



Post-Infection Immunity

Disclaimer:

This *Quick Response Report* was published on April 26, 2020. Given the rapidly changing nature of the coronavirus pandemic, some of the references included in this report may quickly become out-of-date. We further caution readers that researchers at the Newfoundland and Labrador Centre for Applied Health Research are not experts on infectious diseases and are relaying work produced by others. This report has been produced quickly and it is not exhaustive, nor have the included studies been critically appraised.

Original Inquiry

Post- infection immunity: Do individuals that have recovered from COVID-19 have post-infection immunity to the virus? (With attention to healthcare workers returning to work but also for the general population)

Guidance

Alberta Health Services. **COVID-19 Return to Work Guide for Healthcare Workers**. April 21, 2020. ([LINK](#))

- “Like all Albertans, if you have tested positive for COVID-19, then you are legally required to self-isolate for at least 10 days from when your symptoms started or until your symptoms are gone, whichever is longer. At the end of the self-isolation period, you are free to leave your home and tend to any personal responsibilities (e.g. grocery shopping, etc.). However, healthcare workers may not work in any healthcare setting until 14 days have passed since symptoms started AND symptoms have resolved, whichever is longer.”

Canadian Pharmacists Association. **Protecting the Front Line: COVID-19 Day-to-Day Questions**. April 21, 2020 ([LINK](#))

- “In general, all pharmacy staff should follow public health guidelines regarding self-isolation if they have recently travelled, have been exposed to a suspected or confirmed case of COVID-19 or are experiencing COVID-19 symptoms. Symptomatic healthcare workers cannot work. However, every situation is different and at this time we urge you to follow the direction of your public health unit.”
- “Consider screening staff at every shift start prior to entering the pharmacy.”

Alberta Health Services. **COVID-19 Return to Work Guide for Healthcare Workers Decision Chart**. April, 17 2020. ([LINK](#))

- Includes a flow chart of how to decide if you should come to work.

CDC. Return to Work for Healthcare Personnel (HCP) with Confirmed or Suspected COVID-19
April 21, 2020. ([LINK](#))

- “Indicates a preference for use of the Test-based strategy to determine when HCP may return to work in healthcare settings; Adds return to work criteria for HCP with laboratory-confirmed COVID-19 who have not had any symptoms; Aligns with recommendations for universal source control for everyone in a healthcare facility during the pandemic.”

CDC. Coronavirus Disease 2019 (COVID-19): FAQ April 21, 2020 ([LINK](#))

- “CDC and partners are investigating to determine if you can get sick with COVID-19 more than once. At this time, we are not sure if you can become re-infected. Until we know more, continue to take steps to protect yourself and others.”

Infectious Disease Society of America. IDSA COVID-19 Antibody Testing Primer. April 20, 2020 ([LINK](#))

- Outstanding Research Needs: “While extrapolation from other coronavirus infections allows us to be optimistic that detection of an IgG response will likely confer at least some protection to most people, we have no direct evidence of this for SARS-CoV-2. - Understanding which antibodies (if any) are protective is required for vaccine development. There are many different SARS CoV-2 IgG antibodies that may be produced, and each may have a different role. This should also be a consideration in assessing the clinical utility of tests designed to target specific antibodies. - Determine limits of protective immunity (e.g., antibody amount, duration, and efficacy) and correlations with disease severity.”
- Background on Antibody Testing for SARS-Co-V-2 Infection: “The antibody response in infected patients remains largely unknown, and the clinical values of antibody testing have not been fully demonstrated. Seroprevalence data will be important in understanding the scale of the pandemic and future vaccine utility.”

Systematic Reviews

None found at this time.

Other Reviews

Infantino, et al. Serological Assays for SARS-CoV-2 Infectious Disease: Benefits, Limitations and Perspectives. Israel Medical Association Journal. April 22, 2020 ([LINK](#))

- “In any case, it will be necessary to individuate people who have had contact with the virus and have gained immunity, those who are still infectious, although paucisymptomatic, and those who have no antibodies and are therefore potentially susceptible to contagion.”
- “This status is particularly important with the prospect of returning to work, especially for healthcare practitioners.”

Nikolich-Zugich et al. SARS-CoV-2 and COVID-19 in older adults: what we may expect regarding pathogenesis, immune responses, and outcomes. GeroScience. April 10, 2020 ([LINK](#))

- “Here, we briefly review the virus, its structure and evolution, epidemiology and pathogenesis, immunogenicity and immune, and clinical response in older adults, using available knowledge on SARS-CoV-2 and its highly pathogenic relatives MERS-CoV and SARS-CoV-1. We conclude by discussing clinical and basic science approaches to protect older adults against this disease.”
- “The immunological correlates of protection and disease for SARS-2 are still being defined in this nascent field.”
- “There is evidence that immune responses to SARS-1 and suggestion that responses to SARS-2, in our most vulnerable patients, do not effectively switch from innate to adaptive (little to no antibody production) immunity, a topic needing immediate study and offering potential for immune modulation.”

Alberta Health Services. Key Research Question: Can people with previous COVID-19 infection become re-infected by the virus? April 8, 2020 ([LINK](#))

- Rapid Evidence Review that includes Critical Appraisal
- “Although most experts feel that recovered individuals will have some degree of immune protection from reinfection, there is currently not enough data to confirm the proportion of individuals expected to develop a detectable antibody response to SARS-CoV-2 infection, the correlation of this response to protection, and the potential duration of protection.”
- “There is limited information on whether individuals develop protective immunity following COVID-19 recovery.”

Rokni et al. Immune responses and pathogenesis of SARS-CoV-2 during an outbreak in Iran: Comparison with SARS and MERS. Reviews in Medical Virology. April 8, 2020 ([LINK](#))

- “In this review, we investigated the innate and acquired immune responses in patients who recovered from COVID-19, which could inform the design of prophylactic vaccines and immunotherapy for the future.”
- “The important point is, for SARS-CoV-2, the response to viral infection by type I IFN is suppressed.”
- “During the long-term follow-up of survivors, IgG is only detectable in recovered patients at 6 years after SARS infection suggesting decreasing levels of memory B-cells will also be found against SARS-CoV-2.”

Promptchara et al. Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. Asian Pacific Journal of Allergy and Immunology. March, 2020 ([LINK](#))

- “This review aims to provide a comparative view among SARS-CoV, MERS-CoV and the newly epidemic SARS-CoV-2, in the hope to gain a better understanding of the host-pathogen interaction, host immune responses, and the pathogen immune evasion strategies. This predictive view may help in designing an immune intervention or preventive vaccine for COVID-19 in the near future.”

Expert Opinion

National Academies of Sciences (USA). **Rapid Expert Consultation on SARS-CoV-2 Viral Shedding and Antibody Response for the COVID-19 Pandemic.** April 8, 2020 ([LINK](#))

- “Duration of shedding of infectious virus by recovered patients and the relationship to detection of viral RNA, Knowledge of immune mechanisms responsible for virus clearance that might predict recovery and help determine when patients are no longer infectious, Immune correlates of protection Duration of protective immunity”
- **Related News Article:** Posted April 20 2020, STAT News, [Everything we know about coronavirus immunity and antibodies — and plenty we still don’t](#)

Raoult et al. **Coronavirus infections: Epidemiological, clinical and immunological features and hypotheses.** Cell Stress (editorial). February, 2020 ([LINK](#))

- “There are currently no data on the specific role of either humoral or cellular immunity or innate immunity in patients recovering from COVID-19. Only highly specialized laboratories are able to conduct experiments to investigate immune responses against HLA class-I and class-II-restricted viral epitopes mediated by CD8+ and CD4+ T lymphocytes, respectively, to confirm the conjecture of a cellular (rather than humoral) immunity against SARS-CoV-2”

Primary Research

Kissler et al. **Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period.** Science. April 14, 2020 ([LINK](#))

- Uses data to explore a model - “This paper identifies viral, environmental, and immunologic factors which in combination will determine the dynamics of SARS-CoV-2. We integrate our findings in a mathematical model to project potential scenarios for SARS-CoV-2 transmission through the pandemic and post-pandemic periods and identify key data still needed to determine which scenarios are likely to play out. Then, using the model, we assess the duration and intensity of social distancing measures that might be needed to maintain control of SARS-CoV-2 in the coming months under both existing and expanded critical care capacities.”
- “...Longitudinal serological studies are urgently needed to determine the extent and duration of immunity to SARS-CoV-2. Even in the event of apparent elimination, SARS-CoV-2 surveillance should be maintained since a resurgence in contagion could be possible as late as 2024.”

Okba, et al. **Severe acute respiratory syndrome coronavirus 2–specific antibody responses in coronavirus disease 2019 patients.** Emerging Infectious Diseases. July, 2020 ([LINK](#))

- “...We developed serologic assays for detection of SARS-CoV-2 neutralizing, spike protein–specific, and nucleocapsid-specific antibodies. Using serum samples from patients with PCR-confirmed SARS-CoV-2 infections, other coronaviruses, or other respiratory pathogenic infections, we validated and tested various antigens in different in-house and commercial ELISAs. We demonstrated that most PCR-confirmed SARS-CoV-2–infected persons

seroconverted by 2 weeks after disease onset. We found that commercial S1 IgG or IgA ELISAs were of lower specificity, and sensitivity varied between the 2 assays; the IgA ELISA showed higher sensitivity. Overall, the validated assays described can be instrumental for detection of SARS-CoV-2-specific antibodies for diagnostic, seroepidemiologic, and vaccine evaluation studies.”

- Related News Articles: Posted April 20 2020, [Everything we know about coronavirus immunity and antibodies - and plenty we still don't](#) - STAT News

Wu, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. medRxiv. April 6, 2020 ([LINK](#))

- This article is a preprint and has not been peer-reviewed. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.
- “The variations of SARS-CoV-2 specific NAb in recovered COVID-19 patients may raise the concern about the role of NAb on disease progression. The correlation of NAb titers with age, lymphocyte counts, and blood CRP levels suggested that the interplay between virus and host immune response in coronavirus infections should be further explored for the development of effective vaccine against SARS-CoV-2 virus. Furthermore, titration of NAb is helpful prior to the use of convalescent plasma for prevention or treatment.”
- Related News Articles:
 - [What Have Epidemiologists Learned About the Coronavirus?](#)- New Yorker, April 16 2020
 - [Sorry, Immunity to Covid-19 Won't Be Like a Superpower](#) – Wired, April 16, 2020
 - [WHO Says COVID-19 Immunity Is An Unknown; Disease '10 Times Deadlier' Than 2009 Flu](#) – NPR, April 13 2020

Wölfel, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. April 1, 2020 ([LINK](#))

- Note: “This is a PDF file of a peer-reviewed paper that has been accepted for publication. Although unedited, the content has been subjected to preliminary formatting. Nature is providing this early version as a service to our authors and readers.”
- “...Here we provide a detailed virological analysis of nine cases, providing proof of active virus replication in upper respiratory tract tissues. Pharyngeal virus shedding was very high during the first week of symptoms (peak at 7.11×10^8 RNA copies per throat swab, day 4). Infectious virus was readily isolated from throat- and lung-derived samples, but not from stool samples, in spite of high virus RNA concentration. Blood and urine never yielded virus. Active replication in the throat was confirmed by viral replicative RNA intermediates in throat samples. Sequence-distinct virus populations were consistently detected in throat and lung samples from the same patient, proving independent replication. Shedding of viral RNA from sputum outlasted the end of symptoms. Seroconversion occurred after 7 days in 50% of patients (14 days in all), but was not followed by a rapid decline in viral load. COVID-19 can present as a mild upper respiratory tract illness. Active virus replication in the upper respiratory tract puts the prospects of COVID-19 containment in perspective.”

- Related News Article: [Everything we know about coronavirus immunity and antibodies — and plenty we still don't](#) STAT News, April 20 2020,

An, et al. **Clinical characteristics of the recovered COVID-19 patients with re-detectable positive RNA test.** medRxiv. March 30, 2020 ([LINK](#))

- **This article is a preprint and has not been peer-reviewed. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.**
- “Our findings provide empirical information and evidence for the effective management of COVID-19 patients during their convalescent phase.”
- “Our results showed that young and mild COVID-19 patients seem to be RP [re-detectable positive] patients after discharge, who show no obviously clinical symptoms and disease progression upon re-admission.”

Dong, et al. **Characterization of anti-viral immunity in recovered individuals infected by SARS-CoV-2.** medRxiv. March 20, 2020 ([LINK](#))

- **This article is a preprint and has not been peer-reviewed. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.**
- “In this study, we collected blood from COVID-19 patients who have recently become virus-free and therefore were discharged, and analyzed their SARS-CoV-2-specific antibody and T cell responses. We observed SARS-CoV-2-specific humoral and cellular immunity in the patients. Both were detected in newly discharged patients, suggesting both participate in immune-mediated protection to viral infection. However, follow-up patients (2 weeks post discharge) exhibited high titers of IgG antibodies, but with low levels of virus-specific T cells, suggesting that they may enter a quiescent state. Our work has thus provided a basis for further analysis of protective immunity to SARS-CoV-2, and understanding the pathogenesis of COVID-19, especially in the severe cases. It has also implications in designing an effective vaccine to protect and treat SARS-CoV-2 infection.”
- “In summary, we provided the first analysis of SARS-CoV-2-specific humoral and cellular immunity. Both were detected in newly discharged patients, suggesting both participate in immune-mediated protection to viral infection. However, follow-up patients exhibited high titers of IgG antibodies, but with low levels of virus-specific T cells, suggesting that they may enter a quiescent state.”
- Related News Article: [What Immunity to COVID-19 Really Means](#) - Scientific American, Posted April 10 2020

Bao, et al. **Reinfection could not occur in SARS-CoV-2 infected rhesus macaques.** bioRxiv 2020, March 14, 2020 ([LINK](#))

- **This article is a preprint and has not been peer-reviewed. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.**
- “Taken together, our results indicated that the primary SARS-CoV-2 infection could protect from subsequent exposures, which have the reference of prognosis of the disease and vital implications for vaccine design.”

- Related News Article: [Can You Be Re-Infected After Recovering From Coronavirus? Here's What We Know About COVID-19 Immunity](#) - Time online, April 13 2020

Ling, et al. **Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients.** Chinese Medical Journal (English). February 28, 2020 ([LINK](#))

- "...This study analyzed the clearance time and factors influencing 2019 novel coronavirus (2019-nCoV) RNA in different samples from patients with COVID-19, providing further evidence to improve the management of patients during convalescence.";
- "In brief, as the clearance of viral RNA in patients' stools was delayed compared to that in oropharyngeal swabs, it is important to identify viral RNA in feces during convalescence. Because of the delayed clearance of viral RNA in the glucocorticoid treatment group, glucocorticoids are not recommended in the treatment of COVID-19, especially for mild disease. The duration of RNA detection may relate to host cell immunity."

Lan, et al. **Positive RT-PCR Test Results in Patients Recovered From COVID-19.** JAMA. February 27, 2020 ([LINK](#))

- "This case series describes reverse transcriptase–polymerase chain reaction (RT-PCR) test results in 4 health professionals discharged from hospitalization or quarantine after 2 negative RT-PCR test results and resolution of clinical COVID-19 infection."
- "The study was limited to a small number of patients with mild or moderate infection."

News Articles

Boston Globe - Medical workers return to work after recovering from coronavirus. But are they immune? - Posted April 22, 2020 - [Link](#)

- "While people who are infected generally develop antibodies to COVID-19, it's unclear how much protection those antibodies offer, said Dr. Rochelle Walensky, chief of infectious diseases at Mass. General. Scientists are still studying how long any possible protection lasts, and if a person who had a severe case of COVID-19 has greater immunity than someone who had mild disease. "The data that we have so far would suggest that this is like other respiratory illnesses, that those antibodies should be protective — but we haven't proven that," said Dr. Helen Boucher, chief of geographic medicine and infectious diseases at Tufts Medical Center."

WHO - Live from WHO Headquarters - coronavirus - COVID-19 daily press briefing - Posted April 17, 2020 - [Link](#)

- Mike Ryan, Executive Director, WHO Health Emergencies Programme: "There's been an expectation maybe that herd immunity may have been achieved and that the majority of people in society may already have developed antibodies, I think the general evidence is pointing against that. We also need to look at the length of protection that antibodies might give. We're not, nobody is sure, whether someone with antibodies is fully protected against having the disease or being exposed again"

- Dr. Maria Van Kerkhove, Head, Outbreak Investigation Task Force, Center for Global Health: “Right now we have no evidence that the use of a serologic test can show that an individual is immune or is protected from re-infection”
- Other articles addressing the content of this video:
 - The Guardian - **WHO warns that few have developed antibodies to Covid-19** - Posted April 20, 2020 - [Link](#)
 - The Jakarta Post - **Recovery from coronavirus may not confer immunity, warn experts** - Posted April 20, 2020 - [Link](#)
 - The Irish Times - **No proof of immunity in recovered coronavirus patients, says WHO** - Posted April 18, 2020 - [Link](#)
 - RTE - **'No evidence' of virus immunity in recovered patients** - Posted April 18, 2020 - [Link](#)

USA Today - Unproven tests. Inaccurate results. Public health labs worry 'bad data' could taint US recovery from coronavirus crisis. - Posted April 16, 2020 - [Link](#)

- “Anthony Harris, a professor and epidemiologist at the University of Maryland School of Medicine Medical Center, said accurate serology tests could reveal whether health care workers have developed immunity. Such information would alleviate the nation’s strained health care system, he said. Immune workers would be assigned to hospital units treating COVID-19 patients. Nonimmune workers would take care of noninfected patients, Harris said. “It would dramatically decrease anxiety for my health care workers,” Harris said.”

The New Yorker - What Have Epidemiologists Learned About the Coronavirus? - Posted April 16, 2020 - [Link](#)

- “How much immunity and protection it is remains an open question. It could be what we call sterilizing or complete immunity, where you can’t even get infected with the virus, at one extreme. At the other extreme, it could just be very weak immunity that wanes quickly and maybe dampens symptoms a bit but doesn’t stop infection. So it’s clear that there has to be some protection, but the amount of that protection, how long it lasts, how important it is for interrupting transmissions—those are open questions.”

Wired - Sorry, Immunity to Covid-19 Won't Be Like a Superpower - Posted April 16, 2020 - [Link](#)

- “The truth is, our immune responses to this virus aren’t likely to be permanent or perfect. It’s nice to imagine that once someone’s been infected they become a knight in antibody armor, but that’s not really how it works.”

Methodology

Newfoundland and Labrador Centre for Applied Health Research (NLCAHR) COVID-19 Quick Response reports are initiated by, and shared with, our partners in the provincial health system, including the four Regional Health Authorities, the Departments of Health and Community Services and Children, Seniors and Social Development, and public health officials.

NLCAHR staff work with topic submitters to clarify the research question. We then search for related systematic reviews, meta-analyses, other reviews, interim and other guidance statements, primary research, expert opinion and health and science reporting.

We use several search strategies, with a focus on the following databases:

- [CADTH](#)
- [Canadian Pharmacists Association](#)
- [Campbell Collaboration](#)
- [Cochrane Collaboration](#)
- [Centre for Disease Control](#) (CDC)
- [Centre for Evidence Based Medicine](#) (CEBM)
- [Evidence for Policy and Practice Information and Co-ordinating Centre](#)
- [European Centre for Disease Prevention and Control](#)
- [Health Canada](#)
- [Joanna Briggs Institute](#)
- [Johns Hopkins](#)
- [MedRxiv](#)
- [National Institutes of Health](#) (NIH)
- [National Institute of Allergy and Infectious Diseases](#) (NIAID)
- [National Library of Medicine](#)
- [Public Health Agency of Canada](#)
- [Trip Database](#)
- [World Health Organization](#)

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