Revolutionizing Patient Care

Relentlessly pursuing the cure for a rare, fatal disease or finding more effective treatments for a condition that affects millions – UT Southwestern physicians shine at both. Innovative treatments or breakthroughs this past year ranged from a promising stem cell therapy for a paralysis-causing neurologic disorder to pioneering use of robotic surgical tools to improve patient recovery.

DNA sequence results used for finding mutations that can lead to cancer. UTSW has one of the premier clinical cancer genetics programs in the U.S.
Two lifesaving discoveries help four generations of women

Her great-grandmother volunteered in groundbreaking cholesterol research at UT Southwestern in the 1980s. Today, 10-year-old Zoe Allen is benefiting from that decision, receiving the best treatment available for her condition from UT Southwestern’s top heart care specialists.

Four generations of Texas women with a hereditary condition that affects how the body processes cholesterol – familial hypercholesterolemia – form a story interwoven around the discovery of new treatments founded on UTSW research that has helped millions.

It all started in the early 1980s with Zoe’s great-grandmother, Estelle, who took part in UT Southwestern research on cholesterol. Then, just like her mother before her, Kathryn Geddie also had high cholesterol at a young age caused by familial hypercholesterolemia. So the Sunnyvale, Texas, mother of two began taking statin drugs to lower cholesterol levels measured in the upper 300s. (Normal range is less than 200 milligrams per deciliter (mg/dL).)

She also had her then 11-year-old daughter, Shanon, tested. Despite the child’s young age, her cholesterol was soaring at 400 mg/dL.

Little did they know then that their shared medical struggle would lead them on a journey to help reverse the disease – a journey begun by a family member years before.

Statin discovery

In the 1980s, UTSW Professors of Molecular Genetics Drs. Michael Brown and Joseph Goldstein wanted to know why people develop high cholesterol. Their question motivated the study of patients with familial hypercholesterolemia, including Mrs. Geddie’s mother, Estelle. The two scientists identified the basic mechanism of cholesterol metabolism, a significant finding that resulted in their 1985 Nobel Prize in Physiology or Medicine.

Their discovery laid the scientific foundation for the development of statin drugs, which lower cholesterol and help prevent heart disease.

Today, Dr. Goldstein is Chair of Molecular Genetics and Dr. Brown is Director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease. Both are Regental Professors and hold the Paul J. Thomas Chair in Medicine; additionally Dr. Goldstein holds the Julie and Louis A. Beecherl, Jr. Distinguished Chair in Biomedical Research, and Dr. Brown holds The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research.

Changing course

Knowing her mother’s history with medical research, Mrs. Geddie enrolled her daughter in clinical trials with a UT Southwestern pediatric cardiologist. At age 16, Shanon began taking statins, just like her mom. Today, thanks to the drugs, Shanon Allen is a healthy 42-year-old mother of two.

However, Mrs. Geddie’s health story became more complicated. “Three decades after I started taking them, the highest dose statin would no longer work,” Mrs. Geddie said.

Her doctor added a new drug to her regimen called a PCSK9 inhibitor – one of the Julie and Louis A. Beecherl, Jr. Distinguished Chair in Biomedical Research, and Dr. Brown holds The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research.

Cardiologist Dr. Parag Joshi confirmed Kathryn Geddie’s diagnosis of familial hypercholesterolemia with genetic testing in late 2018.
Familial hypercholesterolemia (FH) is a genetic condition that causes extremely high levels of cholesterol at an early age. When one person is diagnosed, other family members can be identified. However, only an estimated 10 percent of the possible 1.2 million Americans with FH know they have it.

“For someone with FH, the risk of heart disease is higher because their clock started early. They’ve been bathed in high cholesterol since birth,” said Professor of Internal Medicine Dr. Amit Khera, who completed his cardiology fellowship at UT Southwestern and holds the Dallas Heart Ball Chair in Hypertension and Heart Disease. “Sometimes by identifying one patient with FH, we find as many as eight or 10 more family members who are at risk.”

A study last year by Dr. Khera in JAMA Cardiology describes how blood donation programs represent a unique opportunity to screen for diseases such as FH. According to the AABB, approximately 6.8 million people in the U.S. donate blood every year, and roughly a third are first-time donors.

Dr. Khera’s team worked closely with Carter BloodCare in Dallas to review almost 1.2 million individual blood donation records specifically for markers of FH. They found more than 3,000 people who met criteria for FH based on their cholesterol levels, similar to the estimated prevalence in the general population. (The retrospective chart review had de-identified data, therefore no patient consent was required for this study, which received Institutional Review Board approval.)

The standard treatment for FH is diet and exercise, followed by the addition of statin medications in later childhood or early adulthood. The UT SW cardiology team is working on a follow-up study to connect those identified as potentially having the disorder with the appropriate medical care – including family screening – and to continue evaluating the effectiveness of these interventions.

In the future, donating blood may provide an alert as to whether you carry the gene for a dangerous inherited cholesterol disorder.

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At a glance: Familial hypercholesterolemia

- This genetic disorder, also known as FH, leaves the body unable to remove low density lipoprotein (LDL) – or bad – cholesterol from the blood, resulting in high levels.
- FH increases the likelihood of narrowing of the arteries and heart attacks at an early age. Some signs of FH include fatty skin deposits over parts of the body, including the heels, elbows, and around the eyes.
- The disease is caused by a mutation in a gene that plays an important role in cholesterol metabolism.
- The condition affects about 1 in 250 people in Europe and the United States.


From left: Kathryn Geddie, Shanon Allen, and Zoe Allen all have a hereditary condition that causes unusually high cholesterol levels.
Dr. Greenberg called Mr. Winspear’s a “whopper of a case” of spinal cord inflammation. It soon forced him to replace favorite hobbies – hiking and canoeing, skydiving and scuba diving – for life as a paraplegic.

Despite the challenges, Mr. Winspear still works as a marketing research consultant and stays physically active, using an elliptical-type glider for cardio exercise and a neuromuscular electrical stimulator.

Dr. Greenberg, a Cain Denius Scholar in Mobility Disorders, is hopeful the new treatment can provide some benefit for TM patients such as Mr. Winspear.

“There’s nothing worse than having a sense of hopelessness, ” Dr. Greenberg said. “It’s exquisitely meaningful to show patients with these rare diseases that science is paying attention. ”

Mr. Winspear and his wife, Ellen, were in North Carolina for their older son’s wedding when he started feeling lower back pain and intense tingling in his feet.

“I took some painkillers, but it only got worse, ” said Mr. Winspear, a longtime Dallas resident.

The night after the wedding, he went to a hospital, where imaging showed a lesion on his spinal cord. Within the hour, Mr. Winspear could no longer uncross his legs as numbness crept up his body.

“I was scared to death, ” Mr. Winspear said. “I was thinking, ‘What if it doesn’t stop?’ ”

After learning the diagnosis, Mr. Winspear’s son did a quick internet search and learned that UT Southwestern is one of only two places in the country focused on this disease.

Mr. Winspear was admitted to UT Southwestern, where he soon met Dr. Greenberg, one of the nation’s leading experts on the disorder, who now manages his care.

If successful, the clinical trial could lead to similar therapies for other conditions, such as multiple sclerosis.

“The trial has been more than 15 years in the making, with a huge number of hurdles, ” said Dr. Greenberg, Professor of Neurology & Neurotherapeutics and Pediatrics, explaining the challenges of developing cells that could both find the damaged area and fix the problem. “It offers real hope to people like Don.”

Transverse myelitis, or TM, is caused by inflammation in the spinal cord that damages myelin, a protective coating around neurons. The damage inhibits communication between nerve fibers in the spinal cord and the rest of the body, resulting in partial or total paralysis. Most patients see at least some improvement in the months after the attack, while a slim minority face permanent paralysis.

UT Southwestern’s clinical trial will study the safety and effectiveness of implanting progenitor cells into the spinal cord, with the hope of reversing paralysis in patients like Mr. Winspear.

The trial is starting with nine participants with the most severe form of transverse myelitis. Each will receive a one-time injection of progenitor cells designed to produce myelin along the damaged area and reestablish critical nerve signaling. The cells have successfully repaired the central nervous system in animals.

The chance of enduring a transverse myelitis attack in any given year is as little as 1 in a million – less likely than getting struck by lightning. It struck Mr. Winspear during one of the happiest times of his life.

UT Southwestern’s Peter O’Donnell Jr. Brain Institute. By injecting patients with stem cells engineered to repair the central nervous system – called progenitor cells – Dr. Benjamin Greenberg and fellow scientists are working to establish the first treatment to repair spinal cords inflamed by transverse myelitis.
Unusual brain cell behavior helps predict epileptic seizures minutes in advance

Elizabeth Delacruz can’t crawl or toddle around like most youngsters her age. A rare metabolic disorder that decimated her mobility has also led to blindness from brain damage and epileptic seizures.

Her mother, Carmen Mejia, is hoping doctors can find a way to detect and prevent Elizabeth’s seizures that stem from the terminal disease known as pyruvate dehydrogenase deficiency (PDHD). In this disease, mitochondria don’t provide enough energy for the body’s cells.

A UT Southwestern study gives Ms. Mejia hope: By monitoring the activity of a specific brain cell type responsible for seizures, scientists now can predict convulsions at least four minutes in advance. The research, published in *Science Translational Medicine*, further shows that an edible acid called acetate may effectively prevent seizures if taken before they occur.

“We’ve found a new approach that should help us and other scientists tackle the root of seizures for many kinds of epilepsy,” said Dr. Juan Pascual, a neurologist with UT Southwestern’s Peter O’Donnell Jr. Brain Institute who led the study.

The study, supported by the National Institutes of Health, The Once Upon a Time Foundation, and other philanthropic donations, shows how astute patient observations can guide transformative research.

Dr. Pascual, a Professor of Neurology & Neurotherapeutics, Pediatrics, and Physiology who has an additional appointment in the Eugene McDermott Center for Human Growth and Development, holds the Ed and Sue Rose Distinguished Professorship in Neurology and The Once Upon a Time Foundation Professorship in Pediatric Neurologic Diseases.

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just one of multiple leading-edge cancer care technologies that the Harold C. Simmons Comprehensive Cancer Center offers patients, in addition to access to clinical trials.

“It’s a great service to the community and offers a lot to women who are facing breast cancer with the busy lives they have today,” said Dr. Asal Rahimi, Associate Professor and Director of Clinical Research in Radiation Oncology at the Simmons Cancer Center. “Our mission is to try to provide very effective treatment in as little time as possible.”

The GammaPod breaks new ground, targeting the tumor within 3 millimeters with high-level radiation without damaging healthy tissue. The device uses vacuum suction that temporarily immobilizes the breast, holding it perfectly still so radiation can hit its target. Suction pulls the breast up against the wall of a fitted plastic cup. Before stereotactic radiation is delivered, a CT scan pinpoints the tumor's exact location. The patient presses against the GammaPod’s table, where there is an opening for the breast cup to slide through. The patient lies face down for treatment, so the breast is downward, eliminating radiation near the heart and lungs.

The GammaPod’s unique configurations allow oncologists to narrow radiation down to a range of just 3 millimeters – less than the width of three stacked pennies. Standard breast cancer radiation treatment typically lasts four to six weeks. But with the stereotactic radiation delivered by the GammaPod, treatment can be shortened to one to five days, potentially lowering toxicity.

Shining a blue light to improve bladder cancer treatment

When Mansfield physician Dr. Robert McMichael was diagnosed with bladder cancer in May 2018, he wanted the best treatment possible. His quest took him to UT Southwestern for exams using a new device, the blue-light flexible cystoscope.

UT Southwestern researchers were among those who tested this technology, so when the Food and Drug Administration cleared it for use in 2018, the Dallas-based institution became one of just four in the country to initially offer it for outpatient use. Dr. McMichael became patient No. 1. Since then, use of the technology has expanded to about a dozen institutions in the U.S.

“Blue light works better than white light (such as light from sunlight) because we instill a photosensitizing agent into the bladder that’s taken up by cancer cells. When you shine a blue light on it, the cancer cells look pink and normal cells don’t,” said Dr. Yair Lotan, a Professor of Urology who completed an internship and two residencies at UT Southwestern.

“Once you have bladder cancer, you have to be monitored indefinitely,” said Dr. McMichael, who remains cancer-free but knows the risk of recurrence can be high for some. “If there’s any cancer to be seen, the blue-light cystoscopy significantly improves the chances of seeing it.”
One of UT Southwestern's first GammaPod patients, Patricia Salcido, 61, of Grand Prairie, said she was a bit nervous before her first treatment, but completely at ease afterward. She was a typical GammaPod patient, requiring five roughly 20-minute treatments. “The new technology is wonderful. I totally believe in it,” Ms. Salcido said at the time of one of her treatments. She finished the therapy last year and has remained cancer-free.

Since installation of the device in March 2019, more than 50 patients have undergone GammaPod treatment at UT Southwestern. Dr. Rahimi co-chairs the GammaPod Consortium with a doctor from the University of Maryland, where the GammaPod was developed. Clinical trials are ongoing and more are planned, she said. Doctors will likely combine the GammaPod with other resources in the Department of Radiation Oncology to personalize treatment to the size of patients’ breasts and tumors.

### Making history

**UTSW is first hospital in Texas to perform single-incision robotic surgery**

In late 2018, UT Southwestern became the first hospital in Texas to perform single-incision robotic surgery – a revolutionary technology that can mean less pain and a faster recovery for patients.

With the technology, all necessary surgical tools are inserted through one small incision. Dr. Jeffrey Cadeddu, Professor of Urology and Radiology, first used the new technique at UTSW in November 2018 to perform surgery on a ureter, the duct that passes urine from the kidney to the bladder, in order to correct a blockage.

Single-incision robotic surgery is a type of laparoscopic surgery, or surgery performed through small incisions and made possible by a tiny video camera that can be inserted into the area of surgery, giving the surgeon a view inside the patient’s body without cutting a large opening.

With this type of surgery, several incisions are usually needed to accommodate both the camera and surgical tools. Standard laparoscopic surgery to repair a ureter, for example, involves four small incisions.

Over the last decade, surgeons have looked for a way to reduce the number of openings. “Every incision means increased pain, increased risk of hitting a blood vessel,” said Dr. Cadeddu, who won the 2018 Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine.

UT Southwestern performs single-incision laparoscopic surgery with a robotic device called the Single Port SP Robot. It has four arms that can insert through a single incision. Intuitive Surgical Inc., the company that makes the SP Robot, initially rolled it out to just a handful of medical centers, including UT Southwestern, considered one of the leaders in robotic surgery.

Besides Dr. Cadeddu, others trained to use the device include Dr. Jeffrey Gahan, Assistant Professor of Urology; Dr. Baran Sumer, Professor of Otolaryngology – Head and Neck Surgery, who holds the T.D. Lupton Family Professorship in Patient Care, in Honor of Dr. John Dowling McConnell and Dr. David Andrew Pistemaa; and Dr. John Truelson, Associate Professor of Otolaryngology – Head and Neck Surgery, who holds the American Airlines Professorship in Cancer Research. UT Southwestern faculty members have completed more than 100 single-incision robotic surgeries to date.

Dr. Cadeddu, who holds the Ralph C. Smith, M.D. Distinguished Chair in Minimally Invasive Urologic Surgery, has also combined single-incision techniques with the innovative use of magnets to control surgical tools inside the body to reduce scarring.

“We expect this to be the start of a cascade of improved surgical procedures with fewer incisions, meaning less pain and fewer complications for patients,” Dr. Cadeddu said.
New living-donor liver transplant program to address severe shortage

More than 1,700 patients in the U.S. die each year waiting for a liver transplant.

UT Southwestern’s new living-donor liver transplant program hopes to lower that heartbreaking statistic by offering patients a route to expedited transplantation and improved survival.

“Living-donor transplantation helps address the critical need for more livers to transplant and is just what it sounds like – a living person can give part of his or her liver to another,” said Dr. Steven Hanish, Surgical Director of UTSW’s Living-Donor Liver Transplantation Program.

“The liver regenerates,” Dr. Hanish explained. “Surgeons can remove a portion of a liver from a healthy donor – up to 70 percent – and transplant it into another person, and it will grow. The portion left behind in the donor will also regrow. That process happens in the first few weeks after surgery.”

Living-donor liver transplantation has better outcomes than deceased-liver transplantation, partly because recipients are not on the waitlist for prolonged periods while their health declines, hoping for an available liver, said Dr. Hanish, also Associate Professor of Surgery.
Not every liver transplant program has a living-donor component, Dr. Hanish noted. Living-donor liver transplant surgery is complex and requires advanced expertise – the kind found at UT Southwestern, he said. The procedure takes between six and eight hours and involves carefully separating the liver so that both pieces can remain functioning in the recipient and the donor.

Only 524 living-donor liver transplants were performed nationally in 2019, according to the United Network for Organ Sharing (UNOS), the nonprofit organization that manages the U.S. organ transplant system under contract with the federal government. UT Southwestern launched its living-donor liver transplant program in 2018.

Donors do not have to be related to the recipient. Historically, though, recipients’ children, parents, and siblings – in that order – have been the most common donors, according to UNOS.

Once a transplant patient identifies a potential donor, the donor contacts UT Southwestern to arrange for a full medical and psychological evaluation, a process that takes place independent of the patient (recipient) evaluation.

If all evaluations are favorable, surgery is then scheduled with the living-donor transplant team.

“Any patient who is on the liver transplant waiting list is potentially eligible to receive a liver from a live donor,” noted Dr. Arjmand Mufti, Medical Director of Living-Donor Liver Transplantation and Assistant Professor of Internal Medicine.

Donors with a compatible blood type for the recipient must also be in good physical and mental health, have a BMI under 35, and range in age from 18 to 60.

The availability of living-donor liver transplantation is the latest mark of distinction for UT Southwestern’s Liver Transplant Program, which saw a 103 percent increase in transplants between 2017 and 2019.

Additionally, the program cut the length of stay after transplant from eight days to only five – one of the lowest in the country, said Dr. Parsia Vagefi, Associate Professor of Surgery, Chief of the Division of Surgical Transplantation, and holder of the Ernest Poulos, M.D. Distinguished Chair in Surgery.

“A leading-edge program in living-donor liver transplantation surgery is entirely consistent with our distinguished record in liver care and our status as one of the nation’s leading academic medical centers,” Dr. Vagefi said. “We’re certainly proud of our past, but even more excited for our future.”
The OCS is about the size of a small shopping cart. Inside, major blood vessels of the donated liver connect to tubes that infuse it with blood. The liver inside the device makes bile and processes medications.

Dr. Parsia Vagefi, Associate Professor of Surgery, Chief of the Division of Surgical Transplantation, and holder of the Ernest Poulos, M.D. Distinguished Chair in Surgery, explained why this might work better than the current system: “The longer a liver sits on ice, the more likely it is to have problems after transplant. It will become unusable if stored too long. With patients waiting for organs, this new way may expand the number of donated livers for transplant.”

One recent beneficiary was Greg Nielsen, a Dallas construction worker. At 59, his liver was failing due to cirrhosis and cancer. When he reached UT Southwestern in June 2018, his options were running out.

After a liver became available, Dr. MacConmara and his team traveled to the donor hospital, carefully placed the liver in the OCS, and returned to UT Southwestern. They monitored it as it produced bile and saw it was functioning well. Dr. Vagefi led the surgical team that transplanted it.

Mr. Nielsen went home three days later. “Before the surgery, I couldn’t walk much at all,” he said. “Now I walk 45 minutes every morning. It’s like a miracle.”

Use of new technology improves odds of liver transplant success

Since the first liver transplant in 1963, donated livers have been immersed in icy fluid inside a cold storage system for transport. Only after the organ is transplanted does the surgeon learn if it functions correctly.

UT Southwestern transplant surgeon Dr. Malcolm MacConmara is leading an international trial to test a better way. The study at 20 U.S. sites is examining the effectiveness of a new device, the portable Organ Care System (OCS) from TransMedics, which keeps donated livers warm and circulates blood during organ transport.

“It’s like a virtual transplant. By putting the liver on the machine, we can truly approximate the conditions of the body.” – Dr. Malcolm MacConmara

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“it’s like a virtual transplant,” said Dr. MacConmara, Assistant Professor of Surgery. “By putting the liver on the machine, we can truly approximate the conditions of the body.”