

WORLD LEADERS IN TRANSPLANTATION

Ajmera Transplant Centre

Through groundbreaking research and highly innovative procedures, the Centre is giving more people a second chance at life.





Transforming lives



ORGAN TRANSPLANTATION is a miracle of modern medicine. It has the power to change people's lives in a way that is truly transformative. Needing a transplant may feel like one of those things that will never happen to you or someone you love, but for the thousands of Canadians on the waiting list for an organ, it's all too real. Vital organs fail. The damage is irreversible. A transplant becomes someone's only hope for survival.

More than 3,000 transplant procedures are performed in Canada each year – but the number of people who could benefit is much higher. The Ajmera Transplant Centre at University Health Network in Toronto is one of the largest and most successful transplant programs in North America, leading the way in clinical care and research, as well as training surgeons, physicians, health professionals and researchers from around the world.

Our exceptional team looks after more than 7,000 patients from more than 550 communities across Canada – people with kidney failure, liver disease, diabetes, lung disease, heart failure and more who are

in need of, or have received, a life-saving transplant.

With a multidisciplinary team of surgeons, physicians, nurses, scientists and many others, we are leading groundbreaking research to improve the availability of organs for transplant and to keep patients well and safe after their transplant. Some of our advances include using cutting-edge technologies to assess and repair organs outside the body; pushing the boundaries of living organ donation; and leading the response to COVID-19 in transplantation, including a first-in-the-world randomized trial proving the benefit of third-dose booster vaccines in transplant recipients.

In these pages you will read about just some of the extraordinary people who make the Ajmera Transplant Centre what it is, a team driven like no other, and patients who have received – or provided – the remarkable and transformative gift of life. I hope their stories will inspire you.

Atul Humar, MD, M.Sc., FRCPC
 Director, Ajmera Transplant Centre
 R. Fraser Elliott Chair in Transplantation Research

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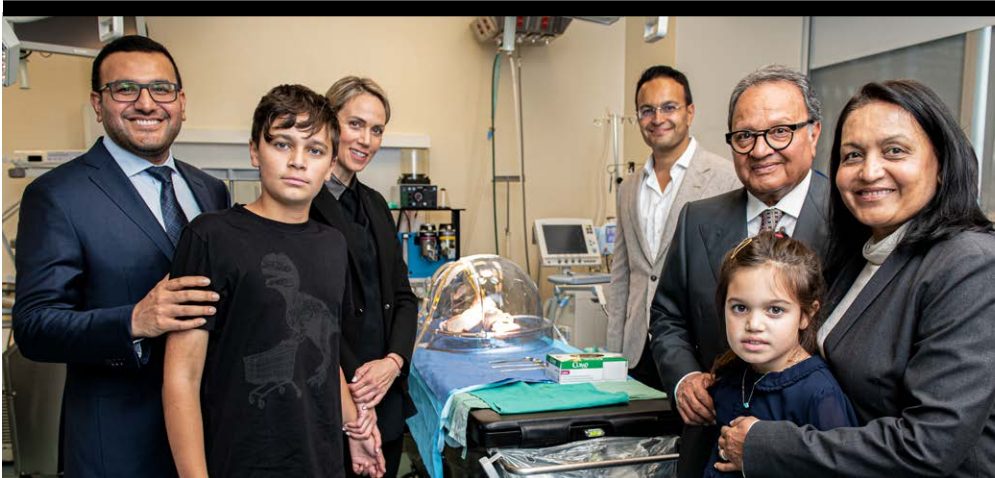
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We want to hear from you! Let us know what you think: publications@uhn.ca

the Waiting room



Sam Ajmera (centre right) and his family stand with an Ex Vivo System at the Ajmera Transplant Centre.

Bringing transplants to life

Big medical breakthroughs are on the horizon, and UHN is where the next great innovations will occur.

BY BRYAN BORZYKOWSKI

Organ transplantation stands out as one of the most significant healthcare innovations of the modern era, with much of the groundbreaking transplant work taking place at the Ajmera Transplant Centre at University Health Network (UHN).

Every year, the Centre's world-renowned team performs often-complex transplants – liver, kidney, heart, lung, pancreas and more – and provides lifelong care to more than 7,000 transplant recipients across the country.

Sam Ajmera, a longtime food entrepreneur who founded FGF Brands in 2004 with his two sons, Ojus and Tejus, generously donated to support the world-leading transplant centre because he was inspired by both its international excellence and its top-notch team. **"To have our family's name associated with such incredible and dedicated people is an honour,"** says Ajmera.

The Centre is growing three key areas of research: repairing, regenerating and building new organs; developing new treatments that can help the body's own immune system fight

disease; and transforming diabetes treatment. Philanthropy, says Dr. Atul Humar, Director of the Ajmera Transplant Centre and the R. Fraser Elliott Chair in Transplantation Research, "will help us build on our momentum of game-changing world firsts and accelerate transplant medicine." ■

A top centre for transplantation

1983

World's first successful single-lung transplant

1990

Canada's first multi-organ transplant

2000

Living Donor Liver Transplant Program created

2008

World's first successful Ex Vivo organ repair transplant

2011

World's first intraoperative stem cell transplant for heart regeneration

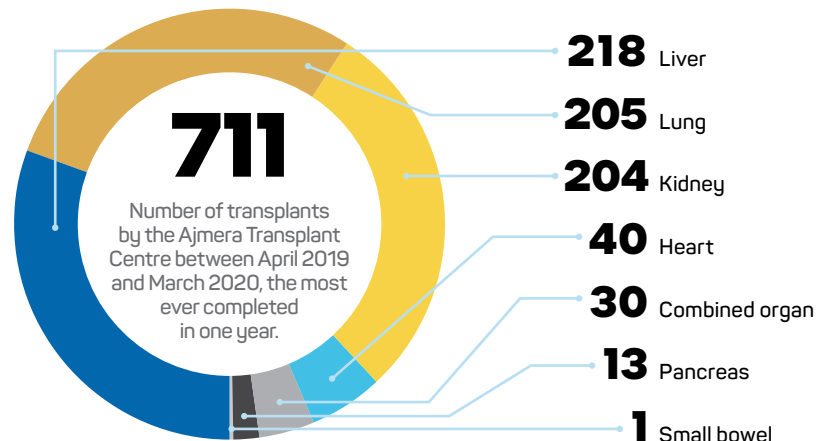
2017

North America's first Ex Vivo kidney transplant

2021

First randomized trial showing third-dose vaccines protect immunosuppressed patients against COVID-19

PHOTO: COURTESY OF ANDREW DOWNS



How transplants work



1. Transplant recipient is called in for surgery.



2. Organ is removed from the donor in the OR.



3. Organ is placed in cold storage for transport.



4. Organ is transplanted into recipient.



5. Lifelong transplant care begins.

The transplant power couple

Drs. Deepali Kumar and Atul Humar conducted COVID-19 transplant research that's been adopted worldwide – and earned them major recognition.



“Our study showed that a third dose of the vaccine significantly boosts immunity in transplant recipients.”

DR. DEEPAI KUMAR

WHILE THE PANDEMIC raged out of control and put the world into lockdown, the Ajmera Transplant Centre’s husband-and-wife team, Dr. Atul Humar, Director of the Centre and the R. Fraser Elliott Chair in Transplantation Research, and Dr. Deepali Kumar, Director of Transplant Infectious Diseases at the Centre and President-Elect of the American Society of Transplantation, was spending countless hours at work trying to keep transplant patients safe from COVID-19.

Over the past year and a half, Drs. Humar and Kumar have developed several innovations and initiatives, all of which have had a global impact on transplant recipients. One major accomplishment – and a world first – was the completion of a randomized placebo-controlled trial of third-dose COVID-19 booster vaccines for these patients, who are especially vulnerable to COVID-19 due to the immunosuppressive medication they need to take. The results, which were published in mid-August in the *New England Journal of Medicine*, showed the third dose dramatically improved protection against COVID-19. Transplant patients had substantially more antibodies that could neutralize the virus and T-cells that could prevent severe COVID-19. This had an immediate impact on transplant patients with the Parenteral Drug Association, a global organization that provides education to the pharmaceutical community, recommending a third dose for this population.

Earlier in the pandemic, the two physicians, who have been married for more than 20 years, developed a donor organ screening and testing tool, which allowed organ transplantation to occur safely in Ontario, and were integral in developing Canadian guidelines. They created a COVID-19 screening questionnaire to guide clinicians

FROM LEFT: DRs. ATUL HUMAR and DEEPAI KUMAR are working to keep transplant patients safe during COVID-19.



who receive organ offers about the status of that organ.

The couple also created guidelines to help clinicians around the world determine how to prioritize transplant operations based on the severity of COVID-19 in their region and the impact the pandemic is having on local healthcare systems. The guidance provided an early framework for safely carrying on transplantation in the midst of a pandemic, including suggestions on ramping transplant activity down, and then back up, in response to surges and waves. This protocol was quickly adopted by many centres.

If that wasn’t enough, they also wrote the Canadian Society of Transplantation guidelines for COVID-19 vaccinations in organ transplant patients – such as when the best time may be to vaccinate a patient and how to prioritize them for vaccines. In Canada, initial guidance was that transplant patients should not receive the vaccine, but Drs. Humar and Kumar advocated strongly for this population. “There was hesitancy about vaccinating transplant patients because there was no data,” Dr. Kumar explains. “But we knew from 20 years of experience studying vaccines that this vaccine was

likely to be safe and should be given.”

When Drs. Humar and Kumar aren’t busy helping people, they are receiving accolades. Last winter, they earned the Transplantation Champion Award from the Trillium Gift of Life Network (TGLN) for their groundbreaking work. It’s one of the most prestigious transplant-related honours; TGLN, the organization that coordinates organ and tissue donations and transplantation in Ontario, has given out this award just seven times before. “It’s an honour to get this award and to share it with somebody who you can bounce ideas off of without actually setting up a formal meeting,” Dr. Kumar jokes. “Our offices are beside each other, so when we’re at work, we’re always walking into each other’s offices.”

Drs. Humar and Kumar are formidable transplant researchers in their own right, but together they’ve proven to be an unstoppable force. Both credit each other, their marriage and their three children for where they are today and for making monumental strides for the Ajmera Transplant Centre during the pandemic. “It helps that the two of us could support each other and work on ideas and really get through this together,” Dr. Humar says. ■



20%

Percentage of transplants in Canada that are performed at the Ajmera Transplant Centre.

SOURCE: UHN



“The whole team, from UHN corporately to our individual teams and programs, was focused on mitigating the risk for patients.”

NIKKI MARKS

NIKKI MARKS helped create a dedicated team to care for transplant patients who contracted COVID-19 and needed hospitalization.

First line of defence

COVID-19 presented a new level of danger for transplant patients. Fortunately, the Ajmera Transplant Centre’s team was already working on ways to minimize the risk of infection.

AS NIKKI MARKS and her colleagues watched the pandemic unfold in early 2020, her immediate worry was not about her own health but about the fate of her current and future patients. “Our big concern was how we could continue to do transplants and provide the safest care to patients who already had transplants,” recalls Marks, a nurse practitioner with the Ajmera Transplant Centre at University Health Network (UHN).

The challenge with organ transplant surgery is that it isn’t a one-and-done operation – post-operative care usually extends for a lifetime. Nurses and clinicians need to monitor a patient’s body for organ rejection and keep an eye on the side effects of

the immunosuppressive medications they’re required to take. What’s worse, because of those drugs, transplant patients are more susceptible to catching infectious diseases, so COVID-19 posed an entirely new level of danger. “The whole team, from UHN corporately all the way down to our individual teams and programs, was very focused on trying to mitigate the risk for patients,” Marks says.

Fortunately, just before the pandemic hit, Marks was part of a team piloting an app with video conferencing technology to help nurse practitioners and clinicians monitor their lung transplant patients remotely. The app also allows patients to text questions to their care team and receive

personalized or generic messages – a useful resource when there were changes in care due to the pandemic. Patients sent information to their team about things like their lung function, temperature, blood pressure, weight and oxygen saturation either every day or every week, depending on the length of time since their surgery. They also received a separate survey, a kind of cue from the physiotherapy department, asking if they were ready to do their exercise for the day and then giving them their routine. Finally, they could enter metrics like their heart rate and their oxygen saturation before and after exercising.

The project, which involved nurses, physiotherapists and physicians, was initially intended for 20 patients across a number of surgical programs, but Marks’ team rapidly enrolled around 300 additional patients between March and early April 2020, as the COVID-19 pandemic ramped up. “We just switched gears and enrolled as many people as we could,” she says. “Being able to pivot like that was a very important strategy, but also it was important that we had access to that technology.”

As well, Marks was part of a secondary group that created a remote COVID-19 clinic made up of UHN team members from across different programs. These experts could monitor patients who tested positive for COVID-19 at UHN. This project became known as Connected COVID Care. There was a documentation app that guided physicians and nurse practitioners, based on the best evidence for monitoring and treating patients with COVID-19. They would also use algorithms to decide if saturation monitors – which assess oxygen saturation levels in the blood – needed to be sent to their homes.

Marks didn’t stop there: along with many nurse practitioners and physicians, she volunteered to be part of a specific team that cared for admitted transplant patients who had COVID-19. “There’s been so much collaboration with different hospital systems and programs, with public health and with the different teams across the hospital,” she notes. “It’s been such a great experience, coming together and bringing our expertise from across different specialties.” ■

300+

Number of patients enrolled in the Ajmera Transplant Centre’s remote care program between March and early April 2020, as the COVID-19 crisis ramped up.

SOURCE: UHN



JARRETT SINGER
is back in school and
cancer free thanks to the
liver transplant he received
from **NADINE YOUNG**, his
organ donor.

Transplanting hope

The Ajmera Transplant Centre's transplant oncology program is giving cancer patients a second chance.

BY ANNA SHARRATT

N 2018 Jarrett Singer, a fit 18-year-old hockey player, had his whole life in front of him. He started his first year of university in September, taking classes to become a nutritionist. In November of that year his appetite suddenly disappeared and he constantly felt lethargic, sleeping in until 3 p.m. Gradually, severe abdominal pain set in. "It got to the point that I contemplated going to the hospital instead of my final exam," he recalls.

In December, still in extreme pain, Singer saw his family physician in Whitby, Ont., who immediately ordered an ultrasound. The results stunned everyone. They showed a 12-centimetre mass on his liver, which was a fibrolamellar hepatocellular carcinoma, a rare form of liver cancer that kills between 32 and 66 per cent of those diagnosed within five years. Singer reeled from the news, having just started a new chapter of his life. "I was shocked," he says. "You never think it's something that can happen to you."

Singer was referred to the Ajmera Transplant Centre at University Health Network (UHN) and placed under the care of Dr. Gonzalo Sapisochin, transplant surgeon at the Centre and part of the Sprott Department of Surgery at UHN, who was confident he could help him. He and his team initially thought they could just remove the cancerous part of his liver when they performed exploratory surgery in early 2019. Then they saw the tumour had wrapped itself around the blood vessels going into the liver, including the bile duct, a thin tube that carries bile, a liquid that helps digest fats in food, from the liver and gallbladder into the small intestine.

Singer's only hope was a liver transplant, which historically has been a non-starter, since implanting a new organ into someone who has cancer carries the risk that the disease will end up attacking that new tissue. The Ajmera Transplant Centre, however, is world

DR. GONZALO SAPISOCHIN performed a liver transplant on cancer patient Jarrett Singer, giving him a new lease on life.

renowned for this type of procedure. It performs 40 per cent of the cancer-related transplants in Canada.

Cancer-fighting transplants

One of the challenges of doing oncology-related transplants is that recipients have to take medications that suppress their immune systems so they won't reject the organ. But these medications also reduce the body's ability to fight off cancer cells. Ajmera Transplant Centre researchers, however, have discovered ways to adjust medications and use chemotherapy in advance of a transplant to ensure operations are successful. "In the last decade, the outcomes of these transplants have really improved," says Dr. Sapisochin.

It's helped that the Ajmera Transplant Centre is a pioneer in living donor transplants, which is when clinicians use an organ – such as a liver or a



Collaboration is key at the Ajmera Transplant Centre.

57

Physicians
and surgeons

+

395

Health
professionals

+

148

Researchers
and scientists

+

32

Fellows
and trainees

632

Total team members

kidney – from someone who is living versus someone who is deceased. Living donor transplants dramatically increase the availability of organs, which means more cancer-related procedures can get done. The Centre conducts about 70 transplants involving living donors every year, with around 30 to 40 per cent of them in liver cancer patients. “We are one of the largest programs in the world doing this,” notes Dr. Sapisochin.

INSTILLING HOPE

It was a living donor who ultimately saved Singer’s life. When it became clear he required a transplant, his firefighter father put out the word in his workplace that his son needed a liver donor. Nadine Young, a 38-year-old firefighter who worked in the same fire hall as Singer’s father but barely knew him, answered the call. She offered up a piece of her liver, in part because, as a parent to a two-year-old girl, she could understand the Singer family’s pain.

Fortunately, Young was a blood and tissue match. She was scared but excited to be selected as a donor. While she was in perfect health, she was also aware of the possible complications: a blood clot or, in extremely rare cases, death. She underwent blood work and psychological testing to determine her readiness, and MRIs and CT scans to assess the health of her liver. When she met Singer, though, she knew she was making the right decision. “I would do it all again in a heartbeat,” she says.

Singer, who had undergone chemotherapy to shrink the tumour ahead of surgery, was incredibly grateful. “It was a special day to see the person who was going to save my life,” he says.

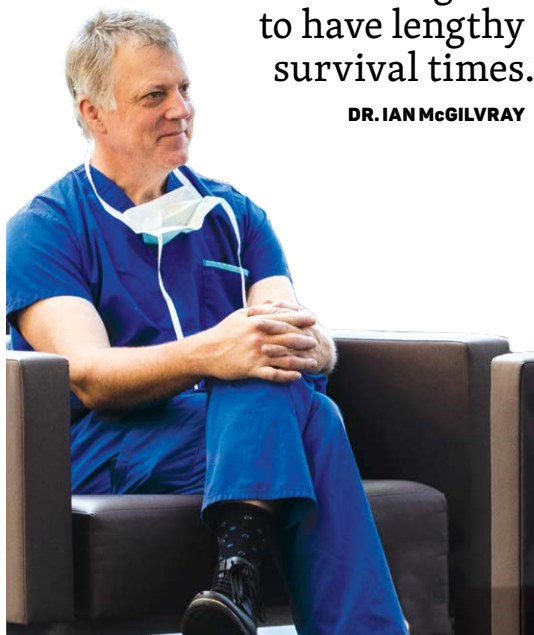
The surgery took more than eight hours and involved removing the right lobe of Young’s liver, which was used to replace Singer’s diseased liver. Young, who was left with a small scar, says her liver regrew after a month and she was back to work after three months. As for Singer, he’s had a smooth recovery and his new liver has been accepted by his body. Best of all? He’s now cancer-free.

NEW OPPORTUNITIES

While stories like Singer’s are becoming more common, clinicians and

“[Post-transplant] some colorectal cancer patients with liver tumours go on to have lengthy survival times.”

DR. IAN MCGILVRAY



researchers are looking at other opportunities in transplant oncology. Dr. Marcelo Cypel, Surgical Director of the Ajmera Transplant Centre, is currently exploring how transplantation can help patients with lung cancers.

Physicians have traditionally done these kinds of procedures on those with early-stage lung cancers, but Dr. Cypel and his team are exploring whether lung transplants can help patients with end-stage lung disease and lung cancer, too. “We are doing this more for patients with lung cancer in the context of other lung diseases, like emphysema,” says Dr. Cypel, who is also part of the Sprott Department of Surgery at UHN, adding that those with lung disease typically can’t have surgery because of a high risk of post-operative complications.

A transplant, though, can prolong a patient’s survival dramatically, says Dr. Cypel. “Most of these patients wouldn’t survive a year if left untreated,” he explains. “If you get a transplant, you have a 65 per cent chance of being alive in five years.”

Colon cancer that has metastasized to the liver and bile duct cancer

“Most of these patients wouldn’t survive a year if left untreated.”

DR. MARCELO CYPEL



are two other malignancies for which surgeons are testing out transplantation. While most of these procedures are currently being done in clinical trials, there have been three colon cancer procedures and one bile duct cancer transplant at UHN, says Dr. Ian McGilvray, abdominal transplant surgeon and scientist in the Ajmera Transplant Centre and Head of Liver and Pancreas Surgery in the Sprott Department of Surgery at UHN. “Some colorectal cancer patients with liver tumours go on to have lengthy survival times,” notes Dr. McGilvray. “There are patients who are alive 10 years after colorectal metastasis,” adds Dr. Sapisochin.

There’s still much work to be done before these transplants become part of standard care. UHN’s immunologists and medical oncologists are trying to determine more ways to modulate immunosuppressive drugs to ensure they don’t suppress the immune system too much, which could then cause cancer cells to grow, explains Dr. McGilvray. Researchers are also exploring ways of preparing the immune system prior to transplantation to attack cancerous tumours and leave the new organ intact.

It won’t be long, though, before doctors treat different types of cancer with transplantation. That’s good news for people like Singer, who initially worried about how his cancer would be treated. He is now 21 and back in school, receiving scans every six months to confirm his cancer hasn’t come back. To date, all is well, but even if his liver cancer recurs, Dr. Sapisochin says surgeons will likely be able to go in and surgically remove any tumours.

Singer encourages people to consider becoming living organ donors.

“We have a shortage of deceased donors,” he notes. “If you’re willing to do it, you can be a true hero for someone else.”

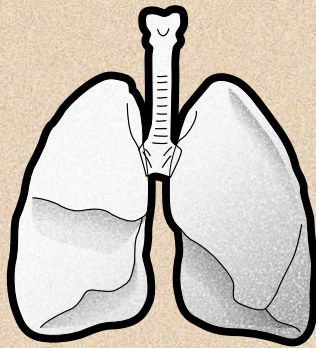
As for Young, she treasures a necklace Singer gave her just before the transplant operation. On it is inscribed, “We needed a miracle. Instead, we got an angel.”

“I never take it off,” she says. ■

BUILDING BETTER ORGANS

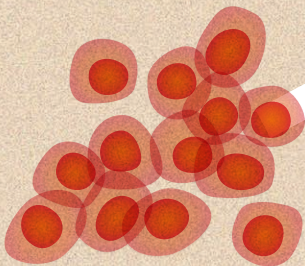
Ajmera Transplant Centre researchers are trying to fill the organ donation gap by creating kidneys, livers and lungs from human cells.

BY CLAIRE GAGNÉ



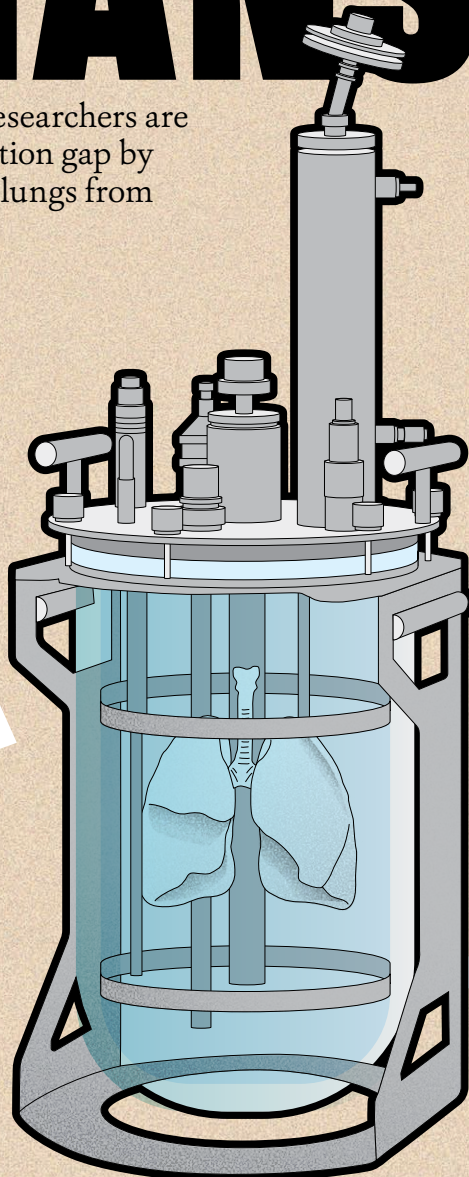
1. Decellularized organ

Cells are stripped from a non-human organ, leaving a scaffold.



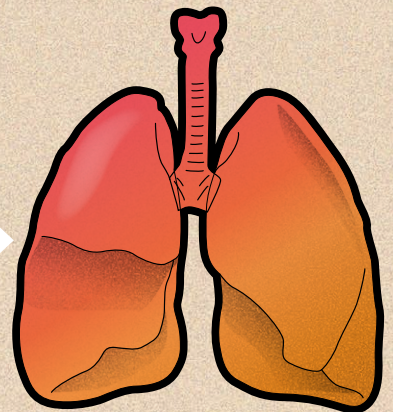
2. Patient cells

In the bioreactor, human cells are put on the scaffold where they repopulate.



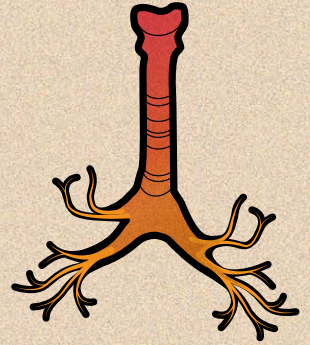
3. Bioreactor

A chamber that can grow organs under controlled conditions.



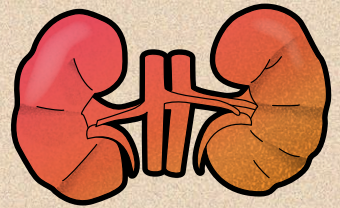
4. New organ

New organs that will one day end up inside the human body are grown in the bioreactor.



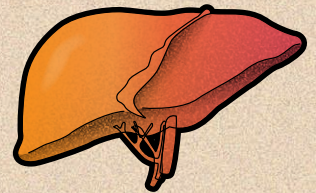
Tracheae

Researchers have repopulated a non-human trachea with human cells.



Kidneys

Two rebuilt kidneys lasted 15 minutes in an Ex Vivo System.



Livers

Researchers are trying to build liver cells out of stem cells.



EVER SINCE the first successful transplant was completed in 1954, patients in need of new organs have had to wait – sometimes for years – to receive an organ from either a deceased

or, more recently, a living donor. But what if clinicians could make one for you, potentially out of your own cells, so you wouldn't have to wait? It sounds wild, but it could be a reality in the not-so-distant future thanks to researchers at the Ajmera Transplant Centre who are at the forefront of this groundbreaking organ-building research.

Developing new kidneys

Clinicians at the Ajmera Transplant Centre have been trying to find ways to make organs from scratch. It's been a long, painstaking process, but one organ that's seen some significant progress is the kidney, in part because it's the organ in highest demand for transplantation. According to the Canadian Institute for Health Information (CIHI), as of December 31, 2019, 76 per cent of the 4,352 people waiting for an organ transplant in Canada were waiting for a kidney.

Dr. Markus Selzner, Surgical Director of

the Liver Transplant Program and scientist at the Ajmera Transplant Centre, is working with stem cell researcher Dr. Ian Rogers, who, several years ago, put out what he calls an "audacious" challenge to his lab team to build a kidney. "There wasn't any technology at the time to suggest this was even possible," he says.

The first step was to figure out how to grow kidney cells, which they did by using what are called induced pluripotent stem cells – stem cells that have been reprogrammed from adult cells and can regenerate to become any kind of cell. "Now I can take cells from people's skin or urine and put them in a dish and make them into kidney cells," says Dr. Selzner, who is also part of the Sprott Department of Surgery at University Health Network (UHN).

Next was figuring out how to take cells in a petri dish and turn them into kidneys – a feat that appeared more feasible after they discovered another researcher had figured out how to strip all the cells from a non-human organ, leaving only the protein framework, called a scaffold, behind. Researchers can then put human cells in this scaffold, where those cells can repopulate. "The human cells are quite happy sitting on this framework," says Dr. Rogers. Dr. Selzner explains it this way: "You would have a hybrid kind of kidney, but the portion of it that the recipient's

body would touch would be entirely human."

Now the team is fine-tuning the kidney-building process by experimenting with different ways of putting human stem cells into the kidney framework and encouraging them to repopulate in a bioreactor, a chamber that can grow organs under controlled conditions. So far they've been able to put two rebuilt kidneys in an Ex Vivo Organ Perfusion System – a device that allows an organ to live outside a human body for several hours – developed by Dr. Selzner. While the rebuilt kidneys only survived for 15 minutes in the Ex Vivo System, the process yielded valuable insights. "It allowed us to ask, 'What went wrong?'" says Dr. Rogers. Bioengineered kidneys aren't far off. "In five to 10 years, we will have something that can be tested in humans," says Dr. Selzner.

Recreating livers

The liver is another organ in high demand, with 610 liver transplants taking place in Canada in 2019 – the second-most out of any organ, according to the CIHI. The process to build a new liver is similar to the kidney, but researchers were one big step behind when they started: they didn't know what cells made up the liver, so they couldn't begin to rebuild it. "The liver is complicated," says Dr. Ian McGilvray, abdominal transplant surgeon

PHOTO: COURTESY OF REGINA GARCIA (DR. WADDELL)

LEADERS IN ORGAN BIOENGINEERING

"In five to 10 years, we'll have something that can be tested in patients."

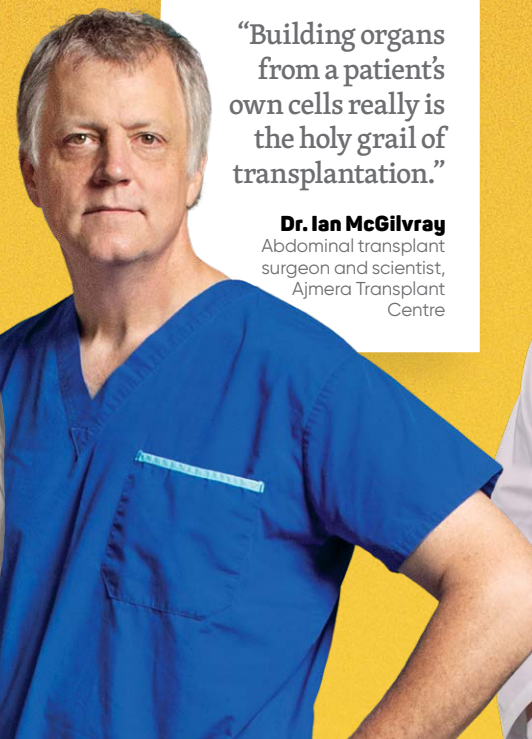
Dr. Markus Selzner
Surgical Director, Liver Transplant Program, Ajmera Transplant Centre



Dr. Ian Rogers
Affiliate scientist, Ajmera Transplant Centre

"Building organs from a patient's own cells really is the holy grail of transplantation."

Dr. Ian McGilvray
Abdominal transplant surgeon and scientist, Ajmera Transplant Centre



and scientist in the Ajmera Transplant Centre and the Head of Liver and Pancreas Surgery in the Sprott Department of Surgery at UHN.

Huge strides were made when, in 2018, Dr. McGilvray, together with Dr. Sonya MacParland, an Ajmera Transplant Centre scientist, published a map of the human liver using a new technology at the time – single-cell RNA sequencing – to look at the individual cells that make up the liver. “Previously, we were able to map out the average of all the cells in the liver, but we couldn’t do it at an individual level,” explains Dr. MacParland. Key to getting this data was a change Dr. McGilvray made about 10 years ago in how surgeons at the Centre do liver transplants so that they now routinely remove an unneeded portion of the liver in order to study it immediately.

Now that they know what cells to grow, another colleague, Ajmera Transplant Centre scientist Dr. Shinichiro Ogawa, is working in the lab to build liver cells out of stem cells. It’s a daunting task. “An individual has 120 to 150 billion liver hepatocyte cells, which make up 80 per cent of the liver,” says Dr. Ogawa, who is also part of the McEwen Stem Cell Institute at UHN.

The next step is to see if diseased livers in animal models can be fixed using these new healthy liver cells made in the lab. “If you

could infuse cells into the scaffolding and have them stick and regenerate, then you might be able to recreate the liver,” explains Dr. McGilvray, who is also working on ways to rebuild a human liver in its entirety.

Growing lungs and tracheae

While kidneys and livers may be the most needed organs, Ajmera Transplant Centre researchers also want to either build or regenerate lungs and tracheae – the latter being the tube that carries air from your throat to your lungs. Once again, they would take a trachea or lung from non-human samples, get rid of all the cellular material that would cause an immune response and then grow new cells over the existing structure, says Dr. Golnaz Karoubi, scientist at the Ajmera Transplant Centre.

So far, researchers have repopulated a non-human trachea with human cells. “The lung is more complicated,” Dr. Karoubi says. “There are more than 40 different cell types within that organ.” Her main challenge is figuring out how to efficiently get the various cells into the lung structure and encourage them to repopulate in such a way that they create an organ that can perform gas exchange. To do this, “we’re looking at how physical forces, like gravity and movement, affect cellular behaviour,” explains Dr. Tom

Waddell, a lung transplant surgeon and scientist with the Ajmera Transplant Centre and the Richard and Heather Thomson Chair in Thoracic Translational Research. “Which genes do they turn on? What chemicals do they secrete? And, to some extent, what shape does the cell adopt?”

Dr. Waddell, who is also part of the Sprott Department of Surgery at UHN, is working on ways to acquire the cells in the first place, adding that while induced pluripotent stem cell technology is useful, it’s expensive. “I’m looking at taking lung cells and only partially reprogramming them,” he says. Instead of turning cells into stem cells, scientists would harvest lung cells that would stay lung cells.

Another approach is to have what’s called universal designer donor cells, where the cell is modified so the immune system doesn’t reject it. The ultimate goal is to have a surgically transplantable lung that does not require immunosuppression.

The possibility of made-to-order organs would completely transform patient care for people with organ failure. “There’s a chronic organ shortage, and as a result, regardless of what organ we’re talking about, there is significant attrition on the wait list because people die waiting,” explains Dr. McGilvray. “Building organs from a patient’s own cells really is the holy grail of transplantation.” ■



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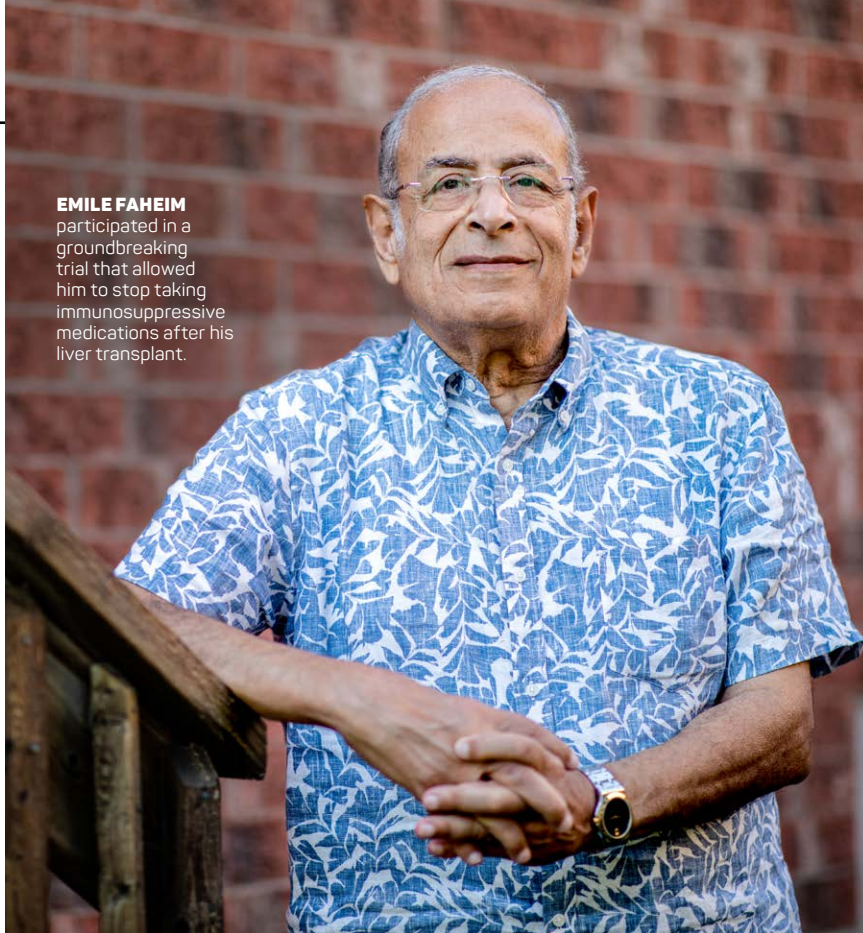
TOLERANCE

The end of rejection

The body doesn't always accept new organs after a transplant. Drs. Sarah Crome and Stephen Juvet hope to change that.

BY GLYNIS RATCLIFFE

EMILE FAHEIM participated in a groundbreaking trial that allowed him to stop taking immunosuppressive medications after his liver transplant.



WHEN EGYPTIAN-BORN Emile Faheim came to Canada in 1990 with his wife and three daughters, he thought he was perfectly healthy. But in 1994, the regional director for a fire safety company went for routine blood work and the results showed something strange: he had elevated liver enzymes in his blood. He had hepatitis C, a viral infection that can cause significant liver damage. "It was shocking, because I felt fine," he says.

Faheim had no idea how he contracted this disease. About 75 per cent of those infected develop chronic hepatitis C, which stays in the body and progresses silently for years or even decades before finally being identified during routine blood work – exactly how Faheim's infection was discovered.

Medications helped keep his liver inflammation under control, but then the drugs stopped working. His body began to deteriorate, with fluid accumulating first in his midsection and later in his lungs, requiring regular trips to the hospital. In 2009, Faheim was placed on a list to receive a liver transplant. In 2013, he received the call from the Ajmera Transplant Centre at University Health Network (UHN): they had found a liver for him. It was in his body the next day. "It was a miracle, truly," Faheim says.

As excited as he was to have a new liver, Faheim wasn't out of the woods yet; his body needed to accept the new organ as its own and he had to ensure his hepatitis C wouldn't

get worse. For the latter, he took a drug called Sovaldi, a "magic cure," he says, that was first trialled by Dr. Jordan Feld, Co-Director of the Schwartz Reisman Liver Research Centre and the R. Phelan Chair in Translational Liver Research at UHN. After three months of treatment the hepatitis C disappeared.

Having his body accept his new liver was

"The central idea of tolerance is about getting T-cells, a type of white blood cell that is part of the immune system, to not respond, despite seeing this foreign organ in the body."

DR. STEPHEN JUVET

Deputy Research Director,
Ajmera Transplant Centre



a bigger challenge. One thing all transplant patients have in common is the potential for the body to reject the new organ. Most have to take strong medications for the rest of their lives to prevent the body from attacking its new addition. The medications can come with serious side effects. For Faheim, they caused his blood pressure to rise and his blood sugar to become unstable. This resulted in him having to take more medications.

Thankfully, Faheim went on to participate in a trial that may make onerous post-operative drug regimens a thing of the past.

Learning not to attack

When the immune system encounters something it doesn't recognize in the body, it mounts a battle to destroy that foreign agent – whether it's an organ, a virus or even a splinter. It's how our bodies fight disease, but it becomes a problem when the foreign object being attacked was placed there to save that person's life.

The immunosuppressive drugs transplant recipients take to prevent the body from rejecting the new organ are toxic medications that don't always work long term, says Dr. Stephen Juvet, Deputy Research Director of the Ajmera Transplant Centre.

With anti-rejection medication, patients can experience high blood pressure, fatigue, decreased blood cell counts, intestinal upset and high cholesterol, among other side effects.

Scientists at the Centre are focused on finding ways to help the body better accept organs.

Dr. Juvet is just one of the clinician-scientists at the Ajmera Transplant Centre who are on the case. He oversees groundbreaking work on immune tolerance, working with all organ types. His other main focus is understanding the mechanisms of chronic lung allograft rejection, or why lungs can continue to be rejected well after they are transplanted into a patient. He wants to find ways physicians can intervene earlier in the chronic rejection process, which is more of a long-term issue. "People think of a transplant as sort of a cure, but it's not that," says Dr. Juvet, noting that a person's new organs don't last forever and other treatment options may be required.

Lungs have the highest rate of rejection, with a 55 per cent patient survival rate at five years post-transplant. Dr. Juvet believes some instances of rejection have to do with the early inflammation that happens at the time of surgery, what's known as ischemia reperfusion injury. This happens when an organ is removed from the donor and put on ice or in cold storage during transportation. As the organ is rewarmed and filled with the recipient's blood, the resulting inflammation may contribute to acute (within the first year) or chronic (long-term) rejection. But another reason is because the lungs are constantly exposed, through the airways, to inflammation triggers like air pollution in the external environment and acid reflux. In both cases, inflammation is the key driver of transplant rejection.

"The central idea of tolerance is about getting T-cells, a type of white blood cell that is part of the immune system, to not respond, despite seeing this foreign organ in the body," Dr. Juvet explains.

A LITMUS test

To help get people off immunosuppressants, Dr. Juvet is overseeing an ongoing clinical trial for liver transplant patients called the

Liver Immune Tolerance Marker Utilization Study (LITMUS).

The trial, which ultimately freed Faheim from the drug regimen he was taking post-transplant, began in 2015 and was created by principal researcher Dr. Gary Levy, former Director of what is now the Ajmera Transplant Centre, who worked on immune tolerance research for years at UHN. Faheim was one of 60 patients the LITMUS research team approached to see if he would be willing to try a controlled weaning off his anti-rejection drugs, after a blood test confirmed the presence of a tolerance biomarker that Dr. Levy had previously identified. That biomarker, which could be a game-changer but needs more study, indicates which transplant patients may be able to stop taking those drugs altogether.

Another scientist pursuing new immune tolerance strategies is Dr. Sarah Crome, a fundamental research scientist with the Ajmera Transplant Centre. Fundamental science aims to understand the underlying basis of disease or health. "My lab is focused on defining how your immune system decides when and when not to attack," explains Dr. Crome. "So, what are the cellular and molecular processes that control immune response?"

A new type of partnership

Dr. Crome uses patient samples wherever possible, because it brings her closer to understanding the mechanisms of disease. She works alongside UHN clinicians for this reason. "We sit together, and they'll say this is the clinical presentation, this is the problem we're having, this is how the disease is manifesting," she says. "And then I take that to the lab and ask, 'Is there something we can find that explains what is observed clinically?'"

This is what led Dr. Crome to look closer at the cells in tissue biopsies from different organs. It turns out that the cells in organ tissues are very different from those in



DR. SARAH CROME wants to know how and why immune systems attack when they do.

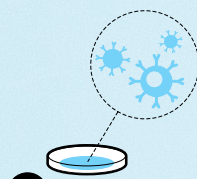
circulation in the blood, with specialized functions that may affect immune tolerance. "If we can identify the cells that are responsible for starting that rejection reaction," she explains, "or understand specific molecules that trigger rejection or prevent it, we could devise new immunotherapy approaches that are more specific and more targeted than general immunosuppression."

The hope is that more transplant recipients will be identified as having higher tolerance biomarkers, moving beyond liver transplant patients like Faheim to potentially include other organs. It would certainly improve many people's quality of life.

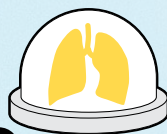
"Now I've had four or five years without any anti-rejection medication," Faheim says. "The doctors call me from time to time to do tests, and my blood sugar and my blood pressure are normal. My liver is like new. It is another miracle." ■

T-CELLS TO THE RESCUE

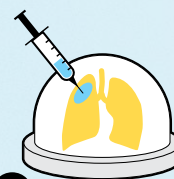
Dr. Stephen Juvet and his team are putting regulatory T-cells, which can block the harmful effects of other T-cells, into donor lungs to see whether they interfere with the process of rejection. The results are promising. Here's how it works.



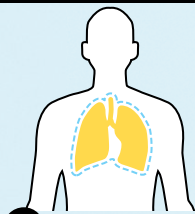
1 Regulatory T-cells are isolated from the recipient's blood, expanded in culture and frozen until needed.



2 Donor lungs are placed on the Ex Vivo Lung Perfusion System, where they're kept at body temperature and continue to "breathe" for several hours.



3 Regulatory T-cells are thawed and infused into the blood vessels of donor lungs, while still on the System.



4 After transplant, the recipient's regulatory T-cells enter their body through the donor lungs, where they can start controlling the rejection response.



ERIC CELENTANO

is more active than ever thanks to the Ex Vivo System-treated lungs he received at the Ajmera Transplant Centre.



IMPROVING THE ODDS

How the Ajmera Transplant Centre's powerful Ex Vivo devices can make damaged organs new again.

BY DIANE PETERS

ERIC CELENTANO thought the pesky pain in his shoulder that began in summer 2012 was from playing golf, his favourite sport. He figured some physiotherapy would fix the issue, or, at worst, he'd need to take a few weeks off. But instead, X-rays of his shoulder revealed something far more troubling than tendonitis: a serious lung condition called idiopathic pulmonary fibrosis (IPF). "I was selling respiratory equipment, so I knew what was going on when I received the diagnosis," recalls Celentano, who's now 64. "But I was scared of what was to come."

He knew that IPF – a progressive disease that causes the lungs to become scarred and stiff over time – could kill him and that his only chance of survival was getting a double-lung transplant.

Celentano's lungs did gradually become worse, and eventually the antifibrotic medication he was on wasn't helping anymore. "By the summer of 2018 I couldn't swing a golf club or even walk up the stairs," he recalls. Celentano needed oxygen whenever he exerted himself, which was depressing for someone used to being busy and active.

In the fall of 2018, with his health in serious decline, a pair of lungs became available. Celentano was prepped for surgery at Toronto General Hospital. However, his surgeon, Dr. Marcelo Cypel, Surgical Director of the Ajmera Transplant Centre at University Health Network (UHN), wasn't sure if the lungs were healthy enough to save Celentano's life.

Fortunately, Dr. Cypel, who is also part of the Sprott Department of Surgery at UHN,

had been part of the team that developed a device more than a decade ago that is able to test and even repair injured donor lungs. It's called the Toronto Ex Vivo Lung Perfusion System, a dome-shaped incubator-like machine that lets organs live outside a body for many hours. Tubes, pumps, ventilators and filters send liquids, oxygen and nutrients into the lung, keeping it alive and allowing it to essentially breathe in and out. While only a few centres around the world have such a device, Dr. Cypel and the Toronto Lung Transplant Program team at the the Ajmera Transplant Centre now use it as their standard of care to assess donor lungs for transplantation.

The first pair of lungs weren't healthy enough, but several weeks later, Dr. Cypel received lungs from a donor who had passed away from a sudden cardiac arrest. Normally



System-treated lungs in 2008 at UHN. Not long after, the Ajmera Transplant Centre fully doubled the number of lung transplants it performed each year. “It transformed the field of transplantation,” says Dr. Cypel.

With the Ex Vivo System, “we can assess an organ’s function in detail, so you can make sure it’s going to work after you transplant it,” explains Dr. Keshavjee, who is also the James Wallace McCutcheon Chair in Surgery, Director of the Toronto Lung Transplant Program at the Ajmera Transplant Centre and Director of the Latner Thoracic Surgery Research Laboratories at UHN. “We pioneered this approach with lungs and demonstrated how to use it. Now, it’s been translated around the world to increase lung transplant access and is being extended to other organs.”

Organs such as the kidneys and liver have their own version of the Ex Vivo System, too, and devices for the heart and pancreas are in development. While they essentially function in the same way, they all look a little different, as each organ needs different supports – including the type of liquid used to keep them going – and are at various stages of development.

“Livers get damaged during the regular preservation process. When they’re cooled, they have no oxygen and they become less healthy,” explains Dr. Markus Selzner, Surgical Director of the Liver Transplant Program at the Ajmera Transplant Centre, who is also part of the Sprott Department of Surgery at UHN. He started his own *ex vivo* research nearly 10 years ago. The device allows doctors to see if the liver can make bile and blood clotting factors, and metabolize toxins. If it can pull off these key functions, it’s likely the organ can be successfully transplanted.

For nearly a decade, there have also been devices that support hearts, but Ajmera Transplant Centre clinicians are trying to improve upon what’s out there. “What exists now has allowed us to take hearts that have stopped and restart them outside the body,” says Dr. Mitesh Badiwala, Surgical Director of the Heart Transplant Program at the Ajmera Transplant Centre, who is also part of the Peter Munk Cardiac Centre and Sprott Department of Surgery at UHN. “But these devices have limitations. They just keep the heart alive. We want to develop an actual Ex Vivo System to be able to test heart function and repair hearts prior to transplantation.”

He’s collaborating with engineers to create a more powerful Ex Vivo System that makes all of a heart’s chambers pump blood – like they do inside a body – which will allow him to test its ability to fully function. He also

in this situation, lungs aren’t suitable for transplant, as they get starved of oxygen and blood for hours while donation is arranged. But Dr. Cypel was leading a new research program for organ donation after cardiac death, which uses the Ex Vivo System to make them ready for transplant.

Like he did before, Dr. Cypel tested the lungs in the Ex Vivo System, and this time they were good to go. Six months later, Celentano was back on the golf course, and a year later, he completed the famed Grouse Grind, a steep hike up Grouse Mountain in North Vancouver. “I didn’t just get back to life – I went back to a better life,” he says.

Modern-day miracle

The Ex Vivo System – which was co-developed by Dr. Shaf Keshavjee, Surgeon-in-Chief of the Sprott Department of Surgery at UHN, and Dr. Cypel – is nothing short of a modern-day medical miracle. If a damaged organ can be kept alive outside a body, where it can then be treated with medications and other procedures to essentially become as good as new again, then the number of organs available for transplant can increase exponentially. That’s a huge deal. Canada has a shortage of organs – in 2019 alone, 249 people died while waiting for a transplant.

In 2006, Dr. Keshavjee wanted to research how to alter some of the genetic components of lungs to make them healthier, and knew it would work best on organs kept warm and moist outside the body. *Ex vivo* technology was aspired to for decades, but no one had gotten it right just yet. “We put the pieces and the physiological concepts together,” recalls Dr. Cypel. He and Dr. Keshavjee oversaw the world’s first transplant of Ex Vivo

DR. SHAF KESHAVJEE (left), Director, Toronto Lung Transplant Program, Ajmera Transplant Centre, and **DR. MARCELO CYPEL**, Surgical Director, Ajmera Transplant Centre, with the Toronto Ex Vivo Lung Perfusion System they created.



Approximate mortality rate of those on the wait list for a lung transplant.

SOURCE: JAMA SURGERY



Approximate percentage of deceased donor kidneys that do not work immediately.

SOURCE: UHN

wants to keep hearts in the device for longer (the current time limit is four hours) so he's working on ways to feed the heart nutrients and clear it of toxins.

Researchers at the Ajmera Transplant Centre are also developing *ex vivo* protocols for the pancreas. "The pancreas is a pretty angry organ," admits Dr. Trevor Reichman, Surgical Director of the Pancreas and Islet Transplant Program at the Ajmera Transplant Centre, who is also part of the Sprott Department of Surgery at UHN. "It doesn't like to be manipulated at all, let alone be transplanted." This organ easily develops inflammation or "pancreatitis," so he's working on a system that calms it down and inactivates some of the enzymes that cause inflammation.

An Ex Vivo System for kidneys is also on the way, to kick-start the organ into operation after coming out of cold storage. "Sometimes the kidney is extremely slow to start working after a transplant," notes Dr. Reichman.

More *ex vivo* innovations

Hours in a device are great; days are even better. Dr. Cypel and his team in the Latner Thoracic Surgery Research Laboratories recently hit a record three days of preserving lungs in the Ex Vivo System. They did it by alternating cold preservation at 10°C instead of 4°C, which slows down the organ but does not shut it down entirely. The lungs are then placed in the Ex Vivo System at body temperature for four hours, to recover and recharge, and then back to cold again for about 18 hours. This process keeps the lungs from needing too many nutrients and extends their ability to live outside the body. Dr. Keshavjee alludes to where this research is leading, "One day, I'm hoping we can have

"WE PIONEERED THIS APPROACH WITH LUNGS AND DEMONSTRATED HOW TO USE IT. NOW, IT'S BEEN TRANSLATED AROUND THE WORLD TO INCREASE LUNG TRANSPLANT ACCESS AND IS BEING EXTENDED TO OTHER ORGANS."

DR. SHAF KESHAVJEE

organs on the shelf, so you just go in and get what you need when you need it."

Meanwhile, innovations in *ex vivo* technology may help imperfect organs improve. Already, the lung team has removed blood clots from organs and treated them with antibiotics. With livers, overweight donors may have organs with a slow fat metabolism. "We're working on research to increase the metabolism of livers," says Dr. Reichman. "We might be able to increase the fat burning of the liver while it's on the Ex Vivo System."

Many organs also harbour infections and viruses that can be removed *ex vivo*. "We give transplant patients anti-rejection medications, which severely knock down their

immune system. So, any minor infection can become pretty life-threatening," says Dr. Atul Humar, Director of the Ajmera Transplant Centre and the R. Fraser Elliott Chair in Transplantation Research. "If you can take the virus out of the organ before it even gets to the recipient, then that's a major advance."

Already, Dr. Humar and his team have shown that a short course of antivirals can eliminate hepatitis C in donor organs. Next, researchers are figuring out how to treat organs for Epstein-Barr virus and cytomegalovirus – a virus that is common but usually harmless in the general population, but can be a dangerous infection in transplant recipients.

An ambitious future

Drs. Cypel and Keshavjee's long-term plan is to use the Ex Vivo System to help physicians engineer better organs. It's years away, but clinicians may be able to change the blood type of an organ so the sickest people can get access to the next available organ instead of waiting for the one that exactly matches their blood. "We could make a universal organ," Dr. Cypel says.

Going back to the idea that inspired the Toronto Ex Vivo Lung Perfusion System years ago, Dr. Keshavjee is working on gene therapy to stop an organ from being attacked by its new host. "We could make the lung look more like 'self' and prevent rejection," he says. This could reduce the risk of transplant failure and, with patients taking fewer anti-rejection drugs or none at all, lower their infection risk and improve their quality of life.

Already, the Ex Vivo System has saved countless lives like Celentano's. "In 10 years," says Dr. Keshavjee, "*Ex vivo* organ perfusion will be the standard of care everywhere." ■

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DR. TREVOR REICHMAN
Surgical Director,
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DR. MARKUS SELZNER
Surgical
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HEART

It takes a village

The Heart Transplant Program at the Ajmera Transplant Centre offers much more than surgery.

BY GLYNIS RATCLIFFE



STELLA KOZUSZKO monitors transplant patients and helps them adjust to post-transplant life.

WHEN YOU HEAR about a heart transplant, the image that most likely comes to mind is that of surgeons and nurses surrounding a body on life support, performing a gruelling operation. Family members pace in the waiting room until the head surgeon appears at the door, hours later, with a tentative smile. Success! The prognosis looks good, and while there's a chance of complications as the patient recovers, they'll be fine once they're released from the hospital.

Heart transplants are not, in fact, the way the movies make them appear. The surgery itself is just one facet of the incredible lifelong relationship each heart transplant patient has with the extensive group of surgeons, clinicians, nurses and other staff at the Ajmera Transplant Centre. Everyone works to optimize the patient's journey – whether it's creating technology to increase the number of viable donor hearts, developing less invasive ways to monitor for rejection post-transplant or other life-saving measures.

"It takes a village to care for one heart transplant recipient," says Stella Kozuszko, a nurse practitioner in the Heart Transplant Program at the Ajmera Transplant Centre, who is also part of the Peter Munk Cardiac

Centre at University Health Network (UHN). She's been with the program for 21 years. "We have amazing cardiologists, heart failure specialists, social workers, pharmacists, intensive care unit (ICU) staff, transplant unit staff, clinic staff – they're all responsible for ensuring every heart transplant recipient has a safe journey through their life."

With patients from the start

When patients first come to the Ajmera Transplant Centre – after they've already been diagnosed with heart disease – they'll meet with a cardiologist, who could be Dr. Michael McDonald, Medical Director of the Heart Transplant Program at the Centre and the Martha Rogers Chair in Heart Failure Training and Education, who is also part of the Peter Munk Cardiac Centre and Ted Rogers Centre for Heart Research at UHN. He and his colleagues make a determination about whether someone is sick enough to require a transplant. If they do need one, the team works with that person to keep them stable while they wait for a heart to become available.

When a heart is matched, the patient gets whisked into the operating room, where some of that movie-like magic takes place,

though the process is more complicated and painstaking than many people think. A typical surgery takes about four hours, but complicated ones – the kinds of rare and difficult cases the Ajmera Transplant Centre often tackles – can take much longer.

Most surgeries, though, are similar. After the patient is put to sleep, a cut in the chest is made and the breastbone is separated in half so physicians can get to the heart. They then connect the person to a heart-lung bypass machine, which supplies the body with blood and oxygen while the heart and lungs are stopped. Once the blood has diverted into the bypass machine, the diseased heart is removed. The surgeon then places the new heart into the body and carefully connects all the blood vessels, ensuring there are no leaks. When the heart is fully connected, the blood that's circulating inside the bypass machine will go back into the heart. The tubes to the machine are then taken out and the surgeon shocks the heart to get it beating again.

As stressful and complicated as the operation may be, it's the post-surgery process that's the most critical aspect of the patient's transplant journey. In the following days,

weeks and even months, Dr. McDonald and his team must make sure the heart takes to the patient's body. As soon as the chest is closed, the transplant patient is wheeled back into the cardiovascular ICU, where their heart function is monitored closely by his team. Dr. McDonald also works with ICU staff to handle the patient's medications, get them through the initial post-operative period and manage their immunosuppression.

Once vital signs and heart function are stable, and patients can breathe without assistance, they're transferred to the Ajmera Transplant Centre's inpatient unit, where they continue to recover and the transplant team prepares them to go home. This involves medication classes, transplant education, drug insurance lessons, regular meetings with social workers, physiotherapy to build their strength and endurance, and occupational therapy to assess whether a patient is physically ready to go home.

As this is happening, Kozuszko is there to ensure heart transplant recipients recover from surgery safely. She monitors them for signs of rejection from the time they're in the ICU and well beyond their release from the hospital. This involves assisting in regular heart biopsies, as well as checking for potential infections or other complications with immunosuppressive medications.

The village approach

The first year following a transplant "is a very intensive process for patients to go through, and we're often reminding them: it's a marathon, not a sprint," Dr. McDonald explains. Many experience side effects from the medications they're taking, which include lowered kidney function, elevations in blood pressure, diabetes and a negative impact on bone health. The key is finding the balance between having the immune system ramp down – so the recipient's body accepts the new heart – but not be so suppressed that opportunistic infections and cancers creep in. That's why



DR. MITESH BADIWALA
(centre) is working on developing an Ex Vivo Heart Perfusion System.

the "village" approach, as Kozuszko calls it, is so important, says Dr. McDonald.

Once that first year of appointments, procedures, medication adjustments and rehabilitation is done, life starts to become a bit more normal. "We then continue to follow them, along with their primary care providers and other specialists, for life," he says.

Solving complex questions

One of the more challenging parts of post-transplant care for patients is the need for regular heart biopsies, in which physicians remove a piece of heart tissue, which is then used to check for any signs of rejection. The biopsies are performed weekly during the first month post-transplant, biweekly for the next month and then monthly for the next year or more. While the biopsies are generally well tolerated by patients, they are invasive and can cause damage to particularly delicate heart tissue.

Fortunately, the Ajmera Transplant Centre is working on a revolutionary new alternative to those heart biopsies, something called a cell-free DNA test. This blood test, referred to colloquially as a "liquid biopsy," can identify two different forms of rejection that would require further tests: cellular (in which the

body's immune cells attack the cells in the new heart) and antibody-mediated (in which antibodies damage the coronary arteries). The best part is that the blood draws can take place at any clinic, reducing the number of hospital visits needed.

Not every heart transplant hopeful goes through this comprehensive process, because there aren't enough donor hearts available. In 2020 alone, 157 Canadians were waiting to get a heart transplant. If Dr. Mitesh Badiwala, Surgical Director of the Heart Transplant Program at the Ajmera Transplant Centre, who is also part of the Peter Munk Cardiac Centre and Sprott Department of Surgery at UHN, had it his way, no one would be left waiting for a new heart.

He and a team of engineers are creating a new machine – the Ex Vivo Heart Perfusion System – based on a lung system pioneered at UHN, which they hope will one day allow surgeons to test a heart's viability before transplant outside one's body. Once the technology is fully developed, a heart that's brought to UHN would be removed from cold storage and put inside the device. Physicians would then clean the damaged organ by pumping it full of infection-fighting drugs or operate to get it working like new.

"We want to put a heart on our device and make it work for an extended period of time," Dr. Badiwala explains. "We can measure function, but also try to create a platform for us to repair hearts or modify them so that they work better."

It's clear that much more goes into a heart transplant than the operation. Whether it's pre-operative care, post-surgical monitoring or the procedure itself, every member of the Centre's team is working together to help patients recover and lead a full life. "I always tell recipients the sky's the limit," Kozuszko says with a smile. "Tell me what you want to do and we will help you do it." ■

"We lean heavily on our primary care colleagues and other specialist colleagues to really help make a team around every patient."

DR. MICHAEL McDONALD
Medical Director, Heart Transplant Program,
Ajmera Transplant Centre



Breaking down barriers

Racialized communities have a harder time finding living organ donors. The Ajmera Transplant Centre wants to change that.

BY WENDY HAAF



JENNEN JOHNSON is trying to raise community awareness about the importance of organ donation, after receiving a life-saving kidney transplant.

JENNEN JOHNSON, then in her late 30s, knew her kidneys were failing due to lupus, but the gravity of her situation didn't hit home until she heard her prognosis outright: without a transplant, she would only live for another four years. Knowing the average wait for a donor kidney could stretch to six years, Johnson, whose daughter Tatianna was then just 12, suddenly felt frozen with shock. "I don't know what was said after that," she recalls. The full emotional impact didn't finally strike until later that evening, when Johnson was telling her mother the news. "I just broke down."

Johnson was fortunate enough to be receiving care at the Ajmera Transplant Centre, which boasts some of the best

transplant outcomes in the world. But the fact that she is a member of the African, Caribbean and Black (ACB) community in Toronto put her at a distinct disadvantage to access her best available treatment option: a living donor kidney transplant. According to research conducted at the Centre, people who identify as African, Caribbean and Black are half as likely as white patients to receive a living donor kidney transplant, even after accounting for medical and socio-demographic factors. The same is true for people who are South or East Asian.

Patients from these communities are less than half as likely to become living donor kidney recipients, compared to white patients, while they're less likely to give an organ, too. Worse yet, individuals from these racialized communities are at a greater risk of developing kidney failure, due to higher rates of

high blood pressure, diabetes and certain inflammatory diseases, including lupus.

Why the disparity between non-white and white transplant patients? Research conducted by Dr. Istvan Mucsi, a transplant nephrologist with the Ajmera Transplant Centre's Kidney Transplant Program, and his colleagues has found that in some non-white communities, there's a distrust of healthcare institutions stemming from previous experiences with racism. There's also a culturally related reluctance to discuss personal health problems. "There are a large number of factors that contribute to these differences, many of which have been around for a long time," he says.

The roots of racialized disparities

Prior to this work, "no comprehensive effort had been initiated to try and understand

and address some of these inequities,” Dr. Mucsi explains, so he and his team undertook the most comprehensive systematic research effort to date to do just that. “In addition to analyzing data from about 1,700 patients transplanted at the Ajmera Transplant Centre, asking approximately 600 patients with kidney failure to complete standard questionnaires about their knowledge and attitudes toward living donor kidney transplant, we also designed a qualitative research project in engagement and partnership with a number of organizations from these communities,” he says. “The most advanced stage of this data collection is with the ACB communities, thanks to the collaboration with the Black Health Alliance.” The Black Health Alliance is a community-based charity aimed at improving the health and well-being of the 1.2 million Black people in Canada.

Lack of ACB representation in the medical and transplant communities and distrust in these institutions due to historic and present-day racism emerged as two leading themes in the research. “Patients in some cases may delay going to the doctor or not seek care because they feel they may not be heard or receive the treatment they require,” says Paula Neves, lead for the Centre for Living Organ Donation at the Ajmera Transplant Centre and a member of the research team. Limited knowledge about transplantation in general and the safety of living kidney donation when strict selection protocols are followed also play a role, as do cultural factors.

For instance, Johnson was reluctant to tell anyone outside her immediate family that she had been diagnosed with lupus or kidney disease, much less ask people if they’d be willing to consider donating a kidney. “For myself, with a Caribbean background, there’s nothing wrong with sharing good news, but anything negative, sad or depressing, you keep within your household,” she explains. Consequently, awareness of the prevalence of kidney disease and possible treatments is low in these communities.

(continued on p. 21)

DR. ISTVAN MUCSI helped design a study to better understand the barriers racialized communities face in finding living donors for kidney transplants.



KIDNEY SWAP

A WORLD-FIRST, THE CENTRE FOR LIVING ORGAN DONATION IS MAKING MORE LIVING TRANSPLANTS POSSIBLE



PAULA NEVES is lead of the Centre for Living Organ Donation.

In her thirties, Joanne Kearney faced an uncertain future: the kidney disease she’d lived with since early childhood had progressed to end-stage renal failure. Her goal was to get a transplant before she needed dialysis. Unfortunately, her husband, Brendan Cahill, couldn’t donate the kidney she so desperately needed: physicians discovered he wasn’t a match, and if his kidney was used, Kearney’s immune system would reject his organ.

Thankfully, they learned about the Kidney Paired Donation Program, which facilitated a multi-way “swap” with a chain of other incompatible donor and recipient pairs. Cahill donated his kidney to a stranger so Kearney could receive one from a stranger as a transformational gift of life. Realizing that few people knew about this option for living organ transplantation, the couple was keen to help establish, with a philanthropic gift, the Centre for Living Organ Donation at the Ajmera Transplant Centre, the first such centre in the world. “We were really lucky,” says Kearney, who has since joined the UHN Foundation Board of Directors. “We thought there has to be a way for everyone in need of a kidney or liver to have the same successful outcome we had.”

In addition to raising awareness of living donation – so more people know it’s an option earlier in their journey with kidney disease – the Centre for Living Organ Donation is focused on making the organ donation process more efficient, while maintaining a lifelong connection with donors. “People might feel better about donating knowing they’re not going to get lost in the system,” explains Cahill.

Improved awareness

A key focus for the Centre is increasing awareness around living organ donation. It organizes Living Donation Week, a national awareness campaign held each September to celebrate and spread the word about this life-changing gift and everyone who makes it possible. For people exploring living organ donation, the Centre provides an info line, email support, webinars on such subjects as “Finding a Living Donor,” access to peer supports and more.

There’s also social media and a YouTube channel with videos describing how organ donation works, and real stories of donors and recipients. It launched in 2019 and garnered 116,000 views within its first year. Finally, the Centre also produces a podcast, in collaboration with the Ajmera Transplant Centre, called Living Transplant, which takes listeners behind the scenes of the transplant program.

Paula Neves, lead for the Centre for Living Organ Donation, says these resources help people feel more comfortable with the donation process. One comment she got said: “We are new to this transplant reality and on a steep learning curve. Connecting with the Centre and hearing the others’ stories made me feel not so alone.” Another said: “We appreciate the opportunity to ask questions and meet a donor and a recipient. This dialogue allows us to ‘normalize’ what feels like a foreign and frightening process.”

“We’re trying to offer hope during a very uncertain time and to take some of that uncertainty away,” enthuses Kearney. “I’m excited to see where all of this will take us – and it’s all going to happen at UHN.”



CLOSED CHAIN

Patients often have a donor in mind, but their organ may not be compatible. The donor would give their kidney to another recipient whose donor is unable to give to them, and so on, until the original patient receives their organ.



CREATING CONNECTIONS

The Kidney Paired Donation Program brings living donors and transplant recipients together, says Dr. Sunita Singh.



When a patient's potential kidney donor doesn't match up, they turn to the Kidney Paired Donation (KPD) Program for help. The program, which is run by Canadian Blood Services (CBS), helps donor and recipient pairs who aren't compatible with one another find matching donors and recipients among the other incompatible donor and recipient couples registered in the program. This enables a "swap," in which the donor from pair one donates to the recipient in pair two, and pair two's donor donates to the recipient in pair one. Using a sophisticated algorithm, the Program "will also create chains of transplants," in domino-like sequences, explains Dr. Sunita Singh, Medical Director of the Ajmera Transplant Centre's Living Kidney Donation Program and Chair of the Living Donation Advisory Committee at CBS.

In some cases, the result is a "closed chain," where donor A can't give to recipient A but can donate to recipient B; donor B gives to recipient C; and donor C donates to recipient A. However, "another really important aspect of the program is non-directed anonymous living kidney donors (NDADs)," Dr. Singh says. As of August 1, 2021, the KPD program has completed 822 kidney transplants, and since the inception of the program there have been NDADs. "They often trigger a cascade of transplants," she adds, similar to the aforementioned chain, but with one addition. The final donor "will then give a kidney to someone on the waiting list," Dr. Singh says. "These are just amazing people who want to help someone in need, and their donation triggers multiple transplants that otherwise may not have happened."

(continued from p. 20)

So is knowledge about organ transplant and trust in the systems behind it. For example, while Johnson's family members were all happy to be tested as possible donors, outside that circle, she ran into a wall. People mistakenly believed donating a kidney could shorten their lives or were reluctant to consider giving an organ to someone outside their family. "Before this, I felt the exact same thing," Johnson says. "I did not sign that organ donor card, but I now know that it's so important."

Community collaboration

After identifying such barriers, Dr. Mucsi and his team again turned to the ACB community for help in finding solutions. "Dr. Mucsi's research really places that emphasis on the people you're interviewing being the guiders of change," says Leslie Williams, a nurse practitioner with the Living Kidney Donation Program at the Ajmera Transplant Centre. "Then it becomes a co-creation that both recipient and provider feel well-invested in."

Some world-leading initiatives that the team is currently working on include designing educational modules "about cultural safety, cultural humility and the impact of racism on health outcomes for nurses and physicians who work with kidneys," Dr. Mucsi says. "We are planning to create clinics that will be more representative of the patient population they serve and also more responsive to their particular needs," he adds. One such clinic is currently being planned with the TAIBU Community Health Centre in Scarborough, which is about an hour east from downtown Toronto. TAIBU exclusively serves Black patients. In addition, "we are working with Black

professionals to deliver culturally safe and appropriate education and information about kidney disease, and provide culturally safe care for patients with kidney disease," Dr. Mucsi notes.

Creating content and resources

One of the groundbreaking developments Johnson is most excited about is a recently launched ACB Organ Health YouTube channel with content almost entirely created by living donors, transplant recipients and healthcare professionals from ACB communities. Its purpose is to bring awareness of signs and symptoms and how to access timely care, and to provide education and resources to people who are either waiting for an organ or have already undergone a transplant. As one of the hosts, "I'll be talking about health, nutrition and exercise," she says. The 30-minute show will include interviews with nutritionists, recipes and cooking segments demonstrating how to make lower-sodium, kidney-friendly versions of Caribbean dishes.

When Johnson started dialysis, she couldn't keep down favourite foods like fried dumplings or many others, including eggs, cucumbers and tomatoes. "Faint smells, even pleasant aromas like food, made me terribly nauseous," she recalls. Nor could she enjoy mother-daughter ice cream dates any longer.

Unfortunately, none of Johnson's family members were medically suitable to donate, and making the "ask" for a living kidney donor can be incredibly difficult. For more than a year, Johnson's search yielded no results. Finally, in desperation, Johnson ran an ad in *NOW* magazine in 2018 outlining her situation, posting it to social media for good measure.

Shared and reshared by friends and family, it caught the eye of Christi Nolan, a self-employed yoga instructor who had once attended the same church as Johnson's cousin Maggie. Nolan offered to be tested and turned out to be a near-perfect match, and today, thanks to Nolan's generosity, Johnson has her life back. Still bowled over by Nolan's transformative gift, Johnson is paying it forward by doing everything she can to raise awareness about organ transplant and the importance of living organ donation.

"If my journey makes a difference in someone's life, then everything I went through was worth it," she says. ■



LESLIE WILLIAMS

is a nurse practitioner with the Living Kidney Donation Program.

LIVER

A thousand lives saved, and counting

The Ajmera Transplant Centre has set a North American record for living donor liver transplants, allowing healthy Canadians to give patients like Lillian Flynn a life-saving gift.

BY TAMAR SATOV



LILLIAN FLYNN
turned one year old in
May, after receiving a
successful liver
transplant in late 2020.

B

BEFORE HER FIRST birthday,

Lillian Flynn had already experienced a lifetime of illness. Her mom, Ashley Flynn, first learned something was wrong at Lillian's eight-week checkup in July 2020, when her family doctor, Dr. Christina Riehl, noticed some abdominal swelling and jaundice in her eyes. A series of tests – including blood work, an ultrasound, a liver biopsy, a nuclear scan and other exploratory surgeries – confirmed the infant's diagnosis: congenital biliary atresia, a blockage of the bile ducts that prevents the flow of bile out of the liver into the gallbladder, which can cause severe liver damage.

A month-long stay in the local children's hospital near their home in Perth, Ont., culminated in surgery to bypass Lillian's blocked ducts and restore normal bile flow, but her condition continued to deteriorate. Her liver was too weak to process fluids, so they collected in her abdomen, a condition called ascites. While she failed to put on weight, dropping to the 10th percentile for her age group, Lillian's belly held two litres of fluid and inflated to the size of a basketball.

In September 2020, the then-four-month-old was admitted to SickKids in Toronto, where they could better deal with the ascites, get her weight up with the help of a feeding tube and assess Lillian for a possible liver transplant. "This is kind of when you realize how sick your child is," says Ashley, who was by Lillian's side through it all, while her husband, Corey, stayed home to look after their other daughter, Grace, then age three. "I was really getting nervous for Lillian."

But, thanks to SickKids' partnership with the Ajmera Transplant Centre at University Health Network (UHN), Lillian would not face the fate of the roughly one-quarter of Canadians waiting for a liver transplant who die before a suitable organ becomes available from a deceased donor. Instead, she would get a life-saving transplant from a healthy donor through the Centre's Living Donor Liver Transplant (LDLT) Program.

The living liver revolution

One of the challenges with traditional transplantation – for the liver and other organs – is that there are never enough deceased donors to go around, leading to about a 25 per cent mortality rate for people on the liver transplant wait list, says Dr. Mark Cattral, Surgical Director of the LDLT Program. In 2000, to increase the pool of liver donors, UHN created this Program, the first of its kind in Canada.



HAPPY ENDING

Lillian Flynn (above left) on the day she received her liver transplant, which she needed after blocked bile ducts caused abdominal swelling (above right). Her parents can smile again with Lillian now healthy (opposite page).

Surgeons can remove part of a donor's healthy liver, which grows back to full size within three months. The procedure is safe – there's been zero mortality or disability to the Program's donors – and once the organ regenerates, donors can return to their busy lives.

Dr. Cattral, who assisted in the very first living donor liver transplant at UHN in 1996, performed the Program's landmark 1,000th surgery this past spring.

The Ajmera Transplant Centre's LDLT Program remains the largest and most active in the Western world, performing a record 78 surgeries in 2020, in spite of the pandemic. About one-third of these living donor liver transplants are in pediatric patients like Lillian, where it's particularly beneficial because deceased donors are usually quite old and have livers in less-than-ideal condition, creating a higher mortality risk.

"Lillian was very sick," says Dr. Cattral, who is also part of the Sprott Department of Surgery at UHN. "Without a living donor transplant, she probably wouldn't have made it."

Angels among us: anonymous donors

Although several friends and family, including Lillian's dad, came forward as potential donors, none were a good match.

"A donor has to match based on the blood group," says Dr. Nazia Selzner, Medical Director of the Ajmera Transplant Centre LDLT Program. "Then, they have to go through a whole set of testing – including scans of their liver – to see if the volume of the liver is appropriate and if the bile ducts and blood vessels are anatomically easy to divide between the donor and recipient."

Above all, donors must be between the ages of 16 and 60, and in optimal health. "You cannot be a donor if you have diabetes, heart disease or fatty liver disease," she explains.

This is something Eric Brousseau, Ashley's uncle, found out the hard way. Long before Lillian was even born, let alone diagnosed with liver disease, he applied to be a living donor when an acquaintance needed a transplant.

"Our son Johnathon passed at age 14 in 2005 from a congenital heart defect, and since then we've tried to help other people in any way we can," says Brousseau. "If being a living donor can give someone a chance to have more

1,000+

Number of living donor liver transplants performed at UHN since 2000.

SOURCE: UHN

3

Number of months it takes a liver to grow back to full size after being partially removed for donation.

SOURCE: UHN



DR. NAZIA SELZNER
is Medical Director of the Living Donor Liver Transplant Program.



DR. BLAYNE SAYED
is a surgeon with the Living Donor Liver Transplant Program.



DR. MARK CATTRAL
performed the Living Donor Liver Transplant Program's 1,000th surgery in 2021.

time with a loved one, then we felt it's worth doing."

Unfortunately, when he went through the testing, he found out he had fatty liver disease, which he'd have to get under control through diet and weight loss. While he hit his goal weight within a few months and got the all-clear, the acquaintance found another suitable donor. But Brousseau decided to stay on the list as an anonymous donor – meaning he'd undergo major surgery for the benefit of a patient he'd never meet and whose name he'd never even know.

The Ajmera Transplant Centre was the first LDLT Program to allow and encourage this kind of anonymous donation, which is still rare around the world. Last year, about 20 per cent of the Program's living donors were anonymous.

"Transplant is the only field in medicine that starts with an altruistic act – with living and anonymous donors, even more so," says Dr. Blayne Sayed, one of seven transplant surgeons on the Ajmera Transplant Centre's LDLT team and the Surgical Lead of Liver Transplantation at SickKids.

Brousseau's surgery took place just days before Lillian got her diagnosis. And while he likely would not have been a good match for Lillian, he and his wife Barbra feel happy they were able to offer some guidance and support to Ashley and Corey throughout the process. By early December, the Ajmera Transplant Centre team found Lillian an anonymous donor of her own – she received her transplant within a couple of weeks. "Our whole family felt that perhaps Eric's surgery put some good karma out into the world and that came back to Lillian," says Barbra.

World-leading clinical experience

When Ashley and Corey met with Dr. Cattral, he patiently explained everything about the procedure,

with pictures to help them understand. "He was so great. We weren't worried at any point," says Ashley, who says the day of the surgery was almost like a celebration. "There were no tears that day. We were so ecstatic. They have done this so many times, we knew she was in good hands."

Dr. Cattral started the delicate procedure to remove Lillian's diseased liver at SickKids at about 9 a.m. Meanwhile, at Toronto General Hospital, home to the Ajmera Transplant Centre, Drs. Anand Ghanekar and Blayne Sayed were removing the left lobe of the donor's liver, which is optimal for a child because it is smaller than the right lobe. At about 4 p.m., a surgical assistant carried the donor organ through the walkway between the hospitals, so the painstaking work of connecting it to Lillian's tiny blood vessels, some just two millimetres wide, could begin.

Lillian was out of surgery by about 10 p.m. and taken to the ICU, where her parents finally saw her at around midnight. "She had a lot of tubes in and was puffy, but I noticed a huge difference in her skin tone even then," says Ashley, referring to the jaundiced yellow tinge that's a marker of liver disease. "She was a pink little baby again."

Just three weeks later, on January 8, the family finally went home. And while Ashley is prepared for hiccups – Lillian must take anti-rejection medication for the rest of her life and may still have episodes of organ rejection that need further treatment – she shares that Lillian is now a normal little kid, hitting the same milestones as her peers. She turned one in May and is starting to walk.

"I have nothing but amazing things to say about our transplant team. They – and our donor – saved our daughter's life," she says. ■

ALLEY ADAMS

received her simultaneous pancreas and kidney transplant in May 2021, eliminating her need for both insulin and dialysis.



A century of life-saving discoveries

Transplanting organs and islets provides life-saving treatments for people with severe diabetes.

BY COLLEEN SETO

A LLEY ADAMS is no stranger to medical challenges. The 35-year-old communications professional with McKinsey

and Company was diagnosed with Type 1 diabetes when she was just five and has grappled with regulating her blood sugar levels, taking insulin and managing an all-consuming chronic disease throughout her life. In November 2018, though, she felt something new – and alarming. She was FaceTiming with a friend and was having trouble following the conversation. “I knew something was wrong,” she says. Adams called 911 and was rushed to hospital, where she learned she was on the brink of a heart attack. Clinicians took a biopsy of her kidney, and she soon found out she was in end-stage kidney failure and was diagnosed with diabetic kidney disease.

It turned out her lifelong diabetes had caused serious damage to her kidneys. Though she displayed few symptoms of kidney failure, which is fairly common, the biopsy showed she needed a transplant. Initially, she

wanted to find a living kidney donor, but her physicians said her best option was a simultaneous kidney and pancreas transplant because, as a diabetic, she ran the risk of needing another kidney transplant in the future. “The survival benefit is much greater for those who get both kidney and pancreas transplants,” says Dr. Trevor Reichman, Surgical Director of the Pancreas and Islet Transplant Program at the Ajmera Transplant Centre and Adams’ surgeon. “The pancreas is protective against diabetic kidney failure, so the benefit of the dual transplant outweighs the risk.”

While waiting for her transplant, Adams received exceptional and comprehensive diabetic kidney care from Dr. David Cherney, through University Health Network’s (UHN’s) CaRE Clinic, allowing her to carry on with day-to-day life. Adams admits she was overwhelmed and scared to get two transplants at once, known as a multi-organ transplant, but after talking to her physicians, it became clear it was the way to go. “It becomes less about how you feel and more about statistically what leads to better outcomes,” she says.

“It’s amazing to see the impact that transplant has for a person like Alley on their quality of life.”

DR. TREVOR REICHMAN

Surgical Director,
Pancreas and Islet
Transplant Program,
Ajmera Transplant
Centre



What Adams didn’t realize at the time was that there may be no place more qualified to help patients with diabetes than the Ajmera Transplant Centre and UHN as a whole. It was at the University of Toronto where, one century ago, in the summer of 1921, Drs. Frederick Banting and Charles Best discovered insulin. In January 1922, the drug was administered at Toronto General Hospital for the first time, saving the life of 13-year-old Leonard Thompson. Ever since then, diabetes has been a key research subject at UHN.

Creating insulin independence

One area of study focuses on replacing organs and islet cells – clusters of cells in the pancreas that make insulin – to potentially eradicate diabetes in those who have it. “We know that islet transplantation works as a means for eliminating the need for insulin injections,” says Dr. Cristina Nostro, affiliate scientist at the Ajmera Transplant Centre and the Harry Rosen Chair in Diabetes and Regenerative Medicine Research at the McEwen Stem Cell Institute at UHN.



DR. CRISTINA NOSTRO is growing surrogate islet cells from regenerated mature stem cells to meet demand for pancreas donations.

When it comes to organ transplants, Ajmera Transplant Centre clinicians have found that simultaneously replacing the kidney and pancreas is the most effective treatment for Type 1 diabetes with end-stage kidney disease. These surgeries dramatically improve quality of life because a new pancreas provides regulated insulin production to treat diabetes, while a new kidney eliminates the need for dialysis.

Islet transplantation is a particularly interesting area of research at the Ajmera Transplant Centre and its Pancreas and Islet Transplant Program. Those with Type 1 diabetes lose the islets that produce insulin, which are the beta cells. With islet transplantation, islets are taken from the pancreas of a deceased organ donor, purified, processed and injected into a vein within the liver of the patient with diabetes. Within two to six weeks of implantation, the beta cells in these islets begin to make and release insulin.

In some cases, islet transplants can result in insulin independence, but it's more often used to prevent

hypoglycemic unawareness, a life-threatening condition in which diabetic patients do not experience symptoms of low blood sugar (hypoglycemia) such as palpitations, sweating or anxiety, says Dr. Reichman, who's also part of UHN's Sprott Department of Surgery.

Islet recovery from a donor pancreas is not perfect, explains Dr. Nostro. It's an hours-long process, while few islet cells survive the isolation and transplantation procedure. Successful transplantations require islets from two or three donors, and there aren't enough donors to go around. To eliminate the issue of donor scarcity, Dr. Nostro is doing groundbreaking work with what are called surrogate islet cells. Instead of relying on donors, Dr. Nostro is producing islet cells from stem cells that have the potential to generate any cell of the body.

More innovations ahead

Dr. Nostro is now tackling the issue of cell survival post-transplant. "We're working on how to mask the cells from the immune system so that we don't

need immunosuppressants," she says. "This is where the future lies."

Regenerative medicine holds immense promise, she says, not just for treating diabetes but other diseases, too. "It would be ideal to make people insulin independent in a less invasive way than an organ transplant, through cellular therapy," adds Dr. Reichman. To this end, his team has also started developing an innovative model for *ex vivo* pancreas transplants, where a pancreas would be kept alive outside the body before being transplanted. This would give clinicians the chance to repair or modify a damaged pancreas, increasing the number and quality of pancreases available for transplantation.

For Adams, her road to insulin independence was long but, thankfully, successful. When she got her first call to come in for surgery in November 2020, the donor organs were not deemed viable – this happened twice more.

Fortunately, the fourth time was a charm. In May 2021, Adams underwent surgery for her simultaneous kidney and pancreas transplant. "I was diagnosed with diabetes on my mom's birthday," she recounts. "I got my transplant on the same day, 30 years later. Transplant of any kind is a gift, but this was particularly serendipitous."

The transplant not only saved Adams' life but also gave her a newfound freedom from dialysis or insulin injections. "It's amazing to see the impact that transplant has for a person like Alley on their quality of life," affirms Dr. Reichman.

Adams, who is now a member of the UHN Impact Collective, a group of young leaders who help raise awareness and funds for important medical initiatives at UHN, "feels amazing," she says. "The transplants have been life-changing to a degree that is hard to articulate and almost impossible to quantify. All of a sudden, I have a sense of normalcy that I have never in my life known. The freedom that comes with a second chance and being free of two chronic diseases is nothing short of a miracle. None of this would be possible without my organ donor and the team at UHN. I'm exceptionally grateful." ■

11M

Approximate number of Canadians who live with diabetes or prediabetes.

SOURCE: DIABETES CANADA

APPRENTICES TO EXCELLENCE

Fellowships at the Ajmera Transplant Centre are keenly sought after by the next generation of transplant leaders.

BY DIANE PETERS

DR. TREVOR REICHMAN
Surgical Director, Pancreas
and Islet Transplant Program

DR. LAURA DONAHOE
Surgical Fellowship
Education Lead, Toronto
Lung Transplant Program

DR. JEFFREY SCHIFF
Medical Director, Pancreas
and Islet Transplant Program

DR. CYNTHIA TSIEN
Education Director, Ajmera
Transplant Centre





DR. CHAYA SHWAARTZ was drawn to the complexity and precision of transplant surgery.



UT OF ALL the work Dr. Chaya Shwaartz did during her surgical residency, it was observing a liver transplant that impacted her most. “I just loved it,” she says. A recent fellowship graduate of the Ajmera Transplant Centre, Dr.

Shwaartz was drawn to the complexity and precision of the surgery and how it changed the patient’s life in a way that other surgical procedures did not. “It’s amazing how someone who is very, very sick gets a new liver and becomes a completely different person,” she explains.

While she was already interested in specializing in hepatobiliary surgery – diseases of the liver, pancreas and biliary system – seeing a transplant inspired her to go further and dedicate her life to transplant surgery as well. So the Israeli-born graduate of the Tel Aviv University School of Medicine applied to the prestigious and competitive Abdominal Organ Transplant Fellowship program at the Ajmera Transplant Centre. “It’s not just the amount of organs we transplant,” says Dr. Shwaartz of the Centre, which she notes does more liver transplants than any other hospital in North America. “It’s also about

the experience you get here.” The hands-on learning, the exposure to a large volume of surgeries, the extremely experienced surgical team and the world-class research made the Centre her first choice.

Getting into the program is not easy, though. The abdominal program, which is one of eight different specialties at the Ajmera Transplant Centre that accepts fellows, garners 150 applicants and accepts just two people a year. Fortunately for Dr. Shwaartz, she was asked to interview for a position and was then accepted for a two-year fellowship starting in 2019.

Every year, a modest group of people gets accepted into the Centre’s world-renowned fellowship program – there are currently 49 fellows working there – which includes lung, liver, heart, pancreas and kidney programs, among others. Each one gives fellows an in-depth and immersive experience working with patients, conducting research and taking part in extra learning opportunities. Surgeons within the program become proficient in transplantation, largely because they actually participate in the operations. At some other centres, surgeons learn by observing, but not here, says Dr. Laura Donahoe, Surgical Fellowship Education Lead of the Toronto Lung Transplant Program at the Ajmera

Transplant Centre and a member of University Health Network’s (UHN’s) Sprott Department of Surgery. “We get them involved,” she explains. “We want to make sure they’re really competent as transplant surgeons when they leave.”

Meanwhile, medical fellows learn how to care for patients “from the instant they leave the operating room until 40 years later,” says Dr. Jeffrey Schiff, Medical Director of the Pancreas and Islet Transplant Program and member of the Kidney Transplant Program at the Ajmera Transplant Centre. Dr. Schiff also heads up the kidney clinical care (nephrology) fellowship program, one of the largest of its kind in North America, which accepts only four people a year. These physicians also learn to help patients with their anti-rejection medications and their risk of infection.

Coveted positions

Fellows are either newly trained residents or working clinicians and surgeons who want to learn more about transplant.

Each program has its own application process – some use a fellowship matching service, similar to those used for medical residencies – and often requires a resumé, a personal statement, letters of reference and a lengthy interview. At the same time, many of these fellows are known to the Centre’s teams. “We often hear a lot about the fellows beforehand from previous fellows or colleagues,” says Dr. Trevor Reichman, Surgical Director of the Ajmera Transplant Centre’s Pancreas and Islet Transplant Program, who also heads up the Centre’s Abdominal Organ Transplant Fellowship. UHN clinicians, he says, are active in the worldwide transplant community and know the rising stars.

Still, it’s a competitive process, with hundreds of applicants for a few positions. Dr. Schiff says the demand keeps growing, too. “There’s definitely an increase in the number of transplants being done around the world,” he notes, which has resulted in more people wanting to specialize in this area. There’s a huge need for nephrologists – physicians who diagnose, treat and manage acute and chronic kidney problems – with transplant experience, for instance.

Besides the hands-on training, clinicians are clamouring to work at the Ajmera Transplant Centre because its fellowships have worldwide clout. Centres around the globe want to hire clinicians who can work with difficult cases and adapt to innovative medical advances. Generally, transplant medicine has become increasingly complex

in recent years, so specialists need the most well-rounded training possible, says Dr. Reichman, who is also part of the Spratt Department of Surgery at UHN.

One of the most attractive parts of the fellowship program is the exposure clinicians get to patients – hundreds of transplants, including many complex ones, are done here every year. “When you’re working somewhere that does about 200 liver transplants a year, you get the benefit of all that clinical experience,” says Dr. Cynthia Tsien, Education Director of the Ajmera Transplant Centre. “The fact that we have these volumes means you’re going to see unusual cases, the type you might only see once in your career, in this program.” For instance, many centres won’t accept patients of advanced age or with other medical conditions, but the Centre often helps these people.

Learning as priority

The other draw, says Dr. Schiff, is the emphasis on learning. “Fellows know they’re not just going to work with transplant patients but that we also dedicate time for them to learn,” he says.

The educational component of the fellowship is rooted in collaboration. While clinicians may specialize in different areas, all of the organ groups are together under one umbrella, says Dr. Tsien. That means all the fellows do orientation and rounds together every two weeks, where they learn about other organ programs and from one another, too.

The Ajmera Transplant Centre’s fellowship leaders are also working together to continually improve the learning experience. They’re currently sharing ideas around how to develop simulation programs that use special custom-made props that fellows can practice medical procedures on. Dr. Tsien is also borrowing ideas from the kidney team to help her fellows practice liver biopsies, while Dr. Donahoe is designing simulation devices to

help practice sewing lungs. “It’s the kind of skill you just can’t get enough practice on,” says Dr. Donahoe. “It’s great to give them tools that they can use to practice at home with as well.”

To further their skills, surgical fellows are encouraged to take advantage of the Toronto Video Atlas of Surgery, a UHN-built website made possible thanks to

“When you’re working somewhere that does about 200 liver transplants a year, you get the benefit of all that clinical experience. You see unusual cases, the type you might only see once in your career.”

DR. CYNTHIA TSIEN

Education Director, Ajmera Transplant Centre

UHN Foundation donors, with dozens of videos on complex surgeries. “When you’re a fellow doing training, you don’t quite know what you’re doing yet,” says Dr. Shwaartz, who’s watched many videos and made her own to share. “It takes the pressure off, because you can view the pitfalls of the surgery before you do it yourself.”

Improving transplants worldwide

During their tenure, fellows are also working with the latest and most innovative technologies, including using artificial intelligence to assess post-transplant outcomes. They’re also doing game-changing research into the social factors that impact access to transplants. Many fellows also publish papers on the rare cases they see at the Ajmera Transplant Centre so people around the world can benefit from their experiences. These fellows have gone on to work in other Canadian hospitals, and also the U.K., Jordan, Saudi Arabia, India and New Zealand, among other locales, says Dr. Schiff. “We’ve had quite a reach with our fellowship program,” he says.

One former fellow went on to create a successful lung transplant program in Florida. “He’s done amazing things,” says Dr. Donahoe, adding that this surgeon then hired more of the Centre’s fellows in subsequent years. “Wherever they go, they can help build their program or contribute to improving their program,” she says of the grads.

Dr. Shwaartz intended to return to Israel after her fellowship, but she’s staying put. UHN just hired her as a hybrid surgeon, dividing her time between hepatobiliary surgeries and abdominal transplants. The job also comes with an academic appointment at the University of Toronto, plus Dr. Shwaartz will be heavily involved in education, working with both the residency and fellowship surgical programs. In fact, she’s just started a master’s degree in education to further this role.

Out of everything, she’s most appreciative of the collaborative spirit at the Ajmera Transplant Centre. “The amazing thing about the fellowship is that it’s a team,” she says. Dr. Shwaartz is looking forward to that continuing – and getting to know her new home in Toronto – as she keeps learning, teaching and operating. “I love it here.” ■

FELLOWS FROM AROUND THE WORLD

In the past five years, UHN’s Ajmera Transplant Centre has trained more than 150 clinical fellows from 18 countries. Many later return to their home countries, where they start their own transplant programs.



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