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– Dr. David Hill, Scientific Director



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Our research happens where patient care is delivered

Lawson Health Research Institute (Lawson) is the research
institute of London Health Sciences Centre (LHSC)
and St. Joseph's Health Care London (St. Joseph's),
working in partnership with Western University.

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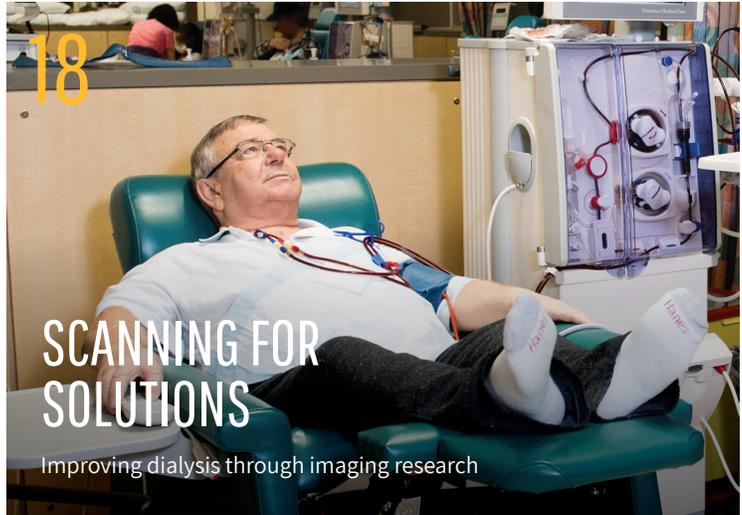
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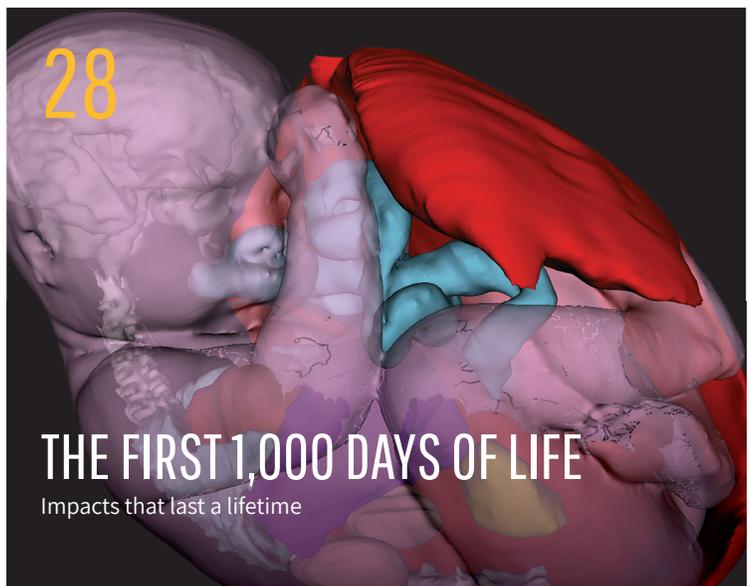
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WORKING WITH THE FIGHTING THE OPIOID CRISIS

It's been called the most complex public health issue of our time. The opioid crisis has transformed the face of addiction, making health care providers question everything from the way pain is managed to underlying causes of disease.

The severity of the epidemic is evident in the lives that are lost. Since 2006, more than 9,000 Canadians have died from an opioid overdose.

"Many of the patients I see with an opioid addiction are very young, often in their 20's or 30's," says Dr. Sharon Koivu, Associate Scientist at Lawson. "When they die, that's too many years that are lost."

Dr. Koivu is a Palliative Care Physician and Addictions Consultant at London Health Sciences Centre (LHSC).

Working in London, Ontario, she sees first-hand the impacts of opioid addiction. London was recently named as the sixth highest city for rate of hospitalizations due to opioid use in Canada.

Recognizing this public health emergency, Lawson researchers are designing and testing solutions with the goal of driving societal change.

Could one opioid be causing an increase in heart infections?

Dr. Koivu began practicing medicine in 1985. It was not until 2011 that she saw her first case of infective endocarditis, a serious and once rare infection of the heart valves. She has now seen hundreds.

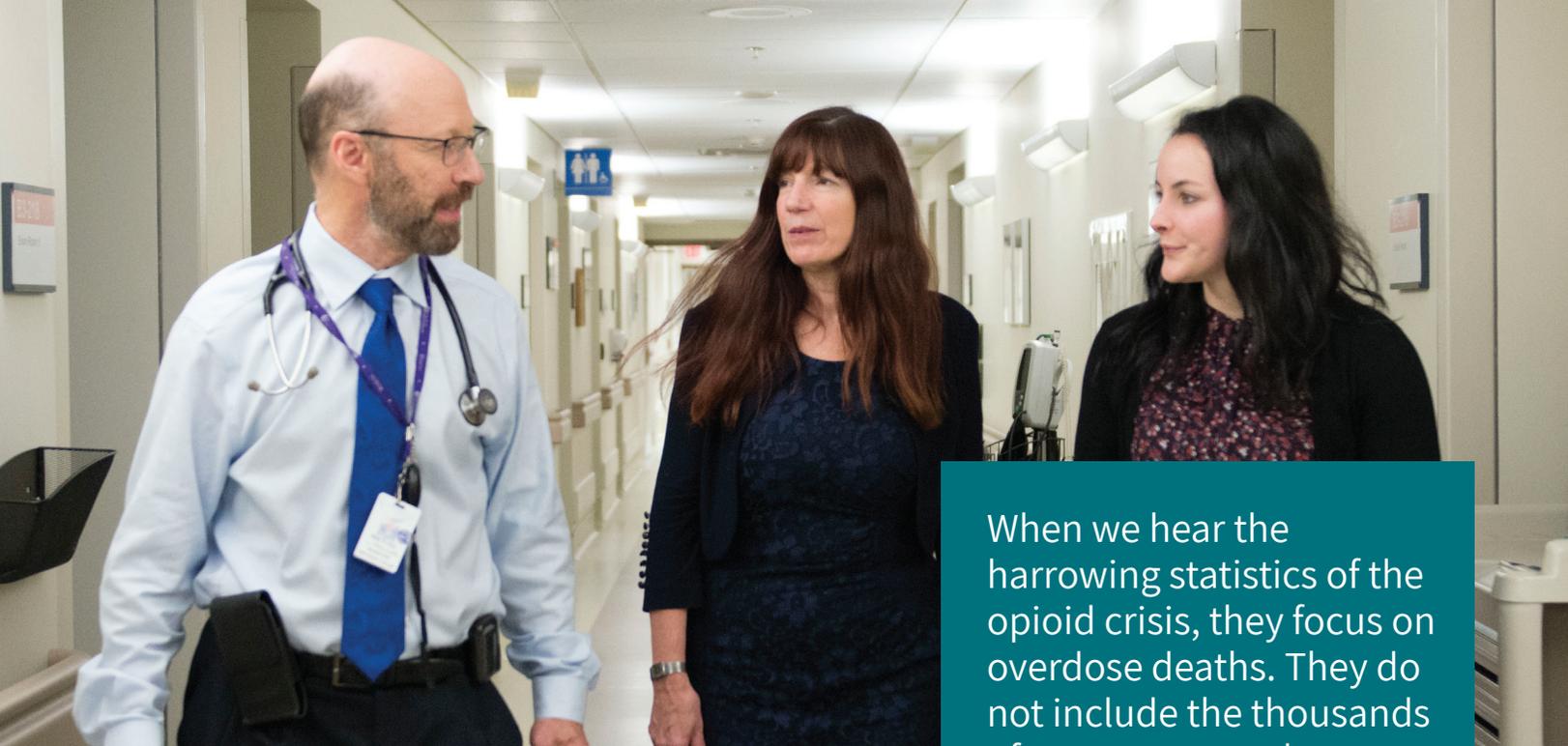
Noting a rise in infective endocarditis and that many of the patients were injection drug users, Dr. Koivu suspected that a specific opioid, hydromorphone, was to blame. She soon joined forces with Dr. Michael Silverman, Associate Scientist at Lawson, to better understand the connection.

In one project, the team examined Ontario health data through ICES for 60,529 hospital admissions related to injection drug use between 2006 and 2015. They showed that rates of infective endocarditis in persons who inject drugs have risen dramatically, more than doubling, and not just in London but across the province.

Hydromorphone prescriptions in Ontario increased from 16 per cent of all opioid prescriptions in 2006 to 53 per cent by 2015, paralleling the rise in infective endocarditis.

People who inject opioids often dissolve them in water, but controlled-release hydromorphone, the most common form of the drug, is difficult to dissolve. As a result, pieces get stuck to injection equipment like the metal 'cookers' used to prepare the drug. Equipment is often saved, so the rest can be dissolved later. This did not happen with controlled-release oxycodone,





From left: Drs. Michael Silverman, Sharon Koivu and Laura Rodger studied which clinical factors are linked to reduced mortality in injection drug users with heart valve infection.

the previous opioid of choice that was removed from market in 2011.

“Reusing equipment allows for bacterial contamination, increasing chances that bacteria will be injected with the drug,” explains Dr. Silverman. “We suspect injection of bacteria may be a contributing factor to the rise in infective endocarditis, and we’re currently studying this in more detail.”

Armed with research knowledge, Drs. Koivu and Silverman are champions for a public health campaign to ‘cook your wash’. It encourages those who inject drugs to heat their injection mixture, known as ‘the wash,’ until it bubbles to kill bacteria.

Discovering effective treatments

When a person who injects drugs develops infective endocarditis, they have a one in three chance of dying.

“When we hear the harrowing statistics of the opioid crisis, they focus on overdose deaths,” says Dr. Koivu. “They do not include the thousands of young men and women who are dying as a result of infectious disease.”

In another study, Drs. Koivu and Silverman set out to improve patient outcomes by understanding what treatments work best. They examined anonymous patient data from 2007 to 2016 at LHSC and St. Joseph’s Health Care London. They found that out of 370 patients with endocarditis, 202 were persons who inject drugs.

When accounting for the severity of a patient’s illness, cardiac surgery resulted in a 56 per cent reduction in mortality. Meanwhile, providing addictions counselling, focused on harm reduction education and support towards recovery while a patient was in hospital, resulted in a 72 per cent reduction.

“We’re not saying every patient needs surgery but our findings suggest it should be considered as a viable option for those most in need,” explains Dr. Silverman.

When we hear the harrowing statistics of the opioid crisis, they focus on overdose deaths. They do not include the thousands of young men and women who die as a result of infectious disease.

– Dr. Sharon Koivu

“Support while in hospital is vital,” adds Dr. Koivu. “The majority of patients don’t understand what they’re doing to cause an infection and this could motivate them for a lifestyle change.”

Reducing prescription numbers

North America has the highest rates of opioid prescriptions in the world.

“By reducing the number of opioids being prescribed, we can decrease the risk of them being misused or ending up in the wrong hands,” says Dr. Luke Hartford, a surgical resident in London.

Dr. Hartford is part of a research team at Lawson and Western University that is tackling this issue. They developed a new clinical protocol for general surgery called STOP Narcotics. It combines education for patients and health care providers with an emphasis on non-opioid pain control.

The protocol was studied with 682 research patients who underwent outpatient gall bladder removal surgery, open hernia repair, breast surgery and anorectal surgery at LHSC and St. Joseph’s. Patients received non-opioid medications like Tylenol and Naproxen to help manage their pain for the first 72 hours after surgery. Physicians were also instructed to write a limited prescription for 10 pills of an opioid that expired within seven days. Patients were told to only fill the prescription if needed, and were instructed on how to properly dispose of unused pills.

The STOP Narcotics protocol cut the number of opioids being prescribed in half and only 45 per cent of patients actually filled their prescription, compared to 95 per cent of patients in a control group. Pain was managed just as effectively, with the same levels of post-operative pain levels reported by both groups. The percentage of patients who properly disposed of their medication tripled.

“We recognized before STOP Narcotics that every surgeon had a different approach to pain control and most were prescribing more opioids than needed,” notes Dr. Ken Leslie, Associate Scientist at Lawson. “The new protocol is effective and also standardizes prescribing practices for clinicians.”

Moving forward, the group hopes to expand the protocol beyond general surgery. “If the protocol is translated to other departments and institutions, we can decrease the number of opioids available for illicit use and significantly impact the opioid crisis through prevention,” says Dr. Hartford.

The STOP Narcotics protocol cut the number of opioids being prescribed in half and only 45 per cent of patients actually filled their prescription, compared to 95 per cent of patients in a control group.

Understanding the individual patient

Tackling the issue in another way, one project is looking at how a patient’s personality traits can affect opioid dosing in chronic pain.

Led by Dr. Robert Teasell, the research team is collecting data that shows patients with chronic pain who possess certain obsessive personality traits related to anxiety and coping experience higher levels of pain-related disruptions to daily activities, greater levels of disability and are at greater risk for mood disorders. Preliminary results suggest that in individuals prescribed opioids, there is a correlation between those personality traits and higher doses.

“While our studies are ongoing, we are very excited about the potential impact of this research,” explains Dr. Teasell, Associate Scientist at Lawson. “If we can use personality measures to predict how individuals with chronic pain will cope,

Dr. Luke Hartford is part of a research team that developed and studied a new clinical protocol after general surgery called STOP Narcotics. The protocol cut opioid prescribing in half.

we can develop more personalized strategies to better manage chronic pain without overreliance on opioids.”

Dr. Koivu is seeing a shift towards alternative methods of pain management that can create real change. “My hope is that we can lower prescription numbers, better understand the effects of individual opioids and support individuals with a substance use disorder. Through this work, we can create real societal change.”

Dr. Sharon Koivu is an Associate Scientist at Lawson, a Palliative Care Physician and Addictions Consultant at London Health Sciences Centre and an Associate Professor at Schulich School of Medicine & Dentistry, Western University.

Dr. Michael Silverman is an Associate Scientist at Lawson and Chair/Chief of Infectious Diseases at Schulich School of Medicine & Dentistry, Western University, London Health Sciences Centre and St. Joseph’s Health Care London.

Dr. Ken Leslie is an Associate Scientist at Lawson and Chair/Chief of General Surgery at Schulich School of Medicine & Dentistry, Western University and London Health Sciences Centre.

Dr. Robert Teasell is an Associate Scientist at Lawson, Medical Director of the Stroke Rehabilitation Program at Parkwood Institute, part of St. Joseph’s Health Care London, and Professor at Schulich School of Medicine & Dentistry, Western University.



See a video about the opioid crisis at lawsonresearch.ca/lawsonlink



A collaborative approach

To help address the opioid crisis in London and surrounding regions, London Health Sciences Centre and St. Joseph’s Health Care London have created the Opioid Stewardship Council (OSC). The OSC is a collaborative group of professionals who are developing new processes to reduce opioid prescriptions for acute pain. Strategies include ensuring patient education materials accompany every narcotic prescription and are reviewed with the patient by their health care provider, limiting the quantity of medications being prescribed, and developing tamper-resistant prescriptions.



GROWING TISSUES IN THE LAB

When challenged by surgeons to find better treatments for difficult-to-manage connective tissue diseases, Dr. David O’Gorman gladly accepted.

Dr. O’Gorman is a Molecular Biologist and Lawson Scientist based at St. Joseph’s Hospital, a part of St. Joseph’s Health Care London. His research focuses on understanding normal and abnormal connective tissue repair. He collaborates with researchers and clinicians working in many different disciplines, including those specializing in reconstructive surgery, orthopedics and urology.

Surgical reconstructions can be hampered by a lack of graft tissue, or graft tissue of

insufficient quality, making it difficult to achieve optimal outcomes for the patients.

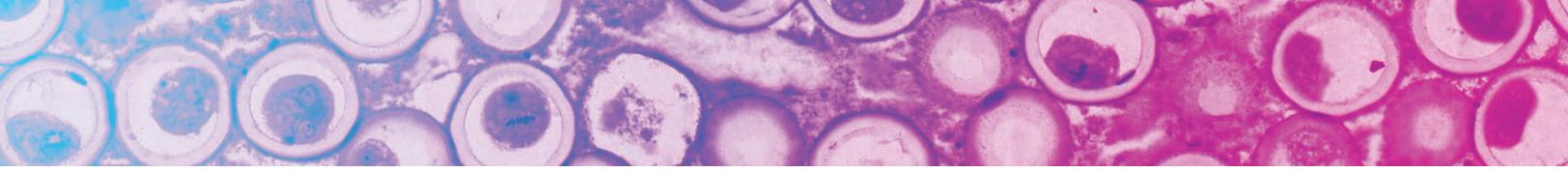
An example is a condition called urethral stricture disease (urethral scarring). This condition occurs in males and typically causes symptoms such as frequent and urgent urination, and slow urinary stream. In extreme cases, it can cause urinary tract infections, permanent bladder dysfunction and renal failure. Recurrence rates after minimally invasive treatments are high, and so many urologists recommend open surgical approaches.

Surgeons can use the patient’s own tissues to reconstruct the urethra after stricture removal. This tissue is normally sourced from the buccal cavity in the mouth but taking large

tissue grafts can result in complications. In cases where buccal grafts have been used for previous reconstructions, there may not be enough intact tissue left.

Dr. O’Gorman sees a solution in growing sheets of human buccal tissues in the lab. “We are currently using buccal graft trimmings as a source of cells, culturing them in a 3D environment and expanding them to create tissues of suitable size, density and elasticity.” The patient’s own cells are used to generate a tissue graft for urethral reconstruction. While several research groups have developed this approach in the past, few have attempted to translate their models for clinical use.

“Our immediate goal is to provide proof of principle – that we can consistently



generate grafts of suitable size and functional characteristics,” explains Dr. O’Gorman, “In the future, we could be providing bioengineered graft tissues for reconstructive surgeries here in London.”

Bioengineered human tissues can also be used as ‘mimetics’ – replications of human tissues – to study diseases, especially those difficult to model using routine laboratory methods.

Dupuytren’s disease (or Dupuytren’s Contracture) affects the palmar fascia in the hand, a connective tissue beneath the skin that extends from the base of the palm into the fingers. This disease can be understood as a type of excessive scarring, where normal tissue repair processes have gone awry and dense scar tissue forms, typically causing permanent palm or finger flexion that restricts hand function.

not found in other species, making animal models impractical. Instead, Dr. O’Gorman’s team extracts cells from the diseased palmar fascia of patients undergoing hand surgeries and bioengineers them into palmar fascia ‘contractures’ in the lab.

“Since the cells from a single palmar fascia sample can be used to grow dozens of little contractures, we can test many different treatments simultaneously to see what works best for each patient.”

This approach may also allow them to determine if Dupuytren’s disease is truly one disease, or a group of similar diseases that cause palm and finger contractures. “Often, Dupuytren’s disease is clearly heritable, but some individuals have no family history of it and develop apparently sporadic disease,” notes Dr. O’Gorman. “We want to determine if these are truly the same disease at the molecular level.”

Another major cause of abnormal connective tissue repair is infection, and tissue mimetics can play a role here, too. While rare, infections of artificial joint replacements are particularly devastating for patients, as they typically require readmission to hospital to remove the infected joint, weeks of antibiotic-based treatment, and an additional surgery to replace the artificial joint. In addition to the associated pain and suffering, these procedures are technically

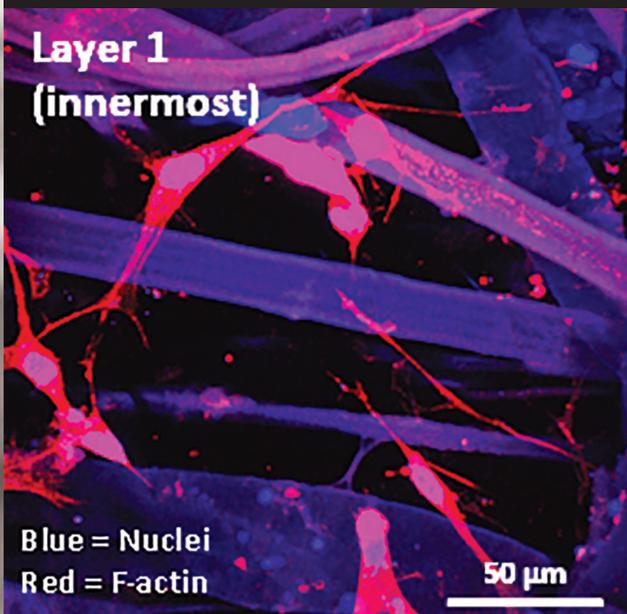
This condition is surprisingly common and may affect more than one million people in Canada. While there are surgical treatment options available, none consistently prevent this disease from recurring in at least a third of patients.

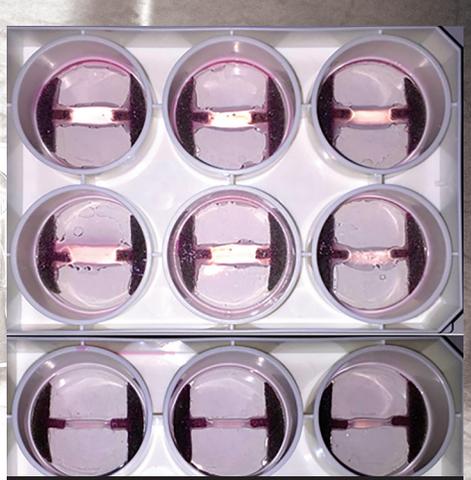
“Due to its high recurrence rate after treatment, Dupuytren’s disease is currently considered incurable. Our challenge is to understand it well enough to develop truly effective treatments,” says Dr. O’Gorman.

Human hands have unique characteristics

Instead of using a growth media or sterile plastic dishes, 3D cell culture is achieved by embedding cells in a matrix of proteins and other molecules normally found in those tissues. In this environment, gene expression and growth is more similar to cells of connective tissues in the body being replicated.

Learn more about 3D cell culture at lawsonresearch.ca/lawsonlink





challenging and costly to our health care system.

Artificial shoulder joint infections are most frequently caused by the microorganism *Cutibacterium acnes* (*C. acnes*). *C. acnes* infections disrupt normal tissue repair processes after surgery, cause shoulder tissues to die and promote loosening of the artificial joint. These infections are difficult to diagnose, and there is a lack of reproducible models in which to study them.

Dr O’Gorman’s team has set out to create the first human Shoulder-Joint Implant Mimetic (S-JIM) of *C. acnes* infection. “While S-JIMs are more complex, they are 3D *in vitro* cell culture systems designed to mimic human tissues, like those that we use for studying Dupuytren’s disease.”

S-JIMs include layers of artificial human tissue, wrapped around cores of titanium alloy or cobalt chrome, the metals used to create artificial joints. They are co-cultured with

C. acnes under low oxygen conditions similar to those that normally occur around artificial shoulder joints.

Studying the connective tissue layers close to the infection allows researchers to investigate processes that promote infection, such as the formation of a biofilm that harbours and protects the bacteria from the body’s immune system. They are also able to test whether novel treatments can disrupt biofilm formation and increase the effectiveness of antibiotics.

Dr. O’Gorman predicts that in the future, medical researchers will routinely use bioengineered 3D human tissue and organ mimetics to accelerate our understanding of disease.

“The technology is in its infancy, but the potential for using bioengineered human tissues for surgical reconstructions or as disease models is huge. At Lawson, we’re ready to take on health care challenges

“We are bioengineering simple 3D cell cultures to more closely mimic the complexity of human tissues, with blood supply, nerves and interactions with other cells.”

– Dr. David O’Gorman

and build on innovative approaches to improve the quality of life for patients.”

Dr. David O’Gorman is a Lawson Scientist and Co-director, Cell and Molecular Biology Laboratory at The Roth | McFarlane Hand and Upper Limb Centre in London, Ontario. He is also an Assistant Professor at Western University.

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Dr. Graham King
Medical Director
Roth | McFarlane Hand
& Upper Limb Centre
Site Chief of Surgery,
St. Joseph’s Hospital

The next generation

Rebecca Sullivan is a trainee working with Dr. Savita Dhanvantari, Lawson Scientist, in her lab at St. Joseph's Hospital, and a PhD candidate at Schulich School of Medicine & Dentistry, Western University.



✓ Rebecca's research

Heart disease is a leading cause of death in Canada. Earlier detection could save thousands of lives and help personalize treatment.

When heart disease is suspected, patients receive a blood test and a combination of imaging methods for diagnosis. Currently used biomarkers can be unreliable and heart disease only shows on imaging after functional changes to the organ.

My research focuses on discovering a biomarker that can detect heart disease at earlier stages. I am currently studying a new biomarker called growth hormone secretagogue receptor (GHSR). I am using heart samples from patients who have undergone a heart transplant or open heart surgery with fluorescent imaging agents, and am also using a combined PET/MRI machine at St. Joseph's Hospital to track this biomarker in the heart to see cellular and physical changes. This combined imaging method allows our research team to understand what is happening in heart disease and work towards developing methods of earlier diagnosis.

✓ Hospital-based research

There is so much happening behind the scenes that most people don't see. It takes years to develop and test a new drug or method and put it into practice. It also takes collaboration. Having different perspectives allows researchers to tackle problems differently. Hospital-based research allows me to collaborate with clinicians, scientists and patients to translate research to care.

✓ Patient impact

For my research, collaboration is essential as the samples are collected during heart surgery and brought back to the research lab. By studying these samples, we're working to better understand heart disease and improve diagnosis. The ultimate goal is to translate our findings back to patient care.

✓ The next step

I would like to learn more about different types of imaging methods, how they work and the new techniques happening locally and globally. Advancements in imaging have created opportunities to personalize detection and treatment of disease. I would also like to pursue a career in academia to help foster students' enthusiasm for research.

✓ Empowering young scientists

I urge female scientists to mentor female trainees and empower them to seek leadership positions. Mentors can make the difference in a trainee's career. I want to show the trainees I mentor that you can move up, be heard and reach leadership positions.

Read more about Rebecca's research and career journey at lawsonresearch.ca/lawsonlink. ▶

A PRIME Team

Collaborating to improve rehabilitation

For many years, Patrick Stapleton would experience severe back pain about once a year, typically leaving him unable to move for a couple of days. “Once I could walk again, I’d go to a chiropractor and be okay,” he recalls.

In May 2015, Patrick was in the midst of one of these events and, while sitting upright in a chair, he noticed his forehead felt cold and clammy and his vision rapidly went out of focus. The next thing he remembers is waking up on the floor with no feeling in his legs.

He acquired a spinal cord injury that day while at home.

“There really is no explanation for what happened to me,” says Patrick. “Many doctors have looked at my case, and after ruling everything out, including stroke or heart attack, their best guess is that I had a muscle seizure and the muscles broke my vertebra.”

Patrick has what is known as an L1 spinal cord injury, and his recovery treatment has been intense. During the first year, he was prescribed multiple medications to manage the pain. He has had spinal





decompression surgery, and now has two titanium rods spanning his T11, T12, L1, L2, and L3 vertebrae.

The road to recovery following a spinal cord injury (SCI) or acquired brain injury (ABI) can be long and challenging. Every patient has a unique condition, with an equally unique set of rehabilitation needs. Optimizing treatment for the individual is the goal of Lawson's Research 2 Practice (R2P) program located at Parkwood Institute, a part of St. Joseph's Health Care London.

Integrating the patient perspective

The R2P team, led by Lawson Scientist Dr. Dalton Wolfe, is guided by the overarching philosophy of health learning systems through clinical and research integration. Embedded Implementation Science Research is part of a fulsome knowledge translation approach used by this team. It involves interdisciplinary collaboration amongst researchers, clinicians, administrators and persons with lived experiences. The team operationalizes new and existing clinical processes and assesses outcomes to inform improvements to practice.

It is easy to see the benefits of this approach in a rehab setting. "By having research embedded into clinical practice, and working directly with clinicians and patients going through rehab, it really makes the work we are doing relevant," explains Dr. Wolfe.

As a person living with spinal cord injury, Patrick has experienced the health system from all angles, and knows the rehabilitation program at Parkwood Institute quite well. "I know the acute care setting, I know the rehab setting, and I know the outpatient setting," he explains.

Including people who live with these conditions is vital in the success of many research projects. Dr. Wolfe stresses that, "Ensuring the patient experience is embedded in our research is integral to this type of model. Patrick adds perspective to the program that you can't get from clinicians."

Parkwood Rehabilitation Innovations in Mobility Enhancement (PRIME) aims to create evidence-based treatment protocols by investigating what combinations of physical or occupational therapies are best for what type of patient. Physio and occupational therapies are integral parts of the rehab process for persons with ABI and SCI, and there are many possible

therapeutic activities a practitioner might prescribe.

R2P researchers work alongside clinicians to carefully track therapeutic activities and patient progress. Through collaborations with computer scientists and engineers, the R2P team hopes to identify which of these activities might be linked with the best physiotherapy practices, with the ultimate goal of providing the best possible clinical recommendations.

Ensuring the patient experience is embedded in our research is integral to this type of model. Patrick adds perspective to the program that you can't get from clinicians.

PRIME members meet regularly to share key findings and identify issues. This is where clinicians can reflect and refine their practice. "The feedback loop, between the researchers and clinicians, is essential to the success of our research. By integrating research into the clinical setting, improvements in care are made frequently, and patients are able to benefit from the research immediately," explains Dr. Wolfe. "Patients experience more effective treatment, faster recovery, and ultimately, better outcomes."

Giving back through research

Today, Patrick's main symptom is neuropathic pain below his knees, which he describes as intense pins and needles, accompanied by a feeling of

"rawness" in different areas. About an hour spent sitting is all he can tolerate. When discomfort sets in, physical movement brings a relieving sensation of pressure to his legs. Twice a week Patrick travels to the Parkwood Fitness Centre for the Functional Electrical Stimulation (FES) cycling program.

FES cycling uses a specialized bike equipped with electrodes which help riders with limited muscle control. The rider has several electrodes positioned in various places on their legs, and an electrical charge is emitted to the leg muscles, stimulating movement. The goal is for the rider to eventually pedal the bike themselves, but when they are unable to generate enough muscle power, the bike provides assistance.

Everyone involved with PRIME has really taken my feedback to heart.

"I started using the FES bike as an inpatient. It has really helped to bring back strength in my right quadriceps, and has improved my mobility," says Patrick. The FES cycling program stemmed from a more traditional research trial; however, having the bikes in hospital has allowed researchers to quickly translate the results of the trial into a clinical program.

"Everyone involved with PRIME has really taken my feedback to heart," Patrick praises. "Being involved has also been helpful for me, and I've had a really positive experience at Parkwood. This is how I can give back." Patrick also works with Spinal Cord Injury Ontario,



offering peer support for other patients.

The mission of all R2P initiatives is to integrate research and clinical activities to enhance clinical practice and improve patient and health system outcomes. The knowledge gained is leading and informing various fields, and helping to identify priority areas that need focus.

Dr. Wolfe and his team are connecting with rehab centres across the country, and working with new therapists to provide validation and help reinforce the relevance of their research. They also plan to increase their collaborations with data analytics experts, who can assist in the development of more advanced clinical decision support systems using artificial intelligence to identify patterns in patient activities and outcomes.

Dr. Dalton Wolfe leads the SCI Research Group at Lawson. He is an Assistant Professor in the School of Health Studies at Western University.



See a video about the Research 2 Practice program at lawsonresearch.ca/lawsonlink

Patrick Stapleton, PRIME member and person with lived SCI experience on the FES bike.



RESEARCH 2 PRACTICE

Interdisciplinary cooperation initiatives

Sexual Health Practice

Aimed at understanding how the sexual health of patients with spinal cord injuries can be better addressed by the health care team, Sexual Health Practice was implemented in the summer of 2018. Sexual health is important to the overall health and wellbeing of any individual; however, it is often a gap in care.

Parkwood Pacing and Planning Program

A research initiative aimed at improving the lives of those with concussion by helping people manage their daily activities without exacerbating their symptoms. The group has developed the Parkwood Pacing and Planning™ app, making the program available to users on their smartphone.

Ontario SCI Implementation & Evaluation Quality Care Consortium

Based on learnings from the SCI Knowledge Mobilization Network, also led by the R2P team, this Consortium aims to connect Ontario SCI academic health centres to implement best practices. This enables optimal and equitable health care services for all Ontarians, ensuring functional recovery, health and wellbeing in persons with SCI.

Self-Management Initiative

A collaborative partnership between the SCI program, SCI Ontario and eHealth, focuses on coordinating care across in-patient, out-patient and community services. It also provides resources for persons with SCI to build their skills to manage their own health. This work is aligned with the Changing Care Initiative aimed at better addressing the needs of family caregivers.

The ROI of Research

Hospital-based research improves health care, creates jobs and contributes to a sustainable knowledge economy.

Why Invest?

Lawson Health Research Institute is one of the top ten hospital-based research institutes in Canada, ranked eighth in the country according to the 2018 edition of Canada's Top 40 Research Hospital list by Research Infosource.

This ranking also places London as one of the top five health research hubs in Ontario. People in this region are the first to benefit when discoveries are made.

As the research institute of London Health Sciences Centre and St. Joseph's Health Care London, Lawson oversees the research mandate of both organizations.

Our world-class scientists are conducting leading-edge research in dedicated labs within hospital sites or alongside care providers in clinical areas, and also in partnership with research patients. Many are health care professionals themselves.

Our research questions are formulated at the point of care, uniquely positioning us to tackle the most pressing issues in health care.

- What frustrations need to be addressed to better serve patients and health care providers?
- How can we improve treatment or fill in an existing gap?
- How do we implement tested solutions to have the best possible outcomes for patients, in the most efficient way for the system?
- Where can we find savings and reduce the cost of health care delivery?



TremorTek

Wearable sensor technology, TremorTek, was developed by Dr. Mandar Jog and his team using commercially available sensor technology. At the London Movement Disorders Centre, operated by Dr. Jog, TremorTek has treated hundreds of research patients suffering from tremors in their upper limbs. Current treatment of tremors involves the use of localized neurotoxin injections. An injection in the wrong place or of the wrong dose can result in negative side effects for the patient. TremorTek allows Dr. Jog and his team to match the dose and location for injection to isolated muscle activity pinpointed by the technology. Spinoff company MDDT Inc. is currently working with numerous stakeholders interested in various other applications.



Learn more at worlddiscoveries.ca

WORLDDiscoveries®, the business development arm of Lawson and a joint venture with Robarts Research Institute and Western University, supports researchers and local inventors to commercialize their discoveries through licensing and new company spin-offs.

Hospital-based research = 3:1 return on investment

CT Perfusion Software

Director of PET/CT Imaging Research at Lawson, Dr. Ting-Yim Lee, invented the use of Computed Tomography (CT) scans to measure blood flow in the body, known as CT perfusion. Dr. Lee's software can be installed on existing CT scanners resulting in fast and easy interpretation of a typically complex algorithm. A product now fully approved for clinical use began as an idea in need of exploration. Through public and private support, Dr. Lee's research has transformed into an economic win. In partnership with GE Healthcare, his software is now installed on 70 per cent of the company's new CT scanners, and is being used in more than 8,000 hospital imaging departments worldwide. Royalties earned through this licensing agreement have enabled Lawson to install Canada's first PET/CT scanner.



MONEY

Lawson attracts over
\$123 million annually
in research income

\$13 million annually

from partnerships with
private industry

**\$616,300 spent per
researcher**

ranking first among large tier
institutes for research intensity



JOB

**60% of Lawson's annual
research income**

is spent on research staff salaries

Over 2,400

researchers, staff, volunteers,
students and fellows



COMMERCIALIZATION

6th

among hospital patent leaders in
Canada with 13 patents in five years

Over 200

business and industry partners in
more than 25 countries

\$2.5 million annually

from commercialization
of discoveries

Lawson Commercialization

- Dr. Matthew Hebb is partnering with STEMCELL Technologies for commercialization of tools for Parkinson's disease research.
- Yabao Pharmaceutical Group in China entered into an exclusive license agreement with Lawson to develop and test a new life-saving drug to treat sepsis, based on a discovery by Dr. Qingping Feng.
- Novare Pharmaceuticals and Lawson were issued a U.S. patent for the composition-of-matter and use of RHAMM-binding peptides with a wide range of potential therapeutic uses. The patent also has claims for the diagnosis and prognosis of cancer, and for prescribing a course of treatment for the diagnosed cancer.

SCANNING FOR SOLUTIONS

Improving dialysis
through imaging

Lloyd Weiss undergoes dialysis three times a week and participates in numerous research studies at Lawson.



Lloyd Weiss was a 10-year-old-boy in Edmonton, Alberta when he had his left kidney removed.

“They told me it wasn’t functioning and so they took it out,” says Lloyd, now 62. “After that, everything seemed fine.”

He went to school, started working as an aircraft maintenance engineer and got married. Then, seven years ago he caught the Norwalk virus, destroying what was left of his remaining kidney.

Lloyd now undergoes dialysis three times a week at the Kidney Care Centre at London Health Sciences Centre (LHSC). He is one of over four million Canadians living with chronic kidney disease and one of 30,000 currently on dialysis.

The kidneys are crucial to human health as they filter waste from the body. When a person loses too much kidney function, they start on dialysis – a process that artificially filters waste from the blood. Unfortunately, dialysis can cause a number of serious side effects.

Dr. Chris McIntyre, Lawson Scientist, and his team are the first in the world to use medical imaging to scan patients while undergoing dialysis.

“A large portion of our work focuses not on creating new treatments but on recognizing the harms in current ones, and then deliberately engineering those harms out,” says Dr. McIntyre.

Protecting the brain

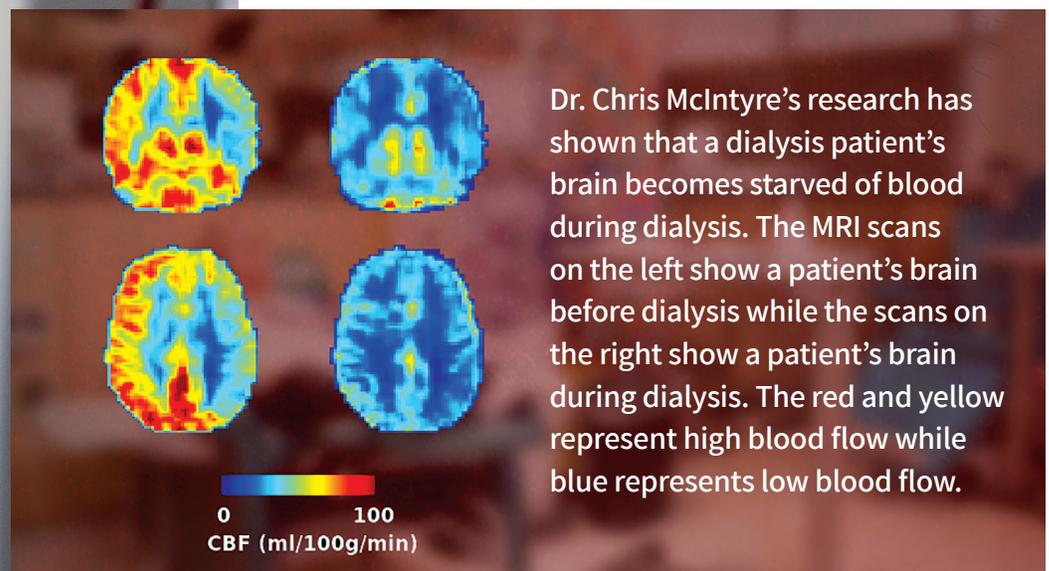
There are two main forms of dialysis, of which hemodialysis is the most common. In hemodialysis, blood is removed from the body, filtered through a machine called a dialyzer and then pumped back in. This sudden removal of bodily fluids can cause low blood pressure and decreased blood flow to multiple organs.

Each round of dialysis is like another recurrent brain injury.

“Our studies show that a patient’s brain becomes starved of blood during dialysis,” explains Dr. McIntyre, also an LHSC Nephrologist. “Each round of dialysis is like another recurrent brain injury.”

Ischemia, a term used to describe restricted blood supply to tissues or organs, leads to less oxygen in the brain which can cause symptoms like abnormal cognitive function and eventually lead to tissue death or stroke.

Dr. McIntyre’s research team is using PET/MRI to determine whether a simple intervention can protect hemodialysis patients from brain injury. Deliberately making one part of the body ischemic may protect other



Detecting cardiovascular stress with a smartphone camera

Through a commercial partnership with Intelomed, Dr. Chris McIntyre is testing a novel mobile app called mCVI™ that can detect changes in a person's physiology with only a cell phone camera. The app uses a smartphone camera to lock onto a person's face and choose a part of the forehead. The picture is made up of three colours. The device measures microscopic changes in the relative intensity of the three colours and interprets those changes as a wave of blood flowing in and out of a person's skin. This wave is used to measure pulse, respiratory rate and oxygen saturation. It can also predict blood flow in the heart, providing insight into cardiovascular health.

Dr. McIntyre's team is validating the app for FDA approval. They are using it to monitor patient response to dialysis and hope it can one day provide early detection of cardiovascular stress.

parts of the body from ischemia, in this case to preserve function to a vital organ. Dr. McIntyre is using a technique called ischemic preconditioning, which consists of inflating a blood pressure cuff on the patient's leg for one to two minutes before dialysis.

"We've already shown that ischemic preconditioning can protect the heart from dialysis. The question now is whether it works the same for the brain. It's an intervention that's completely free and safe, and could be implemented almost immediately."

Preserving kidney function

Ischemia as a result of dialysis affects multiple organs, including the kidneys.

"Kidney function is important even for those whose kidneys are failing," explains Dr. McIntyre. "We need to keep the kidneys as healthy as possible."

His team recently studied the effects of hemodialysis on blood supply to the kidneys, called renal perfusion. Research patients were scanned using CT perfusion imaging while

undergoing dialysis under standard conditions, which resulted in an 18.4 per cent drop in blood supply.

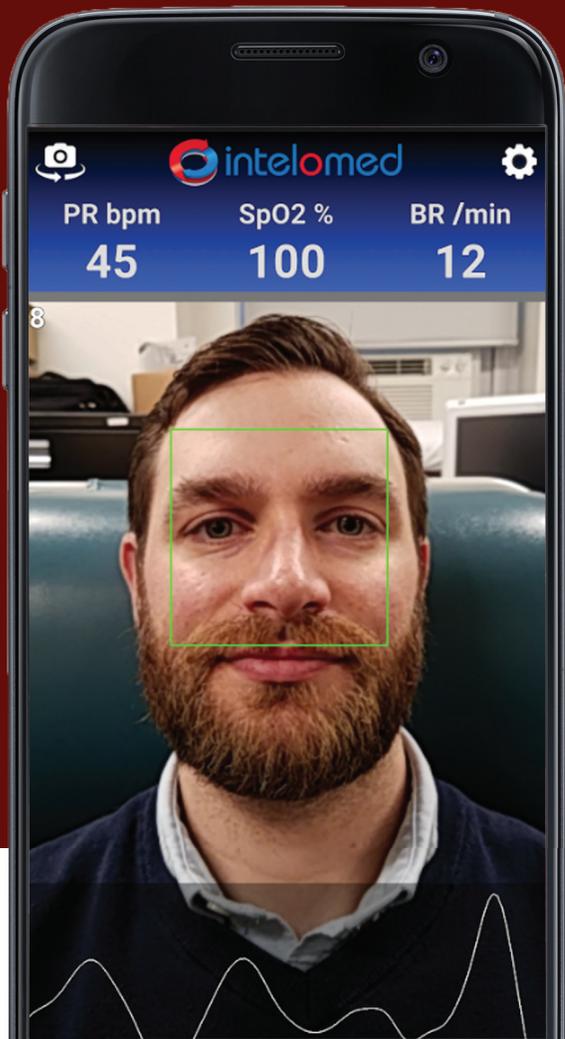
Next, half of the participants were scanned again. This time the dialysate, a fluid used during the dialysis process, was cooled from 36.5 to 35 degrees Celsius. Results show that dialysate cooling improved renal perfusion in two thirds of the patients. Previous studies showed that dialysate cooling can improve overall patient outcomes by limiting cardiovascular stress.

Results show that dialysate cooling improved renal perfusion in two thirds of patients.

"Dialysis may be destroying what's left of remaining kidney function by limiting blood supply," says Dr. McIntyre. "While further study is needed, it appears that dialysate cooling has potential to be used as a therapeutic approach to slow this decline."



Dr. Chris McIntyre is working to improve dialysis and patient outcomes through imaging research.





Lloyd Weiss (right) is participating in research with Dr. Chris McIntyre (left) to study harms caused by dialysis and possible improvements to treatment.

Revealing the harmful effects of salt

The research team was the first in the world to image sodium in the bodies of dialysis patients using PET/MRI. Dialysis cannot fully remove sodium from a patient's body which means salt and its harmful effects remain.

"With a resident physicist on our team, we were able to write the code and produce the imaging coils needed to image salt in the human body," notes Dr. McIntyre.

Using PET/MRI to measure sodium levels in 26 research participants, they found that dialysis patients have significantly higher sodium levels in the skin, muscle and bone of their legs when compared to healthy individuals. The high sodium levels correlated with health issues like

anemia, malnutrition and inflammation.

Imaging coils are now being built to look at sodium in a patient's heart and kidneys.

"We need to better understand the harms that sodium is causing and start looking towards solutions to this problem."

A hope for the future

For Lloyd Weiss, this research has been illuminating.

"I didn't realize sodium was so bad for people on dialysis. I've also noticed how dialysis seems to affect my short-term memory," he says.

"This has been an eye-opener for everything."

Lloyd has participated in multiple studies with Dr. McIntyre's team.

"We're so lucky to live in London with the people and tools to conduct this research. If my

participation helps improve dialysis for patients in the future, I'm happy to do my part."

Dr. Chris McIntyre is a Scientist at Lawson, Nephrologist at London Health Sciences Centre and Professor at Schulich School of Medicine & Dentistry, Western University.

See a video about dialysis research at lawsonresearch.ca/lawsonlink

PROUDLY SUPPORTING

Discovery

London Health Sciences Foundation is pleased to support investment in Lawson Research and all they do to develop new knowledge and translate exciting discoveries that lead to a healthier community and make a real difference in the lives of patients and families at our Hospital.



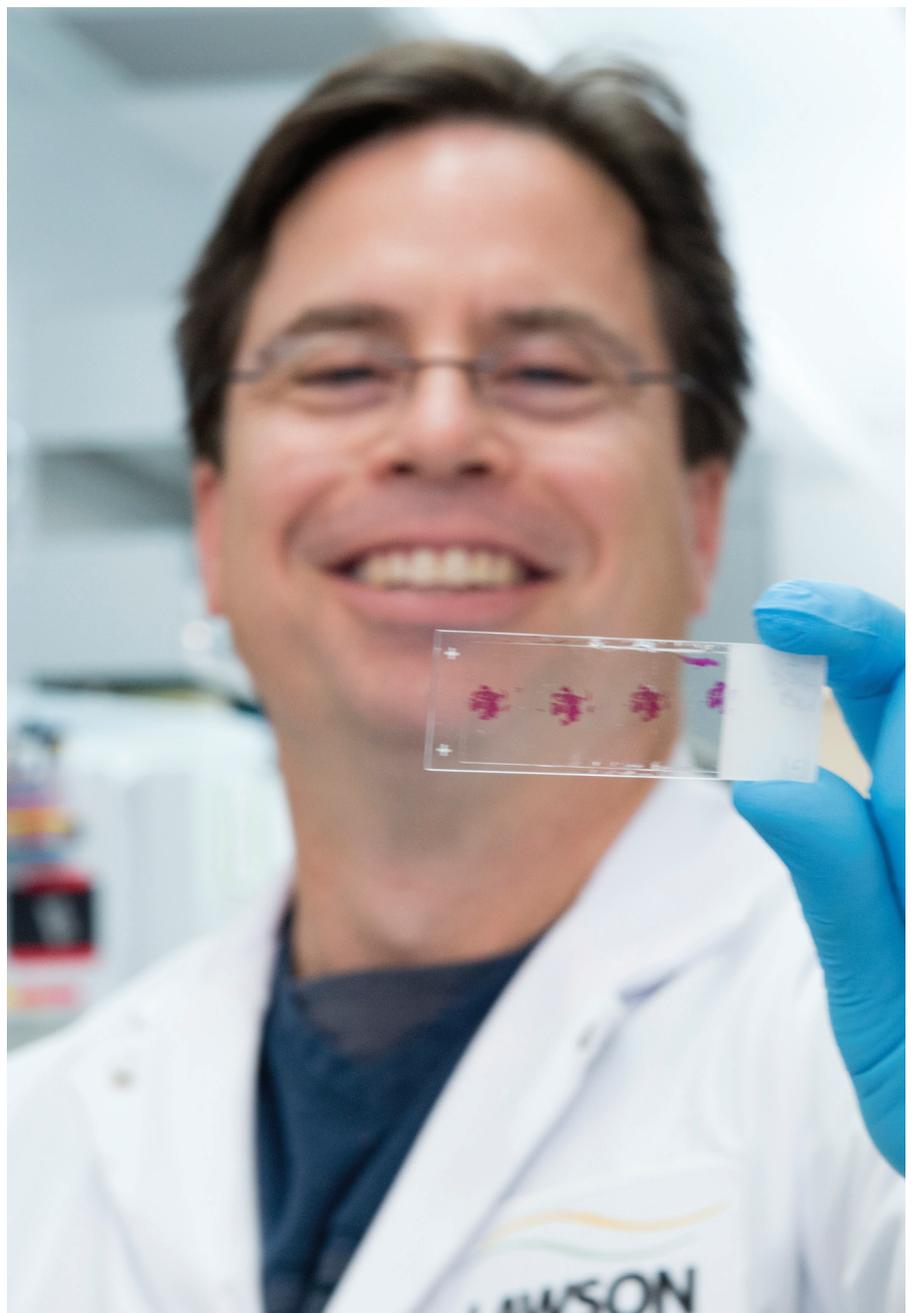
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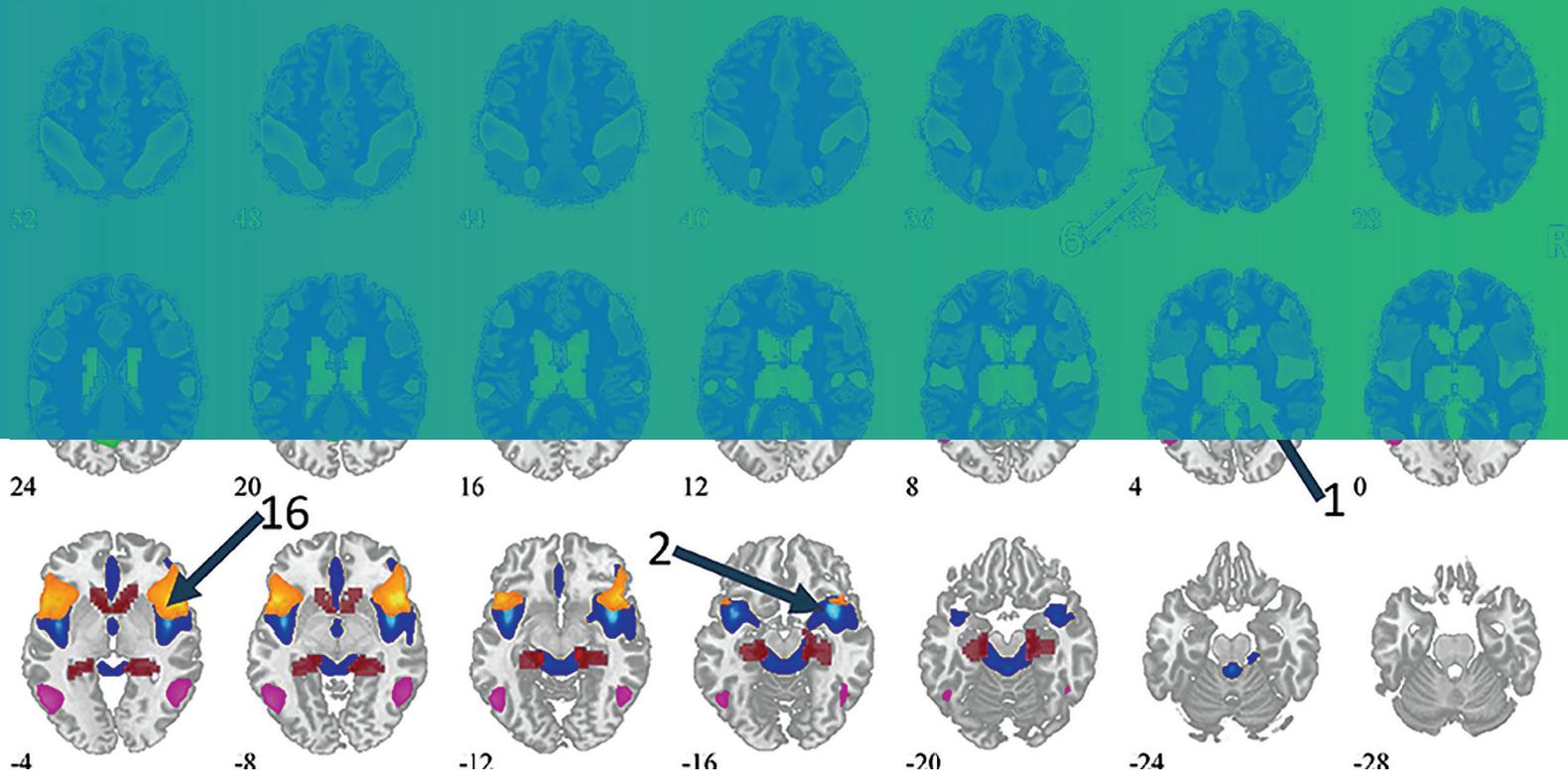
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Cool Science

Genetic mutation may increase risk of pancreatic cancer in females

Pancreatic cancer is a devastating disease that's often diagnosed very late. Researchers from Lawson and Western University have found that mutation of a gene called ATRX may lead to increased risk of developing pancreatitis and pancreatic cancer in females. Led by Dr. Chris Pin, the team discovered through preclinical trials that deleting the gene in females increased susceptibility to pancreatic damage. When comparing results to human samples from the International Cancer Genome Consortium database, 19 per cent of patients carried a mutation within the ATRX gene and 70 per cent of them were female. While not all of the mutations found in human samples would lead to increased susceptibility, they warrant further examination. This marked the first time a potential sex-specific genetic risk factor for pancreatic cancer has been identified.





Using technology to diagnose psychiatric disorders

Psychiatric disorders like major depressive disorder (MDD), bipolar disorder and post-traumatic stress disorder (PTSD) are often difficult to diagnose. Two research teams at Lawson have used technology and brain imaging to better classify psychiatric illness in patients, showing promise as tools for early diagnosis. One study developed an artificial intelligence algorithm that analyzes brain scans to better identify illness in patients with a complex mood disorder and help predict their response to medication. The algorithm correctly classified research participants with a known diagnosis with 92.4 per cent accuracy. The other study combined brain imaging and machine learning to classify with 92 per cent accuracy whether individuals had PTSD, and if it was the dissociative subtype.



Probiotics for respiratory tract infections could save Canada nearly \$100 million a year

Respiratory tract infections are highly contagious infections of the sinus, throat or airways, including influenza or 'the flu.' There is growing evidence that probiotics can reduce the risk of respiratory tract infections and lower their frequency, as well as reduce the duration of infection, absences from work, and antibiotic use. Researchers from Lawson, Western University, Laval University and Utrecht University examined the potential clinical and economic impacts of using probiotics for respiratory tract infections in Canada. They found regular probiotic use could eliminate between 573,000 to 2.3 million days per year of respiratory tract infections, resulting in fewer sick days and antibiotic prescriptions. When accounting for productivity losses due to illness, it could save nearly \$100 million a year.



Oral curcumin shows no benefit in reducing inflammation following vascular surgery

In the largest randomized trial for oral curcumin, researchers at Lawson and Western University showed no benefit in reducing inflammation when curcumin was taken after vascular surgery. Curcumin is the active medicinal ingredient in turmeric and continues to gain popularity as a natural health supplement. Researchers studied 606 patients scheduled for elective surgery for abdominal aortic aneurysm repair at 10 Canadian hospitals. Results showed no positive effect of curcumin on inflammation. In secondary analyses, researchers found there was an increased risk of post-surgical kidney damage in patients in the curcumin group. The study emphasizes the importance of testing turmeric, curcumin and other products marketed as natural supplements in rigorous human clinical trials before claiming any health benefits.

Synthetic surfactant could ease breathing for patients with lung disease and injury

Human lungs are coated with a substance called surfactant which allows us to breathe easily. When this substance is missing or depleted, breathing becomes difficult. Currently, surfactant is taken from animals like cows, then purified and sterilized for use in humans. In a new study, Lawson Scientist Dr. Rudd Veldhuizen collaborated with Dr. Annelise Barron at Stanford University to develop and test a new synthetic surfactant. The synthetic surfactant was evaluated in animal models at Dr. Veldhuizen's research lab at St. Joseph's Health Care London. The study showed the synthetic surfactant equaled or outperformed animal-derived surfactants in every outcome. This included outperforming animal-derived surfactant in oxygenating blood, which is the lungs' main purpose. The team estimates the synthetic surfactant could be produced at as low as one quarter of the cost of animal-derived surfactant.





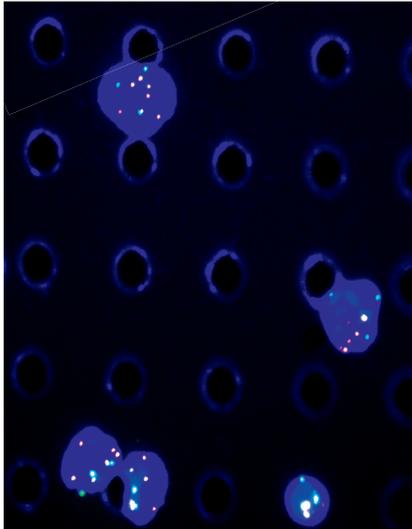
Meditation for mental health

Depression in older adults can be a disabling and debilitating condition often leading to other chronic health problems such as heart disease. In a randomized clinical trial that included 83 research participants, researchers at Lawson and Western University found that meditation can be implemented easily and effectively as a therapy to treat late-life depression and mood related symptoms. Meditation has been shown to have positive impacts, be easy to facilitate, lack negative side effects and be delivered at a low cost. The study showed that participants practicing a form of meditation, called Sahaj Samadhi Meditation, reported a significant improvement in depressive symptoms compared to participants receiving traditional therapies, suggesting it could be beneficial as an additional therapy.



Funding to help tailor patient care

Adverse drug reactions are the fourth leading cause of death among hospitalized patients and cost the Canadian health care system over \$5 billion a year. Studying a patient's unique DNA to ensure they are prescribed the right dose of the right medication at the right time has the potential to transform patient care. Led by Dr. Richard Kim, researchers at Lawson have received \$4.4 million to study an expanded personalized medicine program at London Health Sciences Centre. Personalized medicine is the analysis of a patient's DNA to predict how they will respond to medications. The funding will allow researchers to test personalized medicine for more drugs, follow patient outcomes and assess the cost-effectiveness of the program.



Circulating tumour cells.

Blood test can predict optimal treatment for advanced prostate cancer

Deciding which therapy to pursue next for advanced prostate cancer is a critical point for patients and oncologists. An international collaborative study between Lawson, Memorial Sloan Kettering Cancer Center, the Royal Marsden and Epic Sciences is one of the first to show that a blood test can predict how patients with advanced prostate cancer will respond to specific treatments – helping to extend the lives of patients. The test identifies if a patient's circulating tumour cells contain a protein called AR-V7. The study found that patients who tested positive for the protein responded best to chemotherapy while those who tested negative for the protein responded best to hormone-targeting therapy.

CLINICAL TRIALS

Shaping the treatments of tomorrow

Clinical research plays a crucial role in advancing medical knowledge. Researchers need people to participate in study trials to improve health care and the quality of life for patients and families.



Why should you participate?

- Contribute to important health research and innovation.
- Help yourself and others by advancing medical knowledge and patient care.
- Access cutting-edge diagnostics and treatments.
- Gain additional support and care from a clinical research team.



What is a clinical trial?

A study that enrolls human participants to evaluate the effects of a certain treatment or intervention on health outcomes. Researchers can test and compare methods for the prevention and detection of specific diseases and conditions, or gather data from specific populations. New or improved treatments often begin in a lab before moving on to testing with human participants.

Not all clinical trials are about drugs, medical devices or treatments. They also help develop screening processes and prevention methods to find diseases earlier or prevent them altogether. The value of lifestyle changes like exercise and diet are also studied through clinical trials.

“Would I become involved in a clinical trial again? In a heartbeat. My quality of life has greatly improved and I have much more energy. I also met some great people that were there to support me. Research at our hospitals is so important because it advances treatment options for patients. I would encourage anyone who sees a trial that is appropriate for them to become involved.”

– Wayne Kristoff,
study participant



Who is eligible to participate?

Anyone can participate in a clinical trial, whether you're a healthy individual or have a current medical condition. Eligibility criteria exist for every clinical trial, and could include age, gender, type and stage of disease, previous treatment history or other medical conditions.

Participation is always voluntary. Prior to enrollment in a clinical trial, you will be provided with information so you can understand the risks, potential benefits and alternatives to the study. Throughout the course of the study, new information may be provided and you maintain the right to withdraw at any time.

The four phases of clinical trials



PHASE I – Is it safe?

A Phase I clinical trial is the first time a treatment or intervention is tested in humans. Serious immediate side effects have been ruled out, and now the treatment or intervention is ready for humans under careful observation. These trials are typically very short (two to three months) and involve a small number of participants, often those who are not experiencing major health challenges.

PHASE II – Is it effective?

Once the safety of a treatment or intervention is established through the first phase, it moves on to Phase II to test whether or not the treatment or intervention does what it's supposed to do. Positive or negative effects are recorded. These typically last one to two years, and involve participants who have a relevant disease or condition.

PHASE III – How does it compare?

During a Phase III clinical trial, the effects documented during Phase II are confirmed, and might be compared to a conventional treatment. More safety information is also collected. These trials vary in length depending on the disease or condition. Participant groups are much larger and individuals are randomly put into groups which will receive either different variations of the treatment or no intervention at all. These are known as Randomized Controlled Trials (RCTs), and both the participants and researchers are purposely left unaware of who is receiving what intervention in an effort to decrease bias and avoid, as much as possible, any placebo effect.

PHASE IV – Long term effects?

Once a treatment or intervention makes it past Phase III, it is approved for use in Canada and is made available to the public. Phase IV clinical trials, also known as post-marketing trials, might compare the new treatment to other alternatives, study the treatment in different human populations or look for any further side effects. This phase usually involves use under less controlled conditions and in real-life applications.

“Participation in the REMIT study at Lawson Health Research Institute allowed me to reset my type 2 diabetes. With the professional guidance of Dr. Hramiak and her team, I now manage my diabetes through diet and exercise; medication free.”

– Greg Ackland,
study participant



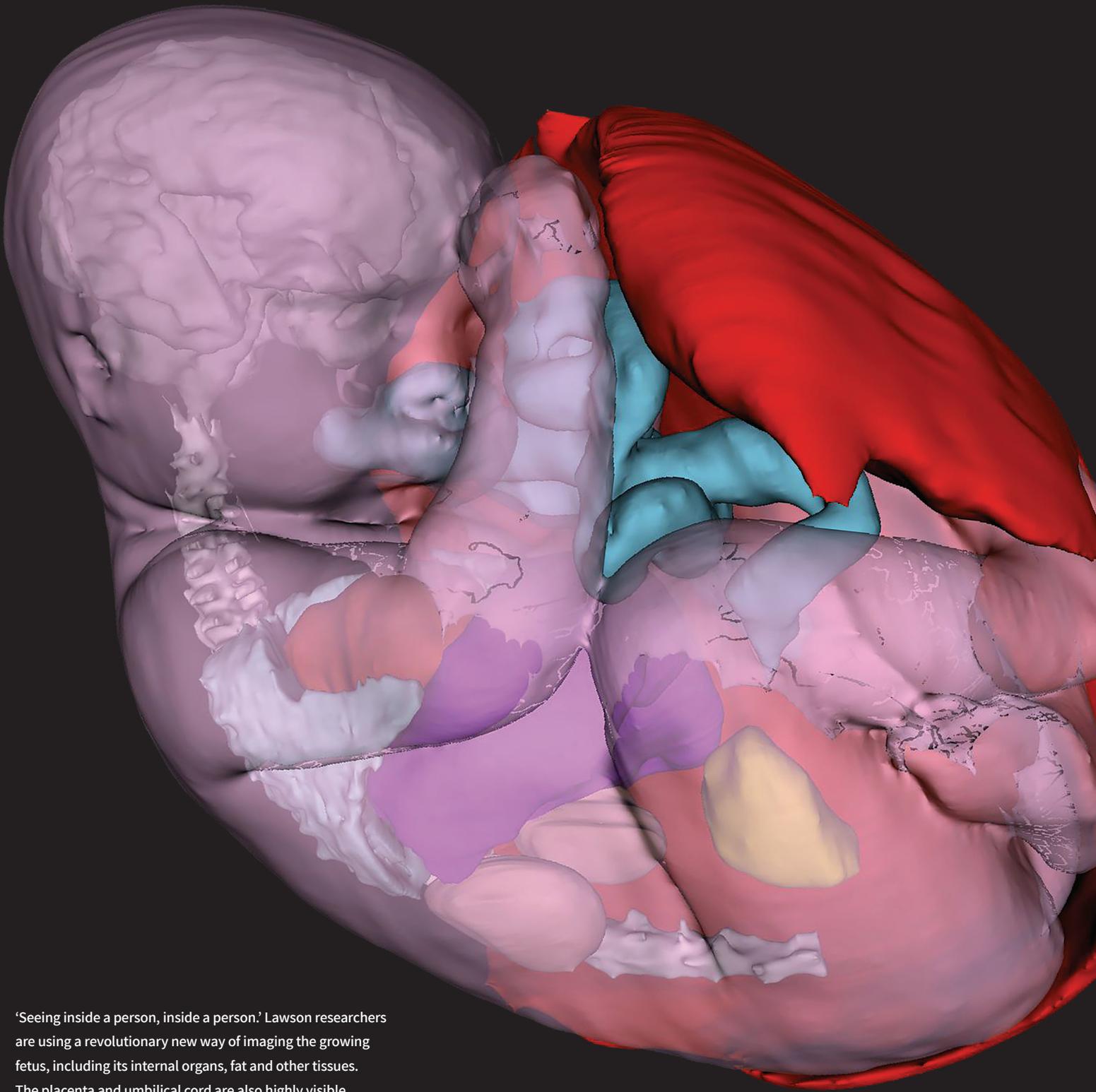
How to find a clinical trial

If you are interested in participating, you are encouraged to ask your primary care provider about any that might exist for your particular disease or condition.

To search for clinical trials in North America, visit www.clinicaltrials.gov.

For cancer clinical trials in Ontario, visit www.ontariocancertrials.ca.

For more information about clinical trials at Lawson, visit lawsonresearch.ca/clinical-research.



'Seeing inside a person, inside a person.' Lawson researchers are using a revolutionary new way of imaging the growing fetus, including its internal organs, fat and other tissues. The placenta and umbilical cord are also highly visible. This MRI technique can track placental and fetal metabolism during pregnancy.

The first 1,000 days of life

Impacts that last a lifetime

The first 1,000 days life, between conception and a child's second birthday, are a critical and unique window of opportunity to support optimal health, growth and brain development. The impacts last a lifetime.

A child's healthy development can be threatened during pregnancy by stressors like maternal obesity, inflammation, and abnormal placental development and function.

The placenta is a key organ in fetal growth and development because it controls maternal-to-fetal exchanges of essential nutrients and hormones. Attacks on metabolic function due to stressors are associated with future life risks for the infant, such as obesity, diabetes and cardiovascular disease.

"Clinicians are still not able to identify which pregnancies or infants are at risk, nor are they able to diagnose abnormalities early enough to suggest interventions or therapies that could help prevent future disease from developing," remarks Dr. Barbra de Vrijer, Lawson Associate Scientist.

As maternal-fetal medicine specialists who noticed this gap, Drs. de Vrijer and Genevieve Eastabrook, Lawson Associate Scientist, formed the Pregnancy Research Group. They collaborate with expert researchers from a variety of fields to promote maternal, fetal and infant health.

Marking chronic inflammation

When a woman becomes pregnant, her immune system responds by allowing – and not rejecting as it would in any other circumstance – the placenta to invade and redirect the mother's blood supply.

"It's quite amazing, considering that a large portion of the pregnancy is not a part of the mom's body itself. Most people would not survive an eight-pound tumour or 40 week-long infection, yet a woman's body deals with pregnancy quite well," says Dr. de Vrijer.

Pregnancy-related suppression of the immune system is often strong enough to protect the placenta against the type of immune response that any other 'stressor' could cause.

But when there is chronic inflammation, the placenta can no longer keep up. Inflammatory markers are found to be increased in early pregnancies that later develop preeclampsia or growth restriction. As Dr. Eastabrook notes, "the performance of these markers as predictors of future development of pregnancy complications is not good enough to be of any clinical use. In fact, the 'best' predictors for pregnancy complications we currently have are pre-pregnancy BMI (Body Mass Index), mean arterial blood pressure and the mother's age."

Despite tremendous progress in neonatal outcomes for preterm births, there have been only modest improvements in the management of at-risk pregnancies. Low-dose Aspirin is advised to all women at risk of preeclampsia, but overall there is no treatment other than to induce labour. Preeclampsia is a complication characterized by high blood pressure and signs of damage to other organ systems.

If the complication occurs early in pregnancy, management is fairly straightforward: wait as long as possible to deliver the baby, and closely monitor placental blood flow and wellbeing of the fetus using ultrasound.

When the placenta is affected by chronic inflammation and preeclampsia develops in the third trimester of pregnancy, ultrasound fails because changes in fetal growth and placental function are often too subtle to detect.

"In order to prevent late onset growth restriction, preeclampsia and stillbirth, we need more reliable tools to identify at-risk patients," says Dr. Eastabrook.

A promising assessment technique is Pulse Wave Velocity (PWV). This portable and non-invasive test measures arterial stiffness, a measure of cardiovascular health that is strongly correlated with inflammation. Arterial stiffness is measured through the velocity of the blood pressure wave travelling through the arteries over time. ▶

Arterial stiffness should decrease very early in pregnancy as part of normal adaptation. These changes are not seen in pregnancies destined to develop late onset complications.

By indirectly measuring the effects of obesity, metabolic changes and inflammation, the team is assessing the cardiovascular system's adaptation to pregnancy. In addition, PWV is a more accurate assessment of cardiovascular health than blood pressure alone, especially for patients with extremely high BMI.

Imaging fetal and placental metabolism

While ultrasound is limited to assessing the baby's size, anatomical structures and umbilical blood flow, the team is now using MRI to study the content of cells, oxygen levels and metabolism.

A recent study looked at the fetal fat content as a marker for metabolic health and found that the normal fetus rapidly accumulates fat during the third trimester.

The research team is now studying whether there are different compartments of fat that are more predictive of abnormal fetal growth and development, and if they can find these differences during pregnancy.

Innovative work is also being done by collaborators Dr. Charles McKenzie and Dr. Timothy Regnault, Lawson Scientists, who are investigating an MRI technique to accurately track placental and fetal metabolism by imaging how sugars are metabolized during pregnancy.



Drs. Barbra de Vrijer and Genevieve Eastabrook

MRI has one disadvantage compared to ultrasound: greater difficulty dealing with motion. During pregnancy it is not only the fetus that moves, but uterine contractions cause the placenta to shift and it is much more difficult for pregnant women to hold their breath for prolonged periods of time. The team is one of the first in the world that is working on adapting computer algorithms to correct for this motion.

"We're really gaining momentum," shared Dr. de Vrijer. "As clinician scientists, we are driven by the goal of providing the best pregnancy care to women, and a healthy life for their children."

Go to lawsonresearch.ca/lawsonlink for a Q&A with the Pregnancy Research Group.

Dr. Barbra de Vrijer is Division Head for Maternal-Fetal Medicine in Obstetrics & Gynaecology at London Health

Sciences Centre; Associate Professor at Western University; and, Associate Scientist at Children's Health Research Institute (CHRI), a Lawson Program.

Dr. Genevieve Eastabrook is Assistant Professor at Western University and Associate Scientist at Children's Health Research Institute (CHRI), a Lawson program.



See a video of this scan at lawsonresearch.ca/lawsonlink



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For more information, visit www.lhsc.on.ca



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Children's Health Foundation is dedicated to raising and granting funds to support Children's Hospital at London Health Sciences Centre, Thames Valley Children's Centre and Children's Health Research Institute. Since 1922, funds raised have helped deliver exceptional care and support for children and their families by providing specialized paediatric care, equipment, education programs, therapy, rehabilitation services and research.

For more information, visit www.childhealth.ca



Renowned for compassionate care, St. Joseph's Health Care London is a leading academic health care centre in Canada dedicated to helping people live to their fullest by minimizing the effects of injury, disease and disability through excellence in care, teaching and research. Through partnership with Lawson Health Research Institute and our collaborative engagement with other health care and academic partners, St. Joseph's has become an international leader in the areas of: chronic disease management; medical imaging; specialized mental health care; rehabilitation and specialized geriatrics; and surgery. St. Joseph's operates through a wide range of hospital, clinic and long-term and community based settings, including: St. Joseph's Hospital; Parkwood Institute; Mount Hope Centre for Long-Term Care; and the Southwest Centre for Forensic Mental Health Care.

For more information, visit www.sjhc.london.on.ca



St. Joseph's Health Care Foundation gathers, grows and grants philanthropic funds to enable St. Joseph's Health Care London to pursue excellence in care, teaching and research. Through donor support, the foundation contributes to advances in the delivery of patient care, specialized equipment, research initiatives and capital funds at St. Joseph's Hospital, Parkwood Institute, Mount Hope Centre for Long-Term Care, Southwest Centre for Forensic Mental Health Care and Lawson Health Research Institute. As one of the largest charitable organizations in Southwestern Ontario, St. Joseph's Health Care Foundation is an accredited member of Imagine Canada's Standards Program, which recognizes the foundation's commitment to ethical fundraising and donor accountability.

For more information, visit www.sjhcfoundation.org



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