unvaccinated: ③ in fig. 2) and the AIS (in the majority of vaccinees: ① in fig. 2), the course of the ongoing pandemics (i.e., P1, P2, P3 as described under fig. 2) can be predicted to primarily affect the unvaccinated whereas the course of the ongoing epidemics of ASLMIs and CSCMIs is primarily affecting the vaccinees. Whereas P1, P2 and P3 are now resulting in reduced disease in the unvaccinated, the opposite applies to the forementioned epidemics taking an increasing toll on lives of the vaccinees. Unfortunately, these concerns will pale in comparison to damages inflicted to this group by yet another global epidemic triggered by P1: An imminent super-epidemic of enhanced severe C-19 disease caused by highly infectious and highly virulent SC-2 variants.

When one grasps the above-summarized dynamics it becomes crystal clear that vaccinating young children against C-19 entails trading a highly ephemeral benefit (short-lived protection from severe C-19 disease) for an immense risk of severe disease from a multitude of other acute or chronic microbial infections or immunopathologies, the consequences of which are simply dramatic. As the forementioned ailments will primarily affect people with poorly trained CBIIS and exhausted AIS, it is reasonable to assume that the unvaccinated and countries with low C-19 vaccine coverage rates will largely resist the pandemic storms as their capacity to build natural and herd immunity

has not been compromised ('Africa will win'). The primary focus of highly vaccinated countries should now be early C-19 treatment of vaccinees and massive distribution of antivirals that are safe and effective and can be provided in sufficient quantities at affordable cost to these individuals.

My predictions are based on a multidisciplinary analysis drawing from fields of immunology, vaccinology, virology, evolutionary biology and biophysical sciences. The endpoint described by the convergence of the governing principles of these scientific disciplines coupled with an overwhelming body of evidence requires **that these conclusions be taken very seriously, even if they seem too dire to be true** ("*How often have I said to you that when you have eliminated the impossible, whatever remains, however improbable, must be the truth?*", Sherlock Holmes)

New pandemics and epidemics in highly vaccinated countries

I. The ongoing pandemic of 'more virulent' SC-2 variants

Hospitalizations and mortality rates due to (not with!) SARS CoV-2 (SC-2) continue to decline as the unvaccinated increasingly train their innate immune response (primarily NK cell-based), while vaccinees are increasingly protected not only against severe C-19 disease (due to the inhibitory effect of high titers of infection-enhancing antibodies [Abs] that block viral *trans* infection in the lungs[1], but now even increasingly against C-19 symptoms in general (due to strong activation [not priming!] of polyspecific MHC class I-unrestricted cytotoxic T cells[2], which naturally enable recovery from C-19 disease). However, as none of the immune mechanisms currently at play within these individuals can prevent productive infection (see figure 1), healthy *vaccinees are now increasingly becoming asymptomatic shedders* of SC-2 immune escape variants.

[1] https://www.voiceforscienceandsolidarity.org/scientific-blog/predictions-gvb-on-evolution-c-19-pandemic
[2] Enhanced activation of these T cells can even protect vaccinees against C-19 disease in the presence of more potent infection-enhancing Abs (see fig.1).

The immune mechanisms preventing (*severe)* C-19 disease in vaccinees are exclusively adaptive in nature (i.e., mediated by antigen [Ag]-specific infection-enhancing Abs and cytotoxic CD8+ T cells) and therefore independent of the innate immune status of the vaccinee.

Deployment of non-replicating C-19 vaccines to fight antigenically shifted SC-2 variants eventually leads to enhanced viral infectiousness in vaccinees that cannot be mitigated by the CBIIS—vaccines of this class are unable to train innate immune cells. Recall of IEABs upon natural infection promotes natural selection and dominant expansion of immune escape variants. As long as the latter do not become resistant to the virulence-inhibiting activity of the IEABs, vaccinees benefit from protection against (severe) C-19 disease.

C-19 vaccines are non-replicating and therefore unable to adequately train the CBIIS. Consequently, loss of neutralizing capacity of vaccine-induced Abs will result in pronounced enhancement of viral infectiousness that cannot sufficiently be countered by CBIIS-mediated viral clearance such as to avoid boosting of S(pike)-specific IEABs. In case the CBIIS is immature, C-19 vaccination will not only enhance viral infectiousness but will even impede the education of the CBIIS because S-specific IEABs induced by C-19 vaccines bind with much higher affinity to SC-2 variants than innate Abs that would otherwise capture the virus (via multivalent binding to self-mimicking sugar patterns) and thereby train the CBIIS for better recognizing SC-2 and other glycosylated viruses[3].
Upon exposure to antigenically shifted SC-2 variants, enhanced viral infectiousness may lead to severe disease in vaccinees, especially if their CBIIS is untrained. As previously explained[4] and partially illustrated in fig. 1, IEABs can bind to SC-2 virus that is tethered to migrating dendritic cells (DCs) and thereby prevent *trans* infection and *trans* fusion (for the purpose of this manuscript I sometimes use the term 'productive'

[3] Recognition of SC-2 and other glycosylated viruses occurs through expression of similar virus-derived self-mimicking peptides on the surface of the host cells they infect: https://www.trialsitenews.com/a/intra-pandemic-vaccination-of-toddlers-with-non-replicating-antibody-based-vaccines-targeted-at-aslvi1-or-aslvd2-enabling-glycosylated-viruses-pr-66e8b959
[4] https://www.voiceforscienceandsolidarity.org/scientific-blog/predictions-gvb-on-evolution-c-19-pandemic

trans infection instead of *trans* fusion). This results in prevention of severe disease from SC-2 in C-19 vaccinees (fig. 2: ① and ②).

It is reasonable to assume that subsequent exposure to more infectious circulating variants will only further boost vaccine-induced IEABs. This implies that these Abs are raising the immune pressure on viral virulence which—for now—is still capable of preventing severe disease. However, this rising population-level immune pressure on viral virulence has already led to the enhanced intrinsic virulence of the virus (BA.4 and BA.5 are 'more virulent' variants[5]).

I postulate that the conserved antigenic site of S-NTD in dominant circulating SC-2 variants is now evolving to strengthen its binding to the IEABs, leading to the simultaneously enhanced viral infectiousness and virulence-inhibiting capacity of these antibodies. This would also imply an increase of SC-2 virions driven into the cytotoxic pathway (fig.1: 3c'-3d') and enhanced abrogation of productive viral infection, dramatically decreasing the incidence rate of severe C-19 disease in <u>all</u> C-19 vaccinees (i.e., regardless of the CBIIS immune status) and enabling asymptomatic shedding.

The very last step the virus needs to take to fully escape the virulence-neutralizing effect of the IEABs is to select an immune escape variant (of the conserved infection enhancing site[6]) which no longer sufficiently binds these Abs when tethered to migrating DCs (see fig. 1). Insufficient or deficient binding of these Abs to DC surface-tethered SC-2 virions will no longer allow them to prevent productive *trans* infection, which leads to syncytia formation and severe disease[7]. <u>When this occurs, protection against severe disease will vanish</u> in all vaccinees (fig. 2: ① and ②). A similar process has already occurred with the 'more infectious' SC-2 variants of the S-RBD (receptor-binding domain of S protein) which were no longer sufficiently bound by previously neutralizing Abs. <u>When this occurred, protection against (moderate) disease vanished</u>.

I predict that i<u>t's only a matter of an additional few months</u> (or maybe only a few weeks, depending on whether vaccination campaigns are extended to children and additional

[5] https://www.biorxiv.org/content/10.1101/2022.05.26.493539v1.full.pdf
[6] This infection-enhancing site is situated within the N-terminal domain of S (S-NTD)
[7] https://www.voiceforscienceandsolidarity.org/scientific-blog/predictions-gvb-on-evolution-c-19-pandemic

booster shots[8] are administered) before the virus overcomes this final hurdle, at which point a super-epidemic will be ignited globally (a so-called 'pseudo-pandemic') . In the vast majority of vaccinees this will likely cause severe disease irrespective of the immune status of their CBIIS or AIS (fig. 2: ① and ②).

If not massively treated with antivirals, highly vaccinated populations will be devastated by massive rates of C-19 morbidity and C-19 mortality. Once SC-2 has become resistant to the virulence-inhibiting capacity of the IEABs, the latter will only contribute to precipitating and accelerating severe disease by virtue of their infection-enhancing effect. Consequently, Ab-dependent enhancement of infection (ADEI) will now prompt manifestation of severe disease. Ab-dependent enhancement of severe disease (ADESD) will first manifest in vaccinees with high titers of IEABs and vaccinated at an early stage of the vaccination program (i.e., before they had an opportunity to train their CBIIS). Hence, elderly and vulnerable vaccinees will be affected first. Provided they had ample opportunity to train their innate immune system prior to vaccination, some vaccinees may have enough natural immune capacity left to survive —but will the hospitals still be able to provide intensive care and treat these patients? Unless we make safe and effective antivirals immediately available in sufficient supply and at affordable cost[9] for prophylactic use of vaccinees at the first sign of the epidemic wave, we're going to face a massive loss of human life. The first sign to look for will be a generalized further improvement of protection against C-19 disease in vaccinees that will soon be followed by an abrupt shift and spectacular increase in the number of previously healthy vaccinees hospitalized due to SC-2 (relative to unvaccinated hospitalized due to SC-2). In a following contribution, I will explain why this is the key parameter to monitor.

[8] Booster shots are more effective in recalling infection-enhancing S-specific Abs than natural infection. This is likely due to the fact that natural infection in vaccinees leads to shielding of the conserved antigenic site by IEABs and to extensive viral clearance by activated cytotoxic CD8+ T cells (for as long as the virulence-inhibiting capacity of the IEABs allows….)

[9] I am not aware of compounds exhibiting strong antiviral activity other than ivermectin and hydroxychloroquine that would fulfill all other conditions (safe, broadly available at low cost and at an affordable price)

Asymptomatic SC-2 infection in the unvaccinated may elicit short-lived, low affinity Abs that can bind to SC-2 without neutralizing it (IgM) and therefore serve as a kind of poorly Ag-specific IEABs. Because enhanced transmission by asymptomatic C-19 vaccinees raises the viral infection rate, rapid re-exposure of some unvaccinated individuals after previous asymptomatic infection may temporarily increase their susceptibility to SC-2 infection and therefore to severe C-19 disease (due to these short-lived IEABs). Whereas this is not normally problematic in a population whose CBIIS is adequately trained, this phenomenon is now responsible for a rise of cases of severe disease in young children (whose CBIIS is not yet trained).

The vast majority of *unvaccinated* individuals are now increasingly unlikely to contract severe C-19 disease from the currently circulating SC-2 variants ((fig. 2: ③). The decline in the incidence rate of severe disease in the unvaccinated is due to improved training of their CBIIS—they can more effectively resist the enhanced infectiousness of these variants. Enhanced SC-2 infectiousness may occur if a person becomes re-infected with SC-2 shortly after a previous asymptomatic infection. Short-lived, non-neutralizing Abs elicited following previous asymptomatic infection are prone to bind to the virus and cause Ab-dependent enhancement of SC-2 infection. Rapid re-exposure is likely to result from a high infection rate due to enhanced viral transmission from asymptomatic reservoirs.

Upcoming variants characterized by a new antigenic shift (i.e., towards resistance to the virulence-inhibiting activity of infection-enhancing antibodies in vaccinees) will soon become dominant in highly vaccinated countries and will likely render the unvaccinated resistant to productive infection[10]. However, in unvaccinated individuals with an untrained CBIIS (young children), the high infection rate is now causing antigenically shifted SC-2 variants to provoke a limited increase in the incidence of severe disease (fig. 2: ④). This can only be explained by rapid re-exposure after primary asymptomatic infection which, in young children, enables short-lived non-neutralizing S-specific Abs (elicited as a result from such asymptomatic infection) to outcompete their innate, neutralizing Abs for binding to the virus and thereby enhance viral infectiousness. As

[10] https://www.voiceforscienceandsolidarity.org/scientific-blog/predictions-gvb-on-evolution-c-19-pandemic

the innate immune effector cells of the young child are untrained, the enhanced viral infectiousness cannot be mitigated by the CBIIS.

II. New pandemics of other glycosylated viruses (see fig. 2)

MHC class I-unrestricted cytotoxic T cells that—in the presence of IEABs—are now increasingly protecting vaccinees against C-19 disease are directed at a conserved CTL epitope that is shared with other[11] glycosylated viruses causing ASLVIs[12] or ASLVDs[13] [https://pubmed.ncbi.nlm.nih.gov/19439480/]. Enhanced activation of these T cells could, therefore, also protect C-19 vaccinees against disease upon their exposure to these other glycosylated viruses.
The extent to which the vaccinated control productive C-19 infection (i.e., the disease) caused by more infectious SC-2 variants is unlikely to depend on the capacity of innate immune effector cells to eliminate virus-infected target cells as IEABs enable the virus to break through this first line of innate immune defense. The resulting lack of training of the CBIIS also fails to strengthen the host's innate immune defense towards other ASLVI- or ASLVD-enabling glycosylated viruses.

In young children, C-19 vaccination will equally raise titers of IEABs towards more infectious SC-2 variants and thereby sideline the CBIIS. How this can reasonably be expected to augment the risk of ADEI and severe disease in toddlers and prevents education of their CBIIS and therefore weakens their innate immune defense towards other ASLVI- or ASLVD-enabling glycosylated viruses has been explained before (https://www.trialsitenews.com/a/intra-pandemic-vaccination-of-toddlers-with-non-replicating-antibody-based-vaccines-targeted-at-aslvi1-or-aslvd2-enabling-glycosylated-viruses-pr-66e8b959).

---

[11] 'Other' means 'other than SC-2'
[12] Examples of glycosylated viruses [other than SC-2] causing ASLVIs: seasonal influenza, RSV and viruses responsible for vaccine-preventable infections: measles, mumps, rubella, varicella, rotavirus.
Note: Given the important asymptomatic reservoir, the occurrence of disease due to common influenza types may no longer be bound to seasonality!
[13] Examples of glycosylated viruses causing ASLVDs: zoonotic influenza (e.g., avian influenza virus), parapox virus (e.g., monkeypox virus)

However, as described above, the virulence-inhibiting activity of the IEABs is now increasingly complemented by cytotoxic CD8+ T cells capable of preventing disease not only due to SC-2 but also to other ASLVI- or ASLVD-enabling glycosylated viruses. Healthy vaccinees are now also increasingly serving as a reservoir[14] for asymptomatic transmission of these other glycosylated viruses[15] (see fig. 2: ① and ②). In a well-mixed and highly C-19 vaccinated population, enhanced transmission from this asymptomatic reservoir to the unvaccinated will lead to a more or less significant increase in the incidence rate of severe disease from ASLVI- or ASLVD-enabling glycosylated viruses, depending on the viral infection rate ('infectious pressure') and the strength of the CBIIS (fig.2: ③ and ④). However, it's important to note that due to enhanced SC-2-mediated training of their CBIIS, the unvaccinated will see an improved ability to counter these infections, resulting in a steady decline in the incidence of severe disease.

III. Ongoing global epidemics of other microbial or immune-mediated diseases

(see fig. 2)

In the meantime, depletion/ exhaustion of adaptive immune effector cells (i.e., IgG-producing B cells and cytotoxic CD8+ T cells) is now rendering C-19 vaccinees (but not the unvaccinated) more susceptible to severe disease due to yet another group of glycosylated pathogenic agents. These can be broken down into three categories:

[14] As the cytotoxic Tc response has no memory and the infection-enhancing antibodies promote the susceptibility of vaccinees to re-infection, vaccinated people can repeatedly be re-infected and acquire mild or moderate disease. Because of the anticipated rise in infection-enhancing and virulence-inhibiting capacity of the evolving SC-2 variants, CTL activation is likely to enable more rapid cytolysis of virus-infected cells (i.e., at an early stage of productive infection). Enhanced abrogation of productive infection is likely to lead to asymptomatic infection but will not provide sterilizing immunity (see fig. 1: B). Although asymptomatic vaccinees tend to shed less virus than unvaccinated individuals (https://www.medrxiv.org/content/10.1101/2022.01.28.22270044v1), they will shed and transmit virus over and over again while boosting their declining infection-enhancing Abs upon each re-exposure.

[15] A C-19 vaccinated population that during childhood has been largely vaccinated with live attenuated viral vaccines (e.g., measles, mumps, rubella, varicella) will not serve as a reservoir for these viruses but could still facilitate asymptomatic transmission of *influenza virus, respiratory syncytial virus* (RSV), dengue virus and other more virulent glycosylated viruses such as *Ebola* or *Marburg* virus

1. Glycosylated bacterial pathogens that normally cause other[16] acute self-limiting microbial infection (ASLMI) such as *Haemophilus influenzae* (Hib), meningococcal bacteria belonging to genus *Neisseria meningitidis* (e.g., serogroups A, C, W and Y; Men ACWY), pneumococcal bacteria belonging to genus *Streptococcus pneumoniae,* fungi such as different types of *Aspergillus, Candida , Cryptococcus.*
2. Glycosylated microbial pathogens that normally cause chronic self-controlled microbial infection (CSCMI) such as HSV-1/ HSV-2, EBV, CMV, HIV, tuberculosis etc.
3. Glycosylated self-proteins that normally enable self-controlled tolerance of self-antigens

The anticipated rise in the incidence of these diseases simply reflects the extent of adaptive immune resources (in terms of IgG Abs and CD8+ T cells) required of vaccinated individuals' immune systems to achieve the level of immune pressure necessary to prevent more infectious and more virulent SC-2 variants from breaking through the protection conferred by the infection-enhancing S-specific Abs and polyspecific cytotoxic CD8+ T cells—which, for now, still provide protection against productive *trans* infection at the lower respiratory tract (i.e., preventing *severe* C-19 disease) and increasingly also against productive infection at the upper respiratory tract (i.e., preventing *moderate* C-19 disease by rapid *abrogation* of productive infection), respectively. In highly vaccinated populations, depletion of IgG Abs and CD8+ T cells will, therefore, likely lead to an increase in the incidence rate of *severe* disease from these other, non-immunogenically related pathogenic agents[17], depending on the overall level of pathogen-related Ag-experience and the level of immune protection conferred by the CBIIS. As the CBIIS in young children is largely pathogen-untrained and the AIS largely Ag-inexperienced, it is logical to postulate that the rise in incidence rate of severe disease due to ASLMI- or CSCMI-enabling glycosylated pathogenic agents will be much more pronounced in vaccinated children than in older vaccinees.

[16] i.e., other than ASLVIs or ASLVDs

[17] For the purpose of this manuscript 'non-immunogenically related pathogenic agents' relates to pathogenic agents other than those sharing the polyspecific CTL epitope comprised within S protein

Many older vaccinees will have sufficient adaptive immune capacity left and/ or had an opportunity to train their CBIIS prior to C-19 vaccination (i.e., due to previous SC-2 exposure) [fig. 2: ② as compared to ①]. An additional accrual of cases of severe disease is likely to occur in young, vaccinated children due to immunopathology (i.e., presumably due to lack of Ag-specific regulatory T cells which are critical to enabling peripheral tolerance) whereas in the remainder of the population cases of cancer are more likely to occur (due to Ag-specific MHC class I-restricted T cells capable of killing neoplastic host cells).

Although adaptive immune depletion will be responsible for an enhanced incidence of severe disease due to ASLVIs or CSCMIs in C-19 vaccinees (especially within young vaccinated children), this is not expected to occur in the unvaccinated as vaccinees are not asymptomatic shedders and should therefore not enhance transmission of this type of pathogens. Consequently, it is probable that ASLMI- and CSCMI-enabling pathogens will ignite epidemics globally in highly vaccinated populations (so-called 'pseudo-pandemics') and therefore be responsible for more and more severe disease amongst vaccinees.

IV. How will these (pseudo-)pandemics evolve, and which populations will they affect?

While emerging pandemics of other ASLVIs (e.g., influenza, RSV) or ASLVDs (e.g., monkeypox and avian flu) will inflict relatively little damage to populations that are highly C-19 vaccinated (as vaccinees benefit from cross-protection conferred by cytotoxic CD8+ T cells while the unvaccinated take advantage of a steadily improved training of their CBIIS), more significant damage will come from epidemics of *other microbial diseases and cancer* as they become more prevalent due to relative exhaustion of the adaptive immune system in these populations. ***However, if communities rapidly proceed with vaccination of young children, global epidemics of infectious and immunopathological disorders could cause incredible damage to this part of the***

population, possibly even before the pseudo-pandemic of 'more virulent' SC-2 variants transitions into its final dramatic stage of ADESD.

Meanwhile, many animal species have also become susceptible to *highly infectious* SC-2 and other 'antigenically shifted' glycosylated viruses (e.g., avian influenza) *for lack of Ag-specific antibodies and adequately trained cell-based innate immunity*. This situation is likely to not only threaten zoo animals but even livestock due to its close proximity with humans and short lifespans that do not allow for the development of robust innate (and thus herd) immunity (owed to lack of endemic circulation of glycosylated viruses). In addition, high stocking density or other unfavorable management or environmental conditions may produce stressors which can negatively impact innate immune function (e.g., within poultry, cattle, pigs).

Countries with low vaccine coverage rates, well-trained innate immunity and younger populations will do best (*Africa will win*!). Loss of human life is likely to be most severe in highly SC-2 vaccinated countries, while unvaccinated individuals in these regions will enjoy exceptional protection due to adequately trained innate immunity and limited susceptibility to emerging SC-2 variants that have evolved to adapt to the immune status of vaccinees. The situation will be dire in countries like China, for example, where not only a high percentage of (elderly) people have been vaccinated and where many unvaccinated may still be at risk of C-19 disease due to poorly trained innate immunity as a result of stringent infection-prevention measures.

Overall conclusion

Massive suboptimal immune pressure exerted by highly C-19 vaccinated populations on the life cycle of SARS-CoV-2 drives natural selection and dominant propagation of highly infectious variants that sideline the cell-based innate immune defense against SC-2. With the onset of a SC-2 pandemic of more virulent viral variants (BA.4 and BA.5), enhanced activation of cytotoxic CD8+ T cells in vaccinees has strengthened their adaptive immunity such as to turn healthy vaccinees in an asymptomatic reservoir responsible for igniting new pandemics of other ASLVI- or ASLVD-enabling glycosylated

viruses while eroding the adaptive immune capacity of other vaccinees in ways that ignite new global epidemics of ASLMI- or CSCMI-enabling glycosylated pathogens. It is reasonable to postulate that this evolution is an indirect consequence of the mass vaccination program and is now exposing both human and animal populations at significant risk of severe disease from SC-2 and other glycosylated microbes in countries with high C-19 vaccine coverage rates. C-19 vaccination of young children in particular will have catastrophic consequences—they will be highly susceptible to a myriad of microbial infections and prone to developing immunopathology. Unless safe and effective antivirals become largely available at an affordable cost, vaccinees in highly vaccinated countries will severely suffer from ADESD once 'more virulent' SC-2 variants have become resistant to the virulence-inhibiting activity of vaccine-induced IEABs, igniting a super-epidemic of SC-2.

Figures

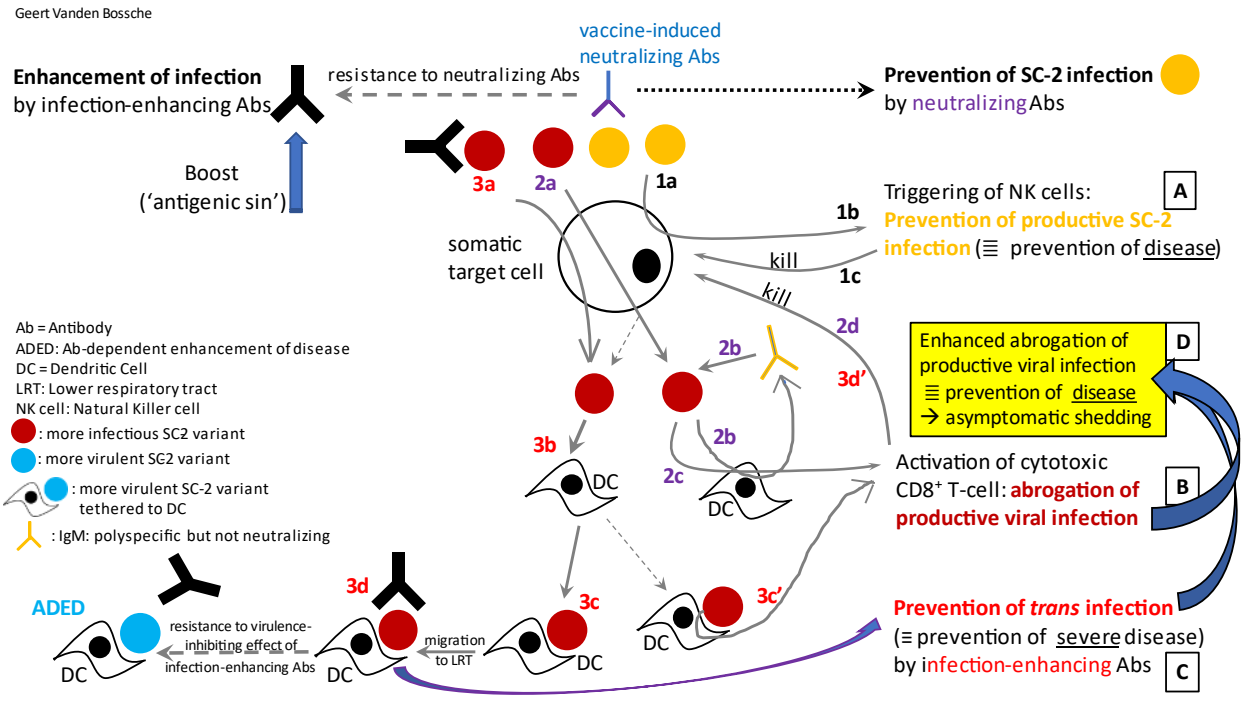


Fig. 1: *Acute, self-limiting viral infections that don't lead to systemic/ severe disease (and possibly death) are terminated by **M**(ajor) **H**(istocompatibility) **C**(omplex)-unrestricted, cytotoxic CD8+ T cells that have no memory and the activation of which is triggered by a universal, pathogen-nonspecific Tc epitope comprised within the spike (S) protein. Unless an infected person progresses to developing severe disease, this is what allows a fairly rapid recovery from disease after primary productive infection (and certainly before fully functional virus-neutralizing Abs peak) [according to **2a-2b-2c-2d** pathway]. However, rather than stimulating de novo generation of new neutralizing Abs towards variants that escaped the neutralizing activity of vaccine-induced Abs, exposure of vaccinees to these immune escape variants will rapidly boost their declining titers of non-neutralizing, infection-enhancing Abs (those are directed against an antigenic site that is conserved within the N-STD of all SC-2 variants and has therefore a license to commit 'antigenic sin' once it has primed the host's immune system).*

*In vaccinees with poor experience in fighting productive infection (and hence, poor training of their innate immune defense according to pathway **1a-1b-1c**) prior to C-19 vaccination, infection-enhancing Abs[18] that are responsible for preventing severe disease by binding to DC-tethered virus (according to **3a-3b-3c-3d** pathway) can synergize with strongly activated cytotoxic CD8+ Tc-mediated killing (**3c**') to even prevent C-19 disease all together and hence, render vaccinees asymptomatic despite their high susceptibility to re-infection (B + C → D). As prevention of disease is not due to prevention of productive infection but to accelerated abrogation of infection, these vaccinees will continue to shed and transmit SC-2 upon re-infection. Whereas innate immune effector cells are MHC-unrestricted and polyspecific (i.e., NK cells) and, therefore, don't drive immune escape, the infection-enhancing-Abs are Ag-specific (i.e., S-specific) and – if produced at high enough titers and with high enough affinity by a large part of the population – will promote natural selection of immune escape variants that can resist the virulence-inhibiting capacity of these Abs. This is because vaccinees cannot prevent productive viral infection; consequently, the immune pressure they exert on viral virulence is suboptimal in that it cannot prevent the expansion in prevalence of immune escape SC-2 variants that have the capacity to overcome this immune pressure. Resistance of viral variants to the virulence-inhibiting activity of infection-enhancing Abs will inevitably cause Ab-dependent enhancement of severe disease (ADESD).*

Fig. 2: *The table below summarizes the relative change in the incidence rate of severe disease (and hence, hospitalization rate) the pandemics or global epidemics described in the text are expected to cause in a well-mixed highly vaccinated population as a result of enhanced asymptomatic transmission or depletion of immune effector cells, respectively. Enhanced viral transmission from asymptomatically infected C-19 vaccinees to other parts of the population causes 4 new types of pandemics[19], i.e., a pandemic of antigenically shifted, **'more virulent' immune escape SC-2 variants enabling ADEI in vaccinees (P1)**, a pandemic of **acute, self-limiting viral infections** (**P2**), a pandemic of **acute, self-limiting***

[18] As previously explained, the non-neutralizing, infection-enhancing Abs are currently hampering *trans* infection at the level of distant organs such as the lower respiratory tract; this is what's currently exerting population-level immune pressure on viral virulence: https://www.voiceforscienceandsolidarity.org/scientific-blog/predictions-gvb-on-evolution-c-19-pandemic).

[19] 'Pandemics' and not 'epidemics' as the spread and transmission of these infectious pathogens will not be restricted to highly vaccinated countries

***viral diseases (P3**). In addition, depletion of IgG Abs and CD8+ T cells in vaccinees gives rise to global epidemics ('pseudo-pandemics') of other glycosylated pathogenic agents (as highlighted in **gold-colored** fonts) whereas viral resistance to the virulence-inhibiting activity of IEABs will trigger a pseudo-pandemic ('super-epidemic') of '**highly infectious and more virulent immune escape SC-2 variants enabling ADESD in vaccinees'** (**in green fonts**).*

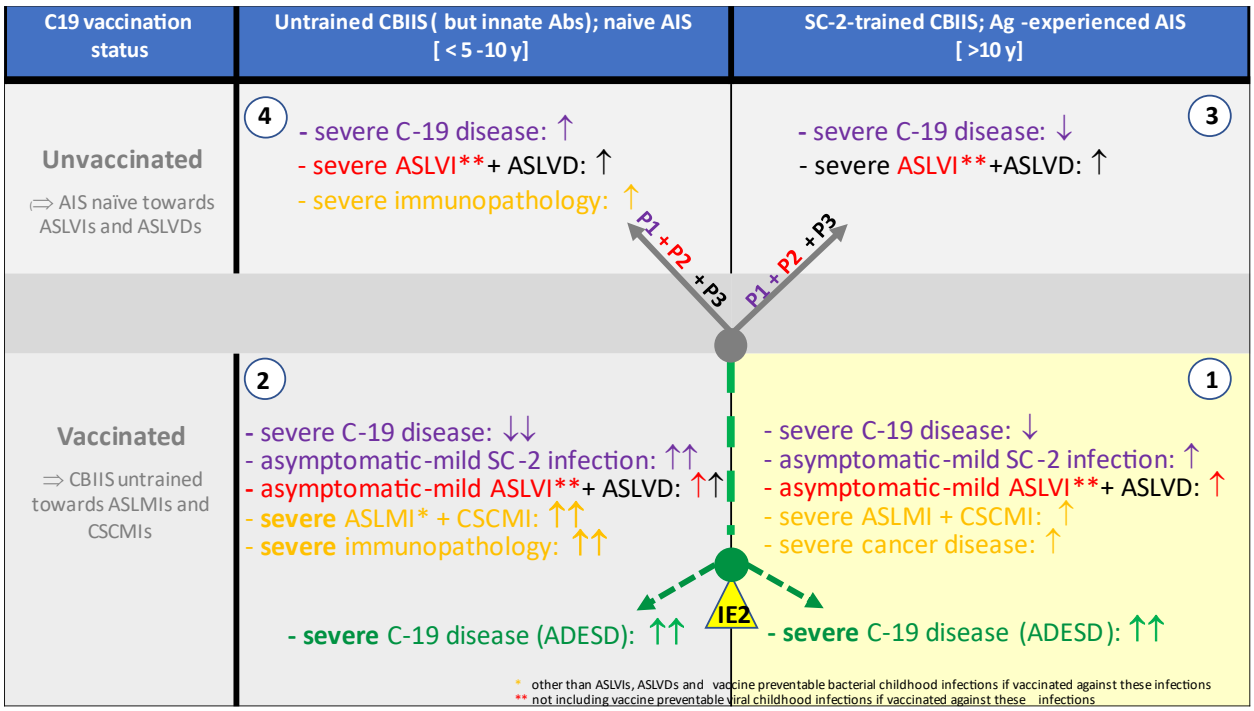
*In highly vaccinated countries, **P2** and **P3** will primarily raise the incidence of severe disease in the unvaccinated whereas the super-epidemic of SC-2 as well as global epidemics of other infectious and immune-mediated diseases (incl. cancer) will primarily affect vaccinees. Whereas the SC-2 super-epidemic is likely to cause severe disease in the vast majority of vaccinees, regardless of their immune status of the CBIIS or AIS, the damage inflicted by the global epidemics will largely depend on the level of innate immune training and Ag-experience the host immune system has at its disposal to fight off glycosylated pathogenic agents that are responsible for these epidemics.*

Abbreviations:

ADESD: Antibody-dependent enhancement of severe disease
Ag: Antigen
AIS: Adaptive immune system
ASLMI: Acute self-limiting microbial infection (other than ASLVI or ASLVD)
ASLVD: Acute self-limiting viral disease
ASLVI: Acute self-limiting viral infection
C-19: Covid-19
CBIIS: Cell-based innate immune system
CSCMI: Chronic self-controlled microbial infection (i.e., self-controlled by the host immune system)
IE2: 2nd immune escape event (triggering resistance of 'more virulent' SC-2 to the virulence-neutralizing/ inhibiting activity of infection-enhancing Abs and thereby rendering vaccinees highly susceptible to severe disease)
SC-2: SARS-CoV-2

P1: ongoing C-19 *pandemic of* antigenically shifted, *'more virulent' immune escape SC-2 variants enabling ADEI in vaccinees* (i.e., BA.4 and BA.5)
P2: ongoing *pandemic of ASLVIs (common Influenza virus types and Respiratory Syncytial Virus [RSV])*
P3: ongoing *pandemic of ASLVDs (Avian influenza virus; Monkeypox virus)*
Characters in green fonts relate to the imminent ***'pseudo-pandemic'***[20] *of new, 'more virulent' immune escape SC-2 variants enabling ADESD in vaccinees.* This is the C-19 pandemic of SC-2 immune escape variants exhibiting 'highly viral infectiousness' and 'high viral virulence' in vaccinees.
Characters in gold-colored fonts relate to the ongoing '*pseudo-pandemics' of glycosylated pathogenic agents enabling ASLMI or CSCMI or immunopathology*[21] *in vaccinees*

[20] For the purpose of this manuscript, a 'pseudo-pandemic' is defined as a global epidemic of an infectious agent that is virulent enough to prevent asymptomatic shedding and spread
[21] including cancer



Note:

- *The age groups don't exactly correspond to the status of the CBIIS and AIS described and only provide a ballpark figure on the age range of groups comprising the majority of people with the indicated immune status*
- *A dramatic increase (↑↑) in '**severe**' disease is highlighted in **bold** as the incidence and evolution thereof will provide guidance on the need for additional hospitalization capacity*
- ***Purple fonts** indicate the reservoir responsible for asymptomatic transmission of 'more infectious' and 'more virulent' SC-2 variants to the unvaccinated in a well-mixed, highly C-19 vaccinated population and initiation of the **P1** pandemic. The resulting rise in infection rate may occasionally cause enhanced viral infectiousness in young, previously asymptomatically infected children and hence, raise the incidence of severe disease in this age group. In contrast, a higher infection rate will improve innate immune training in the remainder of the unvaccinated population. As 'more infectious' variants become more and more resistant to potentially neutralizing vaccinal Abs, they presumably bind with higher affinity to the infection-enhancing Abs (IEABs). The latter are capable of blocking trans infection and, therefore, trans fusion in vaccinees and thereby enhance activation of cytotoxic CD8+ T cells that enable abrogation of productive infection (see **3c'** in fig. 1). Sufficiently high levels of IEABs that bind with increasing affinity to more virulent immune escape SC-2 variants are likely to strengthen inhibition of trans infection and therefore promote viral clearance by cytotoxic CD8+ T cells. Consequently, prevention of severe C-19 disease in C-19 vaccinees will further evolve into prevention of C-19 disease all together (but not in prevention of productive infection!) before any protective effect ultimately fully collapses as a result of viral resistance to the virulence-inhibiting effect of the IEABs.*
- ***Red fonts** indicate the reservoir responsible for asymptomatic transmission of ASLVI-enabling glycosylated viruses to the unvaccinated in a well-mixed, highly C-19 vaccinated population and initiation of the **P2** pandemic. The resulting rise in infection rate (i.e., enhanced infectious pressure)*

may occasionally allow the virus to break through the CBIIS of the unvaccinated and therefore raise the incidence rate of severe disease.

- ***Black fonts*** *indicate the reservoir responsible for asymptomatic transmission of ASLVD-enabling glycosylated viruses to the unvaccinated in a well-mixed, highly C-19 vaccinated population and initiation of the* ***P3*** *pandemic. The resulting rise in infection rate (i.e., enhanced infectious pressure) may occasionally allow the virus to break through the CBIIS of the unvaccinated and hence, raise the incidence of severe disease.*
- ***Green fonts*** *indicate the rise in incidence of ADESD in the C-19 vaccinated caused by natural selection and dominant propagation of 'more virulent' immune escape SC-2 variants that resist the virulence-inhibiting effect of IEABs in vaccinees.*
- ***Gold-colored fonts*** *indicate the rise in incidence of severe disease in the C-19 vaccinated due to depletion of Ag-specific IgGs and CD8+ T cells that are required to fight off glycosylated pathogens causing ASLMIs or CSCMIs or immune-mediated diseases (i.e., cancer or immunopathologies). Alternatively, severe immunopathologies (e.g., autoimmune hepatitis) may also occasionally occur in unvaccinated young children as a result of a high viral infection rate. The latter may occasionally allow the virus to break through the untrained CBIIS of the unvaccinated young child due to insufficient or deficient training.*