The field of heart transplantation has been bolstered recently by techniques to increase the pool of donor hearts, as well as by advances in keeping patients awaiting transplantation stable for longer periods of time.

“The biggest advances really stem from how we’re going to think about organ donation in the future,” says Daniel Cruz, MD, assistant clinical professor of cardiology.

UCLA is a clinical-trial site for the Organ Care System (OCS) Heart, a groundbreaking experimental organ-preservation device that keeps donor hearts beating during transport. The device is a portable perfusion and monitoring system that delivers warm, oxygenated, nutrient-enriched blood to the donor heart and keeps it in a living state until the organ is ready to be transplanted.

continued on p. 4
Pediatric Hem/Onc Clinic Opens in Bakersfield

UCLA's Division of Pediatric Hematology & Oncology has opened an outpatient office in Bakersfield to provide care to children, adolescents and young adults with cancer or blood disorders who reside in the Kern County region.

Women's Heart Health

The UCLA Women's Cardiovascular Center employs diverse clinical expertise and cutting-edge research to provide the best possible care for women with cardiovascular disease.

UCLA Pediatric Sarcoma Program

The multidisciplinary physicians in UCLA's Pediatric Bone and Soft-Tissue Sarcoma Program are expert in treating this exceptionally challenging disease to ensure the greatest chance for survival.

Tuberculosis Sclerosis Program

UCLA's program includes both clinical care and research and is among the few in the nation with the resources and expertise to address the complexities of tuberous sclerosis.

Brachytherapy to Treat Variety of Cancers

High Dose Rate (HDR) brachytherapy delivers a calculated dose of radiation for a more exact amount of time to better target tumors.

3D Mammography

Digital breast tomosynthesis provides radiologists with multiple, thin-section images through the breast to increase breast-cancer detection rates while reducing false-positive results.

Pediatric Lupus Care

UCLA pediatric rheumatologists and pediatric nephrologists see pediatric lupus patients in a convenient clinic that provides coordination of services, careful diagnosis and close monitoring to control flare-ups and mitigate organ damage.

To download these and other clinical advances at UCLA Health, go to: uclahealth.org/clinicalupdates

Prostate-cancer cells have stem-cell qualities

Scientists at the UCLA Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research have shown that the cells responsible for generating deadly prostate cancer share some genetic qualities with the tissue-specific stem cells that naturally reside in the healthy prostate. uclahealth.org/stemcellprostatecancer

Wrist fractures could predict future breaks

Wrist fractures, common among postmenopausal women younger than 65, could predict more serious fractures in other parts of their bodies later in life. uclahealth.org/wristfractures

Improved stroke recovery

UCLA researchers have identified a molecule that, after a stroke, signals brain tissue to form new connections and could help restore brain function. uclahealth.org/strokerecovery

New program to solve genetic mysteries

A new UCLA program offers hope and potential answers for people who have undergone extensive medical testing that has failed to identify their illness. uclahealth.org/遗传学之谜
Innovative Kidney-Exchange Program Expands Options for Matching Recipients and Donors

With more than 100,000 people on the waiting list nationwide, the demand for kidneys for transplantation far exceeds the supply of available donor organs. For some of these patients, it might be eight-to-10 years before a suitable deceased donor becomes available.

Kidney exchange can change that equation. The UCLA Kidney Exchange Program is premised on the fact that many patients on the waiting list have a spouse, parent, sibling or other loved one who is motivated to donate but has an incompatible blood type or cross-match. One way the program expands the living-donor pool is through a kidney swap, in which two donor/recipient pairs who are incompatible trade donors so that each recipient obtains a compatible donor kidney.

Another method involves donor chains, which create even broader opportunities to benefit more patients. The process typically begins when an altruistic individual offers to donate a kidney to a stranger who is on dialysis but has a willing-but-incompatible donor. After receiving the compatible kidney, the organ from the original patient’s incompatible donor is passed on to another patient on dialysis, and that patient’s willing-but-incompatible donor then does the same. This generous “paying it forward” builds the chain of transplants.

To date, UCLA has performed approximately 170 chain kidney exchanges, more than any other center, and in 2015 performed 324 kidney transplants, more than any year in the program’s 50-year history, says Jeffrey Veale, MD, director of the UCLA Kidney Exchange Program.

Most recently, a new innovation in the kidney-exchange program, called the Advance Donation Program, allows a donor to donate a kidney before his or her intended recipient needs one — either because the intended recipient’s kidney failure isn’t yet advanced enough to warrant a transplant or because the patient has a currently functioning kidney transplant but is expected to need a second transplant in the future, as renal allografts tend to last 10-to-20 years.

The first-of-its-kind Advance Donation Program was launched in 2014 when a 64-year-old man approached the UCLA Kidney Exchange Program with the idea of donating his kidney to a stranger in exchange for a “coupon” that his young grandson, who had been diagnosed with kidney disease and was not yet on dialysis, could redeem years later when he needs a transplant.

“There are a lot of people who could donate, but they want to wait until their loved one needs their kidney,” Dr. Veale says. “This gives them the opportunity to donate now with the promise that the loved one will get an organ if needed in the future. In the meantime, we can use that donated organ to start a chain.”

Everyone wins from such actions, Dr. Veale notes. Patients who otherwise might have waited years for a kidney from a deceased donor receive a living-donor kidney, which, on average, lasts twice as long. This also shortens the waiting list for others. The recovery time associated with donation also is much lower than in the past, given the shift toward performing the donor nephrectomy laparoscopically.

“There is a real humanity component to this program,” says Dr. Veale, who has received funding from the National Institutes of Health to study the characteristics of altruistic donors.

“People are so grateful their loved one received a kidney from a stranger that they can’t wait to pass on the generosity to the next person to perpetuate the chain.”

The story of one lifesaving transplant chain in which UCLA was instrumental is depicted in a 2013 online documentary, The Chain: thechain.org

ABO blood type compatibility at a glance

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“There is a real humanity component to this program. People are so grateful their loved one received a kidney from a stranger that they can’t wait to pass on the generosity to the next person to perpetuate the chain.”
UCLA is a clinical-trial site for the Organ Care System Heart, an experimental organ-preservation device that keeps donor hearts beating during transport. In patients with multiple antibodies that preclude a match, physicians are using two medications to prevent antibody-mediated rejection.

STORY HIGHLIGHTS

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COVER STORY

Technology Broadens Pool of Donor Organs

(continued from cover)

The technology allows surgeons to preserve more organs, travel farther distances to obtain organs and monitor the status of the organs from harvest to transplant.

“One of the limitations in organ transplantation is the donor pool, which, for decades, has been very static,” Dr. Cruz says. “Sixty percent of donor organs that are offered are not used. That is due, in part, to distance or the quality of the donor tissue. Because we don’t have a good way of assessing organs, we often turn down marginal hearts. The OCS allows for the donor organ to be monitored to assess its viability and be transported longer distances and matched to a suitable recipient.”

A study led by Abbas Ardehali, MD, director of the UCLA Heart, Lung and Heart-Lung Transplant Programs, and published in The Lancet in June 2015, demonstrated short-term outcomes for recipients of organs transported by OCS similar to outcomes for recipients with organs transported via cold storage.

UCLA physicians also are examining the feasibility of using hearts harvested within 30 minutes of circulatory death and transported via the OCS. “The vision is that we will be able to use the OCS to increase the amount of time the heart is able to stay out of body longer and use organs from circulatory death,” Dr. Cruz says. “This could boost the number of organs by perhaps 10 percent.”
UCLA physicians have led the way in developing improvements for patients awaiting heart transplantation. For patients who have developed multiple antibodies that preclude a match with a suitable donor heart, physicians now, as part of a clinical trial, are using two medications to prevent antibody-mediated rejection, Dr. Cruz says. The C1q assay is used to assess whether antibodies in the recipient will cause harm.

Mechanical-support devices also have greatly affected the prognosis for patients with end-stage cardiomyopathy who are awaiting transplantation. Mechanical circulatory-support devices increasingly are used as a bridge to transplantation, says Ali Nsair, MD, associate director for Mechanical Circulatory Support Device Services. “These patients are in a situation where there is an imminent possibility of death, and they have such poor circulation that other organs are beginning to fail,” Dr. Nsair says. “If appropriate, we implant these devices to restore normal circulation and take over part of the work of the heart. Patients can very often leave the hospital and have a good quality of life while waiting for an organ to become available.”

Recently, UCLA experts began working with a mechanical-support device designed for smaller individuals, such as women and adolescents with congenital heart disease. In addition, research is ongoing to reduce complications such as infection, bleeding, thrombosis, hemolysis, aortic valvular dysfunction, right heart failure and ventricular arrhythmias that are associated with all mechanical-support devices.

UCLA’s program is one of only seven heart-transplant centers nationwide — and the only one in California — to be ranked at the silver level by the Health Resources and Services Administration, which has federal oversight of the nation’s organ-donation-and-transplantation network. UCLA also is a leader in performing heart-kidney and heart-lung transplants, Dr. Ardehali notes. “We have phenomenal records on outcomes after heart transplantation,” he says. “I feel strongly about the progress we have here. This is a program of innovation by expanding the donor pool and recipient criteria, and we are at the forefront of these efforts.”


Assist Devices and Aggressive Medical Therapies Enhance Pediatric Care

A range of medical and surgical advances have led to better outcomes in pediatric heart-transplantation patients and improved health in patients awaiting transplant. We are preventing patients with heart failure and congenital heart disease from needing a transplant, or we are delaying transplant by using novel therapies and aggressive use of medications,” says Juan C. Alejos, MD, medical director of pediatric heart transplantation.

Ventricular-assist devices are an essential tool for the treatment of young patients who are in active heart failure. While such devices aren’t perfect, “they are allowing patients to survive while awaiting further surgery,” says Brian Reemtsen, MD, surgical director of pediatric heart transplantation. Another major advance is the ability to transplant children under 2 years old against blood type, which increases the donor pool and decreases the wait time, Dr. Reemtsen says.

The pediatric program is based on a team approach. “Cardiac-transplantation surgery in pediatric patients is the best example of the need for a team of specialists,” Dr. Reemtsen says. “These patients would not survive, short- or long-term, without the multidisciplinary approach. The child is taken care of by this immense team, and that requires a lot of resources. But it’s the only way to get the best outcomes.”
What is the traditional protocol for hematopoietic cell transplantation?

We perform hematopoietic cell transplantation for the treatment of patients with leukemia, lymphoma and a variety of hematologic malignancies. These transplants have been done as inpatient services where the patient stays in the hospital for up to 60 days to safely undergo the transplant and to recover. But the field has evolved so that a subset of patients can safely receive the hematopoietic cell transplant as outpatients, which we now are doing at UCLA. The procedure entails collecting peripheral blood or bone marrow stem cells from the patient (autologous) or from a healthy donor (allogeneic), administering immunosuppressive chemotherapy to the patient, and then infusing the donor hematopoietic cells into the patient. In allogeneic hematopoietic cell transplant recipients, immune-suppressive medications are administered for three-to-six months.

How does outpatient hematopoietic cell transplantation benefit patients?

Patients have less risk of infection out in the world compared to when they are hospitalized. In addition, psychologically and emotionally, patients and caregivers appreciate not being in a hospital for one-to-three months. Hospitalization for that long can be a depressing experience. The third benefit is that the cost for outpatient treatment is significantly less — thousands of dollars less per day — than for inpatient care.

What are some of the scientific advances that have made outpatient hematopoietic cell transplantation successful?

Our knowledge has increased over the past decade in terms of identifying the lowest-risk patients and understanding how such patients can be treated safely as outpatients. One advance is in our ability to deliver blood products and antibiotics in the outpatient setting. Another is the development of powerful immunosuppressive medications that allow engraftment of donor hematopoietic cells in patients without the need for more toxic, high-dose chemotherapy or irradiation. Healthcare providers have also come to understand that nearly the identical supportive therapies administered in the hospital can be provided in the clinic. Many of these patients will need platelet or red-blood-cell transfusions or antibiotics every day. Previously, such patients required admission to the hospital, but we are now able to administer transfusions and antibiotics efficiently in the clinic or via home healthcare services.

Describe allogeneic transplantation and how this type of transplant is done for an outpatient.

Allogeneic transplantation — cells taken from a healthy donor — traditionally has been done in the hospital. But we will perform non-ablative allogeneic transplantation in the outpatient...
“Our knowledge has increased over the past decade in terms of identifying the lowest-risk patients and understanding how such stem-cell-transplant patients can be treated safely as outpatients.”
Data suggest that keeping organs on ex-vivo perfusion improves the quality of the lungs and potentially will make it possible in the future to accept organs that might not otherwise be considered usable.

Recent advances to transport and maintain donor lungs and improve care of patients awaiting new organs are reshaping the field of lung transplantation. These strategies may increase the number of patients who receive transplants.

UCLA has one of the largest lung-transplant programs in the country. The program also has the largest U.S. enrollment in a closely watched clinical trial on ex-vivo lung perfusion, a technique aimed at improving the quality of donor lungs for transplantation. Abbas Ardehali, MD, surgical director of the UCLA Heart, Lung and Heart-Lung Transplant Programs, is the chief U.S. investigator of the study, dubbed the INSPIRE trial.

“We have access to the newest technologies in organ preservation,” Dr. Ardehali says. “One of the benefits of this technology is to make lungs better for transplantation. Keeping them breathing and perfused is better than keeping the lungs on ice. A body of data suggests that keeping the organs on ex-vivo perfusion improves the quality of the lungs. We hope, through this study, that we can make lungs we don’t typically accept potentially usable in the future.”

Called the Organ Care System (OCS), this novel protocol involves an experimental organ-preservation device that keeps lungs in a near-physiologic state outside the body during transport: perfused with oxygen and a special
solution supplemented with packed red blood. The approach differs markedly from the current standard, which involves transporting donor lungs in a nonfunctioning, nonbreathing state inside an icebox. Among all donor organs, lungs are especially vulnerable to damage and degradation during transport. The OCS protocol may improve lung quality, resulting in a greater number of viable organs and enhanced surgical outcomes. In 2012, UCLA performed the first so-called “breathing-lung” transplantation in the United States.

At UCLA, reduced waiting time to receive a donor organ has resulted in a significantly lower pre-transplant mortality rate of 5.4 percent at 18 months compared to a national mortality rate of 17.5 percent for actively UNOS-listed transplant candidates. Time spent awaiting transplantation has declined even as the qualification criteria for lung transplantation has been expanded to patients who are extremely ill or considered high-risk transplantation candidates.

Lung transplants are performed for a spectrum of cardiopulmonary conditions, such as interstitial pulmonary fibrosis, chronic obstructive pulmonary disease, cystic fibrosis and pulmonary arterial hypertension. Moreover, UCLA’s program is among only a few in the nation that routinely evaluates and transplants complex patients afflicted with scleroderma and other collagen vascular diseases.

“We expect demand to increase as we offer lung transplantation to patients who were not candidates before, such as people in their 70s and those with cardiovascular conditions.”

Better care of the pre-transplant patient also has expanded the criteria of candidates, Dr. Ardehali says. “We are expanding to patients who otherwise would not be candidates or are still not candidates at other centers,” he says.

“One of the benefits of this technology is to make lungs better for transplantation. Keeping them breathing and perfused is better than keeping the lungs on ice.”

The lung-transplant team also offers ambulatory extracorporeal membrane oxygenation (ECMO) as a bridge to transplantation for patients who have not been considered viable candidates previously. Lung transplantation continues to be hindered by a much higher demand for donor lungs than can be supplied, leading to considerable waiting time and mortality among patients awaiting transplantation. This dilemma has led to the search for an alternative bridging strategy, such as ECMO, for patients with end-stage lung disease. The complex technology supplies respiratory and cardiac support to patients with end-stage lung disease and has, in recent years, gained acceptance as a bridge to transplantation for select candidates.

“We have resources to bridge candidates who would otherwise not be transplanted,” Dr. Ardehali says. “All of these things push the frontiers of the field. Just because someone has had heart surgery or needs it doesn’t mean they would be excluded.”
The UCLA Kidney Transplant Program is expanding transplantation to patients who, in the past, would have been unlikely to benefit due to increased immunological sensitivity.

More than a half-century after revolutionizing organ transplantation by pioneering the use of tissue typing to match donors and recipients, the UCLA Kidney Transplant Program is helping to further expand the lifesaving procedure to patients who, in the past, would have been unlikely to benefit from kidney transplantation.

Patients who are highly sensitized — those with particularly high antibody levels that react to foreign tissue — now are among those benefiting from these advances. These patients, including individuals who have had previous transplants, blood transfusions or pregnancies, are more difficult to match with potential donors and more challenging to successfully transplant.

UCLA’s Immunogenetics Center, which is a World Health Organization reference laboratory for human leukocyte antigen (HLA) typing and cross-match testing, “is critical to our ability to reduce the risk of rejection for our patients,” says H. Albin Gritsch, MD, surgical director of the UCLA Kidney Transplant Program.

Under the direction of Elaine Reed, PhD, professor of pathology, the UCLA Immunogenetics Center has developed tests to measure a patient’s response to donor tissue, including the development of anti-donor HLA antibodies. By identifying donor-specific antibodies that indicate a patient is at risk for transplant graft loss, the center has paved the way for tests that prospectively determine which transplant patients are most susceptible to rejection. The immunogenetics center also has worked closely with the transplant program to develop protocols for monitoring patients’ responses to therapy and for more successfully treating patients to prevent rejection. “This has allowed us to be more accurate in selecting patients for transplantation,” Gritsch says.

STORY HIGHLIGHTS

The UCLA Kidney Transplant Program is expanding transplantation to patients who, in the past, would have been unlikely to benefit due to increased immunological sensitivity.
the best drugs for an individual patient, greatly improving our outcomes in the most complicated cases,” Dr. Gritsch says.

Pediatric patients also benefit. “Young children who need a transplant can be challenging because they are smaller and can have more aggressive immune systems than adults,” says Eileen Tsai, MD, medical director of the Pediatric Kidney Transplant Program. “Fortunately, we have had a great deal of experience and success managing these patients’ complications.” Dr. Tsai explains that the program carefully monitors pediatric patients’ immune systems, conducting biopsies as needed, to ensure that medications are optimal.

Like the adult program, UCLA’s pediatric program is experienced in transplanting highly sensitized patients. The pediatric-kidney-transplant team also is taking advantage of new advances to treat diseases that recur in the kidney after transplantation, such as focal segmental glomerular sclerosis. And the program is expanding transplant opportunities to more children by offering paired exchange — allowing, for example, a parent whose kidney is incompatible with his or her child to set up an exchange with another donor-recipient pair to receive a compatible organ (see “Innovative Kidney-Exchange Program Expands Options for Matching Recipients and Donors,” page 3).

One of the biggest concerns related to pediatric kidney transplantation has to do with non-adherence. “We lose a significant number of our kidney allografts as a result of patients not taking their drugs or not following up appropriately, and those patients become much more difficult to transplant again,” Dr. Tsai says. “For adolescents, they are not only struggling with having chronic kidney disease, but they also are going through the developmental stages of adolescence, which can include exploration and defiance.” To meet that challenge, the UCLA Pediatric Kidney Transplant Program is implementing individualized strategies ranging from peer-buddy systems, cell-phone reminders and family counseling to a program that helps transition adolescent patients into adulthood by teaching them age-appropriate life skills, including those involved in posttransplant care.

Organ transplantation has been described as one of medicine’s greatest modern miracles — in many cases resulting in a long and healthy life for individuals who were near death. The expanding number of adult and pediatric patients now able to benefit from a kidney transplant adds to the urgency of encouraging more people to consider becoming a donor, either at the time of death or while they are alive. “The waiting list remains long,” Dr. Gritsch says. “So as physicians, it is incumbent on all of us to make sure people are aware that organ donation saves lives.”

Gabriel Danovitch, MD, medical director of the UCLA Kidney Transplant Program, points out the psychological importance of individuals indicating their willingness to be organ donors while still alive. “It reduces the stress on surviving family members during that time of decision if they know what their loved one wanted,” Dr. Danovitch says. “And the knowledge that some good may come out of the situation can provide some solace during this time of loss.”
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