Join us when Cleveland hosts the 2016 Transplant Games of America — and see the difference a transplant can make.
transplantgamesofamerica.org

About Cleveland Clinic
Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,000 physicians and researchers represent 120 medical specialties and subspecialties. We are a nonprofit academic medical center with a main campus, eight community hospitals, more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City and Cleveland Clinic Abu Dhabi.

In 2014, Cleveland Clinic was ranked one of America’s top 4 hospitals in U.S. News & World Report’s “Best Hospitals” survey. The survey ranks Cleveland Clinic among the nation’s top 10 hospitals in 13 specialty areas, and the top in heart care (for the 20th consecutive year) and urologic care.

The Cleveland Clinic Way
By Toby Cosgrove, MD, CEO and President of Cleveland Clinic
Great things happen when a medical center puts patients first. Visit clevelandclinic.org/ClevelandClinicWay for details or to order a copy.

Survival rates in this publication are calculated by a third party, the Scientific Registry of Transplant Recipients (SRTR), and are from the January 2014 SRTR data release unless otherwise noted. Cleveland Clinic’s observed (actual) and severity-adjusted expected survival rates are reported here, along with the average survival rates for the U.S. as a whole during the same period.
Dear Colleagues,

For Cleveland Clinic’s Transplant Center, 2013 was a year of both looking back and looking forward.

Plenty to look back on …

With gratitude and pride, we marked the 50th anniversary of Cleveland Clinic’s first successful kidney transplant, which established one of the world’s first deceased-donor kidney transplant programs and launched what has evolved into today’s comprehensive Cleveland Clinic Transplant Center.

On a personal level, the conclusion of 2013 gave me a chance to reflect on my first full calendar year as Director of the Transplant Center following my arrival at Cleveland Clinic in mid-2012. Much of what we have accomplished in that time is detailed in the pages that follow, including:

• Extension of our center’s reach with the launch of Cleveland Clinic Florida’s Transplant Program in 2013 and growth of affiliated transplant programs at two more U.S. sites and in Abu Dhabi
• Expansion and refinement of our pediatric transplant services, along with enhancements to other specific transplant programs
• Key contributions to innovations in transplant care, from pioneering work in 3-D-printed organ models for surgical planning to the application of multivisceral transplantation in unprecedented settings

… And an exhilarating future to look toward

Such innovations are at the heart of the forward-looking aspects of the year just ended. The future of transplantation is beckoning from multiple directions, and at Cleveland Clinic we are excited to be at the leading edge of many of these advances, including:

• Development of a center for beta cell therapy for diabetes through close collaboration with medical centers and industry partners at the forefront of innovative beta cell therapeutic modalities, including allotransplantation

We have spotlighted these and other “future of transplantation” developments in sidebars in nearly every one of the following sections of this publication. These sections profile each of the transplant programs that constitute Cleveland Clinic’s comprehensive transplant offerings, focusing on each program’s capabilities, 2013 outcomes and key recent developments.

In between the publication’s glances back at 2013 and glimpses toward the future, we share heartening snapshots of patients whose lives we helped extend and improve in 2013. Their profiles speak to the magic that can result when critically ill patients’ primary providers partner with a premier transplant center to ensure comprehensive pre- and post-transplant care.

I invite you to read more about our center’s singular approach to transplant care and look forward to the chance to collaborate with you to produce similar magic for your patients who may be candidates for transplant or alternative treatment modalities.

In closing, I also invite you to join us in witnessing firsthand the transformative effects that transplantation can have on patients’ quality of life at the 2016 Transplant Games of America, to be held in Cleveland. Stay tuned for more details.

Respectfully,

Kareem Abu-Elmagd, MD, PhD
Director, Cleveland Clinic Transplant Center
abuelmk@ccf.org | 216.445.8876
200+ Transplant Center specialists

50+ years of transplantation experience
Who We Are and What We’re About

The broadest transplant offerings. Cleveland Clinic is one of the world’s few medical centers where both adults and children can receive any type of transplant — all solid organ types, dual-organ, multivisceral, cellular or composite tissue — under one roof.

Vigorous clinical activity. Cleveland Clinic’s Transplant Center maintains one of the nation’s most robust levels of transplant activity, ranking among the four highest-volume U.S. transplant centers in 2013 (according to the United Network of Organ Sharing) and drawing patients from across the nation and around the world.

That 2013 activity included solid organ transplant procedures involving 479 transplanted organs, as well as 191 blood and marrow transplants (see table below).

Deep roots. The Transplant Center draws on one of the world’s largest experience bases in transplantation, having performed kidney transplants for more than 50 years and many other transplant types for multiple decades (see table, next page).

Abundant expertise. At the heart of the Transplant Center is its staff of more than 200 transplant specialists from various patient-centered institutes across Cleveland Clinic. These institutes include Cleveland Clinic’s renowned heart, urology, nephrology and gastroenterology/GI surgery programs, each ranked among the nation’s top one or two programs in its specialty by U.S. News & World Report.

<table>
<thead>
<tr>
<th>2013 transplant volumes at Cleveland Clinic (Cleveland location only)</th>
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<tbody>
<tr>
<td><strong>184 kidney</strong> (includes 11 with pancreas, 7 with liver, 1 with heart and 1 multivisceral)</td>
</tr>
<tr>
<td><strong>128 liver</strong> (includes 7 with kidney and 2 multivisceral)</td>
</tr>
<tr>
<td><strong>98 lung</strong></td>
</tr>
<tr>
<td><strong>44 heart</strong> (includes 1 with kidney)</td>
</tr>
<tr>
<td><strong>16 pancreas</strong> (includes 11 with kidney and 2 multivisceral)</td>
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<tr>
<td><strong>9 intestinal/multivisceral</strong></td>
</tr>
<tr>
<td><strong>479 total organs transplanted</strong></td>
</tr>
<tr>
<td><strong>191 blood and marrow</strong></td>
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Our Commitment to Patients and Advancing Practice

The Transplant Center is committed to the following attributes and principles in its delivery of care before, during and after transplantation:

**Quality** — Demonstrated by patient and graft survival outcomes that are consistently at or above national norms despite Cleveland Clinic’s high volumes of complex procedures in the most critically ill patients, many from far corners of the country and the world

**Comprehensiveness of management options** — Exemplified by the center’s judicious offering of transplantation within a broad mix of options for end-stage disease, from innovative use of circulatory assist devices for heart failure to wide use of inventive surgical techniques for gut reconstruction

**Continuity of care** — Illustrated by ongoing follow-up of 5,261 solid organ transplant recipients as of the end of 2013 (see list at left)

**Innovation** — Manifested by completion of the first near-total face transplant in the U.S., recent introduction of 3-D-printed organ models for surgical planning and development of an Organ Repair Center for normothermic ex vivo perfusion across most organs (see p. 6), among other initiatives

**Active research engagement** — Demonstrated by participation in scores of multicenter trials of new protocols and immune modulation strategies as well as basic research studies to advance transplant outcomes

**Provision of care to more patients** — Evidenced by Cleveland Clinic’s growing geographic footprint in transplantation care, with a dynamic new transplant program at Cleveland Clinic Florida (see p. 7), affiliated transplant programs in West Virginia and Indianapolis, and plans for a multiorgan transplant program at Cleveland Clinic Abu Dhabi (see p. 15 for details)
What Patients and Referring Providers Can Expect*

1) Referral and evaluation. Patients can be referred for transplant evaluations at Cleveland Clinic by calling 800.223.2273, ext. 42394, or 216.444.2394. At the time of referral, a team member collects the basic medical history, results of relevant diagnostic studies and a description of the patient’s current clinical condition.

A transplant evaluation is then scheduled, which includes tests and consults with the following (and others, as needed): transplant physician, transplant surgeon, infectious disease specialist, anesthesiologist, social worker, psychiatrist/psychologist, financial coordinator, nutritionist and transplant coordinator.

Decisions regarding approval of candidacy for transplantation are made by consensus, following a thorough review of each patient’s case at weekly patient selection meetings. For all solid organ transplants except kidney, the final step in the review process includes approval by the Ohio Solid Organ Transplant Consortium. For all solid organ transplants, the final step in evaluation is notification of the patient, referring physician and insurer of the decision about transplantation or any alternative therapy.

2) Ongoing medical therapy review. For patients not approved for transplantation, alternative surgical therapy or continuing specialized medical therapy is available. Patients approved for transplantation are managed by the medical transplant team and placed on the national transplant waiting list. Candidates for kidney and liver transplant may be considered for living-donor transplantation.

3) Transplantation. When a matched organ is available for transplantation, the patient is notified by a transplant coordinator, reports to the hospital and is admitted to the transplant floor. After transplantation, patients may be transferred to an ICU, where their care is jointly managed by the transplant team and ICU staff. The transplant team assumes primary care from the time of transplant through the patient’s stay in the Transplant Special Care Unit; the team also provides long-term follow-up.

Inpatient rehabilitation therapy is available on-site for patients who need it. Additional supportive services before, during and after the patient’s hospitalization are detailed in the section starting on p. 76.

4) Follow-up. After discharge, the patient’s progress is monitored during regular outpatient visits with the transplant team. All patients return to the transplant clinic at scheduled intervals for review and adjustment of medications as necessary. Additional appointments and diagnostic studies are scheduled if needed. All patients are asked to return to Cleveland Clinic annually for follow-up.

Transplant team staff communicate regularly with patients’ referring physicians throughout all phases of care.

For some patients outside Northeast Ohio, arrangements can be made with a local physician for routine follow-up at an agreed postoperative stage. Transplant team staff remain in contact to continue monitoring the patient’s progress.

*For solid organ transplantation. This process may vary depending on the patient’s condition and transplant type.
A multidisciplinary team of transplant surgeons, organ preservation specialists and translational research scientists from Cleveland Clinic’s Transplant Center is working to create a centralized Organ Repair Center, which promises to be one of the nation’s first centers for multiorgan normothermic ex vivo perfusion.

The effort involves remodeling an operating room area at the heart of Cleveland Clinic’s main campus to serve as the Organ Repair Center and house approximately eight stations with the capacity to pump and perfuse most organs using leading-edge technology.

Late 2014 is the target for completing construction, though widespread clinical use of the center will depend on when the perfusion machines and proprietary solutions for normothermic ex vivo perfusion gain FDA approval for various organ types. “As FDA approvals are achieved, we’ll be ready to proceed with this technology on a large scale,” says Transplant Center Director Kareem Abu-Elmagd, MD, PhD.

A promising sign came in August 2014 with FDA approval of the first normothermic ex vivo perfusion system in the U.S., for preserving marginal donor lungs to allow more time to evaluate their function and potential for transplant (see p. 49).

Minimizing ischemia-reperfusion injury

Normothermic ex vivo perfusion aims to minimize the ischemia-reperfusion injury that occurs in organs harvested from brain-dead donors and to allow repair of damage that does occur. Its expected benefits include:

- Further improving the condition of currently usable donor organs, promising reduced length of stay and recovery times and a lower overall cost of care for transplant patients
- Enabling repair or reconditioning of marginal donor organs that currently are not usable, thereby combatting the donor organ shortage and reducing mortality on the waiting list
- Extending the time that donor organs can be preserved prior to transplant compared with traditional cold-storage preservation, allowing better viability testing and creating opportunities to share organs across a wider geographic reach
- Enabling repair or reconditioning of marginal donor organ in an oxygenated state at physiologic temperatures during preservation. The organ is connected to a perfusion machine that pumps oxygen and a nutrient-enriched solution through it to prevent metabolic injury and damage to cell membrane permeability. Principal machine components are a centrifugal pump, a membrane oxygenator and a heat exchanger.

“It’s basically like a miniature bypass circuit, similar to what we use during open-heart surgery,” explains lung transplant surgeon Kenneth McCurry, MD, who leads Cleveland Clinic’s ex vivo lung perfusion efforts.

“Normothermic ex vivo perfusion will buy us time to better assess an organ’s suitability for transplant and enable organ reconditioning and possibly repair,” says liver transplant surgeon Cristiano Quintini, MD, who leads Cleveland Clinic’s ex vivo liver perfusion efforts.

The technology also promises to broaden the donor pool to address chronic organ shortages. “We may be able to retrieve hearts from older donors and donors with left ventricular hypertrophy, which have historically been turned down for transplant,” says heart transplant surgeon Edward Soltesz, MD, MPH.

Testing across multiple organs

Cleveland Clinic is among a small number of U.S. centers studying normothermic ex vivo perfusion across multiple organ types. It has so far tested the technology in the lungs, heart, liver, kidney and pancreas. A few highlights to date:

**Lung transplant.** Cleveland Clinic is one of eight U.S. centers participating in INSPIRE, an international clinical trial comparing transplant outcomes following preservation of donor lungs with either the TransMedics lung perfusion system (OCS™ Lung) or cold storage. As of the end of 2013, Cleveland Clinic had transplanted one lung to a patient after preservation with the system.

**Heart transplant.** Cleveland Clinic was one of eight U.S. centers that participated in PROCEED II, an international trial now closed to enrollment that is comparing transplant outcomes following preservation of donor hearts with either the TransMedics heart perfusion system (OCS™ Heart) or cold storage. As of the end of 2013, Cleveland Clinic had transplanted six hearts to patients after preservation with the system.

**Liver transplant.** Dr. Quintini has conducted pioneering studies of normothermic ex vivo liver perfusion in large animal models, with promising outcomes. Every parameter evaluated has shown perfusion to be superior to traditional cold storage (standard of care). The next step is testing in human liver transplant, which he and his colleagues hope to begin within the next year.
Cleveland Clinic Florida performed its first organ transplants in July 2013 after receiving approval from the United Network for Organ Sharing (UNOS) for liver and kidney transplant services.

Through the end of 2013, surgeons at the Weston, Florida, facility successfully performed nine liver transplants and seven kidney transplants. The pace of transplants accelerated into 2014, and Cleveland Clinic Florida received Centers for Medicare & Medicaid Services approval for its liver and kidney transplant services in mid-2014.

Renowned surgeon at the helm

Cleveland Clinic Florida’s Transplant Program was launched following the hire of internationally renowned transplant surgeon Andreas Tzakis, MD, PhD. Dr. Tzakis was first engaged by Cleveland Clinic as a consultant because of his expertise in abdominal transplantation. In August 2012, he joined the health system to develop and direct Cleveland Clinic Florida’s Transplant Program.

With more than 215 physicians across 35 specialties, Cleveland Clinic Florida has the integrated clinical expertise to support comprehensive transplant services. “We have recruited an outstanding team of transplant professionals who are filling a critical need for highly specialized services from a growing number of patients who might otherwise have to seek care outside South Florida,” says Dr. Tzakis.

One program, two sites

Upon joining the Cleveland Clinic team, Dr. Tzakis spent countless hours over many months with his transplant colleagues in Cleveland to develop a program that was a mirror image of Cleveland Clinic’s Transplant Center on its main campus. Although the Florida transplant program is distinct from the Cleveland program from a regulatory perspective, there’s no distinction from a cultural standpoint:

- Staff from the two programs are in close and regular contact, discussing cases, sharing patient selection meetings and collaborating on administrative issues.
- The two programs share the same protocols, quality measures, electronic medical record system, transplant database — and even personnel. The Florida-based transplant surgeons have obtained licensure in Ohio, and a number of Cleveland-based transplant surgeons have licenses in Florida, to give the newer program the bench depth to offer 24/7 transplant availability.

“IT’s really one program with two sites,” says Charles Miller, MD, director of the liver transplant program in Cleveland and one of the Ohio surgeons with licensure in Florida. “No other U.S. center has this degree of integration of transplant programs across remote locations, with shared surgeons and dual licensures. Each site’s team runs its own program, but we’re communicating all the time.”

Dr. Tzakis continues to come to Cleveland regularly for unified strategic planning, and Transplant Center leaders from Cleveland play an active role in the Florida program’s ongoing development.

Enduring connections, expansive future

“We are delighted to have Dr. Tzakis as a partner to expand Cleveland Clinic’s transplant services in another part of the country,” says Kareem Abu-Elmagd, MD, PhD, Director of Cleveland Clinic’s Transplant Center. “He’s an eminently accomplished surgeon who’s been a colleague of mine since 1990, when we worked together under Dr. Thomas Starzl.”

Dr. Tzakis’ expertise includes intestinal and multivisceral transplantation, and Dr. Abu-Elmagd hopes these services can be offered at Cleveland Clinic Florida before long.

Heart transplant services launching in 2014

The first area of the Florida program’s expansion is heart transplantation, following its mid-2014 receipt of UNOS approval for heart transplant services and the hire of Cedric Sheffield, MD, as surgical director of the facility’s adult heart transplant program.

Dr. Sheffield, a prominent heart transplant surgeon who recently served as director and CEO of the Tampa Transplant Institute, completed a fellowship in thoracic surgery and transplantation at Cleveland Clinic in 1999. He will work with Andrew Boyle, MD, who serves as medical director of Cleveland Clinic Florida’s new heart transplant program.
How We’re Shaping the Future of Transplantation

Beyond working to ensure the best outcomes for today’s patients, Cleveland Clinic’s Transplant Center is committed to advancing care for the patients of tomorrow. Initiatives along these lines are spotlighted in “future of transplantation” sidebars throughout this publication’s sections. They include:

• Development of beta cell therapy expertise for diabetes management through collaboration with academic and industry partners at the forefront of innovative beta cell therapeutic modalities, including allotransplantation (see pp. 20-21)

• Pioneering work to study normothermic ex vivo organ perfusion — including liver perfusion in large animals (see p. 27) and lung perfusion in a clinical trial in humans (see p. 49) — in hopes of improving donor organ quality and enabling repair of marginal donor organs

• Application of visceral transplantation to emerging indications, including a rare (and previously always fatal) congenital syndrome with multiorgan manifestations and in the setting of HIV infection (see p. 36)

• Promising development of a continuous-flow total artificial heart with automatic speed control and self-regulation to balance right-left inlet pressures (see p. 41)

• Early adoption of haploidentical transplantation to expand donor options for selected blood and marrow transplant candidates (see p. 59)

• Progress in animal studies pursuing improved anti-rejection strategies in composite tissue transplantation (see p. 63)

Other Cleveland Clinic efforts to shape the future of transplantation apply across the overall Transplant Center, regardless of transplant type. These include:

Pursuing the secrets of immune tolerance. Immune tolerance has been the holy grail of transplantation medicine, promising freedom from lifelong immunosuppressive therapy for transplant recipients. Real progress is being made toward tolerance induction, and Cleveland Clinic is playing important roles in it:

• Transplant Center Director Kareem Abu-Elmagd, MD, PhD, has reported enduring immunosuppressant-free alloengraftment in a long-term survivor of a liver-containing multivisceral transplant for the treatment of Gardner syndrome (Clin Transpl. 2012;155-166). He continues to follow this remarkable patient for insights into the workings of immune tolerance.

• Transplant Center staff are exploring new, multifaceted anti-donor-specific antibody (DSA) strategies to further improve long-term graft survival.

• The Transplant Center’s basic science program is investigating mechanisms of acute T cell-mediated rejection and antibody-mediated rejection.

• The center has a well-established infrastructure that performs various immune monitoring assays to determine levels of T cell allosensitization and donor sensitization. Staff are near completion of an improved ELISPOT assay that more accurately assesses alloimmunologic risk in patients.
The center contains a robust T cell immunology lab focused on mechanisms of alloreactive memory T cell sensitivity and resistance to CTLA-4Ig.

Establishing the Transplant Research Center. Cleveland Clinic is creating a formalized Transplant Research Center to better coordinate its various transplant research efforts (including those immediately above), promote a more systematic approach to research and speed the translation of bench studies to clinical applications. The effort involves integrating portions of Cleveland Clinic’s renowned Lerner Research Institute with the Transplant Center, establishing a transplant research database, and enhancing transdisciplinary collaboration across transplant immunology, bioinformatics, health services, and clinical and basic science research.

Training tomorrow’s transplant pioneers. Cleveland Clinic offers a range of fellowship programs dedicated to transplantation (see clevelandclinic.org/txfellowships), including the nation’s only transplant ethics fellowship, established in 2013 (see sidebar below).

No area of modern medicine raises more vexing ethical challenges than transplantation. Of some 350 clinical ethics consults at Cleveland Clinic in 2012, 50 of them — 1 in 7 — were for transplant-related cases. That demand for expertise in transplant ethics prompted the creation in 2013 of Cleveland Clinic’s Transplant Ethics Fellowship, the only transplant-specific ethics fellowship currently offered in the U.S.

“The variety and complexity of issues specific to transplant medicine and ethics warrant a dedicated fellowship,” explains Eric Kodish, MD, F. J. O’Neill Professor and Chairman, Cleveland Clinic Bioethics Department. He cites organ shortages, allocation issues and informed-consent policies for living donors among the leading ethics issues grappled with in the transplantation field.

The fellowship was created with a generous donation from former U.S. Treasury Secretary Robert E. Rubin and his wife, Judith.

The first fellow chosen for the two-year Transplant Ethics Fellowship is David Shafran, MD, a pediatric nephrology fellow with a master’s degree in bioethics. He is working with fellowship director Kathryn Weise, MD, MA, to develop a curriculum that will allow fellows to explore the key ethical issues surrounding organ transplantation while pursuing opportunities for independent research.

Combined with real-world experience in transplant ethics consultation, this fellowship program breaks new ground and will help patients, families and providers navigate moral dilemmas raised by transplant medicine well into the future.
Cleveland Clinic has performed more than 4,300 kidney transplants since 1963.
KIDNEY TRANSPLANTATION

A year of two milestones

In 2013, Cleveland Clinic marked the 50th anniversary of its first kidney transplant while achieving another milestone by performing the most kidney transplants in a single year — 184 — in the program’s long history.

The kidney transplant program's graft and patient survival rates compare favorably with national norms, as detailed in the graphs on the following pages. Notable outcomes from the January 2014 report of the Scientific Registry of Transplant Recipients (SRTR) include:

• 36.3-month median time to transplant, one-third shorter than the national median of 54.3 months (see graph, p. 14)
• One- and three-year adult graft survival rates of 94.61 and 89.71 percent, respectively, which are at or above risk-adjusted expected levels and national averages (see graphs, next page)
• Three-year adult patient survival rate of 95.25 percent, exceeding the risk-adjusted expected level and the national average by 3 percentage points
• 100 percent one-year kidney graft survival for simultaneous kidney-pancreas transplants
• 11.3-month median time to transplant for kidney-pancreas transplants (vs. national median of 14 months)

Rise in living-donor transplants bucks national trend

The 184 kidney transplants in 2013 represent a 12 percent increase from 2012. The growth was partly due to an increase in living-donor transplants, which totaled 81 in 2013, representing 44 percent of overall kidney-only transplants.

The program’s rise in living-donor transplants bucks a national trend of declining living-donor kidney transplants. Living donation is generally the best option for recipients because it can provide a very high-quality kidney and the ability to optimally plan the transplant surgery.
More than 90 percent of living-donor procedures in 2013 were performed using laparoscopic techniques. Cleveland Clinic surgeons were instrumental in the development of such techniques beginning in the 1990s, and the program has performed more than 1,000 laparoscopic living-donor nephrectomies to date.

Dual-organ transplant is a setting in which deceased-donor kidneys continue to be essential. In 2013, the surgical team performed 20 dual-organ transplants:

- 11 kidney-pancreas
- 7 kidney-liver
- 1 kidney-heart
- 1 as part of a multivisceral transplant

National Kidney Registry brings more paired donations

One reason Cleveland Clinic has defied the trend against living-donor growth is its participation in the National Kidney Registry to facilitate paired donation, which allows most participating patients to receive a living-donor kidney within six months. Since the program began working with the National Kidney Registry in 2011, it has enabled Cleveland Clinic to perform 22 living-donor kidney transplants (as of the end of 2013) that otherwise would not have been done.

In 2013, Cleveland Clinic ranked seventh out of 75 programs nationally in National Kidney Registry participation volume.

Incompatible donors' kidneys are procured in Cleveland and shipped to recipients elsewhere in the U.S. In return, Cleveland Clinic recipients have received organs from as far away as California. Recipients have fared well, and all grafts have functioned.

In 2013, Cleveland Clinic participated in the second-longest chain of paired donations to date, the 28-patient “Chain 221.” Starting donation chains with altruistic donors has resulted in some transplants in the absence of a reciprocal donor through the registry’s CHIP (Children and High PRA) program for children and highly sensitized patients.
PATRICIA KUNKLE: A THRIVING TESTAMENT TO FIVE DECADES OF TRANSPLANTATION

When Cleveland Clinic marked the 50th anniversary of its kidney transplant program in 2013, Patricia Kunkle was the most appropriate person on hand for the celebration.

A 66-year-old resident of Rocky River, Ohio, Patricia embodies the program’s longevity better than anyone alive today, as the kidney she received from her mother at Cleveland Clinic in 1968 is still serving her well, 46 years later. Since her mother was 46 at the time of the transplant, that means Patricia’s healthy kidney is 92, a remarkable transplant achievement. In the decades since her transplant, Patricia has been able to give birth to and raise three children, earn bachelor’s and master’s degrees, and retire after a career spanning more than 30 years.

“I remember waiting a long time for the transplant surgery because they didn’t have the tissue matching like they do now,” recalls Patricia, who needed the transplant after her kidneys began to shut down secondary to lupus.

“It was just unbelievable how good I felt after the transplant,” she says. “It was like night and day. From there, every day has been a good day.” She adds: “Cleveland Clinic looked at my whole being, not just my kidney. I would never go anywhere else.”

RYAN HULEC: PROOF OF THE POWER OF THE NATIONAL KIDNEY REGISTRY

Full-time student Ryan Hulec struggled with chronic kidney disease but managed to avoid dialysis, thanks to Cleveland Clinic’s participation in the National Kidney Registry and his mother’s generosity.

While not a match for her son, Ryan’s mother agreed to donate her kidney, enabling Ryan to more swiftly obtain a kidney from another living donor. Ryan’s transplant at Cleveland Clinic was a success, and the now 23-year-old Valley View, Ohio, resident is back at school — and his mother is back at work. Both are grateful for Ryan’s renewed health — and for their opportunity to help another patient who was in Ryan’s shoes somewhere else in America.
Short wait times, rapid evaluation, declining length of stay

These aggressive efforts to support living-donor transplants have helped give Cleveland Clinic the shortest kidney waitlist time in Northeast Ohio and a transplant rate that exceeds expectations based on SRTR data. Cleveland Clinic’s median wait time of 36.3 months for patients listed from July 1, 2007, to December 31, 2012 (the most recent data period), is:

- One-third shorter than the national median of 54.3 months
- Shorter than the regional (OPTN Region 10) median of 40.7 months and the local Donation Service Area median of 46.7 months

A number of additional efforts have contributed to the program’s success in trimming wait times:

- To counter the nationwide organ shortage, the program has extended use of the deceased donor pool by using pediatric en bloc and dual adult kidneys and has increased use of organs donated after determination of cardiac death.
- A waitlist IV immunoglobulin desensitization program has been started to enhance transplant opportunities for highly sensitized patients.
- The program takes a proactive, highly communicative approach with patients on the waitlist to ensure that as many as possible are fully ready to be transplanted on short notice.

Additionally, recent operational efficiencies in the program resulted in 60 percent reductions from 2010 to 2013 in:

- Mean time from referral to evaluation for transplant (reduced to 45 days in 2013)
- Mean time from evaluation to wait-listing (reduced to 33 days in 2013)

Post-transplant hospital length of stay (LOS) was also on the decline for the program in 2013. Improved management of the transition from hospital to outpatient care resulted in a reduction in LOS to 5.71 days, the lowest in four years.
Cleveland Clinic’s kidney transplant program has become one of the widest-reaching programs of its kind in the world, with one of the largest collective volumes in the nation — 278 across all U.S. locations in 2013. In addition to the flagship program in Cleveland, kidney transplants (living-donor as well as deceased-donor procedures) are performed by Cleveland Clinic transplant physicians at the following sites:

**Cleveland Clinic Florida**
155-bed Cleveland Clinic hospital in Weston, Fla.
- Program launched in April 2013 under the directorship of world-renowned transplant surgeon Andreas Tzakis, MD, PhD, with an experienced team of surgeons and nephrologists (see p. 7)
- Operated in close collaboration with Cleveland Clinic’s Cleveland program under a “one program” model involving shared protocols, some shared staff, joint patient selection meetings, shared EMR and transplant database, and regular and frequent communications
- 7 kidneys transplanted in 2013
- Patient and graft survival of 92 percent during first 11 months of operation
- Approved by CMS and UNOS

**Charleston Area Medical Center**
Charleston, W.Va.
- An affiliation with Cleveland Clinic since 1987 for kidney transplants and urologic care
- Program team includes Cleveland Clinic transplant surgeon Joseph Africa, MD (program director), certified clinical transplant coordinators, a dietitian, a social worker, attending nephrologists and other clinical support personnel with a supporting histocompatibility lab
- More than 1,000 kidney transplants to date, including 44 in 2013
- Only kidney transplant program in West Virginia
- Approved by CMS and UNOS

**St. Vincent Transplant Services**
Indianapolis
- A partnership between Cleveland Clinic and St. Vincent Indianapolis Hospital since December 2008 for kidney and pancreas transplant services
- Program comprises a dedicated 11-bed unit for kidney transplant patients, an outpatient transplant clinic and a histocompatibility lab
- Directed by Alvin Wee, MD, with support from attending surgeon Islam Ghoneim, MD, PhD, both of whom are renal and pancreatic transplant surgeons with Cleveland Clinic’s Glickman Urological & Kidney Institute
- More than 200 kidney transplants to date, including 44 in 2013, and more than 400 referrals for evaluation annually
- Median time to transplant of 14.8 months, one of the shortest in the nation (national median of 54.3 months)
- Program performed its first simultaneous kidney-pancreas transplant in 2013
- Approved by CMS and UNOS

**Sheikh Khalifa Medical City**
Abu Dhabi, United Arab Emirates (UAE)
- Cleveland Clinic has provided clinical and logistical support for the kidney transplant program at Sheikh Khalifa Medical City in Abu Dhabi, UAE, the only transplant program in the country, since the program’s inception in 2007
- Longtime Cleveland Clinic transplant surgeon Bashir Sankari, MD, took part in Sheikh Khalifa Medical City’s first cadaveric kidney transplant in 2013 after moving to Abu Dhabi in 2012 to practice at Cleveland Clinic Abu Dhabi
- Performed 30 kidney transplants in 2013, its highest annual count to date, including the program’s 100th kidney transplant
- UAE’s legal adoption of a brain death policy laid the groundwork for development of a multiple-organ deceased-donor transplant program at Cleveland Clinic Abu Dhabi after that facility opens in 2015 (see photo above)
Collaborative expert care — conveniently delivered

Kidney transplant patients benefit directly from the multidisciplinary nature of Cleveland Clinic’s Glickman Urological & Kidney Institute, which brings together urologists and nephrologists in an organizational structure designed to pool expertise and promote collaborative management.

Transplant services are also supported by a large dialysis program and the collective clinical acumen of the Urological & Kidney Institute, whose surgeons bring long-standing expertise in complex renal vascular anatomy and renal anomalies. That expertise is reflected in the institute’s ranking among the nation’s top 2 urology and nephrology programs by U.S. News & World Report for multiple consecutive years — and as the No. 1 urology program in 2014-15.

When a patient with end-stage kidney disease is evaluated for transplant, he or she meets in a single care space with a team comprising transplant urologists, transplant nephrologists and other providers. The patient’s evaluation day includes an educational session and visits by transplant physicians, transplant coordinators, social workers, financial counselors and nutritionists.

Advancing the science of kidney transplantation

Cleveland Clinic has a rich history of advancing the care of patients with kidney failure — from the work of Willem Kolff, MD, PhD, to perfect his dialysis machines here in the 1950s, to establishment of one of the first kidney transplant programs in 1963, to pioneering contributions in minimally invasive kidney surgery in the 1990s and beyond.

That tradition continues today across many areas of kidney transplant-related research. Below is a sampling of projects active or published in 2013.

Building a biorepository. Novel biomarkers are fast emerging in basic kidney and pancreas transplant research, but their validation for clinical application requires repetitive tissue sampling in a sizable patient cohort. Cleveland Clinic is one of the few centers that can combine tissue samples from large numbers of transplant recipients with the advanced infrastructure and expertise needed to meet the challenge.

The kidney transplant program got started on that challenge in 2012 by establishing a Renal Transplant BioBank. The goal is to create a patient-linked repository for biologic samples (blood, urine and graft biopsy tissue) for use in research studies related to metabolic, inflammatory and immunologic markers relevant to kidney and pancreas transplant.

Leading a trial of a targeted approach to acute rejection. Organ recipients receive induction therapy with antibodies to make their immune system less able to mount an initial rejection response. Unfortunately, current induction agents, such as anti-thymocyte globulin, have drawbacks related to long-term immune suppression and other immune-mediated side effects.
In search of a safer approach for preventing acute kidney rejection, researchers are studying TOL101, a novel monoclonal antibody that targets a highly specific immune cell type critical to the acute organ rejection response. Cleveland Clinic kidney transplant surgeon Stuart Flechner, MD, is serving as national principal investigator for a multicenter study comparing TOL101 with anti-thymocyte globulin for preventing kidney graft rejection when used as part of an immunosuppression regimen including steroids, mycophenolate mofetil and tacrolimus.

**Using big data to assess safety of living kidney donation.** Living-donor kidney donation is safe and has been getting safer. Those are among the conclusions of a Cleveland Clinic-led research team that published two unprecedented analyses of more than 69,000 living donors between 1998 and 2010. The team found that the incidence of perioperative complications among donors fell from 10.1 to 7.6 percent over that period and that donors’ length of hospital stay declined from nearly four days to less than three days. Complication rates and length of stay were highly comparable with those of other low-risk abdominal surgeries, such as appendectomy. A second analysis found that rehospitalizations among living donors were lower than among patients with comparable surgical procedures but were higher among donors with particular characteristics. The data are assisting in the counseling of living donors around the nation.


**Deep-rooted pediatric program**

In April 1963, just three months after completing its first adult kidney transplant, Cleveland Clinic performed its first pediatric kidney transplant — one of the earliest successful pediatric transplants in the nation.

Since then, the program has transplanted 363 kidneys in patients under age 21. It is northern Ohio’s only pediatric program with a dedicated outpatient pediatric dialysis unit, located at Cleveland Clinic Children’s Hospital for Rehabilitation.

A team of kidney transplant surgeons with expertise in pediatric transplant is supported by a dedicated pediatric kidney transplant medical director, three additional pediatric transplant nephrologists and a growing team of pediatric urologists.

Their collaboration helps produce routinely positive outcomes in pediatric patients, including 100 percent one-year and three-year pediatric patient and graft survival rates in the January 2014 SRTR report.

**2013 QUICK TAKE**

100 percent 1- and 3-year pediatric patient and graft survival rates
100% one-year patient survival for both pancreas and kidney-pancreas transplants

344 pancreas transplants (including 207 kidney-pancreas transplants) through 2013
Cleveland Clinic has been performing pancreas transplants since 1985 and completed 16 such procedures in 2013 (for breakdown by type, see list at right). Its pancreas/kidney-pancreas transplant program has among the largest volumes, best outcomes and shortest wait times of all such programs in its region.

The program’s patient survival rates compare well with national norms (see graphs on p. 21). Notable outcomes from the January 2014 report of the Scientific Registry of Transplant Recipients (SRTR) include:

• 100 percent one-year patient survival for both pancreas and kidney-pancreas transplants
• 11.3-month median time to transplant for kidney-pancreas transplants, shorter than the national median (14.0 months) and the medians for OPTN Region 10 (12.0 months) and the local Donation Service Area (12.9 months)
• 25.5-month median time to transplant for pancreas-only procedures (vs. national median of 27.2 months)

Although the SRTR does not model pancreas graft survival, Cleveland Clinic outcomes are strong on this metric as well. For instance, one-year graft survival among pancreas and kidney-pancreas transplants was 97 percent by Kaplan-Meier survival analysis for the period tracked in the January 2014 SRTR report.

Culture of collaboration

Cleveland Clinic’s pancreas/kidney-pancreas transplant program is a key part of a comprehensive suite of medical and surgical services to manage type 1 diabetes and related conditions. The program team includes transplant surgeons, transplant endocrinologists, transplant nephrologists and a host of supporting clinical personnel.

There is considerable staffing overlap with the kidney transplant team (see preceding section), which promotes close clinical and research collaboration. For the many pancreas transplant candidates with end-stage renal disease, the program is well equipped to offer simultaneous pancreas-kidney (SPK) transplantation or...
sequential pancreas-after-kidney (PAK) transplantation, depending on the patient’s circumstances and needs.

The pancreas transplant team also collaborates regularly with the liver and intestinal/multivisceral transplant teams for en bloc pancreas transplantation, which offers increased immunologic protection from the other transplanted organs and can also reduce the risk of graft thrombosis.

**Expanding geographic reach**

A kidney-pancreas transplant program in Indianapolis was officially started in 2012 by St. Vincent Transplant Services, a partnership for kidney transplantation between Cleveland Clinic and St. Vincent Indianapolis Hospital since 2008 (see p. 15). The program, which is directed by Cleveland Clinic staff, successfully performed its first simultaneous kidney-pancreas transplant in February 2013.

**Beta cell therapy for diabetes**

For patients with type 1 diabetes, innovations in beta cell therapy promise a more comprehensive approach to diabetes management. Cleveland Clinic is helping shape discussion around beta cell therapy for diabetes, such as by convening the 1st Cleveland Clinic Beta Cell Therapy Symposium in November 2014. This singular meeting features a national faculty of experts addressing topics such as bioengineering of beta cells, the bionic pancreas, islet encapsulation, islet allograft rejection in the setting of autoimmune diabetes, and current global activities. Challenges and future directions are also being explored.

A centerpiece of emerging beta cell therapy for diabetes is transplantation of donor islet cells (allogeneic islet cell transplantation), which is being studied as a minimally invasive alternative to whole-organ pancreas transplant. Significant progress has been made in islet allotransplantation, but the procedure remains experimental due to imperfections in the isolation and purification of islet cells from deceased donors as well as inadequate means for preventing rejection of donor islets.

While techniques are being refined to improve islet harvest from deceased donor organs, major translational research activities are underway to establish alternate islet sources, such as islet-producing stem cells from humans and islet cells from nonhuman species (xenotransplantation). Other efforts focus on identifying less-toxic immunosuppressive regimens and inducing immune tolerance to donor islets. New microencapsulation technologies also show promise for providing immunosolation for transplanted islets while still permitting insulin release.

Cleveland Clinic is actively consulting with companies and academic centers at the forefront of beta cell therapy to ensure that it will be among the earliest adopters of these technologies. It is committed to bringing these minimally invasive — and potentially immunosuppressant-free — options to a broad range of patients with diabetes.

For nondiabetic patients, Cleveland Clinic has pioneered the use of pancreatic islet cell autotransplantation following total pancreatectomy secondary to severe chronic pancreatitis (see sidebar). Cleveland Clinic has performed 50 islet autotransplants from 2007 through 2013 and actively offers the therapy for appropriate patients.
FUTURE OF TRANSPLANTATION:
PIONEERING ISLET AUTOTRANSPLANTATION AFTER PANCREATECTOMY FOR CHRONIC PANCREATITIS

For patients with cripplingly painful chronic pancreatitis refractory to medical/endoscopic interventions or traditional surgery, total pancreatectomy is the last resort. Total pancreatectomy has been considered an extreme option because it leads to brittle diabetes, but insulin-dependent diabetes can now be prevented or mitigated by transplanting the patient’s own isolated pancreatic islet cells back to the patient. Islets are injected into the portal vein, which transports them to the liver, their site of implantation (see image). The more islets that can be isolated and infused, the greater the chance of avoiding or controlling the effects of surgical diabetes.

Under the direction of R. Matthew Walsh, MD, Chairman of General Surgery, Cleveland Clinic has been in the vanguard of total pancreatectomy with autologous islet transplantation. Since Dr. Walsh performed the first islet autotransplant at Cleveland Clinic in 2007, 50 such transplants have been performed here through 2013, representing one of the world’s largest experience bases. Significant pain and quality-of-life improvements have been documented (Walsh et al, J Gastrointest Surg. 2012;16:1469-1477).

The procedure holds particular appeal for young patients with refractory chronic pancreatitis, who otherwise face a lifetime of caring for diabetes and its complications. Cleveland Clinic has performed islet autotransplants in numerous adolescents, demonstrating an ability to obtain a sufficient number of islets to allow even very young patients to achieve insulin independence. Earlier effective pain treatment in patients with chronic pancreatitis can also lead to better overall outcomes and rapid transition to productive lives without narcotics. Cleveland Clinic surgeons remain focused on innovating new techniques to efficiently isolate higher numbers of islets following pancreatectomy and to improve the implantation and function of infused islets.
100% one-year patient survival among living-donor liver recipients

1,962 liver transplants through 2013

Median time to transplant less than half the national median
(6.1 vs. 14.4 months)
CLEVELAND CLINIC TRANSPLANTATION

LIVER TRANSPLANTATION

Cleveland Clinic performed 128 liver transplants in 2013. Its liver transplant program is the largest in the region and one of the largest in the nation.

The program’s patient survival rates compare favorably with national norms, as detailed in the graphs on the following pages. Notable data points include the following:

- A 6.1-month median time to transplant, less than half the national median of 14.4 months (January 2014 Scientific Registry of Transplant Recipients [SRTR])
- 100 percent one-year patient survival among adult and pediatric living-donor liver transplant recipients for the period 2011-2013 (N = 20)
- 100 percent three-year patient survival among pediatric patients (January 2014 SRTR)
- Comparable rates of five-year patient survival among primary liver transplant recipients with hepatocellular carcinoma (HCC) (N = 355) and without HCC (N = 768) over nearly three decades (75 vs. 76 percent survival, respectively)

Innovative techniques to broaden the donor pool

A hallmark of Cleveland Clinic’s liver transplant program is its effort to increase the donor pool while maintaining superior outcomes by using a range of alternatives to traditional donation-after-brain-death transplants, including:

- Living-donor transplant, in which part of the donor’s liver is resected
- Split-liver transplant, in which a deceased-donor liver is divided for two recipients
- Donation after cardiac death, in which a non-brain-dead donor is deemed to have no chance of recovery and donation occurs after withdrawal of life support and complete arrest of the cardiac and circulatory system

Cleveland Clinic’s is one of a handful of programs offering all these options, which play a critical role in addressing the shortage of liver grafts, collectively enabling the program to provide 36 more transplants to patients in need in 2013. These

128 liver transplants in 2013 (Cleveland location), including:
- 10 living-donor transplants
- 6 split-liver transplants
- 20 DCD (donation after cardiac death) transplants
- 7 liver-kidney transplants
- 2 as part of multivisceral transplants
- 9 additional liver transplants in 2013 at Cleveland Clinic Florida
innovative approaches can substantially shorten wait times, and patients who are transplanted using these approaches tend to have lower MELD scores, which means lower priority on wait lists even if the need for transplant is urgent.

Leadership in living-donor transplantation

The number of living-donor liver transplants in the U.S. has recently plateaued, however, due to concerns over donor safety and other factors. Many centers are reluctant to perform living-donor transplants because they can pose ethical challenges and are technically demanding and labor-intensive.

Despite these trends, Cleveland Clinic performed 12 living-donor liver transplants in 2012 (its most in a single year), 10 in 2013, and a cumulative total of 67 through 2013. Outcomes have met the highest national standards, and the program is using advanced technology — including intraoperative ultrasound, real-time tracking of surgical instruments, 3-D imaging and now 3-D-printed models of donor livers (see sidebar) — to optimize donor safety.

Successful living-donor transplantation requires high levels of coordination, teamwork and clinical diligence to match the partial donor graft to the recipient anatomically and physiologically — and to ensure both donor and recipient are psychologically ready for the procedure.

Cleveland Clinic’s program is the only one in Ohio performing both adult and pediatric living-donor liver transplants, and it is dedicated to maintaining the collaborative culture, technology and technical skills needed to make this lifesaving option available to as many patients as possible.

Multidisciplinary by nature

The program’s multidisciplinary team brings physicians and surgeons specializing in liver disease, transplant, anesthesiology, infectious disease, bioethics and psychiatry together under one roof — the Liver Transplantation Clinic. This clinic helps improve patient experience by eliminating multiple appointments at various locations and by creating customized treatment plans for each transplant candidate.
CLEVELAND CLINIC TRANSPLANTATION

Cleveland Clinic clinicians and researchers reported in the December Liver Transplantation (2013;19:1304-1310) on the development and clinical application of the world’s first complete 3-D-printed liver replicas.

The highly accurate replica models are being used by Cleveland Clinic liver transplant surgeons for presurgical planning and intraoperative guidance, particularly for resection and graft placement in living-donor liver transplants.

“Imagine you’re a surgeon who will be resecting half a liver for a transplant and you are provided with a 3-D model of the liver you’ll encounter the next day,” says Nizar Zein, MD, Medical Director of Liver Transplantation and principal investigator for Cleveland Clinic’s 3-D model work. “You can look at the 3-D ‘printout’ and better plan your surgery.”

The models were designed to build on 3-D imaging, which has been used for years in liver transplantation but has been limited by the need to still examine images through a 2-D computer screen. Replicas are constructed from 3-D digital files from the optimal visualization phases of contrast-enhanced CT and MRI scans of individual patients’ livers. They are then generated on one of two 3-D printers in the Medical Device Solutions unit of Cleveland Clinic’s Lerner Research Institute. A transparent flexible resin is used to represent the liver’s internal lumen geometry. Dyes are injected to color key structures, allowing easy visualization of the complex vascular and biliary networks.

Through the end of 2013, 24 liver models had been printed for use in transplant planning and guidance as well as for clinical training. Some have helped avert unnecessary surgery in patients with potentially unsuitable anatomy.

The group’s Liver Transplantation paper concluded that the 3-D-printed models demonstrate identical anatomic and geometric landmarks relative to the native livers they aim to replicate, making them highly accurate hands-on tools to aid surgical planning and help reduce surgical complications. The group continues to refine the replicas to improve the efficiency and cost of producing them.
The clinic benefits from frequent communication and shared meetings with the liver transplant team at Cleveland Clinic Florida, directed by renowned liver transplant surgeon Andreas Tzakis, MD, PhD (see p. 7).

Comprehensive in approach and mission

The Liver Transplantation Clinic and liver transplant team are part of a broad hepatology program of unsurpassed size and depth of expertise committed to highly comprehensive liver care. The staff of expert hepatologists in Cleveland Clinic’s Digestive Disease Institute is integral to the liver transplant program, offering superb clinical management to optimize patients for transplant when it is necessary — and to avoid transplant entirely when possible.

One example of how the program’s expertise extends beyond transplant is Cleveland Clinic’s multidisciplinary Liver Tumor Clinic. This clinic, which saw 555 patients in 2013, enables patients with liver tumors to be seen, in a single visit, by a hepatologist, an oncologist, a surgeon and an interventional radiologist. Since the clinic opened in 2009, the time from initial consultation to treatment has been reduced threefold. The Liver Tumor Clinic refers patients to the Liver Transplantation Clinic when transplant may be an option, and the two clinics’ teams collaborate closely.

Innovative use of anti-HCV regimens before and after transplant

Another example is the liver transplant team’s pioneering role in using novel pharmacologic therapies to achieve virologic cure of hepatitis C virus (HCV) infection prior to transplant whenever possible. Doing so greatly reduces the risk of post-transplant HCV recurrence, and avoiding recurrence promotes improved transplant outcomes and survival.

Cleveland Clinic hepatologists have been designing protocols to drive down HCV viral load before transplant for many years, but the advent of new “direct-acting agents” over the past two years has made this possible in many more patients than before. Direct-acting agents produce sustained virologic response at rates far higher than the rates with earlier HCV treatment regimens, and they do so with less toxicity and
FUTURE OF TRANSPLANTATION: LIVER STUDIES LAUNCH EFFORTS TO BRING NORMOTHERMIC EX VIVO PERFUSION TO ABDOMINAL ORGANS

Cleveland Clinic is among a small number of medical centers worldwide testing a new method of preserving abdominal organs. The technology, called normothermic ex vivo perfusion, involves providing oxygen and nutrition to organs for a smooth “live” transition from donor to recipient. (See p. 6 for a profile of Cleveland Clinic’s normothermic ex vivo perfusion efforts across multiple organs.)

By using a miniaturized heart-lung machine and whole blood to perfuse organs awaiting transplantation, the aim is to enable use of more marginal organs that wouldn’t thrive during the traditional cold storage process. A primary goal is to increase the number of organs available for transplant. Organ reconditioning and even organ repair are also possible, which would improve the quality of organs as well.

Cleveland Clinic’s efforts to expand normothermic ex vivo perfusion beyond the lungs and heart have started with the liver. Cristiano Quintini, MD, a surgeon with the liver transplant program, has performed pioneering studies of normothermic ex vivo perfusion in large animal models, with positive outcomes. Every parameter evaluated has shown perfusion to be superior to traditional cold storage (the standard of care). The next step is testing in human liver transplantation, which Cleveland Clinic researchers hope to begin within the next year.

“Normothermic ex vivo perfusion offers the potential to increase the number of donor organs that are usable for transplant by 15 to 20 percent,” says Dr. Quintini. He adds that another groundbreaking feature of the process is the ability to assess the organ during preservation and to predict its function. “The implications are tremendous, considering that transplant of a failing liver almost invariably means the patient’s death unless a retransplant is performed.”

For now, normothermic ex vivo liver perfusion is highly labor-intensive and demands the resources and deep staffing of a center of excellence like Cleveland Clinic. But after development and refinement by a handful of leading programs, normothermic ex vivo liver perfusion may one day become routine, just as machine perfusion is now widely used for kidney transplants.

Continuing research on innovative normothermic ex vivo perfusion to improve the supply and quality of donor livers
Members of Cleveland Clinic’s liver transplant program published in January 2014 the first report, to their knowledge, of successful use of the protease inhibitor telaprevir to treat HCV recurrence after liver transplant in a patient coinfected with HIV (Transplantation. 2014;97[2]:e14-e15).

The patient was a 62-year-old man with a history of HIV infection, chronic HCV genotype 1b infection complicated by cirrhosis, and hepatocellular carcinoma. Nine months after he underwent liver transplant in August 2011, liver biopsy revealed recurrent hepatitis C with grade 2/4 inflammation and stage 2/4 fibrosis.

The patient’s immunosuppression regimen consisted of tacrolimus and mycophenolate mofetil. To address his HCV recurrence while accounting for these immunosuppressants, the team tried triple therapy with the direct-acting protease inhibitor telaprevir plus ribavirin and pegylated interferon. To avoid having the patient on both HCV and HIV protease inhibitors, the darunavir-ritonavir component of his highly active antiretroviral therapy (HAART) regimen for HIV was stopped before telaprevir was started, at which time the integrase inhibitor raltegravir was also initiated.

From day 1 of the telaprevir-based therapy, the team monitored the patient’s serum tacrolimus level very closely. Despite the need for frequent adjustments to his tacrolimus dosage, management was successful: His HCV RNA became undetectable at eight weeks of therapy and remained undetectable 12 weeks after the end of his HCV treatment regimen, indicating sustained virologic response. There were no harmful effects to the liver graft or to renal function. Two months after the end of telaprevir therapy, the patient was switched back to his original HAART regimen.

This case shows that telaprevir-based triple therapy can be used to treat HCV recurrence in patients coinfected with HIV so long as they are monitored closely at a center with experience in transplanting HIV patients. Notably, this patient was treated when telaprevir was the highest level of therapy for patients with HCV; regimens based on newer direct-acting agents would be used now, though the need for vigilant monitoring would still apply.
simpler, shorter dosing schedules. These agents include three new protease inhibitors and the nucleotide analog inhibitor sofosbuvir, which is a component of the first all-oral, interferon-free regimen to be approved by the FDA for HCV infection.

The direct-acting agents are not yet FDA-approved for treating HCV after liver transplant, but Cleveland Clinic is among a few centers studying this off-label use, which requires complex monitoring for toxicity and interactions with immunosuppressants (see case study on opposite page). Outcomes to date have been good, with high virologic response rates and favorable tolerability, and the program is developing protocols for using direct-acting agents in the pre- and post-transplant settings.

**Diverse research to improve outcomes — and sometimes avoid transplant**

In addition to these studies to clear HCV in the transplant setting, Cleveland Clinic is involved in cutting-edge research in multiple areas related to liver transplantation, including:

- Development of 3-D-printed liver replicas for surgical planning and education (see sidebar, p. 25)
- Studies of normothermic ex vivo perfusion for liver preservation in animals (see sidebar, p. 27) with the near-term goal of its use in transplantation of a human liver
- A multicenter clinical trial testing the safety and efficacy of the ELAD® System (Vital Therapies® Inc.) in patients with alcohol-induced liver decompensation. ELAD is a blood pumping system that uses a proprietary line of allogeneic human liver cells to provide continuous liver support to patients with liver failure. It can serve as a bridge to transplant or as destination therapy in patients whose livers may regenerate enough to avoid the need for transplant.

**Prolific pediatric program**

Cleveland Clinic’s pediatric liver transplant program is one of the most experienced in the nation, dating back to 1986. Medical care of the youngest transplant recipients is managed by a dedicated medical director of pediatric hepatology and liver transplantation and a team of additional pediatric hepatologists.

The program offers a full range of liver transplant options for children, including:

- Partial grafts from living donors
- Whole-organ and split-liver transplants from deceased donors (including donation after cardiac death)
- Liver transplant in the context of multivisceral transplantation

These living-donor and split-liver capabilities enable surgeons to place smaller grafts in children’s small bodies, increasing transplant opportunities — and often slashing wait times — for pediatric patients in need (see patient sidebar).

Between 2005 and 2013, the pediatric program performed 45 liver transplants in patients 6 months to 19 years old. More than half of those transplants involved split livers from deceased donors or partial livers (left lateral segments) from living donors.
4.5-fold increase in visceral transplants over 2012

98 surgical procedures for intestinal rehabilitation to avoid transplant in 2013
One year, two key numbers

For Cleveland Clinic’s Center for Gut Rehabilitation and Transplantation, 2013 was in large part a year of two numbers:

- 9, the number of visceral transplants performed — Cleveland Clinic’s second-highest single-year volume to date, including its first pediatric visceral transplant and first visceral transplant in a patient with HIV
- 98, the number of intestinal surgical rehabilitation procedures performed, representing many dozens of patients in whom visceral transplantation (and lifelong immunosuppression) was avoided

These two numbers exemplify the comprehensive approach the Center for Gut Rehabilitation and Transplantation brings to bear for patients with intestinal failure. That approach yielded a number of other notable outcomes and statistics in 2013, as detailed in the graphs that follow and the points below:

- 87.5 percent one-year patient survival among intestinal transplant patients, which compares favorably with the national average of 80.5 percent (per data from the Scientific Registry of Transplant Recipients as of April 2014)
- 211 patients referred to the center in 2013, a fourfold increase over the 2011 level
- 56 percent success rate in achieving nutritional autonomy using autologous gut among patients undergoing surgical intestinal rehabilitation

9 visceral transplants in 8 patients in 2013, including:
- 7 intestine alone
- 1 intestine-liver-pancreas-duodenum
- 1 full multivisceral

Initiated 2008
CMS approval 2010

31 intestinal or multivisceral transplants through 2013

24-hour referrals, 216.312.0308
Transplant: One piece of a comprehensive approach

Cleveland Clinic is among the world’s few centers that offer both intestinal and multivisceral transplantation, and its volume of nine such transplants in 2013 was one of the highest in the U.S. The visceral transplant team draws on the expertise of multiple accomplished abdominal transplant surgeons, a cadre of subspecialized gastroenterologists and a team of transplant coordinators, among others.

But transplantation is just one component of the Center for Gut Rehabilitation and Transplantation, which represents one of the world’s largest and most comprehensive programs for intestinal rehabilitation and restoration of gastrointestinal autonomy.

The multidisciplinary center’s range of options for adult and pediatric patients with intestinal failure is unsurpassed and includes:

- **Home parenteral nutrition** (HPN) support from Cleveland Clinic’s Center for Human Nutrition, which cares for the largest HPN cohort followed by a single U.S. center and is recognized as a program of excellence by the American Society for Parenteral and Enteral Nutrition.

- **Expert medical management** by the Center for Human Nutrition, including intensive, personalized diet counseling with use of oral rehydration solutions, enteral feeding, and (if necessary) medications or growth factors, including the new glucagon-like peptide 2 analog teduglutide (Gattex®). Specialized pharmacists and dietitians work closely with supervising gastroenterologists to reduce or potentially eliminate the need for HPN and improve patients’ quality of life.

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**Transplant: One piece of a comprehensive approach**

87.5% one-year patient survival, better than national average of 80.5%
“Visceral transplantation” generally refers to transplant procedures that include the intestine. There are four main types:

1. Intestine alone
2. Liver, intestine and pancreas
3. Full multivisceral (stomach, duodenum, pancreas, intestine and liver)
4. Modified multivisceral (stomach, duodenum, pancreas and intestine)

The number of patients who undergo visceral transplant is considerably lower than for other solid organ transplants, and far fewer centers perform visceral transplants. Transplants involving the intestine pose a greater immunologic challenge than do other transplant types, but outcomes have improved substantially with the introduction of new immunosuppressive protocols in recent years.

Absolute indications for intestinal transplant alone or with other organs include failure of home parenteral nutrition (HPN) with development of related complications. Current Centers for Medicare & Medicaid Services criteria define HPN failure as:

- HPN-associated liver injury
- Central venous catheter-related thrombosis of two or more central veins
- A single episode of line-related fungal infection
- Frequent episodes of central line bacterial infection
- Frequent episodes of severe dehydration despite IV fluid replacement in conjunction with HPN
- Ultra-short gut syndrome
Innovative surgical procedures for intestinal rehabilitation, to enhance the absorptive function of the residual native intestine in selected patients, many of whom are able to discontinue HPN. The most commonly used procedures are:

- Autologous intestinal reconstruction (67 percent of Cleveland Clinic’s intestinal rehabilitation surgeries in 2013). These procedures include repair of multiple enterocutaneous fistulae and restoration of gastrointestinal continuity with take-down of intestinal and colonic stoma.

- Bowel-lengthening procedures such as the Bianchi procedure and serial transverse enteroplasty procedure (STEP; see images) (17 percent of 2013 surgeries).

- Foregut gastric reconstruction (16 percent of 2013 surgeries). Gastric reconstruction with restoration of gut continuity is increasingly required for patients who undergo gastric bypass surgery at other centers and develop intestinal failure after a catastrophic abdominal event; few if any other centers are able to offer this procedure.

Inventive reconstructive operations for patients with highly complex abdominal pathology (e.g., “hostile abdomen”) that most centers will not take on. These include patients with abdominal cocoon syndrome, extensive abdominal adhesions, multiple enteric fistulae and extensive thrombosis of the portal venous system.

A nuanced, customized approach to challenging cases

The above options are considered for all appropriate patients before visceral transplant, to avoid the unique risks and need for lifelong immunosuppression that transplant confers.

The result is a creative approach to challenging patients that goes far beyond a simple “transplant/no transplant” dichotomy to find the best customized solution for a given patient. The approach includes a novel Intestinal Stroke Center for timely multidisciplinary management of patients with vascular insufficiency of the intestine (see sidebar, opposite page).
The alternatives to visceral transplant are frequently successful: Full nutritional autonomy (freedom from HPN) was achieved in 56 percent of patients (N = 74, who collectively underwent 98 procedures) undergoing surgical rehabilitation at Cleveland Clinic in 2013. The remaining patients underwent continual gut rehabilitation with the new medication teduglutide or proceeded to intestinal transplant.

Even when visceral transplant is unavoidable, the full multidisciplinary resources of the Center for Gut Rehabilitation and Transplantation are deployed for judicious monitoring of organ function and evaluation for infection, malignancy and other systemic disorders while patients await organ availability and during the crucial postoperative and recovery periods.

**Research and innovation: Building on a rich legacy**

The Center for Gut Rehabilitation and Transplantation’s tradition of innovation got a major boost with the arrival of Kareem Abu-Elmagd, MD, PhD, as its new director in August 2012.

Dr. Abu-Elmagd is the world’s most experienced surgeon in intestinal transplantation, having been involved in approximately 20 percent of all such procedures worldwide. His many significant contributions to intestinal and multivisceral transplantation, immunosuppression, transplant immunology and allograft tolerance include the following:

- First demonstration in humans of the immunoprotective effect of the engrafted liver on other simultaneously transplanted visceral organs
- Introduction of a novel tolerogenic immunosuppressive protocol in humans, achieving unprecedented outcomes that include successful complete discontinuation of immunosuppression in a few immune-privileged visceral transplant recipients
- Introduction of the concept of gut rehabilitation with medical and surgical modalities, including innovative autologous reconstructive procedures for patients with complex abdominal pathology and intestinal failure

Dr. Abu-Elmagd is now working with his Center for Gut Rehabilitation and Transplantation colleagues to build on those advances through a number of research and clinical initiatives, including:

- Efforts to develop novel anti-donor-specific antibody strategies for use in liver-free visceral allografts that lack hepatic immunoprotection. This work includes refining a preconditioning protocol involving the proteasome inhibitor bortezomib that Dr. Abu-Elmagd recently introduced for patients with detectable donor-specific antibodies. The protocol has shown encouraging results and is now being implemented by other centers for visceral transplantation.
- Bench research focusing on the repertoire of lymphocytes following visceral transplant to identify a noninvasive clinical biomarker for intestinal allograft rejection to enable earlier detection and treatment of rejection.

**NOVEL INTESTINAL STROKE CENTER PROMOTES SWIFT RESCUE FOR INTESTINAL ISCHEMIA**

Patients with acute intestinal ischemia need optimal management immediately. To provide such management as swiftly as possible, the Center for Gut Rehabilitation and Transplantation recently established an unprecedented Intestinal Stroke Center that employs a multidisciplinary team approach. The aim is to restore blood flow to the intestine and other abdominal organs through innovative combinations of medical management with radiologic and/or surgical intervention. Based on cerebrovascular stroke protocols, the Intestinal Stroke Center ensures 24/7 availability of expert clinicians — including acute care surgeons, intensivists, Center for Gut Rehabilitation and Transplantation surgeons and gastroenterologists, diagnostic and interventional radiologists, hematologists, and infectious disease specialists — and uses a standardized management algorithm to:

- Offer timely intervention to reduce propagation of mesenteric thrombosis and minimize the time of ischemia
- Increase chances of intestinal viability, reduce permanent ischemia to the bowel and salvage as much bowel as possible

In its first 15 months of operation, spanning 2012 and 2013, the Intestinal Stroke Center managed 127 patients across 131 encounters, with most patients being rescued with salvage of the abdominal organs that were viable on referral. The center’s management algorithm ultimately leads to visceral transplant for patients who have permanently lost their gut.
By accepting high-risk patients for visceral transplantation, Cleveland Clinic is helping expand the potential indications and patient populations for the procedure. Two examples stand out from the Center for Gut Rehabilitation and Transplantation’s 2013 case mix:

- A successful transplant of intestine, duodenum, liver and pancreas in a 4½-year-old with Martinez-Frias syndrome, a rare — and previously always fatal — hereditary disorder with multiorgan manifestations (see patient sidebar).
- The world’s first multivisceral transplant in an HIV-infected individual, a 37-year-old man who received six organs — stomach, intestine, duodenum, liver, pancreas and kidney. Although the patient died several months after transplant, this unprecedented attempt at therapy yielded insights into virologic control and immunosuppression that promise to advance management of future cases of visceral transplantation in the setting of HIV.

Leadership in patient advocacy

Dr. Abu-Elmagd has been in the vanguard of patient advocacy in intestinal failure since he played a lead role in convincing the Centers for Medicare & Medicaid Services (CMS) in 1999 to provide reimbursement for intestinal and multivisceral transplantation as the standard of care for irreversible intestinal failure.

Currently Dr. Abu-Elmagd and Cleveland Clinic are helping lead the call for two important initiatives in this area:

- Modification of United Network for Organ Sharing regulations to permit national sharing of deceased donor intestinal allografts according to favorable HLA and virtual cross-match results
- Loosening of CMS controls on current indications for intestinal transplant

Prioritizing pediatric transplant

Cleveland Clinic performed its first visceral transplant in a pediatric patient in 2013 (involving intestine, duodenum, liver and pancreas; see patient sidebar) and is poised to perform increasing numbers to address unmet needs in this population.

Understanding of those needs has been significantly shaped by Dr. Abu-Elmagd’s pioneering research on the quality-of-life aspects of visceral transplantation in children and adults (Ann Surg. 2012;256(3):494-508), which suggests that early consideration should be given to gut rehabilitation, including transplantation, to potentially reduce the risk of autism, developmental delay and behavioral disorders in pediatric patients with intestinal failure.

Appropriate candidates for pediatric visceral transplant include children with short bowel syndrome, congenital anomalies, necrotizing enterocolitis, intestinal atresia, midgut volvulus, gastrochisis and motility disorders.

Cleveland Clinic’s pediatric intestinal and multivisceral transplant services are highly integrated with Cleveland Clinic Children’s well-established Pediatric Intestinal Rehabilitation Program and Pediatric Nutrition Program to ensure a comprehensive overall treatment approach and expert pre- and post-transplant care.
When 3½-year-old Khaled Mahamid arrived at Cleveland Clinic in August 2012, he had already long defied medical expectations.

Born in the Middle East with Martinez-Frias syndrome, Khaled was the first child known to have survived so long with the rare inherited disorder marked by a host of life-threatening complications. In Khaled’s case, these included neonatal diabetes, enterocyte failure and iron overload with end-stage cholestatic liver disease. Since birth, he had required total parenteral nutrition (TPN) and multiple daily insulin doses.

Khaled’s doctors suggested that his parents explore a transplant abroad. They eventually found Kareem Abu-Elmagd, MD, PhD, Director of Cleveland Clinic’s Center for Gut Rehabilitation and Transplantation. He proposed a complex visceral transplant to provide Khaled with a new intestine, duodenum, liver and pancreas.

“The fact that Khaled had survived longer than any other patient with Martinez-Frias syndrome prompted us to try to give him a second chance through transplantation,” explains Dr. Abu-Elmagd.

After more than a year of intricate inpatient care at Cleveland Clinic Children’s to manage Khaled’s TPN, fluid balance and diabetes, suitable donor organs became available. In September 2013, Khaled, then 4½, underwent the 15-hour, five-surgeon transplant procedure. It was a success, with all three organs and the duodenum grafting well.

Khaled was discharged less than two months later on an unrestricted oral diet and with his diabetes cured. At seven months after transplant, he was faring well, with no need for insulin and enjoying his unrestricted diet to full extent. “His favorite foods include mussels, octopus and lobster!” his mother recounts.

Dr. Abu-Elmagd says he is gratified “to be able to show humanity this outcome” in a disease with such a traditionally dismal prognosis, but he is even more pleased to help give Khaled a second chance at life. “I am confident he won’t have recurrent disease with the new organs,” he says.

Khaled is back home in the Middle East, but Dr. Abu-Elmagd and his team will continue to monitor Khaled to study what happens when someone with Martinez-Frias syndrome ages and grows — something that had never been possible before.
1,670 hearts transplanted and
811 mechanical circulatory support
devices placed through 2013

1- and 3-year
adult survival rates above expected
rates and national averages
Cleveland Clinic’s Cardiac Transplantation and Ventricular Assist Device Therapy Program is one of the largest and most experienced heart transplant programs in the nation and the leading program in Ohio. It marks its 30-year anniversary in 2014.

The program’s patient and graft survival rates exceed both national norms and expected rates, as detailed in the graphs on the following pages. Notable outcomes from the January 2014 report of the Scientific Registry of Transplant Recipients (SRTR) include:

- 92.04 percent one-year adult patient survival (vs. expected rate of 90.85 percent and national average of 90.66 percent)
- 90.0 percent three-year adult patient survival (vs. expected rate of 83.39 percent and national average of 83.29 percent)

Standout capabilities in end-stage heart failure

Beyond its outcomes, Cleveland Clinic’s heart transplant program is distinguished by:

- Robust clinical activity, reflected by the 182 adult and pediatric patients who underwent full evaluation for transplant in 2013 from among 242 patients referred, many from far reaches of the nation and the globe
- Two decades of experience in combined heart-lung transplants (see Lung and Heart-Lung Transplantation, p. 44) and combined heart-kidney and heart-liver transplants
- A highly comprehensive approach to patients with end-stage heart failure, including expert medical and interventional management, participation in numerous clinical trials, use of all approved (and many investigational) devices for mechanical circulatory support, and left ventricular reconstruction surgery
- One of the nation’s few dedicated, specialized ICUs for patients with heart failure
- Close integration with the George M. and Linda H. Kaufman Center for Heart Failure and the rest of Cleveland Clinic’s Sydell and Arnold Miller Family Heart & Vascular Institute, ranked by U.S. News & World Report as the nation’s top heart program for 20 years running

44 heart transplants in 2013, including 1 heart-kidney transplant

67 mechanical circulatory support devices placed in 2013, including:

- 35 as bridge to transplant
- 32 as destination therapy

Initiated 1984
UNOS approval 1988
CMS approval 1988

Heart transplant program being initiated at Cleveland Clinic Florida in 2014

One of the few programs placing Berlin Heart Excor LVADs in children
Expansive use of mechanical support devices

Among these points of distinction, the program’s innovative use of mechanical circulatory support devices — dating back a quarter century — is increasingly key. As patients with advanced heart failure continue to outstrip the availability of donor hearts for transplant, the use of these devices — primarily left ventricular assist devices (LVADs) — looms ever larger in the care surrounding heart failure and transplantation.

Mechanical circulatory support devices are used in patients with advanced heart failure either as a bridge to transplantation for patients on the organ waiting list or — increasingly — as destination therapy to improve and prolong the lives of patients who are not candidates for transplantation.

Like many centers, Cleveland Clinic has implanted more LVADs than it has performed heart transplants in recent years, with 67 LVADs implanted in 2013, divided nearly evenly between bridge therapy (n = 35) and destination therapy (n = 32).

Experienced use of LVADs as bridge therapy promises to reduce the mortality rate of patients on the organ waiting list. The proportion of Cleveland Clinic heart transplant patients who had been on mechanical support before transplant has risen steadily from under 15 percent in 2005 to more than half (57.9 percent) by 2013.

Exceptional survival rates in LVAD patients

Comparative trials have consistently shown that mechanical circulatory support lengthens and improves the lives of advanced heart failure patients relative to optimal

### Survival rates of LVAD patients by era of LVAD implantation

<table>
<thead>
<tr>
<th>Survival rates of LVAD patients</th>
<th>2012-2013</th>
<th>2010-2011</th>
<th>Before 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>98%</td>
<td>91%</td>
<td>93%</td>
</tr>
<tr>
<td>6 months</td>
<td>91%</td>
<td>83%</td>
<td>80%</td>
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<tr>
<td>12 months</td>
<td>81%</td>
<td>78%</td>
<td>74%</td>
</tr>
</tbody>
</table>

2013 QUICK TAKE

7.5% in-hospital mortality among LVAD recipients, less than half the expected rate
medical management. And patient survival is steadily increasing over time (see table on previous page) as device technology improves — such as with the replacement of pulsatile-flow devices by newer continuous-flow LVADs — and as experience grows.

Cleveland Clinic has consistently outperformed expectations in terms of in-hospital mortality rates for LVAD patients in recent years. In 2013, Cleveland Clinic’s 7.5 percent in-hospital mortality among LVAD patients was less than half the expected rate of 18 percent, according to data from the University HealthSystem Consortium (UHC) Comparative Database (discharges from January through November 2013).

**FUTURE OF TRANSPLANTATION: A TOTALLY NEW TOTAL ARTIFICIAL HEART**

Biomedical engineers at Cleveland Clinic have joined with their Cardiac Transplantation and Ventricular Assist Device Therapy Program colleagues — and with partners at Cleveland Heart Inc. — to develop a continuous-flow total artificial heart, or CFTAH.

The NIH-funded, potentially groundbreaking innovation advances artificial heart development in two important ways: with automatic speed control and with self-regulation to balance right-left inlet pressures.

The CFTAH is elegantly simple, with just one moving part and one electromechanical component. This single-moving-part design eliminates the need for sensors that balance function of the two sides of the heart, reducing complexity and the risk that the system will fail or wear out over time.

By combining the best features of left and right VADs, the CFTAH promises to address the needs of patients with both left- and right-side heart failure issues that have not been met by right VADs or biventricular assist devices to date.

A slender cable feeds the CFTAH power, which originates from a rechargeable battery that patients can easily strap on under most garments. The entire device, constructed of titanium, weighs less than a pound.

Results of initial biocompatibility tests of the CFTAH have been encouraging, and survival has been achieved in studies of the CFTAH in large animals, but human trials are years away.
Broad leadership in mechanical circulatory support therapy

As more and more patients live for long periods with LVADs, potential complications are emerging, including pump thrombosis, gastrointestinal bleeding, renal failure, stroke and infections. Cleveland Clinic is at the forefront of identifying and reducing such complications through a multidisciplinary approach with the participation of leading specialists.

Beyond this safety vigilance, Cleveland Clinic is dedicated to ensuring that mechanical circulatory support therapy reaches its full potential in the following ways:

- Through active involvement in multiple studies of emerging devices (see “A hub of high-impact research” below) and in development of innovative VAD designs and a new-generation total artificial heart (see sidebar on previous page)
- Through a tenacious focus on using LVADs to keep patients’ original hearts working well enough to stave off transplant for as long as possible, since few transplanted hearts last longer than 20 years

Additionally, Cleveland Clinic is among the few centers that offer inpatient rehabilitation therapy to LVAD patients and heart transplant recipients. Physiatrists and other rehabilitation specialists in the inpatient rehabilitation facility (IRF) on Cleveland Clinic’s main campus work closely with clinicians in the heart transplant program and undergo training specific to managing LVAD patients. Over a 12-month period spanning 2012 and 2013, average length of stay in the IRF for LVAD patients was 16.4 days.

A hub of high-impact research

Cleveland Clinic’s Cardiac Transplantation and Ventricular Assist Device Therapy Program is deeply involved in a wide range of high-impact clinical trials to improve heart transplantation and mechanical circulatory support. Here is a sampling of major active studies and projects:

**CTOT 11.** Cleveland Clinic’s Randall Starling, MD, MPH, is national study chair of this phase 2 trial within the NIH-sponsored Clinical Trials in Organ Transplantation cooperative research program. The study is evaluating whether induction therapy that combines the monoclonal antibody rituximab (for B-cell depletion) with conventional immunosuppression reduces antibody-mediated cardiac allograft vasculopathy after heart transplant and thereby improves graft function and patient survival.

**ENDURANCE.** Cleveland Clinic is participating in this multicenter randomized trial comparing the HeartWare® LVAD with the HeartMate II® LVAD in the setting of destination therapy for patients with end-stage heart failure.

**LVAD Therapy and Mesenchymal Precursor Cells.** This study, coordinated by the Cardiovascular Cell Therapy Research Network and the Cardiothoracic Surgical Trials Network, aims to determine whether intramyocardial injection of mesenchymal precursor cells (MPCs) during LVAD implantation is safe and effective in improving heart function. The trial includes LVADs used as destination therapy or as a bridge to transplant. Cleveland Clinic is one of several participating North American centers, but enrollment is now closed.

ELLA GREEN: A SWIFT PATH FROM CARDIOGENIC SHOCK TO SUCCESSFUL TRANSPLANT

Diagnosed with congestive heart failure, 58-year-old Ella Green passed out in the fall of 2013 after the pacemaker she wore for an irregular heartbeat began to fire repeatedly. Right heart catheterization revealed cardiogenic shock, and she was admitted to Cleveland Clinic.

Although Ella’s surgical team planned to implant an LVAD, she was too weak to undergo surgery without strengthening via arteriovenous extracorporeal membrane oxygenation (AV ECMO). Less than a week after the start of AV ECMO support, a donor heart became available, and on Oct. 29, 2013, Ella underwent a successful orthotopic heart transplant with pacemaker removal.

A few weeks later, including two weeks in rehabilitation, Ella headed home to Columbus, Ohio, to continue physical therapy.

“I feel great!” she said in summer 2014 as she prepared to return to her job as a special-education teacher in the fall. “I feel safe at Cleveland Clinic. I have confidence in the doctors, and the aftercare I’m receiving is great.”
Beyond the above ongoing trials, Cleveland Clinic investigators have published multiple important studies in recent years that have led to improvements in the care of LVAD and heart transplant patients.

**Well-established pediatric program**

Within a year of its first successful adult heart transplant, Cleveland Clinic performed its first successful pediatric heart transplant (March 1985) and has since built one of the nation’s premier programs for pediatric cardiac transplantation, with 140 hearts transplanted through the end of 2013 (including seven heart-lung transplants). Nearly 75 pediatric heart transplant patients are still being followed.

The pediatric program has a low operative mortality rate and patient and graft survival rates that routinely meet or exceed national benchmarks and expected rates. It numbers among the few programs that can perform dual-organ heart transplants — including the lung, liver or kidney — in children.

Two pediatric heart transplant surgeons and a pediatric transplant cardiologist make up the program’s core physician team. They are supported by more than a dozen additional pediatric cardiologists in Cleveland Clinic Children’s, a team of allied health professionals specializing in pediatric heart transplant, and Cleveland Clinic's renowned cadre of pediatric and adult congenital heart disease specialists.

Transplanted patients are followed closely by the pediatric transplant cardiologist — often well into adulthood, thanks to a shared clinic in the Center for Adult Congenital Heart Disease, where adult patients can be seen by both an adult-care congenital disease specialist and their longtime pediatric cardiologist.

**Forestalling pediatric transplant when possible**

The pediatric program’s team does all it can to medically manage failing pediatric hearts and forestall transplant when possible, as few donor hearts last beyond 20 years. This is achieved through intricate medication-based therapy and increasingly with LVADs, which are used in this setting primarily to make patients strong enough to undergo transplantation and buy time until a donor heart becomes available.

Cleveland Clinic placed its first Berlin Heart Excor® LVAD in a child in 2010, under a compassionate-use protocol prior to the device’s FDA approval. Through 2013, the program had bridged four pediatric patients to transplant using the Berlin Heart Excor without a single pump-related major complication. The program’s willingness to use the device as soon as in early infancy requires meticulous management to perfect anticoagulation and avoid infections related to the increased tubing required for small children.

Other LVADs, including the HeartWare and HeartMate II devices, are used in older pediatric patients.

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**HAMZAH CHOUDHRY:**
**EXPERT MANAGEMENT AVERTS NEED FOR LVAD DURING TWO-WEEK TRANSPLANT WAIT**

Hamzah Choudhry, a college student in Blue Springs, Missouri, awoke one morning struggling to breathe. A visit to the student health center began a harrowing journey marked by repeated cardiac arrest and culminating in an emergency flight to Cleveland Clinic.

There, Hamzah learned that he has Uhl anomaly, an extremely rare congenital disorder resulting in partial or total loss of myocardial muscle in the right ventricle. He urgently needed a heart transplant.

During the two weeks he waited for a donor heart, Hamzah was able to avoid the need for an LVAD thanks to expert management in Cleveland Clinic’s heart failure ICU, one of the few of its kind in the nation. He was critically ill yet remained stable until he was successfully transplanted when a matched donor heart surfaced.

“Before the transplant I couldn’t walk because I was always out of breath and got really tired,” says Hamzah, who is now 21 and back at school. “Now I’m twice as active as before.”
Leadership in lung transplant volumes and innovative approaches including the BAR procedure, awake ECMO and normothermic ex vivo perfusion
LUNG & HEART-LUNG TRANSPLANTATION

Cleveland Clinic’s lung and heart-lung transplant program has long been one of the nation’s largest and most active of its kind. The program performed 98 lung transplants (both single and double lung procedures) in 2013. This activity ranks Cleveland Clinic among the four largest-volume lung transplant programs in the nation and the largest in Ohio.

The program's patient survival rates compare well with national norms and expected rates, as detailed in the graph on the next page. Notable program data from the January 2014 report of the Scientific Registry of Transplant Recipients (SRTR) include:

- 87.85 percent one-year adult patient survival (vs. expected rate of 85.71 percent and national average of 86.11 percent)
- 4.5-month median time to transplant, shorter than the regional (OPTN Region 10) median of 6.9 months and the national median of 4.6 months (see graph, p. 47)

These strong clinical outcomes are achieved despite the program’s large number of high-acuity cases and high-risk transplant candidates from far reaches of the nation and the globe, including those with:

- Chronic obstructive pulmonary disease/emphysema
- Fibrotic lung disease
- Primary or secondary pulmonary hypertension
- Cystic fibrosis/bronchiectasis
- Congenital cardiac disease requiring combined heart-lung transplant
- Serious comorbid cardiac disease, requiring concomitant heart surgery in many patients
Points of distinction

The program offers special expertise in a number of areas, including:

**Multiorgan transplants**, including heart-lung and liver-lung.

**Retransplantation** for chronic rejection or bronchiolitis obliterans syndrome.

**Lung transplant with bronchial artery revascularization (BAR).** The world’s first BAR procedure in lung transplantation was performed in 2007 by Cleveland Clinic’s Gösta Pettersson, MD, PhD, who continues with the program today. Cleveland Clinic is one of a small number of centers in the world that perform BAR in the setting of lung transplant, which restores bronchial arterial circulation to transplanted lungs (see images below). Current evidence suggests that BAR may lower early biopsy rejection grades, postpone the onset of bronchiolitis obliterans syndrome and improve long-term survival.

**The difference that bronchial artery revascularization (BAR) can make in selected cases.**

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**Without BAR.** The anastomotic site one week after lung transplant using a standard surgical approach, with evidence of necrosis and ischemia.

**With BAR.** Normal-appearing tracheal anastomosis one week after lung transplant using the BAR surgical technique.
Ambulatory/awake extracorporeal membrane oxygenation (ECMO). Cleveland Clinic was one of the first U.S. centers to use ambulatory ECMO to allow for reconditioning and successful transplant in critically ill patients with respiratory failure.

Use of donation-after-cardiac death (DCD) lungs. Cleveland Clinic is among the few U.S. centers with considerable experience in DCD lung transplants, which represent about 5 percent of the program’s transplants in recent years. The lung transplant team recently published its early and midterm experience with DCD lung transplant (Ann Thorac Surg. 2012;94:406-412), which demonstrated that recipient survival and early graft function with DCD lungs are excellent when standardized selection, procurement and implantation techniques are followed.

Leadership in the development of normothermic ex vivo perfusion to better preserve, assess and even enhance donor lungs, promising to substantially increase the number of usable donor lungs (see sidebar, p. 49).

Expanded options and flexibility for patients

The program’s embrace of options such as DCD and normothermic ex vivo perfusion is part of its commitment to expanding the pool of high-quality donor lungs and trimming wait times for transplant candidates. Not only is its wait time shorter than that of many other centers (see graph above), but Cleveland Clinic’s program allows patients to live at home while awaiting transplant and accepts patients who live within 1,000 miles of Cleveland, enabling patients to avoid the need to relocate.

Because many lung transplant candidates have high-acuity conditions, a good number benefit from the services of Cleveland Clinic’s Critical Care Transport team (see patient profiles, pp. 50 and 51), which deploys specially trained critical care physicians, nurses and paramedics to transfer the most critically ill patients to Cleveland Clinic by mobile ICU vehicles, helicopter or fixed-wing aircraft (see p. 83 for more on Critical Care Transport services).
Comprehensive approach to evaluation and care

When a patient is referred for lung transplant evaluation, he or she is assigned a dedicated multidisciplinary team that includes:

- One or more physicians from the program’s staff of eight pulmonologists and five lung transplant surgeons
- A pretransplant coordinator
- A transplant pharmacist
- A transplant social worker
- A financial team

The team creates a tailored care plan for each patient, which involves determining the timing of transplant listing, testing and addressing specific patient needs. Once a patient is listed, outpatient and inpatient transplant educational programs are started to prepare both the patient and his or her caregiver(s) for all aspects of the waiting and transplant experience.

Because treatment adherence in the post-transplant period is vital to ultimate transplant success, the program supplements standard one-on-one patient education with pretransplant outpatient education on medication regimens and with inpatient group instruction for patients and their caregivers. The inpatient instruction is offered each week in two group sessions led by a post-transplant coordinator on the lung transplant unit. The popular classes have resulted in greater patient knowledge about their medications and post-transplant health issues in general.

Destination program for end-stage lung disease

The comprehensiveness of this management approach is matched by the program’s equally comprehensive approach to end-stage lung disease in general.

For patients who are not yet ready for lung transplant, whose conditions deteriorate while waiting for donor lungs, or who may not be appropriate transplant candidates, the transplant team can partner with colleagues in Cleveland Clinic’s Respiratory Institute, which has been ranked among the nation’s top 3 pulmonology programs for more than a decade by U.S. News & World Report, to offer other advanced therapies for end-stage lung disease. These options, which are considered solely in collaboration with the patient’s referring physician, include:

- Lung volume reduction surgery, which is now performed via a video-assisted thoracoscopic approach to reduce morbidity
- Enrollment in an advanced clinical trial of novel medical therapy for the patient’s underlying condition, such as idiopathic pulmonary fibrosis
- Leading-edge management of patients with primary or secondary pulmonary hypertension via Cleveland Clinic’s premier Pulmonary Hypertension Program

One of eight U.S. centers participating in INSPIRE clinical trial of normothermic ex vivo lung perfusion
**FUTURE OF TRANSPLANTATION:**

**LEADERSHIP IN NORMOTHERMIC EX VIVO LUNG PERFUSION**

Approximately 80 percent of donated lungs cannot be transplanted, due to infection, fluid accumulation or other damage. With thousands of Americans on the lung transplant waiting list, Cleveland Clinic specialists are proud to be engaged in leading-edge research to address these unmet needs by using normothermic ex vivo perfusion to make more donor lungs suitable for transplant. (See p. 6 for a profile of Cleveland Clinic’s normothermic ex vivo perfusion efforts across multiple organs.)

Normothermic ex vivo perfusion involves use of a miniature heart-lung machine that shoots a proprietary solution through a hose into donor lungs hooked up to the machine (see photo). The solution provides nutrients and extracts excess water from the lungs, potentially resuscitating them to function anew. After this “lung washing,” a ventilator mechanically fills the lungs with oxygen via another tube to allow assessment of lung function and prolong the time the lungs can be preserved for potential transplant.

Based on experience in Europe and Canada, where normothermic ex vivo perfusion systems have been approved for use for several years, the technology appears to make a large share — from 40 to 75 percent — of previously untransplantable lungs fit for transplant, functioning as well as donor lungs that didn’t require the treatment.

Normothermic ex vivo lung perfusion remained experimental in the U.S. in 2013, but in August 2014 the FDA approved XVIVO Perfusion’s XPS™ system and STEEN Solution™ for preserving donor lungs that do not initially meet standard criteria for transplant but may be deemed transplantable with more time to evaluate the organs’ function.

Though Cleveland Clinic was not involved in clinical trials of the XVIVO system, it is one of eight U.S. centers participating in the international INSPIRE trial that involves transplanting donor lungs preserved with a similar system (from TransMedics) into human recipients. As of the end of 2013, Cleveland Clinic had transplanted one patient with a lung preserved using that system.

As part of their preclinical preparation and to increase knowledge about ex vivo perfusion strategies, Cleveland Clinic researchers have conducted extensive research on nontransplantable human lungs using various ex vivo perfusion systems. They have presented this work at numerous national and international meetings, including the 2013 and 2014 meetings of the International Society for Heart and Lung Transplantation.

Following the recent FDA approval of the XPS system, Cleveland Clinic plans to implement clinical use of normothermic ex vivo perfusion as soon as possible with systems that have been utilized in the laboratory of lung transplant surgeon Kenneth McCurry, MD, who has led Cleveland Clinic’s lung perfusion efforts. Dr. McCurry says that FDA approval and ultimate use of normothermic ex vivo perfusion systems promise to increase the center’s lung transplant volume by 50 to 100 percent.

Equally exciting are the additional uses to which normothermic ex vivo perfusion might be put, such as to deliver antibiotics or other drugs to donor lungs to thwart rejection. “We might be able to change the lung in some way so that the recipient’s immune system responds to it less vigorously, reducing rejection risk,” Dr. McCurry says.

- Versatile medical and surgical approaches for patients with various congenital diseases offered collaboratively by the heart and pulmonary teams within Cleveland Clinic’s Adult Congenital Heart Disease Center

The result is an agile and highly multidisciplinary approach to care dictated by the patient’s unique needs.

**Forceful lung transplant research**

Cleveland Clinic’s lung transplant team is active in a diverse group of innovative research programs. Major studies that were active in 2013 include:

**INSPIRE trial of ex vivo lung perfusion.** Cleveland Clinic is one of eight U.S. centers in this global trial comparing the TransMedics OCS™ Lung normothermic ex vivo perfusion technology with cold storage techniques for preserving and assessing donor lungs for transplantation in human recipients (see sidebar).
HLA Antibodies After Lung Transplantation (HALT I) study. Cleveland Clinic is one of six U.S. centers participating in this NIH-funded study evaluating long-term outcomes after early development of donor-specific HLA antibodies (DSAs) following lung transplant and the potential benefit of preemptive DSA depletion.

Immune Mechanisms of Rejection in Human Lung Allografts study. Cleveland Clinic is collaborating with Washington University in St. Louis on this NIH-sponsored trial to determine whether downregulation of autoimmune responses by depletion of autoantibodies to self-antigens prior to lung transplant will prevent primary graft dysfunction and reduce the risk of bronchiolitis obliterans syndrome.

Lung Transplant Clinical Trials Network (LT-CTN). Cleveland Clinic is one of five academic centers taking part in this NIH-funded study within the Clinical Trials in Organ Transplantation (CTOT) program. This multicenter trial is addressing two of the most important contemporary graft-limiting problems, cytomegalovirus infection and chronic lung allograft dysfunction, and aims to yield better understanding of the risks, phenotypes and mechanisms of chronic allograft dysfunction to reduce long-term graft loss rates.

TERRY PERROTTA: RECIPIENT OF A DOUBLE LUNG TRANSPLANT AFTER CRITICAL CARE TRANSFER FOR A RARE LUNG CONDITION

Pulmonary veno-occlusive disease (PVOD) accounts for only a small number of cases of pulmonary hypertension, and Terry Perrotta’s case was one of them. Severe deterioration of the condition sent the 53-year-old Rhode Island resident and former professional figure skater into right-sided heart failure in January 2013, and soon she was comatose in the ICU of her local hospital.

Terry’s doctors said her only chance was a double lung transplant, and they arranged her transfer to Cleveland Clinic to have it performed.

After undergoing venoarterial extracorporeal membrane oxygenation (ECMO) as a bridge to transplant to increase chances she’d survive the flight, Terry was rushed to Ohio by Cleveland Clinic’s Critical Care Transport team. She underwent a successful bilateral sequential lung transplant by Cleveland Clinic surgeons. When Terry woke up four days later, a nurse was testing her oxygen level. “It was 100 percent,” she recalls. “I thought it was a dream.”

Lung transplant is the only therapy that appears to significantly prolong the lives of patients with PVOD, but the cumulative transplant experience for the condition is small.

In Terry’s case, it’s been a success. She was discharged home after several weeks of close monitoring and rehabilitation at Cleveland Clinic. “On the drive back to Rhode Island, I walked on a treadmill at a hotel gym for 45 minutes,” she says. “Before the surgery I could barely climb a set of stairs.”

Today Terry says she can breathe as well as before her PVOD developed. “I’ve been able to return to ice skating, and I’m working again. All is well.”
Other studies that the lung transplant team is leading or taking part in include:

- A prospective study of the incidence, prevalence and risk factors for neurocognitive impairment in a cohort of lung transplant recipients
- A multicenter trial assessing gastroesophageal reflux as a contributor to chronic lung allograft rejection
- A single-center prospective investigation to determine the utility of pCLE (probe-based confocal laser endomicroscopy), an optical tool allowing in vivo microscopic imaging of lung tissue during standard bronchoscopy, for detecting rejection after transplant

**Pediatrics: Enhancing offerings for an underserved population**

Fewer than 100 pediatric lung transplants are performed annually worldwide. Several factors explain this low volume:

- The relatively few diagnoses leading to end-stage lung disease in children
- Limited availability of suitable donor lungs for pediatric patients
- An inferior survival rate relative to other solid organ transplant types

Only a few centers perform pediatric lung transplants, and Cleveland Clinic is among them, having completed 25 lung transplants and seven heart-lung transplants in the pediatric population since 1991. It is one of the world’s only centers offering the BAR procedure for pediatric patients undergoing lung transplant.

Cleveland Clinic is now looking to build its volume and expertise in this underserved clinical area with the 2013 arrival of its first dedicated medical director for pediatric lung transplant, Nathan Kraynack, MD, an expert in pediatric cystic fibrosis. Dr. Kraynack is leveraging his background in the medical management of pediatric lung transplant recipients to better position Cleveland Clinic to offer transplant to more children with end-stage lung disorders.

The result is a newly formalized pediatric lung transplant program combining the deep experience of Cleveland Clinic’s lung and heart-lung transplant surgeons with the expertise of Cleveland Clinic Children’s five pediatric pulmonologists, who are skilled in the care of children with conditions such as:

- Cystic fibrosis
- Pulmonary hypertension
- Childhood interstitial lung disease
- Genetic disorders of surfactant dysfunction

The program draws on this collective expertise to make the critical judgment in most pediatric lung transplant decisions: pinpointing the time when a young patient is sick enough to need transplantation yet still well enough to tolerate the surgery. In doing so, the program aims to contribute to knowledge gains to help accelerate progress in outcomes for this underserved population.

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**KATHERINE RUSSELL: BACK TO HER CELLO AFTER A DOUBLE LUNG TRANSPLANT WITH BAR**

“I used to wake up coughing ferociously every morning,” recalls Katherine Russell, a 23-year-old from Amherst, New York. “I would hesitate to go out on the dance floor, and I used to struggle not to cough through classical concerts — a challenge for a performing cellist.”

After battling cystic fibrosis since birth, Katherine experienced rapid health deterioration in 2012 following a bout of influenza that led to pneumonia. Just two weeks after being airlifted to Cleveland Clinic, Katherine was listed for transplant and a pair of donor lungs was identified. She underwent lung transplant with bronchial artery revascularization (BAR), a challenging surgical technique pioneered at Cleveland Clinic to restore bronchial arterial circulation to her transplanted lungs.

“Now my coughing difficulties are all lifted,” Katherine reflects. “The lung transplant has brought more than comfort — it has raised my quality of life.”
Expertise in the full spectrum of BMT procedures and donor cell sources

3,996 transplants through 2013
A dynamic year

2013 was a dynamic year for Cleveland Clinic’s Blood & Marrow Transplant (BMT) Program:

- The program performed 191 transplants, one of its highest annual volumes to date.
- Both the adult and pediatric components of the program achieved three-year Foundation for the Accreditation of Cellular Therapy (FACT) accreditation for all services and facilities inspected.
- It welcomed a new director, Navneet Majhail, MD, MS, an internationally known BMT expert (see sidebar, p. 56), as well as three other new BMT specialist physicians.
- The program introduced its first offerings in haploidentical transplantation (see sidebar, p. 59).

The program is one of the largest of its kind in Ohio and was one of the nation’s earliest BMT programs, with Cleveland Clinic’s first bone marrow transplant dating back to 1975. It has performed 3,996 blood and marrow transplants (or hematopoietic cell transplants [HCTs]) through 2013, and volumes have grown steadily in recent years (see graph on next page).

Full range of transplant types, donor cell sources

This experience has yielded extensive expertise in the full spectrum of transplant types — including autologous, allogeneic with myeloablative conditioning and allogeneic with reduced-intensity conditioning — and donor cell sources, including bone marrow, peripheral blood stem cells and umbilical cord blood. The pie chart on the next spread breaks down the BMT program’s 191 transplants in 2013 by procedure type.

In 2013, the program performed 54 autologous transplants for multiple myeloma/amyloidosis and 55 for non-Hodgkin lymphoma, which were the most common indications. Leading indications for allogeneic transplants were acute and chronic...
myeloid leukemia, acute lymphoblastic leukemia and myelodysplastic syndromes. The program also takes on less common indications ranging from solid tumors and myeloproliferative disorders to aplastic anemia and a growing list of nonmalignant hematologic and immune diseases (see “Progressive pediatric program” below).

Consistently solid outcomes

Patient outcomes are detailed in the table below and remain comparable or superior to national benchmarks. In the publicly available 2013 Report of Survival

<table>
<thead>
<tr>
<th>Transplant type and diagnosis</th>
<th>N</th>
<th>100-day survival</th>
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</thead>
<tbody>
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<td></td>
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<tr>
<td>Non-Hodgkin and Hodgkin lymphoma</td>
<td>126</td>
<td>97%</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>86</td>
<td>99%</td>
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<tr>
<td>MAC, related donor: Acute and chronic leukemia and MDS</td>
<td>31</td>
<td>87%</td>
</tr>
<tr>
<td>RIC, related donor: Acute and chronic leukemia and MDS</td>
<td>20</td>
<td>95%</td>
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<tr>
<td>MAC, unrelated donor: Acute and chronic leukemia and MDS</td>
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<td>97%</td>
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<tr>
<td>RIC, unrelated donor: Acute and chronic leukemia and MDS</td>
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<td>95%</td>
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<tr>
<td>MAC, umbilical cord blood: Acute and chronic leukemia and MDS</td>
<td>12</td>
<td>83%</td>
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</table>

MAC = myeloablative conditioning, RIC = reduced-intensity conditioning, MDS = myelodysplastic syndromes
Statistics for Blood and Marrow Transplantation from the Center for International Blood and Marrow Transplant Research (CIBMTR), Cleveland Clinic’s one-year actual survival probability was 61.7 percent, which was within the program’s predicted survival probability range.

Other 2013 outcomes statistics for Cleveland Clinic’s BMT Program include:

- A median length of stay of 21 days for primary transplant patients
- Rankings above the national 90th percentile for the BMT inpatient unit in overall assessment scores for patient satisfaction on the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) in all four quarters of 2013

Full complement of clinical and support services

Cleveland Clinic’s BMT Program is well equipped and expertly staffed across all aspects and stages of the transplant process, from donor selection and patient preparation through post-transplant follow-up care. The 14 staff physicians across the program’s adult and pediatric components are supported by dedicated infectious disease specialists and by physician partners in various Cleveland Clinic in-house programs:

- An apheresis collection facility
- A progenitor cell processing facility
- Allogen Laboratories, Cleveland Clinic’s wholly owned histocompatibility and transplant immunology lab (see p. 77)

Collaboration with the apheresis unit recently enabled development of algorithms for peripheral progenitor blood cell mobilization that have reduced the number of leukophereses needed for total cell collection, reducing costs and patient inconvenience. Similarly, the program’s partnership with Allogen Laboratories allows a precision and granularity in matching donors (via methods such as maternally inherited compatibility antigens) that few other centers can match.

**Types of transplants performed**

(adult and pediatric), 2013

- Autologous, 124 (55%)
- RIC related, 10 (5%)
- RIC unrelated, 19 (10%)
- MAC related, 16 (8%)
- MAC unrelated, 12 (6%)
- MAC cord, 7 (4%)
- RIC cord, 3 (2%)

**2013 QUICK TAKE**

100-day survival rates of 97–99% for autologous transplants in 2012-2013

**100-day survival rates of 97–99% for autologous transplants in 2012-2013**
This team helped ensure the program’s three-year FACT accreditation award in 2013 for all services and facilities inspected, including:

- Adult and pediatric allogeneic and autologous hematopoietic progenitor cell transplantation
- Marrow and peripheral blood cellular therapy product collection
- Cellular therapy product processing with minimal manipulation

The program’s physicians are also supported by a cadre of transplant nurses, physician assistants, social workers who provide in-hospital and post-discharge psychosocial support, and transplant coordinators who ensure continuity of care across all treatment settings, including exceptional collaboration with community physicians before and after transplant. The program’s support services include a music therapy program (directed by a board-certified music therapist) that received approximately 100 referrals in 2013.

NEW PROGRAM DIRECTOR HAS DEEP ROOTS IN BMT RESEARCH

The new director of Cleveland Clinic’s BMT Program, Navneet Majhail, MD, MS, was recruited from the National Marrow Donor Program (NMDP), where he was Medical Director of Health Services Research, and the University of Minnesota, Minneapolis, where he was an adjunct associate professor of medicine. He also has served as Assistant Scientific Director with the Center for International Blood and Marrow Transplant Research (CIBMTR).

These roles with the NMDP and the CIBMTR have given Dr. Majhail deep experience in coordinating collaborative efforts among national and international BMT experts, which he will bring to bear for Cleveland Clinic.

“We have a strong program with a well-established research infrastructure,” says Dr. Majhail. “My aim is to build on that, mainly by broadening our portfolio of clinical trials and clinical research protocols. We will emphasize making care even more patient-centered. Cleveland Clinic is already on the forefront in that regard, and we are proud of our team-based, multidisciplinary approach to providing high-quality, cutting-edge patient care.”
Ambitious research portfolio

The program also has a robust and diverse clinical research component, demonstrated by its participation in 15 active clinical trials in 2013. These include the following important national collaborative studies:

**Blood and Marrow Transplant Clinical Trials Network (BMT CTN).** As a member of the Case Consortium, Cleveland Clinic serves as a core clinical trial site in this NIH-funded national cooperative group. Two clinical studies — the BMT CTN 0901 and 1101 trials — were open through the BMT program in 2013.

**Chronic Graft-vs.-Host Disease Consortium.** The program is an active member of this NIH-funded multicenter consortium that is investigating biology and novel therapies for the prevention and treatment of chronic graft-vs.-host disease.

**Center for International Blood and Marrow Transplant Research.** Cleveland Clinic participates in two studies through this national NIH-funded initiative:

- A multicenter trial of hematopoietic cell donor safety and quality of life
- A study of killer-cell immunoglobulin-like receptor (KIR) genotyping for unrelated donor selection prior to HCT for acute myeloid leukemia

**Pediatric Blood and Marrow Transplant Consortium.** The program’s pediatric component is part of a national phase 2 study of a conditioning regimen of treosulfan, fludarabine and low-dose total body irradiation for children with acute myeloid leukemia and myelodysplastic syndromes.

**Children’s Oncology Group (COG).** The program’s pediatric component is also an active member of this NIH-funded pediatric oncology group collaborative that is investigating novel therapies and supportive treatments in HCT.

**A collaboration with the Fred Hutchinson Cancer Research Center** on a national study of the use of low-dose total body irradiation and fludarabine with or without alemtuzumab for HCT in children with primary immunodeficiencies and other non-malignant inherited disorders.

The program also directed a number of active investigator-initiated clinical trials in 2013, including:

- A study of personalized monitoring of IV busulfan dosing for patients with lymphoma undergoing autologous stem cell transplantation
- An assessment of low-dose lenalidomide after nonmyeloablative allogeneic stem cell transplantation with bortezomib as prophylaxis against graft-vs.-host disease in high-risk multiple myeloma (see patient profile at right)
- A study of hematopoietic stem cell supermobilization in patients with lymphoma
- Several research projects focusing on psychosocial issues in transplant recipients

The program is likewise an active member of the CIBMTR’s international transplant outcomes registry, and many program staff physicians serve as principal investigators on registry studies.

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**JAMES (RANDY) McCoy:**

**FIRST ENROLLEE IN A TRIAL TO CURB GVHD AFTER TRANSPLANTATION FOR HIGH-RISK MULTIPLE MYELOMA**

As a pilot in the U.S. Air Force, 44-year-old Lt. Col. Randy McCoy is accustomed to high-stakes exploratory flights. Now the recipient of a recent stem cell transplant is helping medicine explore uncharted territory in the control of graft-vs.-host disease (GVHD) following treatment for high-risk multiple myeloma.

Late last year Randy underwent reduced-intensity allogeneic HCT at Cleveland Clinic and became the first patient enrolled in a trial to test the combination of two biologics for multiple myeloma — lenalidomide and bortezomib — for his high-risk form of the disease. A key study objective is to prevent GVHD after transplant by giving 90 days of therapy with standard GVHD prophylaxis using a bortezomib-containing regimen followed by maintenance therapy with lenalidomide.

The National Cancer Institute is serving as a collaborator with Cleveland Clinic on the study of this innovative approach, whose principal investigator is Cleveland Clinic hematologist-oncologist Hien Duong, MD.

Before the transplant, Randy had been on chemotherapy since April 2012 and was eager for the trial to gain FDA clearance. “I knew I was the first patient enrolled and could not wait to get started,” he says.

About four months after his transplant, the resident of central Ohio said he is doing well. “I just passed the 100-day mark without any acute GVHD issues, and I look forward to continued success.”
Progressive pediatric program

Cleveland Clinic has performed blood and marrow transplants in children since the mid-1970s, but its pediatric HCT offerings were invigorated with their formalization into a Pediatric Blood & Marrow Transplant Program in 2011 following the arrival of pediatric HCT specialist Rabi Hanna, MD, who serves as the program’s director.

Pediatric transplant volumes have grown steadily since then (see graph, p. 54), with eight HCT procedures performed in pediatric patients in 2013. Across the 19 primary pediatric transplants performed from 2011 through 2013, 100-day survival was 90 percent.

The pediatric program performs the full range of HCT procedures (autologous, allogeneic with myeloablative conditioning, allogeneic with reduced-intensity conditioning) and has led Cleveland Clinic’s efforts in haploidentical transplantation (see sidebar, opposite page), with participation in several multicenter trials of the procedure in children.

The program added a second pediatric HCT specialist physician in 2013 and expanded its team of dedicated specialized midlevel providers, who provide family-centered care on a 24/7 basis. Facilities include a dedicated pediatric inpatient unit and a pediatric outpatient infusion suite.

Inventive approaches to nonmalignant pediatric conditions

The pediatric program uses HCT protocols to treat a wide range of childhood cancers — leukemias and lymphomas, brain and spinal cord tumors, myelodysplastic and myeloproliferative diseases, and solid organ cancers — and has distinguished itself through the innovative application of HCT to a growing list of nonmalignant conditions including:

- Primary immunodeficiency disorders
- Bone marrow failure syndromes and hematologic disorders, such as sickle cell disease and thalassemia
- Inherited metabolic disorders, such as Hurler syndrome and various leukodystrophies
- Histiocytic disorders
- Other rare disorders, such as osteopetrosis

Young patients benefit from access to emerging therapies and research protocols through the program’s status as a designated Children’s Oncology Group transplant center and a Pediatric Blood and Marrow Transplant Consortium member as well as through its participation in national trial networks such as the BMT CTN (see “Ambitious research portfolio” above).
Ideally, patients in need of HCT can be matched with a sibling who has the same human leukocyte antigen (HLA) tissue type, as such transplants have the greatest chance for success. Yet only about one-third of candidates for allogeneic HCT have HLA-matched siblings.

Improvements in HLA typing have enabled the use of HLA-matched unrelated donors, but the chances of identifying such a match vary significantly by the recipient’s racial and ethnic background, with nearly one-third of minority patients unable to find a suitable unrelated donor.

Until recently, patients without an HLA-matched sibling or unrelated donor were limited to cells derived from umbilical cord blood or from an HLA-mismatched unrelated donor — and both these options carry a high risk of transplant-related mortality.

Enter haploidentical transplant

Cleveland Clinic is among a limited number of institutions that have begun offering patients another option: HLA-haploidentical HCT. Also known as a “half-matched” transplant, the procedure involves a donor who shares identity with the recipient for one HLA haplotype and is variably mismatched for HLA genes on the unshared haplotype.

Because every individual inherits one HLA haplotype from each parent and passes one haplotype to each child, any patient with a living biological parent or child has a potential HLA-haploidentical donor for HCT (see illustration).

The major advantage of haploidentical HCT is that it significantly broadens the donor pool and gives nearly all patients the chance to benefit from a transplant, including those with life-threatening nonmalignant disorders.

FUTURE OF TRANSPLANTATION: EXPANDING OPTIONS THROUGH HAPLOIDENTICAL TRANSPLANTATION

Schematic of a family study illustrating haplotype matching

Sibling 1 is the patient in need of an HCT. Sibling 2 shares 6/6 HLA genes and is considered fully matched with the patient. Siblings 3 and 4 each share only 3/6 HLA genes with the patient and are considered only half-matched, or one-haplotype matches. Sibling 5 does not share any HLA genes with the patient and is considered a mismatch. The patient could consider receiving stem cells from Sibling 2 (preferred, because she is a full match) or, thanks to haploidentical HCT, from Siblings 3 or 4 (haplotype matches) or one of his parents, who are also haplotype matches.

Haploidentical activity at Cleveland Clinic

In 2013, Cleveland Clinic’s BMT Program developed its own protocol using a myeloablative conditioning regimen to reduce relapse risk and improve survival in children and adults undergoing haploidentical HCT. The program also began offering haploidentical transplantation through its participation in multicenter clinical trials of the procedure.

The program continues to develop new haploidentical HCT protocols to individualize treatment choices based on patients’ particular disease, health status and comorbidities.
Performed first near-total face transplant in U.S.

One of the nation’s few centers with composite tissue transplant expertise
2013 was a historic year for vascularized composite allograft transplantation. In July, the U.S. government published a final decision in the Federal Register recognizing vascularized composite allografts as organs. As a result, effective July 3, 2014, allografts for face, hand and similar composite tissue transplants are for the first time allowed to be shared through the nationwide Organ Procurement and Transplantation Network (OPTN) system. This facilitates patient listing and graft procurement and promises an increase in the number of vascularized composite allotransplants performed.

That means more patients stand to benefit from the tremendous progress made over the past decade in addressing technical, logistical and social challenges in face and upper-extremity transplants and other types of reconstructive transplantation.

Cleveland Clinic has played a lead role in that progress, most notably by performing the first near-total face transplant in the U.S. in December 2008. Its Center for Reconstructive Transplantation continues to be a leading contributor to clinical and scientific progress in this field on the worldwide level.

Areas of expertise

Reconstructive transplantation is reserved for patients in whom conventional plastic and reconstructive surgery is unable to produce acceptable results. Potential patients are those who’ve suffered massive loss of complex combinations of tissue — including skin, subcutaneous tissue, neurovascular tissue, bone, muscle, fascia and cartilage — for whom prostheses are unavailable or insufficient for restoring physical integrity and function. The goal is to restore patients’ natural function, quality of life and ability to live independently.

Cleveland Clinic’s Center for Reconstructive Transplantation team consists of plastic and reconstructive surgeons as well as specialists in otolaryngology, neurology, transplant surgery, infectious disease, immunology, endocrinology, urology, anesthesiology and bioethics. This multidisciplinary team offers expertise in several key types of composite tissue transplantation:

**Face** — Face transplant requires exquisitely balanced attention to both form and function across parallel surgeries involving two teams of surgeons: one to remove
The federal government’s recognition of vascular composite allografts as organs means these allografts have been eligible for sharing through the Organ Procurement and Transplantation Network (OPTN) system as of July 2014.

In response, the United Network for Organ Sharing, which operates the nationwide OPTN system, formed a committee to develop national standards and policies for vascular composite allotransplantation.

Cleveland Clinic is likewise setting standards in scientific research in microsurgery and reconstructive transplantation. A few priority areas are profiled below.

**Tolerance induction.** A major focus of Cleveland Clinic research efforts is the induction of tolerance in composite tissue transplantation. Because of the diversity of tissues involved, composite tissue allografts are associated with more intense
rejection compared with vascularized organ grafts such as kidneys or livers. While several experimental designs of tolerance induction have been reported, side effects restrict their use to carefully selected applications.

Cleveland Clinic’s recent approaches to inducing tolerance center on the pivotal role of T cells in allograft rejection. These include exciting efforts to evaluate the role of marrow-derived stem and progenitor cells in tolerance induction following vascularized bone marrow transplantation. Cleveland Clinic staff published two important contributions related to tolerance induction in 2013, as profiled in two of the study summaries in the “future of transplantation” sidebar above.

Face transplant. In 2013 members of the Center for Reconstructive Transplantation reported results of a pathology review conducted four years after they performed the nation’s first near-total face transplant. This paper (Am J Transplant. 2013;13:2750-2764), one of the most comprehensive reports of its kind in the literature, demonstrated the need to correlate pathologic with clinical findings to monitor for rejection and the shortcomings of using histopathology as a sole monitor.

Another patient is now listed for face transplant at Cleveland Clinic, and the Center for Reconstructive Transplantation holds a Department of Defense-funded AFIRM grant (Armed Forces Institute of Regenerative Medicine) to study the clinical care of this patient (see sidebar).

Nerve regeneration. In addition to evaluating surgical techniques for enhancing nerve regeneration, Cleveland Clinic researchers are studying the effects of cyclosporin A on nerve degeneration and the effects of enhancing factors (e.g., DHEA and VEGF 165) on nerve regeneration in normal and diabetic rats.
PETER WILLIAMS: BACK ON HIS FEET AFTER BONE TRANSPLANT FOR LIMB SALVAGE FOLLOWING OSTEOSARCOMA

“I wasn’t that scared because the doctors put together a plan really fast.” So says 13-year-old Peter Williams of Cleveland Heights, Ohio, about the limb salvage surgery he recently underwent at Cleveland Clinic.

After an afternoon spent playing touch football with friends in 2012, Peter began experiencing pain in his leg and started limping. Diagnosed with osteosarcoma in his proximal tibia, Peter soon underwent surgery to remove the tumor and place a tibial allograft/allograft-prosthetic composite to salvage his leg.

The procedure involved two free flaps and close collaboration between Cleveland Clinic orthopaedic and plastic surgeons as well as pediatric oncologists. Peter is now disease-free and resumed walking four months after his surgery.

In addition to its distinctive vascularized composite tissue transplant program, Cleveland Clinic has long used bone and nonvascularized tissue segments in all types of surgical reconstruction — as well as corneal grafts in various corneal transplantation procedures.
NONVASCULARIZED TISSUE AND CORNEAL TRANSPLANTATION

Nonvascularized Tissue Transplantation

Multiple disciplines across 11 Cleveland Clinic institutes collectively used approximately 6,860 tissue or bone segments and tissue valves for various clinical applications in 2013 (see list at right for a breakdown of the major segment types). Among the most frequent clinical applications:

- Cardiothoracic surgery (valve replacement procedures)
- Orthopaedics and spine surgery (repair of joint and bone injuries/malignancies and cartilage defects; meniscal transplants)
- Vascular surgery (repair/reconstruction of weak or diseased blood vessels in various vascular conditions)
- Urology (urethroplasties, pubovaginal sling procedures, reinforcement of soft tissue after surgery, incontinence therapy)
- Colorectal surgery (specialized procedures such as repair of anal fistulas and ventral hernias)
- Plastic surgery (cosmetic procedures, reconstruction of craniofacial defects in children, wound coverage, reconstructive breast surgery)
- Dentistry (surgical repair of extraction sockets and periodontal defects, reinforcement of dental implants)

Cleveland Clinic’s Musculoskeletal Tissue Storage Facility is a model tissue management program that monitors the safety, availability and effectiveness of musculoskeletal tissue grafts. The program ensures full compliance with the standards and guidelines of The Joint Commission, the FDA and the American Association of Tissue Banks. Allograft donors are thoroughly screened via an in-depth medical history, and samples are rigorously tested for viruses and bacteria. All tissues are traceable from the donor or source facility through storage, preparation and use in the recipient.

Number of tissue and bone segments used in 2013, by major types:

- 2,200 valves or pericardial and vascular patches
- 93 homografts/veins
- 1,200 bones/bone segments/demineralized bone matrix products
- 410 skin segments
- 229 corneas/patch grafts
- 62 wound matrix grafts
- 2,436 other biologic segments

Initiated 1983
Approximately 6,860 tissue/bone segments and valves used in 2013
Corneal Transplantation

When the normally transparent cornea becomes distorted or clouded, corneal transplant surgeons in Cleveland Clinic’s Cole Eye Institute can intervene with a range of advanced procedures for the diverse conditions that may be the cause.

Cole Eye Institute surgeons performed 180 corneal transplant procedures in 2013. Less-invasive lamellar procedures — in which only the diseased portion of the cornea is replaced — continued to become an ever-larger part of their mix of interventions, representing nearly two-thirds of all procedures (see list at left).

Outcomes in 2013 were good with both lamellar and traditional methods:
- 98 percent of grafts remained clear at three to 12 months after the lamellar DSAEK procedure (Descemet stripping automated endothelial keratoplasty)
- 90 percent of grafts remained clear at three to 12 months after penetrating keratoplasty

Tailoring diverse procedures to patient needs

To meet diverse patient needs, the corneal transplant program offers a variety of procedures in addition to traditional penetrating keratoplasty:

**DSAEK.** Cole Eye Institute surgeons were among the first in the nation to perform DSAEK, which involves transplanting only the posterior side of the cornea in eyes with endothelial dysfunction. The result is greatly accelerated visual recovery, a reduction in surgically induced astigmatism and a smaller wound with less risk of complications. Institute surgeons have innovated several technique modifications to improve surgical outcomes. DSAEK is used for conditions such as pseudophakic bullous keratopathy and Fuchs endothelial dystrophy.

**Deep anterior lamellar keratoplasty.** This approach is used for corneal scars and keratoconus, in which the anterior cornea is replaced but the patient’s healthy endothelium is retained, eliminating the risk of endothelial rejection.

**Highly specialized procedures,** such as limbal stem cell transplantation and amniotic membrane grafting. These are performed in smaller numbers of patients for uncommon sight-threatening corneal conditions.

**Boston keratoprosthesis placement,** or implantation of a synthetic cornea. This approach is used in patients with end-stage corneal disease who are not candidates for other forms of transplant, allowing them to regain visual function.

---

**2013 corneal transplants by procedure type:**

- 115 lamellar procedures (less invasive; only diseased portion is replaced)
- 109 DSAEKs
- 6 lamellar keratoplasties
- 60 penetrating keratoplasties (traditional full-thickness procedures)
- 5 Boston keratoprosthesis (synthetic cornea) placements

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**Corneal Transplantation**

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Pervasive use of intraoperative OCT

Corneal transplant surgeons at Cole Eye Institute have integrated intraoperative optical coherence tomography (OCT) into their lamellar transplant surgeries on a broad scale, employing it for 50 cases in 2013 and 34 cases in 2012.

This imaging-guided surgical approach allows high-resolution visualization of the layers of corneal tissue, enabling enhanced and real-time visualization of graft placement, interface fluid and dissection depth. Examples of the benefits of intraoperative OCT in transplant procedures include:

• More accurate differentiation of corneal layers in DSAEK for Fuchs dystrophy, allowing selective replacement of endothelial cells and better adherence of donor tissue to the recipient cornea
• More precise visualization of depth during the initial dissection in deep anterior lamellar keratoplasty, yielding better success rates and potentially shorter procedure times

Cole Eye Institute surgeons are co-investigators in the comprehensive prospective PIONEER study of intraoperative OCT in a variety of applications.

FUTURE OF TRANSPLANTATION:
PATIENT-SPECIFIC 3-D MODELS TO GUIDE CUSTOMIZED TREATMENT

Fueled by a recent five-year, $2 million grant from the National Eye Institute and a major gift from Jim and Kathy Pender, Cleveland Clinic Cole Eye Institute researchers are working to develop patient-specific models to measure mechanical properties of the cornea in new ways — and to put that information to clinical use, including for potential transplant applications.

The goal is to use the models for simulation-based therapy that may lead to more customized treatments for conditions such as keratoconus and more optimal treatment of astigmatism and other refractive errors after corneal transplantation.

“We are developing tools to capture 3-D information about corneal material strength and incorporate it in a computerized structural representation of the eye,” explains principal investigator William J. Dupps Jr., MD, PhD, a cornea and refractive surgery specialist.

The hope is that combining corneal shape and material properties in 3-D models will help researchers better develop individualized procedures for correcting optical aberrations that limit vision in many transplant patients, particularly after penetrating or deep lamellar keratoplasty.

“Eyes that have undergone corneal transplantation are the most mechanically and optically complex eyes we care for,” says Dr. Dupps. “Conventional approaches to refractive surgery can help normalize vision, but outcomes are much more variable because most treatment paradigms assume the cornea has normal structural properties. We hope that by modeling an individual eye and running multiple simulations of possible corrective procedures, we can refine the treatment plan and suggest an optimized approach for that particular eye.”
One of the world’s few centers where a child can receive any type of transplant — all solid organ types, dual-organ, multivisceral, cellular or composite tissue
Two leaders, one vision

Cleveland Clinic is one of the world’s few medical centers where a child can receive any type of transplant — all solid organ types, dual-organ, multivisceral, cellular or composite tissue — under one roof.

The institution’s distinctive status in this regard was enhanced by the mid-2012 arrival of two key new leaders at Cleveland Clinic: Giovanni Piedimonte, MD, as Physician-in-Chief of Cleveland Clinic Children’s, and Kareem Abu-Elmagd, MD, PhD, as Director of Cleveland Clinic’s Transplant Center.

These two physicians’ near-simultaneous arrival was a happy coincidence for pediatric patients in need of transplantation. They soon discovered they share a vision and passion for building on Cleveland Clinic’s long, rich history in pediatric transplantation (see table, p. 71) by bringing that expertise to bear for far more young patients overall as well as for pediatric patients in evolving transplant fields, such as multivisceral procedures and composite tissue transplant.

The result was a dynamic year of developments in 2013:

- Key staff additions to further build and refine pediatric transplant-related capabilities
- New initiatives to deepen clinical and research collaboration and support between pediatric and adult-care transplant staff
- Cleveland Clinic’s first pediatric visceral transplant, which took place in a historic patient, the first known long-term survivor of a rare genetic syndrome (see patient profile, p. 37)

Additional developments are detailed in the program-specific profiles below, which are distilled from the pediatric subsections of the transplant program overviews from the preceding pages.
Any profile of Cleveland Clinic's specific pediatric transplant programs must start with a few words about Cleveland Clinic Children's and the special sensibilities and capabilities it brings to transplant care for the youngest of acutely ill patients.

Cleveland Clinic Children's is an integrated network for delivery of inpatient and outpatient pediatric services at more than 40 community locations across Northeast Ohio by more than 350 pediatric specialists and subspecialists.

Transplant patients are cared for at its inpatient unit on Cleveland Clinic's main campus, with 24/7 pediatric hospitalist staffing and extensive dedicated pediatric ancillary services. Among its distinctive offerings and capabilities are several of direct relevance to transplant patients, including:

- Cleveland Clinic Children's Hospital for Rehabilitation, one of only 13 accredited, freestanding rehabilitation hospitals in the U.S. serving pediatric patients exclusively (see sidebar)
- The Judith M. Power Center for Dialysis, a dedicated pediatric center offering on-site hemodialysis and home-based peritoneal dialysis

Cleveland Clinic Children's takes a medical-surgical team approach to transplantation. Child and adolescent patients are evaluated, supported and treated by an elite team of pediatric medical subspecialists and internationally renowned transplant surgeons as well as:

- Pediatric infectious disease specialists
- Pediatric immunologists
- Specialized pediatric nurses
- Pediatric parenteral nutrition experts
- Child psychologists
- Child life specialists
- Social workers
- Pediatric transplant pharmacists

Counseling and care for young patients and their families begin long before transplant and continue through vigilant follow-up for months and years afterward.

Cleveland Clinic Children's proud status as a "children's hospital within a hospital" offers a number of distinctive advantages in transplant care:

- Continuity-of-care benefits for transplant patients with congenital conditions for which smooth transition to adult care is a priority
- Deeper staffing of transplant surgeons compared with freestanding children's hospitals
- Sharing of perspectives, clinical advice and research ideas between adult-care and pediatric transplant specialists

CLEVELAND CLINIC CHILDREN’S HOSPITAL FOR REHABILITATION: UNIQUE ASSET FOR PROMOTING RECOVERY FROM TRANSPLANT

Young patients who require specialized rehabilitative and/or physical therapy following transplantation or placement of a mechanical circulatory assist device benefit from the comprehensive services of Cleveland Clinic Children’s Hospital for Rehabilitation.

The facility, located a few miles from Cleveland Clinic’s main campus, is one of only 13 accredited, freestanding pediatric rehabilitation hospitals in the nation. A formidable team of providers — physiatrists, therapists, psychologists and others, all specialized in pediatrics — offers inpatient and outpatient care through a diverse array of multidisciplinary programs and clinics.

Visit clevelandclinicchildrens.org/rehabhospital for more information.
These benefits have contributed to pediatric patient and graft survival rates that consistently match or exceed expected rates and national benchmarks.

**Kidney and pancreas transplant: 50 years of successful outcomes**

In the more than 50 years since Cleveland Clinic performed its first pediatric kidney transplant in April 1963 — one of the first successful pediatric transplants in the nation — the program has transplanted 363 kidneys in patients under age 21.

Cleveland Clinic has northern Ohio’s only pediatric kidney transplant program with a dedicated outpatient pediatric dialysis unit, located at Cleveland Clinic Children’s Hospital for Rehabilitation.

A team of kidney transplant surgeons with expertise in pediatric transplant is supported by a dedicated pediatric kidney transplant medical director, three additional pediatric transplant nephrologists and a growing team of pediatric urologists.

Their collaboration helps produce routinely positive outcomes in pediatric patients, including 100 percent one-year and three-year patient and graft survival rates in the most recent reporting period (January 2014 report of the Scientific Registry of Transplant Recipients [SRTR]).

The program also performs kidney-pancreas and isolated pancreas transplants in pediatric patients. Moreover, Cleveland Clinic’s pioneering work in pancreatic islet cell autotransplantation has benefited numerous adolescents who have undergone pancreatectomy for chronic pancreatitis (see p. 21), freeing them from a lifetime of caring for diabetes and its complications.

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**Cleveland Clinic’s pediatric transplant programs**

<table>
<thead>
<tr>
<th>Program</th>
<th>Launch date</th>
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<td>Kidney</td>
<td>1963</td>
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<td>Blood &amp; Marrow</td>
<td>1977</td>
<td>102</td>
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<tr>
<td>Heart</td>
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<td>133</td>
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<td>Heart-Lung</td>
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<td>Pancreas</td>
<td>1998</td>
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<td>Intestinal/Multivisceral</td>
<td>2013</td>
<td>1</td>
<td>Kadakkal Radhakrishnan, MD</td>
</tr>
<tr>
<td><strong>Total transplants</strong></td>
<td><strong>732</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Total solid organ transplants</strong></td>
<td><strong>630</strong></td>
<td></td>
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</tbody>
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*Through 2013, for patients under age 21

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**Quick Take**

100% one- and three-year patient and graft survival rates for pediatric kidney transplant
Liver transplant: Aggressive use of living-donor and split grafts

Cleveland Clinic’s pediatric liver transplant program is one of the most experienced in the nation, dating back to 1985. The program, managed by a pediatric liver transplant medical director with a team of three more pediatric hepatologists, offers a full range of liver transplant options for children:

• Partial grafts from living donors
• Whole-organ and split-liver transplants from deceased donors (including donation after cardiac death)
• Liver transplant in the context of multivisceral transplantation

These living-donor and split-liver capabilities facilitate the use of smaller grafts in children’s small bodies, increasing transplant opportunities — and often slashing wait times — for pediatric patients in need (see patient profile, p. 29). Approximately half of the pediatric liver transplants at Cleveland Clinic from 2005 through 2013 involved split livers from deceased donors or partial livers from living donors.

Pediatric liver transplant outcomes are consistently strong, with 100 percent three-year patient and graft survival rates in the January 2014 SRTR report.

Intestinal/multivisceral transplant: Making pediatrics a priority

Cleveland Clinic performed its first visceral transplant in a pediatric patient in 2013 (involving intestine, duodenum, liver and pancreas; see patient profile, p. 37) and is one of just a handful of U.S. centers that offer intestinal/multivisceral transplantation for children.

With the world’s leading visceral transplant surgeon, Kareem Abu-Elmagd, MD, PhD, now directing its intestinal/multivisceral transplant program (see p. 35), Cleveland Clinic is poised to perform increasing numbers of pediatric visceral transplants to address previously unmet needs in this population. In fact, as of mid-2014, another pediatric multivisceral transplant had been performed and at least two more children were listed for multivisceral transplant.

Appropriate candidates for pediatric visceral transplant include children with short bowel syndrome, congenital anomalies, necrotizing enterocolitis, intestinal atresia, midgut volvulus, gastrochisis and motility disorders.

Cleveland Clinic’s pediatric visceral transplant services are highly integrated with Cleveland Clinic Children’s exceptional Pediatric Intestinal Rehabilitation Program and Pediatric Nutrition Program to ensure a comprehensive overall treatment approach and expert pre- and post-transplant care.

When transplant is not an option or not absolutely necessary, Dr. Abu-Elmagd and his team can offer young patients with intestinal failure a range of innovative surgical procedures for autologous intestinal reconstruction (see p. 34).
Heart transplant: Established program turns increasingly to LVADs

Cleveland Clinic performed its first successful pediatric heart transplant in March 1985 and has since built one of the nation’s premier pediatric programs, with 140 hearts transplanted through 2013 (including seven heart-lung transplants). Nearly 75 pediatric heart transplant recipients are still being followed.

The pediatric program has a low operative mortality rate and patient and graft survival rates that routinely meet or exceed national benchmarks and expected rates. It numbers among the few programs that can perform dual-organ heart transplants — including the lung, liver or kidney — in children.

Two pediatric heart transplant surgeons and a pediatric transplant cardiologist make up the program’s core physician team. Transplanted patients are followed closely by the pediatric transplant cardiologist — often well into adulthood, thanks to a shared clinic in the Center for Adult Congenital Heart Disease where adult patients can be seen by both an adult-care congenital disease specialist and their longtime pediatric cardiologist.

The team does all it can to medically manage failing pediatric hearts and forestall transplant when possible, as few donor hearts last beyond 20 years. This is achieved through intricate medication-based therapy and increasingly with left ventricular assist devices (LVADs), which are used in this setting to make patients strong enough to undergo transplant and buy time until a donor heart becomes available.

Charlie McMicken was diagnosed with dilated cardiomyopathy four weeks after birth and was in heart failure as a young infant. Sickness was all Charlie had ever known when Cleveland Clinic Children’s transplant cardiologist Gerard Boyle, MD, first met him. “I knew heart transplant was in his future,” Dr. Boyle says of the boy from Auburn Township, Ohio.

Dr. Boyle and his Cleveland Clinic Children’s colleagues worked hard to manage Charlie medically to strengthen his heart, but at around age 3 Charlie suffered a stroke and began a rapid decline that required moving in to Cleveland Clinic Children’s. “He was shutting down and starting to die,” says his mother, Sarah McMicken.

To keep Charlie going until a donor heart became available, the pediatric cardiology team implanted Charlie with a Berlin Heart Excor LVAD in February 2012. He then progressed back “to almost normal,” say his nurses, whom Charlie regaled with tales of superheroes as he walked the hospital grounds hooked up to the device’s giant external box on wheels.

Despite a significant risk of stroke from the LVAD, Charlie made it safely through five months on the device until a pediatric donor heart surfaced and he was successfully transplanted by pediatric transplant surgeon Robert Stewart, MD. He went home 17 days later and has fared well since, continuing physical and occupational therapy sessions at Cleveland Clinic Children’s Hospital for Rehabilitation to strengthen his left arm and leg. Today Charlie is “a happy, energetic boy who gets into everything,” says his mom. “Cleveland Clinic has saved our son’s life four times. They were like family to us. But it’s a beautiful thing to be home and have our life back to normal.”
Cleveland Clinic placed its first Berlin Heart Excor® LVAD in a child in 2010 under a compassionate-use protocol prior to the device’s FDA approval. Through 2013, the program had bridged four pediatric patients to transplant using the Berlin Heart Excor without any pump-related major complications (see patient profile, previous page). The program’s willingness to use the device as soon as in early infancy requires meticulous management to perfect anticoagulation and avoid infections.

Other LVADs, including the HeartWare® and HeartMate® II devices, are used in older pediatric patients.

**Lung transplant: Enhanced offerings for an underserved population**

Fewer than 100 pediatric lung transplants are performed worldwide, and only a few centers perform them. Cleveland Clinic is among those centers, having completed 25 lung transplants and seven heart-lung transplants (see patient profile) in the pediatric population since 1991. It is one of the world’s only centers offering bronchial artery revascularization (BAR procedure) for pediatric patients undergoing lung transplant.

Cleveland Clinic is now looking to build its volume and expertise in this underserved clinical area with the 2013 arrival of its first dedicated medical director for pediatric lung transplant, Nathan Kraynack, MD, an expert in pediatric cystic fibrosis. Dr. Kraynack is leveraging his background in the medical management of pediatric lung transplant recipients to better position Cleveland Clinic to offer transplant as an option to more children with end-stage lung disorders.

The result is a newly formalized pediatric lung transplant program combining the deep experience of Cleveland Clinic’s lung and heart-lung transplant surgeons with the expertise of Cleveland Clinic Children’s five pediatric pulmonologists, who are skilled in the care of children with conditions such as:

- Cystic fibrosis
- Pulmonary hypertension
- Childhood interstitial lung disease
- Genetic disorders of surfactant dysfunction

The program is drawing on this collective expertise to make the critical judgment in most pediatric lung transplant decisions: pinpointing the time when the young patient is sick enough to require transplantation yet still well enough to tolerate the surgery.

**Blood and marrow transplant: Innovating novel therapy applications**

Cleveland Clinic has performed blood and marrow transplants (i.e., hematopoietic cell transplants [HCTs]) in children since the mid-1970s, with over 100 such transplants performed through 2013. Its pediatric HCT offerings were invigorated with their formalization into a Pediatric Blood & Marrow Transplant Program in 2011 upon the arrival of pediatric HCT specialist Rabi Hanna, MD, as the program’s director.

Transplant volumes have grown steadily since, with eight HCT procedures performed in pediatric patients in 2013. Across the 19 primary pediatric HCT procedures performed from 2011 through 2013, 100-day survival was 90 percent.
The pediatric program marked another milestone in 2013 by receiving three-year accreditation from the Foundation for the Accreditation of Cellular Therapy (FACT) for all services and facilities inspected.

The program performs the full range of HCT procedures (autologous, allogeneic with myeloablative conditioning, allogeneic with reduced-intensity conditioning) and has led Cleveland Clinic’s efforts in haploidentical transplantation (see p. 59), with participation in several multicenter trials of the procedure in children.

The program added a second pediatric HCT specialist physician in 2013 and expanded its team of specialized midlevel providers, who provide family-centered care on a 24/7 basis. Facilities include a dedicated pediatric inpatient unit and a pediatric outpatient infusion suite.

The program uses HCT protocols to treat a wide range of childhood cancers — leukemias and lymphomas, brain and spinal cord tumors, myelodysplastic and myeloproliferative diseases, and solid organ cancers. It also distinguishes itself through the innovative application of HCT to a growing list of nonmalignant conditions including:

- Primary immunodeficiency disorders
- Bone marrow failure syndromes and hematologic disorders (e.g., sickle cell disease, thalassemia)
- Inherited metabolic disorders (e.g., Hurler syndrome, various leukodystrophies)
- Histiocytic disorders
- Other rare disorders, such as osteopetrosis

Young patients benefit from access to emerging therapies and research protocols through the program’s status as a designated Children’s Oncology Group transplant center and a Pediatric Blood and Marrow Transplant Consortium member as well as through its participation in national trial networks.

**Additional pediatric transplant offerings**

**Corneal transplant.** Many children are among the recipients of the nearly 200 corneal transplants performed each year by surgeons in Cleveland Clinic’s Cole Eye Institute and Department of Pediatric Ophthalmology.

**Nonvascularized tissue transplant.** Multiple disciplines across Cleveland Clinic Children’s regularly utilize bone and soft tissue during surgical reconstruction. The tissue segments come from Cleveland Clinic’s extensive tissue storage bank. Frequent applications in pediatrics include bone transplant in orthopaedics, sports medicine and spine surgery, as well as soft tissue transplant in plastic surgery following trauma.

**Composite tissue transplant.** Center for Reconstructive Transplantation Director Francis Papay, MD, specializes in pediatrics as well as adult care, as do other members of the center’s team. The team is fully prepared to accept children and adolescents for listing for face, hand or other composite allograft transplantation.

Began offering haploidentical transplantation to expand donor options for pediatric blood and marrow transplant candidates
Histocompatibility and Immunology Testing

Allogen Laboratories is a full-service, 24/7 histocompatibility and transplant immunology lab accredited by the American Society for Histocompatibility and Immunogenetics (ASHI) in all clinical areas and all testing technologies.

The lab performs a wide range of high-complexity testing to guide transplantation-related clinical decisions. As a wholly owned subsidiary of Cleveland Clinic, it serves all Cleveland Clinic institutes and centers and functions as a reference lab for external healthcare organizations worldwide.

Established in 1968, Allogen Laboratories was one of the first tissue typing laboratories in the U.S. and remains one of the largest today.

Allogen Laboratories performed more than 70,000 tests on samples from potential transplant recipients and donors in 2013 to determine compatibility of blood and tissue types as well as the presence of potential rejection-causing antibodies. The lab’s services are used in evaluations for solid-organ, tissue and hematopoietic stem cell transplantation.

The lab uses and develops cutting-edge technologies such as next-generation sequencing. It is likewise actively engaged in translational research that is supported by extramural funds from organizations including:

- National Institutes of Health
- National Marrow Donor Program
- American Cancer Society
- Roche Organ Transplantation Research Foundation

In addition, Allogen Laboratories supports training of medical students, residents and fellows from many training programs at Cleveland Clinic and other institutions.
Infection Prevention and Management

The Section of Transplant Infectious Disease, part of the Department of Infectious Disease, provides expert consultation for Cleveland Clinic’s various transplant teams, guidance for post-transplant infection prevention and specialized clinical care if an infection should develop. At least one member of the section serves on each transplant team, playing an integral part in the success of the team and its patients’ outcomes.

Deep staffing, broad scope

The section brings together 10 infectious disease physicians (including one who specializes in pediatric infectious disease) and a transplant infectious disease fellow to offer transplant recipients the following:

- Pretransplant evaluations
- Expert management of infectious complications following blood/marrow, solid organ or tissue transplantation
- Post-transplant evaluations and reimmunization (when indicated)

These specialists provide expertise in a wide variety of infection-related challenges that can arise in the setting of transplantation, including:

- Infection with cytomegalovirus
- Fungal infections
- Respiratory viral infections
- Infections with MRSA
- Mycobacterial infections
- Parasitic infections
- Transplantation in HIV-infected individuals, which requires meticulous management of antiretroviral and other antimicrobial agents with close attention to interactions with immunosuppressive agents. Three HIV-infected patients received transplants in 2013 (two kidney and one multivisceral).

In 2013, the section’s specialists saw transplant patients at 999 outpatient visits and 1,396 inpatient consultations. A specialized infectious disease team rounds on both the solid organ and the blood and marrow transplant units at least five days a week, and team members are available for consultations on weekends.
The section developed a detailed document in 2013 to guide clinicians in assessing the risk of infection transmission from deceased organ donors. A section member is available to address such questions 24/7.

What transplant recipients can expect

Transplant recipients can expect the following care related to infection prevention and treatment:

- Pretransplant evaluation for prior infections that could impact the post-transplant course
- Thorough pretransplant efforts to treat past infections (as needed), update vaccinations and design individualized programs for post-transplant infection prevention
- Close monitoring for cytomegalovirus, Epstein-Barr virus and BK virus infections following transplant to enable early treatment, if needed
- Rapid outpatient access if symptoms suggestive of infection develop after transplant
- Scheduled outpatient visits following blood or marrow transplant for reimmunization against preventable infections
- Ready access to Cleveland Clinic’s International Travel Health Clinic to help ensure safe international travel

Leadership in research

Members of the Section of Transplant Infectious Disease are primary investigators for several multicenter studies of investigational agents, providing patients ready access to therapies in development.

Section members also collaborate with the transplant teams on other leading-edge research studies in areas ranging from genetic and immune markers for predicting post-transplant infection risk (e.g., killer cell immunoglobulin-like receptors and use of the QuantiFERON®-CMV assay) to the safety and effectiveness of vaccination in transplant recipients.

Several section members participated in authoring the third edition of the American Society of Transplantation’s Infectious Diseases guidelines, published in March 2013 as an American Journal of Transplantation supplement.

Consistent with this academic focus, the section offers one of only six U.S. fellowship training programs focused on transplant infectious disease.

3 HIV-infected individuals underwent transplants
Dedicated Bioethics Expertise

Each transplant program team includes a dedicated clinical ethicist from the Cleveland Clinic Bioethics Department to ensure that the need to rescue critically ill patients is balanced with optimal use of scarce organs and other transplant resources.

This approach makes each team's "embedded" ethicist intimately familiar with the clinical and psychosocial issues specific to the screening process for a given transplant type, enabling the ethicist to offer highly valued and clinically relevant input.

As a result, the whole team thinks more proactively about ethical questions from the start of a potential transplant case and the quality of the transplant program improves.

Involvement of clinical ethicists is especially critical to Cleveland Clinic’s growing use of living-donor organs in its kidney and liver transplant programs, where ethical perspectives can help ensure proper balancing of donor safety and recipient need. All living liver donors and many living kidney donors meet with an ethics consultant during the screening process.

Cleveland Clinic’s leadership in transplant-related bioethics is demonstrated by its new Transplant Ethics Fellowship (see p. 9), which was launched in 2013 as the only such fellowship in the U.S.

Transplant Ethics Fellowship created in 2013, the only such fellowship in the U.S.

Inpatient Rehabilitation That Goes Beyond Physical Needs

The transition from hospital to home is a critical period for transplant recipients, a fact that’s never lost on the caregivers in Cleveland Clinic Rehabilitation Hospital. The main campus rehabilitation hospital is one of the nation’s few such units that specialize in transplant rehabilitation, with a clear recognition of the central role rehabilitation plays in ultimate transplant outcomes.

Beyond offering expertise in the core physical rehabilitation component of management — i.e., rehabilitation nursing and physical and occupational therapy — the unit is uniquely designed to accommodate transplant patients in the following ways:

• Through tailored education programming and training of patient and family by therapists and nurses who specialize in transplant rehabilitation.

• Through proximity to and collaboration with Cleveland Clinic’s transplant physicians and staff, who are on-site throughout the patient’s stay.
• Through a keen sensitivity to the need to build confidence among transplant patients that they can sustain good health at home. Building this confidence and reassurance is just as important as restoring physical strength and stamina; the unit’s staff has developed expertise in helping patients move beyond perceptions of themselves as being “sick” and back toward empowerment.

**Care Continuity Through Center for Connected Care**

Transplant recipients often require post-hospitalization services. Cleveland Clinic’s Center for Connected Care keeps patients connected to the highest-quality care as they transition from the hospital to home or to a post-acute facility.

The Center for Connected Care’s interdisciplinary home care teams provide skilled care from nurses, therapists, pharmacists, medical social workers, nurse practitioners and physicians. The center also offers a complete range of specialized nursing services, including wound and cardiac care.

Patients transitioning to selected community skilled nursing facilities can be seen by Center for Connected Care physicians and nurse practitioners five days a week, with the goal of improving patient outcomes and avoiding the need for readmission. All care is provided using the same electronic medical record as was used in the hospital, ensuring that all providers are kept informed of the patient’s progress.

**Comprehensive Bone Health Assessment**

Changes in bone health can develop rapidly in transplant recipients, potentially leading to osteoporosis with resulting fractures, debility and death. Anti-rejection immunosuppressants can be a major contributor to low bone mass, but factors present before transplant can play a role as well.

Patients undergoing transplant at Cleveland Clinic typically visit the Center for Osteoporosis and Metabolic Bone Disease in the Department of Rheumatic and Immunologic Diseases prior to their transplant and as needed thereafter to optimize their bone health. This includes a visit shortly after the transplant to ensure patients are on a good bone health program, as bone mass can decline rapidly in the first year after transplant. The priority of the center’s osteoporosis specialists is to maintain transplant recipients’ quality of life in light of the threat that bone mass changes can pose in this population.
Genetic Counseling

Cleveland Clinic’s Genomic Medicine Institute offers comprehensive genetic testing and counseling to patients whose need for transplant may stem from a genetic condition — and to their family members, as needed.

The institute’s team of genetic experts helps patients determine whether genetic testing is appropriate for themselves or family members and offers education about specific inherited conditions, associated health risks and inheritance patterns. They and the transplant team work closely with patients’ primary physicians to develop a care plan as well as a plan for potential family evaluation when genetic risk factors may be at play.

Transplant Dermatology Clinic for Skin Cancer Education and Detection

Skin cancer is the most common malignancy among organ transplant recipients, as ongoing immunosuppressive therapy increases the risk of its development. Organ recipients tend to develop multiple skin cancers and tend to have more aggressive skin malignancies with higher rates of recurrence and metastasis compared with the general population.

In 2011, Cleveland Clinic’s Dermatology & Plastic Surgery Institute established a multidisciplinary Transplant Dermatology Clinic to serve solid organ transplant recipients in light of their high skin cancer risk. Patients are offered education and risk assessments with individualized follow-up intervals. Hundreds of pretransplant and post-transplant skin evaluations are performed by the clinic each year. When cancers are diagnosed, they are managed with a range of surgical interventions as well as systemic and topical chemoprevention and photodynamic therapy.

> 1,390 patients seen and > 560 tumors treated by Transplant Dermatology Clinic since 2011
**Bedside-to-Bedside Transfers Via Critical Care Transport**

The most critically ill transplant candidates benefit from the expert services of Cleveland Clinic’s Critical Care Transport team, which responds to urgent and routine transfer requests 24 hours a day, 365 days a year.

The team is made up of Cleveland Clinic physicians, nurse practitioners, critical care nurses and paramedics who are specially trained for care delivery in the transport environment. Their ability to initiate tertiary care during transfer can improve outcomes for critically ill patients ranging in age from neonates to elderly adults. Patients in extreme conditions can be accommodated, such as those requiring cardiopulmonary bypass or mechanical hearts.

Transfers are available by:

- Ground, via dedicated mobile ICU vehicles
- Helicopter, within a 250-mile radius of Cleveland
- Fixed-wing aircraft for domestic or international transport

Cleveland Clinic’s Critical Care Transport team has transported patients from more than 40 states and over 20 countries, and routinely transfers more than 4,500 patients a year. For more information, visit clevelandclinic.org/cct.

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**THANK YOU**

The Cleveland Clinic Transplant Center thanks its donation and procurement partners and agencies:

**Lifebanc** — As Northeast Ohio’s federally designated nonprofit organ procurement organization, Lifebanc works with more than 80 hospitals to increase organ and tissue donations. 888.558.LIFE (5433) or lifebanc.org

**National Marrow Donor Program** — The NMDP is a nonprofit organization that manages the world’s largest registry of volunteer stem cell donors and cord blood units, facilitating lifesaving blood and marrow stem cell transplants. 800.MARROW2 or marrow.org

**Cleveland Minority Organ & Tissue Transplant Education Program** — This nonprofit organization works to increase awareness about organ and tissue donation through education and advocacy within minority communities in the Cleveland area. 216.229.2690 or clevelandmottep.org

**Cleveland Eye Bank** — The nonprofit Cleveland Eye Bank retrieves, evaluates and distributes donated eyes for use in corneal transplantation as well as research and teaching. It serves nearly 5 million people and 60 hospitals in the region surrounding Cleveland. 216.844.EYES or clevelandeyebank.org
**INFORMATION FOR PHYSICIANS**

**Transplant Referrals**

- **Cleveland**
  - 800.223.2273, ext. 42394, or 216.444.2394
- **Weston, Florida**
  - 954.659.5133
- **Charleston, West Virginia**
  - 304.388.7823
- **Indianapolis**
  - 317.338.6701
- **Hospital Transfers**
  - 800.553.5056

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- [LinkedIn](#)

**Physician Directory**

View our staff online at [clevelandclinic.org/staff](http://clevelandclinic.org/staff).

**Same-Day Appointments**

Cleveland Clinic offers same-day appointments to help your patients get the care they need, right away. Have your patients call our same-day appointment line, 216.444.CARE (2273) or 800.223.CARE (2273).

**Track Your Patients’ Care Online**

Establish a secure online DrConnect account for real-time information about your patients’ treatment at Cleveland Clinic at [clevelandclinic.org/drconnect](http://clevelandclinic.org/drconnect).

**Critical Care Transport Worldwide**

To arrange a critical care transfer, call 216.448.7000 or 866.547.1467. For STEMI (ST elevated myocardial infarction), acute stroke, ICH (intracerebral hemorrhage), SAH (subacute hemorrhage) or aortic syndrome transfers, call 877.379.CODE (2633). Learn more at [clevelandclinic.org/criticalcaretransport](http://clevelandclinic.org/criticalcaretransport).

**Outcomes Data**

View Outcomes books at [clevelandclinic.org/outcomes](http://clevelandclinic.org/outcomes).

**Consult QD Blog for Healthcare Professionals**

Discover the latest research insights, innovations, treatment trends and more at [consultqd.org](http://consultqd.org).

**CME Opportunities: Live and Online**

Visit [ccfcme.org](http://ccfcme.org) to learn about the Cleveland Clinic Center for Continuing Education’s convenient, complimentary learning opportunities.

**Executive Education**

Learn about our Executive Visitors’ Program and two-week Samson Global Leadership Academy immersion program at [clevelandclinic.org/executiveeducation](http://clevelandclinic.org/executiveeducation).

**Physician Referral App**

Contacting us is easier than ever. With our free Physician Referral App, you can view all our specialists, transfer a patient and get in touch immediately with one click of your iPhone®, iPad®, or Android™ phone or tablet. Download today at the App Store or Google Play.

**Cancer Clinical Trials App**

Get the latest on Cleveland Clinic cancer trials with our free mobile app, available from the App Store or Google Play.
Join us when Cleveland hosts the 2016 Transplant Games of America — and see the difference a transplant can make.

transplantgamesofamerica.org

About Cleveland Clinic

Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,000 physicians and researchers represent 120 medical specialties and subspecialties. We are a nonprofit academic medical center with a main campus, eight community hospitals, more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City and Cleveland Clinic Abu Dhabi.

In 2014, Cleveland Clinic was ranked one of America’s top 4 hospitals in U.S. News & World Report’s “Best Hospitals” survey. The survey ranks Cleveland Clinic among the nation’s top 10 hospitals in 13 specialty areas, and the top in heart care (for the 20th consecutive year) and urologic care.