Post-Infection Immunity (updated)

Disclaimer:
This *Quick Response Report* was published on December 3, 2020 to update a previously-released report from 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rapidly changing nature of the coronavirus pandemic, some of the references included in this report may quickly become out-of-date.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 who have recovered from COVID-19 have post-infection immunity to the virus? (With attention to healthcare workers returning to work but also to the general population)

Summary of Findings

- Since our original April 26, 2020, *Quick Response* report:
    - Research into possible long-lasting immunity has increased significantly; however, there remains ambiguity with regard to long-term mechanisms, the strength of the immunity and the implications for treatments or vaccines.
    - It is still not known what level of immune response is protective against future infection or reinfection
    - Guidance on returning to work has coalesced around a set of criteria including time since onset of symptoms and persistence of symptoms, with small variations among jurisdictions. Time to return to work varies with COVID-19 disease severity.
- The available evidence suggests that B-cell-mediated immunity, i.e., antibodies, wanes soon after recovery from COVID-19. In contrast, the available evidence suggests that T-cell-mediated immunity, i.e., CD4+ cells, is longer lasting.
- Evidence on the possibility of re-infection with COVID-19 remains scarce, despite recent reports of isolated cases. The data indicate that a person who has had COVID-19 and recovered may have low levels of virus in their bodies for up to 3 months after diagnosis. A person who has recovered may continue to have a positive PCR test result, even though they are not contagious. (See here for more on serology/antibody and molecular/PCR testing for COVID-19.)
- Research evidence indicates that disease severity modulates infection and long-term immune response. In addition, evidence suggests that immunity to other coronaviruses may play a role in mediating the severity of COVID-19 among those infected.

Guidance

International and National Authorities

WHO. **Coronavirus disease (COVID-19): Serology, antibodies and immunity**. November 13, 2020 ([LINK](#))

- Q&A for key post-infection immunity topics, including: the difference between molecular and serological testing, and the implications of detecting SARS-CoV-2 antibodies.

CDC. **Interim U.S. Guidance for Risk Assessment and Work Restrictions for Healthcare Personnel with Potential Exposure to COVID-19**. November 6, 2020. ([LINK](#))

- "[Healthcare personnel (HCP)]who had prolonged close contact with a patient, visitor, or HCP with confirmed COVID-19:
    - Exclude from work for 14 days after last exposure.
    - Advise HCP to monitor themselves for fever or symptoms consistent with COVID-19.
    - Any HCP who develop fever or symptoms consistent with COVID-19 should immediately contact their established point of contact (e.g., occupational health program) to arrange for medical evaluation and testing.

CDC. **Criteria for Return to Work for Healthcare Personnel with SARS-CoV-2 Infection (Interim Guidance)**. August 10, 2020. ([LINK](#))

- "HCP who are not severely immunocompromised AND were asymptomatic throughout their infection may return to work when at least 10 days have passed since the date of their first positive viral diagnostic test.
- "HCP with mild to moderate illness who are not severely immunocompromised: At least 10 days have passed since symptoms first appeared AND At least 24 hours have passed since last fever without the use of fever-reducing medications AND Symptoms (e.g., cough, shortness of breath) have improved
- "HCP with severe to critical illness or who are severely immunocompromised: At least 10 days and up to 20 days have passed since symptoms first appeared; At least 24 hours have passed since last fever without the use of fever-reducing medications AND Symptoms (e.g., cough, shortness of breath) have improved. Consider consultation with infection control experts."
- "For HCP with severe to critical illness or who are severely immunocompromised, the recommended duration for work exclusion was changed to at least 10 days and up to 20 days after symptom onset"

Related:

- CDC. **Clinical Questions about COVID-19: Questions and Answers**. November 20, 2020. ([LINK](#))
- CDC. **When to Quarantine**. October 27, 2020. ([LINK](#))
    - "People who have tested positive for COVID-19 do not need to quarantine or get tested again for up to 3 months as long as they do not develop symptoms again. People who develop symptoms again within 3 months of their first bout of COVID-19 may need to be tested again if there is no other cause identified for their symptoms."
    - "Cases of reinfection of COVID-19 have been reported but are rare. In general, reinfection means a person was infected (got sick) once, recovered, and then later became infected again. Based on what we know from similar viruses, some reinfections are expected."

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- CDC. **Updated Isolation Guidance Does Not Imply Immunity to COVID-19**. August 14, 2020. ([LINK](#))
  - o "… ==people can continue to test positive for up to 3 months after diagnosis and not be infectious to others. This does not imply a person is immune to reinfection with SARS-CoV-2, the virus that causes COVID-19, in the 3 months following infection==. The latest data simply suggests that retesting someone in the 3 months following initial infection is not necessary unless that person is exhibiting the symptoms of COVID-19 and the

Public Health England. Guidance. **COVID-19: management of staff and exposed patients or residents in health and social care settings**. September 28, 2020. ([LINK](#))
- "Symptomatic staff who test positive for SARS-CoV-2 or who have an inconclusive test result, and symptomatic staff who have not had a test, can:
  - o Return to work no earlier than 10 days from symptom onset, provided clinical improvement has occurred and they have been afebrile (not feverish) without medication for 48 hours and they are medically fit to return.
  - o If a cough or a loss of or a change in normal sense of smell (anosmia) or taste is the only persistent symptom after 10 days (and they have been afebrile for 48 hours without medication), they can return to work if they are medically fit to return (these symptoms are known to persist for several weeks in some cases)."
- Staff who test positive for SARS-CoV-2 and who were asymptomatic at the time of the test must self-isolate for 10 days from the date of the test. If they remain well, they can return to work on day 11. If, during the 10 days isolation, they develop symptoms, they must self-isolate for 10 days from the day of symptom onset. They can follow the same instructions as above."
- Staff who have been notified through the NHS test and trace or other national contact tracing service that they are a contact of a confirmed case of COVID-19 in the community they should inform their line manager and self-isolate for 14 days, in line with the NHS test and trace guidance. This advice should be followed regardless of the results of any SARS-CoV-2 antibody testing. A positive antibody result signifies previous exposure, but it is currently unknown whether this correlates with immunity, including protection against future infections.

Ministry of Health New Zealand. **COVID-19: Advice for all health professionals**. August 27, 2020. ([LINK](#))
- "Mild illness who did not require hospitalization: At the discretion of the health professional responsible for monitoring (currently the public health unit for non-hospitalized probable and confirmed and probable cases), the person can be released from isolation if they meet all the following criteria:
  - o At least 10 days have passed since the onset of symptoms
  - o There has been resolution of symptoms of the acute illness for the previous 72 hours."
- "More severe illness who have been discharged from hospital: The person can only be released from isolation at the discretion of the health professional responsible, based on all the following criteria:
  - o At least 10 days have passed since hospital discharge
  - o There has been resolution of all symptoms of the acute illness for the previous 72 hours
  - o They do not have major immunosuppression (such as being within a year of bone marrow transplantation or receiving chemotherapy).
  - o There has been resolution of symptoms of the acute illness for the previous 72 hours."
- "Cases who remain asymptomatic:

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- o Cases that remain asymptomatic can be released ten days after the date that testing was undertaken."
- "Health care workers who are cases:
  - o Health care workers who are confirmed (or probable) COVID-19 cases should follow the standard advice for release from isolation. There is no longer a requirement to have two negative PCR tests before returning to work."

Australian Government Department of Health. **Communicable Diseases Network Australia (CDNA) and Public Health Laboratory Network (PHLN) joint statement – Revised Australian criteria for the release of persons recovered from COVID-19 from isolation**. August 13, 2020. ([LINK](#))

- "A 10-day period from onset of symptoms in mild cases, and 72 hours after resolution of the acute illness, whichever is the later, is sufficient to indicate that transmission will not occur from a recovered case. This applies regardless of the setting the recovered case may be returning to."
- "A precautionary approach was maintained for cases with more severe illness who are hospitalised. This is due to the risk of a protracted infectious period accompanying prolonged or severe symptoms. The criteria required for release from isolation for these people are:
  - o 10 days from hospital discharge, and
  - o Complete symptoms resolution for 72 hours
    whichever is the later."

Related:
- NSW Government Health. **Release from isolation**. November 22, 2020. ([LINK](#))
  - o "Guidance on when a healthcare worker can return to work"

Sub-National Authorities

Alberta Health Services. **COVID-19 Return to Work Guide for Healthcare Workers.** November 12, 2020. ([LINK](#))

- "… healthcare workers [who have tested positive] may not work in any healthcare setting until 14 days have passed since symptoms started AND symptoms have resolved, whichever is longer."

Related:
- Alberta Health Services. **COVID-19 Return to Work Guide for Healthcare Workers Decision Chart**. November 12, 2020. ([LINK](#))
  - o Flow chart to decide return to work status.

Ontario Ministry of Health. **COVID-19 Quick Reference Public Health Guidance on Testing and Clearance**. October 1, 2020. ([LINK](#))

- Recommendations for Health Care Workers Return to Work:
  - o "Health care workers (HCWs) should follow **isolation and clearance with a non-test based approach;** if they have required hospitalization during the course of their illness, a test based approach may be used at the discretion of the hospital while they are admitted (see above). Some HCWs may be directed to have test based clearance by their employer/Occupational Health and Safety.
  - o Symptomatic HCWs awaiting testing results must be off work
  - o Asymptomatic HCWs awaiting testing results may continue to work using the appropriate precautions recommended by the facility, which will depend on the reason for testing (i.e., asymptomatic HCW is not on self-isolation following a high-risk exposure)."

- "In exceptional circumstances where clinical care would be severely compromised without additional staffing, an earlier return to work under work self-isolation may be considered for an asymptomatic HCW who is self-isolating due to a high-risk exposure."
- "In exceptionally rare circumstances where clinical care would be severely compromised without additional staffing, an earlier return to work of an asymptomatic COVID-19 positive HCW that has not been cleared may be considered under work self-isolation recognizing the HCW may still be infectious (see table below)."

BC Center for Disease Control. **Interim Guidance on Return to Work for Health Care Workers with Symptoms of COVID-19**. April 28, 2020.
([LINK](#))

- "Guidance is available for Workplace Health and Safety, Public Health staff and Medical Health Officers to support decision-making on return to work for health care workers with symptoms of COVID-19. This includes health care workers with confirmed COVID-19, HCWs that developed symptoms following exposure to confirmed cases of COVID-19, and suspected cases of COVID-19. The guidance includes information on:
  o the criteria for return to work,
  o self-isolation for staff with travel history outside Canada,
  o earlier return to work to maintain base staffing levels, and
  o additional precautions including mask usage, restricting access to severely immunocompromised patients and infection prevention and control measures."

Related:
- BC Center for Disease Control. **BC Health Care Worker Return to Work Decision Tree**. ([LINK](#))
  o The Health Care Worker Return to Work Decision Tree summarizes the guidance and can be used as a tool to support decision-making.

Other Provinces:
- Prince Edwards Island Canada. **Health PEI Health Care Workers: COVID-19 FAQs**. November 10, 2020. ([LINK](#))
- Novo Scotia. **Nova Scotia Interim Guidance: Public Health Measures of cases and contacts associated with Novel Coronavirus (COVID-19)**. November 19, 2020. ([LINK](#))
- New Brunswick. **COVID-19 Guidance for Primary Care Providers in a Community Setting.** September 8, 2020. ([LINK](#))
- Saskatchewan. **Health Care Worker Return to Work Assessment**. 2020. ([LINK](#))

Other Authorities

Canadian Pharmacists Association. **Protecting the Front Line: COVID-19 Day-to-Day Questions**. November 11, 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. <mark>Symptomatic healthcare workers cannot work</mark>. However, every situation is different."

Workplace Health and Wellbeing Unit (Ireland). **COVID-19 Telephone Assessment, Testing Pathway and Return to Work of Symptomatic Healthcare Workers Version 7**. September 14, 2020.
([LINK](#))

- A roadmap for healthcare workers to return to work after COVID exposure.

WorkplaceNL. **COVID-19 Guidelines for Employers**. August 28, 2020. ([LINK](#))
- "Fit for work
  Prior to the start of work, the employer must:
  - Review the latest guidance from the Chief Medical Officer of Health, and adjust work practices accordingly.
  - Ensure workers are pre-screened prior to entering the site or workplace. Pre-screening should also be performed for persons who may come into contact with workers where physical distancing measures cannot be maintained (dentists, salons/barbershops, etc.). A COVID-19 "Fit for Work Questionnaire" is included in this guide.
  - If a worker or visitor answers "yes" to any of the screening questions or refuses to answer, then they have failed the screening and cannot enter the site. Explained the next steps to the worker or visitor, which include completing the online COVID-19 self-assessment, calling local public health at 811, and self-isolating.

Related:
- WorkplaceNL. **Covid-19 Client Service Updates. FAQs**. November 26, 2020. ([LINK](#))
  - Guidance for workers believed or confirmed to have COVID-19.

Systematic Reviews
None found at this time.

Systematic Review Protocols (On-Going)
Chivese et al. **Prevalence of immunity to COVID-19 and reinfection: a systematic review and meta-analysis– Ongoing Review**. Prospero. July 30, 2020. ([LINK](#))
- What proportion of people with confirmed COVID-19 infection get immunity, measured by the presence of antibodies specific to SARS-CoV-2 during and immediately after the active phase of the disease?
- How long are antibodies detectable in people after infection with COVID-19 disease?
- What proportion of people with confirmed COVID-19 infection get re-infected after the resolution of the initial infection and what are the determinants of reinfection?"

Ismail et al. **Characterizing the human immune response to SARS-CoV2 infection: a rapid, systematic review – Ongoing Review**. Prospero. June 23, 2020. ([LINK](#))
- "Research Questions are:
  - What are the characteristics of the immune response to SARS-CoV2?
    - How do these vary by age, clinical severity and time since onset of symptoms?
    - What is the relationship between these and other variables and the production of binding and/or neutralizing antibodies to SARS-CoV2?
    - What role might T-cell-mediated immunity play in resistance to severe infection, recovery and immunity?
  - How long does post-infection immunity persist for?"

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Other Reviews

Borsa et al. **Attacking the defense: SARS-CoV-2 can infect immune cells. Nature Reviews Immunology**. August 21, 2020. ([LINK](#))

- "This preprint study reports that immune cells are susceptible to SARS-CoV-2 infection. Post-mortem in situ analysis of lung tissues further confirmed the presence of infected immune cells in COVID-19. As monocytes and lymphocytes do not express ACE2, it remains to be seen whether the virus uses an alternative entry strategy and whether circulating infected immune cells contribute to viral spread and COVID-19 disease progression."

Sekine et al. **Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19**. Cell. August 14, 2020. ([LINK](#))

- "The authors systematically mapped the functional and phenotypic landscape of SARS-CoV-2-specific T cell responses in unexposed individuals, exposed family members, and individuals with acute or convalescent COVID-19."
- "Acute phase SARS-CoV-2-specific T cells displayed a highly activated cytotoxic phenotype that correlated with various clinical markers of disease severity, whereas convalescent phase SARS-CoV-2-specific T cells were polyfunctional and displayed a stem-like memory phenotype. Importantly, SARS-CoV-2-specific T cells were detectable in antibody-seronegative exposed family members and convalescent individuals with a history of asymptomatic and mild COVID-19."
- "The dataset shows that SARS-CoV-2 elicits robust, broad and highly functional memory T cell responses, suggesting that natural exposure or infection may prevent recurrent episodes of severe COVID-19."

Expert Opinion

Kirckcaldy et al. **COVID-19 and Post infection Immunity Limited Evidence, Many Remaining Questions**. JAMA. May 11, 2020. ([LINK](#))

- "The durability of neutralizing antibodies (NAbs, primarily IgG) against SARS-CoV-2 has yet to be defined; persistence up to 40 days from symptom onset has been described. Duration of antibody responses against other human coronaviruses may be relevant in this context. Existing limited data on antibody responses to SARS-CoV-2 and related coronaviruses, as well as one small animal model study, suggest that recovery from COVID-19 might confer immunity against reinfection, at least temporarily. The immune response to COVID-19 is not yet fully understood and definitive data on post-infection immunity are lacking. Amidst the uncertainty of this public health crisis, thoughtful and rigorous science will be essential to inform public health policy, planning, and practice."

Beilicki J, Duval X, Gobat N et al. **Monitoring approaches for health-care workers during the COVID-19 pandemic**. The Lancet Infectious Disease. Volume 20, Issue 10; July 23, 2020. ([LINK](#))

- "Decision making on health-care worker removal from and return to work; a symptom-based algorithm that informs when isolated health-care workers should return to work appears to be best when exposed or infected health-care workers are considered crucial to service maintenance and extended periods of quarantine or isolation are not feasible. Studies are ongoing to assess the possible role of serology as a marker for viral clearance in people with mild illness."

Rueda Garrido J, Vicente-Herrero T, del Campo T et al**. Return to work guidelines for the COVID-19 pandemic**. Occupational Medicine, Volume 70, Issue 5, June 1, 2020. ([LINK](#))
- "Return to work guidelines in any pandemic will depend on the state of the local epidemic, the nature and conditions of each job and on the availability of testing. Guidelines need to be reviewed and updated over time as local epidemic status and supplies may change. In the current situation with a high rate of transmission and limited testing resources, it is important to differentiate between high- and low-risk workers. While low-risk workers' guidelines may rely on clinical criteria, more specific testing-based strategies should be used for high-risk workers."

Primary Research

Mateus et al. **Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans.** Science. August 4, 2020. ([LINK](#))
- "This study demonstrate a range of pre-existing memory CD4+ T cells that are cross-reactive with comparable affinity to SARS-CoV-2 and the common cold coronaviruses... Thus, variegated T cell memory to coronaviruses that cause the common cold may underlie at least some of the extensive heterogeneity observed in COVID-19 disease."
- "Based on these data, it is plausible to hypothesize that pre-existing cross-reactive HCoV CD4+ T cell memory in some donors could be a contributing factor to variations in COVID-19 patient disease outcomes, but this is at present highly speculative."

Related research:
- Braun et al. **SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19 - Accelerated Article Preview**. Nature. July 22, 2020. ([LINK](#))

Ibarrondo et al. **Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19**. NEJM. July 21, 2020. ([LINK](#))
- "The protective role of antibodies against SARS-CoV-2 is unknown, but these antibodies are usually a reasonable correlate of antiviral immunity, and anti–receptor-binding domain antibody levels correspond to plasma viral neutralizing activity. Given that early antibody decay after acute viral antigenic exposure is approximately exponential, the authors found antibody loss that was quicker than that reported for SARS-CoV-1."
- "The findings raise concern that humoral immunity against SARS-CoV-2 may not be long lasting in persons with mild illness, who compose the majority of persons with Covid-19."

Bert et al. **SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls**. Nature Medicine. July 15, 2020. ([LINK](#))
- "The authors studied T cell responses against the structural and non-structural regions of SARS-CoV-2 in individuals convalescing from coronavirus disease 2019 (COVID-19) (n = 36). In all of these individuals, they found T cells that recognized multiple regions of the N protein."
- "We also detected SARS-CoV-2-specific T cells in individuals with no history of SARS, COVID-19 or contact with individuals who had SARS and/or COVID-19 (n = 37). SARS-CoV-2-specific T cells in uninfected donors exhibited a different pattern of immunodominance."

Long et al. **Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections**. Nature Medicine. June 18, 2020. ([LINK](#))

- "This small group of patients (n=37) in China showed that in both asymptomatic and symptomatic individuals with COVID-19, antibody levels dropped significantly during recovery and that the levels became undetectable in 40 percent of the asymptomatic group."

The following articles are preprints and have not been peer-reviewed. They report new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

Dan J, Mateus J, Kato Y et al**. Immunological memory to SARS-CoV-2 assessed for greater than six months after infection**. bioRxiv. doi: https://doi.org/10.1101/2020.11.15.383323, November 16, 2020. ([LINK](#))

- "We analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 185 COVID-19 cases, including 41 cases at ≥6 months post-infection. Spike IgG was relatively stable over 6+ months. Spike-specific memory B cells were more abundant at 6 months than at 1 month. SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months. By studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory to SARS-CoV-2 in an integrated manner, we observed that each component of SARS-CoV-2 immune memory exhibited distinct kinetics."

Seow J, Graham C, Merrick B et al**. Longitudinal observation and decline of neutralizing antibody responses in the three months following SARS-CoV-2 infection in humans**. Nature Microbiology, Volume 5, 1598–1607, October 26, 2020. ([LINK](#))

- "Using sequential serum samples collected up to 94 d post onset of symptoms (POS) from 65 individuals with real-time quantitative PCR-confirmed SARS-CoV-2 infection, we show seroconversion (immunoglobulin (Ig)M, IgA, IgG) in >95% of cases and neutralizing antibody responses when sampled beyond 8 d POS. We show that the kinetics of the neutralizing antibody response is typical of an acute viral infection, with declining neutralizing antibody titres observed after an initial peak, and that the magnitude of this peak is dependent on disease severity."
- "The present study has important implications when considering widespread serological testing and antibody protection against reinfection with SARS-CoV-2, and may suggest that vaccine boosters are required to provide long-lasting protection."

Rodda et al. **Functional SARS-CoV-2-specific immune memory persists after mild COVID-19**. MedRxiv. August 15, 2020. ([LINK](#))

- "A longitudinal assessment of individuals recovered from mildly symptomatic COVID-19 to determine if they develop and sustain immunological memory against the virus.
- "The authors found that recovered individuals developed SARS-CoV-2-specific IgG antibody and neutralizing plasma, as well as virus-specific memory B and T cells that not only persisted, but in some cases increased numerically over three months following symptom onset.
- "The SARS-CoV-2-specific memory lymphocytes exhibited characteristics associated with potent antiviral immunity: memory T cells secreted IFN-γ and expanded upon antigen re-encounter, while memory B cells expressed receptors capable of neutralizing virus when expressed as antibodies.
- "These findings demonstrate that mild COVID-19 elicits memory lymphocytes that persist and display functional hallmarks associated with antiviral protective immunity."

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Wajnberg et al. **SARS-CoV-2 infection induces robust, neutralizing antibody responses that are stable for at least three months**. MedRxiv. July 17, 2020. ([LINK](#))

- "The authors report that the vast majority of infected individuals with mild-to-moderate COVID-19 experience robust IgG antibody responses against the viral spike protein, based on a dataset of 19,860 individuals screened at Mount Sinai Health System in New York City.
- "This study shows that titers are stable for at least a period approximating three months, and that anti-spike binding titers significantly correlate with neutralization of authentic SARS-CoV-2.
- "The data suggests that more than 90% of seroconverters make detectible neutralizing antibody responses and that these titers are stable for at least the near-term future."

Seow et al. **Longitudinal evaluation and decline of antibody responses in SARS-CoV-2 infection**. MedRxiv. July 11, 2020. ([LINK](#))

- "Using sequential serum samples collected up to 94 days post onset of symptoms (POS) from 65 RT-qPCR confirmed SARS-CoV-2-infected individuals, we show seroconversion in >95% of cases and neutralizing antibody (nAb) responses when sampled beyond 8 days POS. The authors demonstrate that the magnitude of the nAb response is dependent upon the disease severity, but this does not affect the kinetics of the nAb response. Declining nAb titres were observed during the follow up period. This transient nAb response is a feature shared by both a SARS-CoV-2 infection that causes low disease severity and the circulating seasonal coronaviruses that are associated with common colds."

News Articles

Nature - **COVID research updates: Immune responses to coronavirus persist beyond 6 months**. Posted on November 20, 2020. ([LINK](#))

- "The immune system's memory of the new coronavirus lingers for at least six months in most people. Shane Crotty at the La Jolla Institute for Immunology in California and his colleagues analysed markers of the immune response in blood samples from 185 people who had a range of COVID-19 symptoms; 41 study participants were followed for at least 6 months (J. M. Dan et al., 2020 Preprint at bioRxiv https://doi.org/ghkc5k).
- The team found that participants' immune responses varied widely. But several components of immune memory of SARS-CoV-2 tended to persist for at least 6 months. Among the persistent immune defenders were memory B cells, which jump-start antibody production when a pathogen is re-encountered, and two important classes of T cell: memory CD4+ and memory CD8+ T cells. The results have not yet been peer-reviewed."

BBC News - **Covid: Antibodies 'fall rapidly after infection'**. Posted on October 27, 2020. ([LINK](#))

- "The Imperial College London team found the number of people testing positive for antibodies has fallen by 26% between June and September."
- "They say immunity appears to be fading and there is a risk of catching the virus multiple times."
- "The fall was greater in those over 65, compared with younger age groups, and in those without symptoms compared with those with full-blown Covid-19."

CIDRAP - Center for Infectious Disease Research and Policy - **Studies show long-term COVID-19 immune response**. Posted on October 26, 2020. ([LINK](#))

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- "A UK study in Nature Microbiology examined 65 individuals with polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection and 31 seropositive healthcare workers (HCWs). More than 95% of patients showed seroconversion—the presence of detectable SARS-CoV-2 antibodies—and neutralizing antibodies in samples 8 days after symptom onset, but the magnitude of the neutralizing antibody response appears to depend on disease severity, with lower peak antibody levels in individuals exhibiting milder disease. In some individuals with low initial levels of peak neutralizing antibodies (mean infectious dose [ID50], 100 to 300), antibodies were undetectable after 50 days, while some patients with high initial levels (ID50, 1,000 to 3,500) maintained neutralizing antibodies for more than 60 days after initial symptoms."
- "Similar findings emerged from a Portuguese study in the European Journal of Immunology that examined antibody levels in more than 500 hospitalized patients, healthcare workers, and volunteers who had recovered from COVID-19. The researchers found that 90% of SARS-CoV-2– positive individuals had detectable antibodies from 40 days up to 7 months post-infection, with higher levels in patients with more severe disease."

BBC Future - **The people with hidden immunity against Covid-19**. Posted on August 18, 2020. ([LINK](#))
- "Though antibodies have proved invaluable for tracking the spread of the pandemic, they might not have the leading role in immunity that we once thought. If we are going to acquire long-term protection, it looks increasingly like it might have to come from somewhere else… a new hope has appeared on the horizon: the enigmatic T cell."

Nature - **What the immune response to the coronavirus says about the prospects for a vaccine**. Posted on August 17, 2020. ([LINK](#))
- "Long-term immunity can vary by type and also by degree of response. Vaccine developers often hope to elicit what's known as sterilizing immunity, a response, typically mediated by antibodies that can rapidly prevent a returning virus from gaining ground in the body. But not all vaccines or infections elicit the neutralizing antibodies required for sterilizing immunity. HIV, for example, rarely induces neutralizing antibodies, a fact that has complicated efforts to develop vaccines against it."
- "Then there's the question of how long antibodies last. When researchers tracked COVID-19 patients over time, they found that the amount of antibody peaked in the days following the onset of symptoms, then began to decline. In some study participants, the antibodies were practically undetectable within about three months."

Nature - **COVID-19 poses a riddle for the immune system**. Posted on August 17, 2020. ([LINK](#))
- "It is unclear why people's immune response to the SARS-CoV-2 coronavirus varies so widely."
- "Differences in immune responses between the different categories of disease severity are even more evident when people with very mild or subclinical disease are included in the analyses."

New York Times – **Scientists See Signs of Lasting Immunity to Covid-19, Even After Mild Infections**. Posted on August 16, 2020. ([LINK](#))
- "What has been observed in people who fought off mild cases of Covid-19 might not hold true for hospitalized patients, whose bodies struggle to marshal a balanced immune response to the virus, or those who were infected but had no symptoms at all. Research groups around the world are continuing to study the entire range of responses. But "the vast majority of the cases are these mild infections"

- "Still, much remains unknown. Although these studies hint at the potential for protectiveness, they do not demonstrate protection in action."

Scientific American - **Concerns about Waning COVID-19 Immunity Are Likely Overblown**. Posted on July 31, 2020. (LINK)
- "Scientists have focused on antibodies because they are relatively easy to measure with a blood test and may be helpful as a treatment for COVID-19. But the adaptive immune system also involves T cells, which may mount a strong response to the novel coronavirus even if antibodies have waned. ==T cells could keep a record of the infection. But its strength may depend on that infection's severity==."
- "Scientists still do not know what level of immune response might be protective against future infection. Only longer-term studies will be able to answer that question."

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 researchers carried out individual internet searches (Google and Google Scholar) and the following databases:

Alberta Health Services
CADTH
Centre for Disease Control
Centre for Evidence Based Medicine
Cochrane Collaboration
COVID-19 Critical Intelligence Unit
Evidence Aid
Guidelines International Network
Health Canada
Health Systems Evidence
HIQA (Ireland)
Joanna Briggs Institute
MedRxiv
National Collaborating Centres on Methods and Tools (NCCMT)

National Institute for Health and Care Excellence
National Institutes of Health COVID-19 Treatment Guidelines
National Library of Medicine
NIPH Systematic Reviews on COVID-19
Once for Scotland guidance
PROSPERO
Public Health Agency of Canada
U Penn Center for Evidence-Based Practice
U.S. Veterans' Affairs (VA) Evidence Synthesis Program
Usher Network for COVid-19 Evidence Reviews
World Health Organization
COVIDEND: Inventory of best evidence syntheses

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