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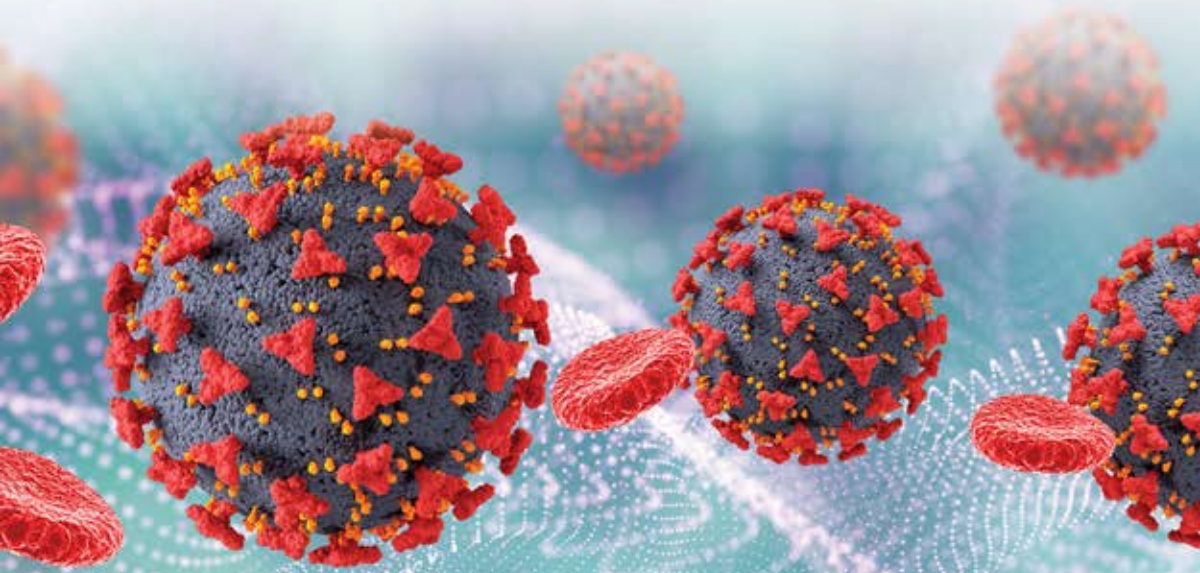
Controversies in the PANDEMIC



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CHAPTER 17

Controversies Concerning the Immunology of the COVID-19 Adaptive Immunity Vaccines

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PREFACE

There were many controversies concerning the immunology of the use of adaptive immunology coronavirus disease 2019 (COVID-19) vaccines to contain an RNA virus pandemic that focused on the development of antibodies to the spike protein. The spike protein is the molecule which mediates the binding of the virus to cells and antibodies to this determinant can often prevent virus entry referred to as neutralization. While in principle, one would ideally like to block the infection of cells which would correlate with resistance to acquisition of COVID-19 of the host and thus would play a role in herd immunity, this is not how it works for pandemic RNA viruses.

If you immunize the host to spike protein and cause the generation of spike-specific IgG1/3 particularly in the upper respiratory tract (URT), this does a number of things. First it causes selection of variants which are then transmitted to others. RNA viruses mutate at high rates and actually exist in the host not as one variant with the same identical RNA sequence but a swarm of mutated related sequences, called quasispecies. When the dominant quasispecies is blocked from replication by the antibodies, the nonblocked quasispecies emerges and then becomes dominant, which is then transmitted from the URT to third parties. This is referred to as "selection of new variants".

Unfortunately, this mismatching of the developed spike-specific (IgG1/3) antibodies with the newly selected variant causes antibody-dependent enhancement (ADE) of infection of the quasispecies into macrophages. This is because macrophages have receptors for these antibodies (that normally are used for phagocytosis), while macrophages do not express the angiotensin-converting enzyme 2 (ACE2) receptor. Now the quasispecies becomes *targeted to the protector macrophages* (and not the ACE2 positive cells in the body) and causes their conversion to disease-causing (pathogenic) macrophages (**Fig. 1)** in which the SARS-CoV-2 virus replicates.

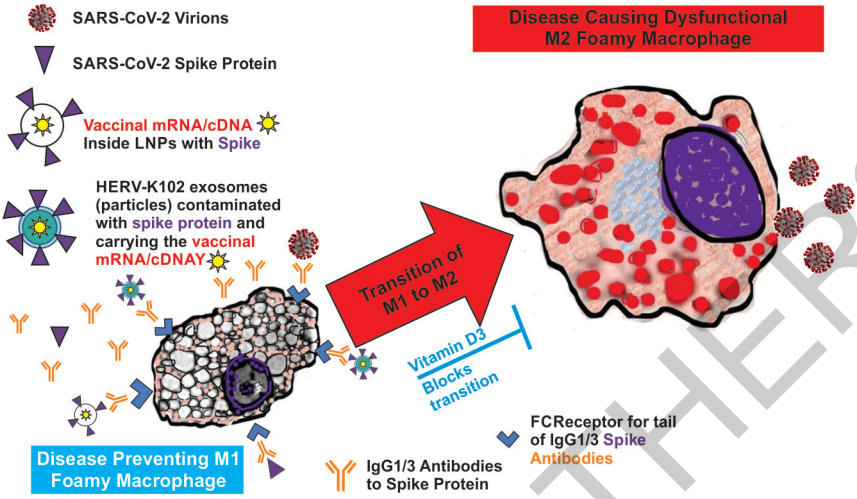

FIGURE 1: Antibody-dependent enhancement (ADE) of spike protein or spike-laden exosomes/particles/LNPs/SARS-CoV-2 virions into the protector M1 foamy macrophages (FM), causing their transition to disease-causing pathogenic and dysfunctional FM (immunosenescence of macrophages, ISM).
(LNPs: lipid nanoparticles)

It is theoretically possible too if the spike gene therapy mRNA/cDNA from the mRNA COVID-19 vaccines becomes integrated in the macrophage that spike protein could also be generated to high levels (with adverse effects on the host due to the toxicity of the spike protein, most importantly, causing macrophage dysfunction).

Note that the cell on the right is resistant to apoptosis induction and persists in the host for a long time. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continuously replicates, produces, and releases SARS-CoV-2 virions from the M2 compromised cells. Alternatively, spike protein or other spike-laden particles/exosomes/lipid nanoparticles (LNPs) *are targeted to the protector FM* via the spike-specific IgG1/3 antibodies. Fortunately, optimal vitamin D3 levels block this transition explaining how vitamin D3 protects against COVID-19 severity, serious side effects of the mRNA gene therapy vaccines, and/or the more deadly vaccinal shedding. Vaccinal shedding may be the most dangerous as (1) it may carry the IgG1/IgG3 from the URT of the recently vaccinated donor (shedding may last up to 3–4 months), and (2) there is very high possibility of integrated vaccinal spike mRNA/cDNA due to hitching a ride with the HERV-K102 particles that contain and utilize functional reverse transcriptase and integrase for their own replication.

Lipid nanoparticles are used to transport the vaccinal spike mRNA/cDNA around the body.

As discussed at length and covered in this chapter, the foamy macrophages hold the *magical power* of deciding recovery or death from COVID-19. Even

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susceptibility to COVID-19 is determined at the level of the macrophage; those with dysfunctional foamy macrophages (referred to as immunosenescence of macrophages, ISM) are at much higher risk of developing severe COVID-19. This is because ISM causes age-associated chronic diseases (from cardiovascular diseases to cancer, autoimmunity, allergy, neurodegenerative disorders, metabolic syndrome, and so on). The COVID-19 disease caused by SARS-CoV-2 is undeniably also via the induction of ISM **(see Fig. 1)**.

It is for this reason, namely ADE, that safe and effective vaccines against emerging or pandemic RNA viruses have never been possible. In other words, they not only select for more transmissible variants, but the vaccinated are at much higher risk of developing severe illness and death in subsequent months or years when they encounter the vaccine selected descendants.

Fortunately, this evolution of dangerous descendants was interrupted by the emergence of the omicron variant in December 2021 and January 2020 globally. Omicron had putatively been selected through the common house mouse and apparently retained little or no affinity for human Basigin (BSG/CD147), but preferring mouse BSG. Before omicron, the severe cases of COVID-19 in the lower respiratory tract (LRT) involved a novel mechanism of ADE where the spike:ACE2 interaction was replaced by spike:BSG (probably via the emergence of the IgG4 isotype of the spike-specific antibodies which blocked SARS-CoV-2 binding to ACE2 on cells). The switch to the spike:BSG interaction was extremely dangerous as BSG is expressed by the macrophages and on several of the innate T and B cell types involved in the critical trained innate immunity needed for COVID-19 recovery. In other words, the switch targeted SARS-CoV-2 directly to the critical HERV-K102 host defense system.

Accordingly, it was said that omicron did not generate pneumonia in the LRT, and thus was less pathogenic although it was much more transmissible due to classical ADE in the URT. Classical ADE in the URT involved SARS-CoV-2 gaining entry to the foamy macrophages via spike-specific IgG1/3 binding to FCGR2A. These foamy macrophages are the sebocytes in sebaceous glands and represent specialized foamy macrophages constitutively producing and releasing HERV-K102 particles to the exterior of the body to coat the mucosal tissues. In the URT, there apparently is no conversion of the ADE promoting spike IgG1/3 to IgG4 despite repeated COVID-19 mRNA vaccination. This is why the multiply vaxed were at higher risk of infection proportional to the number of doses for the workers at the Cleveland Clinic, as it proportionally increased the amount of IgG1/3 to spike protein in the upper respiratory tract (URT).

Had the vaccination against SARS-CoV-2 stopped with two doses and/or upon the onset of omicron, there would have been far less death and injury. As it was, the use of adaptive immunity vaccines to the Wuhan original variant prolonged the COVID-19 pandemic beyond its natural course of extinction predicted to have been by May 2021. However, the use of omicron variants in the bivalent vaccines may have restarted the whole evolutionary process now with selection against the circulating mouse strain of SARS-CoV-2. Some have

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predicted this might have sudden dire consequences for the human race if, in fact, a mutation restores the affinity of the currently circulating SARS-CoV-2 variants for the human BSG. Let us hope not but this is an early warning that to avoid a catastrophic calamity, we must immediately ban all the so-called "gene therapy vaccines".

The main take-home message of this chapter is that *all the evidence* prior to the unexpected and questionable emergency use authorization (EUA) of the COVID-19 mRNA vaccines not only demonstrated but proved beyond a shadow of a doubt, that the development of the spike-specific IgG1/3 antibodies was associated with progression to *more severe disease*, and did *not ever result in the* "protection against COVID-19". This begs the question why the authorities proceeded with the EUAs for the mRNA COVID-19 vaccines, why these adaptive immunology vaccines were deemed "safe and effective", and why would these inherently dangerous vaccines would not only be highly recommended by public health authorities, but mandated!

KEY POINTS

Egregious aspects of the immunology of the COVID-19 mRNA adaptive immunity vaccines:

- *Gene therapy vaccine is an oxymoron.*
- *Adaptive immunity vaccine against pandemic viruses is also an oxymoron. It is impossible for spike IgG1/3 to protect against SARS-CoV-2 or provide herd immunity.*
- Gene therapy vaccination could kill the unvaccinated by shedding from the vaccinated albeit at reduced frequency when compared with the vaccinated (estimated that the mRNA COVID-19 *vaccinated* succumbed to shedding at about *116-fold higher rates* over the *unvaccinated* for England).
- *Stealth gene therapy shedding may have killed far more people than SARS-CoV-2* (at least 14-fold if not more as shedding likely also contributed to COVID-19 deaths).
- *Hiding the truth about risks of death and injury with the gene therapy products was unethical, immoral, and likely criminal.*
- *Using a gene therapy product fraudulently advertised as a safe and effective vaccine was likely criminal.*
- Failing to require proper studies on the risks of shedding of mRNA COVID-19 vaccines prior to awarding the EUAs was probably criminal. *The risk of shedding of gene therapy products was well known prior to the EUA of the mRNA gene therapy shots.*
- Failing to address the all-cause mortality test to establish the gold standard for the risk/benefit profile for the COVID-19 vaccines was likely criminal on behalf of the manufacturers and by the regulatory authorities. (This test should have been performed at 6 months, 12 months, 18 months, and 24 months prior to awarding the EUA.)

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- *Saying the adaptive immunity/gene therapy vaccines were safe and effective was a bold-faced lie and was probably criminal as it led many people to their deaths and/or induced life-altering vaccine injuries.*
- Mandating of vaccines, particularly the COVID-19 gene therapy bio-weapons of mass (stealth) destruction was akin to genocide.
- The indicator used for vaccine effectiveness (levels of spike IgG) had more to do with death and injury than the prevention of a transmissible disease. *The authorities knew this but granted EUAs anyway.*
- An adaptive immunology vaccine cannot protect against emerging pathogens or pandemics. *It is physically/immunologically impossible and the regulators and public health officials well knew and understood this, as did Dr Anthony Fauci.*
- The risk of shedding deaths was enhanced in the donor by the presence of spike-specific IgG1/3 in the URT (from the shedding donor) which was induced by the mRNA gene therapy vaccines and not present (to any great extent) in the unvaccinated.
- The risk of shedding deaths was also enhanced in the recipients of the shed gene therapy products when spike-specific IgG1/3 was systemically present such as in the blood. People who were infected first then received two or more doses of the COVID-19 mRNA vaccines were unlikely to convert to the tolerogenic IgG4, placing them at higher risks of shedding-induced death. The younger the age, the more likely they would have been infected first as the vaccines were distributed in descending order of age.
- The young adults who were at negligible risks of COVID-19 should not have received any COVID-19 vaccines. However, due to shedding there were large increases in excess deaths in the under 50 age groups particularly in the third and fourth quarters of 2021. Many of these deaths were known to involve myocarditis and sudden death (in their sleep or upon exertion). Shedding is likely a major contributor to myocarditis and sudden death exacerbated by having been infected first before the two doses of the mRNA vaccines. An example of a potential shedding incident causing ventricular tachycardia with sweating and high blood pressure during sleep in a 69-year-old female who was infected with SARS-CoV-2 prior to receipt of the two doses of the Pfizer-BioNTech in March 2024 is available online at *https://hervk102.substack.com/p/can-shedding-be-clinically-distinguished*.
- Testing for serum levels of vitamin D3, and topping up where needed, was an easy, safe, affordable, and attainable way to immunologically reduce the risks of severe COVID-19 and would have quenched or eliminated the need for risky vaccine interventions. This would have also reduced the risky congregation at large indoor venues which some noted were associated with SARS-CoV-2 infection especially at the time of the first injection.
- Similarly, ivermectin, hydroxychloroquine, and other repurposed drugs were not only cost effective but exemplary in their ability to promote

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recovery as well as the prevention of COVID-19. These immune protector agents share a common immune enhancing and antiviral property of preventing and/or reversing *ISM* caused by a number of pathogenic agents including SARS-CoV-2.

- It was unlawful of the FDA to suggest ivermectin should not be used off-label to prevent SARS-CoV-2 infection or more severe COVID-19 disease.
- At the heart of COVID-19 disease and indeed most age and/or stress-associated diseases including infections involves the activity of alpha-fetoprotein (AFP) in the macrophages, which is commonly induced by pathogens and exacerbated by stress. AFP antagonists such as ivermectin, zinc, DHEA, or 7-keto-DHEA, genistein, and other isoflavonoids also target the estrogen receptor, and more recently, maraviroc is sure fire means for the prevention and recovery of COVID-19 and any future pandemics.
- There were attempts to validate innate immunity vaccines in clinical trials that started prior to the launch of the COVID-19 mRNA vaccines. But Big Pharma was able to convince Ethics Boards across the nation that no one should be denied the unlawful administration of an experimental intervention known or suspected of causing bodily harm especially where mandated. So, all these legitimate clinical trials were in fact ruined by interception by mRNA COVID-19 vaccines. Some of the reports of such trials concluded that the innate vaccines were ineffective against COVID-19 when in fact the trials were stopped early due to the unjustifiable interference by Big Pharma.
- The most abhorrent and reprehensible was the labeling of personal accounts of vaccine injury and death as disinformation or conspiratory theories, and thus, this abrogated the ability to warn others about the risks on social media. As well these people who needed immediate support allegedly caused by the governments' mandates were denied rapid compensation. Some in dire straits were instead offered medically assisted dying.
- Not only did the FDA and other regulators abandon the responsibility to report in real time on vaccine deaths and serious injuries, but in Canada just for these bioweapons only, the reporting structure was changed. The new system required reporting only to the municipal level which then was sent up to the provincial and federal levels which contradicted the point of rapid responses to faulty products on the market. Moreover, a Canadian citizen could no longer report a death or serious injury, while licensed physicians were afraid to lose their license if they reported COVID-19 gene therapy-associated deaths. Ergo virtually none were reported.
- The continued censorship on the reporting and discussion of the death and destruction caused by the COVID-19 vaccines especially the gene therapy shots is frankly undemocratic and unconstitutional. This will cause poor choices for future pandemics on how to immunologically handle the "next one".

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- Saying that hybrid immunity was the best of both worlds was certainly not the case for people who were infected prior to receipt of the gene therapy shots. These people were at higher risk of SARS-CoV-2 and the shed gene therapy products transmitted via exosomes.
- Saying that the protection from the vaccines only lasted 6 months or less refers to the protection induced by innate immunity and little to do with waning of the spike IgG1/3 antibodies.
- Many researchers did not realize that using the pseudovirus assay in neutralization experiments which involves the culture of the pseudovirus in human cells instead of the green monkey Vero cell line actually detected innate neutralizing antibodies that reacted with HERV-K102 envelope present both on the particles and on the surface of such human but not nonhuman cell lines. The same is true for uncultured SARS-CoV-2 virus directly isolated from humans. Showing neutralizing antibody activity with these methods instead of the classical culture of the intact virus in green monkey cells and tested on green monkey cells as the indicator cell line misled some to conclude broader protection against SARS-CoV-2 variants. Some sloppy researchers actually reported spike neutralizing antibodies when by ELISA no antibodies to spike protein could be detected. Less commonly human cell lines were used as indicator cell lines which could led to false positive or false negative results due to the presence of the HERV-K102 particles in the plasma/serum, which is believed to cause lysis in susceptible human cell lines but not Vero cells at 24 hours.

INTRODUCTION

Single Cell RNA Sequencing has Revealed the Importance of Innate Immunity, Especially Macrophages

Single cell RNA (scRNA) sequencing has substantially revolutionized the ability to gauge cell fate and developmental programs such as for immune cells in sickness and in health.[1,2] Such investigations have revealed the importance of innate immune mechanisms in recovery from or protection against many common diseases.

For example, an initial investigation involving 39 cancer types and about 18,000 tumors unexpectantly determined in 2015 that the gamma-delta 2 (GD2) T cells and/or other innate T cells were frequently correlated with protection against many although not all cancers.[3] This discrimination was largely based on the expression of KLRB1 (CD161) on these innate T cells. KLRB1 is a lectin-like receptor that binds galactose-a-(1,3) galactose which is a carbohydrate marker of nonhuman cells and where humans have IgM against this moiety.[4] On the other hand, FOXM1 considered a marker of poor prognosis tended to identify neutrophil populations within many cancers.

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More recently, using scRNA sequencing, M1-like proinflammatory macrophages have been implicated in remission from acute myeloid leukemia,[5] and as correlates of protection in patients with lung cancers.[6]

In addition, via scRNA sequencing, monocytes/macrophages have been identified as essential to a reduced risk of *Simian immunodeficiency virus*/*Simian-human immunodeficiency virus* (SIV/SHIV) acquisition in nonhuman primate (NHP) animal studies and were implicated in the partial vaccine efficacy against human immunodeficiency virus HIV-1 infection demonstrated in the RV144 trial.[7] At a more detailed level, the induction of hypoxia with inflammasome activation in CD14 monocytes has been associated with a decreased risk of SIV_{mac251} acquisition in NHP models.[8] It should be appreciated that hypoxia and inflammasome activation results in foam cell formation in M1-like proinflammatory macrophages.[9] Accordingly, it appears, proinflammatory foamy macrophages provide protection against HIV-1 acquisition, a conclusion reached earlier on entirely different evidence.[10,11]

Macrophages although long considered the central orchestrator of both innate and adaptive immunity, are primarily associated with innate immunity, the antigen nonspecific arm of the immune system involving interferon responses and intrinsic pathogen detection systems termed pattern recognition receptors (PRRs). Dendritic cells that are the antigen presenters for adaptive immune responses are derived from a separate set of bone marrow progenitors, called the common lymphoid progenitors (CLPs). Instead, macrophages (and monocytes) are derived from the common myeloid progenitors (CMPs) which then generate the granulocyte-macrophage progenitors (GMPs) and the megakaryocyte-erythroid progenitors (MEPs).[12] Accordingly, discussions of monocytes in the blood or macrophages in the tissues refer and pertain to innate immunity.

The Clue of Antibody Dependent Enhancement of Infection into Macrophages

Historically, a major line of evidence emphasizing the importance of macrophages in the control of infectious diseases and outcomes has been the concept of ADE of infection into monocyte/macrophages. Disease escalation involving antibodies that mediate the enhanced infection of macrophages through Fc receptors was first documented for dengue in 1967. Since that time ADE has been observed for various viral infections[13] such as measles, SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), HIV-1, West Nile virus, Japanese encephalitis virus, Ross River virus, Ebola virus, respiratory syncytial virus, feline infectious peritonitis virus, porcine reproductive and respiratory syndrome virus, and now SARS-CoV-2.[14] Most notably, it has been suggested that COVID-19 disease progression from moderate to severe commonly relates to ADE-mediated infection of SARS-CoV-2 into monocytes/macrophages[14] (which will be examined and validated

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in more detail below). This view is, however, not supported by everyone, as some profess that ADE has not been observed clinically during COVID-19 infection.[15]

Despite the controversy in opinion, incontrovertible evidence had emerged that even before the COVID-19 vaccines were authorized for emergency use that demonstrated IgG antibodies to spike protein were not protective but instead were associated with progression to more severe COVID-19 disease including death during natural infection.[16-30] Despite this unanimous finding, three papers claimed exceptions to the consensus finding based on assumptions about neutralizing activity.[31-33] However, these could be discounted based on technical grounds. All three excursions were based on neutralizing antibody data generated from pseudotyped virus produced in human 293T cells rather than live SARS-CoV-2 virus grown and tested in the non-human, green monkey cell line and Vero cells. As virus pseudotyped in human cells likely carries human innate immunity target antigens, the authors did not address and exclude the possibility that the neutralization they observed was due to innate neutralizing antibodies rather than those reactive with spike protein.

As also noted by Ricke,[14] the main problem which led to more severe disease during natural infection was that the onset of IgG to spike protein preceded the clearance of SARS-CoV-2 by the innate immune system.[34-38] This earlier onset leading to more severe disease was also documented previously for spike IgG antibody to SARS-CoV-1.[39,40] In contrast when SARS-CoV-2 was neutralized or cleared from the URT before the onset of spike-specific IgG in the blood, this invariably resulted in mild COVID-19 disease.[41]

The problem of ADE following vaccination particularly for RNA viruses is believed in part to reflect the rapidity at which new variants are generated in the host following the introduction of antibodies to spike protein that can and do readily select for new variants. For example, in immunosuppressed high-risk individuals, it took 10 days on average for a neutralizing monoclonal antibody (MAb), bamlanivimab to spike protein to generate escape mutants and establish a rebound viremia.[42] Fortunately, in many instances but not all patients studied, convalescent plasma was able to provide recovery presumably related to innate neutralizing antibodies and other innate humoral immune mechanisms found in plasma.

Perhaps more importantly, a growing body of evidence implies for natural infection unless the case of COVID-19 was severe/critical, there were few IgG1 or IgG3 antibodies to spike RBD in the nasal secretions and none in the saliva.[43,44] However, with the second dose of COVID-19 vaccines (mRNA or virus vectored), these IgG1/3 antibodies to spike protein capable of mediating ADE were commonly detected at high levels in the URT.[43,44] Thus, the global mass vaccination with COVID-19 vaccines not only greatly increased the likelihood of the emergence of variants, but led to increased transmission and infection rates, all of which would and did prolong the pandemic beyond May 2021.[45]

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Given the importance of the selection of SARS-CoV-2 variants and increased infection rates as salient proof of ADE, which in turn validates that the macrophage provides the most important correlate of protection against COVID-19, data supporting each of these statements will be briefly discussed.

Evidence from Canada for Selection of SARS-CoV-2 Variants Correlating with Vaccination Milestones

For both the Pfizer and Moderna mRNA COVID-19 vaccines, it was about 14 days after the second dose of vaccines, when the IgG antibodies to spike protein became significantly detectable in most individuals.[46,47] Also, it was known that the first dose which provoked trained innate immunity-induced heterologous protection against all-cause mortality. Negative excess all-cause mortality was clearly demonstrated in countries especially those that postponed the second dose (Canada[48] and the UK) at the time that the first dose was administered.[49] For the USA, a study of seven integrated healthcare organizations in the USA demonstrated that heterologous protection against non-COVID-19 mortality was induced upon the first dose and which was not appreciably altered upon receiving the second dose, at least for the first 7.5 months of the vaccination campaign.[50]

In Canada, the selection of variants (initial emergence or when the variant became dominant) was observed[51] either (1) when the percentage of the eligible population who received two doses over those who had only received one dose exceeded 0.5 **(Table 1)** or (2) when the negative excess all-cause mortality (heterologous protection against all-cause mortality comparing 2021 to the average for 2015–2019) reversed direction and started to trend positive **(Fig. 2)**. In either case, these parameters are alternative ways of looking at the relative impact of the induction of ADE-promoting, spike-specific IgG1/3 by the second dose relative to the heterologous protection by trained innate immunity of the first dose. Both sets of parameters examine and reflect ADE. As detailed elsewhere,[51] and reproduced here by the author, when the second dose to first dose ratio exceeded 0.5, this was associated with the initial emergence of the alpha variant and was also associated with the dominance of the delta variant **(Table 1)**. Conversely, when the negative excess all-cause mortality reversed direction (i.e., the heterologous protection of trained innate immunity against mortality became less, **Fig. 2**) this correlated with the alpha variant becoming dominant and with the initial emergence of the delta variant.

Accordingly, these tight correlations indicate a high likelihood that the COVID-19 vaccines through ADE mechanisms were causally related to selection of the alpha and delta variants. In further substantiation of this notion, the global selection of immune escape variants did not appreciably occur until the COVID-19 vaccines were introduced.[49] For clarification, the initial emergence of the alpha variant which occurred by December 2020 in the UK could have reflected that over 600,000 UK residents had taken part

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TABLE 1: The two over one dose ratios for COVID-19 vaccination in Canada: December 22, 2020 to August 1, 2021 (from Our World in Data[49]).

Date	% at least one dose	% two doses	% one dose	Two/One ratio	Events	Notes
22-Dec	0.071	None	0.071	**N/A**		
29-Dec	*0.19*	None	*0.19*	**N/A**		
03-Jan	0.3	None	0.30	**N/A**		EACM decreases
10-Jan	0.84	0.1	0.74	**0.135**		
17-Jan	1.5	0.6	0.9	**0.667**		**EACM temporarily flattened**
24-Jan	2.03	0.15	1.88	**0.080**		
31-Jan	2.3	0.3	2	**0.150**		
07-Feb	2.4	0.47	*1.93*	**0.244**		
08-Feb	2.4	0.5	1.9	**0.263**		
10-Feb	2.5	0.6	1.9	**0.316**		**Enters Neg EACM**
14-Feb	2.59	0.81	1.78	**0.455**		
21-Feb	2.9	1.1	1.8	**0.611**		
22-Feb	3	1.2	1.8	**0.667**	Alpha emerges	
25-Feb	3.2	1.3	1.9	**0.684**		
26-Feb	3.4	1.4	2	**0.700**		
27-Feb	3.5	1.4	2.1	**0.667**	NACI intervention around Feb 27	
28-Feb	3.63	1.41	2.22	**0.635**		
07-Mar	4.85	1.52	3.33	**0.456**		Uptick in Neg EACM
08-Mar	5.1	1.6	3.5	**0.457**		
11-Mar	5.67	1.59	4.08	**0.390**		
14-Mar	6.5	1.6	4.9	**0.327**		
15-Mar	6.8	1.6	5.2	**0.308**		
21-Mar	8.83	1.7	7.13	**0.238**		Lowest Neg EACM (Nadir)
22-Mar	9.2	1.7	7.5	**0.227**	Alpha dominates	
28-Mar	11.81	1.81	10	**0.181**		Uptick in Neg EACM
04-Apr	15.07	1.92	13.15	**0.146**		
11-Apr	19.04	2.19	16.85	**0.130**		Uptick in Neg EACM
18-Apr	24	2.5	21.5	**0.116**		
19-Apr	25	2.5	22.5	**0.111**		

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Date	% at least one dose	% two doses	% one dose	Two/One ratio	Events	Notes
25-Apr	29.18	2.75	26.43	**0.104**		
26-Apr	30	2.8	27.2	**0.103**		
28-Apr	31	2.9	28.1	**0.103**		Exit Neg EACM
02-May	33.58	3.05	30.53	**0.100**	Delta emerges	
03-May	34	3.1	30.9	**0.100**		
09-May	39	3.4	35.6	**0.096**		
16-May	45	3.8	41.2	**0.092**		
17-May	46	3.9	42.1	**0.093**	Max alpha at 59%	
23-May	51	4.05	46.95	**0.086**		
30-May	56.69	5.45	51.24	**0.106**		
02-Jun	58.8	6.11	52.69	**0.116**		
11-Jun	63.87	10.82	53.05	**0.204**		
14-Jun	64.86	13.11	51.75	**0.253**		
20-Jun	66.29	18.85	47.44	**0.397**		
26-Jun	67.38	26.47	40.91	**0.647**		
04-Jul	68.31	35.02	33.29	**1.052**		50% of the eligible receive 2nd dose
12-Jul	69.27	44.33	24.94	**1.777**	Delta dominant	
19-Jul	69.99	50.61	19.38	**2.611**		50% fully vaccinated
25-Jul	71	55	16	**3.438**		
01-Aug	71	59	12	**4.917**		

Note:

- Max alpha at 59% means the maximal portion of the sequenced variants was recorded at 59%.
- All of the data provided[49] is freely available for both academic and commercial use under Creative Commons Attribution 4.0 (CC-BY 4.0) license terms.

[EACM: excess all-cause mortality; NACI: National Advisory Committee on Immunization (Canada); Neg: negative; N/A: not applicable]

in vaccine clinical trials. Presumably, the use of neutralizing MAbs to spike protein and/or use of convalescent plasma may have also contributed to the earlier emergence of the alpha variant in the UK. Conversely, Canada did not participate in mRNA vaccine clinical trials. This enabled an assessment of both the emergence of the alpha and delta variants associated with mass immunization.

There is additional published data supporting the above conclusions that the COVID-19 vaccines were likely causally related to the selection of variants. SARS-CoV-2 variants sequenced from the two-dose vaccinated when compared with the unvaccinated had significantly higher percentages

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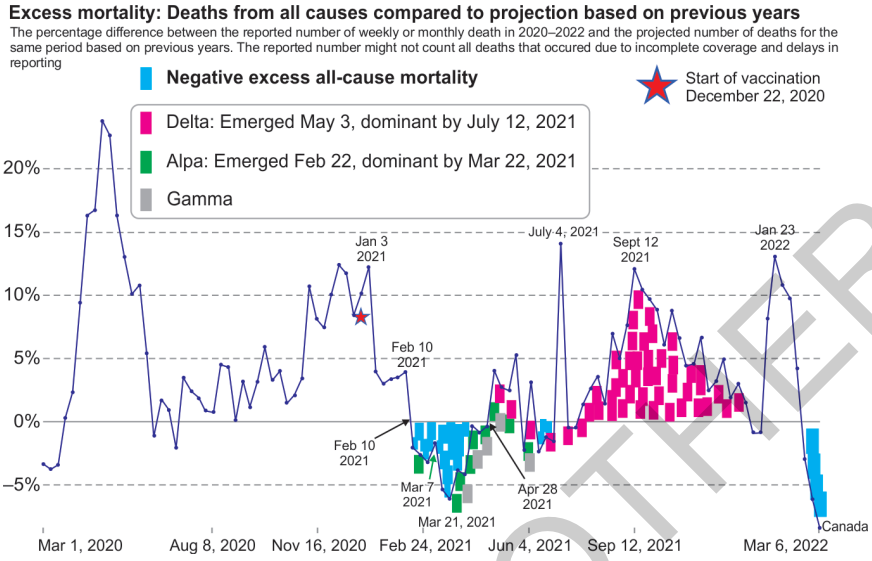

FIGURE 2: Negative excess all-cause mortality in spring 2021 (February 10–April 28) in Canada associated with postponement of second COVID-19 vaccine dose by up to 120 days.[48] Negative excess mortality relative to the average mortality per week for 2015–2019 is highlighted in turquoise as provided by Our World in Data.[49] Bright green highlights pertain to emergence and dominance of the alpha variant (emerged February 22, 2021 and became dominant by March 22, 2021 but never exceeded 57% of the total variants); hot pink highlights pertain to emergence (May 3, 2021) and dominance of the delta variant (July 12, 2021) and reached 99% of the total variants by Aug 30, 2021; and the gamma variant appearance is shown in gray and never reached higher than 26%. Mass vaccination started in Canada on December 22, 2020. There were no variants of concern selected prior to December 22, 2020, implicating mass vaccination as the cause. Note that the peak in excess all-cause mortality recorded on July 4 pertained to 619 heat wave related deaths from June 25 to July 1, 2021, in British Columbia[52] and thus are immaterial to the discussion.

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Source: Human Mortality Database (2022) and World Mortality Dataset (2022).

of immune escape variants as well as variants associated with higher infectivity.[53] Furthermore, in a separate report, boosted innate immunity (the first 6 days after the second dose) showed 100% vaccine effectiveness (VE) from April 2021 to August 2021 while during the same period the VE for adaptive immunity (7 days or longer after the second dose) declined from 78 to 48% as determined in a large integrated health system in the USA[54] (see their Supplemental Table 5c, in reference 54). The latter findings are consistent with the notion that the neutralizing antibodies of innate immunity can provide sterilizing or lasting herd immunity against SARS-CoV-2, whereas adaptive immunity neutralizing antibodies cannot. In other words, as expected due to ADE, adaptive immunity vaccines particularly producing IgG1 and IgG3 antibodies to spike protein are not very useful and may be harmful to control a pandemic.

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Controversies in the PANDEMIC

This book is a stellar example of international collaboration written by several renowned scientists, clinicians, and scholars. The majority of authors are not only clinicians, scientists, and scholars, but have also personally cared for thousands of patients afflicted and critically ill with COVID-19. It is not an ivory tower group; they truly represent a boots-to-the-ground approach to care of these complex patients. Paul Marik, who has coauthored several chapters, is one of the most published intensivists in the world who has spent the last year and a half taking care of critically ill patients in the intensive care units. The unique selling points of this book include the points listed below. There are no authentic textbooks on the pandemic other than "Challenges in the Pandemic" which the above editors have edited and authored. The pandemic is by no means over, and it is anticipated that more waves will follow. The editors and authors provide distilled information obtained through careful and meticulous analysis and research about the pandemic gained over the past 2 years so that we can help others in a useful no-nonsense manner. Confusion still exists in the medical world as to what works and what does not. Social media and governmental policies with their constant U-turns and flip flops have added to the confusion. Our book attempts to offer clarification on all major issues. The book is structured on issue-based problems, offering rare clarity and resolution with deep but clear scientific insight.

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