

SYNOPSIS

12/04/2020

Review of “Shedding of viable SARS-CoV-2 after immunosuppressive therapy for cancer”

Article citation: Aydillo T, Gonzalez-Reiche AS, Aslam F, van de Guchte A, Khan Z, Obla A, et al. Shedding of viable SARS-CoV-2 after immunosuppressive therapy for cancer. *N Engl J Med.* 2020 Dec 1 [Epub ahead of print]. Available from: <https://doi.org/10.1056/NEJMc2031670>

One-minute summary

- This study investigated the shedding of live severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 20 patients with cancer and immune system compromise. Patients were from a single cancer centre in New York City and diagnosed with Coronavirus Disease 2019 (COVID-19) between March 10 and April 20, 2020.
- **Patient characteristics:**
 - Median age: 61 years (range: 35–77)
 - Male patients: 55.0% (11/20)
 - Pre-existing conditions: lymphoma (40.0%, 8/20), multiple myeloma (35.0%, 7/20), acute leukemia/myelodysplastic syndrome (20.0%, 4/20), and chronic leukemia (5.0%, 1/20)
 - Patients with hematopoietic stem cell transplant (HPSCT): 80% (16/20) of which 6 had active graft vs host disease
 - Patients undergoing chemotherapy: 60.0% (15/20)
- **Disease severity:**
 - Mild (no oxygen requirement): 30.0% (6/20)
 - Moderate (nasal cannula required for oxygen): 15.0% (3/20)
 - Severe (high oxygen requirement; e.g., mechanical ventilation): 55.0% (11/20)
- **Three patients had viable virus detected later than 20 days since symptom-onset (i.e., 25, 26 and 61 days).** Two of these patients had undergone allogeneic HPSCT and one patient had undergone chimeric antigen receptor T-cell therapy within the last 6 months. All three patients remained negative for SARS-CoV-2 IgG. Two of the three patients had severe disease.
- A unique genetic variant of SARS-CoV-2 infected each patient and there were no major differences across genomes within each patient, indicating **patients had persistent infections rather than re-infections.**
- Based on their findings, the authors suggest that the Centers for Disease Control and Prevention’s current 20-day isolation guidelines for severely ill patients may need to be revised.¹

Additional information

- The authors used real-time reverse transcription polymerase chain reaction (RT-PCR) to detect SARS-CoV RNA on nasopharyngeal (NP) swabs and sputum samples. To detect viable virus, the

authors inoculated Vero E6 cells with RT-PCR-positive samples and observed cultures daily for cytopathic effects. Whole genome sequencing was performed on serially collected NP swabs and viral cultures.

- **Viral isolation on 57 NP swab samples from the 20 patients (number of patients with positive culture/number of patients with culture performed):**
 - Day zero (day of first positive RT-PCR): 71.4% (10/14)
 - Days 1–10: 50.0% (1/2)
 - Days 11–20: 33.3% (2/6)
 - Days 21–30: 15.4% (2/13)
 - Days 31–40: 0.0% (0/8)
 - Days 41–50: 28.6% (2/7)
 - Days 51–60: 20.0% (1/5)
 - Past 60 days: 0.0% (0/2)
- **Median time of viral RNA shedding (RT-PCR) in upper respiratory tract samples:**
 - Since symptom-onset: 51 days (range: 12–82)
 - Since first positive RT-PCR: 47 days (range: 9–78)
- **Treatments for COVID-19:**
 - Hydroxychloroquine: 65.0% (13/20)
 - Corticosteroids: 45.0% (9/20)
 - Convalescent plasma: 40.0% (8/20)
 - Azithromycin: 25.0% (5/20)
 - Tocilizumab: 25.0% (5/20)
 - Remdesivir: 10.0% (2/20)
 - N-acetyl cysteine: 5.0% (1/20)

PHO reviewer's comments

- The authors did not identify the cause of prolonged shedding of viable virus in this study. However, in this cohort of patients with different types of blood cancer, prolonged shedding of viable virus was likely due to immune system suppression therapies and severe disease. Further research is needed to identify how much each of these factors contributes to prolonged shedding of live virus.
- Currently, Ontario recommends a non-test based approach to deciding when to discharge patients from isolation.² For patients with severe illness who required intensive care unit admission or with severe immune system compromise, isolation can be discontinued after 20 days since symptom-onset date or from first RT-PCR-positive date (if initially asymptomatic). In addition, patients must be afebrile without the use of fever-reducing medications and have improvement of symptoms over the previous 24 hours.
- It remains unclear how the three patients identified in this study represent the broader population of patients with severe illness or with severe immune system compromise.

Additional references

1. Centers for Disease Control and Prevention (CDC). Duration of isolation and precautions for adults with COVID-19 [Internet]. Atlanta, GA: CDC; 2020 [last updated 2020 Oct 19; cited 2020 Dec 02]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html>

2. Ministry of Health. COVID-19 quick reference public health guidance on testing and clearance [Internet]. Toronto, ON: Toronto, ON: Queens’s Printer for Ontario; 2020 [last updated 2020 Nov 20, cited 2020 Dec 02]. Available from: http://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/2019_testing_clearing_cases_guidance.pdf

Citation

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