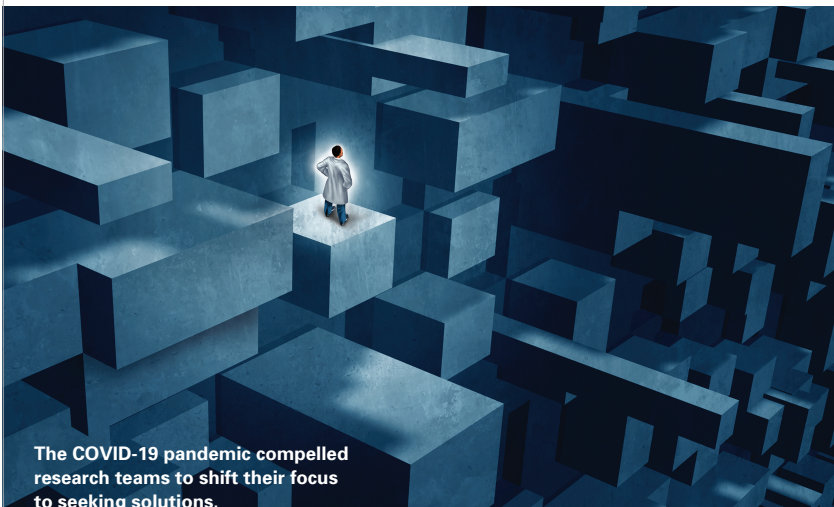


# The **AJT** Report

News and issues that affect organ and tissue transplantation

## Three Platforms: Ways to Pivot in a Pandemic

*As COVID-19 took hold across the globe, these three transplant researchers were rising to the moment*



The COVID-19 pandemic compelled research teams to shift their focus to seeking solutions.

**S**preading rapidly from Wuhan, China, to Lombardy, Italy, to New York City, COVID-19 ushered in a season of overwhelmed medical systems, paralyzed communities and death. Suddenly, “the city that never sleeps” went silent, except for the intermittent whine of ambulance sirens. No one was immune, least of all health workers. At New York-Presbyterian/Columbia University Irving Medical Center, transplant surgeon Tomoaki Kato, MD, MBA, was unexpectedly stricken with the virus and hospitalized. For two months, Dr. Kato fought for his life as his colleagues rallied to provide the continuous support and assistance that he and exploding numbers of fellow sufferers so desperately needed.

“We were being redeployed to do ICU, ICU triage and night shifts at the hospital,” recalls Dr. Elizabeth C. Verna, MD, MSc, director of clinical research at the Transplant Clinical Research Core at Columbia. The hepatologist and research manager/coordinator was now compelled to shift much of her team’s effort to COVID-19. However, even as medical staff worked around the clock, some continued to engage in research activity on the side.

During the initial uncertain months of the pandemic, transplant researchers like Dr. Verna pivoted their teams of investigators toward seeking answers to the important questions of the moment. Paolo Cravedi, MD, PhD, a nephrologist at Mount Sinai in New York City, watched as both his adopted home and his birth town in

Lombardy became overrun by the virus. He turned his focus to finding solutions to the pandemic. And a thousand miles away at Northwestern University in Chicago, where the medical center’s laboratories closed as the hospital prepared for the pandemic to hit the Midwest, Ankit Bharat, MBBS, head of the Lung Transplant Program, pondered ways in which his team could bring innovation to the care of critically ill COVID-19 patients.

For Drs. Verna, Bharat and Cravedi, the switch to studying an acute infectious problem required overcoming many logistical barriers. Ultimately, however, the concentrated effort produced meaningful results and reinforced their appreciation of problem-based science.

### Research from the Front Lines

Dr. Verna’s group published one of the first major papers on COVID-19 in solid organ transplant recipients, which confirmed the suspicion that such recipients were at high risk for SARS-CoV-2 infection and poor associated outcomes.<sup>1</sup> Acknowledging that testing limitations likely led to undercounting of mild/asymptomatic cases, the team reported that 18% of the 90 patients diagnosed with COVID-19 died.

#### KEY POINTS

- In the early months of the COVID-19 pandemic, three transplant research teams turned their focus to seeking solutions.
- Columbia University published one of the first major papers on COVID-19 in solid organ transplant recipients.
- The lung transplant team at Northwestern University transplanted patients who had COVID-19 respiratory failure.
- An international transplant consortium reported key findings regarding hospitalized kidney transplant recipients with COVID-19.

As COVID-19 research became a priority at Columbia, researchers from the School of Public Health and the Medical Center shifted their efforts and rapidly published their findings. One matched case-control study reported the effect of tocilizumab as a treatment for COVID-19 in solid organ transplant recipients.<sup>2</sup>

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The group found that while tocilizumab appeared to be safe, it was not associated with decreased 90-day mortality.

Looking back, Dr. Verna feels that her research group was “uniquely positioned” to do this work because “our hospital was completely overrun by COVID in early spring,” she says. “We had, early on, enough patients to say something decisive. . . . We felt that it was an obligation to get some initial reports out about this disease, especially in transplant recipients.” Dr. Verna and colleagues continue to focus their research on the virus.

### Surgical Solution

In Chicago, which did not experience the same crisis as New York City, Dr. Bharat’s team continued to push to identify more paths to saving patients. “I never thought I’d find a vaccine. That’s outside my scope as a surgeon,” he says. Instead, he developed a surgical solution for patients with severe COVID-19.<sup>3</sup>

Recognizing that despite optimal medical therapy, some patients with severe COVID-19 develop irreversible lung injury, Dr. Bharat and his team transplanted lungs into patients who had COVID-19 respiratory failure. As they reported, although SARS-CoV-2 RNA could not be detected in the explanted lungs of these patients, the researchers observed fibrotic pathology and transcriptional changes that resembled the lungs from patients with pulmonary fibrosis. Dr. Bharat credits his team’s accomplishment to a culture of innovation in his division.

### International Access

On the phone with his friends and parents in Lombardy, Dr. Cravedi could hear the wailing of Italian ambulance sirens. He turned to Post-Transplant Glomerular Diseases (TANGO), the international network he had established with colleague Dr. Leonardo RIELLA, MD, PhD, the medical director of Kidney Transplantation at Massachusetts General Hospital in Boston, to study posttransplant glomerular diseases.<sup>4</sup>

In May 2020, TANGO addressed the issue of whether kidney transplant recipients were at a high risk of developing critical COVID-19 due to chronic immunosuppression and comorbidities.<sup>5</sup> They reported that hospitalized kidney transplant recipients with COVID-19 had high rates of acute kidney injury and mortality. Globally, approximately one-third of such patients hospitalized due to COVID-19 had died. These patients, who tended to be older, had lower lymphocyte counts and estimated glomerular filtration rate levels, and higher serum lactate dehydrogenase, procalcitonin and interleukin-6 levels.

TANGO also provided a platform that allowed the international kidney transplant community to easily share information that not only helped to treat patients in the moment, but that could be published and shared. In August, Dr. Cravedi and colleagues wrote that, contrary to initial predictions, the humoral immune activity of COVID-19–infected kidney transplant recipients was not impaired.<sup>6</sup> Their findings raise the possibility that empiric reductions in immunosuppressive therapy for all kidney transplant recipients with active COVID-19 may not be necessary.

The group continues to work actively on this topic. “Being so connected to Europe and other areas where the epidemic arrived first has allowed us access to clinical data and human samples to analyze,” explains Dr. Cravedi.

### Common Themes

As an infectious disease, COVID-19 falls directly within the field of transplant, particularly because disease results not only from the viral infection, but also from the body’s immune response to the virus. The crisis of a rapidly spreading and deadly pandemic mobilized and affected transplant doctors and researchers in powerful and unexpected ways. Dr. Kato, having survived his critical bout with COVID-19, has documented his experience in a first-person account.<sup>7</sup>

Looking back, Drs. Verna, Bharat and Cravedi emphasize the intellectual satisfaction of studying a new disease and note the importance of adaptability when meeting a medical crisis. “Don’t be afraid to seize new opportunities. It’s about understanding your passion and skill set,” says Dr. Verna, who views the experience as an honor. “The bravery and work ethic and compassion in the middle of a crisis at all levels was really overwhelming and inspiring. . . . We are part of a remarkable community.” **AJT**

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## Transplant Milestones

**F**ifty years ago, Angela Dunn was surviving on dialysis and not expected to live beyond 30 years old. Then she received a kidney from a man who had died in a traffic accident. In July 2020, the now-74-year-old French resident celebrated her golden anniversary of living a healthy life with the same kidney graft. Ms. Dunn, who received her transplant from Prof. Sir Roy Calne, a surgeon and pioneer of organ transplantation working at Addenbrooke’s Hospital in Cambridge, UK, is now reportedly the longest living kidney transplant recipient.

In 1970, a 6-year-old boy in Zurich, Switzerland, had developed end-stage kidney disease due to hemolytic uremia syndrome and had received hemodialysis three times a week for 6 months to improve his nutritional state to allow renal transplantation. He received a kidney graft from a deceased donor and was subsequently able to attend regular

school and grow to live a normal adult life with no major health problems. For him, December 2020 marked 50 years of functioning with the same graft. He continues to receive the “basic” immunosuppressive treatment of prednisone (20 mg/48 hours) and azathioprine (62.5 mg/day).

Prof. Ernst Leumann (emeritus pediatric nephrologist from Zurich), who managed and performed Switzerland’s first pediatric transplant with the now-deceased transplant surgeon Prof. Felix Largiader, reflects on the milestone. “Fifty years is really very special,” he says, and adds that it would be interesting to gather and analyze these pioneering patients’ stories, and look for any common factors that may contribute to optimal renal graft function maintenance. **AJT**

