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- Lawson delivers disruptive innovation with the potential to positively impact the health of individuals in the region, and across Canada and the world

Lawson delivers disruptive innovation with the potential to positively impact the health of individuals in the region, and across Canada and the world.

Lawson scientists bring knowledge to clinical care providers and to industry partners so they can move it forward for the benefit of patients. To do that, we have a simple philosophy: follow your curiosity.”

– Dr. David Hill, Scientific Director
Growing up with type 1 diabetes

Lawson researchers are finding ways to ease the transition from paediatric to adult care.

Nicole Pelcz was 13 years old and had just started grade nine when she found out she had type 1 diabetes. “I kept feeling sick at school and eventually my mom said it looked like I’d lost quite a bit of weight. She told me she could see it in my face. So I went and weighed myself, and I had lost almost 20 pounds. I went to the doctor the next day and was diagnosed with diabetes,” she says.

Type 1 diabetes occurs when the body attacks and destroys cells in the pancreas that make insulin. Our body needs insulin to use the sugar found in many foods for energy. Without it, sugar builds up in the blood, which can damage organs, blood vessels and nerves.

It is a chronic disease that requires a high level of patient self-management and engagement. Blood glucose (sugar) levels need to be monitored throughout the day and insulin must be delivered through daily injections or an insulin pump. Diet, exercise, stress or other factors can impact how much insulin is needed.

Although type 1 diabetes can occur later in life, it is most often seen in young patients. Parents of children and young adults with diabetes need to have a very active role in the management of their child’s condition.

But what happens when children grow up, leave home for school or work, and have to manage their diabetes independently?

“Unfortunately, 30 per cent of young adults drop out of medical care when they transition from paediatric to adult care. This impacts long-term health,” says Dr. Cheril Clarson, associate scientist at Children’s Health Research Institute, a program of Lawson, and a paediatric endocrinologist at Children’s Hospital at London Health Sciences Centre (LHSC).

“Sometimes our patients transfer to adult care and then we hear a year or two later that they’re not being seen. Often their diabetic control deteriorates and this can lead to increased diabetes-related hospital admissions and acceleration of diabetic complications. It’s been well-recognized for decades that transition of care is a huge problem,” Dr. Tamara Spaic, Lawson associate scientist and adult endocrinologist at St. Joseph’s Health Care London (St. Joseph’s), has always shared Dr. Clarson’s concerns about transition of care for young adult patients.

“Dr. Clarson and I have a close collaborative relationship. I became interested in transition when I spent time at Children’s Hospital during my fellowship training. When I established my own practice in diabetes and saw some of the difficulties that young adults who had transitioned from paediatric care were experiencing, I realized that we needed to change the care model to improve the transition process,” says Dr. Spaic.

When you have type 1 diabetes you have to think about it throughout the day and in any circumstance.”

– Dr. Tamara Spaic

In 2012, Drs. Clarson and Spaic launched a multi-centre randomized controlled trial with the goal of improving the transition from paediatric to adult care through a structured transition program.

The program provided additional support to patients as they began adult care and included having a Certified Diabetes Educator act as a dedicated transition coordinator. The coordinator attended the patients’ clinic visits, and was accessible between visits by email, text or phone to problem solve specific diabetes care issues, and to help patients adjust to care at a new facility.

Just after starting grade nine, Nicole Pelcz was diagnosed with type 1 diabetes. When she was 19 years old, a new transition program guided her through the process of moving from paediatric to adult care.

Nicole was one of Dr. Clarson’s patients and heard about the study from her care team. She enrolled when she was 19 years old and transitioning from paediatric care at Children’s Hospital to adult care at St. Joseph’s.

“At the time I was just starting university. I was moving away from home and would be living on my own. Before that, my mom had always come with me to my appointments but I knew that she wasn’t going to be coming with me anymore. I felt like it would be helpful to have someone there to guide me through the transition,” says Nicole.

“When you have type 1 diabetes you have to think about it throughout the day and in any circumstance. Your life is not that spontaneous and this is not easy for young adults. They’re trying to gain their own independence and figure out who they are as a person: their personality, sexuality, friends, what they’re going to be in life. These things seem so much more important than thinking about their health every day,” explains Dr. Spaic. “On top of all this, hormonal changes during this time period can make blood sugar harder to control.”

Another factor that makes this transition period difficult is the difference between paediatric and adult care.
“Paediatric care is very family-oriented and you meet with the whole care team at the same appointment, including an endocrinologist, nurse, dietitian and social worker. Adult care requires more independence as the patient schedules how often they want to see their care team and makes separate appointments to see their endocrinologist, nurse, dietitian and social worker,” says Dr. Clarson.

The structured transition program was successful in helping patients meet the challenges of managing diabetes as a young adult. Drs. Spaic and Clarson found that the program led to better clinic attendance, and patients reported being more satisfied with their care and felt that the emotional burden of their diabetes had decreased.

“Having my transition coordinator attend my appointments with me made me feel more comfortable talking to my new healthcare team. Following appointments, as well as any other time during the transition, she answered all the questions I had,” says Nicole. The study enrolled 205 young adults with type 1 diabetes between the ages of 17 and 20. Patients were recruited with type 1 diabetes between the ages of 17 and 20. Patients were recruited with type 1 diabetes between the ages of 17 and 20. Patients were recruited with type 1 diabetes between the ages of 17 and 20.

Patients were seen in the paediatric care setting for six months and then transferred to adult care, where they continued with either the transition program or standard care for one year. “Our hope is that support from a transition coordinator will become a standard of care for young adults with type 1 diabetes during the transition from paediatric to adult care. A similar model could also be considered for other chronic childhood conditions, such as cystic fibrosis, congenital heart disease and inflammatory bowel disease,” says Dr. Spaic.

Nicole is now 23 years old and a recent graduate of the Food and Nutrition program at Brescia University College, an affiliate of Western University. She is working towards becoming a dietitian and a Certified Diabetes Educator like her transition coordinator so that she can help other type 1 diabetes patients and ensure they have a positive care experience.

The structured transition program Dr. Cheril Clarson (left) and Dr. Tamara Spaic (right) developed led to improved clinic attendance and satisfaction with care among young adult patients with type 1 diabetes. Nicole Pelcz (centre) was one of the patients enrolled in the study.

Why is the transition from paediatric to adult care challenging for patients with type 1 diabetes?

- The transition coincides with multiple other changes in the lives of young adults, including starting post-secondary education.
- It is a time when they are becoming more independent and their parents may not be monitoring their care as closely.
- Paediatric and adult care are different.

Paediatric care is family-oriented and patients meet with their whole care team at the same appointment. Adult care requires more independence as the patient schedules how often they want to see their care team and makes separate appointments to see each member of the team.
A GUT REACTION

Tackling colorectal cancer using ‘mini-guts’

In Dr. Samuel Asfaha’s laboratory you will find...

The hallmark of medical research from petri dishes to high-powered microscopes. More unusually, you will find ‘mini-guts’ — gastrointestinal (GI) structures developed from stem cells. The mini-guts are only one cell thick but their structure is similar to a normal GI tract in humans. “The ability to grow a fully structured gut lining in a dish is unique,” explains Dr. Asfaha, a Lawson scientist and gastroenterologist at London Health Sciences Centre. “The gut contains stem cells that regenerate normal, healthy cells every few days. This allows us to grow healthy gut cells indefinitely,” says Dr. Asfaha.

Colorectal cancer, cancer of the colon or rectum, is the second leading cause of cancer death in Canada. Dr. Asfaha’s team is growing mini-guts from both healthy tissues and cancerous ones, and mutating genes to see how they affect the tissues and their response to injuries caused by inflammation and radiation. The team is also using new technology to test different drugs on the mini-guts. This allows them to see what drugs work in preventing and treating colorectal cancer without harming healthy tissue.

The role of inflammation

Inflammation is often associated with the development of cancer. For example, research has shown that inflammatory bowel disease (IBD), including Crohn’s disease and ulcerative colitis, can increase a patient’s risk of colon cancer. But we also know that colorectal cancer develops over several years. “The gut is a fascinating system as its cells are regenerated every two to five days by stem cells. For a cell in the gut to be mutated over several years and turn into cancer, it is reasonable to think it is a stem cell being transformed because they are long-lived and have the ability to regenerate other cells,” says Dr. Asfaha.

Before relocating to London, Ontario, Dr. Asfaha was part of a team of researchers at Columbia University in New York City. The team discovered a unique cell in the gut that has a long lifespan but is resistant to genetic mutation. As soon as they added inflammation to the cell’s environment, like that associated with IBD, the cell led to the development of tumours. They termed the cell a facultative stem cell: it only takes on the characteristics of a stem cell in the condition of inflammation.

A new stem cell population

The team is also growing mini-guts to examine the role of a newly discovered stem cell and its role in radiation-resistant cancer. The stem cells of the gut were first identified in 2007. In 2015, Dr. Asfaha identified another stem cell population in the gut and proved its importance to the growth of colon cancer. When mutated, these particular stem cells lead to tumours that are resistant to radiation therapy. “Radiation therapy is very important for treatment of rectal cancer, but not all patients respond to it,” says Dr. Asfaha. “We’re trying to determine if some patients don’t respond to therapy because their cancers were formed from mutation of this newly discovered stem cell.”

Dr. Asfaha’s team is studying both stem cell populations in the GI tract using their mini-gut system. They want to further characterize each stem cell and the tumours that develop. They hope to understand the mechanisms that make some tumours resistant to radiation therapy and identify a drug that can make these tumours more sensitive to radiation.

Dr. Asfaha also has a goal of one day using the mini-gut system to study patient-specific tumours. “No two cancers are the same as cancer genetics differ between patients,” explains Dr. Asfaha. “We hope to eventually take individual patient samples, grow a mini-gut from their tumour and see what therapies work best against it.”

Through continued innovation, the team hopes these mini-guts will help drive colorectal cancer research forward.

Dr. Asfaha and his Lawson team are growing mini-guts to understand how inflammation changes this particular cell and transforms it into a cancer. This includes studying two proteins highly expressed by the cell called CDX1 and CDX2, which are the enzyme targets of aspirin, a drug previously shown to reduce patients’ risk of colorectal cancer.

Dr. Asfaha is currently conducting research to examine whether taking aspirin or other anti-inflammatory drugs can inhibit the transformation of this particular cell. “Aspirin can be toxic to the gut, especially when taken regularly at high doses, and can lead to the development of ulcers,” he explains. “If we can better understand how aspirin might inhibit the transformation of this cell, we can develop a new class of drugs that work in a similar way but with less toxicity.”

Dr. Asfaha is a part of the Cancer research program at Lawson. He is an assistant professor in the Departments of Medicine and Oncology, Schulich School of Medicine & Dentistry at Western University.
When Judy Williams slipped on a patch of ice and broke her wrist six years ago, she could not imagine the health journey she was embarking on. The months that followed were sleepless ones. Judy was in excruciating pain, her hand swelled and her fingers turned blue. She visited the emergency department four times to have her cast removed and reapplied.

Judy was eventually referred to the Hand and Upper Limb Centre (HULC) at St. Joseph’s Health Care London (St. Joseph’s). Dr. Robert Richards, a plastics and microvascular surgeon, realized her injury was not a simple break and that she had complex regional pain syndrome (CRPS). Dr. Richards referred Judy to St. Joseph’s Pain Management Clinic where Dr. Collin Clarke, a Lawson scientist and an anaesthesiologist, confirmed her diagnosis.

CRPS is a chronic neuropathic pain condition that occurs after injury to a limb. After the injury heals, pain persists. “The exact mechanisms behind CRPS are not clear, but the initial injury triggers a firing of neurons in the patient's central nervous system that is perceived by the body as chronic pain,” explains Dr. Clarke. “Essentially the brain keeps a memory of the pain even after the injury has healed.”

The diagnosis was life changing for Judy. “It may sound strange but I was extremely relieved,” says Judy. “The pain I was experiencing was not logical. There’s a certain relief in knowing what’s wrong with you and working towards management of the condition.”

Under the care of Dr. Clarke, Judy has seen improvements to her health through a variety of treatments. These have ranged from pharmaceutical therapies to a spinal cord stimulator. Judy has also participated in pain research at Lawson. Judy sees her participation as a way to give back to London’s medical and research community, and help future generations of patients.

DRIVING PAIN RESEARCH FORWARD

London, Ontario is home to a large multidisciplinary pain research team with collaborators across Lawson, London Health Sciences Centre, St. Joseph’s and Western University. A primary area of interest for these researchers is neuropathic pain.

In 2008, Dr. Dwight Moulin, a Lawson scientist and neurologist at St. Joseph’s Pain Management Clinic, spearheaded a national collaborative team that set up a neuropathic pain patient registry. This registry has recruited over 800 patients to the Canadian Neuropathic Pain Database. The powerful tool has allowed neuropathic pain researchers across Canada to collaborate on nine studies published in leading pain research journals.

In one of these studies, led by Dr. Moulin, researchers examined the long-term outcomes of patients who visit pain clinics to manage neuropathic pain conditions like CRPS. Patients were followed over one year to study any improvements in pain intensity, quality of life and other treatment outcomes. Researchers found that at 12 months only 23.7 per cent of patients experienced significant improvements.

“This study shows that only one in four patients get adequate pain relief,” says Dr. Moulin. “This suggests that our current treatments are not good enough. We need more research to better understand and treat chronic neuropathic pain.”

USING MRI TO STUDY COMPLEX REGIONAL PAIN SYNDROME (CRPS)

Lawson researchers are conducting a number of studies to better understand neuropathic pain. In one project Dr. Keith St. Lawrence, a Lawson Imaging scientist, collaborated with Drs. Clarke and Moulin to study brain plasticity, defined as lasting changes to the brain, in patients with CRPS.

“Previous studies have shown that there are structural changes to the brains of patients with CRPS,” says Dr. St. Lawrence. “However, little was known about the differences in brain changes...”
Lawson researchers such as Dr. Dwight Moulin (left) and Dr. Keith St. Lawrence (right) are conducting studies to gain more understanding of neuropathic pain and improve treatments.

“MOST PEOPLE DON’T UNDERSTAND CHRONIC PAIN. I WANT TO DO WHATEVER I CAN TO HELP OTHERS.”

– Judy Williams

The researchers discovered different patterns of brain changes between the two groups. In early-stage CRPS patients, they found shrinkage in the volume of grey matter in areas of the brain associated with pain processing. Meanwhile, no changes were detected in areas of the brain associated with emotional response to pain.

“This research could provide clues as to why pain persists in patients with CRPS,” says Dr. St. Lawrence. “It’s showing there are unique early changes to the brain. This highlights how an injury to a limb can cause alterations in the central nervous system.”

The researchers hope their findings might also provide clues for improving treatments. They want to further study whether they can predict a patient’s response to treatment based on early changes they see in the brain. They also hope their research can lead to new treatments, perhaps by targeting areas of the brain that are changing.

This is an exciting prospect, especially for CRPS patients like Judy Williams who participated in the study. “When Dr. Clarke approached me about joining the study, I saw it as my chance to give back,” says Judy. “Most people don’t understand chronic pain. I want to do whatever I can to help others. If we can link this to the prevention or treatment of CRPS, that’s amazing.”

“Recognizing the burden of chronic pain, our team is committed to research in this field,” says Dr. Clarke. “Utilizing state-of-the-art neuroimaging technologies, we have been able to look into the brain to see changes that occur in those with CRPS.”

UNDERSTANDING THE INDIVIDUAL EXPERIENCE OF PAIN

Researchers are also looking at psychological factors associated with chronic pain. There is a growing interest in how these factors influence patient outcomes. In one project, researchers studied catastrophizing and its relation to patient outcomes. Catastrophizing is a tendency to focus on, exaggerate and feel helpless towards pain.

“We often see catastrophizing in those with high anxiety levels,” says Dr. Moulin. “The injury might be minor but their experience of it is magnified by their psychological state.”

The study, led by Dr. Melanie Racine, formerly a Lawson trainee and current research associate at Western University, recruited 538 patients from across Canada as part of the Canadian Neuropathic Pain Database, including those recruited from St. Joseph’s Pain Management Clinic. The research participants were asked to complete measures of their own catastrophizing and pain intensity when first seen in the clinic and then at three and six-month follow-up appointments.

The study showed that when catastrophizing was reduced early in treatment, it predicted improvement in pain intensity later in treatment. Similarly, improving pain intensity early in treatment predicted a reduction in catastrophizing later in treatment.

“Those results suggest that treatments targeting catastrophizing might positively influence other pain outcomes and vice versa,” says Dr. Moulin. “There may be multiple paths to achieving positive outcomes.”

Cognitive behavioural therapy (CBT) is currently the most common psychosocial treatment for addressing pain-related catastrophizing. This research suggests that CBT could be beneficial as an alternate therapy for patients with neuropathic pain.

Through continued work, Lawson researchers are working to advance knowledge of neuropathic pain and uncover even more potential therapies for patients like Judy Williams in the future.

Dr. Collin Clarke is a part of the Imaging research program at Lawson. He is an assistant professor in the Department of Anaesthesia and Peri-Operative Medicine, Schulich School of Medicine & Dentistry at Western University.

Dr. Dwight Moulin is a part of the Neurological Disorders research program at Lawson. He is the Earl Russell Chair, Pain Medicine and a professor in the Departments of Clinical Neurological Sciences and Oncology, Schulich School of Medicine & Dentistry at Western University.

Dr. Keith St. Lawrence is a part of the Imaging research program at Lawson. He is an associate professor in the Departments of Medical Biophysics and Medical Imaging, Schulich School of Medicine & Dentistry at Western University.

WHAT IS CHRONIC NEUROPATHIC PAIN?

• Chronic neuropathic pain results from a disease or damage that affects nerves in the somatosensory system.
• The somatosensory system is part of the peripheral and central nervous system that is linked to sensory receptors throughout the body. The system helps the brain to understand what an individual is feeling both inside and on the surface of their body.
• With neuropathic pain, nerves become damaged and send pain signals to the brain.
• Neuropathic pain conditions include complex regional pain syndrome (CRPS) and nerve pain due to diabetes and shingles.
Family environment influences emotional well-being of children with epilepsy

Children with epilepsy have a higher risk of developing emotional and behavioural disorders, including depression, anxiety and poor self-esteem, yet it has been difficult to pinpoint why this occurs. Researchers at Children’s Health Research Institute (CHRI), a program of Lawson, studied a group of children aged four to 12 with new-onset epilepsy, investigating factors at the time of diagnosis and their impact on the emotional well-being of the children two years later. They found that clinical factors, such as the type of epilepsy and frequency of seizures, were not associated with emotional well-being. Instead, several family characteristics, including family stresses, functioning and resources, were strongly associated with emotional well-being. The study was led by Dr. Kathy Speechley, chair of the Children’s Health & Therapeutics Division at CHRI, and Dr. Shane Goodwin, who was a PhD candidate in the Department of Epidemiology & Biostatistics at Western University’s Schulich School of Medicine & Dentistry and a trainee at CHRI at the time the study was conducted.

Radiation techniques to improve quality of life for lung cancer patients

While palliative radiation therapy is used to ease pain in patients with advanced lung cancer, it often has adverse effects on the esophagus, which leads to symptoms like heartburn and difficulty swallowing. Through the PROACTIVE clinical trial, Lawson scientist Dr. Alexander Louie is testing new palliative radiation techniques to spare these effects on the esophagus and improve quality of life for lung cancer patients. PROACTIVE first launched at the London Regional Cancer Program (LRCP) at London Health Sciences Centre in late 2016. It is now active at multiple centres across Canada. The clinical trial uses more precise radiation techniques to reduce the dosage of radiation to the esophagus or ‘swallowing passage’ with the hope of easing pain, building comfort and allowing for a nutritious diet.

New test can identify P. acnes shoulder infection, a complication of arthroplasty surgery, within 24 hours

Propionibacterium acnes (P. acnes, or as it has been recently re-named, Cutibacterium acnes) is a type of bacteria typically found deep in the hair follicles and sebaceous pores of the skin. A P. acnes infection of the shoulder is a common and serious complication that occurs after arthroplasty (surgery to replace a damaged joint, most commonly with artificial material), which can cause pain in the shoulder joint and often loosens the implant. It can be difficult to diagnose a P. acnes infection as it often presents without symptoms that would be characteristic of an infection, such as pain, skin reddening, or wound drainage. A team of researchers led by Dr. David O’Gorman, Lawson scientist and co-director of Molecular and Cellular Research at the Roth McFarlane Hand and Upper Limb Centre (HULC) at St. Joseph’s Health Care London, developed the PCR-RFLP assay, a test which can accurately identify P. acnes infection within 24 hours. Current methods take an average of six or more days, and are prone to sample contamination and false-positive results.
Healthy aging and a healthy gut

In one of the largest microbiota studies conducted in humans, researchers at Western University, Lawson and Tianyi Health Science Institute in Zhenjiang, Jiangsu, China, showed a potential link between healthy aging and a healthy gut. With the establishment of the China-Canada Institute, the researchers studied the gut bacteria in a cohort of more than 1,000 Chinese individuals in a variety of age-ranges from three to over 100 years-old who were self-selected to be extremely healthy with no known health issues and no family history of disease. The overall microbiota composition of the healthy elderly group was similar to that of people decades younger, and the gut microbiota differed little between individuals from the ages of 30 to over 100.

Brains of patients with schizophrenia have the capacity to reorganize and fight the illness

Schizophrenia has long been considered a degenerative illness with no possibility of a cure. Research led by Dr. Lena Palaniyappan, Lawson scientist and medical director for the Prevention & Early Intervention Program for Psychoses (PEPP) at London Health Sciences Centre, is providing new insights that are challenging this perception. Using imaging data, the team was the first to show that the brains of patients with schizophrenia have the capacity to reorganize and fight the illness. Schizophrenia is an illness generally associated with a widespread reduction in brain tissue volume, but the study found that, given sufficient time, a subtle increase in tissue also occurs in certain brain regions. The project is the result of an international collaboration among scientists in Nottingham, UK; Shanghai and Changsha, China; Lawson; and Robarts Research Institute at Western University.

Potential for new glaucoma treatment

Glaucoma is a group of diseases that affect nearly 70 million people worldwide. In some patients with primary open-angle glaucoma, the structure of the trabecular meshwork, a porous tissue in the eye through which the clear fluid that fills the eye drains out, is damaged by fibrosis. Fibrosis is a thickening or scarring of tissue caused by excess matrix molecules, such as collagen, deposited in the trabecular meshwork. This prevents fluid in the eye from draining out normally, which leads to increased pressure in the eye and damage to the optic nerve. A team of Lawson researchers at St. Joseph’s Health Care London led by Dr. Sunil Parapuram found that inactivation of a protein called “phosphatase and tensin homolog” (PTEN) can cause too many matrix molecules to be deposited in the trabecular meshwork, leading to fibrosis. However, when PTEN activity was increased, it reduced the amount of matrix molecules deposited. This means that drugs that can activate PTEN have the potential to be used as a treatment for open-angle glaucoma.

Preventing family homelessness

Lawson, Western University, the City of London, and Mission Services of London, Ontario, partnered to assess the effectiveness of a shelter diversion pilot-program at Rotholme Women’s and Family Shelter (Mission Services). The Prevention of Homelessness Among Families (PHAF) project showed that a low percentage of families ended up in shelter when accessing the program, and as many as 90 per cent of the families were known to still be housed 18 months later. Rotholme’s shelter diversion program works with families to maintain stable housing prior to eviction. Families at risk of homelessness who contact the shelter before leaving their home are immediately connected with a housing crisis worker. Together, parents and the crisis worker explore alternate housing arrangements, services, and supports. The study was led by Dr. Cheryl Forchuk, Beryl and Richard Ivey Research Chair in Aging, Mental Health, Rehabilitation and Recovery at St. Joseph’s Health Care London’s Parkwood Institute.

From left: Hong Liu, research technician; Venkat Arutla, fourth year undergraduate student working in Dr. Sunil Parapuram’s lab; and Dr. Parapuram, Lawson scientist

From left: Jan Richardson, manager, Homelessness Prevention, City of London; Dr. Cheryl Forchuk, assistant scientific director at Lawson, and professor of Nursing at Western University; Gordon Russell, director of shelters at Mission Services of London; and Peter Rozeluk, executive director at Mission Services of London
Most of us think of hydrogen sulfide, known for its rotten egg smell, and carbon monoxide, often called the “silent killer,” as poisonous gases harmful to human health. While they can be lethal in large quantities, they are also part of a family of small molecules called gasotransmitters that are produced in our own bodies. Lawson researchers Drs. Alp Sener and Gedas Cepinskas are using controlled doses of these molecules to pioneer new solutions to health care challenges.

**Hibernating kidneys**

The inspiration for Dr. Sener’s research on hydrogen sulfide and kidney transplantation came in part from a paper in the journal Science that his father showed him one day while he was an undergraduate student. The paper focused on the protective effects of hydrogen sulfide in hibernating animals. Hydrogen sulfide levels increase in animals when they hibernate and hibernation-like states can be induced in these animals by administering hydrogen sulfide.

Years later, during his postdoctoral training, he made a connection between the findings in the paper and the hibernation-like state that kidneys and other organs go into when they are being preserved in cold temperatures before transplant. He wondered what role hydrogen sulfide could play in improving this process.

Now a transplant surgeon in the Multi-Organ Transplant Program at London Health Sciences Centre (LHSC), Dr. Sener has investigated this question to address a major issue in kidney transplantation.

“Everywhere in the world there is a large discrepancy between the number of patients on the kidney transplant waiting list and the number of available organs,” says Dr. Sener. “Due to the lack of donor supply we often have to use ‘marginal’ deceased donor kidneys, which can be kidneys from older donors, donors with existing medical issues, and donors after circulatory death (loss of function of the heart and lungs). These kidneys often don’t work as long and are slower to recover after transplantation.”

After a kidney is taken from a donor, the typical process to prepare the organ for transplant can cause further injury to the cells and tissues. This process involves flushing the kidney with cold preservation solution and then putting it in cold storage for an average of 18-24 hours while it is being transported to the recipient. Dr. Sener and his research team found that if hydrogen sulfide molecules are added to the preservation solution, organ storage can be prolonged without risk of tissue injury, dangerous inflammatory cells decrease, kidney function is recovered quicker after transplant, the kidneys have greater urine output, and recipient survival is improved.

“Instead of a kidney lasting ten years, what if our treatment could make it last eleven?”

– Dr. Alp Sener

Researchers in Dr. Alp Sener’s lab are able to create a transplantation-like environment for kidneys without actually transplanting the organ. They use this ex-vivo perfusion apparatus for experimental storage and perfusion of animal and unusable donated human kidneys. The machine enables them to control perfusion pressures and oxygenation, and to measure urine output and other physiological variables.

**Poisons that heal**

Discovering the therapeutic potential of hydrogen sulfide and carbon monoxide

Researchers in Dr. Alp Sener’s lab are able to create a transplantation-like environment for kidneys without actually transplanting the organ. They use this ex-vivo perfusion apparatus for experimental storage and perfusion of animal and unusable donated human kidneys. The machine enables them to control perfusion pressures and oxygenation, and to measure urine output and other physiological variables.
molecule that is already approved for use in renal failure patients to existing organ preservation solutions. The drug does not have to be given to a recipient or a donor, only to the organ while it is in storage. Their goal is to begin clinical trials once enough data is collected from their current studies that use discarded human grafts – kidneys from organ donors who have consented to research and whose organs were not candidates for transplantation due to disease, injury or having no match on the transplant list. While he is now a leader in this growing field, Dr. Sener says it was hard convincing people at first that hydrogen sulfide, a smelly toxic molecule, could be used to improve kidney transplantation.

“When we started this research a lot of people said it was a crazy idea. We spent many years determining the correct dosage to ensure no toxic effects. As this research becomes more mainstream, we hope it will eventually help improve outcomes of organ transplantation all over the world.”

Harnessing the silent killer

Carbon monoxide – a colourless, odourless gas produced by the burning of fuels – is widely known as the “silent killer.” While carbon monoxide can be lethal when inhaled at high concentrations, powdered carbon monoxide-releasing molecules (CORMs) have the potential to treat systemic inflammation. Many conditions or illnesses can cause systemic inflammation, inflammation that simultaneously affects multiple organs. One of the most severe forms of systemic inflammation is sepsis, a life-threatening complication of an infection. Sepsis is the leading cause of death in Intensive Care Units worldwide.

Apart from the use of antibiotics, treatments for systemic inflammation are limited. From his lab at LHSC’s Victoria Hospital, Dr. Cepinskas was the first to study the therapeutic potential of CORMs to treat systemic inflammation and is still one of very few researchers in the world working in this field.

Systemic inflammation occurs when many inflammatory molecules are released into the blood stream. These molecules activate cells in the blood vessel wall resulting in a loss of tight connections between these cells and creating microscopic gaps. Inflammatory molecules also activate white blood cells, which adhere to blood vessel walls and create more gaps. The gaps allow white blood cells and inflammatory molecules in the blood to escape from the blood vessels.

Normally, white blood cells protect our bodies by eliminating bacteria, but when inflammation is severe, too many white blood cells escape from the blood vessels into organs, including the brain and lungs, and cause serious tissue damage with their arsenal of biochemical “weapons” designed to kill bacteria. Neutrophils, a type of white blood cell, release elastase and myeloperoxidase (MPO) enzymes, which kill bacteria, but at the same time contribute to the formation of gaps between cells in the blood vessel walls, further amplifying inflammation.

“We found that CORMs not only reduce the number of white blood cells entering inflamed tissue, but they also inhibit elastase and MPO activity,” says Dr. Cepinskas.

In addition, CORMs are “broad spectrum” inhibitors of several inflammation-associated signaling pathways, which are unique sequences of biochemical reactions that take place in the cells in response to interaction with a specific molecule. “Many drugs are designed to target a very specific signaling pathway. Unfortunately, all clinical trials using this approach to treat sepsis have failed because there are so many different inflammatory molecules produced during systemic inflammation, each with its own unique signaling pathway. CORMs, on the other hand, simultaneously target many signaling pathways,” says Dr. Cepinskas.

CORMs can be administered through an injection, which does not cause the toxic effects that occur when carbon monoxide gas is inhaled. In addition to sepsis-focused research, Dr. Cepinskas has also studied the role CORMs can play in the treatment of other conditions that cause systemic inflammation, including muscle injury.

“In addition, CORMs have the potential to treat systemic inflammation, such as a bone fracture or crushed muscle, characterized by severe swelling of the muscle. Currently, the only treatment is a surgical procedure to cut fascia (tissue that encapsulates muscle) to relieve tension and pressure in the limb. Dr. Cepinskas and Dr. Abdel-Rahman Lawendy, a Lawson scientist and orthopaedic surgeon at LHSC, were the first to demonstrate that CORMs could minimize muscle damage caused by compartment syndrome. Dr. Cepinskas is also collaborating with Dr. Sener and Dr. Patrick Luke, a Lawson scientist and co-director of the Multi-Organ Transplant Program at LHSC, to examine how CORMs could be used to improve organ transplantation. After an organ is transplanted, it is connected to the body’s blood vessels to restore blood flow. This causes inflammation throughout the body, which is very difficult to control.

“Now that carbon monoxide is accepted and recognized for its anti-inflammatory effects, there is huge potential for broader clinical applicability.”

- Dr. Gedas Cepinskas

Their research has shown that administering CORMs to kidneys before transplantation suppresses inflammation after the organ is transplanted and reduces the risk of transplant rejection.

“Now that carbon monoxide is accepted and recognized for its anti-inflammatory effects, there is huge potential for broader clinical applicability.” Dr. Gedas Cepinskas

Lawson Internal Research Fund

During the early stages of their research, both Dr. Sener and Dr. Cepinskas received funding from Lawson’s Internal Research Fund (IRF), which helped them to secure grants from large external funding agencies. Lawson’s IRF is designed to allow Lawson scientists the opportunity to obtain start-up funds for new projects with potential to obtain larger funding, to be published in an important journal, or to provide a clinical benefit to patients.

The IRF is supported financially by the clinical departments at London Health Sciences Centre and St. Joseph’s Health Care London, as well as London Health Sciences Foundation and St. Joseph’s Health Care Foundation.

Dr. Alp Sener was the first to study carbon monoxide-releasing molecules as a potential treatment for systemic inflammation.

Dr. Gedas Cepinskas leads the Critical Illness research program at Lawson. He is an associate professor in the Department of Surgery and Microbiology and Immunology, Schulich School of Medicine & Dentistry at Western University.

Dr. Gedas Cepinskas was the first to study carbon monoxide-releasing molecules as a potential treatment for systemic inflammation.

Dr. Alp Sener is a part of the Transplantation research program at Lawson. He is an associate professor in the Departments of Surgery and Microbiology and Immunology, Schulich School of Medicine & Dentistry at Western University.
Walk the talk

Walking and talking can be an early predictor of dementia

Roy Bratty, 82, and his wife Annabel McMillan, made a family decision to participate in research when they recognized that Roy was beginning to show signs of memory issues. “When we met with our doctor, a few different research projects were suggested to us,” recalls Annabel. They decided Roy would participate in the “Gait and Brain Study” led by Dr. Manuel Montero-Odasso, a Lawson scientist and geriatrician at St. Joseph’s Health Care London (St. Joseph’s). With his team, Dr. Montero-Odasso is currently assessing 150 seniors with mild cognitive impairment (MCI), a slight decline of memory and other mental functions which is considered a pre-dementia syndrome, in order to detect an early predictor of cognitive and mobility decline and progression to dementia. Annabel and Roy chose to participate in the study because it is non-invasive and only requires bi-annual visits to St. Joseph’s Parkwood Institute over a six year period. “My hope is that participating in the project can help me monitor my memory loss, but also that through my participation and the information I provide, others will benefit too,” says Roy.

For the study, researchers ask participants to walk while simultaneously performing a cognitively demanding task (dual-tasking), such as counting backwards or naming animals. “While walking has long been considered an automatic motor task, emerging evidence suggests cognitive function plays a key role in the control of walking, avoidance of obstacles and maintenance of navigation,” adds Dr. Montero-Odasso. “We believe that gait, as a complex brain-motor task, provides a golden window of opportunity to see brain function.” The “gait cost,” or speed at which participants completed a single task (walking) versus a dual-task, was higher in those MCI individuals with worse episodic memory and who struggle with executive functions such as attention keeping and time management. Moreover, those individuals with MCI that slow down more than 20 per cent while performing the dual-task are at a higher risk of progressing to dementia. “Our results reveal a ‘motor signature’ of cognitive impairment that can be used to predict dementia,” elaborates Dr. Montero-Odasso. “It is conceivable that we will be able to diagnose Alzheimer’s disease and other dementias before people have significant memory loss. Our hope is to combine these methods with promising new medications to slow or halt the progression of MCI to dementia.” The study was made possible through community support, which helped to purchase key equipment and enhance research space – enabling the work of Dr. Montero-Odasso and his team. Roy says the experience has made him more aware about the importance of taking care of himself and he regularly challenges his mind and memory by solving Sudoku puzzles. His goal to help others by participating in research may someday be realized should the research project translate into a simple test clinicians can utilize in any care environment.

Roy Bratty decided to participate in the “Gait and Brain Study” after he began to show signs of memory issues.

Dr. Manuel Montero-Odasso is the director of the Gait and Brain Lab, which is part of Parkwood Institute Research, a program of Lawson. He is also a professor in the Department of Medicine, Schulich School of Medicine & Dentistry at Western University.
Zain Awamleh is a trainee at Children’s Health Research Institute, a program of Lawson, and a PhD candidate in the Department of Biochemistry, Schulich School of Medicine & Dentistry at Western University.

The research
Normal development of the placenta is critical to ensure proper fetal growth. Preeclampsia, characterized by high blood pressure and damage to the kidney or liver, and intrauterine growth restriction (poor growth of the fetus) are two of the most common pregnancy-related complications resulting from abnormal placental development. My research assesses the role of microRNAs, part of a protein processing chain of cells that play a key role in gene expression, in human placenta complicated by preeclampsia and/or intrauterine growth restriction. I also assess the potential use of these microRNAs as biomarkers to predict the onset of these complications, as placental microRNAs can enter maternal circulation during pregnancy.

Interacting with patients
To enroll patients in my study, I describe the purpose of the research, any risk factors and how they can contribute. I value my interactions with patients and their families, and take the opportunity to educate patients about the importance of hospital-based research and, when appropriate, other ongoing research projects. When interacting with patients I believe it is important to keep in mind the patient’s condition, to be compassionate, and to listen and address their concerns.

The next step
I would like to further my training in health research, particularly in the fields of molecular oncology and bioinformatics. Advancements in technologies used for genetic diagnostics have created a need for individuals skilled in analyzing high-throughput data using machine learning, but who also possess the biological knowledge to make sense of the data.

Bench to bedside
In the first two years of my project, there was a heavy focus on obtaining patient samples. I dedicated time to raising awareness of my research on the obstetrical care unit at London Health Sciences Centre’s Victoria Hospital because I required the assistance of caregivers, particularly nurses, to identify patients and obtain samples at the time of delivery. After obtaining a sufficient number of samples, I transitioned to the laboratory to start working on the samples. For the following two years, I worked in the lab, but also continued to enroll patients and collect samples.

Empowering young scientists
I always see myself achieving my goals in Canada. However, it has been particularly challenging for young Canadian scientists to transition into more senior and stable careers at home. It is our responsibility as Canadian scientists to showcase our achievements to our government and advocate for ourselves and our peers.
LAWSON EXPERTISE

CLINICAL RESEARCH
Lawson has clinical research experience in all medical disciplines from prenatal and paediatric care to aging and geriatric care. Opportunities exist for Phase I – IV Trials, sponsored, peer-reviewed or investigator-initiated clinical research.

LAWSON RESEARCH

Lawson Clinical Research Services (LCRS)

LCRS is a versatile, fully staffed facility that provides increased clinical trials capacity to investigators from London Health Sciences Centre and St. Joseph’s Health Care London, as well as community physicians and dentists. LCRS provides the expertise and facilities to manage the clinical, technical and administrative aspects of both investigator and industry-sponsored research. The facility offers clients the opportunity to contract services, in whole or in part, required to successfully conduct clinical research.

Gerald C. Baines Centre for Translational Cancer Research

Located in Victoria Hospital at London Health Sciences Centre (LHSC), the Gerald C. Baines Centre was established as a partnership between Lawson, LHSC’s London Regional Cancer Program, the Schulich School of Medicine & Dentistry and Western University. The centre supports citywide translational cancer research by linking researchers from multiple disciplines with academic clinicians and facilitating knowledge transfer between teams.

Lilith Caberto Kidney Clinical Research Unit (KCRU)
The KCRU is dedicated to clinical research in the areas of kidney health, kidney disease and treatments of dialysis and kidney transplantation. There are over 70 active clinical research studies being coordinated through the KCRU, a 4,000 square-foot facility located at London Health Sciences Centre’s Victoria Hospital. The KCRU also fosters strong ongoing collaboration with the ICES Kidney Dialysis and Transplant Program, which is sited adjacent to the KCRU facility.

Clinical Research and Chronic Disease Centre (CRCDC)
The CRCDC at St. Joseph’s Hospital is the first dedicated clinical research space for chronic disease in our region, bringing together researchers in one state-of-the-art healthcare facility. Diabetes, cardiac rehabilitation, and breast cancer research are core research areas utilizing the CRCDC with the goal of translating research findings from “bench-to-bedside.” Research done in these areas will improve outcomes for those individuals living with chronic disease.

TRAINING AND EDUCATION
Lawson is an international training centre for students: co-op, summer, pre-graduate, graduate, postdoctoral fellow and resident. The Lawson environment is unique for its first-class facilities, its location in an active biomedical research community and the pleasant surroundings of the city of London, Ontario. Most training opportunities are coordinated through our academic partner Western University, with many positions affiliated with divisions of the Schulich School of Medicine & Dentistry. With Lawson’s guidance, our students are ready for the global workplace. We’re proud to say that all of them continue to enhance the reputation of Lawson and Western University.

Lawson Association of Fellows & Students (LAFS)
LAFS is comprised of postdoctoral fellows, technicians and graduate students. The group ensures an engaging research and academic setting, offers a political voice in the future direction of Lawson, and organizes social events across the London research community.

FACILITIES & TECHNOLOGY

At Lawson, we have joined with our partner research and clinical institutions to provide core research facilities and expertise for highly technical areas in a cost effective manner.

ICES Western
ICES Western is a satellite site of the Institute for Clinical Evaluative Sciences, a not-for-profit research institute encompassing a community of research, data and clinical experts, and a secure and accessible array of Ontario’s health-related data. ICES researchers use this data to produce unique scientific insights that improve understanding of health care issues, guide decision-making and inform changes in care delivery in Ontario.

TRAINING AND BUSINESS DEVELOPMENT

Commercialization opportunities at Lawson are managed through WORLDDiscoveries®.

WORLDDiscoveries®
WORLDDiscoveries® is the business development arm of London’s extensive research network, created through a partnership between Lawson, Robarts Research Institute and Western University. With their industry connections, sector-specific market knowledge, and business development expertise, the WORLDDiscoveries® team helps researchers and local inventors commercialize their discoveries through licensing and new company spin-offs.

London Health Research Day
London Health Research Day is a partnership between Lawson and the Schulich School of Medicine & Dentistry at Western University. It is the region’s premier research showcase event, highlighting outstanding research by students, trainees, clinical fellows and postdoctoral scholars from across the city of London. As the largest research day of its kind in Ontario, more than 700 people attend this event each year. The day includes poster and platform presentations, The Lucille & Norton Wolf Health Research Lecture Series, and a networking session for trainees and industry partners.

Talks on Friday’s (TOFS)
Talks on Friday’s (TOFS) is a weekly, student-run seminar series hosted by Lawson. It is designed to provide students with opportunities to develop professional skills and experience, including presenting conference-style oral presentations to an audience; preparing for internal competitions, such as London Health Research Day, and networking with other members of Lawson’s research community, with the potential to identify prospective career and collaborative opportunities.
LAWSON
HEALTH RESEARCH INSTITUTE

The Research Institute of London Health Sciences Centre and St. Joseph’s Health Care London.

lawsonresearch.ca