

**2019-nCoV (Coronavirus):
FAQs for Organ Transplantation**

Updated: June 18, 2020

The AST's Infectious Disease Community of Practice has received queries from transplant colleagues regarding the novel coronavirus (2019-nCoV). The following FAQs were developed to relay information on the current state of knowledge. This document is subject to change as more information becomes available.

Also see OPTN information link: <https://optn.transplant.hrsa.gov/news/information-fortransplant-programs-and-opos-regarding-2019-novel-coronavirus/>

Please note, the organ donor resources previously included in this document are now in a separate document.

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 was first recognized in the Hubei province of China in December 2019 subsequently spreading across China and has continued to spread worldwide being declared a pandemic on March 11, 2020. While the first infections with SARS-CoV-2 likely came from a non-human host it is currently transmitted from person to person.

There are 7 coronaviruses known to infect humans. Four seasonal coronavirus strains 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. There is no laboratory cross reactivity between the seasonal coronaviruses and SARS-CoV-2. 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 is acquired from someone who is shedding virus. Person-to-person transmission was recognized early in the pandemic during close exposure (<6 feet) to a person infected with COVID-19, primarily via respiratory droplets produced when the infected person coughs or sneezes. Most frequently, transmission is presumed to be from symptomatic individuals with

COVID-19 via droplet spread. However, shedding from asymptomatic and pre-symptomatic individuals can also transmit infection. In addition, indirect transmission from fomites with infected particles is presumed to occur. While stool has tested positive for SARS-CoV-2 in some cases by nucleic acid testing (NAT), it is not known whether this is replicative virus. The incubation period is usually between 2-14 days in the general population although longer incubations have been documented (Bai Y et al JAMA 2020).

Healthcare transmissions of COVID-19 have occurred; given the potential for greater infectivity, strict isolation precautions should be followed for anyone with suspected SARS-CoV2 infection. Studies show that asymptomatic individuals can spread the virus and therefore, on April 3, 2020, CDC recommended that people wear face coverings such as cloth masks when going out in public or in instances where social distancing may be challenging. The public has been encouraged to make masks as [recommended by the CDC \(https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-to-make-cloth-face-covering.html\)](https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-to-make-cloth-face-covering.html).

All healthcare personnel should wear a facemask at all times while in the healthcare facility. Personal protective equipment such as N95 masks should be used by all healthcare workers who enter the room of a patient with known or suspected COVID-19 or as specified by institutional policies. Surgical masks are acceptable alternatives when supplies are limited. During such periods of limited supplies, the N95 masks or their equivalents should be reserved for procedures that are more likely to generate respiratory aerosolization (including bronchoscopy, intubation, and nasal swab procurement). In addition to facemask, eye protection (i.e. goggles or disposable face shield that covers the front and sides of the face) can be worn to protect from splashes and sprays of infectious materials from others. Local institutional guidelines should be followed for personal protective equipment (PPE).

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

Data on transplant recipients with COVID-19 are still limited but experience is accumulating. Mild infections are common in transplant recipients. However, preliminary experience suggests that infection, once acquired by immunosuppressed transplant recipients, may be of greater severity than in normal hosts after the initial incubation period. Experience with other viruses including prior outbreaks of coronaviruses, also suggests that severe infections will occur in some transplant recipients. The New York City experience revealed high rates of respiratory failure and mortality in transplant recipients but was likely impacted by the sudden and severe surge of infection that hit the city.

At this time, the risk factors for severe disease have not been fully characterized. Initial report by Pereira *et al* (Am J Transplantation, 2020) reported advanced age was associated with severe disease in their transplant cohort, which is not different from reports of non-immunocompromised host. Many of the risk factors for severe COVID-19 disease in normal hosts (renal dysfunction, obesity, diabetes, cardiovascular disease, chronic respiratory illness) are also common in the transplant population. 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 to postponing non-essential transplant clinic visits to avoid exposing vulnerable populations.

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

The CDC has recommended to suspend all non-essential travel and restrictions continue to be in place in multiple locations.

We recommend that transplant patients not travel unless it is essential. Should transplant recipients need to travel, we recommend taking additional essential medicines with them, to ensure they have a sustainable supply in the event of an unexpected quarantine or travel delay. We also suggest that transplant patients' immediate household contacts not travel unless absolutely essential. Regardless, the household contact should avoid travel to high-risk areas. Given the rapidly evolving epidemiology of COVID-19, all nonessential travel should be carefully evaluated.

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>
- CDC COVID Data Tracker: <https://www.cdc.gov/covid-data-tracker/index.html#cases>
- World Health Organization: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- In Canada: <https://www.canada.ca/en/publichealth/services/diseases/2019-novel-coronavirusinfection.html>

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

The CDC recommends all people wear masks or face coverings when in public. Frequent handwashing or hand sanitizer use helps prevent infection. Transplant patients should exercise caution about being in overcrowded situations and practice social distancing.

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 SARSCoV-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.

6. When should COVID-19 be considered in the differential diagnosis for transplant recipients?

Transplant patients with symptoms of a flu-like illness may have infection with SARS-CoV-2 as well as other infections. Many symptoms of COVID-19 are typical of respiratory viral infections. Transplant patients should be instructed to call the transplant center or their local physician if they have symptoms including, but not limited to, *fever, chills, rigors, cough, dyspnea, myalgias, headache, sore throat, diarrhea, or new loss of sense of taste and/or smell*. They should notify the transplant center or hospital before presenting for care if possible. If patients are instructed to present for medical evaluation at a clinical center, transplant patients should wear a mask during transit and immediately upon entering the building. If the transplant patient has a medical emergency (e.g., shortness of breath, chest pain, or stroke/weakness), **they should call 911** and notify the dispatcher if they have been exposed to SARS-CoV-2 or have suggestive symptoms 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; these may vary seasonally in your geographic area. Consult your local hospital practices for outpatient COVID-19 screening availability or visitor restrictions for transplant recipients as these will change over time.

Patients suspected of COVID-19 should wear a surgical mask, 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. Specific testing for SARS-CoV-2 must be requested. Testing is done via a nucleic acid test (most often RT-PCR on nasopharyngeal or oropharyngeal swabs) either as a single test or as part of a panel of tests for respiratory viruses. Testing guidelines vary by institution and availability may be limited.

7. Are all transplant patients at greater risk for severe infection due to SARS-CoV-2?

Immunosuppressed transplant patients may be at risk for more severe infection due to SARS-CoV-2. It is important whenever a transplant patient has persistent fever or other symptoms of infection that they contact their transplant center for guidance. Many transplant patients have risk factors for more severe infection including:

- Immunosuppressive medications
- Advanced age (over 60, but increasing with greater age)
- Hypertension
- Heart Disease
- Diabetes

- Obesity
- Cancer therapy
- HIV infection.

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

Each transplant program needs to decide their own policy for new transplants and outpatient visits when COVID-19 is circulating in the region.

Elective ambulatory appointments may be moved to virtual visits (e.g., telemedicine) and telephone contacts. Likewise, the urgency for bloodwork at the center, or for nonurgent procedures such as bronchoalveolar lavage and surveillance biopsies should be reviewed. Laboratory testing may be performed at centers outside the hospital or in the home if data can be provided expeditiously to the Transplant Center. Organizational leadership will need to be involved in prioritization plans. Some institutions may require SARS-CoV-2 testing prior to performing procedures on patients in both in and outpatient settings.

9. Should we be transplanting now?

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, blood products, dialysis supplies, and hospital staffing. In addition, local centers with circulating virus need to consider the risk of nosocomial transmission to a new transplant recipient, living donor or to healthcare workers. Temporary suspension of elective living donor transplantation or non-urgent deceased donor transplants may be considered.

On April 7, CMS released [recommendations regarding elective surgeries and non-essential procedures](#) that include transplantation. Transplants fall into Tier 3b, noting that they should not be postponed in “high acuity/unhealthy patients.” As infection rates decline regionally, centers have started to make individual decisions regarding the timing of less urgent transplantation. Centers will need to explore expansion of deceased donor transplants with organizational leadership. Issues impacting this decision may include the level of circulating infection in their areas and/or operational issues (e.g. testing availability, bed space, availability of basic supplies and equipment, including PPE).

The current outbreak is unpredictable, and virus is still circulating in most communities. The status of organ procurement varies by region depending on the availability of viral testing, of procurement teams, and of uninfected deceased donors. Local healthcare infrastructure and capacity issues may also impact transplantation. Local rules will adapt to the changing epidemiology and new information regarding treatment and testing.

10. Should transplant candidates be counseled about potential risks for COVID-19 infection?

At this time, with active circulation of SARS-CoV-2 in many parts of the world, it is appropriate to counsel all candidates about the risk for acquisition from the community, the hospital environment and theoretically from a donor although definitive proof of donor transmission is still absent. Candidates should be educated about preventive strategies such as social distancing, masking when in proximity to non-household contacts and frequent hand washing.

The risk - benefit of transplantation during the COVID-19 pandemic should be reviewed with each patient considering individual risks of progression of underlying disease while on the wait-list and local infection and transmission rates. In general, all deceased and live donors should be tested for COVID-19 based on local testing availability and sensitivity.

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

If available, all patients in regions where SARS-CoV-2 is circulating should be tested for virus prior to transplantation, even if asymptomatic. It is not known if patients with active or recent COVID-19 can be safely transplanted. It is anticipated that transplantation of these patients with active viral infection and need for immunosuppression could result in adverse outcomes. The risk of transplantation must always be balanced against the need for life-saving transplantation. Given the absence of definitive treatment or effective vaccination, candidates with active COVID-19 should be deferred from transplantation. Some patients continue to have positive PCR swabs for viral mRNA long after symptom have resolved (out past 40 days in some patients). It is not known whether positive tests indicate shedding of active virus. Blood tests that demonstrate antibodies to SARS-CoV-2 are encouraging, but it is not yet known whether the individual is protected against further infection or whether relapse could occur. As more is learned about serologic conversion, antibody testing may aid in the pre-transplant evaluation. The meaning of these tests remains to be investigated.

The ideal disease-free interval is unknown. Based on currently available data it is recommended that a candidate have complete symptom resolution and have a negative SARS-CoV-2 PCR from the upper respiratory tract prior to transplantation. This will also help to protect the hospital environment and the healthcare team. Some transplant physicians recommend two negative PCR tests at least 24 hours apart due to the limited sensitivity (~70%) of each test; the optimal timing of multiple tests is unknown.

12. Are there any effective treatments for COVID-19?

There are no curative treatments for COVID-19. Potential antiviral medications are undergoing testing and vaccines are under development. However, it may be several months before any of these are approved and widely available

Stable transplant patients with COVID-19 may be managed at home if they have social supports and access to medical care should the infection progress. In this setting, the main treatment is supportive care.

In patients requiring hospital admission, various antiviral and anti-inflammatory therapies are under investigation.

While some trials data are encouraging, available agents appear to shorten the symptomatic period rather than eradicating viral infection. Physicians are encouraged to follow new or emerging data. Similarly, prospective trials are underway to examine the risks and benefits of immunomodulatory therapies for the acute inflammatory state associated with severe COVID-19. Some concerns exist for use of such therapies when coupled with immunosuppression for transplantation due to the potential risk for superimposed infection. Data are required. Reactivations of viruses such as hepatitis B virus (HBV), hepatitis C virus (HCV), or herpesviruses (HSV, CMV, VZV) or of latent infections such as tuberculosis or *Strongyloides* may occur in patients receiving steroids or immunomodulation.

Remdesivir is an investigational antiviral that is being studied in clinical trials for severe and moderate COVID-19 cases. The Adaptive COVID-19 Treatment Trial (ACTT)-1 Study (NEJM, 2020) revealed that remdesivir shortens the time to recovery in adults hospitalized with COVID-19 pneumonia. The FDA issued an Emergency Use Authorization (EUA) for remdesivir on May 1, 2020 to permit the emergency use of the unapproved product intravenously for treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in adults and children hospitalized with severe disease, defined as those with oxygen saturation (SpO₂) \leq 94% on room air or requiring supplemental oxygen or mechanical ventilation or extracorporeal membrane oxygenation (<https://www.fda.gov/media/137566/download>). There is no transplant specific sub-analysis from this trial; data regarding the relative efficacy in SOT are pending.

Several agents including chloroquine, hydroxychloroquine, lopinavir/ritonavir, interferon-1 β , and tocilizumab were evaluated for its antiviral or anti-inflammatory response; however, published data on efficacy have been variable. No specific recommendations for the use of these medications can be provided and should be only used under clinical trial settings (NIH guidelines, June 11,2020). More recently, the FDA EUA has been removed for chloroquine and hydroxychloroquine and these agents should be used with caution. Patients receiving hydroxychloroquine require careful monitoring of QTc interval and for drug interactions.

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 CYP3A-mediated inhibition of their metabolism by ritonavir. We recommend against the use of lopinavir/ritonavir for first line therapy given early data that it lacks efficacy and the potential for severe drug-drug interactions.

The suggestion that continued ARB and ACE inhibitor therapy may be detrimental to COVID-19 outcomes is not yet supported by data; there is no firm recommendation regarding discontinuation of these medications. The impact of immunosuppression on COVID-19 is not currently known but decreasing immunosuppression should be considered for infected recipients who have not had recent rejection episodes. Many providers have decreased or discontinued cell cycle inhibitors or reduced calcineurin inhibitor levels, but comparative data

regarding these interventions are not yet available. Whether adjunctive corticosteroid therapy for patients with severe ARDS may be beneficial is also unknown. Recent data, as yet unpublished, suggest that adjunctive corticosteroids may be beneficial (<http://www.ox.ac.uk/news/2020-06-16-low-cost-dexamethasone-reduces-death-one-third-hospitalised-patients-severe>). Further data are required. Low dose corticosteroid to reverse adrenal insufficiency may be considered in setting of refractory shock in COVID-19 (NIH guidelines, June 11, 2020).

13. How do we approach clearance of transplant patients after COVID-19 infection for removal of enhanced isolation in the hospital and return to outpatient clinics?

Patients with COVID-19 have variable clearance of clinical symptoms as well as in testing for SARS-CoV-2 from nose, pharynx, lungs and other sites. It is unknown whether the virus detected by sensitive PCR assays remains infectious and what risk remains of infection for social contacts and healthcare providers and the community in general. It is also unknown whether positive antibody testing (serology) is predictive of a protective immune response or of reduced infectivity, although this may be the case.

Based on other viral infections in immunocompromised individuals, it is expected that viral shedding in the respiratory tract as detected by nucleic acid testing (NAT) using molecular amplification (PCR) will be prolonged (>4-6 weeks) in many transplant recipients. Both false negative and false positive (pre-liver patients) antibody testing may be observed. Seroconversion may be delayed. Chest radiographs will lag behind resolution of symptoms and viral shedding.

Patients *with prior positive SARS-CoV-2 assays* should have resolution of symptoms, including fever, before enhanced respiratory precautions are removed. Some centers use two negative nasopharyngeal swab assays (PCR) at least 24-48 hours apart as a basis for removal of COVID-19 precautions. For patients with a clinical diagnosis of COVID-19 without positive tests, it is reasonable to await symptom resolution; further viral testing (sputum, tracheal aspirate, blood, stool) and serology have been utilized in some cases to assist in decision-making.

Further data are required. Public health and hospital guidelines should be followed.

14. Useful links:

Hygiene, physical distancing, masks, isolating, quarantining, what to do if you are sick:

- [CDC: How to Protect Yourself/What to Do If you are Sick](#)
- [CDC: Printable Handouts for Patients](#)

NIH Treatment Guidelines: <https://www.covid19treatmentguidelines.nih.gov/>

Infectious Disease Society of America Treatment Guidelines:

<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>