

Appendix “G”



Canadian Covid Care Alliance
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VACCINE VERSUS NATURALLY-INDUCED IMMUNITY

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Which is better for future COVID-19 prevention:

Immunity Following Natural Infection or Vaccine-Induced Immunity?

A review of a collection of 15 studies compiled by Daniel Horowitz at TheBlaze.com - all credit to Horowitz with additional references and commentary prepared for the Canadian Covid Care Alliance (<https://www.canadiancovidcarealliance.org/>)

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1) [***Discrete Immune Response Signature to SARS-CoV-2 mRNA Vaccination versus Infection | New York University, May 3, 2021***](#)¹

The authors of this study examined the contrast between vaccine-induced immunity and immunity from SARS-CoV-2 infection as it relates to stimulating innate host defense as well as B- and T-cell immunity. It is relevant to note that the appropriate combination of innate and adaptive host defense mechanisms generally generates more durable adaptive immunity than antibodies alone. The authors concluded, "In COVID-19 patients, immune responses were characterized by a highly augmented interferon response which was largely absent in vaccine recipients. Increased interferon signaling likely contributed to the observed dramatic up

¹ Ivanova, E., Devlin, J., Buus, T. et al. (2021, May 3). *Discrete immune response signature to SARS-CoV-2 mRNA vaccination versus infection*. medRxiv. Preprint. <https://doi.org/10.1101/2021.04.20.21255677>.



regulation of cytotoxic genes in the peripheral T cells and innate-like lymphocytes in patients but not in immunized subjects.”

Other authors established that early in the pandemic, the interferon class of cytokines were important in control of viral replication and in making the appropriate transition from innate to adaptive immune responses.²

The study by Ivanova *et al.*¹ - currently still a preprint - further notes, "Analysis of B and T cell receptor repertoires revealed that while the majority of clonal B and T cells in COVID-19 patients were effector cells, in vaccine recipients clonally expanded cells were primarily circulating memory cells." Horowitz suggests this could indicate that, "Natural immunity conveys much more innate immunity, while the vaccine mainly stimulates adaptive immunity." The authors write in the discussion that, "**We observed the presence of cytotoxic CD4 T cells in COVID-19 patients that were largely absent in healthy volunteers following immunization.** While hyper-activation of inflammatory responses and cytotoxic cells may contribute to immunopathology in severe illness, in mild and moderate disease, **these features are indicative of protective immune responses and resolution of infection.**"

These authors also point out that, "COVID-19 patients had a striking expansion of antibody-producing plasmablasts, with evidence of clonal cells in this cluster. However, **we did not detect appreciable expansion of plasmablasts in circulation of individuals immunized with SARS-CoV-2 BNT162b2 mRNA vaccine**, despite a robust antibody response." Plasmablasts are the cells specialized to go on to produce large amounts of antibodies.

It is important to understand that **not all antibodies are created equal**. Some can neutralize viruses and others do not. Some antibodies are more important at mucosal surfaces, such as IgA which can be found in the upper respiratory tract. Antibodies of the IgG class are found lower in the respiratory tract and play a more important role than IgA at that location. Since natural exposure to SARS-CoV-2 is via the upper respiratory tract, which later can move down to lower regions of the tract, this has a propensity to generate both IgA in the upper track and IgG antibodies in the lower airway to various components of the virus. Conversely, intramuscular vaccination is known to preferentially generate IgG, but not necessarily mucosal IgA. Consequently, upon re-exposure, people who have previously been exposed to the live virus will quickly generate a robust and broad-based set of innate and adaptive immune responses, both IgA and IgG, along with other cellular responses. This is why immunity following natural exposure is durable, often lasting the duration of the declared pandemic as discussed in various reports below. In contrast, **vaccine-induced immunity is clearly shorter term and must lack the breadth of immunity following natural exposure since the response is limited only to the viral spike (S) protein**. Consequently, multiple vaccine boosters have been rapidly rolled out. Testing for evidence of immunity

² Lei, X., Dong, X., Ma, R. *et al.* (2020, July 30). *Activation and evasion of type I interferon responses by SARS-CoV-2*. *Nat Commun* 11, 3810 (2020). Published. <https://doi.org/10.1038/s41467-020-17665-9>.



following natural infection would negate the need for mandatory vaccination, spare vaccine doses, and certainly multiple booster shots. Although not mentioned in the manuscript by Ivanova *et al.*¹ another important consideration is that with natural exposure, the polyclonal antibody response will allow for the generation of a wide variety of memory cells. When the virus mutates, the immune response can respond with expansion of appropriate neutralizing effector cells. In contrast, vaccination will elicit a much smaller diversity of memory cells that are more likely to result in antibody-dependent enhancement, often due to non-neutralizing antibodies that actually facilitate the uptake of virus into the host cells.

To summarize, **the results of this paper demonstrate distinct differences in the quality, quantity, location, and the overall nature of the innate and adaptive immune responses generated following vaccination versus natural infection.** Understanding these differences is important to determine who needs to be vaccinated and for designing better vaccines that more closely mimic the responses of immunity following natural infection, for example mucosal delivery systems. It has always been the goal of immunologists and vaccinologists to design vaccines that mimic the protective and durable immunity found in those who successfully recovered from natural infections.

2) [**SARS-CoV-2 Infection Induces Long-lived Bone Marrow Plasma Cells in Humans | Washington University, St. Louis, Missouri, May 24, 2021, published in Nature**](#)³

As Horowitz states, the media has been promoting the idea that if antibody levels wane, it means immunity is weakening, as we are indeed seeing with the vaccines today. But as author Ewen Callaway writes in a Nature News article entitled, Had COVID? You'll probably make antibodies for a lifetime,⁴ as he highlights this paper by Turner *et al.*, **"People who recover (even) from mild COVID-19 have bone-marrow cells that can churn out antibodies for decades."**

More specifically, Turner *et al.*³ explained in the primary research article that, "After a new infection, short-lived cells called plasmablasts are an early source of antibodies. But these cells recede soon after a virus is cleared from the body, and other, longer-lasting cells make antibodies: memory B cells patrol the blood for reinfection, while bone marrow plasma cells (BMPCs) hide away in bones, trickling out antibodies for decades" as needed. Turner and colleagues conclude in the discussion section of the paper, **"Overall, our data provide strong evidence that SARS-CoV-2 infection in humans robustly establishes the two arms of humoral immune memory: long-lived bone marrow plasma cells (BMPCs) and memory B-cells."** This means that even though

³ Turner, J.S., Kim, W., Kalaidina, E. *et al.* (2021, May 24). *SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans*. Nature 595, 421–425 (2021). Published. <https://doi.org/10.1038/s41586-021-03647-4>.

⁴ Callaway, E. (2021, May 27). *Had COVID? You'll probably make antibodies for a lifetime*. Nature. Published. <https://www.nature.com/articles/d41586-021-01442-9>.



antibody levels will eventually wane, there are long-lived cells in the bone marrow that have memory of the virus and can quickly produce the needed antibodies against the virus upon re-infection.

Horowitz then went on to correctly point out, “It’s therefore not surprising that early on in the pandemic, an in-vitro study in Singapore published in *Nature* found **immunity against SARS-CoV-2 to last even 17 years later from SARS-1-infected patients who never previously had COVID-19.**”⁵ This paper by Le Bert *et al.* looked specifically at T-cell responses against the structural nucleocapsid (N) protein of the virus and found both CD4 and CD8 T cells that recognized multiple regions of the N-protein. The CD4 and CD8 T-cells are lymphocytes critical in generating both helper and cytotoxic T-cell responses. The authors conclude, “Thus, infection with betacoronaviruses induces multi-specific and long-lasting immunity against the structural N protein.”

3) [***Necessity of COVID-19 Vaccination in Previously Infected Individuals*** | Cleveland Clinic, June 19, 2021](#)⁶

Howowitz then talked about a study involving **1,359 previously SARS-CoV-2 infected health care workers** in the Cleveland Clinic system, where “**not a single one of them was re-infected 10 months into the pandemic**, despite some of these individuals being around COVID-positive patients more than the regular population.”

The idea of reinfection with SARS-CoV-2 is a contentious one, being dependent on individual health status and stress levels, but most studies indicate that reinfection is rare and the immunity following natural infection is highly protective even against any new variants to date. A large study of UK health workers discussed by *Nature News* in January 2021 concluded that, “The data suggest that repeat infections are rare — they occurred in less than 1% of about 6,600 participants who had already been ill with COVID-19.”⁷ In the original paper published by Hall *et al.* in the *Lancet*,⁸ the authors interpreted their findings as follows, “A previous history of SARS-CoV-2 infection was associated with an 84% lower risk of infection, with median protective effect observed 7 months following primary infection. **This study shows that previous infection with SARS-CoV-2 induces effective immunity to future infections in most individuals.**” Further, a May 2021 paper published in the *Lancet’s* *EClinicalMedicine* elaborates that, “based on current evidence, we hypothesize that antibodies to both S and N-proteins after natural infection may persist for longer than previously thought, thereby providing

⁵ Le Bert, N., Tan, A.T., Kunasegaran, K. *et al.* (2020, July 15). SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. *Nature* 584, 457–462 (2020). Published. <https://doi.org/10.1038/s41586-020-2550-z>.

⁶ Shrestha, N. K., Burke, P. C., Nowacki, A. S. *et al.* (2021, June 19). *Necessity of COVID-19 vaccination in previously infected individuals*. medRxiv. Preprint. <https://www.medrxiv.org/content/10.1101/2021.06.01.21258176v3>.

⁷ Ledford, H. (2021, January 14). COVID reinfections are unusual — but could still help the virus to spread. *Nature News*. Published. <https://www.nature.com/articles/d41586-021-00071-6>.

⁸ Hall, V. J., Foulkes, S., Charlett, A. *et al.* (2021, April 9). SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). *The Lancet*, 397(10283), 1459–1469. Published. [https://doi.org/10.1016/s0140-6736\(21\)00675-9](https://doi.org/10.1016/s0140-6736(21)00675-9).



evidence of sustainability that may influence post-pandemic planning.”⁹ Their hypothesis was indeed correct since the authors, “demonstrated a sustained positivity rate of antibodies against the SARS-CoV-2 spike protein past ten months post-PCR confirmed COVID-19 infection using data from over 39,000 patients, with linear trends indicating a substantial population half-life.”

In immunology anything is possible, but not everything is probable. Therefore, although a few people have shown to test positive more than once for SARS-CoV-2, these occurrences appear rare.⁷ They may indicate a true reinfection, persistence of viral RNA in phagocytic cells, a false positive PCR test, or may even be due to SARS-CoV-2 RNA integration into the host genome later expressed in human cells, although the latter needs to be confirmed in vivo.¹⁰

Cumulatively, these studies indicate that there is no need of further vaccination or advantage of vaccinating those previously infected with SARS-CoV-2. Although vaccination following natural infection may increase antibody titers to the spike protein, this is not required for further protection. Additionally, as discussed above the responses induced by the vaccine are distinct from that of natural infection and much less durable. Further, amplification of naturally induced antibody responses by vaccination cannot be recommended in the absence of long-term safety studies. This is important because overly robust antibody responses can predispose people to unwanted autoimmune sequelae.

4) [**Longitudinal Analysis Shows Durable and Broad Immune Memory after SARS-CoV-2 Infection with Persisting Antibody Responses and Memory B and T Cells | Fred Hutchinson Cancer Research Center, Seattle/Emory University, Washington, July 14, 2021, published in Cell Medicine**](#)¹¹

The study found that most recovered patients produced durable antibodies, memory B cells, and durable poly-functional CD4 and CD8 T cells that target multiple parts of the virus. Horowitz concluded, "Taken together, these results suggest that **broad and effective immunity may persist long-term in recovered COVID-19 patients.**" Horowitz, in support of the growing body of literature, stated, “unlike with the vaccines, **no boosters are required to assist natural immunity.**”

⁹ Alfego, D., Sullivan, A., & Poirier, B. (2021, May 14). *A population-based analysis of the longevity of SARS-CoV-2 antibody seropositivity in the United States*. *EClinicalMedicine*, 36, 100902. Published. <https://doi.org/10.1016/j.eclinm.2021.100902>.

¹⁰ Zhang, L., Richards, A., & Barrasa, M. I. (2021, May 25). *Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues*. *Proceedings of the National Academy of Sciences*, 118(21), e2105968118. Published. <https://doi.org/10.1073/pnas.2105968118>.

¹¹ Cohen, K. W., Linderman, S. L., Moodie, Z. et al. (2021, July 14). *Longitudinal analysis shows durable and broad immune memory after SARS-CoV-2 infection with persisting antibody responses and memory B and T cells*. *Cell Reports Medicine*. Published. [https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00203-2](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00203-2).



5) [**Single Cell Profiling of T and B cell Repertoires Following SARS-CoV-2 mRNA Vaccine | University of California, Irvine, July 21, 2021**](#)¹²

Horowitz quotes the authors conclusion on their preprint paper - "**Natural infection induced expansion of larger CD8 T cell clones occupied distinct clusters, likely due to the recognition of a broader set of viral epitopes presented by the virus not seen in the mRNA vaccine.**" This makes sense given that following vaccination, a person is only exposed to the viral spike protein; whereas, following natural infection the person is exposed to all components of the virus giving the individual the opportunity to make a much broader immune response using multiple T cell clones that recognize various parts (epitopes) of viral antigens. This becomes highly pertinent when a person comes in contact with the virus for a second time, since even if the spike protein has been altered producing a variant of concern (VOC), the immune system still can activate other clones against the membrane protein for example, as well as other components of the virus.

In fact, each infected person can have antibodies generated against hundreds of epitopes in the virus. VOC's typically differ by less than 0.5% from other strains in their overall protein structures. Moreover, the actual regions in which the mutations associated with the common VOC's are located do not appear to be particularly immunogenic in patients that recovered from COVID-19.¹³ Consequently, the mutations in the known VOC's should not readily impact overall immunity following natural exposure to the virus.

6) [**mRNA Vaccine-induced T Cells Respond Identically to SARS-CoV-2 Variants of Concern but Differ in Longevity and Homing Properties Depending on Prior Infection Status | University of California, San Francisco, May 12, 2021**](#)¹⁴

This preprint article concluded that, "**In infection-naïve individuals, the second (vaccine) dose boosted the quantity but not quality of the T cell response, while in convalescents (recovered individuals), the second dose helped neither.** Spike protein-specific T cells from convalescent vaccinees differed strikingly from those of infection-naïve vaccinees, with phenotypic features suggesting superior long-term persistence and ability to home to the respiratory tract including the nasopharynx." This reiterates the findings of Ivanova¹ and further supports that the nature of the immunity generated following natural infection is distinct from that following vaccination.

¹² Sureshchandra, S., Lewis, S. A., Doratt, B. et al. (2021, July 15). *Single cell profiling of T and B cell repertoires following SARS-CoV-2 mRNA vaccine*. bioRxiv. Preprint. <https://www.biorxiv.org/content/10.1101/2021.07.14.452381v1>.

¹³ Pelech, S. University of British Columbia, Vancouver, B.C., Canada, Personal Communication.

¹⁴ Neidleman, J., Luo, X., McGregor, M. et al. (2021, July 29). *mRNA vaccine-induced T cells respond identically to SARS-CoV-2 variants of concern but differ in longevity and homing properties depending on prior infection status*. bioRxiv. Preprint. <https://www.biorxiv.org/content/10.1101/2021.05.12.443888v2>.



Horowitz correctly explains that, “Given that we know the virus spreads through the nasopharynx, **the fact that natural infection conveys much stronger mucosal immunity makes it clear that the previously infected are much safer to be around than infection-naïve people with the vaccine.** The fact that this study artfully couched the choices between vaccinated naïve people and vaccinated recovered rather than just plain recovered doesn't change the fact that **it's the prior infection, not the vaccine, conveying mucosal immunity.** In fact, studies now show that **infected vaccinated people contain just as much viral load in their nasopharynx as those unvaccinated,** a clearly unmistakable conclusion from the **virus spreading equally or in greater amounts among the vaccinated.**”¹⁵ The CDC also recognized in its July 28, 2021 report that, “preliminary evidence suggests that fully vaccinated people who do become infected with the Delta variant can be infectious and can spread the virus to others”¹⁶; this is now commonly acknowledged.

It is relevant to mention at this point that **there are also risks associated with the current nucleic acid vaccines against SARS-CoV-2.** These have been recently discussed in several papers, including one by Kostoff *et al.*¹⁷ in Toxicological Reports entitled, “Why are we vaccinating children against COVID-19?”. These authors stated, “A novel *best-case scenario* cost-benefit analysis showed *very conservatively* that there are **five times the number of deaths attributable to each inoculation versus those attributable to COVID-19** in the most vulnerable 65+ demographic. The risk of death from COVID-19 decreases drastically as age decreases, and the longer-term effects of the inoculations on lower age groups will increase their risk-benefit ratio, perhaps substantially.” Similarly, a paper by Walach and colleagues, which appeared in *Science, Public Health Policy and the Law*, calculated the Number Needed to Vaccinate (NNTV) to prevent one death from a field study.¹⁸ They used the Adverse Drug Reactions database of the Dutch National Register (Lareb) to extract the number of cases reporting severe side-effects and the number of cases reporting fatal side-effects and concluded that for 6 deaths prevented by vaccination, approximately 4 deaths were reported to Dutch Lareb that occurred after vaccination, yielding a potential risk/benefit ratio of 2:3. Their overall conclusion was that, “**these data indicate a lack of clear (vaccine) benefit,** which should cause governments to rethink their vaccination policy.” The Ontario Civil Liberties Association has concluded the same in a recent Open Letter to Public Health by Canadian virologist, Dr. John Zwaagstra, posted on their website September 21, 2021.¹⁹

¹⁵ Riemersma, K. K., Grogan, B. E., & Kita-Yarbro, A. et al. (2021, August 24). *Shedding of infectious SARS-CoV-2 despite vaccination.* medRxiv. Preprint. <https://doi.org/10.1101/2021.07.31.21261387>.

¹⁶ National Center for Immunization and Respiratory Diseases. (2021, July 7). *Interim Public Health Recommendations for Fully Vaccinated People.* Centers for Disease Control and Prevention. Published. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html>.

¹⁷ Kostoff, R. N., Calina, D., & Kanduc, D. (2021). *Why are we vaccinating children against COVID-19?* Toxicology Reports, 8, 1665–1684. Published. <https://doi.org/10.1016/j.toxrep.2021.08.010>.

¹⁸ Walach, H., Klement, R. J., & Aukema, W. (2021, August). *The Safety of COVID-19 Vaccinations—Should We Rethink the Policy?* *Science, Public Health Policy, and the Law*, 3, 87–99. Published. https://www.researchgate.net/publication/354223836_The_Safety_of_COVID-19_Vaccinations_-_Should_We_Rethink_the_Policy_newly_and_independently_peer-reviewed_version.

¹⁹ Zwaagstra, J., PhD. (2021, September 21). *Vaccine concerns weighed against natural immunity.* Ontario Civil Liberties Association. Published. <https://ocla.ca/vaccine-concerns-weighed-against-natural-immunity/>.



7) [**Large-scale Study of Antibody Titer Decay Following BNT162b2 mRNA Vaccine or SARS-CoV-2 Infection | Israeli researchers, August 22, 2021**](#)²⁰

Regarding this preprint paper, Horowitz says, "Aside from more robust T cell and memory B cell immunity, which is at least as important as antibody levels, Israeli researchers found that **antibodies wane slower among those with prior infection**. Specifically, "In vaccinated subjects, antibody titers decreased by up to 40% each subsequent month while in convalescents they decreased by less than 5% per month." This supports the studies mentioned above which show evidence of long-term antibody producing cells following natural infection that are not necessarily found post-vaccination.

8) [**Quantifying the Risk of SARS-CoV-2 Reinfection Over Time | Irish researchers, published in Wiley Review, May 18, 2021**](#)²¹

In this study, the researchers conducted a review of 11 cohort studies with over **600,000 total recovered COVID-19 patients** who were followed up for more than 10 months. Horowitz provided the key finding, stating that **unlike the vaccine, after about four to six months, they found "no study reporting an increase in the risk of reinfection over time."**

9) [**SARS-CoV-2 Antibody-positivity Protects against Reinfection for at Least Seven Months with 95% Efficacy | Cornell University, Doha, Qatar, published in the Lancet, April 27, 2021**](#)²²

Horowitz describes this study as, "one of the only studies that analyzed the population-level risk of reinfection based on whole genome sequencing in a subset of patients with supporting evidence of reinfection. Researchers estimate the risk at 0.66 per 10,000 person-weeks". Most importantly, **the study found no evidence of waning of immunity for over seven months of the follow-up period**. The few reinfections that did occur, "were less severe than primary infections," and "only one reinfection was severe, two were moderate, and none were critical or fatal." Also, unlike many vaccinated breakthrough infections in recent weeks that have been very symptomatic, "most reinfections were diagnosed incidentally through random or routine testing, or through contact tracing."

²⁰ Israel, A., Shenhar, Y., Green, I. et al. (2021, August 22). *Large-scale study of antibody titer decay following BNT162b2 mRNA vaccine or SARS-CoV-2 infection*. medRxiv. Preprint. <https://www.medrxiv.org/content/10.1101/2021.08.19.21262111v1>.

²¹ O Murchu, E., Byrne, P., Carty, P. G. et al. (2021, May 27). *Quantifying the risk of SARS-CoV-2 reinfection over time*. *Reviews in Medical Virology*, 2021;e2260. Published. <https://doi.org/10.1002/rmv.2260>.

²² Abu-Raddad, L. J., Chemaitelly, H., & Coyle, P. et al. (2021, May 1). *SARS-CoV-2 antibody-positivity protects against reinfection for at least seven months with 95% efficacy*. *EClinicalMedicine*, 35, 100861. Published. <https://doi.org/10.1016/j.eclinm.2021.100861>.



10) [**Protection of Previous SARS-CoV-2 Infection is Similar to that of BNT162b2 Vaccine Protection: A Three-month Nationwide Experience from Israel**](#) | Israeli researchers, April 24, 2021²³

As Horowitz explained, “Several months ago, **Israeli researchers studied 6.3 million Israelis and their COVID status and were able to confirm only one death in the entire country of someone who supposedly already had the virus, and he was over 80 years old.**” Horowitz contrasted that to the hospitalization and deaths now reported in the vaccinated in Israel. There are other studies in Israel, Vietnam and elsewhere confirming breakthrough infections despite full vaccination. For example, the study of Vietnamese health care workers concluded, “**Breakthrough Delta variant infections are associated with high viral loads, prolonged PCR positivity, and low levels of vaccine-induced neutralizing antibodies,** explaining the transmission between the vaccinated people.”²⁴ In this study, the viral loads in the vaccinated people with COVID-19 with the Delta variant were estimated to be 251-times higher than in unvaccinated people previously diagnosed with COVID-19 a year before with earlier strains.²⁴

11) [**Live Virus Neutralisation Testing in Convalescent Patients and Subjects Vaccinated against 19A, 20B, 20I/501Y.V1 and 20H/501Y.V2 Isolates of SARS-CoV-2**](#) | French researchers, May 11, 2021²⁵

Horowitz described in this preprint article, “Researchers tested blood samples from health care workers who never had the virus but got both Pfizer shots against blood samples from those health care workers who had a previous mild infection and a third group of patients who had a serious case of COVID.” The authors state that they found, “No neutralization escape could be feared concerning the two variants of concern [Alpha and Beta] in both populations of those previously infected.”²⁵ However, the authors state, “The reduced neutralizing response observed towards the 20H/501Y.V2 (variant 2) in comparison with the 19A (initial strain) and 20I/501Y.V1 (variant 1) isolates in fully immunized subjects with the BNT162b2 vaccine is a striking finding of the study.”²⁵ In other words, **the virus neutralizing capacity of the antibodies in the previously infected were minimally impacted by the variants** examined in this study compared to the vaccinated where viral neutralization to certain variants was substantially reduced.

²³ Goldberg, Y., Mandel, M., Woodbridge, Y. et al. (2021, April 24). *Protection of previous SARS-CoV-2 infection is similar to that of BNT162b2 vaccine protection: A three-month nationwide experience from Israel*. medRxiv. Preprint. <https://doi.org/10.1101/2021.04.20.21255670>.

²⁴ Chau, N. V. V., Ngoc, N. M., & Nguyet, L. A. et al. (2021, August 10). *Transmission of SARS-CoV-2 Delta variant among vaccinated healthcare workers, Vietnam*. SSRN Electronic Journal. Published. <https://doi.org/10.2139/ssrn.3897733>.

²⁵ Gonzalez, C., Saade, C., Bal, A. et al. (2021, May 11). *Live virus neutralisation testing in convalescent patients and subjects vaccinated against 19A, 20B, 20I/501Y.V1 and 20H/501Y.V2 isolates of SARS-CoV-2*. medRxiv. Preprint. <https://doi.org/10.1101/2021.05.11.21256578>.



12) [**Highly Functional Virus-specific Cellular Immune Response in Asymptomatic SARS-CoV-2 Infection** | Duke-NUS Medical School, Singapore, published in Journal of Experimental Medicine](#)²⁶

Horowitz posed the question that many people are asking, “If they got only an asymptomatic infection, are they less protected against future infection than those who suffered infection with more evident symptoms?” This research study by le Bert *et al.*²⁶ showed the opposite to be true. **“Asymptomatic SARS-CoV-2–infected individuals are not characterized by weak antiviral immunity; on the contrary, they mount a highly functional virus-specific cellular immune response,”** Horowitz pointed out, “If anything, they found that those with asymptomatic infection only had signs of non-inflammatory cytokines, which means that **the body is primed to deal with the virus without producing that dangerous inflammatory response that is killing so many hospitalized with the virus.**” The fact that asymptomatic people infected with SARS-CoV-2 recovered with minimal disease clearly demonstrates a high degree of immunological responsiveness in these individuals in the first place. Likewise, anyone who fully recovers from SARS-CoV-2 ultimately has had to develop an effective immune response to overcome the viral infection. In vaccinated people, the effectiveness of the induced immunity remains equivocal until tested, due to large variability in the antibody and T-cell responses amongst individuals, especially when narrowly focused on a single viral protein.

13) [**SARS-CoV-2-Specific T cell Memory is Sustained in COVID-19 Convalescent Patients for 10 Months with Successful Development of Stem Cell-like Memory T Cells** | Korean researchers, published in Nature Communications on June 30, 2021](#)²⁷

Horowitz highlighted this paper by Jing *et al.*²⁷ by saying, “The authors found that the T cells created from convalescent patients had “stem-cell like” qualities. After studying SARS-CoV-2-specific memory T cells in **recovered patients** who had the virus in varying degrees of severity, the authors concluded that **long-term “SARS-CoV-2-specific T cell memory is successfully maintained regardless of the severity of COVID-19.”**”

14) [**Anti-SARS-CoV-2 Receptor Binding Domain Antibody Evolution after mRNA Vaccination** | Rockefeller University, July 29, 2021](#)²⁸

²⁶ le Bert, N., Clapham, H. E., & Tan, A. T. (2021, March 1). *Highly functional virus-specific cellular immune response in asymptomatic SARS-CoV-2 infection*. *Journal of Experimental Medicine*, 218(5). Published. <https://doi.org/10.1084/jem.20202617>.

²⁷ Jung, J.H., Rha, M.S., Sa, M. *et al.* (2021, June 30). *SARS-CoV-2-specific T cell memory is sustained in COVID-19 convalescent patients for 10 months with successful development of stem cell-like memory T cells*. *Nature Commun* 12, 4043. Published. <https://doi.org/10.1038/s41467-021-24377-1>.

²⁸ Cho, A., Muecksch, F., Schaefer-Babajew, D. *et al.* (2021, August 30). *Anti-SARS-CoV-2 receptor binding domain antibody evolution after mRNA vaccination*. *bioRxiv*. Preprint. <https://doi.org/10.1101/2021.07.29.454333>.



In agreement with the other papers referenced here, Horowitz made a remark about this preprint article by Cho *et al.*²⁸ stating, "The researchers note that far from suffering waning immunity, memory B cells in those with prior infection **express increasingly broad and potent antibodies that are resistant to mutations found in variants of concern.**" The authors concluded that, "**memory antibodies selected over time by natural infection have greater potency and breadth than antibodies elicited by vaccination.**"

15) [**Differential Effects of the Second SARS-CoV-2 mRNA Vaccine Dose on T Cell Immunity in Naïve and COVID-19-recovered Individuals | Researchers from Madrid and Mount Sinai, New York, March 22, 2021**](#)²⁹

In this final Camara *et al.*²⁹ preprint cited by Horowitz, he concluded, "Until now, we have established that natural immunity provides better adaptive B cell and innate T cell responses that last longer and work for the variants as compared to the vaccines. Moreover, those with prior infection are at greater risk for bad side effects from the vaccines, rendering the campaign to vaccinate the previously infected both unnecessary and dangerous. But the final question is: **Do the vaccines possibly harm the superior T cell immunity built up from prior infection?**"

Immunologists from Mount Sinai in New York and Hospital La Paz in Madrid have raised serious concerns about this question. In a remarkable discovery, after monitoring a group of vaccinated people both with and without prior infection, they found, "**in individuals with a pre-existing immunity against SARS-CoV-2, the second vaccine dose not only failed to boost humoral immunity but determines a contraction of the spike-specific T cell response.**" They also noted that other research has shown, "**the second vaccination dose appears to exert a detrimental effect in the overall magnitude of the spike-specific humoral response in COVID-19 recovered individuals.**"

CONCLUSION and FURTHER READING

We would be remiss not to mention several other key studies demonstrating the value of immunity following natural infection with SARS-CoV-2 that are published in reputable peer-reviewed journals. These include the early studies of Sette and Crotty that showed that CD4 T cells, CD8 T cells, and neutralizing antibodies all contributed to control of SARS-CoV-2 in non-hospitalized and hospitalized patients with COVID-19.³⁰

²⁹ Camara, C., Lozano-Ojalvo, D., Lopez-Granados, E. *et al.* (2021, March 22). *Differential effects of the second SARS-CoV-2 mRNA vaccine dose on T cell immunity in naive and COVID-19 recovered individuals.* bioRxiv. Preprint. <https://doi.org/10.1101/2021.03.22.436441>.

³⁰ Sette, A., & Crotty, S. (2021, February 18). *Adaptive immunity to SARS-CoV-2 and COVID-19.* Cell, 184(4), 861–880. Published. <https://doi.org/10.1016/j.cell.2021.01.007>.



A Canadian study also demonstrated that 90% of healthy adults tested in the Greater Vancouver area had antibodies or cross-reactive antibodies to various components of the virus using a highly sensitive multiplex array.³¹ This evidence of immunity in non-vaccinated Canadians was recently substantiated in a small pilot study of unvaccinated individuals between June-August 2021 residing in South Western Ontario using the same assay.³²

Another study by Braun *et al.* showed that both healthy donors and patients with COVID-19 have SARS-CoV-2 reactive T-cells.³³ The study concluded, “the presence of spike-protein cross-reactive T cells in a considerable fraction of the general population may affect the dynamics of the current pandemic, and has important implications for the design and analysis of upcoming trials investigating COVID-19 vaccines.”

A recently published study by Wang *et al.* also showed **stable B-cell immunity six to 12 months following infection**.³⁴ The authors reported, “In the absence of vaccination, antibody reactivity to the receptor binding domain (RBD) of SARS-CoV-2, neutralizing activity and the number of RBD-specific memory B cells remain relatively stable between 6 and 12 months after infection. They did however see increases in antibodies to the viral spike protein following vaccination of these individuals, which would be expected. However, keep in mind as explained above, the nature of vaccine-induced immune responses is not the same as that following natural infection. In fact, when all the evidence is considered, there appears to be no additional protective benefit from vaccinating those previously recovered from COVID-19. **This would impose an unnecessary risk of vaccination.** Whether vaccinating those previously immune from natural infection reduces or enhances the clonal diversity against SARS-CoV-2 remains controversial. This may differ depending on whether or not the studies examined B or T cell clones. Either way, the functionality and location of the clones post-vaccination would be critical to know when addressing this question.

Collectively, the current literature unequivocally demonstrates protective immunity following natural infection with SARS-CoV-2 that is durable and long lasting. Therefore, there is no need for mandated vaccination of individuals with previous SARS-CoV-2 infection, particularly in those with proof of previous immunity based on evidence of antibody or T-cell responses. This becomes increasingly important now that it is

³¹ Majdoubi, A., Michalski, C., & O’Connell, S. E. (2021, March 15). *A majority of uninfected adults show preexisting antibody reactivity against SARS-CoV-2*. JCI Insight, 6(8). Published. <https://doi.org/10.1172/jci.insight.146316>.

³² Mallard, B. University of Guelph, Guelph, Ontario, Canada, Personal Communication.

³³ Braun, J., Loyal, L., & Frentsch, M. (2020, July 29). *SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19*. Nature, 587(7833), 270–274. Published. <https://doi.org/10.1038/s41586-020-2598-9>.

³⁴ Wang, Z., Muecksch, F., & Schaefer-Babajew, D. (2021, June 14). *Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection*. Nature, 595(7867), 426–431. Published. <https://doi.org/10.1038/s41586-021-03696-9>.

As we reference several preprint articles, we do not claim to represent those current findings as conclusive as they may continue to change until accepted for publication. However, the accumulating body of evidence in the preprint articles cited here also supports the published literature in support of long-lasting and durable immunity following natural exposure to SARS-CoV-2.



clear that both fully and partially vaccinated people, without prior viral exposure, can become infected and transmit the pathogen.

It is also important to accurately classify people based on their prior vaccine exposure. It is not reasonable to classify individuals as completely unvaccinated simply because they have not yet received the full series or the next booster in the series. Therefore, a standard system needs to be adopted to identify people who have received one, two or even three shots, and the timing of those injections. Maximum immune responses will be mounted differently depending on whether this is the first or subsequent exposure to the virus or the vaccine. More rapid anamnestic (memory) responses are generally generated on subsequent exposures. It is essential to keep in mind that the timing of maximal immune responses will differ from the reported timing of vaccine injury, and these timelines should not be confused. For example, immediate hypersensitivity reactions (e.g. anaphylaxis) can occur within minutes of exposure to a foreign substance, intermediate reactions can occur hours to days later, and long-term reactions may occur even years later. These timelines are distinct from the normal acquired immune responses which generally peak 7-21 days following primary exposure and 3-7 days following secondary exposure. The exact timeline of the immune response can vary somewhat depending on the antibody isotype (e.g. IgM versus IgG), the antigenic dose, the route of injection, and the genetics of the host. It is pertinent to mention here that the actual dose of spike antigen given with the current nucleic acid vaccines is essentially unknown. The amount of nucleic acid (DNA or mRNA) delivered is known but because each person generates the foreign protein within their own cells after nucleic acid delivery, the amount of spike protein generated by each individual can differ depending on age, gender, body metabolism and so on. This is in contrast to traditional vaccines where the amount of foreign protein in each dose is precisely known.

Moreover, as described earlier, vaccination of individuals with established immunity may place them at greater risk of vaccine injury. From a societal perspective to help end the SARS-CoV-2 pandemic, the establishment of immunity from natural acquisition plays an important role given the scope and durability of these immune responses. **The relevance of natural immunity needs to be fully recognized and accepted by society as one of the valid means of achieving protection as has long been the case with other infectious diseases.** Natural immunity has several protective advantages as outlined above and also reduces the vaccine implementation costs which are solely relying on extensive and repeated inoculations. The various societal damages associated with recurring lockdowns of the population must also be considered. Safe and selective vaccination of those at the highest risks of severe COVID-19 and the adoption of a myriad of effective early treatment protocols is the most logical course of action at this time.

Finally, **the spread of the virus in unvaccinated people recovered from COVID-19 is highly unlikely** given their broad and durable immunity shown to date. As such, **it makes sense to abandon the notion of separating society into two groups based on variable vaccination status.** Individuals have the right to consent to medical treatments that align with their needs and preferences, and the COVID-19 vaccines are no different. **We**



propose a multi-faceted path forward that fully embraces the underlying immunology demonstrated in the above series of articles, as well as integrating preventative and early treatment protocols into outpatient and healthcare systems to best serve patients in Canada.

Original article: <https://www.theblaze.com/op-ed/horowitz-15-studies-that-indicate-natural-immunity-from-prior-infection-is-more-robust-than-the-covid-vaccines>, Daniel Horowitz is senior editor.