July 8, 2022

The Honorable Ron Johnson  
United States Senate  
Washington, DC 20510

Dear Senator Johnson:

Thank you for your letter of September 15, 2021, regarding natural (hereinafter “infection-induced”) immunity from COVID-19. I am pleased to respond on behalf of the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and the National Institutes of Health (NIH).

The U.S. Department of Health and Human Services (HHS) and our federal partners are working together with state, local, tribal and territorial governments, public health officials, health care providers, researchers, private sector organizations, and the public to execute a whole-of-America response to the COVID-19 pandemic that protects the health and safety of the American people and moves the country forward safely.

The President’s National COVID-19 Preparedness Plan focuses on four key goals:
1. Protect against and treat COVID-19
2. Prepare for new variants
3. Prevent economic and educational shutdowns
4. Continue to lead the effort to vaccinate the world and save lives

America must maintain the tools – vaccines, boosters, treatments, tests, and masks – to protect against COVID-19 and dramatically decrease the risk of the most severe outcomes. Thanks to robust investments in research and development, we have a diverse medicine cabinet filled with more treatments now than at any point in the pandemic.

Thank you again for your time and dedication to this matter. Your questions are restated in bold in the enclosure, followed by HHS’s responses. Should you have additional questions, please do not hesitate to reach out to the Office of the Assistant Secretary for Legislation at 202-690-7627.

Sincerely,

Melanie Anne Egorin  
Melanie Anne Egorin, PhD
Assistant Secretary for Legislation

Enclosure
Approximately 20 months into this pandemic, why have U.S. health agencies not fully studied COVID-19 natural immunity?

HHS Response: On October 29, 2021, the CDC released a science brief, “SARS-CoV-2 Infection-induced and Vaccine-induced Immunity,” which evaluated more than 90 published reports and pre-print studies on infection-induced immunity.\(^1\) We know from this evaluation that SARS-CoV-2 (the virus that causes COVID-19) infection provides some protection from subsequent infection; there are data that show the risk of reinfection may be low for some individuals in the first six months following infection. We are still evaluating how long immunity lasts, how it may vary based on the severity of initial infection, and how it may be affected by new SARS-CoV-2 variants. Current evidence shows that antibody responses after SARS-CoV-2 infection also vary widely by individual. Certain people, such as older adults and people who are immunocompromised, may have a less robust immune response and thus a lower level of protection. CDC continues to investigate these questions. We regularly publish research on COVID-19 transmission, hospitalizations, and immunity, much of which can be found on CDC’s Morbidity and Mortality Weekly Report website.\(^2\)

The National Institute of Allergy and Infectious Diseases (NIAID), within the National Institutes of Health NIH, supports basic, translational, and clinical research to increase our understanding of the immune responses to a variety of pathogens, including SARS-CoV-2. Since early in the COVID-19 pandemic, NIAID-supported research has been informed by the NIAID Strategic Plan for COVID-19 Research, which has been updated to reflect the current status of the science on COVID-19.\(^3\) A major component of this Strategic Plan involves research to enhance our knowledge of immunity against SARS-CoV-2 and to identify components of the immune response that provide protection against COVID-19.

Over the course of the COVID-19 pandemic and in line with the Strategic Plan, NIAID has conducted and supported numerous studies examining the immune response generated by infection with SARS-CoV-2. These studies include a large, international collaboration, led by NIAID researchers, to explore the immune responses during acute COVID-19 and after recovery.\(^4\) NIAID also supports a large-scale, multi-year surveillance program analyzing the immune responses following SARS-CoV-2 infection or COVID-19 vaccination in health care personnel and other high-risk populations. This effort aims to identify components of the immune response that provide protection and determine how long that immunity lasts.

Data on immunity from infection with SARS-CoV-2, including studies by NIAID scientists and NIAID-supported researchers, demonstrate that most individuals generate a protective immune

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\(^2\) https://www.cdc.gov/mmwr/Novel_Coronavirus_Reports.html


response to COVID-19 after infection and during the period of the study. NIAID continues to conduct and support projects that aim to elucidate more fully the immune response to SARS-CoV-2 infection and/or COVID-19 vaccination. Importantly, we would note that ongoing research to assess the protective immune responses following infection with SARS-CoV-2 will require additional time to determine how long these immune responses persist and how immunity may differ from individual to individual.

It also is important to continually track how emerging SARS-CoV-2 variants interact with existing immunity from SARS-CoV-2 infection and/or COVID-19 vaccination. The Administration is engaged with these efforts through multiple collaborative initiatives. For example, HHS established the SARS-CoV-2 Interagency Group (SIG), which includes representatives from NIAID, CDC, BARDA, and other federal agencies, to coordinate the characterization of emerging SARS-CoV-2 variants to evaluate their impact on available medical countermeasures, disease severity, and transmissibility. Based on CDC genomic surveillance data, the SIG identifies emerging variants to prioritize for further characterization. As part of the SIG, NIAID coordinates the SARS-CoV-2 Assessment of Viral Evolution team, comprised of NIH, CDC, and academic scientists, who work to rapidly prioritize variants for studies to characterize their properties, including whether immunity is maintained against these variants. For example, NIAID scientists examined the T cell response against SARS-CoV-2 in patients who recovered from COVID-19 early in the pandemic and found that their T cells could recognize the Omicron variant, suggesting a level of cross-protection against this variant.

2. Please explain why Dr. Fauci supports vaccine mandates for all individuals without apparently considering studies that show the effectiveness of natural immunity against the virus.

HHS Response: COVID-19 vaccines undeniably reduce the risk of infections, hospitalizations, and deaths. The Administration seeks to reduce the number of unvaccinated Americans by encouraging COVID-19 vaccination for individuals who are eligible to receive it wherever possible, including for the Federal workforce. Studies of the antibody responses elicited by COVID-19 vaccination in individuals previously infected with SARS-CoV-2 have shown that vaccination is safe and greatly increases the protective antibodies against the virus present in

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7 SARS-CoV-2–specific CD8+ T cell responses in convalescent COVID-19 individuals. *JCI.* [https://www.jci.org/articles/view/145476](https://www.jci.org/articles/view/145476)

8 SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. *Nature.* [https://www.nature.com/articles/s41586-021-03647-4](https://www.nature.com/articles/s41586-021-03647-4)

Additionally, the durability of immunity and protection against other variants generated by SARS-CoV-2 infection has not been definitively established, and this immune response can differ significantly from individual to individual. More needs to be known about protective immune responses to SARS-CoV-2, whether resulting from prior infection or vaccination. There is uncertainty about how a number of variables affect the generation of a protective immune response to SARS-CoV-2, including the age of the individual; the immune status of the individual; which medical treatments the individual has received; the impact of SARS-CoV-2 variants; and the impact of the severity of initial infection and time since infection, if applicable. Additionally, some studies show that people who are vaccinated after infection have broader and/or more potent antibody responses, and one study found that people who remained unvaccinated after infection had a two-fold greater risk of being reinfected compared to those who were fully vaccinated after infection. These findings support COVID-19 vaccination for eligible individuals regardless of history of symptomatic or asymptomatic SARS-CoV-2 infection. As noted in the response to your first question, NIAID continues to extensively study immunity generated by infection with SARS-CoV-2.

It is important to note that infection with SARS-CoV-2 carries significant risks and relying on immunity from infection for protection from COVID-19 could result in unnecessary suffering and deaths. The Administration will continue to monitor the most current scientific data on SARS-CoV-2 immunity to help inform the COVID-19 response.

3. Did Dr. Fauci recommend to study the protection offered by natural immunity prior to President Biden’s decision to impose vaccine mandates? If not, why not?

HHS Response: As noted in response to the previous questions, NIAID, the Institute within the NIH that Dr. Fauci directs, has studied immunity generated from infection with SARS-CoV-2 since early in the COVID-19 pandemic. NIAID continues to support research to understand immune responses to SARS-CoV-2 infection and/or COVID-19 vaccination, including projects

10 mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection. Science. https://science.sciencemag.org/content/372/6549/1413
11 Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. Science. https://science.sciencemag.org/content/372/6549/1418
12 SARS-CoV-2 Antibody Responses in Infection-Naive or Previously Infected Individuals After 1 and 2 Doses of the BNT162b2 Vaccine. JAMA Network Open. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782762
14 Serum from COVID-19 patients early in the pandemic shows limited evidence of cross-neutralization against variants of concern. Scientific Reports. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC813826/
16 Antibodies elicited by mRNA-1273 vaccination bind more broadly to the receptor binding domain than do those from SARS-CoV-2 infection. Sci Transl Med. https://pubmed.ncbi.nlm.nih.gov/34103407/
18 Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May–June 2021. CDC MMWR. https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e1.htm
investigating how durable the protective response is; whether immunity differs in certain populations; and how SARS-CoV-2 variants may affect immunity.

4. **Did FDA and CDC consider the January 2021 NIH article titled, “Lasting immunity found after recovery from COVID-19,” or other studies on natural immunity, when deciding that individuals, regardless of previous COVID-19 infection, should be vaccinated? If not, why not?**

**HHS Response:** CDC has reviewed the NIH article, “Lasting immunity found after recovery from COVID-19,” as well as the peer-reviewed, published paper, “Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection,” which the article describes. In addition, CDC reviewed the research that the article cites. This paper, and many of the articles it cites, are part of a growing and extensive body of literature that CDC reviews on an ongoing basis to inform CDC’s “Interim Clinical Considerations for Use of COVID-19 Vaccines” and other recommendations.

Findings from CDC’s science brief on infection-induced immunity demonstrate that the immunity provided by vaccination and prior infection are both high but not complete (i.e., not 100 percent). Although multiple studies have demonstrated that higher antibody titers (a marker of immunity) are associated with decreased risk of subsequent symptomatic infection, there is not a test approved, cleared, or authorized by FDA that can be used to determine whether a person is protected from SARS-CoV-2 infection after previous infection or vaccination. The antibody response following SARS-CoV-2 infection also varies, with higher antibody levels following severe disease than after mild or asymptomatic infection. While there is a wide range in antibody titers in response to infection with SARS-CoV-2, COVID-19 vaccination typically leads to a more consistent and higher-titer initial antibody response or immunity.

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26 Khoury, D.S., et al., Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nature Medicine, 2021: p. 1-7. [https://doi.org/10.1038/s41591-021-01377-8](https://doi.org/10.1038/s41591-021-01377-8)
CDC’s review of reports and studies for the science brief28 confirmed that vaccination remains an effective, evidence-based strategy for preventing COVID-19 for all eligible people, including those who have a history of prior SARS-CoV-2 infection. Multiple immunologic studies have shown that vaccination further strengthens the existing immune response in individuals who have been previously infected, and more specifically, have shown that this higher immune response increases a previously infected person’s ability to neutralize more transmissible SARS-CoV-2 variants, such as Delta and more recently the Omicron variant.29,30,31,32 In one of these studies of health care workers vaccinated seven to 11 months after infection with SARS-CoV-2, antibody titers measured six days following their first vaccination dose were twice as high as the antibody titers measured the month after their initial infection, and were able to neutralize wild-type, Alpha, and Beta variants, irrespective of vaccine type, number of doses, or pre-vaccination antibody titers.33 There is also a growing body of data that show vaccinating people who were previously infected not only boosts their antibody levels, but also significantly reduces their risk of subsequent infection, as well as severity if re-infected.

In a study published August 6, 2021, in CDC’s Morbidity and Mortality Weekly Report (MMWR), investigators found that people who were not vaccinated after their COVID-19 illness had more than two times the odds of reinfection compared to those who became fully vaccinated (meaning they received their primary series of COVID-19 vaccines) after their COVID-19 illness.34 And a recent study from the Cleveland Clinic published in Clinical Infectious Diseases showed that with increasing time since prior SARS-CoV-2 infection, vaccination of previously infected individuals provides greater protection against COVID-19 compared to prior infection alone.35

If a person has previously been infected with SARS-CoV-2, the most reliable way to be protected from reinfection is vaccination, which provides additional protection using a known dose of a well-characterized antigen, without further engendering the risk of getting and spreading the SARS-CoV-2 virus.

32 SARS-CoV-2 Omicron Variant Neutralization in Serum from Vaccinated and Convalescent Persons | NEJM
Among individuals with evidence of SARS-CoV-2 infection prior to vaccination enrolled in clinical trials of Pfizer-BioNTech, Moderna, and Janssen COVID-19 vaccines, vaccination elicited robust neutralizing antibody responses and has not been associated with safety concerns. Furthermore, data from CDC support that vaccination following previous infection confers protection against clinically significant COVID-19 beyond protection conferred by infection alone. Therefore, it is reasonable to conclude that the benefits of vaccination outweigh its risks.

FDA focuses on evaluating evidence submitted in support of emergency use authorization (EUA) and biologics license application (BLA) requests.

5. Does the FDA and CDC agree with the World Health Organization’s statement that “[a]vailable scientific data suggests that in most people immune responses remain robust and protective against reinfection for at least 6-8 months after infection”? If not, why not?

HHS Response: The statement from the World Health Organization was published in a Science Brief in May 2021.36

Prior to Omicron, most individuals were protected following infection for at least six months, but this protection does wane over time, whereas those who are vaccinated following infection had greater protection.37,38

Since that time, during Omicron multiple studies showed that the protection from a prior history of infection decreased dramatically, even in countries that previously reported very high protection from infection.39,40,41,42 Among those who survive SARS-CoV-2 infection, the risk of reinfection is low when the circulating variant is sufficiently similar to the variant of the primary infection. Immunity following both vaccination and infection wanes over time and may be

42 “Coronavirus Disease 2019 (COVID-19) Vaccine Boosting in Persons Already Protected by Natural or Vaccine-Induced Immunity.” Nabin K. Shrestha, Priyanka Shrestha, Patrick C. Burke, Amy S. Nowacki, Paul Terpeluk, Steven M. Gordon medRxiv 2022.02.10.22270744; doi: https://doi.org/10.1101/2022.02.10.22270744
further reduced in the setting of novel variant circulation. Vaccination can boost the immune response in a previously infected individual and can further increase ability to neutralize variants of concern.

Although many people may be protected after infection, there is no test approved, cleared, or authorized by FDA that can be used to determine whether someone is fully protected against SARS-CoV-2 infection.

In a study examining more than 7,000 people across nine states, CDC found vaccine-induced immunity was more protective than infection-induced immunity against laboratory-confirmed COVID-19. The study, published October 29, 2021, in MMWR, showed that among adults hospitalized with symptoms similar to COVID-19 during January to September 2021, unvaccinated people with prior SARS-CoV-2 infection 90 to 179 days earlier were 5.49 times more likely to have laboratory-confirmed COVID-19 than those who received their second mRNA COVID-19 vaccine dose 90 to 179 days prior.

Another study published in MMWR in January 2022 analyzed cases and hospitalizations by vaccination status and previous COVID-19 diagnosis from May 2021 to November 2021 before widespread circulation of the Omicron variant and before most people had received additional primary series or booster COVID-19 vaccine doses to protect against waning immunity. Case rates were initially lowest among vaccinated people without a previous COVID-19 diagnosis; however, after emergence of the Delta variant and over the course of time, incidence increased sharply in this group, but only slightly among both vaccinated and unvaccinated people with previously diagnosed COVID-19. Across the entire study period, people with vaccine-and infection-induced immunity had much lower rates of hospitalization compared with people who were unvaccinated without previous COVID-19 diagnosis. These results suggest that vaccination protects against COVID-19 and related hospitalization and that surviving a previous infection protects against a reinfection and related hospitalization. Importantly, infection-induced protection was greater after the highly transmissible Delta variant became predominant, coinciding with the early decline of vaccine-induced immunity in many people. Similar data accounting for booster doses and as new variants (including Omicron) circulate will be studied and assessed.

6. **Is the FDA or CDC aware of any adverse events in previously infected individuals that have been vaccinated? Please provide a complete list of these adverse events.**

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43 Bozio CH, Grannis SJ, Naleway AL, et al. Laboratory-Confirmed COVID-19 Among Adults Hospitalized with COVID-19–Like Illness with Infection-Induced or mRNA Vaccine-Induced SARS-CoV-2 Immunity — Nine States, January–September 2021. MMWR Morb Mortal Wkly Rep 2021;70:1539–1544. DOI: [http://dx.doi.org/10.15585/mmwr.mm7044e1](http://dx.doi.org/10.15585/mmwr.mm7044e1)

**HHS Response:** There is no evidence that prior SARS-CoV-2 infection increases a person’s risk for clinically serious adverse events following COVID-19 vaccination. For adverse reactions for which there is evidence of a causal association with COVID-19 vaccines (allergic reactions, myocarditis after mRNA vaccination, thrombosis with thrombocytopenia syndrome after vaccination with Johnson & Johnson’s Janssen vaccine, and possibly Guillain-Barré syndrome after vaccination with Johnson & Johnson’s Janssen vaccine), signals have not been detected indicating any increased risk associated with prior SARS-CoV-2 infection. People who are vaccinated after recovery from SARS-CoV-2 infection and COVID-19 illness experience many of the minor side effects of vaccinations experienced by people who have not been previously infected. More serious side effects are rare, and CDC has not detected an increased risk associated with prior SARS-CoV-2 infection. CDC has a study in progress to further evaluate this issue.

Vaccine Adverse Event Reporting System (VAERS) reports are designed to capture information about the vaccinee’s adverse event experience following immunization and do not systematically capture information on the patient’s COVID-19 disease history. Thus, VAERS is not suited to study rates of infection in those with prior SARS-CoV-2 infection versus those without. However, review of VAERS reports for the above adverse events, which in many cases have included collection and review of relevant medical records, has not identified an association of those adverse events with prior infection with SARS-CoV-2.

FDA and CDC continue to closely monitor the safety of COVID-19 vaccines through both passive and active surveillance systems to ensure that any safety concerns are identified and evaluated in a timely manner.45

7. **How many Americans received a vaccination after having COVID-19? If this data is unavailable, please explain why.**

**HHS Response:** At this time, CDC does not have an estimate of how many people with prior SARS-CoV-2 infection were subsequently vaccinated. CDC uses seroprevalence surveys to estimate the proportion of the population that has antibodies as a result of vaccination, infection, or both. Both vaccination and infection result in the production of antibodies. A combination of antibody tests and vaccine history can be used to distinguish if someone has been infected, vaccinated, or both.46,47,48

Current data from the seroprevalence surveys do not indicate, in individuals who had COVID-19 prior to receiving a COVID-19 vaccine, whether SARS-CoV-2 infection took place prior to COVID-19 vaccination. Furthermore, existing information collected from blood donors does not include information on a donor’s SARS-CoV-2 infection status, COVID-19 vaccination status, or COVID-19 test date, if any. To identify which came first, this information needs to be linked to the laboratory data. Also, not everyone with infection-induced antibodies knows

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48 https://covid.cdc.gov/covid-data-tracker/#national-lab
when they were infected, and many would not be able to provide a date if asked for that information.

CDC is working with national blood collection organizations to estimate the number of vaccinated people who were previously infected with SARS-CoV-2 based on vaccine history and antibody testing. Using seroprevalence data referenced above, CDC is currently drafting a manuscript that describes the estimated total immunity for antibodies from either SARS-CoV-2 infection or COVID-19 vaccination versus antibodies from just infection.

8. Provide the current estimated total number of infections of COVID-19 in the U.S.

**HHS Response:** As of March 21, 2022, the total number of COVID-19 cases in the United States reported to CDC is approximately 79.5 million and the total number of deaths is 969,114. These and other U.S. COVID-19 data can be found on CDC’s COVID Data Tracker.49

9. Do the FDA and CDC dispute the findings of the two Israeli studies cited in this letter? If so, please provide the data that contradict these studies.

**HHS Response:** The research findings and inferences presented by Goldberg et. al.50 and Gazit et al.51, were derived using accepted methods for large datasets. Their findings are consistent with other data that infection-induced immunity appears to provide protection against reinfection at least comparable to that induced by vaccination against primary infection for at least 3 months (90 days).

More recent data demonstrate that hybrid immunity – protection from infection-induced immunity and vaccination induced-immunity – provides greater protection than infection-induced immunity alone.52 In addition, and as referenced in the response to your fifth question, among COVID-19–like illness hospitalizations in adults age 18 years or older whose previous infection or vaccination occurred 90 to 179 days earlier, the adjusted odds of laboratory-confirmed COVID-19 among unvaccinated adults with previous SARS-CoV-2 infection were 5.49-fold higher than the odds among people who had received their second mRNA COVID-19 vaccine and who had no previous documented infection.43

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49 https://covid.cdc.gov/covid-data-tracker/#datatracker-home
50 Yair Goldberg, et al, Protection of previous SARS CoV-2 infection is similar to that of BNT162b22 vaccine protection: A three-month nationwide experience from Israel, Apr. 24, 2021, (preprint) available at https://www.medrxiv.org/content/10.1101/2021.04.20.21255670v1
10. Provide the estimated number of breakthrough infections in vaccinated persons versus reinfections in previously infected persons.

**HHS Response:** At this time, CDC does not have an estimate comparing the total number of SARS-CoV-2 infections in vaccinated people versus reinfections in people who previously had the virus. CDC is engaged in a range of work to understand infections after vaccination (commonly known as breakthrough infections),\(^{53,54}\) including leading studies in various populations, locations, and settings that allow the agency to obtain representative, scientifically valid information. CDC’s efforts to monitor breakthrough infections include multi-state collaborations with COVID-19 case data linked to immunization records to compare SARS-CoV-2 infection incidence among people who are vaccinated to people who are unvaccinated. CDC is also engaged in multi-state study platforms to assess vaccine effectiveness against infections, hospitalizations, and deaths using scientific methods that help minimize bias to improve the accuracy of our estimates. In addition, CDC is using several data sources to understand reinfections, including cohort studies, review of data from electronic health record systems, and by working with local jurisdictions as they link cases over time.\(^{55}\)

In terms of surveillance, CDC worked closely with public health jurisdictions and the Council of State and Territorial Epidemiologists to update the national surveillance case definition of COVID-19 in 2021 and enable states to count repeat infections in the same individuals over time.\(^{56}\) The new COVID-19 case definition specifies criteria for listing new cases in people previously classified as a probable or confirmed case (i.e., reinfections). This update will allow CDC to track rates of reinfection over time and in the setting of different variants.

The rate of reinfections depends on both the level of protection provided by previous infection, for which there is increasing evidence, and the general rate of infections in the population, which is highly variable. Unlike ascertaining vaccine status, ascertaining prior infection status relies on data systems linking multiple episodes in local jurisdictions or on widespread sequencing.

CDC is actively working to learn more about breakthrough infections and reinfections to inform public health action. As described in the responses to your fourth and fifth questions, data continue to highlight the importance of vaccination, including for those who previously had

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\(^{53}\) [https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html](https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html)


\(^{55}\) Reinfections and COVID-19 | CDC

COVID-19 illness.\textsuperscript{57,58,59,60}

To reduce their likelihood of future infection, all eligible people should be offered COVID-19 vaccine — even those who were previously infected with SARS-CoV-2 and had COVID-19 illness. CDC recommends that everyone 5 years and older get their primary series of COVID-19 vaccines and receive a booster dose when eligible.\textsuperscript{Error! Bookmark not defined.}

11. Please explain why “antibody testing is not recommended to determine whether you are immune or protected from COVID-19.”

HHS Response: The presence of antibodies in an unvaccinated individual only indicates they have experienced a SARS-CoV-2 infection. Detection of antibodies provides no information about the quality of their immunity after the infection or how well they may be protected against reinfection. As noted above, although multiple studies have demonstrated that higher antibody titers are associated with decreased risk of subsequent symptomatic infection,\textsuperscript{61,62,63,64} no validated methods have been established to determine what level of antibodies indicates if the tested person has sufficient protection against reinfection with SARS-CoV-2.

FDA has noted that results from currently authorized SARS-CoV-2 antibody tests should not be used to evaluate a person’s level of immunity or protection from COVID-19 at any time. If antibody test results are incorrectly used for these purposes, there is a potential risk that people that receive positive results may take fewer precautions against SARS-CoV-2 exposure. Taking fewer steps to protect against SARS-CoV-2 can increase their risk of SARS-CoV-2 infection and may result in the increased spread of SARS-CoV-2.\textsuperscript{65}

\textsuperscript{57} Minimal Crossover between Mutations Associated with Omicron Variant of SARS-CoV-2 and CD8 + T-Cell Epitopes Identified in COVID-19 Convalescent Individuals. mBio. \texttt{https://pubmed.ncbi.nlm.nih.gov/35229637/}
\textsuperscript{58} mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection. \textit{Science}. \texttt{https://science.sciencemag.org/content/372/6549/1413}
\textsuperscript{59} Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. \textit{Science}. \texttt{https://science.sciencemag.org/content/372/6549/1418}
\textsuperscript{60} SARS-CoV-2 Antibody Responses in Infection-Naive or Previously Infected Individuals After 1 and 2 Doses of the BNT162b2 Vaccine. \textit{JAMA Network Open}. \texttt{https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782762}
\textsuperscript{61} Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. \textit{Science}. \texttt{https://pubmed.ncbi.nlm.nih.gov/33408181/}
\textsuperscript{62} CD8+ T cell responses in COVID-19 convalescent individuals target conserved epitopes from multiple prominent SARS-CoV-2 circulating variants. \textit{Open Forum Infectious Diseases}. \texttt{https://academic.oup.com/ofid/article/8/7/ofab143/6189113}
\textsuperscript{63} SARS-CoV-2–specific CD8+ T cell responses in convalescent COVID-19 individuals. \textit{JCI}. \texttt{https://www.jci.org/articles/view/145476}
\textsuperscript{64} SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. \textit{Nature}. \texttt{https://www.nature.com/articles/s41586-021-03647-4}
12. Has the FDA or CDC examined the duration of natural immunity compared to vaccine immunity? If not, why not?

**HHS Response:** Yes, as noted above, CDC published a review of more than 90 peer-reviewed studies and pre-print publications to understand the level of protection against COVID-19 illness in people who have immunity from prior SARS-CoV-2 infection and those with immunity from vaccination. Available evidence shows that people vaccinated against COVID-19 and people previously infected with SARS-CoV-2 each have a low risk of subsequent infection for at least six months. Prior to Omicron, most individuals were pretty well protected following infection for at least six months, but this protection does wane over time, whereas those who are vaccinated following infection had greater protection. For people with SARS-CoV-2 infections, those with more severe symptoms and worse illness tend to generate a much higher antibody response than people without symptoms or with mild illness. Also, certain people, such as the elderly and immunocompromised, may have a less robust immune response and lower level of protection.

At this time, there are insufficient data to extend the findings related to infection-induced immunity to people with very mild or asymptomatic infection or to children. In addition, while many people may be protected after infection, scientists do not know what level of antibodies are needed for protection from reinfection. Importantly, there is no FDA-approved, cleared, or authorized test that can determine whether someone is fully protected against SARS-CoV-2 infection. CDC continues to review the science comparing infection- and vaccine-induced immune response and it is a priority question in our “CDC Public Health Science Agenda for COVID-19.”

For people who have been infected, studies have shown that vaccination provides a boost in the immune response and further reduces the risk of a repeat infection. Even if someone has had COVID-19 before, getting vaccinated will help prevent severe illness, hospitalization, and death if they get reinfected with SARS-CoV-2. CDC recommends that everyone 5 years of

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66 Protection and waning of natural and hybrid COVID-19 immunity | medRxiv
69 mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection. Science. https://science.sciencemag.org/content/372/6549/1413
70 Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. Science. https://science.sciencemag.org/content/372/6549/1418
71 SARS-CoV-2 Antibody Responses in Infection-Naive or Previously Infected Individuals After 1 and 2 Doses of the BNT162b2 Vaccine. JAMA Network Open. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782762
72 Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. Science. https://science.sciencemag.org/content/372/6549/1418
73 SARS-CoV-2 Antibody Responses in Infection-Naive or Previously Infected Individuals After 1 and 2 Doses of the BNT162b2 Vaccine. JAMA Network Open. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782762
age and older get their primary series of COVID-19 vaccines and receive a booster dose when eligible, including unvaccinated people who were previously infected with SARS-CoV-2.  

74 mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection. Science. https://science.sciencemag.org/content/372/6549/1413