How Many More Times Will I Have To Tell You That This ‘Immune Escape’ Pandemic Will Not Have a Happy Ending?

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General Manager at Voice for Science and Solidarity | The biggest challenge in vaccinology: Countering immune evasion

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Opinion Article

The exotic and highly infectious nature of the currently circulating variants raises questions. New emerging variants are now succeeding each other at a rapid pace (e.g., FL.1.5.1, BA.2.86, EG.5). While they share a phylogenetic relationship, they have become so antigenically distinct from their predecessors that they should no longer be considered mere *variants* but rather *different serotypes*.

Mutations, as identified by mutation-spotters and confirmed by molecular epidemiologists, are no longer converging to a well-defined spike (S)-associated domain. It appears that mutations enhancing the virus's intrinsic infectivity are currently thriving and competing with each other. This suggests that the viral evolutionary dynamics are no longer driven by 'herd' immune selection pressure on viral infectivity.

In the absence of immune selection pressure on viral infectivity and with highly infectious variants in circulation, variants which incorporated spontaneous mutations conferring an even higher level of intrinsic

viral infectivity are now more likely to emerge. This is because the higher the viral infectivity, the more the virus replicates and the more likely it is for variants with even higher infectivity to gain a competitive advantage over existing lineages or less infectious offspring. If not constrained by selective immune pressure, variants with steadily increasing infectivity can lead to higher rates of asymptomatic transmission among COVID-19 vaccinees and compete for dominance.

Because public health authorities do not fully comprehend the dynamics of the population-level immune adaptation at play, they do not consider the current evolution very threatening for several reasons:

- Antibodies in vaccine recipients are mistakenly believed to have the capability to effectively neutralize the newly emerging variants *in vivo*, even those that are highly infectious, albeit with somewhat reduced effectiveness.

- Although hospitalization and morbidity rates are now gradually increasing, most hospitalizations are primarily *associated with* SARS-CoV-2 but are *not directly attributed* to it.

- Cases of mild to moderate COVID-19 disease, whether in the vaccinated or unvaccinated, have become increasingly rare.

- While viral transmission rates are increasing, they remain lower than during the initial circulation of Omicron and its early variants.

Few appear to acknowledge that the spread of more infectious Omicron-derived lineages is resulting in reduced attachment of *S variant-nonspecific*, *non-neutralizing* antibodies to a *highly conserved* antigenic site within the N-terminal domain of S protein (therefore also called 'polyreactive', non-neutralizing antibodies; PNNAbs). This site is exposed on the surface of S proteins found on progeny virions that adhere to migrating dendritic cells (DCs) surveying the upper respiratory tract. This diminished binding can result in flawed inhibition of viral *trans* infection in distal organs and may lead to the cell-to-cell *trans* fusion of virus-infected host cells.
Trans fusion of SARS-CoV-2-infected cells is indicative of high viral pathogenicity, which can clinically manifest as severe or systemic COVID-19 disease. When the segment of the population exerting *suboptimal* PNNAb-mediated immune pressure on viral *trans* infectivity surpasses a specific threshold, the entire population represented by that segment will collectively exert *immune selection pressure* on this trait. This will inevitably lead to the natural selection and spread of a new variant that combines high viral infectivity with high viral *trans* infectivity (i.e., enhanced virulence) when infecting a population experiencing such immune selection pressure (i.e., highly COVID-19 vaccinated populations).

So, whereas Omicron resisted the infection-inhibiting activity of neutralizing Abs (NAbs) and redirected population-level immune selection pressure on the infectivity of SARS-CoV-2 to population-level immune selection pressure on *trans* infectivity of Omicron descendants, a novel (O-glycosylated) variant, which I've termed "**Hi-Vi-Cron**" as an acronym for "**Hi**ghly

Virulent Omicron descendants," might possess the capability to withstand the *trans* infection- inhibiting effects of PNNAbs while leveraging these antibodies to amplify viral infectivity. This increased viral infectivity, in conjunction with heightened virulence, is likely to lead to hyperacute systemic COVID-19 disease, instead of facilitating the adaptation of the host immune response through immune refocusing (as explained in my recently published book: "The Unescapable Immune Escape Pandemic"; drgeert.com).

Understanding the immunological consequences of mass vaccination during a pandemic of a virus causing acute self-limiting infection (e.g., SARS-CoV-2) is essential. The advent of Omicron signaled the irrevocable loss of the opportunity for the population to develop herd immunity and instead turned mass vaccination into an unprecedented and life-threatening "gain-of-function" experiment with the global population as guinea pigs. Just as Omicron came like a thief in the night, so too will Hi-Vi-Cron surprise society.

Predicting complex biological dynamics requires a rigorous scientific analysis of the fundamental causes of these dynamics and their alignment with forthcoming data and observations, rather than extrapolation from *ad hoc* data or previous observations. Regarding the ongoing immune escape pandemic, the dominant biological patterns are governed by the evolving dynamics of the virus, molded and remolded by the population-level immune response imprinted by mass vaccination. As these viral evolutionary dynamics were initiated in the wrong direction (the immune response should ideally adjust to the virus, not the other way

around!), Nature is now compelled to eliminate all incorrect immune adaptations from the population. This scenario will, however, leave many vaccinated individuals (i.e., those who were vaccinated in ways that made them exclusively reliant on this mistaken immune imprinting) entirely unprotected. *I cannot imagine how this would not lead to significantly increased mortality rates before protective herd immunity can be achieved*. However, this may only transpire once the rate of excess deaths in vaccinees due to immune suppression or immune-related pathology indirectly resulting from mass vaccination has further increased.

The scenario depicted above represents the only means through which nature can transform the ongoing *herd immune selection pressure* (on viral virulence) exerted by highly COVID-19-vaccinated populations into a state of optimal, sterilizing *herd immunity* (primarily conferred by the unvaccinated).

The rise in hospitalization and mortality rates could rapidly strain healthcare and funeral service systems in highly COVID-19-vaccinated countries. I therefore urge all healthy unvaccinated individuals to be prepared to assist in such scenarios, whenever and wherever they may arise.

COVID-19 Immunity Pandemics SARS-CoV-2

Comments (10)

What do you think?