### **'Original Antigenic Sin' Is a Real Problem with COVID-19** Vaccines

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Studies have now confirmed that "original antigenic sin", or a detrimental fixation on a suboptimal immune response, is a real problem for people who've gotten COVID-19 vaccines.

#### Introduction

There is a phenomenon in immunology known as "original antigenic sin" that studies have now confirmed to be a real problem with COVID-19 vaccines.

In brief, what can happen is that an initial viral infection or vaccination can result in an individual's immune system becoming fixated on generating responses to the original antigen even during subsequent infection with different strains characterized by different epitopes, or molecular structures capable of being recognized and responded to by the immune system. Thus, the immune response to a new strain can result in an *inferior* immune response in immunologically experienced people relative to the immune response induced by the new strain in immunologically naïve individuals.

Other terms that are sometimes used to describe this phenomenon include "viral interference", "immune interference", "antigenic fixation", and "immune imprinting".

Of course, the imprinting of an immune response to a virus is not in itself a bad thing. On the contrary, the induction of immunological "memory" to a virus is what provides long-term protection. It is only when a previously primed immune system fails to adequately *adapt* its responses to a newly infecting strain that the effect can be detrimental.

It is also not necessarily a question of whether original antigenic sin occurs or not; the more relevant question might be to what degree it occurs. For example, it has been observed with both natural immunity to influenza and with flu shots, but since infection induces a broader repertoire of immune responses than vaccination, natural immunity still represents an *opportunity cost* of vaccination.

In other words, priming the immune system by vaccination comes at the cost of the lost opportunity to prime the immune system by infection, resulting in a fixation of the immune response to subsequent infections with mutated strains that is *suboptimal* relative to superior natural immunity.

In fact, original antigenic sin has been hypothesized as a mechanism that could explain observations of an *increased* risk of illness due to the 2009 pandemic influenza A(H1N1) virus, also known as the "swine flu", among individuals who received the seasonal flu shot.[1]

Policymakers eager to get jabs into arms perpetually fail to consider natural immunity as an opportunity cost of vaccination. I have long been <u>warning</u> that if original antigenic sin turns out to be a problem with COVID-19 vaccines, the policy aim of achieving a high vaccination rate could result in a prolonging of the pandemic and *worsening* of mortality outcomes in the long run.[2]

For instance, three months before the first COVID-19 vaccine received emergency use authorization from the US Food and Drug Administration (FDA), the UN published a written statement to the UN Human Rights Council that I authored on behalf of the non-governmental organization Planetary Association for Clean Energy, Inc. (PACE). Published on September 14, 2020, as General Assembly document <u>A/HRC/45/NGO/43</u>, the document included the following warning about <u>the potential risks</u> of forcing COVID-19 vaccines on the population:

There are many legitimate concerns about vaccines in addition to their non-specific effects. Policymakers do not consider the opportunity costs of vaccination, such as the superiority of immunity acquired naturally compared to that conferred by vaccination.

For example, studies have found that having a flu shot annually could increase the risk of infection with novel influenza strains, as well as with non-influenza viruses, in part due to the lost opportunity to acquire the cross-protective, cell-mediated immunity conferred by infection.

A complementary hypothesis is the phenomenon of "original antigenic sin", whereby the first experience of the immune system with an antigen determines future responses. Priming the immune system with antigen components of the influenza vaccine could potentially cause a mismatched antibody response to strains that the vaccine is not designed to protect against, thereby increasing the risk of infection as compared to an immune response in which naive T and B cells are instructed to fight off the infecting virus.

This phenomenon might help explain an increased risk of serious dengue infection among Filipino children who received the dengue vaccine and who had not already experienced a prior infection. This finding led the Philippines to the withdrawal of the vaccine, which the government had implemented into its childhood schedule upon the recommendation of WHO, despite earlier data having indicated that the vaccine might cause precisely that outcome.[3]

Unsurprisingly, the phenomenon of original antigenic sin has received scant attention in the mainstream media, which generally do policy advocacy rather than journalism when it comes to the topic of vaccines.

A rare early exception was an article in *The Conversation* on March 8, 2021, written by Matthew Woodruff, an instructor at the Lowance Center for Human Immunology at Emory University whose research is funded by the National Institutes of Health (NIH). The current COVID-19 vaccines are designed to elicit an immune response to the spike protein of the original Wuhan strain of SARS-CoV-2 (the coronavirus that causes COVID-19), which is no longer circulating. Woodruff <u>anticipated</u> that attempts to update the vaccines to generate antibodies specific to newer variants of SARS-CoV-2 might fail due to original antigenic sin. [4]

Woodruff's cautionary remarks, like my own, have proven prescient.

Indeed, it has been demonstrated that a booster dose of an mRNA vaccine modified to express the spike protein of the Beta variant still results in generation of neutralizing antibodies more specific to the original Wuhan strain than to the Beta variant. As the authors of a <u>study</u> published in the journal *Cell* on January 24, 2022, pointed out, this suggests that

"some degree of immune imprinting, or preferential responses to the viral variants initially encountered by the immune system, may affect the development of antibodies against new viral variants."[5]

Similarly, a study comparing the antibody response in macaques from either the Moderna mRNA COVID-19 vaccine or an updated vaccine designed to induce antibodies specific to the Omicron variant of SARS-CoV-2 found *no* protective advantage of the Omicron-matched vaccine compared to the vaccine designed to induce antibodies to the ancestral Wuhan strain, which is now extinct outside of laboratories.[6]

These findings help to explain why, despite the acknowledgment that the vaccines are much less effective against Omicron, and despite early promises from "public health" officials that the mRNA vaccines could be easily updated to match new variants, there remains no Omicron-specific vaccine.

Since very early into the mass vaccination campaign, there were indications in the scientific literature that original antigenic sin would turn out to be a major obstacle for policymakers intent on getting the population to accept COVID-19 vaccines. Several recent studies have now confirmed that this is a real problem, with startling implications for the long-term protection of vaccinated individuals.

## Scientists Have Known about "Original Antigenic Sin" for Over Half a Century

The first mention of "original antigenic sin" in the medical literature, to my knowledge, was in a paper discussing immunity to influenza titled "<u>On the Doctrine of Original Antigenic Sin</u>", which was published in the *Proceedings of the American Philosophical Society* in 1960. The paper provides a helpful explanation of the phenomenon that is worth reviewing.

First, it is important to understand that an "antigen" is a substance that induces an immune response, and an "antibody" is "a serum protein whose production is stimulated by antigen." With that understood, the paper observed:

The antibody of childhood is largely a response to the dominant antigen of the virus causing the first Type A influenza infection of the lifetime. As the group grows older and subsequent infections take place, antibodies to additional families of the virus are acquired. But the striking feature is that the antibody which is first established continues to characterize that cohort of the population throughout its life. The antibody forming mechanisms have been highly conditioned by the first stimulus, so that later infections with strains of the same type successively enhance the original antibody to maintain it at the highest level at all times in that age group. The imprint established by the original virus infection governs the antibody response thereafter. This we have called the doctrine of original antigenic sin.

The effect is attributed not merely to continuation of initial antibody levels but to repeated stimulation by persistence of the first dominant antigen as a lesser or secondary component of later Type A strains.[7]

It stands to reason also that the effect may be exacerbated *by repeated stimulation from vaccination*. If an individual's first antigenic exposure was either infection with the ancestral strain of SARS-CoV-2 or a COVID-19 vaccine designed to induce antibodies specific to the spike protein of the ancestral strain, and then if the person experiences repeated immunological stimulation with subsequent doses of the vaccine, the anticipated effect would be to more strongly fixate the immune response on the ancestral strain at the opportunity cost of generating a more appropriate immune response to subsequently circulating variants, such as the now-predominant Omicron variants.

The relevant data available to date are consistent with this hypothesis.

#### The Role of Pre-Existing Immunity to Common Cold Coronaviruses

One observation made early during the COVID-19 pandemic was that immune responses induced by prior infection with common human coronaviruses that are a cause of the common cold are cross-reactive with SARS-CoV-2. An enlightening <u>study</u> published in *Nature* in November 2021 found that certain individuals who never developed symptoms and *never generated a detectable antibody response* to SARS-CoV-2 nevertheless experienced an "abortive" infection wherein pre-existing T cells induced by prior infection with common cold coronaviruses cross-reacted with SARS-CoV-2 and appeared to be sufficient to limit and clear the infection.[8]

Pre-existing immunity from common colds has also been <u>proposed</u> as one of the reasons why children are at such low risk from SARS-CoV-2 infection, whereas pre-existing immune responses might contribute to severe disease in the context of "a dysregulated immune response", as observed more often in elderly people.[9]

Consistent with this idea, a <u>study</u> published in the *Journal of Clinical Investigation* in September 2021 found cases of severe COVID-19 to be associated with a boost in *pre-existing* cross-reactive antibodies that *poorly* neutralized SARS-CoV-2.[10]

A <u>study</u> published in *Cell Host & Microbe* in December 2021 observed that *most* people have pre-existing antibodies from prior common coronavirus infections and that antibody responses to SARS-CoV-2 infection and COVID-19 vaccination are consistent with a cross-reactive *memory* response, which could either be beneficial or detrimental.

As noted by the authors, "Imprinting can hinder immunity to a novel virus if pre-existing antibodies against conserved epitopes dominate the immune response but do not neutralize the novel virus." The pre-existing memory B cells, which are involved in the production of antibodies, "can outcompete B cells specific for novel epitopes and hinder immunity to the novel virus."

Pre-existing immunity from common colds has also been proposed as one of the reasons why children are at such low risk from SARS-CoV-2 infection.

Children tend to be more exposed to common cold coronaviruses than adults, but the immune response of children is biased toward production of IgM antibodies and consistent with "a more adaptable repertoire, which may explain why younger individuals exhibit less disease severity than older individuals."

Relevantly, the authors noted that cross-reactive antibody responses "showed strikingly distinct patterns in infected versus vaccinated individuals", and since "the vaccine does not induce a robust IgM response in most individuals, it is currently not known whether IgM antibody levels after vaccination impact vaccine efficacy."[<u>11]</u>

As noted in a <u>commentary</u> reviewing that study's findings in *JAMA* (the primary journal of the American Medical Association), "it will be important to test whether immunity to the vaccine strain negatively influences protection from variants like Omicron that are substantially different."[<u>12]</u>

### The Accumulating Evidence of "Original Antigenic Sin" with COVID-19 Vaccines

The phenomenon of original antigenic sin has relevance for serological testing intended to determine the prevalence of SARS-CoV-2 infection in the population. Because the vaccines are designed to provoke an immune response *only* to the spike (S) protein of the ancestral strain of SARS-CoV-2, the scientific community has turned to antibody tests designed to detect antibodies to the nucleocapsid (N) protein in order to determine whether an individual has experienced a prior infection with the virus.

This is a fairly reliable method of determining whether unvaccinated individuals have previously been infected with SARS-CoV-2 since most people who survive infection do produce anti-N as well as anti-S antibodies (although the former antibodies tend to wane faster than the latter to undetectable levels, resulting in underestimation of prevalence).

However, anti-N assays have proven to be *unreliable* when it comes to determining prior infection in *vaccinated* individuals.

One of the earliest observations of this problem was a <u>letter to the editor</u> published in the *Journal of Infection* on August 9, 2021, in which researchers from Ireland observed that individuals who had experienced "breakthrough" infection after vaccination appeared to have an *impaired* ability to generate anti-N antibodies.

The letter authors reported their finding that only 26 percent of vaccinated individuals had detectable anti-N antibodies compared to 82 percent of individuals with naturally acquired immunity. They suggested that this might be explained by early virus neutralization at the mucosal surface of the respiratory tract playing a key role in generation of anti-N antibodies, which was a reasonable hypothesis since the COVID-19 vaccines *were not designed to induce mucosal immunity*.[13]

This design limitation was usefully explained in a <u>review</u> of COVID-19 vaccines then under development published in *Nature* on September 23, 2020, three months before the FDA's first emergency use authorization. As the review author observed:

[I]t is important to note that natural infection induces both mucosal antibody responses (secretary immunoglobulin A (IgA)) and systemic antibody responses (IgG). The upper respiratory tract is thought to be mainly protected by secretory IgA, whereas the lower respiratory tract is thought to be mainly protected by IgG. Vaccines that are administered intramuscularly or intradermally induce mainly IgG, and no secretory IgA. It is therefore possible that most vaccines currently in development induce disease-preventing or disease-attenuating immunity, but not necessarily sterilizing immunity.[14]

In other words, the vaccines might be expected to moderate disease symptoms but would not be expected to prevent infection and transmission of the virus.

("Sterilizing" immunity refers to protection against infection due to antibodies effectively neutralizing the virus before it has a chance to enter and replicate inside of host cells. Once the virus has gained access to the cells, the immune system has other mechanisms of limiting and clearing the infection.)

This expected inability to prevent infection and transmission, of course, has proven to be the case, with "public health" officials having acknowledged even before the emergence of the Omicron variant that the sterilizing immunity induced by the vaccines is short-lived.

"It is therefore possible that most vaccines currently in development induce diseasepreventing or disease-attenuating immunity, but not necessarily sterilizing immunity."

On October 26, 2021, a <u>study</u> by researchers from Public Health England was published on the preprint server *medRxiv* similarly finding a lower rate of seroconversion of antinucleocapsid antibodies among vaccinated individuals, suggesting that the use of anti-N assays in seroprevalence studies was "likely to underestimate the proportion of the population who have experienced COVID-19 in the highly-vaccinated UK population, particularly following the Alpha-variant wave or in younger populations who often experience mild infections, as well as due to waning."[<u>15]</u>

In addition to a blunted antibody response against the nucleocapsid protein, people whose immune systems are primed by vaccination appear to have impaired cellular immunity relative to those with natural immunity.

A <u>study</u> by researchers in Norway published at *medRxiv* on January 13 of this year observed that vaccinated people with breakthrough infection produced a lower level of *T cells* specific to the virus's membrane and nucleocapsid proteins than seen in people with naturally acquired immunity.

"The importance of T cells", the authors emphasized, "has been underlined in previous reports as T cells are necessary for rapid and efficient resolution of COVID-19, for protection against severe COVID-19 in settings of low antibody levels, and for rapid viral control in the absence of antibodies—aborting infection in healthy individuals."

In addition to a blunted antibody response against the nucleocapsid protein, people whose immune systems are primed by vaccination appear to have impaired cellular immunity relative to those with natural immunity.

In addition to the reduced ability to generate T cells against the virus, the authors observed a "relative lack of neutralizing antibodies" in Omicron breakthrough infections. It remained unknown, they pointed out, whether immune systems primed by vaccination and then challenged with Omicron would be able to adapt the antibody response to be more specific to this variant.[16]

While a breakthrough infection boosts the immune response to SARS-CoV-2 in vaccinated people, as would be expected with an increased number of antigenic exposures, the ability of boosted antibodies to neutralize the virus was only "moderate", as described by the authors of a <u>study</u> published in *Cell* on January 19.[<u>17]</u>

Further evidence that antigenic sin might prove to be a problem with vaccination was provided by the aforementioned <u>study</u> published in *Cell* on January 24, which noted that immune imprinting appeared to be an obstacle to developing variant-specific COVID-19 vaccines.

The authors noted that while, in *immunologically naïve* individuals, infection with a SARS-CoV-2 variant "elicits variant-specific antibodies", "prior mRNA vaccination imprints serological responses toward" the original Wuhan strain of the virus "rather than variant antigens."

Vaccination also generates an immune response biased toward production of IgG antibodies, with comparatively "weak IgM and IgA responses" toward the spike protein. "Unlike infection," the authors commented, "which stimulates robust but short-lived IgM and IgA responses, vaccination shows a pronounced bias for IgG production even at early time points."

"Correlates of immunological protection from SARS-CoV-2 infection following vaccination or prior infection are still under investigation", the authors further noted. While they didn't explicitly say so, this means that just because vaccinated people generate a high level of IgG antibodies that bind to the spike protein of variants—even higher than observed in naturally immune people—does not necessarily mean that vaccinated people have greater protection. [18]

(In fact, a consistent observation in the literature is that a *higher* level of IgG antibodies is associated with *more severe* COVID-19, which association exists independently from age, whereas people whose immune systems are highly effective at fighting the virus tend to produce a comparatively low level of antibodies.[<u>19</u>])

Additionally, with natural immunity, the binding of IgG antibodies to the receptor binding domain (RBD) of the spike protein of variants, which is the specific part of the protein that enables the virus to enter human cells, was observed to improve over time relative to binding to the ancestral strain, "suggesting evolution of the antibody response through at least 7 weeks post-onset of symptoms"; whereas variant binding ratios in vaccinated people "did not change from day 21 onward." There was "improvement in variant recognitions over time in the infected patients", but not so much in vaccinated people.

The study went further, testing the hypothesis that original antigenic sin occurs with vaccination:

To test whether prior exposure to one SARS-CoV-2 RBD variant causes imprinting of humoral immunity, we analyzed plasma from individuals vaccinated with Wuhan-Hu-1 [ancestral strain] antigens and subsequently infected with Alpha or Delta variants. Despite breakthrough infection with Alpha or Delta viral variants, the vaccinated individuals showed patterns of IgG binding to viral variant RBDs similar to those of individuals exposed to only Wuhan-Hu-1.

In other words, the study findings suggest that while the immune responses of people with natural immunity are adaptive, resulting in an "updated" antibody response over time that is more specific to a newly infecting variant, the immune system of vaccinated people has an

impaired ability to do so and instead persists in generating antibodies specific to the extinct ancestral strain.

There was "improvement in variant recognitions over time in the infected patients", but not so much in vaccinated people.

Oddly, the authors nevertheless speculated that "antibodies from infection may provide somewhat decreased protection against virus variants compared to comparable concentrations of antibodies stimulated by vaccination."

That conclusion appears to ignore their observation that correlates of immunity have not yet been established as well as their finding of greater adaptability of the immune response in people with natural immunity, whereas "vaccine-derived imprinting affects subsequent antibody responses stimulated by vaccination as well as infection."[20]

Importantly, it is also *not* what is observed in real world data on the effectiveness of vaccineinduced versus natural immunity. Studies have consistently demonstrated that superior protection is conferred by natural immunity. Even CDC researchers have since acknowledged this fact, despite the CDC having previously propagated the disinformation that "people get better protection by being fully vaccinated compared with having had COVID-19."[21]

A possible explanation for the inclusion of that obvious non sequitur fallacy in the *Cell* paper is the fact that the study was funded by the NIH and its subagency the National Institute for Allergy and Infectious Disease (NIAID), under the directorship of Dr. Anthony Fauci.

"[V]accine-derived imprinting affects subsequent antibody responses stimulated by vaccination as well as infection."

Tangentially, the study authors noted that—contrary to <u>claims from faux "fact checkers"</u> that the mRNA from the vaccines is rapidly eliminated from the body "within days"—vaccine mRNA was found to persist in some cases "for up to two months" following receipt of the second dose.[22]

Similarly, while the ridiculous "fact checkers" have insisted that the spike protein generated by the mRNA COVID-19 vaccines is harmless and eliminated from the body "within days", the study authors observed circulation of spike protein in the blood and persistence of abundant spike antigen in vaccinated individuals two months after receipt of the second dose.[23]

Additionally, <u>numerous studies have shown that the spike protein by itself is pathogenic</u>, which has been <u>hypothesized</u> as a potential mechanism explaining the association of COVID-19 vaccines with <u>an increased risk of myocarditis.[24]</u>

The occurrence of original antigenic sin in vaccinated people was further confirmed by a <u>study</u> whose lead author, Jasmin Quandt, is affiliated with BioNTech, the German company that partnered with Pfizer to produce the Pfizer-BioNTech COVID-19 vaccine. The study, published on the preprint server *bioRxiv* on April 1, showed that Omicron infection in individuals whose immune system was primed by vaccination results in a boosting of antibodies capable of neutralizing the variant. However, this was *not* because their immune repertoire was adaptive and expanded to become more specific to the variant.

Instead, it was simply because the spike protein of Omicron, despite numerous mutations, is similar enough to the spike protein of the original Wuhan strain that vaccinees' fixated immune response to the ancestral strain still managed to recognize the variant.

The authors observed "imprinting of the immune response by previous vaccination" so that Omicron breakthrough infection "primarily expands preformed memory B cells that recognize epitopes shared broadly by different variants, rather than inducing new B cells against strictly Omicron-specific epitopes." In fact, in contrast to the boost in the memory B cell response "directed against epitopes shared by both Wuhan and Omicron BA.1 SARS-CoV-2 variants", the researchers "could hardly detect only Omicron-RBD-specific" memory B cells.

Naturally, the authors spun their concerning finding of "possible imprinting of the immune response by previous vaccination" into a positive outcome, lauding the ability of vaccinated individuals to still generate immune responses against the Omicron variant.[25]

Federal regulators and "public health" officials are not unaware of the problem of original antigenic sin. Dr. Paul Offit, a member of the FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC), which has made recommendations for the FDA to authorize or approve COVID-19 vaccines for various populations, wrote a commentary published in the *New England Journal of Medicine* on April 28 acknowledging this risk.

Astonishingly, Offit admitted that—contrary to how the vaccines were originally sold to the public—it was always "expected" that the protection against symptomatic infection would be short-lived. Studies by Pfizer, he noted, had shown that a booster dose could restore protection against mild illness, but "unfortunately, this protection did not persist for more than a few months."

Even more remarkably, he acknowledged:

In addition, because boosters are not risk-free, we need to clarify which groups most benefit. For example, boys and men between 16 and 29 years of age are at increased risk for myocarditis caused by mRNA vaccines. And all age groups are at risk for the theoretical problem of an "original antigenic sin"—a decreased ability to respond to a new immunogen because the immune system has locked onto the original immunogen. An example of this phenomenon can be found in a study of nonhuman primates showing that boosting with an omicron-specific variant did not result in higher titers of omicron-specific neutralizing antibodies than did boosting with the ancestral strain. This potential problem could limit our ability to respond to a new variant.[26]

In another <u>study</u> funded by the NIH and NIAID, published at *medRxiv* on April 19, researchers reexamined data from the clinical trials for Moderna's COVID-19 vaccine and confirmed that people whose immune system is primed by the vaccine, which is narrowly focused on eliciting antibodies to the spike protein, have an impaired ability to generate antibodies to other parts of the virus. Whereas antibodies to the nucleocapsid protein were generated in 93 percent of people with lab-confirmed COVID-19 in the placebo group, the anti-N antibody seroconversion rate with breakthrough infections among the vaccinated was only 40 percent.

A potential explanation for this was that unvaccinated people experience a higher viral load than vaccinated individuals, resulting in a higher level of antibodies against the N protein. However, after taking this hypothesis into account, they found that "viral copies at the illness visit did not fully explain the large differences" in seropositivity between the vaccine and control groups. In fact, "for any given viral copy number, the odds of anti-N seropositivity were 13.67 times higher for the placebo arm than the vaccine arm."

The primary relevance the authors saw in this finding was that "Conclusions about the prevalence and incidence of SARS-CoV-2 infection in vaccinated persons based on antinucleocapsid antibody assays need to be weighed in the context of these results." In other words, if studies use anti-N assays to determine the rate of breakthrough infections among vaccinated individuals, they are likely to underestimate the rate of breakthrough infections.

They offered no comment about how their finding showed that evidence of original antigenic sin *was always right there in the clinical trial data* that the FDA used as the basis for its emergency use authorization and subsequent licensure of the Moderna vaccine.[27]

"And all age groups are at risk for the theoretical problem of an 'original antigenic sin'—a decreased ability to respond to a new immunogen because the immune system has locked onto the original immunogen."

The occurrence of original antigenic sin might help to explain the finding of another recent <u>study</u> that while a booster dose in individuals whose immune systems were primed by vaccination results in protection against the Omicron variant "beyond that afforded by the

primary series", which was "low" to begin with, *no such benefit* of a booster dose was found in individuals who had acquired natural immunity prior to getting vaccinated.[28]

That could be explained simply because the immunological imprinting from infection enables more broadly adaptive immune responses compared to the antigenic fixation that occurs with people whose imprinting is due to vaccination.

The medical establishment's cognitive dissonance on this point is startling. To illustrate, we are being told that a reinfection is bad, an outcome to be avoided by getting vaccinated, while fully vaccinated and boosted individuals are being reassured that breakthrough infection is a *good* thing. The media have <u>reported</u> on studies' findings that breakthrough infection serves as a natural booster by describing the outcome as "<u>super immunity</u>".[29]

"We should think about breakthrough infections as essentially equivalent to another dose of vaccine," immunologist John Wherry told *WebMD*.[30]

Never mind that we can anticipate from the evidence available to date that an asymptomatic or mild reinfection with Omicron among individuals who had previously acquired natural immunity from infection with another variant of SARS-CoV-2 will also serve as *an even more effective* natural booster. (The sustenance of immunity against disease due to reexposure to previously encountered pathogens is an important phenomenon that is sometimes referred to as "<u>exogenous boosting</u>" in the medical literature.[<u>31</u>])

One notable shortcoming among most studies examining the varying immune responses of individuals based on differing combinations of antigen exposures is failure to control for the time since the last exposure. Whether induced by infection or vaccination, immunity does wane over time, so the duration of potential waning is an important factor to consider.

"Importantly, the CDC study also showed no significant benefit of vaccination for those with pre-existing natural immunity when it came to protection against hospitalization."

For example, a CDC <u>study</u> showing that natural immunity offered superior protection against the Delta variant compared to being fully vaccinated also claimed that the rate of COVID-19 diagnosis was lowest among those who got vaccinated after recovering from infection (so-called "hybrid immunity"). However, this could simply be an artifactual finding resulting from the failure of CDC researchers to control for time since last antigen exposure rather than being a true effect of vaccination among those with prior infection. Essentially, *by virtue of the study's design*, those who were also vaccinated would be more likely to have had a more recent antigen exposure (i.e., the vaccination).

Importantly, the CDC study also <u>showed no significant benefit of vaccination</u> for those with pre-existing natural immunity when it came to protection against hospitalization.[32]



Uniquely, a <u>study</u> published in the *New England Journal of Medicine* on May 25 took this into consideration and controlled for "time since the last immunity-conferring event", with findings that once again indicate that the immune imprinting from vaccination *impairs* the immune response relative to the imprinting that results from infection.

Their results showed that natural immunity still offered significantly better protection *even after a full year of potential waning* than being fully vaccinated *at only two to four months* since receipt of the second dose. (The rate of confirmed infection among those with natural immunity was 30.2 [28.5–32.0] per 100,000 person-days at risk at twelve months or more since infection, compared to a rate of 88.9 [88.2–89.5] among the fully vaccinated at two to four months.)

Additionally, the study showed that among those with "hybrid" immunity, those whose immune systems were primed by infection (with subsequent vaccination) were significantly better protected than those whose immune systems were primed by vaccination (with subsequent breakthrough infection). (The rate was 11.6 [10.0–13.5] per 100,000 person days at risk among the former compared to 16.2 [14.0–18.5] among the latter, with no overlap in confidence intervals.)

Importantly, the supposed "super immunity" induced by breakthrough infection in fully vaccinated individuals was *not* significantly greater than natural immunity alone. At six to eight months since the last immunity-conferring event, which was the longest duration observed for vaccinated individuals, the respective case rates for those with natural immunity, those who got vaccinated after recovering from infection, and those who

experienced infection after getting vaccinated had overlapping confidence intervals. (The rates, respectively, were 14.0 [13.3–14.8] per 100,000 person-days at risk, 11.6 [10.0–13.5], and 16.2 [14.0–18.5].)

Cohort and Subcohort	Adjusted Rate (95% CI)†	Rate Ratio (95% CI)	Rate Ratio (95% CI)
		Reference Subcohort vs. Other Subcohort	Subcohort with Most Recent Immunity-Conferring Event vs. Other Subcohort
	no. of confirmed infections/ 100,000 person-days at risk		
Recovered, unvaccinated coho	rt		
4 to <6 mo subcohort	10.5 (8.8-12.4)	2.0 (1.7-2.4)	Reference
6 to <8 mo subcohort	14.0 (13.3-14.8)	1.5 (1.4-1.6)	0.7 (0.6-0.9)
8 to <10 mo subcohort	20.6 (19.1-22.1)	1.0 (0.9–1.1)	0.5 (0.4-0.6)
10 to <12 mo subcohort	28.5 (26.9-30.2)	0.7 (0.7–0.8)	0.4 (0.3–0.4)
≥12 mo subcohort	30.2 (28.5-32.0)	0.7 (0.6-0.8)	0.3 (0.3-0.4)
Three-dose cohort			
0 to <2 mo subcohort	8.2 (8.0-8.4)	2.6 (2.4–2.7)	Reference
Two-dose cohort			
0 to <2 mo subcohort	21.1 (20.0-22.4)	Reference	Reference
2 to <4 mo subcohort	45.1 (43.8-46.5)	0.5 (0.4-0.5)	0.5 (0.4-0.5)
4 to <6 mo subcohort	69.4 (68.7–69.9)	0.3 (0.3-0.3)	0.3 (0.3-0.3)
6 to <8 mo subcohort	88.9 (88.2-89.5)	0.2 (0.2-0.3)	0.2 (0.2-0.3)
Recovered, one-dose cohort			
0 to <2 mo subcohort	3.7 (3.1-4.5)	5.7 (4.6-6.9)	Reference
2 to <4 mo subcohort	4.3 (3.5-5.2)	5.0 (4.0-6.1)	0.9 (0.7-1.2)
4 to <6 mo subcohort	10.3 (9.4–11.4)	2.0 (1.8-2.3)	0.4 (0.3-0.4)
6 to <8 mo subcohort	11.6 (10.0–13.5)	1.8 (1.5-2.2)	0.3 (0.3-0.4)
One-dose, recovered cohort			
4 to <6 mo subcohort	10.6 (7.6–15.0)	2.0 (1.4-2.8)	Reference
6 to <8 mo subcohort	16.2 (14.0-18.5)	1.3 (1.1-1.5)	0.7 (0.5-0.9)



Humorously, the study authors noted that their findings "did not appear to support" the CDC's claim that vaccination provides greater protection than natural immunity, which might be due to the CDC's failure to control for time since last antigen exposure (i.e., comparing the protectiveness of natural immunity after a year or more of potential waning with the protectiveness within just a few months since vaccination, prior to the dramatic waning of immunity observed in vaccinated people by six months out).

The authors chose *not* to highlight, however, the implication from their data that immunologic priming by vaccination appeared to *impair* the ability of vaccinated individuals to mount a protective immune response relative to those who were vaccinated after first having acquired natural immunity.[<u>33]</u>

The occurrence of original antigenic sin in vaccinated individuals was again demonstrated in a <u>study</u> published at *bioRxiv* on June 2 appropriately titled "Imprinted antibody responses against SARS-CoV-2 Omicron sublineages". The authors observed an "immunological imprinting" whereby antibodies derived from plasma cells or memory B cells in vaccinated individuals with an Omicron breakthrough infection were characteristic of a response to the ancestral strain that happened to cross-react with Omicron variants, whereas antibodies in individuals whose acquired immunity came from primary infection with Omicron were specific to the infecting variant.

As the authors bluntly stated, "Omicron breakthrough infections failed to elicit BA.1- or BA.2 RBD-specific antibodies", which findings "illustrate how immunological imprinting from prior exposure, i.e., 'original antigenic sin', can strongly affect the response to antigenically novel antigens."

Whereas their findings indicated that, due to this immunologic imprinting, "an Omicron-based vaccine might only elicit narrow antibody responses directed towards the vaccine-matched antigen", Omicron infection in people with pre-existing natural immunity "recalls cross-reactive memory B cells which may further mature over time to enhance their affinity and neutralizing potency against Omicron, but also to broaden their neutralizing activity against past and future variants."[<u>34</u>]

The mainstream media, of course, naturally spin such findings into *good* news for vaccinated people—just as the failure of vaccines to protect against infection has been spun as inducing "super immunity", whereas exogenous boosting among the unvaccinated with natural immunity, regardless of symptoms (or lack thereof), is characterized as a lamentable and indeed condemnable outcome, blamed on a failure of the individuals to adhere to "public health" officials' recommendations to get vaccinated.

As an example of media spin that would be laughable were it not such a serious matter, *Fortune* magazine reported on the study by claiming it showed that unvaccinated people who had an Omicron infection "did not have a similarly robust and protective immune response" as vaccinated people with Omicron breakthrough infection—a curious interpretation indeed given the explicit acknowledgment that original antigenic sin is a problem for individuals whose immune systems are primed by vaccination, whereas those with a primary Omicron infection developed effective immune responses specific to the infecting variant, and whereas the immune responses of those with pre-existing immunity from a prior infection were capable of adaptation to the new variant.

#### The Cognitive Dissonance of the "Public Health" Establishment

Finally, another <u>study</u> published in *Science* just last week, on June 14, further confirmed that the phenomenon of original antigenic sin is relevant for cellular immunity as well as the antibody response of vaccinated people.

While sterilizing immunity depends on the ability of antibodies to neutralize the virus before it has a chance to infect cells, the authors noted that cellular immunity is critical for limiting and clearing infection and thereby protecting against severe COVID-19. So, they set out to examine both B cell and T cell responses to Omicron breakthrough infection among triple-vaccinated individuals.

Studies had already demonstrated "that people at this stage in the pandemic carry heterogeneous, immune-imprinted repertoires derived from their distinctive histories of infection and vaccination", so they further explored "how these differences manifest in differential, cross-recognition of B.1.1.529 (Omicron)" relative to other "variants of concern" and "the extent to which prior encounter with spike antigen through infection and vaccination shapes subsequent immunity" to the Omicron variant "through immune imprinting."

In keeping with the spin that breakthrough infection induces "super immunity", the authors remarked that it is possible that Omicron breakthrough infection "may confer a benign, live booster to vaccine immunity"—while omitting any mention that an Omicron infection in people who had previously recovered from infection with an earlier variant can also be generally expected to confer a benign boost to their natural immunity.

Importantly, while attempting to blame the occurrence of original antigenic sin on the immune response to *infection*, the study authors *only* examined the immune responses of *triple-vaccinated* individuals.

Looking at B cell immunity, they found that those who were infected early in the pandemic with the ancestral Wuhan strain showed "a significantly reduced" level of antibodies targeting the receptor binding domain of the respective spike proteins of Beta, Gamma, and Omicron variants, although cross-reactive antibodies against Omicron "were significantly reduced" compared to other variants "irrespective of previous SARS-CoV-2 infection history", as were frequencies of memory B cells against Omicron after receipt of the third dose of vaccine.

Astonishingly, they found that "more than half"—54 percent—of triple-vaccinated individuals "made no T cell response" against the "S1" domain of the Omicron spike protein "irrespective of previous SARS-CoV-2 infection history", which compares with only 8 percent who made no T cell response against the ancestral Wuhan strain.

Looking beyond the spike protein, they found that 42 percent of triple vaccinated people "make no T cell response at all" against mutated Omicron peptides distinguishing this variant from the ancestral strain. (A peptide is a chain of amino acids typically shorter than a protein, either of which can be an epitope, or a molecular region on the surface of an antigen capable of eliciting an immune response.)

Additionally, breakthrough infection with Omicron "produced potent cross-reactive antibody" against earlier variants, "but less so against B.1.1.529 (Omicron) itself."

Triple vaccinated individuals *without* Omicron breakthrough infection, by contrast, made *no* neutralizing antibodies against Omicron by fourteen weeks after the third vaccine dose, "indicating rapid waning" of the neutralizing antibodies induced by the booster shot.

Similarly, fourteen weeks after the third dose, 90 percent of triple-vaccinated individuals with no prior history of infection "showed no cross-reactive T cell immunity" against the Omicron spike protein. *None* of those with a history of infection with the ancestral strain showed such immunity, indicating that three doses of vaccine were "unable to boost T cell immunity" against Omicron in these individuals.

The effect of original antigenic sin was observed to be greatest among those who were infected with the ancestral strain and then later got fully vaccinated and boosted. Whereas Omicron breakthrough infection was seen to boost binding and neutralizing antibody responses to the Omicron variant in triple vaccinated but previously uninfected individuals, this did *not* occur in those previously infected with the Wuhan strain.

The authors remarked that "Immune imprinting by prior Wuhan Hu-1 infection completely abrogated any enhanced nAb [neutralizing antibody] responses against B.1.1.529 (Omicron) and other VOC [variants of concern]".

However, what they really meant is that immune imprinting by prior infection with the ancestral strain *followed by three doses of COVID-19 vaccine* completely abrogated the antibody response against other variants.

"Importantly, while attempting to blame the occurrence of original antigenic sin on the immune response to infection, the study authors only examined the immune responses of triple-vaccinated individuals."

Similarly, they commented that "immune imprinting from prior Wuhan Hu-1 infection resulted in absence of a T cell response" against the S1 domain of the Omicron spike protein, the true meaning of which, of course, is that this immune imprinting was the effect of infection *plus three doses of a vaccine designed to elicit an immune response against the spike protein of the ancestral strain.* 

In another illustration of cognitive dissonance, the authors observed that "functional neutralization by vaccine-primed sera is considerably blunted" against the Omicron variant *regardless of prior infection history*, which they blamed the effect of immune imprinting from natural infection by stating, "That previous SARS-CoV-2 infection history can imprint such a profound, negative impact on subsequent protective immunity is an unexpected consequence of COVID-19."

Recall again the observation from over half a century ago that the effect of original antigenic sin is attributable not merely to the initial antigen exposure but also to "repeated stimulation" with the same antigen.

Shockingly, the study authors appear to have completely dismissed the possibility that it may have been the subsequent three-dose vaccination of these individuals that resulted in this immunologic fixation on the spike protein of a variant that is no longer circulating among the human population.

Their implicit claim that three vaccine doses did *not* exacerbate the problem of original antigenic sin in those with a prior history of infection with the ancestral strain is unsupportable by their data, which did *not* provide a comparison of the immune responses of *unvaccinated* individuals with a prior history of infection and who then became infected with Omicron.[35]

As already noted, other studies have indicated that, in most people, a history of prior infection, far from being associated with an impaired immune response to SARS-CoV-2, results in a robust immune repertoire characterized by well-coordinated cellular and humoral responses and induction of long-term immunologic memory capable of specific adaptation to newly emerging variants.

The study authors' effort to avoid pointing out the elephant in the room—the fact that having received three doses of COVID-19 vaccine would exacerbate the effect of original antigenic sin—is a remarkable testimony to the level of cognitive dissonance required to maintain faith in these pharmaceutical products as a universally necessary medical intervention.

### Original Antigenic Sin Helps Explain Negative COVID-19 Vaccine Effectiveness

The occurrence of original antigenic sin among vaccinated people helps to explain repeated observations of *negative* vaccine effectiveness over time, as the short-term protective effect of these pharmaceutical products wears off.

As I have <u>previously reported</u>, a <u>study</u> by researchers in Denmark published at *medRxiv* on December 23, 2021, found a statistically significant negative effectiveness against infection with the Omicron variant among fully vaccinated individuals. Vaccine effectiveness waned rapidly from about 55 percent during the first month to *no significant effectiveness* after just one month.

Moreover, three months after receipt of the second dose, effectiveness became *significantly negative*, meaning that fully vaccinated people were *more* likely than unvaccinated people to become infected with SARS-CoV-2.[<u>36</u>]



Time (days) since full vaccine protection (14 days post 2nd dose)

**Figure** Vaccine effectiveness against SARS-CoV-2 infection with the Delta and Omicron variants, shown separately for the BNT162b2 and mRNA-1273 vaccines. Vertical bars indicate 95% confidence intervals.

The authors of the study attributed that finding to differences in behavior between vaccinated and unvaccinated people, which is somewhat plausible considering the policy discrimination against unvaccinated people during the study period. It may be that, while unvaccinated people were restricted from participation in society, vaccinated people were simply more likely to put themselves into situations where there was a high chance of exposure to the virus.

It is also plausible that the finding was at least in part due to the inferiority of vaccine-induced immunity relative to natural immunity and the occurrence of detrimental immune imprinting among the fully vaccinated. This latter interpretation is supported by data from other studies likewise showing negative vaccine effectiveness.

A <u>study</u> by researchers in Canada published at *medRxiv* on January 1 of this year similarly found that "receipt of 2 doses of COVID-19 vaccines was not protective against Omicron at any point in time". While a booster dose provided "some protection in the immediate term", effectiveness peaked at only 37 percent—and it is known that the protective effect of booster shots wanes rapidly just as with the primary series.

Moreover, among the fully vaccinated and unboosted, statistically significant *negative* effectiveness was observed after just four months since receipt of the second dose.



Receipt of at least 1 mRNA vaccine for the 2-dose primary series

While the authors of that study also proposed that this could be an artifact of differences in behavior between vaccinated and unvaccinated people, they acknowledged the possibility that their data was evidence that "antigenic imprinting" by vaccination had a detrimental long-term effect on immunity.[<u>37]</u>

While a booster shot might delay the negative consequences, as the head of the Biological Health Threats and Vaccines Strategy division of the European Medicines Agency (EMA), Marco Caveleri, has <u>warned</u>, "While use of additional boosters can be part of contingency plans, repeated vaccinations within short intervals would not represent a sustainable long-term strategy."

The EMA official further cautioned, "If we have a strategy in which we give boosters every four months approximately, we will end up potentially having problems with the immune response, and the immune response may end up not being as good as we would like it to be, so we should be careful in not overloading the immune system with repeated immunization."[38]

A press release from the EMA on January 11 cited preliminary data provided by a UK Health Security Agency technical briefing indicating that a booster dose increased vaccine effectiveness against hospitalization to 90 percent (which was rounded up from the actual figure presented in the briefing of 88 percent).[<u>39</u>]

However, that was the observed effect at only two weeks since administration of the booster, and the same data <u>showed</u> that the effectiveness of the booster dose against symptomatic infection *rapidly waned* from around 70 percent within two to four weeks after third-dose administration to 45 percent after just two months.

Furthermore, the same dataset revealed that two doses of COVID-19 vaccine resulted in significantly *negative* effectiveness against Omicron within six months.[40]



As I <u>reported</u> earlier this month, studies have also been published showing negative COVID-19 vaccine effectiveness in children.[41]

A <u>study</u> by researchers from the New York State Department of Health published at *medRxiv* on February 28 showed rapidly waning vaccine effectiveness against Omicron infection among children. Among adolescents aged twelve to seventeen, effectiveness dropped from 76 percent initially to under 50 percent *after just five weeks* since receipt of the second dose.

For children aged five to eleven, vaccine effectiveness dropped from 65 percent to just 12 percent after only one month, and thereafter the data indicated significantly *negative* effectiveness. Within six weeks of the second dose, vaccine effectiveness fell to negative 10 percent, and within seven weeks, it plummeted further to negative 41 percent.

# Figure 2: Incidence rate ratios, comparing cases during January 3 - January 30, 2022 for unvaccinated versus children newly fully-vaccinated December 13, 2021-January 2, 2022, by Time Since Full Vaccination



<sup>a</sup> Negative VE values observed in later timepoints likely reflect estimator instability and/or residual confounding, as opposed to true relativelyincreased risk for those vaccinated.

The authors asserted that there was nevertheless "sustained protection against severe disease" among adolescents. However, that description hardly seems appropriate considering the fact that their data showed vaccine effectiveness against severe disease falling from 94 percent to 73 percent after just two months. Vaccine effectiveness against hospitalization among younger children lost statistical significance within the same time frame.

The health department researchers relegated their comment about this observed negative effectiveness to a footnote, stating that estimates of negative effectiveness "likely reflect estimator instability and/or residual confounding, as opposed to true relatively-increased risk for those vaccinated." However, this dismissal is irresponsibly speculative, and this finding could very well indicate a detrimental effect of COVID-19 vaccines in children.[42]

The data from New York were also <u>published</u> in *JAMA* on May 13. Gone from this version were the corresponding estimates of vaccine effectiveness, but the reported incident rate ratios presented, which compare the rate of COVID-19 cases among fully vaccinated children with unvaccinated children, still show *negative* vaccine effectiveness for children aged five to eleven within six weeks of receipt of the second dose. Within seven weeks, the negative effectiveness reached statistical significance.



Figure. New COVID-19 Cases Among Unvaccinated Children vs Fully Vaccinated Children by Time Since Vaccination and Age Group

Once again, the health department researchers demonstrated reckless disregard for the health of children by dismissing this finding as an artifact, bewilderingly concluding that their findings "support efforts to increase vaccination coverage in children and adolescents".[43]

This is a useful illustration of how authors' conclusions frequently are either unsupported or *contradicted* by their own data. It also illustrates the tendency of "public health" officials to succumb to confirmation bias, accepting data that supports their policy recommendations while willfully ignoring findings that do not, such as this data suggesting that by urging parents to vaccinate their children, they might be ultimately causing these children to be *more* susceptible to COVID-19 *throughout their lifetimes*.

Another illustration of official confirmation bias comes from a separate <u>study</u> by CDC researchers also published in *JAMA* on May 13. Their data showed that vaccine effectiveness for children aged five to eleven years fell from 60 percent to 29 percent within two months, which was the extent of the observational follow-up for this age group.

Furthermore, the study showed *negative* vaccine effectiveness for children aged twelve to fifteen years by five months since receipt of the second dose.[44]



Since February, data published on the CDC's website has also <u>shown</u> a *higher* rate of COVID-19 among *vaccinated* children aged five to eleven than among unvaccinated children. As of this writing, the latest reported figures are a rate of 137 COVID-19 cases per 100,000 population among unvaccinated children compared to 194 cases per 100,000 population among those who are fully vaccinated.[45]



The CDC's own data showing that the protection afforded by COVID-19 vaccines in children rapidly wanes into *negative* vaccine effectiveness has naturally not prevented the agency from telling parents that they must get their children vaccinated—even though CDC data also indicates that <u>at least 75 percent of children</u> have already had SARS-CoV-2 infection, which means that those who weren't already vaccinated before becoming infected have already acquired the superior protection afforded by natural immunity.

Incidentally, the authors of the study showing that most children have already been infected noted that their estimate was conservative in part "because infections after vaccination might result in lower anti-N titers"—evidence for original antigenic sin conveniently ignored by the CDC apart from its interpretive relevance for seroprevalence.[46]

#### Conclusion

The COVID-19 vaccines were rushed through the developmental and regulatory processes with the pre-determined intent among policymakers to mass vaccinate the population. The clinical trials upon which emergency use authorization or licensure is based provided early evidence that the immunological phenomenon of "original antigenic sin" might be a problem with these pharmaceutical products, yet the "public health" establishment willfully blinded itself to this risk and has pushed these products on the population anyway, including now increasingly on children, who were already at very low risk of severe COVID-19 to begin with and are at even lower risk now that most have already acquired immunity.

Consequently, by recommending parents to vaccinate their children *without considering the opportunity cost*, policymakers may be responsible for *increasing* the risk of COVID-19 throughout their lifetimes. This is a reasonable conclusion to draw based on the data currently available, which consistently show that the vaccines offer only short-term protection, with waning of immunity to statistical insignificance and then to significantly *negative* effectiveness. We can also anticipate that booster shots will only delay rather than prevent this outcome.

Such observations of negative vaccine effectiveness are also being willfully ignored by public vaccine policy advocates, yet these observations are consistent with studies that have now demonstrated beyond any reasonable doubt that original antigenic sin is a real problem with these pharmaceutical products.

This also serves as another illustration of how public vaccine policy violates the right to informed consent. Logically, anyone unfamiliar with the term "original antigenic sin" is incapable of exercising truly informed consent when it comes to making a decision about whether or not to get vaccinated. While there have been rare acknowledgements of the risk of this phenomenon in the medical literature, such as by VRBPAC member Paul Offit, the risk has *not* been communicated to the public via statements from "public health" officials or reports in the mainstream media.

This speaks to intent. Rather than aiming to empower people with the knowledge they need to make a truly informed choice about whether to vaccinate themselves or their children, the "public health" establishment along with the media have chosen to engage in policy advocacy, aiming instead to persuade everyone to get vaccinated by exaggerating the benefits and downplaying or ignoring altogether the risks.

In short, what government officials and agencies like the CDC do is to issue endless propaganda, while the media advocate public vaccine policy rather than doing journalism. As always, what the government and media *say* science says about vaccines and what the science actually tells us are two completely different things. This is certainly no less true for COVID-19 vaccines than for other vaccines recommended by the supposed "authorities" who are evidently more concerned with exercising power and control over the population and generating profits for the pharmaceutical industry than in ensuring good public health.

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