Opinion

iMedPub Journals
www.imedpub.com

Journal of Clinical Immunology and Infectious Diseases

2022
Vol.6 No.3:42

Time for Fresh Constructive Scientific Debate on the Origin Of, Immune Response To, And Optimal Vaccination Strategy For, Infection with SARS-Cov-2

Reginald M Gorczynski [1*], N Chandra Wickramasinghe[2,3,4], Robyn A Lindley[5,6], Edward J Steele[6,7]

[1]Department of Medical Sciences, University of Toronto, Institute of Medical Science, Toronto, Canada

[2]Department of Astrobiology, University of Buckingham, Buckingham Centre for Astrobiology, MK18 1EG, UK

[3]Department of Astroeconomics, Soka University, Institute for the Study of Panspermia and Astroeconomics, Gifu, Japan

[4]Department of Fundamental Studies, University of Peradeniya, National Institute of Fundamental Studies, Kandy, Sri Lanka

[5]Department of Clinical Pathology, University of Melbourne, Dentistry and Health Sciences, Melbourne, VIC, Australia

[6]Melville Analytics Pty Ltd, Melbourne, VIC, Australia

[7]Department of Astrobiology, University of Ruhuna, Matara, Sri Lanka

[*]**Corresponding author:** Reginald M. Gorczynski, Department of Medical Sciences, University of Toronto, Institute of Medical Science, Toronto, ON, Canada, E-mail: reg.gorczynski@utoronto.ca

Received date: May 23, 2022, Manuscript No. ipciid-22-13555; **Editor assigned date:** May 25, 2022, PreQC No. ipciid-22-13555 (PQ); **Reviewed date:** June 07, 2022, QC No. ipciid-22-13555; **Revised date:** June 15, 2022, Manuscript No. ipciid-22-13555 (R); **Published date:** June 21, 2022, DOI: 10.36648/Ipciid.6.3.42

Citation: Gorczynski RM, Wickramasinghe NC, Lindley RA, Steele EJ(2022) Time for Fresh Constructive Scientific Debate on the Origin Of, Response Immune To, And Optimal Vaccination Strategy For, Infection with SARS-Cov-2. Clin Immunol Infect Dis Vol.6 No. 3: 42.

Abstract

The authors comment on, and discuss the flaws inherent in, a recently published review by the Chair of Global Public Health at the University of Edinburgh which concluded with her summation that some scientists just refuse to accept that they "got in wrong" in their discussion of many of the faults with the way governments, scientists and clinicians in general handled the response to the SARS-CoV-2 pandemic. We suggest that this polemic has added nothing useful in terms of meaningful discussion of the pandemic, and worse, belittles the conflicting cogent arguments that there is indeed a wealth of data which has not be adequately understood/interpreted, and lessons which can be learned from so doing.

Introduction and Discussion

We are now more than two years into discussing the epidemiology and optimal responses (medical/scientific/political) to SARS-CoV-2, and yet major conundrums persist, at least in the minds of those controlling the scientific discussion.

In a recent article in the Guardian, Professor Devi Sridhar, chair of global public health at the University of Edinburgh, argued, correctly, that "The essence of science is asking questions, forming hypotheses for possible answers, and then revising these based on new data. COVID has been a constantly changing situation." However she moves from this to a more personal opinion, "I have respect and admiration for scientists who have admitted what they got wrong, and also understand that each stage of the pandemic has required a different response, based on the latest data, tools and analysis." She goes further, emphasizing "(that) "Living with COVID", now that science has largely defanged it, involves ensuring widespread vaccination, as well as creating schemes such as the US government's "test to treat". " At no time does she give credence to the likelihood that we are still, as she surmises, viewing the pandemic through a fog", likely of our own making, simply because we have from the outset refused to go back to first principles of biology/immunology, and consider, before arguing for any one plan of campaign (to reduce infectivity/morbidity/mortality), what are the essentials for the optimal host resistance to this pathogen.

SARS-CoV-2 is one of a family of coronaviruses (including SARS-1; MERS; SARS-2 (COVID-19/SARS-CoV-2) described over the last 2 decades causing significant respiratory disease in a number of species, for which no effective vaccine has yet to be confirmed (1-3). Host resistance to respiratory pathogens (infecting at mucosal surfaces) is a function of an active innate immune system and local acquired immunity, based on IgA producing B lymphocytes and activated T cells (4)-the same seems to be the case for natural infection with SARS-CoV-2 (7-8). For SARS-CoV-2, much has been made of the rise in serum (systemic) IgG responses to the virus following natural infection, suggesting this may point towards a method to test vaccine efficacy (9). This may indeed be a surrogate marker of activation, within the respiratory tract, of B/T cells activated for IgA production, but that has never been tested. The historical control for this methodology, of course, lies in the annual testing of new influenza vaccines, where a key issue in the strategy for mass vaccination is to show the vaccine enhances an immune function which can be shown to be responsible for protection, is easily measured, and can be used for monitoring. For influenza a wealth of experimental and human data suggests that influenza serum hemagglutination antibody titres are a marker for immune protection (10)–though it should be noted that while stringent criteria must be met for licensure of annual influenza vaccines, with a pre-determined increase in titre: e.g. >40 in

18-60 year olds with a 4-fold increase in titre post vaccination and >40% seroconversion in the same group, historically such vaccines are still associated only with ~50% reduction in influenza risk (10). This level of protection may be even less, given that vaccines are raised against variants circulating in the previous season, during antigenically unmatched years (11-14).

There are likely many reasons why current influenza vaccines are sub-optimal in protective efficacy, but we would highlight their failure on at least two key fronts addressed below:

- A complete failure to acknowledge effects associated with Cosmic Biology: Each new season is likely to have fresh unanticipated in-fall variants from viral-laden dust of cometary/cosmic origin introduced into the stratosphere and upper atmosphere. Furthermore there is growing evidence, particularly from data bases newly generated in the aftermath of SARS-CoV-2 infections, for the reality of such an effect and its potential influence with regard to our response to future infections (15).
- No local (to the site of infection) induction of immunity. There has been no conscious emphasis on ensuring these vaccines induce the necessary protective mucosal respiratory tract immune system, both Innate Immunity and Adaptive secretory IgA immunity and locally activated cytotoxic T cells. Recent studies clearly show now in mice that defective/attenuated coronavirus and influenza virus preparations applied intra-nasally seem to provide far superior protection (16-18).

Even here, however, it is recognized that in the elderly, in whom standard vaccine therapy is often ineffective (19), strict analysis of HI titres are not as useful in guidance of vaccination, and monitoring of cell mediated immune responses may be more valid predictors of efficacy (19,20). There are no published data of equivalent scientific rigor for SARS-C0V-2 vaccines, but others have commented further on the clinical value of mucosal IgA immunity in protection (21,22), and on the increased susceptibility of individuals with IgA deficiency diseases to SARS-CoV-2 (23,24), and we have stressed the same conceptual strategy as likely to be successful (25).

Furthermore, there is the strong evidence for a crucial role for innate immunity in response to respiratory viruses, including SARS-CoV-2. Infection with SARS-CoV-2 of individuals with impaired innate defenses causes severe, often life-ending, disease (26-32). However, the value of any (vaccine) strategy deliberately to boost such immunity was never at the forefront of any early attempts to control this pandemic. It may be that the adjuvant used in vaccines to date does indeed augment innate immunity, and this may (not any antigen-specific moiety in the vaccine) even be responsible for any observed vaccine protection-this too has never been investigated. Instead all effort has been made to develop vaccines which are then tested, using serum IgG as a marker, for their efficacy in inducing a response to the injected material-this is simply a test of the ability of the host to respond immunologically, not of the clinical utility of the vaccine, nor of the value of serum IgG to be a surrogate marker for such utility. To argue that vaccines have reduced the numbers of individuals testing positive for SARS-CoV-2 who are admitted to ICUs ignores the bias of the medical community to admit such individuals to hospitals, and ICUs, simply because they are not vaccinated, with the foregone assumption that this is a prime consideration as to whether it represents the best surrogate marker for a high risk group. There is no valid scientific reason for this presumption, and in doing so we have defined our own self-fulfilling prophesy! It should be noted here that similar dubious procedures of validation of hypotheses have become all too common in recent times.

Regrettably, it seems that despite the wealth of new data which has been uncovered in the last 2-3 years, the response in many countries to a growing number of infections with various new viral variants of SARS-CoV-2, is to fall back on emphasizing conduct which has never been shown, scientifically, to be of value, including the mandatory use of masks (33); coercive or mandatory vaccination policies (34); and inordinate ostracism of those attempting to voice alternative opinions which challenge the prevailing paradigms (35), an issue we have commented on earlier. In the latter instance we are witnessing an outrageous travesty of freedom of expression on a scale not seen since Europe in the 1930's, and in Canada at least, such individuals have been accused by the Prime Minister as equivalent to racist bigots. Professor Sridhar seems to fall into the same trap, demeaning those who hold alternate opinions to her own, suggesting that what she deems as "extreme positions" have received disproportionate exposure in comparison to the "silent majority" who seem to understand the complexity of the situation – and the need to rely on expertise grounded in data". This bias has no place in structured and enlightened scientific discourse.

Conclusion

We conclude that such ostensibly arrogant attitudes as were laid out in this publication, both in regard to the matters discussed above as well as in the still unexplained question of the origin of the virus itself, will continue to hold back our understanding of the current infection immeasurably. To quote Carl Sagan, "The suppression of uncomfortable ideas may be common in religion or in politics, but it is not the path to knowledge, and there's no place for it in the endeavor of science".

References

1. Yong CY, Ong HK, Yeap SK, Ho KL, Tan WS (2019) Recent advances in the Vaccine development against middle east respiratory Syndrome-Coronavirus. Front. Microbiol 10: 1781.
2. Liu YV, Massare MJ, Barnard DL, Kort T, Nathan M et al. (2011) Chimeric severe acute respiratory syndrome coronavirus (SARS-CoV) S glycoprotein and influenza matrix 1 efficiently form virus-like particles (VLPs) that protect mice against challenge with SARS-CoV. Vaccine 29(38): 6606-6613.
3. Keshavarz B, Richards NE, Workman LJ, Patel J, Muehling LM et al. (2022) Trajectory of igg to SARS-cov-2 after vaccination with BNT162b2 or mrna-1273 in an employee cohort and comparison with natural infection. Front Immunol 13: 850987.
4. Hellfritzsch M, Scherlieb R (2019) Mucosal vaccination via the respiratory tract. Pharmaceutics 11(8): 375.

5. Froberg J, Diavatopoulos DA (2021) Mucosal immunity to severe acute respiratory syndrome coronavirus 2 infection. Curr Opin Infect Dis 34(3): 181-186.

6. Focosi D, Maggi F, Casadevall A (2022) Mucosal Vaccines, Sterilizing Immunity, and the Future of SARS-cov-2 virulence. Viruses 14(2): 187.

7. Jeyanathan M, Afkhami S, Smaill F, Miller MS, Lichty BD et al. (2020) Immunological considerations for COVID-19 vaccine strategies. Nat Rev Immunol 20: 615–632.

8. Wang Z, Lorenzi JC, Muecksch F, Finkin S, Viant C et al. (2021) Enhanced SARS-cov-2 neutralization by dimeric iga. Sci Transl Med 13: 577.

9. Gluck V, Tydykov L, Mader AL, Warda AS, Bertok M et al. (2022) Humoral immunity in dually vaccinated SARS-cov-2-naive individuals and in booster-vaccinated COVID-19-convalescent subjects. Infection 1–7.

10. Benoit A, Beran J, Devaster JM, Esen M, Launay O et al. (2015) Hemagglutination inhibition antibody titers as a correlate of protection against seasonal A/H3N2 influenza disease. Open Forum Infect Dis 2(2): ofv067.

11. Debbink K, McCrone JT, Petrie JG, Truscon R, Johnson E et al. (2017) Vaccination has minimal impact on the intrahost diversity of H3N2 influenza viruses. PLoS Pathog 13(1): e1006194.

12. Osterholm MT, Kelley NS, Sommer A, Belongia EA (2012) Efficacy and effectiveness of influenza vaccines: A systematic review and meta-analysis. Lancet Infect Dis 12: 36–44.

13. Skowronski DM, Chambers C, Sabaiduc S, De Serres G, Winter A-L et al. (2015) Integrated sentinel surveillance linking genetic, antigenic, and epidemiologic monitoring of influenza vaccine-virus relatedness and effectiveness during the 2013–2014 influenza season. J Infect Dis 212: 726–739.

14. Cohen J (2017) Why is the flu vaccine so mediocre. Science 357(6357): 1222-1223.

15. Steele EJ, Gorczynski RM, Lindley RA, Carnegie PR, Rebhran H et al. (2022) Overview SARS-cov-2 Pandemic as january-february 2022: Likely cometary origin, global spread, prospects for future vaccine efficacy. Infect Dis Ther Volume 3(1): 1-16.

16. Xiao Y, Lidsky PV, Shirogane Y, Aviner R, Wu CT et al. (2021) A defective viral genome strategy elicits broad protective immunity against respiratory viruses. Cell 184: 6037-6051.

17. Oh JE, Song E, Moriyama M, Wong P, Zhang S et al (2021) Intranasal priming induces local lung-resident B cell populations that secrete protective mucosal antiviral IgA. Science Immunology 6: eabj5129.

18. Afkhami S, Agostino DMR, Zhang A, Stacey HD, Marzok A et al. (2022) Respiratory mucosal delivery of next-generation COVID-19 vaccine provides robust protection against both ancestral and variant strains of SARS-CoV-2. Cell 185: 896–915

19. Thorrington D, van Leeuwen E, Ramsay M, Pebody R, Baguelin M (2019) Assessing optimal use of the standard dose adjuvanted trivalent seasonal influenza vaccine in the elderly. Vaccine 37:2051-2056.

20. Andrew MK, Bowles SK, Pawelec G, Haynes L, Kuchel GA et al. (2019) Influenza vaccination in older adults: Recent innovations and practical applications. Drugs Aging 36(1): 29-37.

21. Hennings V, Thorn K, Albinsson S, Lingblom C, Andersson K et al. The presence of serum anti-SARS-CoV-2 IgA appears to protect primary health care workers from COVID-19.Europ J Immunol 52(5):800-809

22. Cokaric Brdovcak M, Materljan J, Sustic M, Ravlic S, Ruzic T et al. (2022) Chadox1-s adenoviral vector vaccine applied intranasally elicits superior mucosal immunity compared to the intramuscular route of vaccination. Eur J Immunol 52(6): 936-945.

23. Quinti I, Mortari EP, Fernandez Salinas A, Milito C, Carsetti R (2021) IgA Antibodies and IgA Deficiency in SARS-CoV-2 Infection. Front Cell Infect Microbiol 11:655896.

24. Colkesen F, Kandemir B, Arslan S, Colkesen F, Yildiz E et al. (2021) Relationship between selective iga deficiency and COVID-19 prognosis. Jpn J Infect Dis 75(3): 228-233.

25. Gorczynski RM, Lindley RA, Steele EJ, Wickramasinghe NC (2021) Nature of Acquired Immune Responses, epitope specificity and resultant protection from SARS-cov-2. J. Pers. Med 11: 1253.

26. Galani IE, Andreakos E (2021) Impaired innate antiviral defenses in COVID-19: Causes, consequences and therapeutic opportunities. Semin Immunol 55: 101522.

27. Achary D, Liu GQ, Gack MU (2020) Dysregulation of type I interferon responses in COVID-19. Nat Rev. Immunol 20: 397-398.

28. Blanco-Melo D, Nilsson-Payant BE, Liu W-C, Uhl S, Hoagland D et al. (2020) Imbalanced host response to SARS-CoV-2 drives development of COVID-19. Cell 181: 1036-1045.

29. Hadjadj J, Yatim N, Barnabei L, Corneau A, Boussier J et al. (2020) Impaired type I interferon activity and exacerbated inflammatory responses in severe Covid-19 patients. Science 369: 718-724.

30. Netea MG, Giamarellos-Bourboulis EJ, Dominguez-Andres J, Curtis N, Reinoutvan C et al. (2020) Trained Immunity: A tool for reducing susceptibility to and the severity of SARS-cov-2 infection. Cell 181: 969-977.

31. Zhang Q, Bastard P, Liu Z, Le Pen J, Moncada-Velez M et al. (2020) Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. Science 370: eabd4570.

32. Lucas C, Wong P, Klein J, Castro TBR, Silva J et al. (2020) Longitudinal analyses reveal immunological misfiring in severe COVID-19. Nature 584: 463-469.

33. Bundgaard H, Bundgaard JS, Raaschou-Pedersen DET, von Buchwald C, Todsen T et al. (2021) Effectiveness of adding a mask recommendation to other Public Health Measures to prevent SARS-Cov-2 infection in Danish mask wearers. Ann Int Med 174(3): 335-343.

34. Dunne CP, Spain E (2022) Compulsory vaccination against COVID-19: A legal and ethical perspective on public good versus personal reticence. Ir J Med Sci 25: 1-6.

35. Leach M, MacGregor H, Scoones I, Wilkinson A (2020) Post-pandemic transformations: How and why COVID-19 requires us to rethink development. World Dev 138: 105233.