Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Even as the worst of the COVID pandemic subsides, transplant patients are left not knowing which way to turn to stay safe.

BY LARA C. PULLEN, PHD

News and issues that affect organ and tissue transplantation

Guiding Transplant Patients in a Postpandemic World

More vulnerable than the general population, transplant recipients are far from living a safe, post-COVID life

However, despite all his research and attention to the experts, Mr. Stautzenbach remains at a loss as to how best to manage his risk during the pandemic. The problem, he says, is due to a lack of clear guidance. “Transplant centers were late to the game getting out information and, if you are listening critically like our community is, they’re not consistent,” he says.

Transplant recipients crave specific guidance. Instead, what they most often hear is that they should “act as if they are unvaccinated.” Mr. Stautzenbach feels that this advice is, at best, unhelpful and at worst, confusing. Most transplant recipients know that they need to be careful. They also know that they are more susceptible to the flu than the general population, as well as to COVID. So, if they are more vulnerable than the general population even when they are vaccinated, wonders Mr. Stautzenbach, is it truly sufficient for them to manage their risks as if they were healthy unvaccinated individuals? Should they travel on airplanes? Should they return to a mask-free work environment?

As a patient and as an employer, Mr. Stautzenbach worries that transplant recipients may be pressured to return to in-person work and jeopardize their lives in the process. He also sees potential for employment disability problems arising from the faulty assumption that “healthy and unvaccinated” is the same as “vaccinated with a health condition.” Transplant-specific guidance, he believes, could help prevent this problem. “Part of it is giving direction to us as transplant recipients and part of it is explaining to the rest of society,” he adds.

This past summer, as vaccinations were distributed throughout the US and cities reopened, many individuals started to laud “the end of the pandemic.” However, this can be a risky attitude for transplant patients. “There’s a lot of social pressure for transplant patients to be more easygoing,” says Candida Moss, PhD, a kidney transplant recipient who wrote a guest essay in The New York Times entitled, “I’m a Vaccinated Transplant Recipient. I Don’t Have Antibodies. Now What?” In response, she received hundreds of emails from transplant recipients, many of whom expressed surprise to learn that the COVID vaccine was likely ineffective for them and that they, like Dr. Moss, may be entering a more dangerous and isolating phase of the pandemic.

Seeking Consistent Guidance

Tom Stautzenbach will soon celebrate his 18th kidney transplant anniversary. He has a close relationship with his transplant center, maintains connections with the transplant community, attends webinars hosted by multiple transplant centers and is active on transplant social media. Mr. Stautzenbach recognizes that the solid organ transplant community is at heightened risk for COVID and understands the risk to kidney transplant recipients to be even higher still. He knows that certain types of immunosuppression are more likely to diminish the efficacy of the vaccine and that he is on such medications.

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KEY POINTS

- Transplant recipients may be entering a more dangerous and isolating phase of the pandemic.
- Transplant centers have been slow getting information to patients, and messages have been inconsistent.
- Lacking guidance, frustrated transplant recipients are taking matters into their own hands.
- Clinical trials will soon be underway to provide scientific evidence to direct recommendations for transplant recipients.

What would this specific guidance look like? Mr. Stautzenbach points to the U.S. Centers for Disease Control and Prevention (CDC)’s green, yellow and red risk assessment chart, which was created for
the general public and has been updated throughout the pandemic. He wonders why the transplant community has not created a similar chart geared for its population when this is clearly so needed. He conjectures that, given the paucity of data on transplant recipients, the chart would likely be based on professional consensus at first. This way, he explains, the transplant chart could be updated to reflect the science like the chart provided by the CDC for the general population.

Taking Initiative
“It's really understandable that patients are frustrated, confused and scared,” says Dorry Segev, MD, PhD, director of the Epidemiology Research Group in Organ Transplantation at Johns Hopkins University in Baltimore. He receives hundreds of emails daily from patients searching for guidance from their providers.

Absent this guidance, patients are trying to reach their own understanding and then matters into their own hands. One way they are doing this is by obtaining a third booster dose of the COVID vaccine, even though the current U.S. Food and Drug Administration emergency use authorization (EUA) limits patients to two doses and prohibits physicians from prescribing a third dose. Dr. Segev estimates that hundreds of transplant patients have gone this route. Dr. Moss reports that some transplant recipients have written to confide that they secretly decreased their immunosuppression prior to COVID immunization. Dr. Segev declares this approach to be “very unwise and not recommended at all.” Going to get a third dose is one thing but reducing your own immunosuppression at a time when you are also activating the immune system is pretty risky. I really hope that people do not do this.”

As things stand, each transplant center must counsel the individual patient. “Transplant centers need to make sense of the situation in real time and do that collaboratively with our patients,” says Lara Danziger-Isakov, MD, MPH, director of Immunocompromised Host Infectious Disease at Cincinnati Children’s Hospital Medical Center in Ohio. This means weighing many variables for each patient. Dr. Danziger-Isakov advises that all individuals who spend significant time with a transplant recipient become vaccinated first, to create a “circle of protection.”

Future Clinical Trials
Dr. Danziger-Isakov acknowledges that transplant recipients vary widely in their responses to vaccine. However, individual responses cannot be expressly considered because the American Society of Transplantation does not currently recommend measuring antibody titers. “There’s a wide variety in what the antibody tests actually measure as well as the level of antibodies required to prevent severe disease,” she says, noting that even without this specific information, patients require very individualized conversations with their providers to understand which behaviors are safest for them. Moreover, this individual counseling must occur against a backdrop of few scientific data, a process that frustrates physicians and patients alike.

Fortunately, upcoming clinical trials could help remedy this situation. Daniel Rotrosen, MD, director of the Division of Allergy, Immunology, and Transplantation at the National Institute of Allergy and Infectious Diseases (NIAID), describes NIAID scientists’ phased approach to a better understanding of vaccine efficacy in transplant recipients. “The first phase will assess humoral and cellular immunogenicity of a homologous boost (third dose) of an mRNA vaccine in approximately 200 kidney transplant recipients who have low or nondetectable SARS-CoV-2 antibodies after receiving a full course of the emergency use authorization vaccine,” he says. The NIAID received the “safe to proceed” go-ahead in July 2021, and participant screening is underway.

The next phase of research will examine varying approaches to modifying transplant recipient immunosuppressive regimens to enhance vaccine immunogenicity. Dr. Segev is the protocol chair for this adaptive design, multi-arm, multi-site study of approximately 800 solid organ transplant recipients. The study will examine the effect of modifying immunosuppressive medications as well as the role of boosters.

“NIAID is also developing studies for patients who are immunosuppressed due to treatment for autoimmune diseases. The focus initially will be on patients with rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, scleroderma and pemphigus,” says Dr. Rotrosen. “That study will be conducted through the NIAID Autoimmunity Centers of Excellence and will ask if vaccine immunogenicity can be enhanced with short-term modification or withholding of immunosuppressive medications.” Although Dr. Rotrosen does not have a figure on total federal funding for COVID research in transplant recipients, he says that the U.S. Department of Health and Human Services will provide EUA vaccines and up to 40 million dollars to conduct the solid organ transplant studies.

Certainly, these studies will be welcomed by transplant patients, many of whom are beginning to feel expendable. As Mr. Stautzenbach observes the decrease in COVID mortalities across the nation, he realizes that his community of transplant recipients will contribute to the eventual tolerable death count. Transplant recipients like him do not yet live in a post-COVID world, and he is asking the transplant community to help him explain this to the rest of society.

References
1. Moss C. I’m a Vaccinated Transplant Recipient. I Don’t Have Antibodies. Now What? The New York Times. May 24, 2021; https://www.nytimes.com/2021/05/24/opinion/organ-transplant-covid-vaccine.html. Accessed July 16, 2021.

On June 30, 2021, Howard Bauchner, MD, stepped down from his role as editor-in-chief of the Journal of the American Medical Association (JAMA). Dr. Bauchner had already been on administrative leave for months, pending investigation over race-related comments that were made on a JAMA podcast episode. Prior to the broadcast, a promotional tweet posted by JAMA had stated that “no physician could be racist.” Although Dr. Bauchner himself did not write the tweet, as editor-in-chief, he acknowledged responsibility for its posting and for the podcast. Leaders of the American Medical Association admitted to serious missteps and proposed a 3-year plan to “dismantle structural racism,” not just within the organization, but within medicine.

Last year, the American Society of Transplantation announced the members of its Inclusion, Diversity, Equity, and Access to Life (IDEAL) Task Force, people whose voices have informed the American Journal of Transplantation (AJT). They include IDEAL chair Marie Chisholm-Burns, PharmD, MPH, MBA, of the University of Tennessee College of Pharmacy in Memphis, and Elisa Gordon, PhD, MPH, of Northwestern University in Chicago.1-3 AJT and “The AJT Report” are committed to continue serving as a vehicle for these critical conversations.

References
1. Pullen LC. A path toward improving health literacy and transplant outcomes. Am J Transplant. 2019;19:1871-1872.
2. Pullen LC. Striving for equity in transplant. Am J Transplant. 2020;20:2293-2294.
3. Pullen LC. Stepping up to reduce racial disparities in transplantation. Am J Transplant. 2018;18:773-774.