Interim guidelines for detecting cases of reinfection by SARS-CoV-2

29 October 2020

The Pan American Health Organization / World Health Organization (PAHO/WHO) encourages Member States to compile evidence on cases of SARS-CoV-2 reinfection in order to contribute to and expand the existing knowledge of COVID-19 and its prevention, control, and clinical management.

Introduction

SARS-CoV-2 has been classified within the genus *Betacoronavirus* (subgenus *Sarbecovirus*), belonging to the *Coronaviridae* family. In the past, reinfections with other coronaviruses have been documented as well as with another *Betacoronavirus* (hCoV-OC43)[1,2]; therefore, the occurrence of reinfection with SARS-CoV-2 cannot be ruled out.

SARS-CoV-2 is the seventh coronavirus identified as infectious for humans (HCoV). Four of these viruses, HCoV-229E, HCoV-NL63, HCoV-HKU1, and HCoV-OC43, are endemic, seasonal, and often cause mild respiratory disease. The other two viruses, both of zoonotic origin and more virulent, are the Middle East respiratory syndrome coronavirus (MERS-CoV) and the severe acute respiratory syndrome coronavirus type 1 (SARS-CoV-1).

In fact, in recent months, cases of reinfection by SARS-CoV-2 have been documented worldwide. With the information available to date, there is insufficient evidence that people who have recovered from SARS-CoV-2 infection generate neutralizing antibodies that can protect them from reinfection.[3]

Because confirmation of SARS-CoV-2 reinfection requires relatively complex laboratory support, especially to rule out recurrence or prolonged viral excretion, detecting suspected cases of reinfection may be more manageable. To this effect, an operational case definition and an ad-hoc surveillance system are necessary to detect suspected cases of reinfection.

A summary of some cases of SARS CoV-2 reinfection is provided in **Table 1**[4].

[1] Edridge AWD, Kaczorowska J, Hoste ACR, Bakker M, Klein M, Loens K, et al. Seasonal coronavirus protective immunity is short-lasting. Nat Med. 2020 Sep 14. https://doi.org/10.1038/s41591-020-1083-1

[2] Kiyuka PK, Agoti CN, Munywoki PK, Njeru R, Bett A, Otieno JR, et al. Human Coronavirus NL63 Molecular Epidemiology and Evolutionary Patterns in Rural Coastal Kenya. J Infect Dis. 2018 May 5;217(11):1728-39. https://doi.org/10.1093/infdis/jiy098

[3] WHO. "Immunity passports" in the context of COVID-19. Scientific note, 24 April 2020. Available at: https://bit.ly/31o6peP

[4] For more detailed information, please see references 3-7.

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Table 1. Description of select SARS-CoV-2 reinfections documented until 19 October 2020.

Characteristics of the cases	Case A	Case B	Case C	Case D	Case E*	Case F*
Age (Years old)	52	33	46	25	25	28
Sex	Female	Male	Male	Male	Male	Female
Health status	Asthma	Inmunocompetent	Inmunocompetent	Inmunocompetent	Inmunocompetent	Inmunocompetent
Clinical evolution during the first episode	Symptomatic	Symptomatic	Symptomatic	Symptomatic	Asymptomatic	Asymptomatic
Type of first sample	Oropharyngeal swab	Oropharyngeal swab and saliva	Oropharyngeal swab	Oropharyngeal swab	Oropharyngeal swab	Oropharyngeal swab
Type of first testing	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR
Time between the first and the second positive PCR	93 days	142 days	63 days	48 days	108 days	111 days
Clinical evolution during the second episode	Symptomatic	Asymptomatic	Symptomatic	Symptomatic - Hospitalization	Asymptomatic	Asymptomatic
Type of second sample	Oropharyngeal swab	Oropharyngeal swab and saliva	Oropharyngeal swab			
Type of second testing	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR
Country of report of the case	Belgium	China (Hong Kong)	Ecuador	United States of America	India	India

Note:
* Corresponds to a healthcare worker
Source: European Centre for Disease Prevention and Control. SARS-CoV-2 Reinfection: Considerations for the Public Health Response: ECDC; 2020. Available at: https://bit.ly/31B9et3

Guidance and recommendations for national authorities

The Pan American Health Organization / World Health Organization (PAHO/WHO) provides the following provisional case definitions and criteria for documenting cases of reinfection by SARS-CoV-2. The definitions are based on current available information and are subject to periodic review as new information is generated.

The following considerations should be taken into account for determining the occurrence of reinfection by SARS-CoV-2:

- Reinfection is defined as the process by which a person was once infected with SARS-CoV-2, was no longer infected, and becomes reinfected with SARS-CoV-2.

- The detection of cases of SARS-CoV-2 reinfection should not change public health and clinical management measures for cases of primary infection, or the management of subsequent secondary SARS-CoV-2 infections.

- Adequate collection and storage of samples from COVID-19 cases is key to ensuring confirmation of reinfection; reinfection can only be confirmed through the availability of at least two samples (primary sample and secondary sample), from which primary infection and secondary infection can be verified.

Provisional case definitions

Suspected case of SARS-CoV-2 reinfection

- A symptomatic or asymptomatic person with a positive test result for SARS-CoV-2 following a period of ≥90 days from the first infection with SARS-CoV-2 for which prolonged shedding of SARS-CoV-2 or viral RNA and infection by another agent have been ruled out.

OR

- A person with symptoms compatible with COVID-19 , and a positive test result for SARS-CoV-2 following a period ≥45 days from the first infection with SARS-CoV-2 for which prolonged shedding of SARS-CoV-2 or viral RNA and infection by another agent have been ruled out.

Confirmed case of SARS-CoV-2 reinfection

A suspected case of SARS-CoV-2 reinfection for which the following criteria are met:

Epidemiological criteria:

- Period of time during which the case did not present with symptoms of primary infection by SARS-CoV-2.

OR

- Period of time during which the case did not excrete SARS-CoV-2 or viral RNA.

OR

- A negative laboratory test for SARS-CoV-2 or viral RNA following primary infection.

Laboratory criteria:

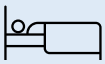
- Complete genomic sequencing of SARS-CoV-2 for both the primary infection sample and secondary infection sample indicating they belong to different genetic clades or lineages, regardless of the number of single nucleotide variations (SNV). The virus is expected to mutate by approximately two SNVs per month.

OR

- Complete genomic sequencing indicating that the number of SNV among SARS-CoV-2 infections, including differences in high-confidence minority variants, correlate with the probability that different episodes are caused by different viral lineages.

PAHO/WHO maintains the recommendations published through previous Epidemiological Alerts and Updates on COVID-19 issued to date and available at:
https://www.paho.org/en/epidemiological-alerts-and-updates

The following are links to a series of guidance documents, scientific reports, and other resources published by PAHO/WHO and WHO.

Surveillance, rapid response teams, and case investigation 	**Clinical care** 
WHO resources, available at: https://bit.ly/30zjmCj PAHO/WHO resources available at: https://bit.ly/36DJi3B	WHO resources, available at: https://bit.ly/3li6wQB PAHO/WHO resources available at: https://bit.ly/36DJi3B
Laboratory 	**Infection prevention and control** 
WHO resources, available at: https://bit.ly/3d3TJ1g PAHO/WHO resources available at: https://bit.ly/36DJi3B	WHO resources, available at: https://bit.ly/3d2ckuV PAHO/WHO resources available at: https://bit.ly/36DJi3B
Critical preparedness, readiness, and response actions 	**Travel, Points of entry and border health** 
WHO resources, available at: https://bit.ly/3ljWHBT PAHO/WHO resources available at: https://bit.ly/36DJi3B	WHO resources, available at: https://bit.ly/3ivDivW PAHO/WHO resources available at: https://bit.ly/36DJi3B
Schools, workplaces, & institutions 	**Other resources**
WHO resources, available at: https://bit.ly/3d66iJO PAHO/WHO resources available at: https://bit.ly/36DJi3B	WHO resources, available at: https://bit.ly/33zXgRQ PAHO/WHO resources available at: https://bit.ly/36DJi3B

References

1. WHO. Diagnostic tests for SARS-CoV-2. Interim Guidance, 11 September 2020. Available at: https://bit.ly/2HjNb33

2. WHO. "Immunity passports" in the context of COVID-19. Scientific note, 24 April 2020. Available at: https://bit.ly/31o6peP

3. Van Elslande J, Vermeersch P, Vandervoort K, Wawina-Bokalanga T, Vanmechelen B, Wollants E, et al. Symptomatic SARS-CoV-2 reinfection by a phylogenetically distinct strain. Clinical Infectious Diseases. 2020. Available at: https://bit.ly/3lMOvdG

4. To K, Hung I, Ip J, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clinical Infectious Diseases, ciaa1275. Available at: https://doi.org/10.1093/cid/ciaa1275

5. Prado-Vivar B, Becerra-Wong M, Guadalupe JJ, Marquez S, Gutierrez B, Rojas-Silva P, et al. COVID-19 Reinfection by a Phylogenetically Distinct SARS-CoV-2 Variant, First Confirmed Event in South America. SSRN. 2020 3 September 2020. Available at: https://bit.ly/2FsL646

6. Tillett, Richard, Sevinsky, Joel, Hartley, Paul et al. Genomic Evidence for a Case of Reinfection with SARS-CoV-2 (25 August 2020). Available at SSRN: https://ssrn.com/abstract=3680955 and http://dx.doi.org/10.2139/ssrn.3680955

7. Gupta V, Bhoyar RC, Jain A, Srivastava S, Upadhayay R, Imran M, et al. Asymptomatic reinfection in two healthcare workers from India with genetically distinct SARS-CoV-2. [Internet]. 2020 [updated 15 September 2020; cited 17 September 2020]. Available at: https://osf.io/4fmrg/

8. European Centre for Disease Prevention and Control. SARS-CoV-2 Reinfection: Considerations for the Public Health Response: ECDC; 2020. Available at: https://bit.ly/31B9et3