https://jamesfetzer.org/2021/07/letter-to-physicians-four-new-scientific-discoveries-regarding-the-safety-and-efficacy-of-covid-19-vaccines/

Letter to Physicians: Four New Scientific Discoveries Regarding the Safety and Efficacy of COVID-19 Vaccines

James Fetzerblog

By Doctors for COVID Ethics

SCIENTISTS CONCLUDE
THE BENEFIT OF COVID-19 VACCINATION IS "HIGHLY DOUBTFUL"
BUT VACCINE INJURY IS "WELL SUBSTANTIATED"

Doctors for Covid Ethics has sent the following letter to tens of thousands of doctors in Europe, summarising four recent scientific findings critical to the COVID-19 vaccination program. The letter explains each finding as it relates to the biology of COVID-19 vaccines, including interactions with the immune system. Taken together, the letter warns that these new pieces of evidence force all physicians administering COVID-19 vaccines to re-evaluate the merits of COVID-19 vaccination, in the interests of their own ethical standing, and their patients' safety and health. A video explanation of the underlying immunology by **Professor Sucharit Bhakdi** MD is here, with German subtitles here.

Dear Colleague:
Four recent scientific discoveries are herewith brought to your urgent attention. They alter the entire landscape of the COVID-19 pandemic, and they force us to reassess the merits of vaccination against SARS-CoV-2.

Summary

Rapid and efficient memory-type immune responses occur reliably in virtually all unvaccinated individuals who are exposed to SARS-CoV-2. The effectiveness of further boosting the immune response through vaccination is therefore highly doubtful. Vaccination may instead aggravate disease through antibody-dependent enhancement (ADE).

Discovery 1: SARS-CoV-2 spike protein circulates shortly after vaccination

SARS-CoV-2 proteins were measured in longitudinal plasma samples collected from 13 participants who received two doses of Moderna mRNA-1273 vaccine [1]. With 11 of the 13, the SARS-CoV-2 spike protein was detected in the blood within only one day after the first vaccine injection.
Significance. Spike protein molecules were produced within cells that are in contact with the bloodstream—mostly endothelial cells—and released into the circulation. This means that a) the immune system will attack those endothelial cells, and b) the circulating spike protein molecules will activate thrombocytes. Both effects will promote blood clotting. This explains the many clotting-related adverse events—stroke, heart attack, venous thrombosis—that are being reported after vaccination.

Discovery 2: Rapid, memory-type antibody response after vaccination

Several studies have demonstrated that circulating SARS-CoV-2-specific IgG and IgA antibodies became detectable within 1-2 weeks after application of mRNA vaccines [1–3].
Significance. Rapid production of IgG and IgA always indicates a secondary, memory-type response that is elicited through re-stimulation of pre-existing immune cells. Primary immune responses to novel antigens take longer to evolve and initially produce IgM antibodies, which is then followed by the isotype switch to IgG and IgA. A certain amount of IgM was indeed detected alongside IgG and IgA in some studies [1,4]. Importantly, however, IgG rose faster than IgM [4], which confirms that the early IgG response was indeed of the memory type. This memory response indicates pre-existing, cross-reactive immunity due to previous infection with ordinary respiratory human coronavirus strains. The delayed IgM response most likely represents a primary response to novel epitopes which are specific to SARS-CoV-2. Memory-type responses have also been documented with respect to T-cell-mediated immunity [5–7]. Overall, these findings indicate that our immune system efficiently recognizes SARS-CoV-2 as "known" even on first contact. Severe cases of the disease thus cannot be ascribed to lacking immunity. Instead, severe cases might very well be caused or aggravated by pre-existing immunity through antibody-dependent enhancement (ADE, see below).

Discovery 3: SARS-CoV-2 elicits robust adaptive immune responses regardless of disease severity

Serum antibody profiles were reported for 203 individuals following SARS-CoV-2 infection [8]. 202 (>99%) of the participants exhibited SARS-CoV-2 specific antibodies. With 193 individuals (95%), these antibodies prevented SARS-CoV-2 infection in cell culture and also inhibited binding of the spike protein to the ACE2 receptor. Furthermore, CD8+ T-cell responses specific for SARS-CoV-2 were clear and quantifiable in 95 of 106 (90%) HLA-A2-positive individuals.
Significance. This study confirms the above assertion that the immune response to initial contact with SARS-CoV-2 is of the memory type. In addition, it shows that this reaction occurs with almost all individuals, and particularly also with those who experience no manifest clinical symptoms. The goal of the vaccination is to stimulate production of antibodies to SARS-CoV-2, but we now know that such antibodies can and will be rapidly generated by everyone upon the slightest viral challenge, even without vaccination. Severe lung infections always take many days to develop, which means that if the antibodies generated by the memory response are needed, they will arrive on time. Therefore, v accination is unlikely to provide significant benefit with respect to the prevention of severe lung infection.

Discovery 4: Rapid increase of spike protein antibodies after the second injection of mRNA vaccines

IgG and IgA antibody titres were monitored before vaccination and after the first and the second injection of mRNA vaccines [3]. Antibody titres rose with some delay after the first injection, then plateaued, but rose again very shortly after the second injection.

Significance. Even though the antibody response to the first injection is of the memory type, the small time lag after the injection may mitigate adverse reactions, because the abundance of spike protein on the cells in the blood vessel walls and in other tissues may have already passed its peak when the antibodies arrive. The situation changes dramatically with the second injection. Then the spikes are produced and protrude into the bloodstream that is already swarming with both reactive lymphocytes and antibodies. The antibodies will cause the complement system [9,10] and also neutrophil granulocytes to attack the spike protein-bearing cells. The possible consequences of all-out self-attack by the immune system are frightening.

Antibody-dependent enhancement of disease

As described, memory-type immune responses ensure the rapid rise of antibody titres after initial exposure to SARS-CoV-2, rendering the benefit of vaccine-induced antibody response exceedingly doubtful. Regardless, we should not assume that high antibody titres against SARS-CoV-2 will always improve the clinical outcome. With several virus families—in particular with Dengue virus, but also with coronaviruses—antibodies can aggravate rather than mitigate disease. This occurs because certain cells of the immune system take up antibody-tagged microbes and destroy them. If a virus particle to which antibodies have bound is taken up by such a cell, but it then manages to evade destruction, it may instead start to multiply within the cell. Overall, the antibody will then have enhanced the replication of the virus. Clinically, this antibody-dependent enhancement (ADE) can cause a hyperinflammatory response (a “cytokine storm”) that will amplify the damage to the lungs, liver and other organs of our body. Attempts to develop vaccines to the original SARS virus, which is closely related to SARS-CoV-2, repeatedly failed due to ADE. The vaccines did induce antibodies, but when the vaccinated animals were subsequently infected with the virus, they became more ill than the unvaccinated controls (see e.g. [11]). The possibility of ADE was not adequately addressed in the clinical trials on any of the COVID-19 vaccines. It is therefore prudent to avoid the danger of inducing ADE through vaccination and instead rely on proven forms of treatment [12] for dealing with clinically severe COVID-19 disease.

Conclusion

The collective findings discussed above clearly show that the benefits of vaccination are highly doubtful. In contrast, the harm the vaccines do is very well substantiated, with more than 15.000 vaccination-associated deaths now documented in the EU drug adverse events database (EudraVigilance), and over 7.000 more deaths within the UK and the US [13].

ALL PHYSICIANS MUST RECONSIDER THE ETHICAL ISSUES SURROUNDING COVID-19 VACCINATION.

Notes

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SINTESI IN ITALIANO: sui benefici della vaccinazione covid ci sono grossi dubbi, mentre i danni da vaccino sono molto ben documentati

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0. i non vaccinati reagiscono in modo rapido ed efficace a ogni esposizione a sarscov2, e quindi aumentare le difese coi vaccini è inutile e rischioso.
1. la proteina spike dei vaccini giunge a contatto con il sangue e attiva i trombociti causando, dopo il vaccino, trombosi, infarti, ictus, e coagulazioni.
2. gli anticorpi ci sono già prima del vaccino (IgG più precoci delle IgM), quindi il covid si aggrava per eccesso di anticorpi, cioè con la vaccinazione.
3. anche gli asintomatici sarscov2 hanno elevate difese immunitarie che sono pre-eeistenti al vaccino e più rapide dell'insorgenza dei sintomi covid.
4. la prima dose di vaccino riattiva anticorpi pre-esistenti, ma la seconda dose causa reazioni terrificanti, dove l'organismo può attaccare se stesso.
5. la rapida difesa naturale al sarscov2 rende dubbia l'utilità del vaccino, perché il vaccinato può ammalarsi molto più gravemente del non vaccinato.

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IJCP THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

PERSPECTIVE | Open Access

Informed consent disclosure to vaccine trial subjects of risk of COVID-19 vaccines worsening clinical disease

Timothy Cardozo, Ronald Veazey

First published: 28 October 2020 | https://doi.org/10.1111/ijcp.13795 | Citations: 2

il consenso informato per i "vaccini" covid e' viziato dalla grave omissione del rischio di ADE (covid piu' grave per colpa del vaccino)

Abstract

Aims of the study

Patient comprehension is a critical part of meeting medical ethics standards of informed consent in study designs. The aim of the study was to determine if sufficient literature exists to require clinicians to disclose the specific risk that COVID-19 vaccines could worsen disease upon exposure to challenge or circulating virus.

Methods used to conduct the study

Published literature was reviewed to identify preclinical and clinical evidence that COVID-19 vaccines could worsen disease upon exposure to challenge or circulating virus. Clinical trial protocols for COVID-19 vaccines were reviewed to determine if risks were properly disclosed.

Results of the study

COVID-19 vaccines designed to elicit neutralising antibodies may sensitise vaccine recipients to more severe disease than if they were not vaccinated. Vaccines for SARS, MERS and RSV have never been approved, and the data generated in the development and testing of these vaccines suggest a serious mechanistic concern: that vaccines designed empirically using the traditional approach (consisting of the unmodified or minimally modified coronavirus viral spike to elicit neutralising antibodies), be they composed of protein, viral vector, DNA or RNA and irrespective of delivery method, may worsen COVID-19 disease via antibody-dependent enhancement (ADE). This risk is sufficiently obscured in clinical trial protocols and consent forms for ongoing COVID-19 vaccine trials that adequate patient comprehension of this risk is unlikely to occur, obviating truly informed consent by subjects in these trials.

Conclusions drawn from the study and clinical implications

The specific and significant COVID-19 risk of ADE should have been and should be prominently and independently disclosed to research subjects currently in vaccine trials, as well as those being recruited for the trials and future patients after vaccine approval, in order to meet the medical ethics standard of patient comprehension for informed consent.

JOURNAL OF INFECTION

il rischio di ADE (anticorpi che invece di bloccare il virus lo aiutano, producendo sintomi covid più gravi nei vaccinati rispetto ai non vaccinati) adesso è ancora più alto perché le varianti delta del sarscov2 in pratica resistono ai vaccini

LETTER TO THE EDITOR | ARTICLES IN PRESS

Infection-enhancing anti-SARS-CoV-2 antibodies recognize both the original Wuhan/D614G strain and Delta variants. A potential risk for mass vaccination ?

Nouara Yahi • Henri Chahinian • Jacques Fantini

Published: August 09, 2021 • DOI: https://doi.org/10.1016/j.jinf.2021.08.010

Highlights

- Infection-enhancing antibodies have been detected in symptomatic Covid-19
- Antibody dependent enhancement (ADE) is a potential concern for vaccines
- Enhancing antibodies recognize both the Wuhan strain and Delta variants
- ADE of Delta variants is a potential risk for current vaccines
- Vaccine formulations lacking ADE epitope are suggested

Abstract

News

Covid-19: Delta infections threaten herd immunity vaccine strategy

BMJ 2021 ; 374 doi: https://doi.org/10.1136/bmj.n1933 (Published 02 August 2021)
Cite this as: *BMJ* 2021;374:n1933

i "vaccinati" covid si infettano ugualmente e la loro carica virale e' identica a quella dei non vaccinati; in altre parole i "vaccinati" sono contagiosi tanto quanto i non vaccinati

Owen Dyer

Author affiliations

Epidemiologists are adjusting their expectations for the future course of the pandemic after data from a recent outbreak in Massachusetts in the US suggest that while vaccination remains highly protective against the worst consequences of infection, it may not be sufficient on its own to stop the spread of the delta variant.

Testing conducted among Massachusetts residents during an outbreak in Provincetown, a popular weekend getaway spot, from 3 to 17 July found that 75% of those infected were fully vaccinated, in a state where 69% of adults were fully vaccinated.[1]

Among the vaccinated with breakthrough infections, the difficulty of detecting virus in the nasal passages, known as the cycle threshold value, was almost identical to that seen in the unvaccinated. This finding suggests that both groups carried equal viral loads and were equally likely to pass on their infections, the US Centers for Disease Control and Prevention (CDC) warned.

The results support claims that vaccinated people are playing a role in the summer surge in delta variant infections and led the CDC to reinstate its recommendation that vaccinated people wear masks indoors.

The CDC published the Provincetown data on 30 July, but a slide presentation mentioning the findings on viral load

Association of American Physicians and Surgeons Says COVID Shots Risk Millions of Lives

August 2, 2021 WND 0

Dr. Paul Kempen, MD, who leads the Association of American Physicians and Surgeons (AAPS), responded to mandatory COVID vaccines for health-care workers by pointing out that 30-million people have recovered from COVID-19 in the US and now have natural immunity. For them, the shots confer only risk with no benefit. It is absurd that they are not exempt from these mandates. A statement from AAPS warns that COVID cases, hospitalizations and deaths have increased at the same time that half of the US population was taking the inoculation. Long-term effects are unknown and may cause autoimmune disorders, antibody-enhanced disease, infertility, cancer, and birth defects. The benefit to the public is mythical, because uninfected people cannot transmit COVID. but vaccinated people can. Instead of taking the jab, the AAPS recommends early-treatment options, of which there are many. The AAPS acknowledges that everyone has a right to liberty, "which they do not forfeit when they serve the sick or the disabled." -GEG

The chief of an influential physicians organization that represents doctors in a multitude of practices is warning that making COVID-19 vaccinations mandatory could endanger millions.

The comments come from Dr. Paul Kempen, M.D., who leads the Association of American Physicians and Surgeons.

The Pfizer mRNA vaccine: pharmacokinetics and toxicity

Michael Palmer, MD and Sucharit Bhakdi, MD

July 23rd, 2021

Abstract

We summarize the findings of an animal study which Pfizer submitted to the Japanese health authorities in 2020, and which pertained to the distribution and elimination of a model mRNA vaccine. We show that this study clearly presaged grave risks of blood clotting and other adverse effects. The failure to monitor and assess these risks in the subsequent clinical trials, and the grossly negligent review process in conjunction with the emergency use authorizations, have predictably resulted in an unprecedented medical disaster.

1 Introduction and background

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Covid vaccines have now
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Moderna and Pfizer vaccine trials RIGGED by vaccinating the control group… blatant science FRAUD exposed

Tuesday, August 10, 2021 by: Lance D Johnson

Tags: badhealth, badmedicine, clinical fraud, Clinical trials, Collusion, control arm, corruption, deception, effectiveness, FDA, FDA approval, informed consent, Integrity, long-term effects, medical fraud, mutations, obscure data, pandemic, placebo, safety, science fraud, susceptibility, vaccine force

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La vaccination Covid à l'épreuve des faits. Deuxième partie : une mortalité inédite

La pharmacovigilance des vaccins anti-covid est déniée car elle menace l'idéologie de la vaccination intégrale portée par les industries pharmaceutiques, les gouvernements et les principaux médias. Cette vaccination de masse conduit pourtant à une mortalité inédite dans l'histoire de la médecine moderne. Il y a urgence à la suspendre pour évaluer la balance bénéfice/risque au cas par cas.

INSIDER

CDC says fully vaccinated people spread the Delta variant and should wear masks: 'This new science is worrisome'

Aria Bendix

Tue, July 27, 2021, 10:15 PM · 4 min read

THE LANCET

CORRESPONDENCE | VOLUME 398, ISSUE 10298, P385-387, JULY 31, 2021

Spike-antibody waning after second dose of BNT162b2 or ChAdOx1

Madhumita Shrotri • Annalan M D Navaratnam • Vincent Nguyen • Thomas Byrne • Cyril Geismar • Ellen Fragaszy • et al. Show all authors

Published: July 15, 2021 • DOI: https://doi.org/10.1016/S0140-6736(21)01642-1

Coronavirus COVID19

Fully Vaccinated People Are Contagious And Spread Delta Variant To The Unvaccinated Says CDC

July 29, 2021

People who have been fully vaccinated for COVID-19 yet still get infected with the delta strain could transmit the infection to unvaccinated people, Centers for Disease Control and Prevention Director Rochelle Walensky said Tuesday in justifying renewed recommendations for mask-wearing.

New Results

SARS-CoV-2 Lambda variant exhibits higher infectivity and immune resistance

Izumi Kimura, Yusuke Kosugi, Jiaqi Wu, Daichi Yamasoba, Erika P Butlertanaka, Yuri L Tanaka, Yafei Liu, Kotaro Shirakawa, Yasuhiro Kazuma, Ryosuke Nomura, Yoshihito Horisawa, Kenzo Tokunaga, Akifumi Takaori-Kondo, Hisashi Arase, The Genotype to Phenotype Japan (G2P-Japan) Consortium, Akatsuki Saito, So Nakagawa, Kei Sato

doi: https://doi.org/10.1101/2021.07.28.454085

Summary

SARS-CoV-2 Lambda, a new variant of interest, is now spreading in some South American countries; however, its virological features and evolutionary trait remain unknown. Here we reveal that the spike protein of the Lambda variant is more infectious and it is attributed to the T76I and L452Q mutations. The RSYLTPGD246-253N mutation, a unique 7-amino-acid deletion mutation in the N-terminal domain of the Lambda spike protein, is responsible for evasion from neutralizing antibodies. Since the Lambda variant has dominantly spread according to the increasing frequency of the isolates harboring the RSYLTPGD246-253N mutation, our data suggest that the insertion of the RSYLTPGD246-253N mutation is closely associated with the massive infection spread of the Lambda variant in South America.

Shedding of Infectious SARS-CoV-2 Despite Vaccination when the Delta Variant is Prevalent - Wisconsin, July 2021

Kasen K. Riemersma, Brittany E. Grogan, Amanda Kita-Yarbro, Peter Halfmann, Anna Kocharian, Kelsey R. Florek, Ryan Westergaard, Allen Bateman, Gunnar E. Jeppson, Yoshihiro Kawaoka, David H. O'Connor, Thomas C. Friedrich, Katarina M. Grande

doi: https://doi.org/10.1101/2021.07.31.21261387

The SARS-CoV-2 Delta variant and its sublineages (B.1.617.2, AY.1, AY.2, AY.3; [1]) can cause high viral loads, are highly transmissible, and contain mutations that confer partial immune escape [2,3]. Using PCR threshold cycle (Ct) data from a single large contract laboratory, we show that individuals in Wisconsin, USA had similar viral loads in nasal swabs, irrespective of vaccine status, during a time of high and increasing prevalence of the Delta variant. Infectious SARS-CoV-2 was isolated from 51 of 55 specimens (93%) with Ct <25 from both vaccinated and unvaccinated persons, indicating that most individuals with Ct values in this range (Wilson 95% CI 83%-97%) shed infectious virus regardless of vaccine status. Notably, 68% of individuals infected despite vaccination tested positive with Ct <25, including at least 8 who were asymptomatic at the time of testing. Our data substantiate the idea that vaccinated individuals who become infected with the Delta variant may have the potential to transmit SARS-CoV-2 to others. Vaccinated individuals should continue to wear face coverings in indoor and congregate settings, while also being tested for SARS-CoV-2 if they are exposed or experience COVID-like symptoms.

International Journal of
Environmental Research and Public Health

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Article

COVID-19 and the Political Economy of Mass Hysteria

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Abstract: In this article, we aim to develop a political economy of mass hysteria. Using the background of COVID-19, we study past mass hysteria. Negative information which is spread through mass media repetitively can affect public health negatively in the form of nocebo effects and mass hysteria. We argue that mass and digital media in connection with the state may have had adverse consequences during the COVID-19 crisis. The resulting collective hysteria may have contributed to policy errors by governments not in line with health recommendations. While mass hysteria can occur in societies with a minimal state, we show that there exist certain self-corrective mechanisms and limits to the harm inflicted, such as sacrosanct private property rights. However, mass hysteria can be exacerbated and self-reinforcing when the negative information comes from an authoritative source, when the media are politicized, and social networks make the negative information omnipresent. We conclude that the negative long-term effects of mass hysteria are exacerbated by the size of the state.

Keywords: mass hysteria; nocebo effects; contagion; mass media; social media; public health; law and economics; political economy; groupthink; culture of fear; emotional contagion; anxiety; policy error; COVID-19

Citation: Bagus, P.; Peña-Ramos, J.A.; Sánchez-Bayón, A. COVID-19 and the Political Economy of Mass Hysteria. *Int. J. Environ. Res. Public Health* **2021**, *18*, 1376. https://doi.org//10.3390/ijerph18041376

Received: 26 December 2020
Accepted: 27 January 2021
Published: 3 February 2021

1. Introduction

Public healthcare systems form a vital part of the welfare state. Indeed, it is generally taken for granted that one main purpose of the modern welfare state is to improve public health. It is supposed that the state positively contributes to public health. In this article, we question this narrative in relation to the phenomenon of mass hysteria. We analyze how the modern state influences the development and extension of mass hysteria, arguing that the state exacerbates this phenomenon with adverse consequences for public health. By developing a political economy of mass hysteria, we fill an apparent gap in the literature. There have been many illuminating studies on psychological issues related to the phenomena of mass hysteria. As a consequence of the COVID-19 crisis, there have been several studies examining the adverse psychological effects of state-imposed lockdowns [1–4]. There are also studies that examine the contribution of digital media and the internet to anxiety [5,6], emotional contagion [7,8], anxiety transmissions [9,10], and nocebo effects [11,12]. However, to our knowledge, there has been no study that analyzes how different political institutions and the state affect the development and extension of mass hysteria. The interplay of media, science, politics, and public is a real research gap [13]. Building on the psychology related to the phenomenon of mass hysteria, we develop a political economy of mass hysteria deriving important insights from a public health perspective.

In a multidisciplinary analysis (beyond Law and Economics or Sociological Economics), we show that the size of the state exacerbates the negative consequences of mass

International Journal of Infectious Diseases 107 (2021) 172–175

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Short Communication

First case of postmortem study in a patient vaccinated against SARS-CoV-2

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ARTICLE INFO

Article history:
Received 25 February 2021
Received in revised form 13 April 2021
Accepted 14 April 2021

Keywords:
SARS-CoV-2
Vaccine
Autopsy
Histology
RT-PCR

ABSTRACT

A previously symptomless 86-year-old man received the first dose of the BNT162b2 mRNA COVID-19 vaccine. He died 4 weeks later from acute renal and respiratory failure. Although he did not present with any COVID-19-specific symptoms, he tested positive for SARS-CoV-2 before he died. Spike protein (S1) antigen-binding showed significant levels for immunoglobulin (Ig) G, while nucleocapsid IgG/IgM was not elicited. Acute bronchopneumonia and tubular failure were assigned as the cause of death at autopsy; however, we did not observe any characteristic morphological features of COVID-19. Postmortem molecular mapping by real-time polymerase chain reaction revealed relevant SARS-CoV-2 cycle threshold values in all organs examined (oropharynx, olfactory mucosa, trachea, lungs, heart, kidney and cerebrum) except for the liver and olfactory bulb. These results might suggest that the first vaccination induces immunogenicity but not sterile immunity.

We report on an 86-year-old male resident of a retirement home who received vaccine against SARS-CoV-2. Past medical history included systemic arterial hypertension, chronic venous insufficiency, dementia and prostate carcinoma. On January 9, 2021, the man received lipid nanoparticle-formulated, nucleoside-modified RNA vaccine BNT162b2 in a 30 μg dose. On that day and in the following 2 weeks, he presented with no clinical symptoms (Table 1). On day 18, he was admitted to hospital for worsening diarrhea. Since he did not present with any clinical signs of COVID-19, isolation in a specific setting did not occur. Laboratory testing revealed hypochromic anemia and increased creatinine serum levels. Antigen test and polymerase chain reaction (PCR) for SARS-CoV-2 were negative.

Gastroscopy and colonoscopy were performed to investigate the cause of diarrhea further. Colonoscopy, in particular, demonstrated an ulcerative lesion of the left colonic flexure, which was histologically diagnosed as ischemic colitis. PCR-analysis on biopsy specimens, following a previously reported method (Kaltschmidt et al., 2021), was negative for SARS-CoV-2. Treatment was supportive with mesalazine and intravenous iron substitution. Subsequently, the patient's condition deteriorated under the development of renal insufficiency. On day 24, a patient in the same hospital room as our case tested positive for SARS-CoV-2. On day 25, our patient tested SARS-CoV-2 positive by real-time PCR (RT-PCR), with a low cycle threshold (Ct) value indicating high virus load. On further analysis of the swab sample, there was no evidence for mutant SARS-CoV-2 variants B.1.1.7, B.1.351 or B.1.1.28.1. Taken together, it appears the patient became infected from the patient in his hospital room. Our patient now presented with fever and respiratory discomfort, and lung auscultation displayed crackles. Despite starting supplemental oxygen (2 l per minute) and antibiotic therapy by ceftriaxone, the patient died from acute renal and respiratory failure on the following day.

Immunogenicity assessment by measuring spike protein (S1) antigen-binding immunoglobulin (Ig) G in the serum samples obtained at day 25 showed antibody response (8.7 U/ml, reference value <0.8–1.2 U/ml; Roche ECLIA™), while (nucleocapsid) NCP-

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https://doi.org/10.1016/j.ijid.2021.04.053

Table 1
Summary of major features of the patient's history, clinical symptoms and laboratory findings, including SARS-CoV-2 testing (reference values given in brackets).

	Day 1	Day 15	Day 18	Day 19	Day 20	Day 23	Day 24	Day 25	Day 26
Major event	Vaccination	Collapse during breakfast	Admission to hospital; gastroscopy (mild gastritis)	Abdominal ultrasound, initiating intravenous iron application	Colonoscopy (ischemic colitis), initiating mesalazine	Acute renal insufficiency, initiating intravenous glucose application	Patient in same hospital room has positive SARS-CoV-2 RT-PCR test (Ct, 15)	Patient somnolent, initiating antibiotic therapy, chest radiograph with minimal infiltrates	Death at 14:30
Leading clinical symptoms	No relevant symptoms recorded	No further relevant symptoms recorded	Diarrhea	Anemia	Anemia	Lung auscultation with any pathological signs, hypernatremia	Hypernatremia	Dehydration, lung auscultation with crackles	Acute renal and respiratory failure
Temperature (°C)	Not recorded	Not recorded	36.4	Not recorded	Not recorded	36.8	36.2	38.8	Not recorded
Blood pressure (mmHg)	Not recorded	130/70	187/83	Not recorded	Not recorded	180/80	166/73	160/80	Not recorded
Oxygen saturation (SpO_2)	Not recorded	Not recorded	97%	Not recorded	Not recorded	Not recorded	Not recorded	97% + 21 O_2	Not recorded
SARS-CoV-2 test	No data	No data	Antigen-test: negative PCR-test: negative	No data	PCR-test: negative	No data	No data	RT-PCR-test: positive (Ct, 20)	No data
White-cell count (4–9/nl)	No data	No data	6.6	7.1	12.1	13.5	No data	9.2	15.2
Platelet count (140–400/nl)	No data	No data	267	263	262	254	No data	204	196
Hemoglobin (14.0–18.0 g/dl)	No data	No data	7.4	7.1	7.2	8.0	No data	8.6	9.3
Lactate dehydrogenase (135–250 U/L)	No data	No data	179	165	No data	No data	No data	No data	439
Creatinine (0.7–1.2 mg/dl)	No data	No data	1.91	1.78	No data	2.04	No data	2.17	3.23
C-reactive protein (<0.5 mg/dl)	No data	No data	1.0	0.8	No data	2.0	No data	No data	8.8
Sodium (135–145 mmol/l)	No data	No data	138	138	No data	154	155	No data	156

RT-PCR, real-time polymerase chain reaction; Ct, cycle threshold.

IgG/IgM was not elicited (<0.1 U/ml, reference value >1.0 U/ml; Roche ECLIA™). These results indicate that the patient had already developed relevant immunogenicity through vaccination.

Postmortem study revealed acute bilateral bronchopneumonia with abscesses, sometimes being surrounded by bacterial cocci (Figure 1). There were no findings of commonly described manifestations of COVID-19-associated pneumonitis. In the heart, we found biventricular hypertrophy (weight 580 g) and histologically, we diagnosed ischemic cardiomyopathy. We detected amyloidosis of the transthyretin type in the heart and to a lesser extent in the lungs. The kidneys revealed both chronic damage with arteriolosclerosis and interstitial fibrosis, and acute renal failure with hydropic tubular degeneration. The examination of the brain revealed a left parietal pseudocystic tissue necrosis, which was diagnosed as an old infarction area.

We conducted molecular mapping of 9 different anatomical parts of formalin-fixed paraffin-embedded tissue as previously described (Kaltschmidt et al., 2021). RNA was extracted from paraffin sections using the Maxwell RSC (Promega, Madison, WI, USA). Multiplex RT-PCR analysis targeted 2 independent genes of the SARS-CoV-2-genome (Fluorotype SARS-CoV-2 plus Kit; HAIN/Bruker, Nehren, Germany): RNA-dependent RNA polymerase (Target 1) and nucleopeptide (Target 2). The negative cut-off value was Ct >45. We examined 9 different tissue samples for known and relevant pathways of virus spreading in the human body (Figure 1). To prevent cross-contamination, each specimen was directly embedded in separate tissue cassettes and separately fixed in 4% phosphate-buffered saline-buffered formalin. We demonstrated viral RNA in nearly all organs examined except for the liver and the olfactory bulb (Figure 1).

A detailed autopsy study including molecular virus mapping of a patient vaccinated against SARS-CoV-2 with a positive SARS-CoV-2 test post-vaccination has not previously been reported, to the authors' knowledge. We suggest that a single treatment with BNT162b2 RNA vaccine elicited significant immunogenicity, as reflected in the reported spike protein-based neutralizing IgG serum values. From the weeks before vaccination, through vaccination (day 1), to shortly before death (day 24), the patient was free of any clinical symptoms typically ascribed to COVID-19. Furthermore, blood work did not show an IgM titer that is generally observed 7–14 days after symptom onset (Kim et al., 2020). However, the patient tested SARS-CoV-2 positive. Both the Ct value measured in nasopharyngeal swab and values measured in formalin-fixed paraffin-embedded autopsy specimens indicate viral load and suggest transmissibility. Because our patient died approximately 2 days after his first positive SARS-CoV-2 test result, we suppose that the molecular mapping data reflects an early stage of viral infection. An early stage of infection might also explain why different regions such as the olfactory bulb and liver were not (yet) affected by systemic viral spread.

We did not observe any characteristic morphological features of COVID-19 reported in comprehensive morphological autopsy studies so far (Schaller et al., 2020; Edler et al., 2020; Ackermann et al., 2020). We did not find any typical signs of diffuse alveolar damage in the lungs, but we identified extensive acute bronchopneumonia, possibly of bacterial origin. We concluded that the patient died from bronchopneumonia and acute renal failure.

Our findings are in line with previous evidence from animal models that immunization against SARS-CoV-2 by vaccination appeared to reduce the severity of pathogenesis, especially with regard to severe lung disease, while viral RNA persisted in nasal swabs (Van Doremalen et al., 2020; Vogel et al., 2021). Recently, Amit et al. (2021) published results on a clinical trial on

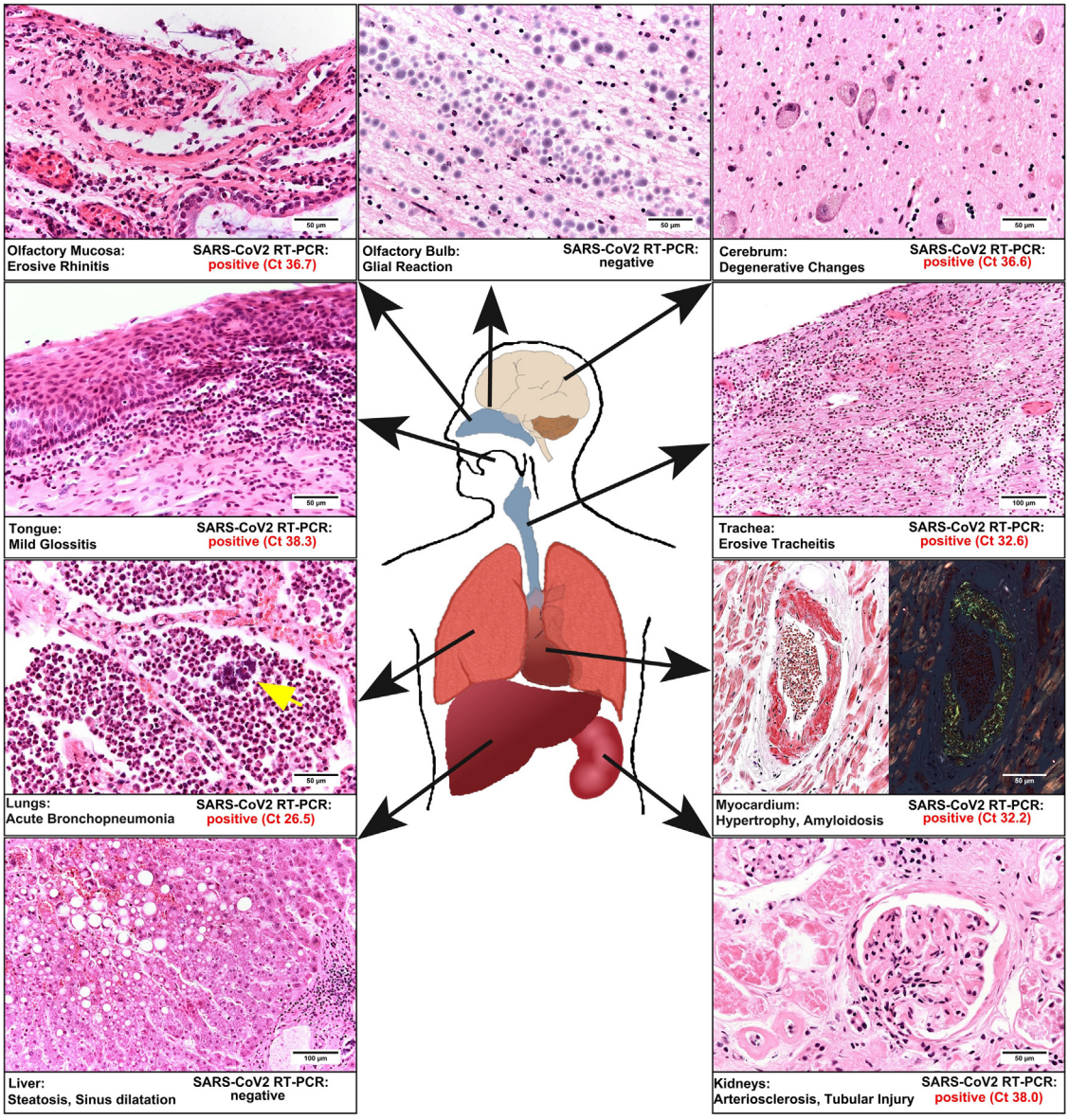

Figure 1. Synopsis of the relevant histological findings and the results of molecular mapping is presented. The histomorphology is obtained by standard hematoxylin and eosin reaction, except for the myocardium on the right side (Congo red staining). The magnification is shown by bars. Note that in the lungs, we also observed colonies of cocci (arrow) in granulocytic areas. In addition, the results of molecular mapping are given as evaluated cycle threshold values of the real-time polymerase chain reaction for SARS-CoV-2. Note that only in the olfactory bulb and the liver SARS-CoV-2 could not be detected.

healthcare workers using vaccine BNT162b2 that demonstrated substantial early reductions in SARS-CoV-2 infection and symptomatic COVID-19 rates following administration of the first vaccine dose.

Concerning major adverse effects in patients receiving vaccination against SARS-CoV-2, local effects predominate, and severe systemic reactions are rarely described (Yuan et al., 2020). However, recent reports of an increased risk of blood clots, particularly of cerebral venous sinus thrombosis in the case of the Oxford-AstraZeneca vaccine (Mahase 2021), raised a matter of debate on the safety of COVID-19 vaccine in general. Comprehensive analysis of autopsy data must be performed to provide more detailed insights into lethal adverse effects and any deaths associated with vaccination.

In summary, the results of our autopsy case study in a patient with mRNA vaccine confirm the view that by first dose of vaccination against SARS-CoV-2 immunogenicity can already be induced, while sterile immunity is not adequately developed.

Conflicts of interest

The authors do not have any commercial or financial conflict of interest.

Ethical approval

This case study was performed in the setting of the German national “Defeat Pandemics” project, approved by the Medical Association of Westphalia-Lippe, Münster, Germany (Ref. 2020-575-b-S) and carried out in accordance with the ethical principles of the Helsinki Declaration. Informed consent by the next-of-kin was available.

Funding source

There was no funding received from any individual or organization.

Acknowledgements

We are grateful for the expert technical assistance of Ralf Bode and Nadine Weber (University Hospital of OWL of the University of Bielefeld, Campus Lippe, Detmold).

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JCI The Journal of Clinical Investigation

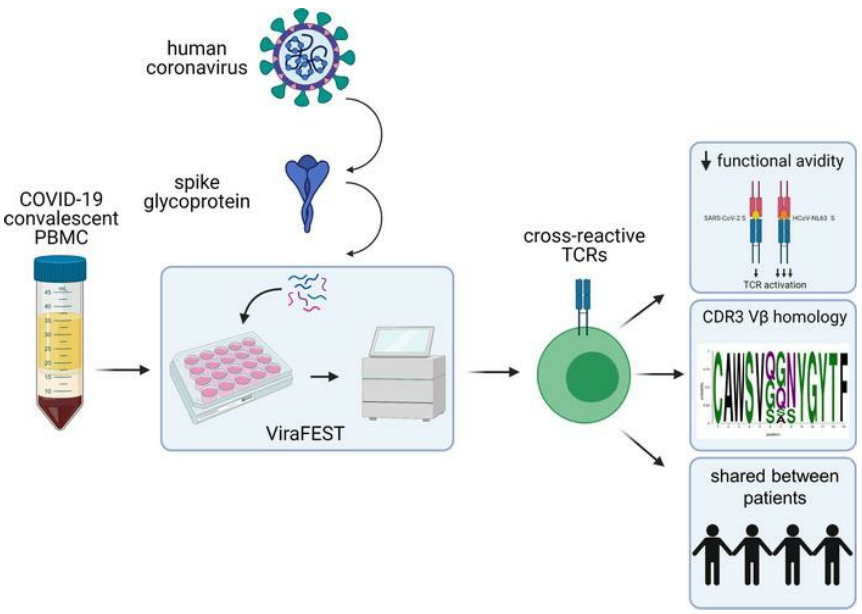
Functional characterization of CD4+ T cell receptors crossreactive for SARS-CoV-2 and endemic coronaviruses

Arbor G. Dykema, … , Joel N. Blankson, Kellie N. Smith

J Clin Invest. 2021;131(10):e146922. https://doi.org/10.1172/JCI146922.

Clinical Medicine COVID-19 Immunology

Graphical abstract



Functional characterization of CD4+ T cell receptors crossreactive for SARS-CoV-2 and endemic coronaviruses

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BACKGROUND. Recent studies have reported T cell immunity to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in unexposed donors, possibly due to crossrecognition by T cells specific for common cold coronaviruses (CCCs). True T cell crossreactivity, defined as the recognition by a single TCR of more than one distinct peptide-MHC ligand, has never been shown in the context of SARS-CoV-2.

METHODS. We used the viral functional expansion of specific T cells (ViraFEST) platform to identify T cell responses crossreactive for the spike (S) glycoproteins of SARS-CoV-2 and CCCs at the T cell receptor (TCR) clonotype level in convalescent COVID-19 patients (CCPs) and SARS-CoV-2–unexposed donors. Confirmation of SARS-CoV-2/CCC crossreactivity and assessments of functional avidity were performed using a TCR cloning and transfection system.

RESULTS. Memory CD4+ T cell clonotypes that crossrecognized the S proteins of SARS-CoV-2 and at least one other CCC were detected in 65% of CCPs and unexposed donors. Several of these TCRs were shared among multiple donors. Crossreactive T cells demonstrated significantly impaired SARS-CoV-2–specific proliferation in vitro relative to monospecific CD4+ T cells, which was consistent with lower functional avidity of their TCRs for SARS-CoV-2 relative to CCC.

CONCLUSIONS. Our data confirm, for what we believe is the first time, the existence of unique memory CD4+ T cell clonotypes crossrecognizing SARS-CoV-2 and CCCs. The lower avidity of crossreactive TCRs for SARS-CoV-2 may be the result of antigenic imprinting, such that preexisting CCC-specific memory T cells have reduced expansive capacity upon SARS-CoV-2 infection. Further studies are needed to determine how these crossreactive T cell responses affect clinical outcomes in COVID-19 patients.

FUNDING. NIH funding (U54CA260492, P30CA006973, P41EB028239, R01AI153349, R01AI145435-A1, R21AI149760, and U19A1088791) was provided by the National Institute of Allergy and Infectious Diseases, the National Cancer Institute, and the National Institute of Biomedical Imaging and Bioengineering. The Bloomberg~Kimmel Institute for Cancer Immunotherapy, The Johns Hopkins University Provost, and The Bill and Melinda Gates Foundation provided funding for this study.

Authorship note: AGD and BZ contributed equally to this work.

Conflict of interest: DMP and KNS have filed for patent protection on a subset of the technologies described herein (MANAFEST – A Novel Sensitive, Specific, Salable and Simple Method to Identify Functional Anti-Tumor T Cell Responses, US provisional patent application no. 62/407,820). AGD, ALC, FRD, DMP, JNB, and KNS have filed for patent protection on a subset of the technologies described herein (SARS-CoV-2-specific T cell receptors and Related Materials and Methods of Use, US provisional patent application no. 63/135,534). SZ is a founder of, holds equity in, and serves as a consultant to Personal Genome Diagnostics. SZ holds equity in Thrive Earlier Detection and has a research agreement with BioMed Valley Discoveries Inc. DMP reports stock and ownership interests in Aduro Biotech, DNAtrix, Dracen Pharmaceuticals, Dragonfly Therapeutics, Ervaxx, Five Prime Therapeutics, Potenza Therapeutics, RAPT, Tizona Therapeutics, Trieza Therapeutics, and WindMIL; a consulting or advisory role in Amgen, DNAtrix, Dragonfly Therapeutics, Ervaxx, Five Prime Therapeutics, Immunocore, Immunomic Therapeutics, Janssen Pharmaceuticals, MedImmune/AstraZeneca, Merck, RAPT, and WindMIL; research grants from Compugen; patent royalties, and/or other intellectual property through their institution with Aduro Biotech, Arbor Pharmaceuticals, Bristol-Myers Squibb, Immunomic Therapeutics, NexImmune, and WindMIL; and travel, accommodations, and expenses from Bristol-Myers Squibb and Five Prime Therapeutics. KNS receives commercial research funding from Bristol-Myers Squibb, AstraZeneca, and Enara Bio and has received travel support/honoraria from Illumina Inc. KNS, DMP, and SZ own founder's equity in ManaT Bio. These arrangements have been reviewed and approved by the Johns Hopkins University in accordance with its conflict-of-interest policies.

Submitted: December 15, 2020; **Accepted:** April 7, 2021; **Published**: April 8, 2021.

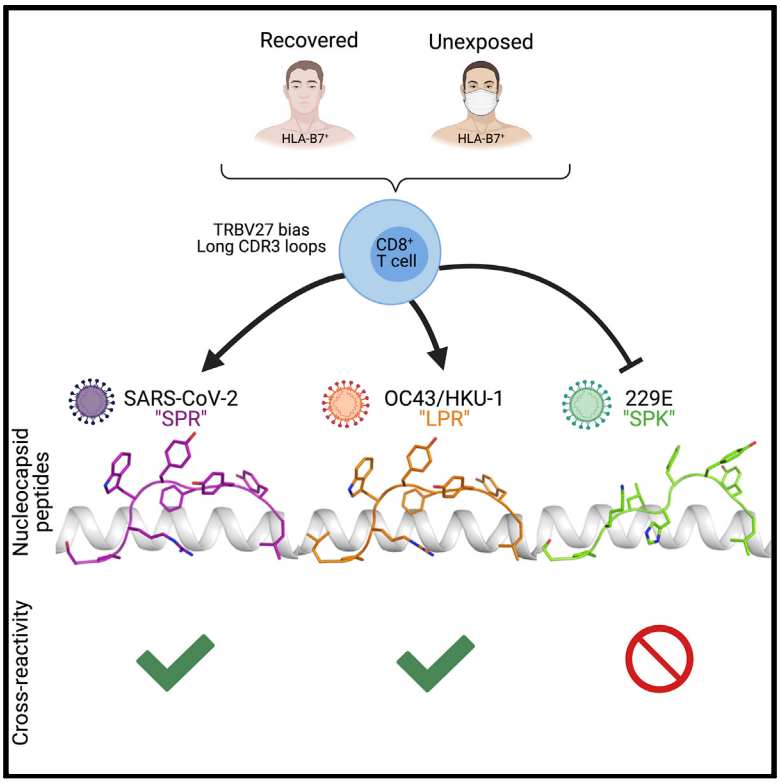
Reference information: J Clin Invest. 2021;131(10):e146922. https://doi.org/10.1172/JCI146922.

Article

Immunity

CD8+ T cells specific for an immunodominant SARS-CoV-2 nucleocapsid epitope cross-react with selective seasonal coronaviruses

Graphical abstract



Highlights

- ICS assay detects SARS-CoV-2-specific T cells in unexposed and recovered donors
- Epitope mapping identifies one dominant HLA-B7-restricted epitope
- Identical TCR clonotypes recognize SARS-CoV-2 and betacoronaviruses epitopes
- Crystal structures reveal distinct peptide conformations between alpha- and betacoronaviruses

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In brief

The impact of seasonal coronaviruses on immune responses to SARS-CoV-2 is an active area of research. Lineburg et al. identify CD8+ T cells specific for a conserved and immunodominant SARS-CoV-2 epitope in HLA-B7+ individuals. Furthermore, SARS-CoV-2 epitope-specific CD8+ T cells display cross-reactivity to beta- but not alphacoronaviruses because of distinct peptide-HLA conformations.

Lineburg et al., 2021, Immunity *54*, 1055–1065
May 11, 2021
https://doi.org/10.1016/j.immuni.2021.04.006

CellPress

Immunity

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Article

CD8+ T cells specific for an immunodominant SARS-CoV-2 nucleocapsid epitope cross-react with selective seasonal coronaviruses

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https://doi.org/10.1016/j.immuni.2021.04.006

SUMMARY

Efforts are being made worldwide to understand the immune response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for the coronavirus disease 2019 (COVID-19) pandemic, including the impact of T cell immunity and cross-recognition with seasonal coronaviruses. Screening of SARS-CoV-2 peptide pools revealed that the nucleocapsid (N) protein induced an immunodominant response in HLA-B7+ COVID-19-recovered individuals that was also detectable in unexposed donors. A single N-encoded epitope that was highly conserved across circulating coronaviruses drove this immunodominant response. *In vitro* peptide stimulation and crystal structure analyses revealed T cell-mediated cross-reactivity toward circulating OC43 and HKU-1 betacoronaviruses but not 229E or NL63 alphacoronaviruses because of different peptide conformations. T cell receptor (TCR) sequencing indicated that cross-reactivity was driven by private TCR repertoires with a bias for TRBV27 and a long CDR3β loop. Our findings demonstrate the basis of selective T cell cross-reactivity for an immunodominant SARS-CoV-2 epitope and its homologs from seasonal coronaviruses, suggesting long-lasting protective immunity.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an emerging virus responsible for the ongoing coronavirus disease 2019 (COVID-19) pandemic. Over 97 million individuals have been infected and over 2 million individuals have succumbed to infection (Dong et al., 2020). Although some vaccines against SARS-CoV-2 are already being administered, and others are in development, many questions remain regarding the immune response toward this virus. Cytotoxic CD8+ T cells are key players in the immune response to viral infections because they participate directly in viral clearance. Among the 26 viral proteins of SARS-CoV-2, some surface proteins, such as the spike protein (S), are more variable, whereas others are internal and more conserved, such as the nucleocapsid protein (N). The sequence conservation of non-surface proteins makes them ideal vaccine targets for activating cytotoxic CD8+ T cells. CD8+ T cells recognize small peptides (typically 8–10 amino acids) together with human leukocyte antigen (HLA) molecule with varying affinity. Although HLA-A2, the most prevalent HLA molecule (~40% frequency worldwide; Ellis et al., 2000), can present SARS-CoV-2 N-derived peptides (Szeto et al., 2021), they are only weakly immunogenic (Habel et al., 2020). However, it remains unclear whether this is a characteristic

OPINION | COMMENTARY

Eradication of Covid Is a Dangerous and Expensive Fantasy

It seemed to work in New Zealand and Australia, but now ruinous, oppressive lockdowns are back.

Main Street: The CDC should scrap its confusing guidance and make Covid-19 vaccination the only priority. Images: AFP via Getty Images
Composite: Mark Kelly

By Jay Bhattacharya and Donald J. Boudreaux
Aug. 4, 2021 6:16 pm ET

Much of the pathology underlying Covid policy arises from the fantasy that it is possible to eradicate the virus. Capitalizing on pandemic panic, governments and compliant media have used the lure of zero-Covid to induce obedience to harsh and arbitrary lockdown policies and associated violations of civil liberties.

Among all countries, New Zealand, Australia and especially China have most zealously embraced zero-Covid. China's initial lockdown in Wuhan was the most tyrannical. It infamously locked people into their homes, forced patients to take untested medications, and imposed 40-day quarantines at gunpoint.

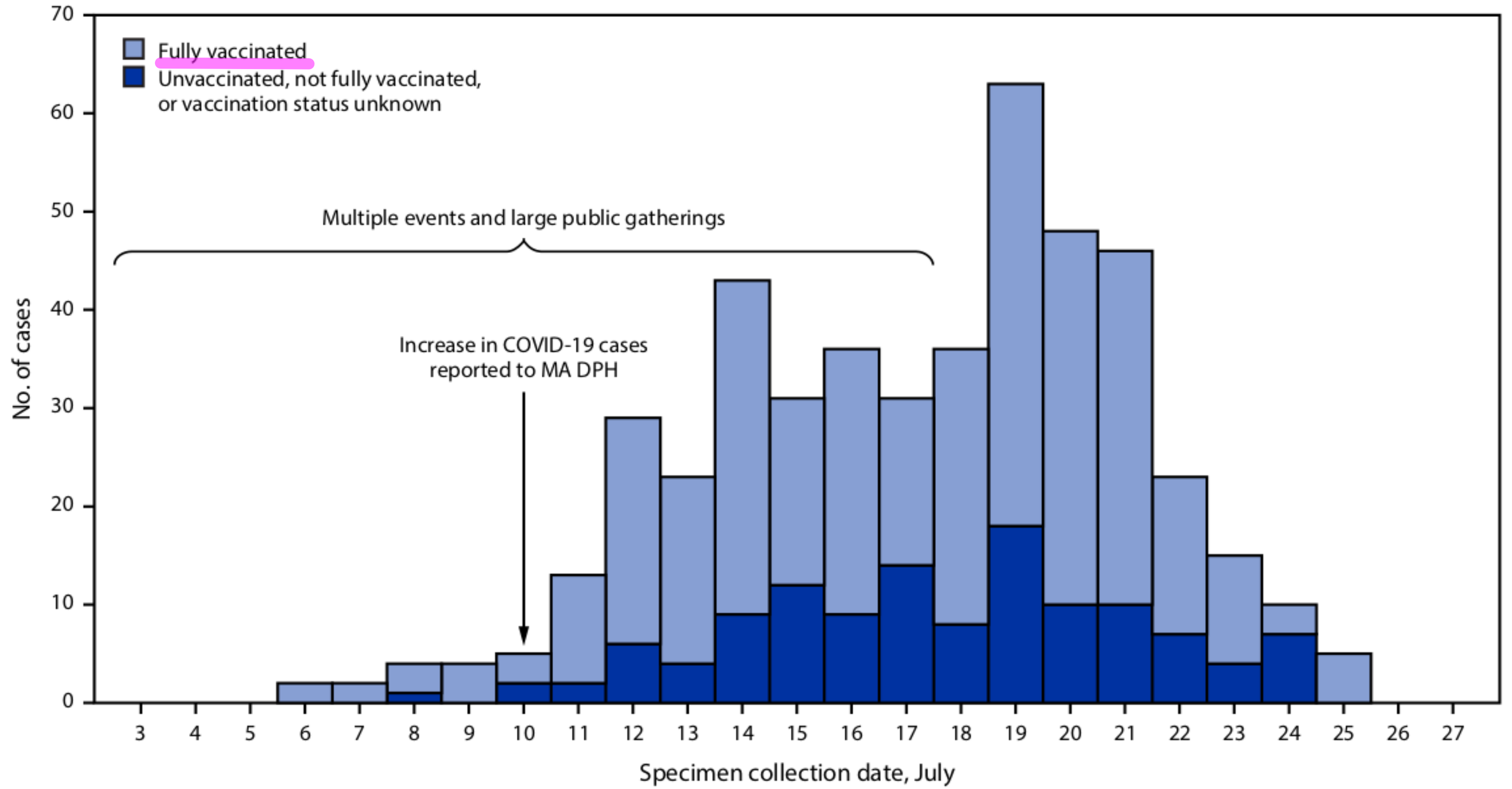
On March 24, 2020, New Zealand imposed one of the most onerous lockdowns in the free world, with sharp restrictions on international travel, business closures, a prohibition on going outside, and official encouragement of citizens to snitch on neighbors. In May 2020, having hit zero-Covid, New Zealand lifted lockdown restrictions, except quarantines for international travelers and warrantless house searches to enforce lockdown.

Australia also took the zero-Covid route. While the initial steps focused on banning international travel, the lockdowns there also involved closed schools, occasional separation of mothers from premature newborns, brutal suppression of protests, and arrests for wandering more than 3 miles from home.

New Zealand's and Australia's temporary achievement of zero-Covid and China's claimed success were greeted with fanfare by the media and scientific journals. China's authoritarian response seemed so successful—despite the country's record of lying about the virus—that panicked democratic governments around the world copied it. The three countries lifted their lockdowns and celebrated.

Early Release

FIGURE 1. SARS-CoV-2 infections (N = 469) associated with large public gatherings, by date of specimen collection and vaccination status* — Barnstable County, Massachusetts, July 2021



Abbreviation: MA DPH = Massachusetts Department of Public Health.

* Fully vaccinated was defined as ≥14 days after completion of state immunization registry–documented COVID-19 vaccination as recommended by the Advisory Committee on Immunization Practices.