What happens if a pandemic involving a virus naturally causing acute self-limiting infection fails to generate herd immunity?

Showcase: SARS-CoV-2

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https://www.voiceforscienceandsolidarity.org/

General considerations

Abbreviations:
Ab: Antibody
APC: Antigen (Ag)-presenting cell
C-19: Covid-19
CII: Cell-based innate immunity
CTL: Cytotoxic T lymphocyte
DC: Dendritic cell
NAb: Neutralizing Ab
NK cell: Natural Killer cell
PNNAB: Polymeric non-neutralizing Ab
RBD: Receptor-binding domain
S: Spike (protein)
SC-2: SARS-CoV-2
SIR: Steric immune refocusing
(V)BTI: (Vaccine) breakthrough infection

- A lack of comprehensive understanding of immunology poses a significant hurdle to the development of effective public health interventions and prevention strategies during pandemics.

- Key stakeholders in pandemic management, including epidemiologists, virologists, public health experts, and authorities, lack profound insights into the adaptive dynamics of the host immune response that develops during a pandemic. Even the concept of herd immunity isn't correctly understood.

- Any (large-scale) intervention in population immunity that does not prevent viral transmission may have catastrophic consequences on public and individual health. The idea that viruses evolve to become benign — like the coronavirus evolving into the "common cold" — is a "myth" and was never guaranteed.

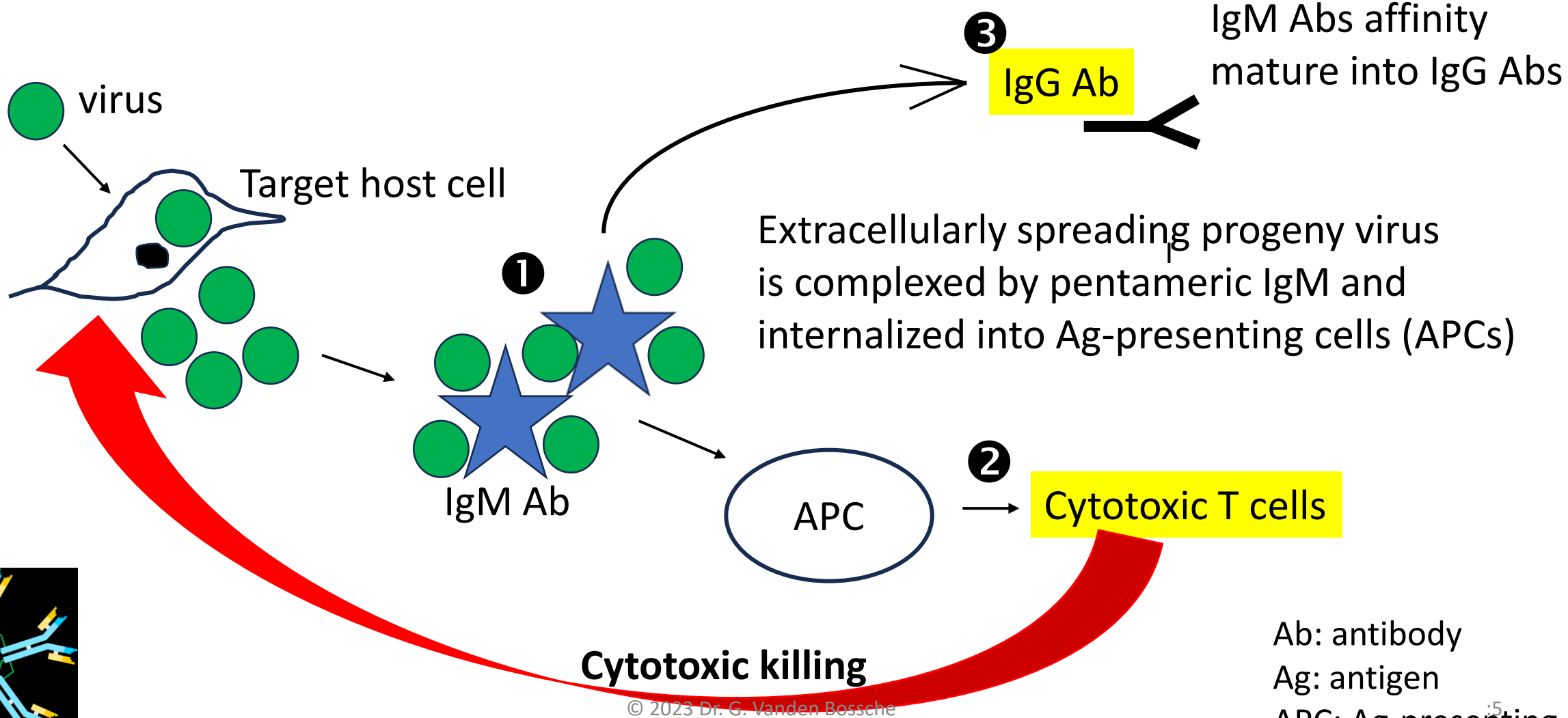
- Implementing widespread measures to impede viral growth —i.e., viral transmission in the case of an acute self-limiting viral infection— eventually drives a spectacular gain in viral fitness. This can manifest as gain in resistance to NAbs in the case of large-scale immune pressure on virus neutralizability (e.g., Omicron BA.1) or gain in intrinsic viral infectiousness in the case of large-scale immune pressure on viral infectiousness (e.g., BA.2.86).

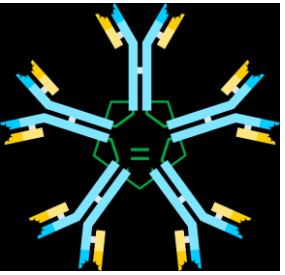
- Failure to comprehend the impact of adaptive, population-level immune pressure has resulted in failure to understand why and how mass vaccination has transformed a natural pandemic into one marked by more infectious variants.

HERD IMMUNITY

- In the context of acute, self-limiting infections, herd immunity refers to a level of population-level immunity that reduces the level of (viral) transmission down to a threshold where individuals who have not been immunized (for lack of exposure to wild or live attenuated vaccine) are protected against infection. Herd immunity therefore stops viral spread in the population.
- Herd immunity is achieved when a sufficiently large portion of the population develops sterilizing immunity towards the circulating virus/ pathogen.
- No pandemic of an acute, self-limiting viral infection can be contained without herd immunity!
- Due to its self-limiting nature, a pandemic of an acute self-limiting viral infection can never be considered a health emergency of international concern!
- Because the threshold for seroconversion (SC) to attain herd immunity following natural infection varies based on pre-existing population-level innate immunity and viral transmissibility, the SC rate is not be a reliable metric for assessing herd immunity. Conversely, vaccine-induced SC rates are not a reliable metric either as C-19 vaccines do not stimulate cell-based innate immunity.

Acute self-limiting infection or disease entails sterilizing immunity & protection from infection

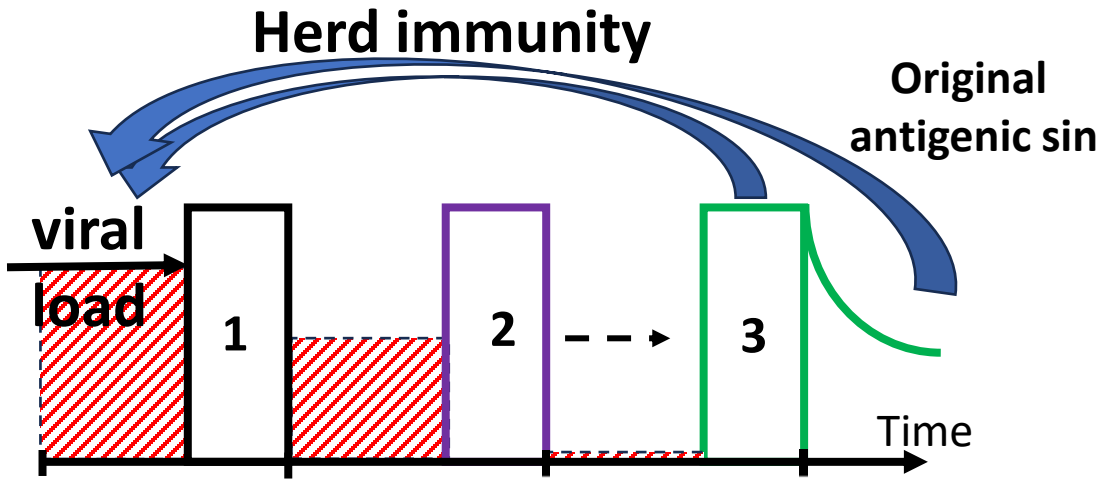




Ab: antibody
Ag: antigen
APC: Ag-presenting cell

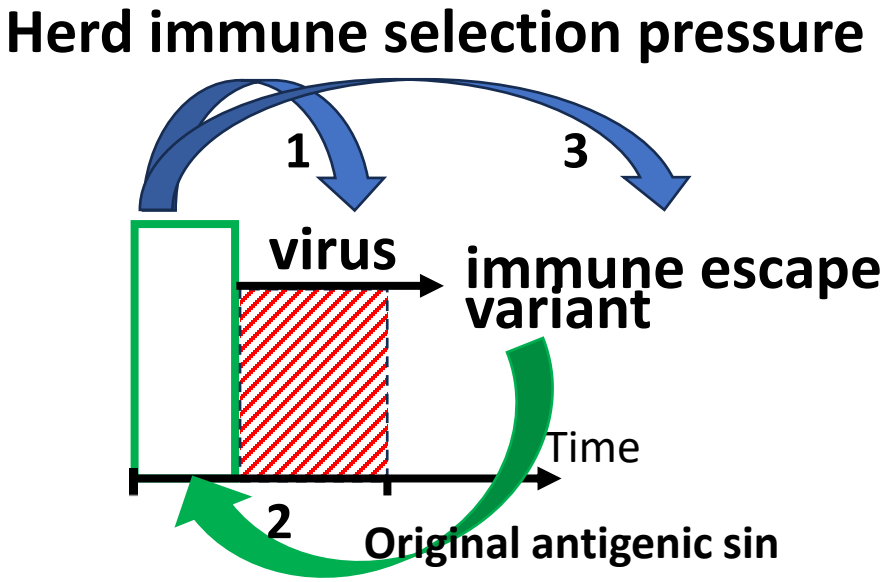
Priming of S-specific NAbs in the presence of virus (pandemic!) inevitably leads to immune escape

infection-primed NAbs



1: innate cell-based immunity (NK cells)
2: CTL (without memory)
3: adaptive humoral immunity (high affinity NAbs)
: viral load

vaccine-primed NAbs

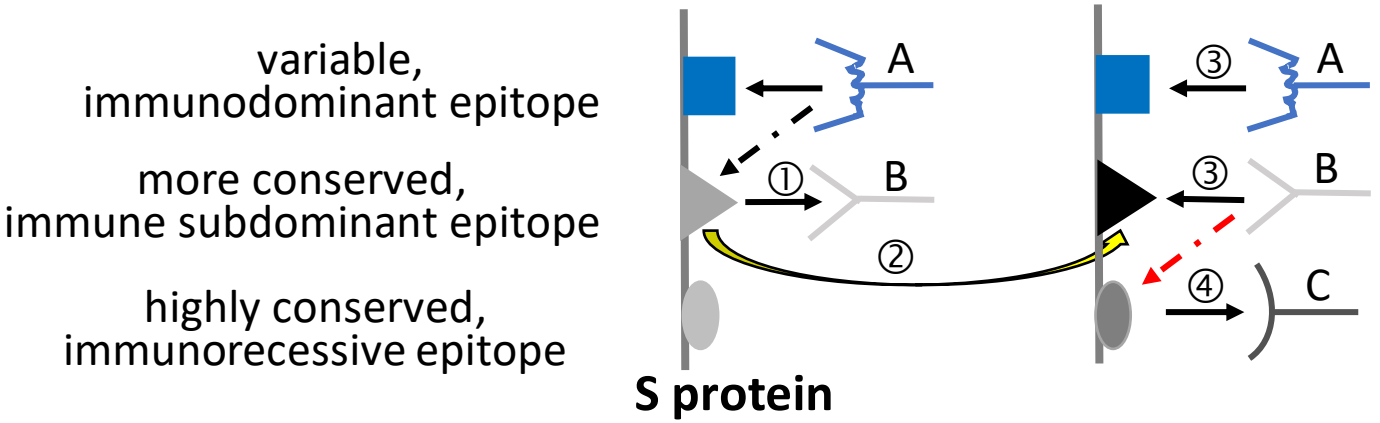


NO innate cell-based immunity
NO CTL
Only adaptive humoral immunity (high affinity NAbs)

- As some so-called ‘experts’ are confounding herd (i.e., population-level) immune pressure with herd immune protection, they have claimed that the ‘acute phase’ of the pandemic is over. They don’t seem to understand that when the acute phase of a pandemic involving a virus causing acute self-limiting infection were over, this would mean that the pandemic is over altogether!
- As others ignore how adaptive immune responses evolve as a consequence of mass vaccination, they consider the emergence of Omicron BA.1 and BA.2.86 ‘unnatural’ and rely on conspiracy theories or scapegoat immune-suppressed individuals to explain the sudden dominant propagation of these highly mutated, highly transmissible immune escape variants*.
- When a virus reaches peak infectiousness while still facing sustained immune pressure on its transmissibility, it may unleash the brakes on systemic viral dissemination to increase viral replication and propagation within the host → enhanced viral virulence.
- Contrary to being a blessing, Omicron must be considered a scourge, triggering vaccine breakthrough infections that shift immune responses from suboptimal S variant-specific NAbs to suboptimal S variant-cross-reactive, infection-inhibiting Abs. This perpetuates a cycle of suboptimal immune pressure, facilitating ongoing viral immune escape.
- As infection-mitigating Abs lose efficacy, Ab-mediated immune pressure increasingly shifts to CTL-mediated immune pressure.

STERIC IMMUNE REFOCUSING (SIR)

Pre-existing Abs that bind with low affinity to immunodominant S-associated epitopes cause steric masking of these epitopes



SIR-1: weak binding of S variant-specific pNAbs (A) → cross-neutralizing Abs (B)

SIR-2: weak binding of S variant-specific pNAbs (A) and cross-reactive pNAbs (B) → broadly neutralizing Abs (C)

pNAb: Potentially neutralizing Ab
S: Spike protein
SIR: Steric immune refocusing

Boosting of cross S variant-reactive Abs will quickly result in suboptimal immune pressure on viral infectiousness, allowing highly C-19 vaccinated populations to exert *large-scale immune selection pressure* on viral infectiousness. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10138620/

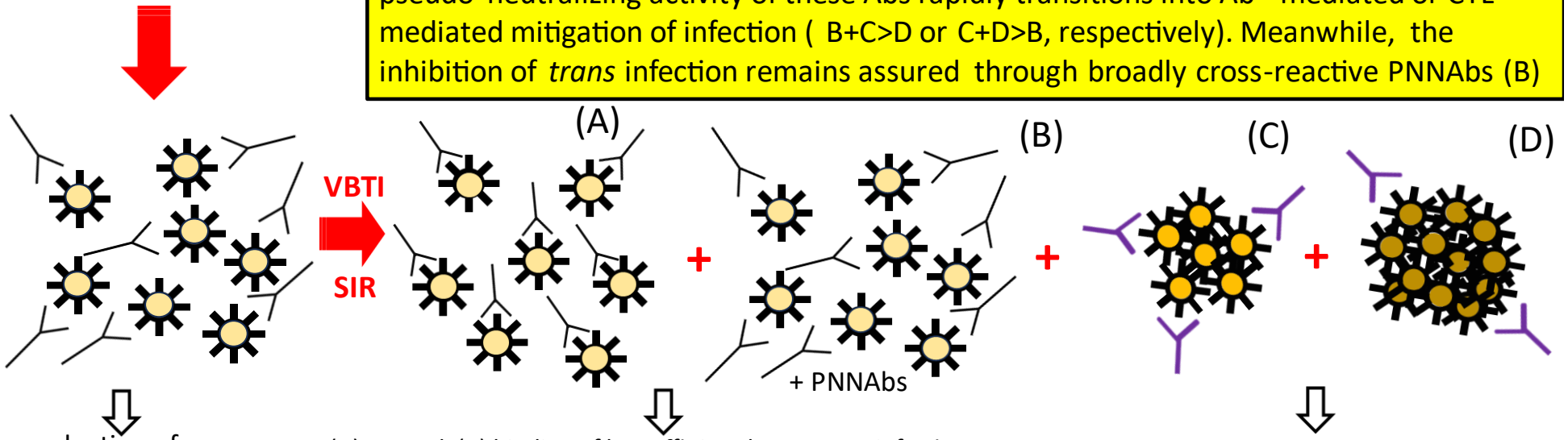
Longitudinal Variations in Antibody Responses against SARS-CoV-2 Spike Epitopes upon Serial Vaccinations

What you need to know about immune steric refocusing (SIR)

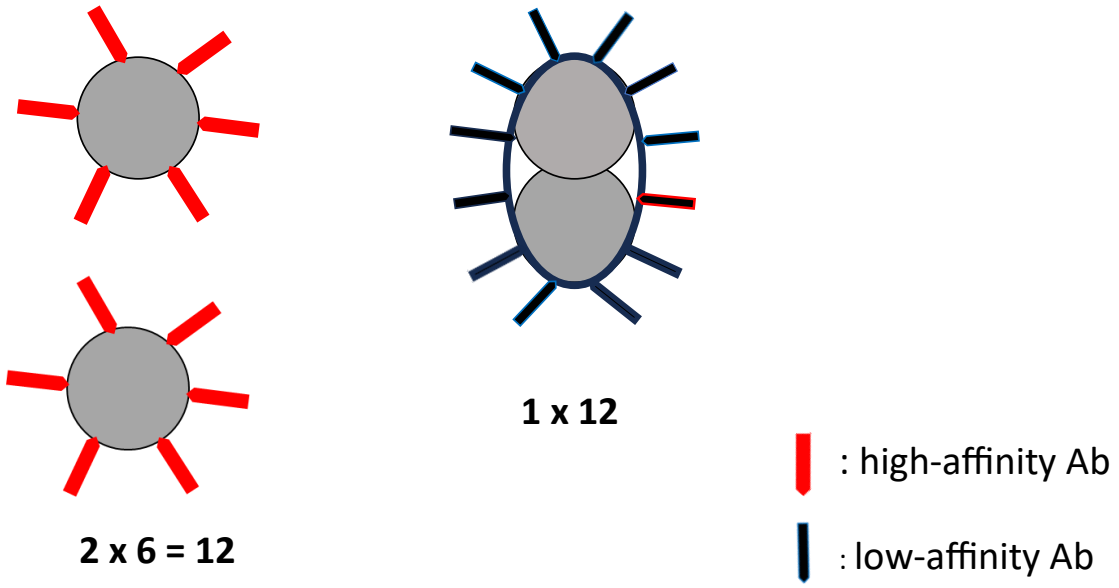
- Immune refocusing is triggered by VBTIs and updated vaccine boosters; mRNA vaccines promote SIR in their own right, even in the absence of VBTIs.
- Immune refocusing drives immune escape
- Infections with newly emerging variants in C-19 vaccinees inevitably cause SIR-enabling VBTIs. Highly C-19 vaccinated populations are therefore driving irreversible viral immune escape.
- SIR makes the host immune response not only weaker (less affinity), but also broader (less specific) and eventually shifts the immune response from humoral to cell-mediated.

VBTI with Omicron or more infectious Omicron descendants enable (transient) protection from infection or trans infection, respectively.

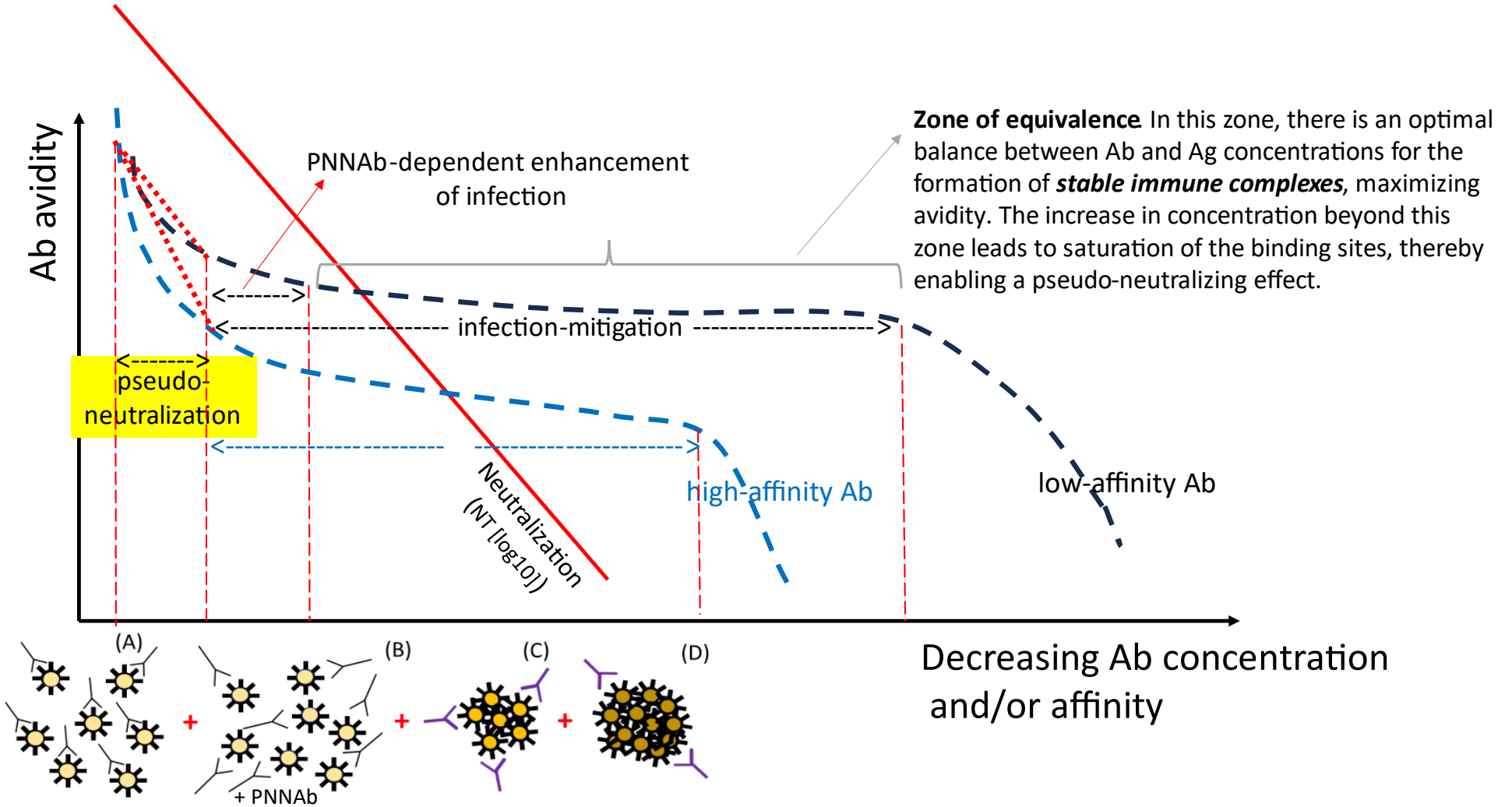
PNNAb-dependent VBTI primes cross S variant-reactive Abs via SIR. New VBTIs or updated vaccine boosters activate the pseudo -neutralizing activity of these previously SIR-primed Abs (A). Upon subsequent VBTIs or a decline in Ab concentration, the pseudo-neutralizing activity of these Abs rapidly transitions into Ab -mediated or CTL-mediated mitigation of infection (B+C>D or C+D>B, respectively). Meanwhile, the inhibition of *trans* infection remains assured through broadly cross-reactive PNNAbs (B)



Low-affinity Abs stabilize viral complexes/ aggregates



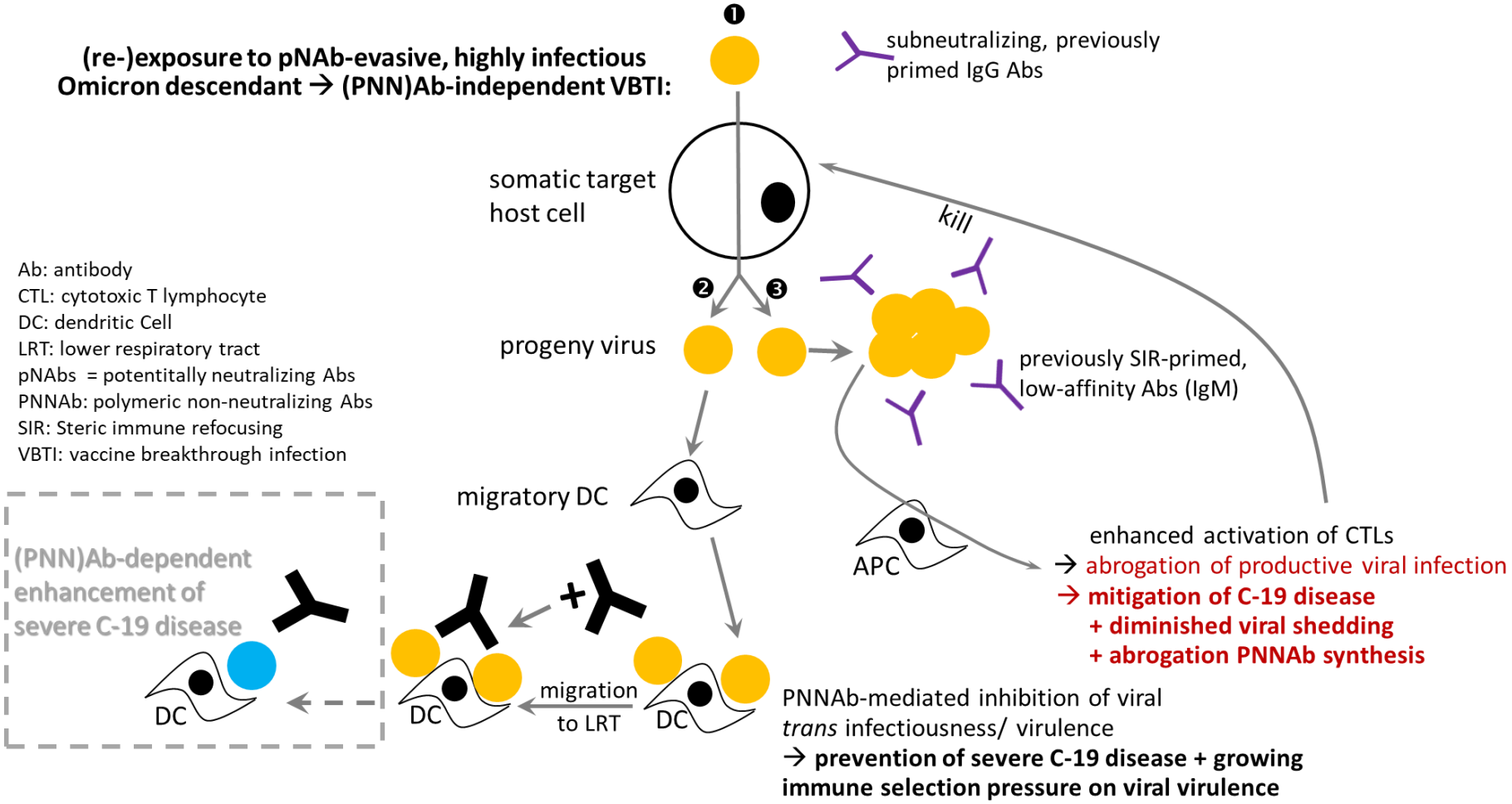
Avidity is a measure of the overall strength and stability of interactions between multiple binding sites on a bivalent or multivalent Ab and its corresponding multivalent Ag. Low-affinity Abs cover a broader scope of variants and can stabilize viral particulates over a broader range of dilutions. These Abs can, therefore, exert much broader and stronger immune selection pressure on viral infectiousness (via their prolonged infection-mitigating activity) compared to high-affinity Abs. At excessively high concentration, though, the latter have much higher pseudo-neutralizing capacity than low-affinity Abs

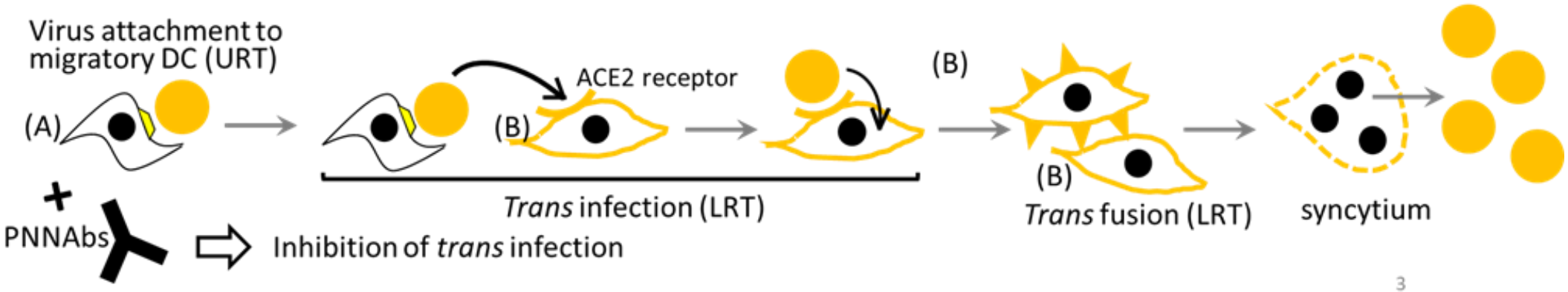


- CTL-mediated abrogation of viral transmission becomes suboptimal as more infectious virus increasingly adsorbs to APCs instead of being internalized into these cells. This lowers the concentration of PNNAbs down to suboptimal levels, thereby leading highly C-19 vaccinated populations to exert immune selection pressure on *viral virulence*.
- Finally, as immune refocusing promotes the recognition of more conserved S-associated B cell epitopes with degenerate specificity✶, VBTIs (and mRNA vaccines!) likely promote an increased incidence of autoimmune diseases and cancers.
- In essence, a comprehensive understanding of immunology is crucial for understanding that the collective natural immunity within a population (i.e., herd immunity) is the most effective immune strategy to combat pandemics and avoid the emergence of more infectious viral variants.

✶Flexibility in MHC and TCR Recognition: Degenerate Specificity at the T Cell Level in the Recognition of Promiscuous Th Epitopes Exhibiting No Primary Sequence Homology: https://pubmed.ncbi.nlm.nih.gov/11359825/

Newly emerged, highly infectious Omicron descendants do not rely on PNNAbs to infect target host cells (❶). Replication of highly infectious variants generates an immunological environment that promotes their adsorption onto tissue-resident DCs. PNNAbs bind in high quantities to progeny virus tethered to these DCs, which subsequently migrate to the lungs and other distal organs (❷)





A: Productive infection triggers innate inflammatory stimuli such as interferons. The latter upregulate lectin expression on DCs. Lectins are attachment receptors for SC-2.

B: Lectins on DCs enable viral adsorption in the upper respiratory tract (URT); virions tethered to DCs promote viral dissemination as activated tissue-resident DCs do not support productive infection but migrate and facilitate infection in *trans* of epithelial cells (low expression of ACE2) in the lower respiratory tract (LRT) https://www.nature.com/articles/s41586-021-03925-1

C: S-mediated membrane fusion and formation of syncytia. The latter is pathognomonic for severe C-19 disease

And this is how it all started…..and how it is likely to end….

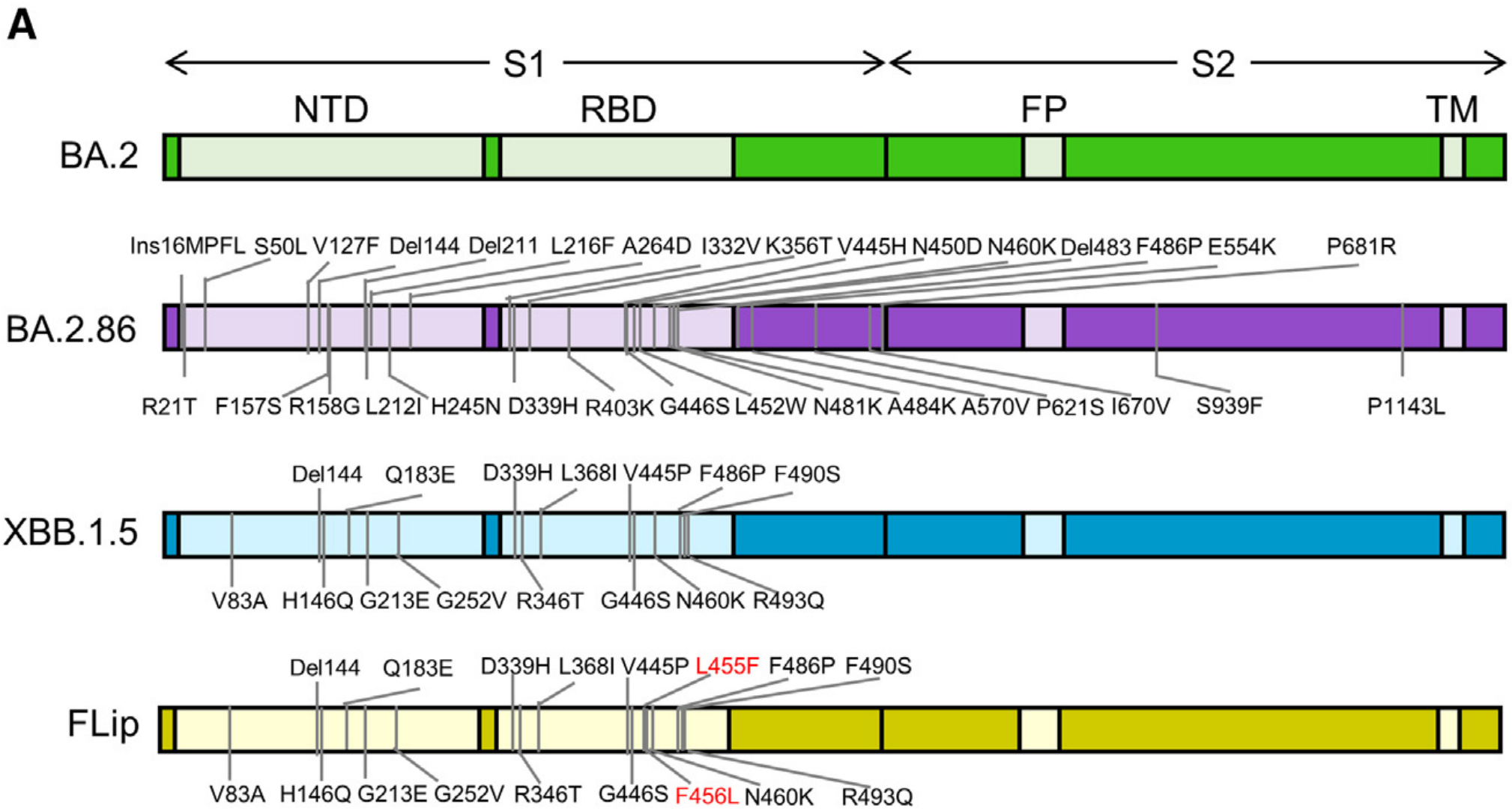
- Large-scale immunization against S protein (responsible for viral infectiousness) during an acute viral pandemic fails to generate herd immunity and instead generates 'herd' immune pressure.
- Collective (mass vaccination!), highly selective immune pressure exerted by 'neutralization-mitigating' Abs on the specific immunodominant domain of the 'infectious' protein (i.e., S-RBD) eventually promotes dominant propagation of an immune escape variant (Omicron) that collectively resists S-specific NAbs (> 30 mutations).
- Diminished neutralizing capacity of previously primed Abs promotes production of PNNAbs (IgMs), thereby triggering PNNAb-dependent VBTIs (https://pubmed.ncbi.nlm.nih.gov/34384810/ The latter restimulate previously vaccine-primed Abs at high titers, thereby triggering SIR, while PNNAbs inhibit viral *trans* infectiousness.
- SIR leads to boosting of previously primed, broadly cross S variant-reactive B cells, which produce low-affinity Abs with suboptimal neutralizing capacity. These low-affinity Abs stably mitigate viral infectiousness while recognition of more conserved S-associated B cell epitopes with degenerate specificity promotes early onset autoimmune diseases and cancers (IgG4 Abs)

And this is how it all started…..and how it is likely to end….(cont'nd)

- Suboptimal S variant-nonspecific immune pressure exerted by 'infection-mitigating' Abs on viral infectiousness promotes co-circulation of a diversified spectrum of newly emerging, more infectious immune escape variants, thereby ensuring perpetuation of VBTIs and immune refocusing.
- Collective (large-scale VBTIs), suboptimal immune pressure on viral infectiousness promotes natural selection of highly immune evasive variants that have incorporated additional mutations enabling their resistance to infection-mitigating S variant-cross-reactive Abs and nonS-specific CTLs. These mutations have been found in proteins responsible for viral entry (> 30 mutations) and productive viral infection and are driving dominant propagation of these variants (BA.2.86/ JN.1 clan).
- Enhanced intrinsic infectiousness of the BA.2.86 clan triggers Ab-independent VBTIs and thereby causes PNNAb concentrations to collectively decline, thereby causing highly C-19 vaccinated populations to exert S variant-cross-reactive immune pressure on viral virulence (i.e., on the specific infection-enhancing site within S-NTD).
- Suboptimal S variant-nonspecific immune pressure collectively exerted on viral virulence likely promotes dominant propagation of an immune evasive, highly infectious immune escape variant that collectively resists the virulence-mitigating, S variant-cross-reactive PNNAbs. This could occur through a conformational change in the infection-enhancing site of SC-2 particles adsorbed on migratory DCs, thereby allowing the new variant to unleash the PNNAb-mediated blockade on viral *trans* infection/ virulence.

BA.2.86: > 30 mutations in S protein (compared to BA.2);

https://pubmed.ncbi.nlm.nih.gov/37745517/



Backup slides

Why could Omicron not train the CII of non-previously exposed C-19 vaccinees?

- Following its initial VBTI (or 2nd mRNA dose), Omicron was readily neutralized by high concentrations of mismatched, previously vaccine-(SIR-)primed Abs that bind with low affinity to S-associated immunodominant epitopes (thereby triggering SIR). Prevention or mitigation of infection of susceptible cells following initial VBTI prevented training of naïve/ unexposed innate immune systems
- Subsequent exposure to newly emerged immune escape variants boosts previously SIR-primed cross-reactive Abs at high titers, thereby ensuring strong infection-mitigating activity and further preventing triggering and training of CII

How are the unvaccinated protected from highly infectious variants?

- Their innate immune system is able to quickly lower viral loads and kill virus-infected cells (via trained, i.e., epigenetically re-programmed, innate immune cells) without causing a strong recall of previously infection-primed pNAbs (and, therefore, preventing SIR).
- The better the innate immune system is trained, the weaker the recall effect and the lower the likelihood of PNNAb-dependent BTI.
- Unvaccinated individuals **who are in good health and avoiding overcrowding** can now successfully rely on their innate immune system to handle their immune defence entirely

Never immunize during a pandemic!

- Work on prevention:
  - Avoid overcrowding (especially of vulnerable people),
  - Foster good health practices
  - Apply standard hygiene/ sanitation

- Let the (asymptomatically/ mildly) infected spread and treat vulnerable people with antivirals

Multi-country epidemics of an acute viral disease are being reported. How will you proceed to determine your scientific advice re: scientifically sound public health measures to be taken?

- Forget about vaccination!!
- Mandate isolation/ quarantine of individuals with symptomatic disease
- Provide **early** treatment (incl. antivirals) to symptomatically infected patients
- Avoid (over)crowding
- No masks, no infection-prevention or social distancing in healthy population
- Monitor overall disease/ hospitalization rate and morbidity rate in vulnerable people (metric for development of herd immunity)
  - If ASLVD (e.g., MERS, SARS): rapid ↓ of morbidity/ hospitalization rate in the overall population (due to isolation)

    → disease-free population if no contact with animal reservoir (no vaccination in endemic regions)
  - If ASLVI (e.g., SC-2): rapid ↓ of morbidity/ hospitalization rate in vulnerable people

    → disease-free population once herd immunity is established (vaccination in endemic and nonendemic area if no animal reservoirs)

Note: virus isolation- RT-PCR + Ag testing: only for DIAGNOSTIC purposes

What does a rationale approach to pandemic *preparedness* consist of?

- Prevention is always better than cure:

  healthy nutrition, healthy lifestyle, strong physical and mental health
- Avoid overcrowding (especially of vulnerable people)
- Use standard hygiene and sanitary practices (clean water/ ventilation)
- Ensure sufficient isolation/ quarantine capacity
- Childhood vaccination to fill up gaps in herd immunity (if no nonhuman reservoirs)
- Train doctors on early pathogen-nonspecific treatment
- Train epidemiologists on immunology

How will the outcome of the C-19 pandemic be described in future science books?

"Due to suboptimal neutralization of its infectiousness, SC-2 acquired enhanced intrinsic infectiousness. As enhanced intrinsic infectiousness led to suboptimal neutralization of its trans infectiousness in C-19 vaccinees, SC-2 acquired enhanced intrinsic virulence in C-19 vaccinees."

"The C-19 mass vaccination program will indisputably be remembered as the largest and most dangerous gain-of-function experiment ever conducted in the history of biology- – one which mankind has unleashed on its very own species."

Key messages from my book:
The inescapable immune escape pandemic

https://bit.ly/3NYokkE

This book delves into various aspects of the evolutionary consequences stemming from the widespread COVID-19 vaccination program. It stands out by emphasizing the scientific intricacy of population-level interactions between the SARS-CoV-2 virus and the host immune system. These interactions are not only complicated but also varied, depending on the infectiousness of the circulating variant and the type of immunity induced (infection-based versus vaccine-based). The book demonstrates how mass vaccination influences these interactions, transforming a natural pandemic into one characterized by immune escape variants. I caution that the ramifications of this could lead to uncontrollable evolutionary viral dynamics due to insufficient herd immunity and potentially cause a massive rebound effect from the hasty and ill-advised deployment of new vaccine technologies (such as rapid mass vaccination during a pandemic). Additionally, I discuss how the adaptability of the human immune system has postponed the emergence of a more virulent variant, contrary to my initial predictions. While some sections may be challenging to comprehend, if the book aids in understanding the complexity of these issues and highlights nature's superiority over the overconfidence of technocrats, my primary objective for writing will be fulfilled.

C-19 vaccination does not promote herd immunity!

- mRNA vaccines and vaccine breakthrough infections promoted resistance of new Omicron sublineages to previously SIR-induced antibodies and therefore expedited viral infectivity instead of developing herd immunity
- Highly C-19 vaccinated populations exert *herd immune pressure on viral infectiousness* instead of generating *herd immunity against productive infection.*
- Mass vaccination programs imposed by health authorities and policy makers have turned highly C-19 vaccinated populations into a breeding ground for immune escape variants and thereby transformed a natural pandemic into a pandemic of immune escape variants. Pretending that a pandemic of immune escape variants generates herd immunity is a *contradictio in terminis*….. and without herd immunity a pandemic cannot transition into endemicity….
- *Natural infection/ immunization during a natural pandemic prevents immune escape and thereby generates herd immunity* while providing *long-lived sterilizing immune capacity to the individual*. In contrast, *mass vaccination during a natural pandemic drives natural immune selection of non-neutralizable and more infectious immune escape variants and, therefore, fails to generate herd immunity or provide long-lived sterilizing immunity to the individual*.

In the case of a pandemic, natural immunity, including trained innate immunity, is far more efficient (and safe!) than vaccine-induced immunity!

- In the absence of a robust adaptive immune mechanism that protects against viral virulence, the best alternative to protect against severe C-19 disease during an immune escape pandemic is to avoid breakthrough infection via *trained cell-based innate immunity.*
- Whereas both cell-based innate immunity and virulence-inhibiting, non-neutralizing antibodies (NNAbs) are *S variant-nonspecific*, the cell-based innate immune system (*CBIIS) is endowed with adaptive memory* whereas deficient T help will eventually prevent recall of NNAbs.
- Due to their thoroughly trained CBIIS, healthy unvaccinated people are protected from severe C-19 disease and will likely improve their protection when highly infectious SC-2 variants evolve to exhibit high virulence in 'untrained' C-19 vaccinees.
- In conclusion: Large-scale natural immunity is required but sufficient to durably protect an individual from a virus causing ASLVI and to end a natural pandemic.

Why and how is the majority of vaccinees still protected against (severe) C-19 disease?

- The currently observed protection against (severe) disease in C-19 vaccinees fully relies on short-lived NNAbs and strong activation of CTLs. (Re-)exposure to circulating Omicron descendants or vaccine booster doses initially extended this protection, but only temporarily and not without enhancing large-scale immune selection pressure on viral virulence.
- However, once the NNAbs collectively decline below an optimal threshold, the virus will likely break through their virulence-inhibiting capacity and unleash a major wave of severe C-19 disease in highly C-19 vaccinated populations.

Where has all the science gone?

- Key opinion leaders and health experts are erroneously interpreting diminished pathogenicity as an indication that the virus is transitioning into endemicity. They do not understand that reduced pathogenicity of SC-2 does not result from herd immunity but is triggered by broadly infection-mitigating immune response. Repeated activation of broadly infection-mitigating CTLs upon re-exposure to highly infectious circulating variants results in enhanced immune selection pressure on the virus' capacity to prevent NNAb-mediated inhibition of viral virulence. This is now preparing the virus to lift the immune blockade on severe C-19 disease.
- Massive exercises in mutational stamp collection combined with *ad hoc* interpretations of epidemiological, biological and clinical data have prevented scientists from seeing the forest for the trees and are the biggest obstacle for them to understand the disastrous consequences of this mass vaccination experiment; their mutational analyses and predictive epidemiological models merely reflect snapshots and don't consider the immunologic dynamics that are driving natural adaptation of the virus.

Where has all the science gone? (cont'd)

- Although scientists seem to agree that Spike (S)-associated viral mutations are driven by population-level immune selection pressure, *none of them dares to mention that mass vaccination and subsequent booster immunizations caused populations to exert large-scale immune pressure on viral infectiousness*.
  Why does no one investigate the origin of this large-scale immune selection pressure placed on the virus?
- While our experts claim that mRNA vaccination and vaccine breakthrough infections (VBTIs) protect against severe C-19 disease, they seem to ignore that both prevent or even abrogate training of the cell-based innate immune system and promote viral immune escape.
- Not understanding that updated vaccine booster doses will only recall previously primed Abs, thereby expedite immune refocusing and leading to immune escape, is one of the most blatant examples of immunological illiteracy. On the other hand, VBTI infections fail to prime new NAbs towards the infecting circulating variant.

Where has all the science gone? (cont'd)

- Neither health experts nor scientists seem to understand how enhanced susceptibility to Omicron infection can be reconciled with prevention against (severe) disease in C-19 vaccinees whose antibodies no longer possess sufficient neutralizing capacity.
- No scientist even seems to be considering the risk of this virus evolving a major - but immunosilent (glycan-based!)- shift transforming it into a variant that enhances viral virulence in highly vaccinated populations.
- Regardless of their astonishing lack of understanding and insight, many scientists continue to blindly endorse the proposal of incompetent public health experts and authorities to continue the mass vaccination experiment with mRNA-based vaccines and to even recommend use of the latter for fighting other diseases.

Many experts pretended Omicron would end the pandemic. Why have they been wrong?

- Since the advent of Omicron, the pandemic has evolved into a self-catalyzing chain of large-scale immune escape instead of transitioning into endemicity.
- Because Omicron self-catalyzed its evolution into a series of highly infectious co-circulating descendants, it rapidly caused immune escape dynamics to reach a point of no return. What this means is that Omicron descendants are now paving the way to the likely emergence of a naturally selected immune escape variant with high virulence potential in highly C-19 vaccinated populations
- In conclusion: Early Omicron descendants, the i*nfectiousness* of which could no longer be sufficiently *neutralized* by *pre-existing potentially neutralizing* Abs, acquired *enhanced infectiousness* in vaccinated individuals whereas subsequent Omicron descendants, the *trans infectiousness* of which can no longer be sufficiently *inhibited* by *pre-existing non-neutralizing Abs, will likely acquire enhanced virulence.*

Vaccinated -but not unvaccinated people - in highly C-19 vaccinated populations have turned the natural pandemic into a pandemic of immune escape variants

- Because trained cell-based innate immunity provides strong sterilizing immunity the unvaccinated did not contribute to viral immune escape and were not responsible for turning the natural SARS-CoV-2 pandemic into a pandemic of immune escape variants.

- Each highly C-19 vaccinated population is now planting the seeds for the emergence of a new Omicron descendant with high virulence potential (HI-VI-CRON).

Why will the mass vaccination program be remembered in the history of mankind as a colossal blunder?

- Mass vaccination with C-19 vaccines during this pandemic drove immune escape and diminished the neutralizing capacity of vaccine-induced Abs towards the circulating virus. This allowed Omicron to cause vaccine breakthrough infections (VBTIs) that caused the immune system to produce poorly functional Abs (a phenomenon called ‘immune refocusing’). VBTIs irreversibly compromised the cell-based innate immune system of C-19 vaccinees while fueling large-scale viral immune escape, thereby eventually raising immune selection pressure on viral virulence in vaccinees.
- In their incredibly naive belief that through technology, they can control biology, technocrats have been seduced into pursuing sophisticated technologies without fully understanding their biological impact. When they realized the complexity, they decided to turn their ‘program’ into a global clinical - but purely empirical- vaccine experiment that doesn’t even meet the routine regulatory requirements for preclinical testing.

Why will the mass vaccination program be remembered in the history of mankind as a colossal blunder? (cont'd)

- This mass vaccination experiment has caused a profound disturbance of the naturally balanced virus-host immunity ecosystem. By converting *antibody(Ab)-mediated protection against C-19 disease* into ***Ab-independent enhancement of severe C-19 disease***, it will have turned a natural pandemic into the largest and most dangerous gain-of-function experiment ever conducted in the history of biology-– one which mankind has unleashed on its very own species.

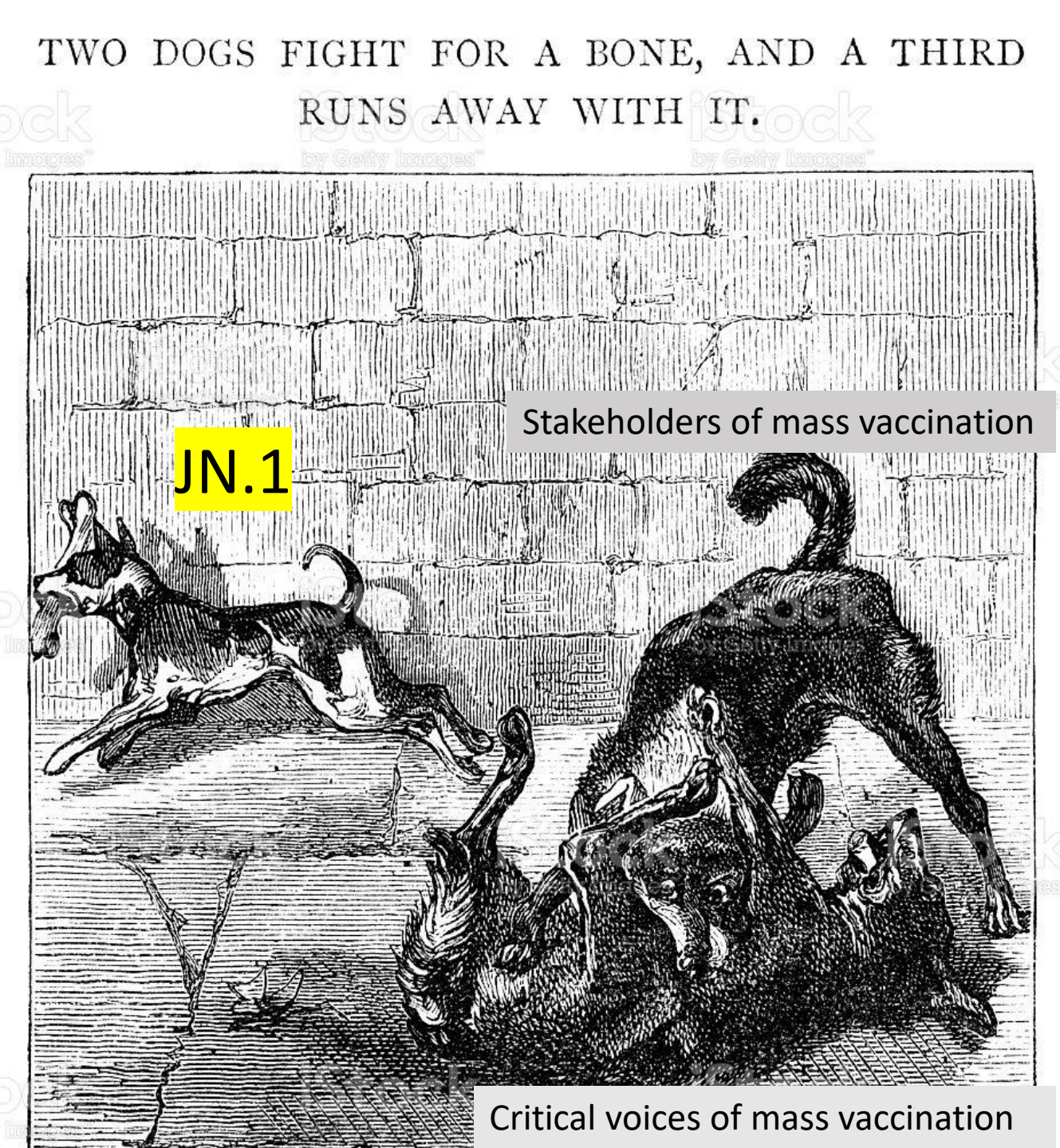
- Mandatory vaccination during a pandemic cannot be scientifically justified. It is therefore completely unethical. Even individuals with a frail innate immune system should not have received C-19 vaccines but rather allowed prophylactic antiviral or early multidrug treatment.

Why am I predicting that SARS-CoV-2 (SC-2) will soon evolve into a highly virulent variant in highly vaccinated populations before ending the pandemic?

- Viral survival will require the blockade on viral virulence to be lifted in highly C-19 vaccinated populations.
- Adaptation of viral immune escape variants to large-scale enhanced immune pressure on viral virulence is likely to select a new type of SC-2 variant that is capable of breaking through vaccine-mediated immune protection against severe disease and shift viral replication and spread to susceptible organ tissues of the vaccinated host itself rather than to other susceptible hosts.
- I predict that this will lead to an extraordinary high loss of human lives (i.e., excess deaths) and thereby curtail viral transmission to an extent where the virus can no longer survive in the affected population.
- However, my analysis strongly suggests that all healthy unvaccinated individuals who trained their cell-based innate immune system (CBIISduring this immune escape pandemic will be protected from severe C-19 disease and even from C-19 disease all together.
- Biology always encompasses gray areas and offers hope for C-19 vaccinees who adequately trained their CBIIS before vaccination.

Which C-19 vaccines are most problematic? Which C-19 vaccinees are less impacted?

- While mRNA vaccines promote immune refocusing, they must be considered highly problematic both from an individual and public health viewpoint.
- Healthy vaccinees who only received a single injection of an mRNA-based C-19 vaccine or no more than 2 injections with a non-mRNA-based vaccine prior to developing a symptomatic vaccine breakthrough infection are thought to have preserved their capacity to train their cell-based innate immune system.
- Whereas mRNA-based vaccination shortly after SC-2 infection promotes immune refocusing and expedites the emergence of an immune escape variant that has the potential to cause *enhancement of severe C-19 in highly C-19 vaccinated populations*, C-19 vaccination shortly before exposure to a new SC-2 variant likely promotes *individual cases of Ab-dependent enhancement of C-19 disease*.


TWO DOGS FIGHT FOR A BONE, AND A THIRD RUNS AWAY WITH IT.
JN.1
Stakeholders of mass vaccination
Critical voices of mass vaccination