

**COVID-19 (Coronavirus):
FAQs for Organ Donation and Transplantation**

Updated: March 11, 2020

The AST's Infectious Disease Community of Practice has received queries from transplant colleagues regarding the novel coronavirus (COVID-19). The following FAQs were developed to relay information on the current state of knowledge. This document will be updated as more information becomes available.

Please note, information regarding organ donors has now been added to this resource.

1. What is the origin of the novel coronavirus?

COVID-19 is the disease caused by the novel coronavirus named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) that emerged in the Hubei province of China in December 2019 spread across China and has continued to spread to include over 100 countries as of today's date. While many cases outside of China have been linked to travelers from China or other areas with high circulation of SARS-CoV-2, cases have also been diagnosed without obvious travel-related exposure. Humans likely contracted COVID-19 from an intermediate host but now it is transmitted human-to-human.

There are many different types of coronaviruses with 7 known to infect humans. There are four seasonal coronavirus strains that normally circulate in humans. These are usually mild common cold viruses but on occasion can cause viral pneumonia in immunosuppressed persons and can be identified using multiplex respiratory virus panels. Two previous outbreaks from more virulent coronaviruses have been caused by Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS CoV). There are published case reports of transplant patients acquiring SARS and MERS viruses, in some cases with fatal outcomes (AJT 2003; 3(8): 977-81 and AJT 2015; 15(4):1101-4).

2. How is SARS CoV-2 transmitted?

Infection needs to be acquired from someone who is shedding virus. Most frequently, transmission is felt to be from symptomatic individuals with COVID-19 via droplet spread. Less commonly asymptomatic transmission has occurred, and it is presumed that transmission is possible from infected fomites. While stool has tested positive for SARS-CoV-2 in some cases by nucleic acid testing (NAT), it does not appear to be infectious at this time. The incubation period is usually between 2-14 days in the general population; however recent reports suggest incubation can be as long as 24 days (Bai Y et al JAMA 2020).

Healthcare transmissions of COVID-19 have occurred and given the potential for greater infectivity, strict isolation precautions should be followed for anyone with suspected SARS-CoV2. Although the virus is not airborne, CDC has recommended use of airborne precautions and N95 masks while they remain available. Surgical masks are acceptable alternatives when supplies are limited. During periods of limited supplies, the N95 masks or their equivalents should be reserved for procedures that are more

likely to generate respiratory aerosolization. Local institutional guidelines should be followed for personal protective equipment (PPE).

3. Are transplant patients at higher risk for COVID-19?

Complete data on transplant recipients with COVID-19 are still lacking. However, based on data from influenza and SARS, if infection occurs, progression to pneumonia may be more common in the immunocompromised population, including transplant recipients. In addition, it is anticipated that transplant recipients may have a greater viral burden and shedding resulting in greater infectivity and potential spread to other individuals.

For Healthcare centers with active cases of COVID-19, consideration should be given for postponing non-essential transplant clinic visits to avoid inadvertent nosocomial transmission to a vulnerable population.

4. Are there any treatments for COVID-19?

Currently, the treatment is supportive care. Potential antiviral candidates are undergoing testing and vaccines are under development. However, it may be a number of months before any of these are approved. Remdesivir is an investigational antiviral that is being studied in clinical trials for severe and moderate COVID-19 cases. It may be possible to obtain this via clinical trial or compassionate use. Its efficacy is still unknown. Similarly, chloroquine, hydroxychloroquine, lopinavir/ritonavir, interferon-1 β and several other compounds are being evaluated or considered as experimental therapy. Drug-drug interactions with immunosuppressant medications need to be evaluated and managed, particularly with the HIV drug lopinavir/ritonavir which leads to marked elevations in the levels of calcineurin inhibitors and mTOR inhibitors due to profound CYP3A4-mediated inhibition of their metabolism by ritonavir. The impact of immunosuppression on COVID-19 is not currently known but decreasing immunosuppression should be considered for infected recipients, if no recent rejection episodes.

5. Are there any specific travel restrictions for transplant patients?

The CDC has recommended to suspend all non-essential travel by air for all people at increased risk for getting very sick from COVID-19 including transplant recipients.

We recommend that transplant patients not travel to locations where SARS-CoV2 is currently circulating. Travel restrictions to other locations will depend on virus activity and will change over time. Since this is changing rapidly, postponing all non-essential travel should be considered for transplant recipients. The CDC advises against cruise travel, given the recent outbreaks associated with cruise ships. We also suggest that transplant patients' immediate household contacts not travel to high-risk areas.

The CDC and WHO maintain websites that are being updated as the outbreak evolves, and travel recommendations will likely change over time.

- CDC: <https://www.cdc.gov/coronavirus/2019-nCoV/summary.html>
- World Health Organization: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>

- In Canada: <https://www.canada.ca/en/publichealth/services/diseases/2019-novel-coronavirus-infection.html>

6. Should transplant patients wear a mask or avoid public places?

In general, transplant patients should exercise caution about being in overcrowded situations. The benefit of wearing masks in public is controversial even for transplant patients, and it is unknown how much wearing a mask will help prevent infection. Most surgical masks are not tight fitting and aerosols can get through. However, they may prevent patients from touching their nose and mouth. It is unclear if an N95 mask is better than a regular surgical mask since proper fit testing has not been performed. N95 mask can be uncomfortable to wear for prolonged periods. The CDC is not recommending mask use for infection protection outside the hospital at this time. N95 masks should be reserved for healthcare workers. Frequent handwashing or hand sanitizer use helps prevent infection.

Transplant candidates, recipients, and potential living donors should be educated about the importance of performing frequent hand hygiene, avoidance of crowds, and applying social distancing. If SARS-CoV-2 is circulating in the recipient's area, avoid public places including school, and stay at home as much as possible to reduce risk of exposure SARS-CoV-2.

7. What is the approach to transplant recipients with flu-like/respiratory symptoms?

Transplant patients should be instructed to call the transplant center if they have symptoms of fever or cough instead of presenting to the clinic without notifying the center in advance. If patients are instructed to present for medical evaluation, transplant patients should wear a mask immediately upon entering the building. If the transplant patient has a medical emergency (e.g., shortness of breath), they should call 911 and notify dispatch if they've been exposed to SARS-CoV-2 so that appropriate safety precautions can be taken.

There are many different causes for flu-like/respiratory symptoms. Each hospital should have protocols in place for transplant patients with flu-like/respiratory symptoms in the era of COVID-19. Consult your local hospital practices for outpatient transplant clinic screening or visitor restrictions for transplant recipients as these may evolve over time. A travel history or contact with recently returning travelers from high-risk geographic areas internationally and geographic areas including those in the US and Canada where there is local transmission, should be elicited. Other causes of respiratory illness including influenza and RSV should be assessed but COVID-19 should also be considered based on epidemiologic factors and local transmission.

Patients suspected of COVID-19 should have a surgical mask placed on them, be placed in isolation and local infection control should be notified. CDC has updated guidelines for infection control <https://www.cdc.gov/coronavirus/2019-ncov/infection-control.html>.

The CDC has also established interim risk criteria for exposure to the SARS-CoV-2 <https://www.cdc.gov/coronavirus/2019-ncov/php/risk-assessment.html>.

Testing for SARS-CoV-2 is done via a specific RT-PCR on nasopharyngeal and oropharyngeal swabs. However, testing capabilities are still limited in much of the US and abroad.

SARS-CoV2 is not detected using the standard respiratory virus multiplex tests.

8. What is the approach to transplant candidates and recipients coming for routine appointments?

In general, if COVID-19 is circulating in the vicinity of a transplant center, issues of resource availability need to be balanced against the need for urgent organ transplantation. Local centers with circulating virus will need to consider the risk of nosocomial transmission to a recipient or to healthcare workers. Temporary suspension of elective living donor transplantation or non-urgent deceased donor transplants may need to be considered. Likewise, the need for performance of nonurgent procedures such as bronchoalveolar lavage and surveillance biopsies should be reviewed, and consideration given for deferring elective appointments. Increased use of telemedicine or phone consultation for nonurgent visits should be evaluated.

In addition, the need for routine elective ambulatory appointments should be considered. In some stable patients with scheduled routine visits, virtual/telemedicine visits may be appropriate and laboratory testing may be performed locally. Organizational leadership will need to be involved in prioritization plans.

9. What is the approach to ill transplant candidates who are actively listed for transplant?

Given the paucity of data, it is not known if patients with active or recent COVID-19 can be safely transplanted. However, it is anticipated that transplantation of these patients could result in adverse outcomes. Given the absence of definitive treatment for COVID-19, it is preferable to defer transplantation in a candidate with active COVID-19. The ideal disease-free interval is unknown at this time. However, median duration of viral shedding in one study was 20 days from illness onset (range 8 to 37 days) (Zhou F the Lancet published on line March 9, 2020). The risk of transplantation must be balanced with the risk of not transplanting a patient with acute or recent COVID-19.

Information on ORGAN DONORS

1. Should living and deceased donors be screened?

Yes, donors should be screened for concern for COVID-19 infection.

Screening encompasses three different methods

- 1) Epidemiologic screening for travel and potential exposures
- 2) Screening for symptoms suggestive of COVID-19
- 3) Laboratory screening: (Nucleic acid testing of specimens)

The risk of a COVID-19 infection from an infected donor is unknown at this time. Factors that could impact the risk of SARS_CoV-2 transmission include epidemiological risk factors, incubation period, degree of viremia and viability of the virus within the blood and specific organ compartments. Other factors to consider during organ acceptance are the risk of the transplant candidate's mortality while on

the transplant waitlist, as well as the impact that a COVID-19 donor-derived infection could have on the recipients' medical system and community.

The optimal approach to donor screening may change over time as more data accumulates. At this time, organ procurement organizations (OPOs) and living donor hospitals should screen potential donors for exposure and clinical symptoms compatible with COVID-19 (Table 1). OPO's and living donor hospitals can consider use of the FDA emergency application for COVID-19 testing. If available, diagnostic testing for SARS-CoV-2 is indicated for donors with a history of COVID-19 exposure or clinical symptoms suggestive of COVID-19. For deceased organ donors we recommend testing upper (nasopharyngeal and oropharyngeal) or lower respiratory samples (bronchoalveolar lavage) for COVID-19. If donor testing is not available, or if the COVID-19 test result will not be available pre-procurement, then the criteria in Table 2 should be used to stratify deceased donors into high, intermediate, or low risk of a COVID-19 donor-derived infection. The recommendations for the different deceased donor scenarios are summarized in Table 3.

In general, if COVID-19 is circulating in the transplant center community, issues of resource availability need to be balanced against the need for an organ transplant. This should include evaluating availability of intensive care beds, ventilators and hospital staffing. In addition, local centers with circulating virus need to consider the risk of nosocomial transmission to a new transplant recipient or to healthcare workers.

Temporary suspension of elective living donor transplantation or non-urgent deceased donor transplants may need to be considered with involvement of organizational leadership based on prioritization planning.

Table 1: Exposure and clinical screening of potential donors for COVID-19

EPIDEMIOLOGIC SCREENING

Does the deceased donor meet any of the following criteria?	Yes, No or Unknown
<ul style="list-style-type: none">• Travel to or residing in an area in the preceding 21 days, where local COVID-19 transmission is occurring• Travel to or from a CDC high-risk area (Level 2- 3)• Direct contact with known or suspected case of COVID-19 in the preceding 21 days*• Confirmed Diagnosis of COVID-19 in the last 28 days	

*this includes being within six feet of a person with suspected or proven COVID-19.

Close contact can occur while caring for, living with, visiting, or sharing a healthcare waiting area or room with a COVID-19 case or having direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on)

CLINICAL SCREENING:

Has the deceased donor experienced any of the following symptoms in the last 21 days? Yes, no or unknown

- Fever (>38°C or 100.3°F or subjective fever)
- Malaise or flu like symptoms, + /- myalgias
- New cough
- Shortness of breath

Table 2: Donor Classification for Donor Derived COVID-19 based on Clinical symptoms and epidemiologic screening above

High Risk <ul style="list-style-type: none">• Yes, to one or more of the epidemiology screening criteria PLUS <ul style="list-style-type: none">• Yes, to one or more of the clinical screening criteria
Intermediate Risk <ul style="list-style-type: none">• Yes, to one or more of the epidemiology screening criteria AND <ul style="list-style-type: none">• No or Unknown to the clinical screening criteria
Intermediate Risk <ul style="list-style-type: none">• No or unknown to the epidemiology screening criteria AND <ul style="list-style-type: none">• One or more clinical symptoms without another clear diagnosis and in the absence of testing for COVID-19
Low Risk <ul style="list-style-type: none">• No epidemiologic risk factors AND <ul style="list-style-type: none">• No clinical symptoms

Table 3 Preliminary Deceased Donor Recommendations to mitigate risk of COVID-19 Donor Derived Infection

<ul style="list-style-type: none"> • We do not recommend using organs from deceased donors at this time who: <ul style="list-style-type: none"> ○ Have active COVID-19 infection ○ Test positive for COVID-19 as part of the OPO evaluation ○ Classified as high-risk on screening tool and SARS-CoV-2 testing not available or feasible
<ul style="list-style-type: none"> • Deceased donors who are classified as intermediate risk should be tested for COVID-19 <ul style="list-style-type: none"> ○ If testing is not available, we recommend NOT using lungs or intestines ○ The use of other organs should be made with caution after careful consideration of the risks and benefits. The decision-making should include the candidate or their proxy and explaining lack of currently approved therapies. Transplant programs accepting organs from these donors should consider placing recipients in contact, and airborne isolation
<ul style="list-style-type: none"> • Organs from deceased donors that met epidemiological or clinical criteria and test negative during the OPO evaluation should be used with caution given the reports of false negatives. <ul style="list-style-type: none"> ○ The decision-making should include the candidate or their proxy. Transplant programs accepting organs from these donors should consider placing recipients in airborne isolation.
<ul style="list-style-type: none"> • Organs from deceased donors classified as low risk may be used <ul style="list-style-type: none"> ○ This recommendation is subject to modification if COVID-19 transmission from asymptomatic donors is confirmed in the future
<ul style="list-style-type: none"> • Organs from deceased donors who have recovered from COVID-19 and have resolution of symptoms greater than 28 days prior to procurement and repeated negative testing are likely safe to use

Table 4 Preliminary Living Donor Recommendations to mitigate risk of COVID-19 Donor Derived infection

<ul style="list-style-type: none"> • We do not recommend using organs from a living donor with active COVID-19 at this time
<ul style="list-style-type: none"> • Living donors who are classified as high risk should have donation postponed until they are at least 28 days beyond symptom resolution and have a negative SARS-CoV-2 PCR test
<ul style="list-style-type: none"> • Consider delaying transplant for living donors who are classified as intermediate risk due to exposure questions but who have no symptoms of illness for 14 days <ul style="list-style-type: none"> ○ They should be counseled about ways to decrease transmission ○ They should be tested for SARS-CoV-2 prior to transplant to document negative status (NP/OP) and blood NAT testing
<ul style="list-style-type: none"> • During periods of local transmission of SARS-CoV-2, temporary suspension of elective living donor transplantation may need to be considered to protect the potential donor as well as the recipient

The current outbreak is unpredictable. If widespread community-transmission occurs, healthcare infrastructure and capacity issues may have further impact on donation and transplantation. These recommendations will be regularly updated to account for the changing epidemiology and new information regarding treatment and testing.

Acknowledgement:

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