Review of: "The Changing Trajectory of Covid-19 and How Immunity is Evolving with It"

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The Changing Trajectory of Covid-19 and How Immunity is Evolving with It

https://www.qeios.com/read/42934U/pdf

This well-written article summarizes officially recognized knowledge on the evolution of the SARS-CoV-2 virus. But all the reasoning in this article is based on paradigms that are commonly accepted but should be discussed

Vaccines have not been proven to reduce the spread of the virus, since they do not prevent transmission of the virus as early as 2021.

A U.S. Department of Defense AI program called "Project Salus," run in cooperation with the JAIC (Joint Artificial Intelligence Center), analyzed data from 5.6 million Medicare beneficiaries aged 65.

. The alarming results show that the vast majority of hospitalizations for covid occur among fully vaccinated individuals, and that the condition of fully vaccinated individuals worsens from week to week.

[Effectiveness of mRNA COVID-19 Vaccines Against the Delta Variant Among 5.6M Medicare Beneficiaries 65 Years and Older

Weekly update of September 28, 2021

https://www.justfacts.com/document/waning_effect_covid-19_vaccines_humetrix_2021.pdf

Part of a U.S. Department of Defense study called "Project Salus,"https://www.galp.in/work/project-salus : https://www.humetrix.com]

SARS-CoV-2 Vaccine Breakthrough Surveillance and Case Information Resource

Washington State Department of Health June 9, 2021

https://doh.wa.gov/sites/default/files/2022-02/420-339-VaccineBreakthroughReport.pdf

From February 12 - July 29, 2021, the Washoe County Health District identified and traced 6,128 out of 6,399 reported cases across the sample period. 338 (5.5%) of all cases were identified as breakthrough infections, and 289 (86%)

vaccinated individuals had symptomatic infections. Severe clinical outcomes were infrequent with 17 hospitalizations (5% of VBT) and no deaths. Cycle threshold values were not statistically different between vaccinated and unvaccinated individuals.

An Analysis of SARS-CoV-2 Vaccine Breakthrough Infections and Associated Clinical Outcomes

Heather Kerwin, Rex Briggs, Sameer Nair-Desai, Andrew Gorzalski, Mark Pandori, Stefanie Friedhoff, Thomas C. Tsai

medRxiv 2021.09.09.21262448; doi: https://doi.org/10.1101/2021.09.09.21262448

Omicron period : Koutsakos M, Lee WS, Reynaldi A, Tan HX, Gare G, Kinsella P, Liew KC, Taiaroa G, Williamson DA, Kent HE, Stadler E, Cromer D, Khoury DS, Wheatley AK, Juno JA, Davenport MP, Kent SJ. The magnitude and timing of recalled immunity after breakthrough infection is shaped by SARS-CoV-2 variants. Immunity. 2022 Jul 12;55(7):1316-1326.e4. doi: 10.1016/j.immuni.2022.05.018. Epub 2022 May 27. PMID: 35690062; PMCID: PMC9135796.

Infection has been shown to provide better protection against reinfection than vaccination

“By analyzing results of more than 460,000 individuals, we show that while recent vacci-nation reduces Omicron viral load, its effect wanes rapidly. In contrast, a significantly slower waning rate is demonstrated for recovered COVID-19 individuals.” Woodbridge, Y., Amit, S., Huppert, A. et al. Viral load dynamics of SARS-CoV-2 Delta and Omicron variants following multiple vaccine doses and previous infection. Nat Commun 13, 6706 (2022).https://doi.org/10.1038/s41467-022-33096-0

Covid-19 : Natural immunity versus vaccine immunity october 2021

DOI: 10.32388/DP264J https://www.qeios.com/read/DP264J

https://www.qeios.com/read/DP264J

The correlation between antibody levels and protection is unclear: Perry J, Osman S, Wright J, Richard- Greenblatt M, Buchan SA, Sadarangani M, et al. (2022) Does a humoral correlate of protection exist for SARS-CoV-2? A systematic review. PLoS ONE 17(4): e0266852. https://doi.org/10.1371/journal.Pone.0266852

Calculations taken from a CDC publication [https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e1.htm] show that the vaccinated are more likely to test positive for COVID-19 than the unvaccinate and that the vaccine effectiveness in preventing a positive COVID-19 test was -17% for people who had received two shots, -36% for three shots and -45% for four shots.

The discrepancy between immunogenicity data and lack of protection against infection needs to be explained

The role of antibodies in coronavirus disease needs to be discussed [Banoun (2021).

The role of antibodies in the light of the theory of evolution.

African Journal of Biological Sciences. 3(3), 1-9.

https://www.afjbs.com/files/1627021759_(1)_AFJBS20210145_(p_1-9).pdf

COVID19: Cross-Immunity with Other Coronaviruses, Immunopathological Phenomena

http://ssrn.com/abstract=3654264

Banoun H. Why are children and many adults not affected by COVID-19? Role of the host immune response. Infect Dis Res. 2022;3(3):18. doi:10.53388/IDR20220825018) https://www.tmrjournals.com/article.html?J_num=4&a_id=2275]

For a discussion of the evolution of the virus in the face of the host immune system, see:https://pubmed.ncbi.nlm.nih.gov/33910211/

Banoun H. Evolution of SARS-CoV-2: Review of Mutations, Role of the Host Immune System. Nephron. 2021;145(4):392-403. doi: 10.1159/000515417. Epub 2021 Apr 28. PMID: 33910211; PMCID: PMC8247830.

It would also be useful to discuss protection against coronavirus infection: is it due to innate or adaptive immunity?

What is immune evasion, and can it be deleterious or beneficial? Define immunoevasion: why do successive variants increasingly escape the immune system, but at the same time become less and less pathogenic?

How can a vaccine be expected to produce sterilizing immunity, when disease or coronavirus infection does not?

Detailed comments throughout the text

Introduction

defining host 'immunity: innate or adaptive

Defining a case: are 44 million cases sick with symptoms or just PCR- or antigen-positive?

Emergence of new variants

The continuous evolution of SARS-CoV-2 has resulted in the emergence of numerous subvariants that often exhibit growth advantages over previous variants

why often and not always? There are no cases where a new variant has proved more pathogenic than its predecessors

studies indicate that the variants can elude some of the antibodies produced after coronavirus vaccinations and infections

These are still studies on blood antibodies, which by definition are not found in the upper airways first exposed to the virus.

These studies do not say whether the variants escape the innate or adaptive immunity of the upper respiratory tract

"This is particularly concerning since antibody therapies have proved popular and effective against other variants and subvariants of SARS-CoV-2.

this requires a reference

Explanation of the higher transmissibility: consider surface electrostatic potential, see Fantini Fantini, J.; Chahinian, H.; Yahi, N. Convergent Evolution Dynamics of SARS-CoV-2 and HIV Surface Envelope Glycoproteins Driven by Host Cell Surface Receptors and Lipid Rafts: Lessons for the Future. Int. J. Mol. Sci. 2023, 24,1923.https://doi.org/10.3390/ijms24031923

Fantini J. Lipid rafts and human diseases: why we need to target gangliosides. FEBS Open Bio. 2023 Apr 13. doi: 10.1002/2211-5463.13612. Epub ahead of print. PMID: 37052878.

Fantini J, Azzaz F, Chahinian H, Yahi N. Electrostatic Surface Potential as a Key Parameter in Virus Transmission and Evolution: How to Manage Future Virus Pandemics in the Post-COVID-19 Era. Viruses. 2023 Jan 19;15(2):284. doi: 10.3390/v15020284. PMID: 36851498; PMCID: PMC9964723.

Define immunoevasion: how can we explain the fact that successive variants increasingly escape the immune system but are at the same time less and less pathogenic?

See Banoun H. Evolution of SARS-CoV-2: Review of Mutations, Role of the Host Immune System. Nephron. 2021;145(4):392-403. doi: 10.1159/000515417. Epub 2021 Apr 28. PMID: 33910211; PMCID: PMC8247830.

The chance for the emergence of a new dominant variant, which causes more severe disease or has immune escape is still there, so continued monitoring is of paramount importance.

This has never been shown for a human coronavirus, and in particular for SARS-Cov-2.

How Host Immunity is Evolving with SARS-COV-2

While the current vaccines may be sufficient to provide individual protection against severe disease, they have little effect on protection against infection and reduction in transmission, and therefore do not adequately generate community immunity.

See the Cleveland Clinic publication showing a correlation between risk of infections and vaccine doses received Nabin K Shrestha and others, Effectiveness of the Coronavirus Disease 2019 Bivalent Vaccine, Open Forum Infectious Diseases, Volume 10, Issue 6, June 2023, ofad209, https://doi.org/10.1093/ofid/ofad209

Innate immunity is the first to respond to intruding pathogens and can exert strong selection pressure on the Covid-19 virus, which could explain the rapid spread of the two most recent and dominant variants. One of the ways in which innate immunity protects the host against infection is by recruiting antiviral proteins to combat invading viruses; studies have shown that SARS-CoV-2 can inhibit the activation of these essential antiviral proteins [24].

Here again, we need to distinguish between immunity that prevents transmission (which probably does not exist - except in the very short term - for coronaviruses) and immunity that prevents systemic invasion by the virus.

Once again, it is contradictory to assert that successive mutations make it possible to escape innate immunity [24], while at the same time emphasizing that successive variants are less and less pathogenic.

A recent study compared the antibody-mediated response between patients with severe and mild disease and found that patients with severe disease had a more robust humoral immune response due to increased levels of B-cell receptor activation and clonal expansion.

There is a correlation between disease severity and antibody levels.

Banoun, 2020, http://ssrn.com/abstract=3654264

Kream and colleagues have proposed that convalescent memory T-cell immunity in people with mild or asymptomatic SARS-CoV-2 infection may result from an evolutionarily adapted immune response to coronavirus and the "common cold" [35].

It seems that protection against severe Covid is not due to cross-reactivity with common cold viruses, but rather to a sufficient innate response in individuals who remain asymptomatic https://www.tmrjournals.com/article.html?J_num=4&a_id=2275

Banoun H. Why are children and many adults unaffected by COVID-19? Role of the host immune response. Infect Dis Res. 2022;3(3):18. doi:10.53388/IDR20220825018

It has recently been shown that people suffering from allergic conditions such as hay fever, rhinitis and atopic eczema may have a positive immune response to COVID-19 lower risk of Covid-19 infection, especially if they also have asthma [48].

They may also be at lower risk of Covid-19 infection, particularly if they also suffer from asthma.

This could be due to the protective role of antihistamines against COVID-19:https://www.researchgate.net/profile/Annwyne-Houldsworth-2/post/Are-Angiotensin-Receptor-Blocker-Trials-as-Therapy-Inhibiting-COVID-19-Infection-Successful/attachment/5eb02081c005cf0001882c60/AS%3A887470908530693%401588600961846/download/Antihistamines+as+a+therapeutic+care+plan+of+Covid-19+About+26+cases+%281%29.pdf

Reznikov LR, Norris MH, Vashisht R, et al. Identification of antiviral antihistamines for COVID-19 repurposing. Biochem Biophys Res Commun 2021;538:173-179. http://dx.doi.org/10.1016/j.bbrc.2020.11.095

Palma G, Pasqua T, Silvestri G, et al. PI3Kδ Inhibition as a Potential Therapeutic Target in COVID-19. Front Immunol 2020;11:2094. http://dx.doi.org/10.3389/fimmu.2020.02094

Ciprandi G, Licari A, Filippelli G, Tosca MA, Marseglia GL. Children and adolescents with allergy and/or asthma seem to be protected from coronavirus disease 2019. Ann Allergy Asthma Immunol 2020;125(3):361-362.http://dx.doi.org/10.1016/j.anai.2020.06.001

Freedberg DE, Conigliaro J, Wang TC, et al. Famotidine Use Is Associated With Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study. Gastroenterology 2020;159(3):1129-1131.e3. https://doi.org/10.1053/j.gastro.2020.05.053

Hogan Ii RB, Hogan Iii RB, Cannon T, et al. Dual-histamine receptor blockade with cetirizine - famotidine reduces pulmonary symptoms in COVID-19 patients. Pulm Pharmacol Ther 2020;63:101942. https://doi.org/10.1016/j.pupt.2020.101942

Morán Blanco JI, Alvarenga Bonilla JA, Homma S, Suzuki K, Fremont-Smith P, Villar Gómez de Las Heras K. Antihistamines and azithromycin as a treatment for COVID-19 on primary health care - A retrospective observational study in elderly patients. Pulm Pharmacol Ther 2021;67:101989. https://doi.org/10.1016/j.pupt.2021.101989

. Another study found that patients with severe Covid-19 disease had genetic

mutations that resulted in a deficient type 1 interferon (IFN) response or autoimmune antibodies affecting type I IFN In fact, recent studies highlighted that many of the genes associated with severe disease were associated with inflammation or immunoregulatory pathways particularly those associated with the IFN signaling pathway.

We should mention the double-edged role of interferon, which is antiviral but can also exacerbate immunopathological phenomena (Banoun H. Why are children and many adults not affected by COVID-19? Role of the host immune response. Infect Dis Res. 2022;3(3):18. doi:10.53388/IDR20220825018) https://www.tmrjournals.com/article.html?J_num=4&a_id=2275)

Of note, most genome wide association studies conducted early on were

skewed due to small sample sizes and the selection of severely ill patients

Indeed, this problem has been highlighted here https://pubmed.ncbi.nlm.nih.gov/33910211/

One known [60] exception is cutaneous Leishmaniasis in which one primary natural infection may lead to life-long immunity

And measles (https://www.xiahepublishing.com/2472-0712/ERHM-2022-00018

Banoun H. Measles and Antibody-Dependent Enhancement (ADE): History and Mechanisms. Explor Res Hypothesis Med. Published online: Apr 29, 2022. doi: 10.14218/ERHM.2022.00018.)

A new study from Yale University and the University of North Carolina at Charlotte suggests healthy people should get annual Covid-[62]19 boosters to prevent widespread outbreak

See the results of the Cleveland Clinic study showing a correlation between the number of doses of vaccine received and the risk of being infected by the virus https://doi.org/10.1093/ofid/ofad209

The appeal for IN vaccinations lies in the fact that they have shown promise to induce sterilizing immunity against mucosal

[66] pathogens

How can a vaccine be expected to induce sterilizing immunity when disease or coronavirus infection does not?

Furthermore, there is a note of caution about the frequent use of booster shots with short gaps in between, which may overburden the immune system and lead to immune exhaustion, as has been observed in the case of HIV infections[72].

Immune exhaustion has also been shown with repeated covid vaccinations.

The impact of BNT162b2 mRNA vaccine on adaptive and innate immune responses

Konstantin Föhse, Büsra Geckin, Martijn Zoodsma, Gizem Kilic, Zhaoli Liu, Rutger J.Röring, Gijs J. Overheul, Josephine S. van de Maat, Ozlem Bulut, Jacobien J. Hoogerwerf, Jaap ten Oever, Elles Simonetti, Heiner Schaal, Ortwin Adams, Lisa Müller, Philipp NiklasOstermann, Frank L. van de Veerdonk, Leo A.B. Joosten, Bart L. Haagmans, Reinout van Crevel, Ronald P. van Rij, Corine GeurtsvanKessel, Marien I. de Jonge, Yang Li, JorgeDomínguez-Andrés, Mihai G. Netea

medRxiv 2021.05.03.21256520; doi:https://doi.org/10.1101/2021.05.03.21256520

Gao et al, iScience 25, 105479 December 22, 2022 a 2022https://doi.org/10.1016/j.isci.2022.105479

Uversky, V.N.; Redwan, E.M.; Makis, W.; Rubio-Casillas, A. IgG4 Antibodies Induced by Repeated Vaccination May Generate Immune Tolerance to the SARS-CoV-2 Spike Protein. Vaccines 2023,11,991. https://doi.org/10.3390/vaccines11050991

Irrgang et al Class switch toward noninflammatory, spike-specific IgG4 antibodies after repeated SARS-CoV-2 mRNA vaccination. Sci Immunol. 2023 Jan 27;8(79):eade2798. doi: 10.1126/sciimmunol.ade2798. Epub 2023 Jan 27. PMID: 36548397; PMCID: PMC9847566.

Deleterious role of IgG4: https://www.ejinme.com/article/S0953-6205(21)00312-5/fulltext ,

Rispens, T., Huijbers, M.G. The unique properties of IgG4 and its roles in health and disease. Nat Rev Immunol (2023). https://doi.org/10.1038/s41577-023-00871-z

Experts do not expect the recent vaccination of children ages 6 months to 5 years old to alter the trajectory of the pandemic due to sustained vaccine hesitancy in parents; seven out of ten parents in the USA remain hesitant about vaccinating their children mainly due to the lack of transparency in the trial process and dosing determination [76][77].

In fact, FDA documents prove that boosters for children aged 6 months to 5 years are ineffective and toxic.

https://www.researchgate.net/publication/366440489_FDA_approves_COVID-19_vaccine_for_babies_6_months_and_older_non-existent_scientific_bases

FDA approves COVID-19 vaccine for babies (6 months and older): non-existent "scientific bases".