COVID-19 Patients with Persistent or Recurrent Positive PCR Tests

Ending home isolation after detection of SARS-CoV-2 RNA by PCR assay:

- People who have had a positive PCR for SARS-CoV-2 and were symptomatic can end home isolation when:
  - 3 days have passed with no fever; and
  - Respiratory symptoms have improved (e.g. cough, shortness of breath); and
  - 10 days have passed since symptoms first appeared.

- People who have had a positive PCR for SARS-CoV-2 and were asymptomatic can end home isolation when:
  - 10 days have passed since their positive test.

Detection of SARS-CoV-2 RNA after clinical recovery from COVID-19:

- Many people with COVID-19 recover from their clinical illness and subsequently do not have detectable SARS-CoV-2 RNA in upper respiratory tract specimens.
- In others, viral RNA can be persistently detected by PCR in respiratory tract samples after clinical recovery, sometimes for weeks (persistent positive results).
- Also, in some people, after testing negative by PCR in two consecutive samples, later samples can test positive again (recurrent positive tests).
- Whether persistent or recurrent, data from the Centers for Disease Control and Prevention (CDC) indicate:
  - These repeated detections of viral RNA consistently are associated with higher cycle threshold (Ct) values (i.e., fewer RNA copies) than were found in earlier PCR results in samples collected shortly after or and during clinical illness.
  - Live virus has not been isolated when viral isolation in tissue culture has been attempted in people who have clinically recovered yet have persistent or recurrent positive tests.

The implications of persistent or recurrent positive SARS-CoV-2 PCR results:

- It is unknown whether people who have clinically recovered from COVID-19 but who have persistent or recurrent detection of SARS-CoV-2 are infectious.
  - Experience with other viruses suggests it is unlikely that such individuals are infectious. Usually the amount of detectable virus decreases over time after the onset of illness, and this decrease in the amount of virus is associated with a decreased ability to isolate live virus.
  - In studies to date with SARS-CoV-2, live virus was not isolated from upper respiratory tract specimens collected more than 10 days after illness onset.
There is no evidence that people who have clinically recovered from COVID-19 with persistent or recurrent detection of virus with PCR have transmitted infection to others.

After viral infection, antibodies directed against the virus become detectable and increase over time. These antibodies then prevent viral infection in in vitro studies. However, there is no conclusive evidence yet that antibodies developed after SARS-CoV-2 infection are protective. If such antibodies are protective, the antibody titers associated with protection from reinfection is not known. In addition, the magnitude and persistence of the immune response following recovery from infection may vary from one person to another, with various factors (e.g., age) likely influencing protection.

The implications of persistent or recurrent positive SARS-CoV-2 PCR results in people who have not clinically recovered from COVID-19 or who have experienced a new clinical illness concomitant with positive SARS-CoV-2 PCR results are not clear, especially with regard to home isolation and exclusion from work, school, or other group settings.

Use of cycle threshold (Ct) values in assessing whether an individual is no longer infectious:

- Ct values are not a measure of viral burden, are not standardized by PCR platform, and have not been approved by the U.S. Food and Drug Administration for use in clinical management.
- Therefore, although attempts to culture virus from upper respiratory specimens have been largely unsuccessful when Ct values are in high but detectable ranges, Ct values are not recommended by the CDC as a way to assess when a person is no longer infectious.

Use of viral culture in assessing whether an individual is no longer infectious:

- Viral culture is not widely performed for SARS-CoV-2 because:
  - It must be conducted in Biosafety Level 3 (BSL-3) laboratories using BSL-3 practices by experienced virologists; and
  - Results can take a week or more.
- Therefore, while persons whose specimens do not yield live virus are considered no longer infectious, the complexity of such testing and the time required to complete it mean that it is unlikely to be useful to guide management of infected persons.
- Viral culture is not available in Vermont.

REQUESTED ACTION:

- Consider enrollment of people with recurrent positive PCR tests for SARS-CoV-2 into an ongoing study organized by the Emerging Infections Network (a cooperative agreement program of the Infectious Diseases Society of America (IDSA) and the CDC). Contact AHS.VDHRecurrentInfections@Vermont.gov for assistance in enrolling people into that study.
If you have any questions, please contact the HAN Coordinator at 802-859-5900 or vthan@vermont.gov

HAN Message Type Definitions

*Health Alert:* Conveys the highest level of importance; warrants immediate action or attention.

*Health Advisory:* Provides important information for a specific incident or situation may not require immediate action.

*Health Update:* Provides updated information regarding an incident or situation; unlikely to require immediate action.

*Info Service Message:* Provides general correspondence from VDH, which is not necessarily considered to be of an emergent nature.