

# The End of Dialysis?



Dr. Stanley Jordan's research has led to major advances in diagnostic and treatment approaches in the care of patients receiving transplanted organs.

BY LAURA RANDALL

Soraya Kohanzadeh was lucky. Of the tens of thousands of people who need a new kidney, she wasn't among the nearly 75,000 in the United States who must wait years for a compatible organ to turn up. The high school algebra teacher had a matching, and very willing, donor in her mother Joan.

**W**HAT SORAYA DID NOT KNOW IS THAT SHE had high levels of "antidonor" antibodies in her blood due to an earlier series of transfusions. She was told she was unlikely to ever receive a transplant and would have to remain on dialysis for the rest of her life. "Dialysis was a painful, horrible existence," recalls Soraya. "I couldn't work, I was sick all the time. The likelihood of living past the next 15 years was very slim."

An estimated 33 percent of patients on the nation's kidney transplant lists are found to be, like Soraya, highly sensitized: Their immune systems are hypervigilant and would likely reject a donor organ. Until recently they had little chance of receiving a new kidney.

It was this group Stanley C. Jordan, MD, hoped to help, when more than a decade ago he began exploring the use of intravenous immunoglobulin (IVIG) as a way to reduce the high incidence of organ rejection. Although tissue compatibility is an issue for anyone receiving a transplanted organ, rejection risks are particularly high for patients with immune systems that have been exposed to "nonself" human leukocyte antigens (HLAs). HLAs are proteins present on the surface of all cells that regulate the way the body recognizes foreign substances. They are coded to allow the immune system to distinguish between "self" and "nonself." Exposure to "nonself" HLAs may occur through an organ transplant, blood transfusions (as in



Soraya's case), or pregnancy, when the mother is exposed to foreign tissue from the fetus.

"This has been a problem in transplantation for as long as there have been transplants; people are prone to rejection," Dr. Jordan says. Today, Jordan is medical director of Kidney Transplantation and Transplant Immunology at Cedars-Sinai's Comprehensive Transplant Center.

Immunoglobulins are a class of proteins secreted by blood cells that are induced in response to invasion by foreign antigens. Administered to patients through intravenous infusion during dialysis, IVIG lowers the level of HLA antibodies and blocks their ability to attack the transplanted organ. Unlike other antirejection drugs it modulates the system instead of suppressing it, making patients less susceptible to infectious complications after a transplant, Dr. Jordan explains. "It is a therapy that has the potential to offer the patient a new life."

In 1997, Dr. Jordan began a five-year multicenter study on IVIG therapy at Cedars-Sinai with funding from the National Institutes of Health. Led by Ashley Vo, PharmD, a clinical transplant pharmacist, the team administered either IVIG or a placebo to 101 highly sensitized patients while they were awaiting kidney transplantation. The rates of successful transplantation for patients who had IVIG were double that of the placebo group, and triple for patients who had already received a transplant and rejected it.

IVIG became a Medicare-approved therapy in 2004, the same year the Transplant Immunotherapy Program opened at Cedars-Sinai. So far more than 150 highly sensitized patients have successfully received transplants from living or deceased donors through the program. "We have now become a national referral center for patients with this problem," Dr. Jordan says.



Above: Ashley Vo, PharmD, and LaKeisha Hall (left) share a few laughs as LaKeisha gets set up for IVIG therapy a few days before receiving a kidney from her brother Howard. Bottom right: Registered Nurse Lourdes Begg sets up a dialysis machine to be used in the four-hour IVIG treatment.

It is also the only program in the country to treat sensitized patients who are waiting for a kidney from a deceased donor, notes Dr. Vo, administrative director of the program. “We wait until a patient has been on the waiting list for five years and has started getting frequent deceased donor offers,” she explains. “Then we start to desensitize them with IVIG and get them ready for the transplant.” This requires an enormous amount of coordination among staff members, laboratories, and other medical facilities.

More medical centers around the country are looking into starting their own transplant immunotherapy programs, but the reality is that it is easier to focus on the “healthy” transplant candidates who pose less of a risk for rejection, says Dr. Jordan.

“Other centers are reticent to start desensitization since a comprehensive program is required,” he explains.

Today Dr. Jordan and his colleagues are exploring ways to improve on IVIG therapy and help patients live better lives post-transplant. Among their discoveries: the development of a specialized test that enables them to more accurately predict which patients will most likely benefit from IVIG, thereby increasing their chances of a successful transplant. They also pioneered a treatment that combines IVIG with Rituxan®, an antibody used to treat non-Hodgkin’s lymphoma and B-cell leukemia, which lessens the time it takes to desensitize pre-transplant patients from 16 weeks to five weeks.

The hope is that IVIG therapy can eventually be applied to other types of organ transplants as well as the kidney. The therapy is already being used on heart- and liver-transplant patients and has worked especially well for patients awaiting heart transplants, says Dr. Jordan.

**T**HE INNOVATIVE WORK TAKING PLACE AT the Transplant Immunotherapy Program is what attracted Nancy Reinsmoen, MD, when she accepted the position of director of the HLA Laboratory at Cedars-Sinai in September 2006. Building on research she has conducted over the last two decades, Dr. Reinsmoen is currently exploring ways to improve the post-transplant outcome of highly sensitized

patients by identifying parameters that predict short- and long-term survival rates of organs. An immunologist who has overseen the transplant immunology laboratories at Duke University Medical Center and the University of Minnesota, she was aware of Dr. Jordan’s pioneering work in IVIG therapy long before her arrival at Cedars-Sinai.

“We want to predict which transplant patients will have a good outcome versus those who might not, so we can better tailor immunosuppression and help alleviate some of the side effects,” Dr. Reinsmoen says. “If we could predict, pre-transplant, which patients are going to have early acute rejection episodes, the clinicians and surgeons could think about different types of immunosuppression.”

“At the same time,” she adds, “if I could tell them which patients look like they’ll be just fine, they could lower the doses of immunosuppressive drugs or use different types of drugs for these patients.” Dr. Reinsmoen is in the process of asking the NIH to support her continued research in this area at Cedars-Sinai.

Another promising area of research is a specialized test that may be better able to determine whether a highly sensitized patient is at risk for rejection before the transplant process even begins. Developed by Mieko Toyoda, MD, director of the Transplant Immunology Laboratory at Cedars-Sinai, it uses a cellular assay to measure a patient’s B-cell response to new donors or to third-party cells and predict what the body’s reaction will be to them.

Several standard tests are currently used to evaluate the efficacy of the desensitization treatment, says Dr. Toyoda, but they often do not go any further to show which patients are likely to reject an organ after their transplants.

The results of an earlier study were promising, and the test is now in a clinical trial setting and will be evaluated scientifically. “We are very excited about this, because it does look like it gives us

a different measure of risk for rejection besides the antibody,” says Dr. Jordan.

In the meantime, the medical and insurance communities are becoming increasingly aware of IVIG’s cost-effectiveness and ability to help patients who were once considered hopeless, Dr. Jordan points out. IVIG therapy currently costs between \$7,000 and \$10,000 a dose, and patients receive an average of four doses before their transplant, depending on their levels of antibodies. In contrast, notes Jordan, it costs \$150,000 to \$200,000 a year to keep a person on dialysis, and a transplant itself costs about \$14,000 to \$15,000, long-term. “The cost of this therapy is minuscule compared to having patients stay on chronic dialysis,” he says.

**A**ROUND A TABLE IN DR. JORDAN’S SMALL corner office, he and Dr. Vo discuss their research and goals in measured, confident tones. Dr. Jordan, a silver-haired father of three, was raised in North Carolina’s Blue Ridge Mountains and was inspired to study medicine by the doctors and nurses who treated him when he contracted polio as a young boy. Dr. Vo was raised in Saigon, Vietnam, and fled to the United States as a young girl. The two share a quiet pride in their work, ticking off the rewards it has



yielded, such as the gratitude conveyed by patients and the respect the immunotherapy program at Cedars-Sinai has garnered in the international transplant community.

“Our clinic is a gratifying place to be,” Dr. Jordan says. “You see people who have gone from being very sick to being healthy, and they’re very appreciative of that. I do enjoy seeing people get their lives back.”

A little over a year ago, after undergoing immunotherapy treatment at Cedars-Sinai Medical Center, Soraya was able to receive her mother’s kidney, and both women recovered well from the surgery. Last August, Soraya, now a teacher at a Marin County juvenile hall, celebrated her 30th birthday with friends and family at her favorite restaurant. She is passionately advocating IVIG, and feels incredibly lucky to be dialysis-free. Then again, luck is always with her: “Soraya” is ancient Persian for “Seven Lucky Stars,” the constellation we call the Big Dipper. ♡

