

# The **AJT** Report

News and issues that affect organ and tissue transplantation

## COVID-19: Transplant Works Toward Adaptation

Research is key to helping transplant adjust to the reality of the pandemic



**A**s the northern hemisphere braces for a winter season with COVID-19, many questions remain about the virus' effect on transplant. Maryl Johnson, MD, past president of the United Network for Organ Sharing, categorizes these questions into three buckets: management of transplant recipients; care and selection of candidates for transplant; and donors, including determination of safe transplant use from donors with a history of COVID-19.

### Managing Risk

Many transplant centers question how to manage patients who succumb to infection. "This is something we had to deal with in the first wave of the pandemic here in Italy," says Luciano Potena, MD, PhD, medical director of heart and lung transplantation at the University of Bologna, Italy. When COVID-19 first hit the country, his team reduced immunosuppression in the few patients (4 of 400) who experienced symptomatic infection. Although there was no evidence at the time to support this decision, Dr. Potena feels that this instinctive response based on the precautionary principle was the right choice. All the patients who tested positive for COVID-19 recovered, although one did experience a mild episode of myocardial rejection. Even so, Dr. Potena still has questions, particularly regarding the optimal dosages and types of immunosuppression regimens to employ during the pandemic.

Recent guidance from the American Society of Transplant Surgeons and other groups presumes that patients with active or recent COVID-19 who are transplanted will likely have worse outcomes.<sup>1,2</sup> Based on this assumption, transplantation in candidates with active or recent COVID-19 has been deferred. In Italy, however, a joint committee of the Italian Society of Organ Transplantation (ISOT) and the Italian Society of Nephrology has provided its own recommendations, as explained by Giuseppe Remuzzi, MD, director of the Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Italy, and "Chiara Farma" professor of nephrology, University of Milan. These recommendations state that during the COVID-19 pandemic, deceased donor kidney transplantations should be performed only if it is possible to transplant a SARS-CoV-2 negative organ into a SARS-CoV-2 negative patient, and that renal transplantation should be prioritized for recipients facing urgent clinical

conditions "because frequent healthcare contact due to the severity of their underlying disease means that these patients will remain at high risk for acquiring SARS-CoV-2, a risk that might be greater than the risk of SARS-CoV-2 acquisition through successful transplantation," says Dr. Remuzzi.<sup>2</sup>

### KEY POINTS

- The optimal immunosuppression management strategy for transplant recipients during a pandemic is not known.
- Questions remain on whether candidates for transplantation with active/recent COVID-19 should be deferred.
- As the potential for donor-derived COVID-19 infection is not understood, transplant centers and organizations err on the side of caution.
- The fall and winter seasons will bring additional challenges related to identifying and managing COVID-19.

Despite the establishment of such guidelines, questions remain: Is it important to defer transplant for candidates who are positive for COVID-19? And, if such a deferral is necessary, how soon can these patients be transplanted?

Currently, the American Society of Transplantation and the ISOT do not recommend the use of organs from living donors who are SARS-CoV-2 positive or classified as high risk after screening.<sup>2</sup>

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Unfortunately, however, there are no clinical data that accurately define the risk of transplant transmission of SARS-CoV-2. Thus, transplant centers and organ procurement organizations apply the precautionary principle and look to small studies of SARS-CoV-2 as well as studies of related coronaviruses for guidance.

Although transfusion and transplantation during the SARS-CoV and MERS-CoV outbreaks do not appear to have resulted in viral transmission, this may not apply to SARS-CoV-2. Recently, colleagues at Dr. Remuzzi's institution reported the presence of SARS-CoV-2 in the kidney, and the potential for donor-derived COVID-19 infection remains unknown.<sup>3</sup>

Access to transplantable organs may become even more limited if research indicates that organs from recovered patients should not be transplanted. "We may find chronic organ damage even in those who do not develop any symptoms," says Dr. Potena, noting concerns about lasting lung damage or sustained myocarditis.

### Coexisting with the Virus

As Italy's cases plateau, the country's healthcare system is finding a way to coexist with the virus. Effective strategies begin in communities and extend into hospitals and transplant centers, with basic questions about how best to live within a pandemic.

Currently, much of the northern hemisphere permits outdoor gatherings. Summer is safer because the common cold is not circulating, and most people are not coughing or sneezing. With fall, however, the transplant community will be challenged to dissect and identify a COVID infection from other respiratory infections. Anticipating a difficult season, Dr. Potena reflects on the lessons that Italy has learned. "We had a quite prolonged phase of total lockdown, and it was like in the war," he says. During that time, medical care that was not COVID-driven went unattended, including crucial cancer visits and follow-ups. Dr. Potena does not believe the Italian healthcare system will derail again this fall. "We have a majority of people who are educated to wear masks and wash hands..." he says. "It could be better, but it is something."

Dr. Potena estimates that in a typical winter, 20 to 25% of the transplant center's patients have COVID-like symptoms. He anticipates the same this year, and, although a minority of them will actually have COVID, it will be challenging to identify these individuals so as to create the separate paths needed to reduce the

spread. Healthcare centers must also screen asymptomatic patients for infection, especially if the patients are poised to receive a transplant. Thus, a rapid, sensitive PCR test must be readily available and must be implemented at a massive scale, he emphasizes.

Transplant centers also need to better understand the role of serology screening. It is not known whether positive serology means that the patient is protected from SARS-CoV-2 infection and if so, how long protection will last. Likewise, if a vaccine becomes available, research is needed to determine whether immunosuppressed patients will respond to it and if that response will last.

Once transplant centers have established separate treatment paths, they will need to collect data on how best to manage patients with respiratory symptoms. Some patients may not require a visit, and infection risk will outweigh the likely benefit of a visit. Information technology infrastructure can be developed to support telemedicine, but research is needed to determine which visits can be most effectively done via telemedicine.

Best practices will vary from country to country. However, the world will benefit from an exchange of ideas and a willingness to learn from the mistakes and successes of other countries. "Despite the fact that the current COVID-19 pandemic continues to spread and resurge worldwide, certainly we should, and hopefully will, learn to coexist with the circulating SARS-CoV-2," says Dr. Remuzzi. "To do this, we need to take lessons from countries like Italy, where measures to contain the transmission of the infection so far have been valuable and efficient. This includes coordinating the easing of various containment measures for COVID-19 to avoid the situation that can currently be observed in the United States, where this approach has not been adopted and a dramatic resurgence of COVID-19 cases and an increase in the number of deaths have been reported across the country." **AJT**

#### References

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## Xenotransplantation Through a New Lens

**M**any in the transplant community believe that xenotransplantation has the potential to solve the shortage of human organs for transplant.<sup>1</sup> However, the COVID-19 pandemic has driven attention to the risk of zoonotic diseases and fueled concerns about nonhuman sources of infection. "We in the xenotransplant field have been appropriately nervous about infection for a long time," says Richard Pierson, MD, scientific director, Center for Transplantation Sciences at Massachusetts General Hospital, Boston. After all, every form of transplantation brings a risk for disease transmission.

A 2018 minireview published in the *American Journal of Transplantation* describes the possible infectious risks of xenotransplantation to transplant recipients as well as the community at large. While many flu viruses are capable of infecting pigs, it is not yet known whether the same is true of SARS-CoV-2 or other coronaviruses. Moreover, absent human studies, the absolute risk for infections in xenotransplantation is unknown. According to Dr. Pierson, "xenotransplantation should be safer than allotransplantation," because

the background and exposure of the pigs is thoroughly documented via prior identification and testing for pathogens, a luxury not always possible for deceased donors. Xenogeneic tissue is also resistant to infections by human pathogens such as HIV (1 and 2) hepatitis B virus, hepatitis C virus, and herpes viruses including human cytomegalovirus.

As the pandemic persists, the resulting decrease in transplantable human organs may render the idea of xenotransplantation more viable to the transplant community and the general public. "When xeno comes forward, it will be appropriate for the press and the public to ask these questions about zoonotic disease," notes Dr. Pierson. "Our first obligation as doctors is to first do no harm, and this precautionary principle is baked into our planning for any clinical xenotransplantation trial." **AJT**

#### References

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