

Should We Be Concerned About SARS-CoV-2 Reinfections?

Series | COVID-19 & response strategy

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[This document is a part of a series of discussion notes addressing fundamental questions about COVID-19 and response strategies. These documents are based on the best scientific information available and may be updated as new information comes to light.]

16 October 2020

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The most reliable estimates suggest that one in ten people worldwide have already been infected by the SARS-CoV-2 coronavirus¹. In this context, the possibility that people could be reinfected with the virus casts a shadow over the strategy against COVID-19. Reports of second episodes of infection in people who had already been infected have recently started to emerge.

So far, cases of reinfection remain **anecdotal**. At least six cases have been documented in such disparate locations as Hong Kong, the United States, Belgium, Ecuador and India. Although four of these reports are still in the pre-print stage and the cases identified are the exception in a pool of more than 36 million confirmed infections worldwide, the reality is that the **lack of data** and the **limitations of tracing systems** may be obscuring other similar episodes.

From a scientific point of view, there are **three fundamental questions** about reinfection that we cannot answer with certainty on the basis of the information currently available:

- What is the **frequency** of reinfections?
- How **serious** is the second infection compared to the first one?
- To what extent do reinfections contribute to the **spread** of the virus?

The answer to each of these questions will have both clinical and epidemiological implications and will therefore have an impact on the social and public-health response to COVID-19. This document contains **recommendations** regarding various aspects pertaining to this debate ●

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¹ 10% Of Global Population May Have Contracted The Coronavirus, WHO Says. NPR. 5 October 2020.

Figure 1. Cases of Reinfection Reported in Scientific Publications.



Location	Age of patient	First episode	Interval	Second episode	Publication
Hong Kong	33 years	Symptomatic	142 days	Asymptomatic	Peer-reviewed
Nevada, USA	25 years	Symptomatic	48 days	Symptomatic with hospitalisation	Pre-print
Belgium	52 years	Symptomatic	93 days	Symptomatic	Peer-reviewed
Ecuador	46 years	Symptomatic	63 days	Symptomatic	Pre-print
India	25 years	Asymptomatic	108 days	Asymptomatic	Pre-print
India	28 years	Asymptomatic	111 days	Asymptomatic	Pre-print

Source: [Reinfection with SARS-CoV-2: considerations for public health response. Threat assessment brief](#). European Centre for Disease Prevention and Control (ECDC). September 2020.

1. What Do We Currently Know About the Immune Response to SARS-CoV-2?

“If immunity is short-lived, the incidence of reinfection may increase 6-12 months after the first infection. Better monitoring of reinfections will therefore be critical in the next phase of the pandemic.”

a) Possibility of reinfection

Although the data suggest that reinfection may be exceptional, we cannot rule out the possibility that reinfections may so far have been underestimated due to the strain on the health, epidemiological and scientific services and/or because infections go undetected if they are mostly asymptomatic. Most experts agree that reinfections **are to be expected**, but are **likely to be mild and with limited consequences**, although serious cases associated with individual risk factors cannot be ruled out.

b) Post-infection immunity

Early studies showed that most people produce antibodies. Further research has shown that most people also generate cellular responses. Cross-reactivity between SARS-CoV-2 and the coronaviruses that cause the common cold could provide partial protection against COVID-19, especially in children. However, as research advances, it is becoming clear that the immune response is **highly heterogeneous among individuals**. Some people do not produce antibodies, although all appear to generate SARS-CoV-2-reactive T cells. We still do not know what type and threshold of antibodies and T cells protect against infection and disease (correlates of protection). This is a fundamental limitation.

c) Duration of the immune response

We do not yet know whether SARS-CoV-2 immunity resembles that of the common-cold coronaviruses (limited duration, 6-12 months) or that of the SARS and MERS coronaviruses (long duration, several years). Recent studies that followed cases for up to four months reported that antibodies tend to decrease over time, although T cells may be more stable. Therefore, the risk of reinfection may increase as immune responses drop below the protective threshold, but with great variability among individuals. If immunity is short-lived, the incidence of reinfection may increase **6-12 months after the first infection**. Better monitoring of reinfections will therefore be critical in the next phase of the pandemic. The first generation of **vaccines** could delay a possible upsurge of reinfections. However, the same uncertainties surrounding natural immunity apply to vaccine-induced immunity: **Will immunity last over time, or will people need to be revaccinated periodically?** ●

2. How Can We Answer the Questions Surrounding Reinfection?

“The only way to answer these questions is to actively monitor cases over time to determine the type, magnitude and duration of the immune responses.”

The only way to answer these questions is to **actively monitor cases** over time to determine the type, magnitude and duration of the immune responses and their impact on protection against reinfection. In particular, it will be necessary to:

- **Create cohorts** of people who have had the disease and people who have been vaccinated.
- **Standardise the criteria and protocols** for defining reinfections, preferably at the European level.
- **Collect as much information as possible** about both episodes of infection:

genomic information (viral sequencing), epidemiological information (contacts, exposure), clinical information (risk factors, symptom severity) and immunological information (presence of antibodies and T cells). Common protocols for obtaining and collecting this information would be very useful.

Until more information is available and as long as the risk of infection remains significant, people who have already had the disease must keep following the **same preventive measures**, including mask-wearing and hand hygiene ●

3. Response and Resilience of Health Systems and Clinical Care

“The possibility that people who have been infected with the virus could be reinfected, become ill again and pass the disease on to others should be taken into account in the preparation of health systems.”

The **foresight of health systems** is a key factor in the response to COVID-19. The possibility that people who have been infected with the virus could be reinfected, become ill again and pass the disease on to others should be taken into account in the preparation of health systems in several relevant areas:

- Diagnosis and assessment of SARS-CoV-2 infection is necessary even in patients who have previously been infected. This means that **rapid testing capacity must also be guaranteed for cases with confirmed previous infection** and compatible symptoms. When such a person tests positive, contact tracing and testing should be carried out and quarantine protocols should be applied.
- Based on what we know so far, the **clinical management** of reinfected patients should be **no different from that of patients infected for the first time**.

Although none of the reinfection cases reported to date have transmitted the infection to other people, we cannot rule out the possibility that they could spread the disease just like people infected for the first time.

In short, the **limited evidence currently available** suggests that, on a large scale, reinfections could have a limited epidemiological impact on transmission (assuming that the virus is relatively genetically stable, as observed to date). Even so, public health activities and the response of health care systems should **take this possibility into account**, applying and, where appropriate, adapting their existing protocols and ensuring coordination in the information and management of transmission prevention and control actions ●

4. Global Vaccination Strategy

“Reinfection does not mean that vaccines are not effective. What it could mean is that a large part of the population might require one or more booster doses after a certain period of time.”

It is important to note that we do not yet know whether the **immunity conferred by the vaccines** currently in development will be of the same type and duration as natural immunity. Vaccines are expected to induce stronger, longer-lasting and more homogeneous immunity than the immunity conferred by natural infection, particularly in cases with mild or no symptoms, but this has yet to be proven (several of the more advanced candidate vaccines use technology that has never before been used in humans).

In any case, **reinfection does not mean that vaccines are not effective**. What it could mean is that much of the population might require **one or more booster doses** after a certain period of time. Logistically, this will require an even greater effort to produce, distribute and purchase billions of additional vaccine doses. But this is also true of many other vaccines; indeed, the yellow fever vaccine is one of the few that confer lifelong protection.

It is also possible that vaccines will **only reduce symptoms rather than prevent**

infection. If this is the case, **vaccinated people** would become **asymptomatic carriers** of the virus and could therefore infect members of vulnerable groups. Therefore, both vaccinated and unvaccinated people should continue to observe the **usual preventive measures**—mask-wearing, hand hygiene, etc.—until this hypothesis can be tested or until a sufficiently large percentage of the population has been vaccinated.

If reinfections turn out to be marginal—i.e. infrequent and without negative health impacts—a possible strategy in countries where **serological surveillance** is feasible would be not to include those who have already been infected in national vaccination plans (about 10% of the population, according to the WHO estimate cited above). Given that, at least initially, the demand for the vaccine will be much greater than the supply, this strategy would make it possible to **prioritise groups that have not yet developed immunity** ●

Box 1. Managing Education and the “New Normal”.

The possibility of reinfection has little effect on the routines devised for a **safe return to school**. In schools, the main goal is to identify positive cases and isolate them quickly, while at the same time tracing the infected person’s direct contacts within their so-called “bubble” group.

The reinfection scenario would simply **enlarge the pool of potentially “infectable” children and adults**. If reinfection becomes more frequent, all close contacts of a positive case would need to be traced and isolated in anticipation of a possible reinfection. However, this would not affect the established routines; it would simply increase the number of people at risk.

5. The Challenge of Public Information

“Reinfections should be considered in light of what is known about other respiratory viruses and always in the context of the magnitude of the problem, so as not to create unnecessary alarm.”

It is essential that information on reinfections be provided to the public in a **timely and transparent** manner and that the uncertainty currently surrounding the issue of reinfection be duly explained. Reinfections should be considered in light of what is known about other respiratory viruses and always in the context of the magnitude of the problem, **so as not to create unnecessary alarm.**

The **messages** that should be conveyed, given the information currently available, include the following:

- At present, reinfections are not a cause for alarm. Reinfections are also seen in many other respiratory viruses.
- We do not yet know how frequently reinfections occur. **Very few cases** have been documented so far.
- We do not yet understand the consequences of reinfection at the individual level (severity of symptoms after the second infection) or at the population level (ability to spread the virus). This is why it is important for people who have already had the infection to **keep observing the same hygiene and prevention measures** as the rest of the population.
- **More information is needed** on the type and duration of natural and vaccine-induced immunity.

- If reinfections are marginal and do not exacerbate the disease, people with antibodies need not be included in the **first vaccination campaigns.**

- If reinfections are frequent, **booster doses may need to be administered regularly or after a certain period of time** ●

TO LEARN MORE:

- [Reinfection with SARS-CoV-2: considerations for public health response. Threat assessment brief.](#) European Centre for Disease Prevention and Control (ECDC). September 2020.
- [Coronavirus reinfections: three questions scientists are asking.](#) *Nature*. 4 September 2020.
- [What the immune response to the coronavirus says about the prospects for a vaccine.](#) *Nature*. 17 August 2020.
- [Robust T Cell Immunity in Convalescent Individuals with Asymptomatic or Mild COVID-19.](#) *Cell*. 14 August 2020.
- [A systematic review of antibody mediated immunity to coronaviruses: kinetics, correlates of protection, and association with severity.](#) *Nature Communications*. 17 September 2020.

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