Consensus guidance for organ donation and transplantation services during COVID-19 pandemic

The most current version of this document will reside on the Organ and Tissue Donation and Transplantation professional education website.

Background

On March 12, an urgent teleconference meeting of the Organ Donation and Transplantation Expert Advisory Committee (ODTEAC) was held, bringing together donation and transplantation leaders from across the country. The aim of the meeting was to develop a consensus which can be used by provincial organ donation organizations and regional transplant and donation programs to guide the administration of organ and tissue donation and transplantation services in light of the COVID-19 pandemic. It is understood that each organization, program and jurisdiction will develop their own policies.

Because the situation is rapidly evolving, going forward, a teleconference will be held at least once a week to discuss and update the consensus guidance. These discussions and the consensus itself will continue to be informed by recommendations from Canadian Blood Services' advisory committees, Health Canada, Public Health Agency of Canada, WHO, provincial agencies, and international partners (including UK and Spain).

This document was **last updated May 15, 2020**, and will be updated after each national teleconference as required.

Key Considerations

Guiding principles

1. Organ donation and transplantation is an essential life-saving and life-preserving medical intervention.

2. Transplant recipients are, or are likely to become, immunocompromised, and may be at increased risk of more severe outcomes related to COVID-19. Although data from Canada is lacking, preliminary data from Spain (not yet peer-reviewed) suggests that the risks of transplant recipients acquiring COVID-19 is two to three times higher than the general population. Mortality rates are three to four times higher. The vast majority of transplant recipients acquire the infection through community transmission. There have been no confirmed cases of donor-to-recipient transmission.
3. Recommendations must balance the incidence trends in provinces and territories, the risk posed to potential recipients who will become immunocompromised, and the risks of suspending or delaying transplantation.
4. A consistent and principled approach for all jurisdictions is preferred.

Current level of risk

COVID-19 is a serious health threat, and the situation is evolving daily. The risk will vary between and within communities, but given the increasing number of cases in Canada, the risk to Canadians is considered **high**. Continued vigilance will be required.[i]

There is likely an increased risk of more severe outcomes for Canadians:

- aged 65 and over
- with compromised immune systems
- with underlying medical conditions

Current risk factors for acquiring COVID-19:

1. Those who show clinical symptoms compatible with COVID-19. Significant variation exists in COVID-19 symptomatology, including non-respiratory symptoms.
2. In addition, there is evidence that asymptomatic or mildly symptomatic carriers can also serve as a source of community or institutional spread.
3. The epidemiology of COVID-19 in Canada is continually evolving. For example, currently, residence or working in a long-term care facility is a significant risk factor.
4. The increasing or variable incidence of COVID-19, associated with increased hospital occupancy by COVID-19 positive patients, and/or acquisition by health care providers also can make hospital/clinic visits or hospital admission an additional risk factor.

Modes of transmission:

1. There have been no confirmed cases of donor-to-recipient transmission. Based on the available evidence, donor-to-recipient transmission is unlikely.
2. Donor to recipient
    a. droplet/respiratory or aerosolization spread

   b. +/- viremia (unknown but presumed likely; RNA-emia reported in up to 15% of cases but in a recent study of 300 patients, the RNA-emia incidence is 1% (Wang et al., JAMA, 2020). Most RNA-emic patients also have detectable virus in the respiratory tract.
   c. Virus present in organ (lung especially; gastrointestinal tract; but other organs possible).
3. Nosocomial
   a. other patients, visitors, health care staff
   b. droplet spread, aerosolization and potential surface contamination
4. Community-acquired

COVID-19 Testing

1. It appears there is no gold standard for sample collection, whether from nasopharyngeal (NP) or oropharyngeal (OP) swabs, or both, given the lack of data available to accurately assess sensitivity[ii]. A NP swab and/or an OP swab are often recommended for screening or diagnosis of early infection. A single NP swab has become the preferred swab, as it is tolerated better by the patient and is safer to the operator[iii]. Some reports have shown that indication of viral pneumonia on a CT scan may precede a positive RT-PCR result in some patients[iv]. In some cases, lower respiratory tract specimens are more sensitive than upper tract specimens for the PCR detection of SARS-CoV-2[v]. There is limited data on sensitivity and specificity in the setting of donor screening. CT chest has good sensitivity in patients with symptoms, but has lower sensitivity in asymptomatic individuals. The sensitivity and specificity in deceased donors is not known.
2. For intubated patients with COVID-19 respiratory failure, a broncho-alveolar lavage (BAL) has higher sensitivity than NPA. The BAL can be performed bronchoscopically which is an aerosol generating procedure, or can be performed as a modified BAL, using an in line endotracheal tube suction catheter wedged deep into the airway. If a BAL is not performed, an endotracheal aspirate should be sent as an alternative.
3. Clearance criteria for confirmed cases may vary between settings. The Ontario Ministry of Health criteria for when to discharge someone from isolation outlines scenarios for home isolation, hospital, and healthcare workers.
   a. For hospitalized patients, isolate in hospital until two negative tests (single NP swab), obtained at least 24 hours apart.
   b. If discharged home within 14 days of symptom onset, follow advice for individuals at home where viral clearance swabs are not required.
   c. If discharged to a long-term care home/retirement home, maintain isolation (droplet and contact precautions) until two consecutive negative tests, obtained at least 24 hours apart. If testing for clearance is not feasible, maintain isolation until at least 14 days from symptom onset.[vi].

4. There is growing evidence that patients may still be shedding virus after two PCR-negative swabs.[vii]
5. Some countries request lung CT scan in potential donors to rule out evidence of COVID-19 infection.
6. Rates of RNA-emia have been described as being possibly around one per cent in a larger sampling of hospitalized patients.[viii] Rates can vary depending on patient illness presentation and the sample size used. Results may have inherent sampling biases in small studies. Increasing numbers of publications describe nucleic acid testing of serum or plasma. These assays may not be validated or available in all settings.[ix] It is also unclear if RNA detected in the blood represents viable virus or damaged virions or simply RNA. The clinical utility is uncertain, since it is expected that most or all viremic donors will have a positive respiratory sample.
7. Serology assays (IgG and IgM) are becoming available. They have higher sensitivity later in the course of disease. Their potential utility in donor screening has not been evaluated.

Consensus guidance (as of May 15, 2020, 12:00 EDT)

Recommendations for ICU, OR and transplant services

Decision to proceed with organ donation and transplantation is predicated on hospital capacity and resource considerations, and it is understood that it may be affected by provincial and facility incidence and severity of COVID-19.

1) Adult and pediatric intensive care units are asked to test all patients that meet the following criteria:
   a) They are admitted to intensive care;
   b) The presenting condition is an acute community-acquired respiratory infection of any kind OR a febrile illness, regardless of known or suspected causative pathogen and clinical features. This includes ECMO active or eligible cases.
   c) Depending on jurisdiction and degree of community transmission, many ICU's will routinely test for COVID-19 for all admissions, regardless of presenting illness.
2) All health care personnel involved in organ donation and transplantation services should be fit-tested for masks and have personal protective equipment training.
3) N95 masks should be required for all ICU and OR staff, when deemed appropriate by hospital safety protocols (e.g., procedures that may lead to aerosolization of the virus such as intubation, bronchoscopy, surgical cautery, bone saw), and are not expected to be required for general care.
4) We suggest all health care professionals deploy routine universal precautions (surgical masks, gloves) during the care of COVID-negative donors and recipients.

a) It is acknowledged that there is regional and institutional variability with respect to:
   i) COVID-specific PPE
   ii) Universal precautions
   iii) No routine precautions
b) Given community spread, risk of asymptomatic carriage, limitations in NPA screening sensitivity and the inability to reliably distinguish COVID-positive from COVID-negative patients, many centers have adopted universal precautions for all health care professionals during all patient interactions.
c) Due to immunocompromised status, transplant recipients may have heightened risk for adverse outcomes and mortality from COVID-19. This information is based on non-validated international reports, emerging from Italy, Spain and the UK. Currently reported but unpublished data from Spain show that the overall incidence of COVID-19 in transplant recipients is 18 per cent, with 84 per cent acquisition of COVID-19 via community transmission, a median of 56 months from transplant, and an unadjusted mortality rate of 18-29 per cent.

5) Health Canada regulations determine the criteria for “exceptional distribution” relevant to organ donation. During the COVID-19 pandemic, the risk to potential transplant recipients is more significant in relation to the circumstances of transplantation and post-transplantation recovery than transmission from the donor. As a result, during this time all transplant recipients should be advised of the increased risk (see bullet 3 under “Recommendations for transplant programs”.)
6) Transplant candidates should be prioritized for testing. As new tests become available, each jurisdiction should consider how they can be used for this population to expedite access to results prior to transplant.

Recommendation for living donor programs

Based on a March 13 meeting of the chairs and co-chairs of the Kidney Transplant Advisory Committee and the Living Donation Advisory Committee and Canadian Blood Services OTDT leadership, it is recommended that:

1) All living donor kidney transplant programs in Canada should consider postponing living donor transplants on a case-by-case basis and/or until this issue has resolved.

2) Living donor liver transplantation generally caries greater urgency. Living donor liver transplantation should continue on a case-by-case basis, taking into account recipient medical need and hospital resource utilization depending on the severity of the pandemic in the local jurisdiction.

Recommendations for transplant programs

Effective May 15, it is recommended:

1) All transplant programs should consider suspending deceased kidney transplants, except for highly sensitized recipients (PRA>=99%) or because of an urgent medical need due to a lack of access to dialysis. However, transplant restart should be considered in the setting of flattening of COVID-19 activity, and adequate hospital capacity, coupled with adequate donor screening and a post-transplant COVID-free pathway to ensure recipient safety.

2) All transplant programs should consider avoiding the use of lymphocyte depleting therapies. However, choice of immunosuppression remains with transplant programs.

3) During the pandemic, recipients of solid organ transplants should be fully informed at time of organ offer of the potential risk of severe complications should they contract the virus at the time of transplant, during the hospital stay, or once discharged from the hospital while being immunosuppressed. This informed consent should be clearly documented in the hospital chart.

4) All transplant programs should, whenever possible, recover organs locally and ship them. For those centres that cannot recover organs locally, the decision to send a surgical team can be assessed on case-by-case basis, relative to recipient urgency.

5) If surgical recovery teams travel, the teams should be as small as possible. Every effort should also be made to minimize the team's potential exposure to COVID-19. For example, upon arrival in locality, teams should go directly to the OR, they should avoid the emergency department whenever possible, and they should return directly to the plane as soon as they are able.

6) Please also see bullet #6 of "Recommendations for ICU, OR and transplant services."

Recommendations for donor criteria

CRITERIA FOR DECEASED DONORS

1. Organs from donors with active COVID-19 should not be used.
2. Donors with a previous diagnosis of COVID-19 require two negative tests before being considered for donation and another negative test at the time of donation. Extreme caution is still recommended until more data are available.

3. All potential donors must be tested for COVID-19. The optimal choice of specimen for testing is unknown but options include NP swab, Broncho-alveolar lavage (BAL) (bronchoscopic or modified), or deep endotracheal aspirate or a combination of above. Concerns about aerosolization with bronchoscopic BAL sampling should also be taken into account. Current evidence of sensitivity and specificity in the setting of deceased donor screening is lacking. A reasonable screening may include two samples: a NP swab plus a lower respiratory tract specimen. The utility of CT chest screening in this setting is unknown but could provide added information especially for lung transplantation.
4. ICU/OR capacity allowing, a negative COVID-19 result must be available prior to proceeding (except in exceptional circumstances).
5. All organ offers from programs, such as in the United States, where testing of donors may not have reliably occurred, should be considered on a case-by-case basis.

CRITERIA FOR LIVING DONORS (IF TRANSPLANT IS NOT SUSPENDED)

1. All potential living donors should undergo a symptom screen prior to donation. Any donor with compatible symptoms should be deferred but should also be tested to allow for future planning.
2. All potential living donors must be tested for COVID-19 with the testing occurring as close as possible prior to donation (within 24–48 hours). Current data suggests the optimal test type in this ambulatory setting is a nasopharyngeal swab.
3. All potential living donors who travelled outside Canada must wait at least 14 days before donating (as per Health Canada's *Measures to Address the Potential Risk of Transmission of the novel coronavirus responsible for COVID-19 by Human Cells, Tissues and Organ Transplantation)*. Current public health guidelines require all returned travelers to self-isolate for 14 days.
4. All potential living donors should be advised to practice significant social distancing for 14 days prior to surgery. All living donors should not travel and be very careful to avoid contact with others who have respiratory or flu like symptoms in the 14 days prior to donation.
5. A living donor is eligible to donate only if they have tested negative for COVID-19 with the testing taking place within 24–48 hours prior to surgery, AND have a negative symptom screen AND have not travelled outside of Canada in the previous 14 days.
6. All living donors with a previous diagnosis of COVID-19 require two negative tests before being considered for donation and another negative test at the time of donation.
7. Living donor transplants are considered deferable (especially kidney), if it is in the best interest of the donors and patients except in the case of medical urgency for a transplant candidate.

Recommendations for recipient criteria

CRITERIA FOR RECIPIENTS OF DECEASED DONATION

1. All recipients of deceased donation should undergo a symptoms screen and a screening NP swab at the time they are called in for transplant. Those with a positive symptom screen should be deferred.
2. In patients with a negative symptom screen, whenever possible, every attempt should be made to have the screening swab result available prior to proceeding with surgery. It is recognized that this may not be possible in all situations, given current constraints on test-turnaround time.

CRITERIA FOR RECIPIENTS OF LIVING DONATION (IF TRANSPLANT IS NOT SUSPENDED)

1. All recipients of living donation should undergo a screening NP swab in the 24–48 hours prior to surgery and should not proceed if positive.

Impacts to Canadian Blood Services Kidney Paired Donation and Highly Sensitized Patient Programs

In light of the current COVID-19 pandemic concerns, Canadian Blood Services leadership and the chairs and co-chairs of the Kidney Transplant Advisory Committee and the Living Donation Advisory Committee have assessed the current evidence and information available in this rapidly changing environment. With the goal of ensuring the safety of both living donors and transplant recipients the following decisions have been made:

1. Highly Sensitized Patient (HSP) Program:

   The HSP registry will continue to operate and be available to the country. The decision to proceed with accepting a kidney offer will be made by local/provincial programs based on their hospital's current policies and processes for deceased donor organ transplantation during the COVID-19 situation.

2. Kidney Paired Donation (KPD) Program:

   On May 12, Canadian Blood Services' Kidney Transplant Advisory Committee, Living Donation Advisory Committee, and OTDT leadership agreed to restart the Kidney Paired Donation Program in three phases. The program was put on-hold, effective March 16, 2020, to minimize the possibility of exposing living donors, transplant candidates, and recipients to COVID-19.

   The three phases are:

1. The first priority will be to resolve the donation and transplantation chains affected by the suspension of the program on March 16, 2020. The goal is to complete or collapse all affected chains by August 2020.
2. With an anticipated start date of June 2020, match runs will take place every month, as opposed to three times per year. The purpose of this change is to better accommodate provincial programs, as it is expected they will incrementally return to normal operations. The greater frequency of match runs will also help to identify as many matches as possible, given the limited number of opportunities for matches that are anticipated going forward. Programs will also be encouraged to ship and receive kidneys, instead of asking donors to travel, with some local travel by donors taking place at the discretion of programs.
3. It is expected that most provincial programs will have returned to normal operations by Fall 2020. The KPD program will work with provincial programs to identify opportunities for innovation and adapt for the new environment.

Update on Impact to Blood Supply

Blood components are a vital resource supporting health care in Canada. Canadian Blood Services operates a national blood inventory and, in collaboration with our provincial and territorial partners, continues to monitor the impact of COVID-19 on the supply of these resources and will continue to keep the community apprised of the blood situation as it evolves.

Additional resources

1. As they become available, we will share additional resources related to the COVID-19 pandemic on *Organ and Tissue Donation and Transplantation professional education website.* Additionally, a Google Doc and Dropbox folder has been established for ease of sharing documents requiring limited access.

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[i] See https://www.cidrap.umn.edu/sites/default/files/public/downloads/cidrap-covid19-viewpoint-part1_0.pdf and https://www.cmaj.ca/content/192/19/E497.long

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[iii] Tang YW, Schmitz JE, Persing DH, et al. "The Laboratory Diagnosis of COVID-19 Infection: Current Issues and Challenges." *J Clin Microbiol*. 2020;10.1128/jcm.00512-20.

[iv] Xie X, Zhong Z, Zhao W, et al. "Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing." *Radiology.* 2020 Feb 12:200343. doi: 10.1148/radiol.2020200343. [Epub ahead of print]

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[v] Hase R, Kurita T, Muranaka E, Sasazawa H, Mito H, Yano, Y. "A case of imported COVID-19 diagnosed by PCR-positive lower respiratory specimen but with PCR-negative throat swabs." *Infect Dis (Lond)*. 2020 Apr 2:1-4. doi: 10.1080/23744235.2020.1744711. [Epub ahead of print]

[vi] Ontario Ministry of Health. "Public health management of cases and contacts of COVID-19" in Ontario, March 25, 2020. Health System Emergency Management Branch; 2020.

[vii] Xiao AT, Tong YX, Zhang S. "False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence." *J Med Virol*. 2020 Apr 9. doi: 10.1002/jmv.25855. [Epub ahead of print]

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