2019-nCoV (Coronavirus): FAQs for Organ Transplantation

Updated: May 11, 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 early cases outside of China were linked to travelers from China or other areas with high circulation of SARS-CoV-2, cases are now more often diagnosed without obvious travel-related exposure. 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. Shedding from asymptomatic individuals has also led to transmission of 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 and given the potential for greater infectivity, strict isolation precautions should be followed for anyone with suspected SARS-CoV2. 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. N95 masks should be reserved for healthcare workers. Surgical masks are acceptable alternatives when supplies are limited. However, 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). The public is encouraged to make masks as recommended by the CDC.

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

Data on transplant recipients with COVID-19 are still limited to case series but experience is accumulating. However, based on data from other viruses and SARS, severe infection in the immunocompromised population, including transplant recipients has occurred. Mild infections have also been reported. The New York City experience revealed high rates of 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 infection have not been fully characterized. 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 treatments for COVID-19?

Currently, the treatment is supportive care. Potential antiviral medications 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. A press release from the NIH revealed that remdesivir decreased time of illness in the recent trial but the publication is not yet available. The FDA issued an Emergency Use Authorization 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 (https://www.fda.gov/media/137566/download). There is no transplant specific sub-analysis from this trial at this time; data regarding the relative efficacy in SOT are pending.

Similarly, chloroquine, hydroxychloroquine, lopinavir/ritonavir, interferon-1$_{\beta}$, tocilizumab and several other compounds are being evaluated or considered as experimental therapy; results have been variable and based on small case series and not specific recommendations for the use of these medications can be provided.

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 CYP34A-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.

There is a suggestion that continued ARB and ACE inhibitor therapy may be detrimental but data on this association are extremely limited and there is no firm recommendation for discontinuation of these medications at this time. 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. Many providers have decreased or discontinued cell cycle inhibitors but comparative data regarding this intervention is not yet available. Whether adjunctive corticosteroid therapy for patients with severe ARDS may be beneficial is also unknown and there is no current recommendation for the use of adjunctive corticosteroids.

5. 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 absolutely 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
- 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

6. 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.

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 COVID-19 including, but not limited to, fever, chills, rigors, cough, myalgias, headache, sore throat, flu-like symptoms, unexplained gastrointestinal symptoms, 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, 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), they should call 911 and notify dispatch if they have 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; these may vary seasonally in your geographic area. Consult your local hospital practices for outpatient transplant clinic screening or visitor restrictions for transplant recipients as these may evolve over time.

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 availability is highly variable in much of the US and abroad. SARS-CoV2 is not detected using the standard respiratory virus multiplex tests at this time, so specific testing must be requested.

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 and laboratory visits 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. The risk of transplantation must always be balanced with the risk of not transplanting an

individual patient with acute or recent COVID-19. Given the absence of definitive treatment, candidates with active COVID-19 should be deferred from transplantation. The ideal disease-free interval is unknown at this time. Likewise, the need for PCR negativity is not known as 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).

However, with the 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 to avoid adverse events post-transplant as well as avoid exposure to the healthcare team. Some transplant physicians recommend two negative PCR tests; the optimal timing of multiple tests is unknown. As more is learned about serologic conversion, antibody testing may also aid in the pre-transplant evaluation.

10. Should candidates be counseled about the risk for COVID-19 infection?

At this time, with active circulation of SAR-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.
It is not known if asymptomatic candidates should be screened by SARS-CoV-2 PCR of the upper respiratory tract prior to proceeding to transplantation, but if available testing should be strongly considered.

In addition, the risk - benefit of transplantation during the COVID-19 pandemic should be reviewed taking into account individual risks of becoming more ill on the wait-list and local transmission rates.

11. Should we be transplanting right 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 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.

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.” Some centers may still need to explore temporary suspension of elective living donor transplantation or non-urgent deceased donor transplants with involvement of organizational leadership based on prioritization planning. 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. 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.