

I have to admit that I don't know exactly when the COVID-19 tsunami will begin, but I do know that it will happen and here is how it will unfold.



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JAN 21, 2025 · PAID



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This article is short but critically important if you want to understand the evolution ahead. I hope you understand how the evolutionary dynamics of this pandemic, with its numerous transitions, continue to surprise us.

The redirection of cellular immunity^[1] towards dendritic cell (DC)-mediated virus inactivation shifts the acute phase of COVID-19 (C-19) disease into a more chronic form ('long COVID'). This transition induces a shift in population-level immune pressure—from targeting *viral infectiousness* to targeting *viral trans infection* and *trans fusion*.

As the prevalence of chronic infections is now increasing, the occurrence of cryptic variants[2] capable of *intra-host* transmission[3] and shed by chronically infected individuals also rises. Over time, this gradually increases the likelihood of a 'suitable'[4] (i.e., virulent) cryptic variant emerging—one that happens to gain a fitness advantage over the increased immune pressure on viral *trans* infection and *trans* fusion (i.e., on viral virulence) exerted by highly C-19 vaccinated populations. As such a variant would suddenly enjoy large-scale natural immune selection, it would likely cause a rapid surge in *enhanced severe C-19 disease*, thereby affecting all parts of the population unable to eliminate it at an early stage of infection. Avoiding such an unfortunate outcome would require either *trained cell-based innate immunity* or *sufficiently high pre-existing concentrations of antivirals*.

In conclusion:

The more the prevalence of chronic C-19 disease replaces that of acute C-19 disease, the closer we come to a tsunami of C-19 hospitalizations and mortality.

As long as the 'suitable' variant doesn't emerge, the pandemic situation remains '*metastable*,' giving society the impression that the pandemic is subsiding. However, the sudden emergence of a new, 'suitable' SARS-CoV-2 lineage is highly likely to result in a hyper-acute, *multi-country* epidemic (i.e., in highly C-19 vaccinated countries), leaving society in these countries caught off guard.

[1] The *redirection of cellular immunity* occurs following the *refocusing of humoral immunity* and involves a shift from cytotoxic T lymphocyte (CTL)-mediated elimination of virus-infected host cells at an early stage of infection to dendritic cell (DC)-mediated adsorption of infectious virions.

[2] Cryptic SARS-CoV-2 (SC-2) variants may harbor novel mutations that are selected during chronic SC-2 infections and are not commonly seen in acute infections. Although they may eventually be shed into the population, they do not spread widely in populations that either do not exert immune pressure or exert a type of immune pressure that fails to provide these variants with a fitness advantage. These variants are, therefore, not regularly identified in wastewater analyses or through standard viral surveillance and tracking methods, which is why they are referred to as 'cryptic'. However, *under specific collective immune pressure*, such as that exerted by highly C-19 vaccinated populations*, *a specific emerging cryptic variant* could, however, gain a competitive advantage.

*but not in previously SC-2 infected populations, as the latter do not exhibit a high prevalence of subneutralizing anti-Spike protein antibodies

[3] Chronic infections provide a prolonged environment for viral replication and evolution, enabling the virus to acquire mutations that improve its fitness within the specific host. These adaptations may make the virus better suited for *intra-host*

transmission between cell types or tissues.

[4] For the purpose of this article, 'suitable' means 'being well adapted to overcome the suboptimal population-level immune pressure on viral *trans* infection and *trans* fusion.'



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Eamonn Blaney 20h



Are those of us who are healthy, non-mRNA injected and with vitamin D bloods of 150nmol (50ng/ml) be at equal risk of serious illness from a cryptic variant, as those how received multiple injections?

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Sam Young 20h

