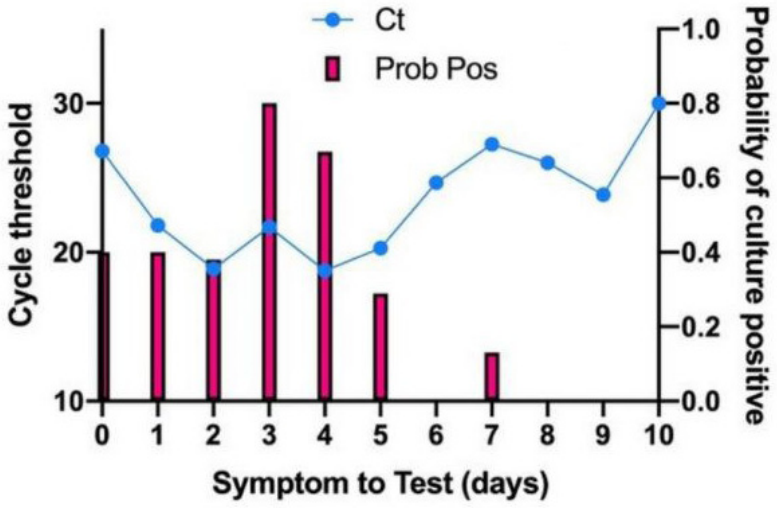
THE PATHCARE NEWS

Retesting after a positive PCR outcome for SARS-CoV-2

The presence of viral RNA in respiratory samples is critical information in the diagnosis of an acute SARS-COV-2 infection. The real-time reverse transcription-polymerase chain reaction (RT-PCR) detects these pieces of RNA. But RT-PCR is a poor test of cure. The presence of RNA does not imply the presence of infectious or replication-competent virus. Viral culture techniques, where laboratory cell lines are injected with clinical samples to detect cell damage and death and the release of a new generation of viruses (implying the presence of infectious viruses in the sample), are no longer readily available in diagnostic laboratories. Thus data is sparse on how PCR results relate to viral culture results (i.e. replication-competent virus).

In one of the few studies comparing viral culture results with PCR data and time of symptom onset, the probability of SARS-COV-2 infectious virus was greater when the cycle threshold (Ct value) of the PCR was lower. The lower the cycle threshold level the greater the amount of RNA (genetic material) in the sample. Beyond 8 days, however, no live virus was detected.



Comparing symptom onset to test (days) to the probability of successful culture on Vero cells (bar graph) and SARS-CoV-2 E gene RT-PCR cycle threshold (Ct) value (line graph).

Early in the pandemic de-isolation guidelines were based on retesting with two consecutive negative PCR outcomes required at least 24 hours apart. Most patients with mild COVID-19 infection continue to shed SARS-CoV-2 nucleic acid from their upper airways for a median of approximately 7-12 days. However, several cases were reported with prolonged periods of positive PCR outcomes (up to 84 days and beyond) in spite of resolution of symptoms. With a few exceptions infectious viruses could only be isolated up to about 9 days.

With higher Ct values and intermittent shedding of virus, PCR test outcomes may alternate between positive and negative outcomes for the patient in the convalescent period and beyond. Furthermore, the detection vs replication-competent conundrum is ubiquitous for RNA viruses. SARS-CoV, MERS, Influenza, Ebola and Zika viral RNA can be detected long after the disappearance of the infectious virus.

With limited data available current recommendations and guidelines for SARS-CoV-2 clinical management can only balance risks and benefits, and not remove risk. Guidelines for de-isolation and/or retesting (South African NDOH, CDC and WHO) now adopt a symptom based rather than a test based strategy. Current CDC recommendations clarify the approach for retesting:

1. Duration of isolation and precautions

- For most persons with COVID-19 illness, isolation and precautions can generally be discontinued 10 days *after symptom onset** and resolution of fever for at least 24 hours, without the use of fever-reducing medications, and with improvement of other symptoms.

- A limited number of persons with severe illness may produce replication-competent virus beyond 10 days that may warrant extending duration of isolation and precautions for up to 20 days after symptom onset; consider consultation with infection control experts.

- For persons who never develop symptoms, isolation and other precautions can be discontinued 10 days *after the date of their first positive RT-PCR test for SARS CoV 2 RNA.*

2. Role of PCR testing# to discontinue isolation or precautions

- For persons who are severely immunocompromised, a test-based strategy could be considered in consultation with infectious diseases experts.

- For all others, a test-based strategy is no longer recommended except to discontinue isolation or precautions earlier than would occur under the strategy outlined in Part 1, above.

3. Role of PCR testing after discontinuation of isolation or precautions

- For persons previously diagnosed with symptomatic COVID-19 who remain asymptomatic after recovery, retesting is not recommended within 3 months after the date of symptom onset for the initial COVID-19 infection.

- For persons who develop new symptoms consistent with COVID-19 during the 3 months after the date of initial symptom onset, if an alternative etiology cannot be identified by a provider, then the person may warrant retesting; consultation with infectious disease or infection control experts is recommended. Isolation may be considered during this evaluation based on consultation with an infection control expert, especially in the event symptoms develop within 14 days after close contact with an infected person.

- For persons who never developed symptoms, the date of first positive RT-PCR test for SARS-CoV-2 RNA should be used in place of the date of symptom onset.

4. Role of serologic testing

- Serologic testing should not be used to establish the presence or absence of SARS-CoV-2 infection or reinfection.

* *Symptom onset* is defined as the date on which symptoms first began, including non-respiratory symptoms.
\# *PCR testing* is defined as the use of an RT-PCR assay to detect the presence of SARS-CoV-2 RNA.

The possibility of re-infections (even in the presence of antibodies) cannot be excluded based on current knowledge and should be taken into consideration when following guidelines.

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