The fulminant spread of JN.1 is a highly worrisome prognostic indicator…

The Omicron descendants, bred in highly C-19 vaccinated populations, have transformed a naturally occurring pandemic into an 'inescapable immune escape pandemic' through the generation of significant immune selection pressure and immune refocusing.

As the evolution of this pandemic will undoubtedly escalate at this stage, I am presenting a summary below of the article I am currently writing on the ultimate outcome of this crisis. As a seasoned vaccinologist, I consider it my duty to scientifically document that those who have been providing scientific advice to our (public health) policymakers have consistently been wrong, and as a result, they bear responsibility for the significant health catastrophe I am anticipating. My predictions are exclusively rooted in a comprehensive and multidisciplinary scientific analysis of the consequences of the mass vaccination they vigorously endorsed (and continue to support). I have diligently conducted my research, whereas they have chosen to vilify me and numerous others, despite the absence of any scientifically grounded analysis of the evolutionary dynamics of this pandemic on their part.

I am sorry that the summary of my analysis contains complex scientific and technical language that may be challenging for some readers to understand without additional context. For them, belief or disbelief in my predictions has now become a matter of credibility. However, wWe will know very soon who has been speaking the truth. As I repeated so many times: 'Society in highly C-19 vaccinated countries will be caught off guard'.

Summary:

Many scientists trust that updated booster vaccines will continue to provide protection against severe Covid-19 (C-19) disease. Their assumption is based on seroneutralization data collected before and after an updated C-19 booster dose (or natural re-exposure) in previously mRNA-vaccinated individuals. They don't seem to realize that what they are looking at are new, cross variant-reactive anti-spike (S) antibodies (Abs) that only manifest virus-neutralizing activity at high serum titers. These Abs are primed as a result of steric immune refocusing (SIR) to more conserved S-associated epitopes following vaccine breakthrough infections (VBTIs) or mRNA vaccination alone (https://braintrain.mykajabi.com/the-inescapable-immune-escape-pandemic). Boosting of these low-affinity anti-S Abs upon re-exposure to newly emerged SARS-CoV-2 (SC-2) variants or updated booster vaccines yields high Ab titers that confer a broadly reactive, but short-lived infection-neutralization effect. However, as their titers decrease, *these low-affinity Abs primarily stabilize virus-Ab complexes through high avidity interactions, thereby exerting a suboptimal infection-inhibiting effect. Mitigation instead of inhibition of infection causes highly C-19 vaccinated populations to exert large-scale immune selection pressure on viral infectiousness,*

*thereby promoting natural selection and enhanced propagation of more infectious immune escape variants (*https://www.voiceforscienceandsolidarity.org/scientific-blog/misinterpretation-of-acute-antibody-responses-after-administration-of-updated-booster-vaccines-to-covid-19-vaccine-recipients-conveys-a-dangerously-misleading-public-health-message; see fig. attached below).

Previously SIR-primed cross S variant-reactive Abs with strongly diminished neutralizing capacity towards these newly emerged, more infectious variants can still bind to these new variants and thereby elicit the production of polymeric, non-neutralizing IgM Abs (NNAbs). These NNAbs bind with low affinity to the infection-enhancing site comprised within the N-terminal domain of S protein (S-NTD), thereby enhancing viral infectiousness and triggering NNAb-dependent VBTI.

Re-boosting of previously primed cross S variant-reactive Abs following another NNAb-dependent VBTI initiates a new SIR event. This primes anti-S Abs to recognize even more conserved S-associated domains, demonstrating increased cross-variant reactivity. As long as re-exposure to newly emerged SC-2 variants (or updated booster vaccines) results in boosting of previously SIR-primed cross S variant-reactive Abs, subsequent immune selection pressure on viral infectiousness will result in the rapid succession of more infectious SC-2 variants dominating one after another.

The highly alarming observation is that the SC-2 variant JN.1[1] is now rapidly outpacing other co-circulating variants. This rapid dominance is attributed to additional mutations in viral proteins, extending beyond the S protein and accounting for a growing proportion of SC-2 variants globally. The dominant propagation of JN.1 suggests that the population's immune response does no longer primarily consist of broadly cross S variant-reactive Abs but of newly emerging immune effectors that are no longer S-specific but still exert immune pressure on viral infectiousness. This fully aligns with my theory that immune refocusing has shifted from *cross S variant-reactive* Abs to *cross SC-2-reactive* cytotoxic T lymphocytes (CTLs). As the latter are MHC class I-unrestricted and abrogate productive viral infection at a later stage of infection, their activation in highly C-19 vaccinated populations results in suboptimal non-S-specific immune selection pressure on viral infectiousness.

Consequently, enhanced CTL activity drives natural immune selection of more infectious variants that have incorporated non-S-specific infection-enhancing mutations (i.e., including mutations in other viral proteins that enhance the efficiency of viral protein synthesis or increase the intracellular viral replication rate). This phenomenon elucidates the dominant selection and propagation of JN.1, the increased intrinsic infectiousness of which is characterized by less commonly observed S-associated viral entry-enhancing mutations and replication-enhancing

[1] JN.1 is a descendant of the highly mutated Omicron BA.2.86 subvariant (nicknamed “Pirola”)

mutations found in other viral proteins (https://www.forbes.com/sites/williamhaseltine/2023/10/26/jn1-the-odd-man-out-among-omicron-sublineages/?sh=74aa039b3e47&s=03). Simultaneously, enhanced CTL activity impedes T help-dependent (!!) boosting of previously primed cross-S variant-reactive Abs—rather than hindering viral entry into susceptible cells. The diminished boosting of these Abs prevents the *de novo* production of polymeric, non-neutralizing IgM Abs. The latter enhance viral infectiousness or inhibits viral *trans* infectiousness by attaching to the conserved enhancing site within S-NTD exposed on free virions or dendritic cell (DC)-bound virions, respectively (https://www.voiceforscienceandsolidarity.org/scientific-blog/predictions-gvb-on-evolution-c-19-pandemic). As inhibition of viral *trans* infectiousness implies inhibition of viral *trans* fusion (syncytia), the attachment of NNAbs to the enhancing site within S-NTD, exposed on DC-tethered virions, inhibits viral virulence. A collective decrease in the *de novo* synthesis of these virulence-inhibiting Abs is expected to lead highly C-19 vaccinated populations to exert suboptimal immune pressure on viral virulence. It is reasonable to assume that this will occur *dramatically and rapidly* as the immune pressure becomes concentrated on a single antigenic site -the conserved, infection-enhancing site within S-NTD. Since this site must maintain its sequence integrity to preserve its infection-enhancing capacity, compensating for a likely fitness cost on viral entry, I had previously predicted that extensive mutational changes in the S-associated glycosylation profile would be necessary. Any SC-2 variant acquiring appropriate O-glycosite mutations would be able to significantly alter the conformation of this conserved antigenic site within S-NTD, displayed on DC-tethered virions, without changing the integrity of its amino acid sequence (https://www.voiceforscienceandsolidarity.org/scientific-blog/predictions-gvb-on-evolution-c-19-pandemic). Such conformational changes would exclusively hinder the binding of NNAbs to this conserved antigenic site when the latter is presented on the surface of variant virions adsorbed onto migratory DCs following viral exposure to highly infectious SC-2 variants. The removal of NNAb-mediated inhibition of *trans* infection would unleash the unbridled virulence potential of the new variant in C-19 vaccinees. The greater the intrinsic infectiousness of newly emerging variants, the more widespread this novel form of immune refocusing becomes in the population, and the more a highly C-19 vaccinated population will exert non-S-specific immune selection pressure on the virus's ability to evade the virulence-inhibiting effect of NNAbs.

Last but not least, heightened CTL activity will not only obstruct the recall of cognate T memory cells to assist boosting of previously SIR-induced cross S variant-reactive Abs **but will also impede the *de novo* priming of neutralizing Abs (NAbs) toward any C-19 vaccine (including so-called 'updated boosters')**.

In essence, the fulminant spread of JN.1 simply reflects the refocusing of the immune response towards 'universal' CTL responses, thereby indicating a growing immune selection pressure on S-NTD to thwart the attachment of virulence-inhibiting non-neutralizing anti-S Abs. Diminished

production of NNAbs upon Ab-dependent VBTIs caused by co-circulating SC-2 variants (not just JN.1) has already resulted in a rise in C-19 hospitalizations in several heavily C-19 vaccinated countries. The current surge in C-19 hospitalization and mortality rates observed across all circulating SC-2 variants is, therefore, *not linked to an intrinsic increase in virulence of JN.1*. This clarifies why our ignorant public health experts maintain that the spectacular spread of JN.1 does not pose an immediate threat to highly C-19 vaccinated populations. Relying on the (temporary!) neutralization effect seen with previous updated C-19 vaccine booster shots, they strongly advocate for vaccination with the updated XBB.1.5 mRNA vaccine, **even though updated C-19 vaccines can no longer work** *due to the progression of immune refocusing towards CTL-mediated infection mitigation* (as explained above).

In conclusion, while the rapidly spreading JN.1 variant does not evoke concerns about increased *intrinsic* virulence, its widespread dominance is of high concern. The presence of additional, productivity-enhancing mutations in viral proteins other than the S protein indicates the exertion of immune selection pressure by MHC class I-unrestricted (i.e., non-S-specific) CTLs and therefore strongly suggests a reduction in the production of virulence-inhibiting NNAbs.

Based on the experience with Omicron, it is difficult to imagine how collective immune pressure exerted on a single antigenic site (this time located within S-NTD instead of S-RBD[2]) would not prompt the rapid emergence of a new and spectacularly different variant with high virulence capacity in populations that collectively exert suboptimal immune pressure on S-NTD (i.e., highly C-19 vaccinated populations).

According to my analysis of the evolutionary dynamics of the interactions between currently circulating variants and the adaptive immune responses in C-19 vaccinees, I fear that society in highly C-19 vaccinated populations will be caught off guard when a very different variant suddenly emerges and provokes a dramatic surge in severe C-19 disease and death in highly C-19 vaccinated populations.

As I have emphasized on multiple occasions, healthy unvaccinated individuals will not be affected by this new variant, as they have long since transitioned from adaptive humoral immunity to trained cell-based innate immunity (CBII). Due to the failure of mass vaccination to achieve herd immunity during a pandemic, it has consequently generated highly infectious variants that further disrupted ('refocused') the adaptive immune response of vaccinees while failing to train their CBII (due to SIR-enabling VBTIs). *Those who advocated for mass vaccination over mass immunization through natural infection were destined to face the catastrophic consequences of their foolish decisions from the very outset of this experiment.*

[2] RBD: Receptor-binding domain

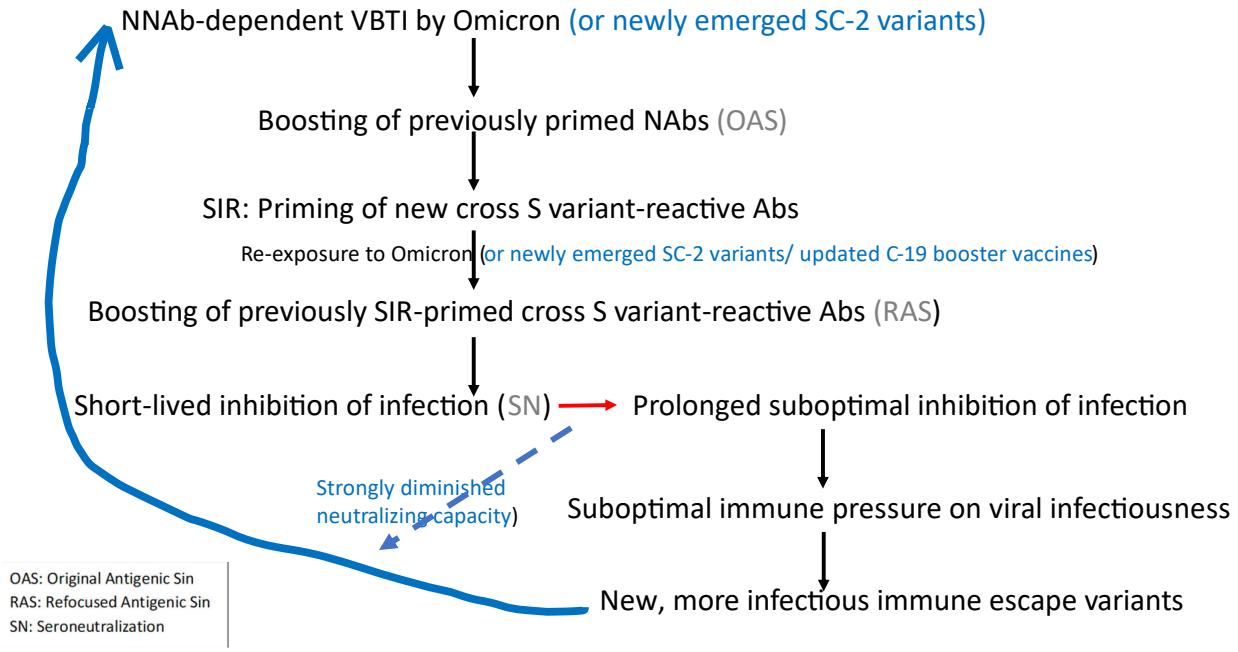

Fig.: **Misinterpretation of serological data in C-19 vaccinated populations conveys a dangerously misleading public health message**.

Painfully, several scientists and so-called 'experts' persist in the belief that currently circulating variants, including JN.1, remain neutralized after vaccination with updated booster vaccines (e.g., with the XBB.1.5 vaccine). ***They erroneously conclude that the updated (2023-2024) C-19 vaccine works against the new JN.1 variant!*** However, they don't grasp that updated booster vaccines only confer a *short-lived* neutralization activity to the ***cross variant-reactive*** anti-S Abs previously induced as a result of steric immune refocusing (SIR) following vaccine breakthrough infections (VBTIs) with newly emerging variants. This short-lived neutralization effect rapidly transitions into a more stable *suboptimal* infection-inhibiting (i.e., infection-*mitigating*) effect. The latter causes highly C-19 vaccinated populations to collectively exert immune selection pressure on viral infectiousness and, therefore, drives the propagation of more infectious variants! *By boosting previously SIR-induced cross variant-reactive Abs, updated booster vaccines will only expedite SIR upon VBTIs with newly emerging variants, thereby accelerating the emergence of more infectious immune escape variants*!

In highly C-19 vaccinated populations, immune refocusing to MHC class I-unrestricted T cells results in diminished boosting of previously induced neutralizing Abs[3], thereby dampening the production of non-neutralizing anti-S Abs. NNAbs have repeatedly been reported to facilitate VBTIs with newly emerging SC-2 variants by virtue of their infection-enhancing effect. NNAbs also have the potential to inhibit viral *trans* infection, thereby preventing viral *trans* fusion and, consequently, impeding viral virulence (https://braintrain.mykajabi.com/the-inescapable-immune-escape-pandemic).

As the production of these NNAbs produced upon VBTIs in highly C-19 vaccinated populations will soon collectively decrease to *suboptimal* levels, SC-2 is poised to undergo a spectacular mutation to overcome the immune selection pressure collectively exerted by these Abs on the virus's capacity to prevent their virulence-inhibiting activity.

[3] The production of polymeric (IgM) NNAbs is thought to be triggered by the interaction of previously induced NAbs that exhibit a strongly diminished neutralizing capacity towards the new infecting S variant.