IPC Management of Severely Immunocompromised COVID-19 Patients

Part 1: Definition for "Severely Immunocompromised"

Rationale:
Immunocompromised patients may require an extended duration of Additional Precautions for one or more of the following reasons:

- reduced immune response in clearing certain infections
- prolonged shedding of a microorganism
    - severely immunocompromised patients may produce replication-competent SARS-CoV-2 virus for prolonged periods beyond 21 days after COVID-19 symptom onset (or after first positive COVID-19 test if asymptomatic throughout)
    - the exact criteria that determine which patients will shed replication-competent virus for longer periods are not known
- greater risk of developing or re-activating certain infections
- inadequate or quickly waning protective immune response post-infection
- an atypical presentation of a communicable illness.

[See: Infection Prevention and Control Considerations for Immunocompromised Patients]

Definition:
For the purposes of COVID-19 IPC-related patient management, special consideration is given to a subset of immunocompromised patients who are considered to be "severely immunocompromised."

This list is considered current to the date provided, and is to be used as guidance by ICPs (and others) to identify which patients need further discussion with an IPC physician regarding COVID-19 management related to clearing of COVID-positive status, cohorting when recovered, re-testing within 90 days of initial infection, etc.

"Severely immunocompromised" includes:

- Congenital and acquired immunodeficiency including severe combined immunodeficiency (SCID) and profound hypogammaglobulinemia
- HIV infection with CD4 T lymphocyte count < 200 (or less than 15%) and unsuppressed viral load
    - For Paediatrics:
        - Less than 5 years – use CD4 <15%
        - 5 years or older – use CD4 count <200
- Any haematological malignancy
- Within 24 months of stem cell transplant
- Solid organ transplant until on stable immunosuppression
- Current receipt of prednisone >20mg/day (or equivalent) for more than 14 days
    - For Paediatrics:
        - >2mg/kg body weight for more than 14 days
- Chimeric antigen receptor (CAR) T-cell therapy
- Anti-B cell therapy (current or within last 6 months)
    - Most common: rituximab, ocrelizumab

For more information contact
ipcsurvstdadmin@ahs.ca

Original date: March 2021
Revised date: 25 June 2021
ECC Approval: 29 June 2021

Alberta Health Services

- Others: 90Y-ibritumomab tiuxetan, ofatumumab, veltuzumab, 131I-tositumomab, obinutuzumab, ocaratuzumab, ublituximab, blinatumomab, inebilizumab, combotox
- Note: Rituximab and ocrelizumab can be used for autoimmune disorders such as rheumatoid arthritis and multiple sclerosis in addition to chemotherapy regimens.

Part 2: Discontinuation of COVID-Related Precautions for Severely Immunocompromised Patients

COVID-19 test negative

- same as other pts
- see: Discontinuation of Contact and Droplet Precautions for Suspected or Confirmed COVID-19

COVID-19 test positive

- depends on patient-specific factors
- will always be case-by-case

General considerations for clearing COVID-positive status:

1. At least 21 days since symptom onset (or from COVID-positive test if symptom onset date not known or patient remains asymptomatic)
2. Fever: Resolution of fever
3. Other symptoms: Symptom stabilization/improvement to new or pre-existing baseline for at least 48h
4. Follow-up testing
    - Collect nasopharyngeal (NP) swab on day 22 i.e. NOT throat swab or anterior nares swab
        - Consult IPC physician if specimen type other than NP was submitted for testing
    - Use laboratory-based PCR testing
        - Request ProvLab laboratory-developed test (LDT) on requisition
    - ***A negative test is not required ***
        - Use cycle threshold (ct) value ≥30 if previous values and no symptoms OR use serial ct values
        - Determine on case-by-case basis in discussion with IPC physician
        - Contact COVID virologist-on-call if ct value not otherwise readily available
    - Frequency & duration
        - Usually weekly starting after day 21, but frequency & interval to be decided on case-by-case basis after day 22 swab
    - For outpatients: arrange for testing as required on a case-by-case basis

Is there a role for serology?

- Can be considered on a case-by-case basis.
- Unlikely to be of use in patients with hypogammaglobulinemia or who are B-cell depleted.

For more information contact
ipcsurvstdadmin@ahs.ca

Original date: March 2021
Revised date: 25 June 2021
ECC Approval: 29 June 2021

Alberta Health Services

Part 3: Severely Immunocompromised Outpatients

- Management is similar to inpatients.
- If patient is not cleared of COVID-positive status, then they must be kept on Contact and Droplet Precautions in private space when they receive healthcare.
- Communication is key:
  - Community health care providers
  - Public Health – ensure they are aware of general IC approach provincially and about specific patients in the zone
  - Patient letter provided by IPC
- Duration of isolation in community to be decided on a case-by-case basis.
  - Consider risk of transmission to be different in community versus hospital.
- Other measures are included in the patient letter.

Part 4: Management of COVID Recovered Severely Immunocompromised Patients

Symptoms	Any Risk Factor(s)	Strain of original Infection	Strain of new exposure (if known)	Contact & Droplet Precautions	COVID-19 Test
ASYMPTOMATIC					
Asymptomatic	No	Any strain or unknown strain	n/a	n/a	n/a
Asymptomatic	Yes	Any strain or unknown strain	Any strain or unknown strain	Yes - regardless of interval - continue C+D precautions until 14d since last exposure - do not cohort	No -only if symptoms or as directed by IPC
SYMPTOMATIC with NO RISK FACTORS					
Symptomatic [core resp or GI]	No	Any strain or unknown strain	n/a	Yes - do not cohort	Yes - request ProvLab laboratory-developed test (LDT)
Symptomatic [expanded]	No	Any strain or unknown strain	n/a	Yes - do not cohort	Yes - request ProvLab laboratory-developed test (LDT)

For more information contact
ipcsurvstdadmin@ahs.ca

Original date: March 2021
Revised date: 25 June 2021
ECC Approval: 29 June 2021

Alberta Health Services

SYMPTOMATIC & RISK FACTOR(S) PRESENT					
Symptomatic [core resp or GI]	Yes	Any strain or unknown strain	Any strain or unknown strain	Yes - regardless of interval since initial COVID-19 infection - do not cohort	Yes - request LDT - if COVID-negative, continue C+D precautions until 14d since last exposure or until symptoms improve/stabilize for at least 48h, whichever is longer - consider re-testing as necessary
Symptomatic [expanded]	Yes	Any strain or unknown strain	Any strain or unknown strain	Yes - regardless of interval since initial COVID-19 infection - do not cohort	Yes - request LDT - if COVID-negative, continue C+D precautions until 14d since last exposure or until symptoms improve/stabilize for at least 48h, whichever is longer - consider re-testing as necessary

Note:
Currently, COVID-19 immunization status does not change management (regardless of whether patient is fully or partially vaccinated, or not vaccinated). This will continue to be re-assessed as more data becomes available and as local epidemiology evolves.

For more information contact
ipcsurvstdadmin@ahs.ca

Original date: March 2021
Revised date: 25 June 2021
ECC Approval: 29 June 2021

REFERENCES

PCR positive references:

Choi, Bina, et al. "Persistence and Evolution of SARS-CoV-2 in an Immunocompromised Host." *N Engl J Med* 383.23 (2020): 2291-3. Web.

Corsini Campioli, Cristina, et al. "Clinical Predictors and Timing of Cessation of Viral RNA Shedding in Patients with COVID-19." *Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology* 130 (2020): 104577-. *PubMed.* Web.

Italiano, Jack, et al. "Persistent Viral Shedding Despite Seroconversion in a Kidney Transplant Recipient with Severe Extrapulmonary COVID-19." *BMJ Case Reports* 13.11 (2020): e239612. Web.

Man, Zhang, et al. "Viral Shedding Prolongation in a Kidney Transplant Patient with COVID-19 Pneumonia." *American Journal of Transplantation* 20.9 (2020): 2626-7. Web.

Nakajima, Yukiko, et al. "Prolonged Viral Shedding of SARS-CoV-2 in an Immunocompromised Patient." *Journal of Infection and Chemotherapy* 27.2 (2021): 387-9. Web.

Nam, Hannah, et al. "540. Prolonged Viral Shedding of SARS-CoV-2 in Solid Organ Transplant Recipients." *Open Forum Infectious Diseases* 7 (2020): S337-. Web.

Shingare, Ashay, Madan M. Bahadur, and Shailesh Raina. "COVID-19 in Recent Kidney Transplant Recipients." *American Journal of Transplantation* 20.11 (2020): 3206-9. Web.

Wang, Aileen X., et al. "Influence of Immunosuppression on Seroconversion Against SARS-CoV-2 in Two Kidney Transplant Recipients." *Transplant Infectious Disease* 23.1 (2021): e13423. Web.

Wei, Jia, et al. "SARS-CoV-2 Infection in Immunocompromised Patients: Humoral Versus Cell-Mediated Immunity." *Journal for immunotherapy of cancer* 8.2 (2020): e000862. *PubMed.* Web.

Yousaf, Muhammad, et al. "COVID-19: Prolonged Viral Shedding in an HIV Patient with Literature Review of Risk Factors for Prolonged Viral Shedding and its Implications for Isolation Strategies." *Clinical Case Reports* 9.3 (2021): 1397-401. Web.

Zhong, Zibiao, et al. "Clinical Characteristics and Immunosuppressant Management of Coronavirus Disease 2019 in Solid Organ Transplant Recipients." *American Journal of Transplantation* 20.7 (2020): 1916-21. Web.

Zhu, Lan, et al. "Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China." *European urology* 77.6 (2020): 748-54. Web.

sgRNA positive references:

Avanzato, Victoria A., et al. "Case Study: Prolonged Infectious SARS-CoV-2 Shedding from an Asymptomatic Immunocompromised Individual with Cancer." *Cell* 183.7 (2020): 1901,1912.e9. Web.

Culture positive references:

Aydillo, Teresa, et al. "Shedding of Viable SARS-CoV-2 After Immunosuppressive Therapy for Cancer." *N Engl J Med* 383.26 (2020): 2586-8. Web.

For more information contact
ipcsurvstdadmin@ahs.ca

Original date: March 2021
Revised date: 25 June 2021
ECC Approval: 29 June 2021

Alberta Health Services

Baang, Ji Hoon, et al. "Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 Replication in an Immunocompromised Patient." *The Journal of infectious diseases* 223.1 (2021): 23-7. *PubMed.* Web.

Decker, Annegrit, et al. "Prolonged SARS-CoV-2 Shedding and Mild Course of COVID-19 in a Patient After Recent Heart Transplantation." *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* 20.11 (2020): 3239-45. *PubMed.* Web.

Rajakumar, Irina, et al. "Extensive Environmental Contamination and Prolonged Severe Acute Respiratory Coronavirus-2 (SARS CoV-2) Viability in Immunosuppressed Recent Heart Transplant Recipients with Clinical and Virologic Benefit with Remdesivir." Infection Control & Hospital Epidemiology (2021): 1-3. Cambridge Core. Web. 2021/04/29.

Sepulcri, Chiara, et al. "The Longest Persistence of Viable SARS-CoV-2 with Recurrence of Viremia and Relapsing Symptomatic COVID-19 in an Immunocompromised Patient – a Case Study." Open Forum Infectious Diseases (2021)Web.

Tarhini, Hassan, et al. "Long-Term Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infectiousness among Three Immunocompromised Patients: From Prolonged Viral Shedding to SARS-CoV-2 Superinfection." *The Journal of infectious diseases* (2021)Web.

Truong, Thao T., et al. "Increased Viral Variants in Children and Young Adults with Impaired Humoral Immunity and Persistent SARS-CoV-2 Infection: A Consecutive Case Series." EBioMedicine 67 (2021): 103355. Web.

van Kampen, Jeroen J. A., et al. "Duration and Key Determinants of Infectious Virus Shedding in Hospitalized Patients with Coronavirus Disease-2019 (COVID-19)." *Nature Communications* 12.1 (2021): 267. Web.

Guidelines:

Manuel, Oriol, Michele Estabrook, and the American Society of Transplantation Infectious Diseases Community,of Practice. "RNA Respiratory Viral Infections in Solid Organ Transplant Recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice." *Clinical transplantation* 33.9 (2019): e13511. Web.

Michaels, Marian G., et al. "Coronavirus Disease 2019: Implications of Emerging Infections for Transplantation." *American Journal of Transplantation* 20.7 (2020): 1768-72. Web.

References used for definition:

Bridger NA, Allen UD; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Safe living strategies for the immunocompromised child. Last updated 2020. Web. <https://www.cps.ca/en/documents/position/immunocompromised-child>

CDC. "**Discontinuation of Transmission-Based Precautions and Disposition of Patients with SARS-CoV-2 Infection in Healthcare Settings**." 2021. Web. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html>.

CDC. "**Interim Guidance on Duration of Isolation and Precautions for Adults with COVID-19**." 2021. Web. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html>.

For more information contact
ipcsurvstdadmin@ahs.ca

Original date: March 2021
Revised date: 25 June 2021
ECC Approval: 29 June 2021

Alberta Health Services

European Centre for Disease Prevention and Control.
Guidance for Discharge and Ending Isolation of People with COVID-19 . Stockholm: ECDC, 2020. Print.

Fraaij, P. L., et al. "Viral Shedding and Susceptibility to Oseltamivir in Hospitalized Immunocompromised Patients with Influenza in the Influenza Resistance Information Study (IRIS)." *Antiviral Therapy* 20.6 (2015): 633-42. Web.

For more information contact
ipcsurvstdadmin@ahs.ca

Original date: March 2021
Revised date: 25 June 2021
ECC Approval: 29 June 2021

Alberta Health Services