

LAWSON LINK

2020 EDITION

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DISEASES

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HOSPITALS



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– Dr. David Hill, Scientific Director



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AND CYNTHIA YI.

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SPECIAL UPDATE

To our readers,

This edition of Lawson Link was written in early 2020, before COVID-19 began to impact our community. The stories in our magazine showcase the innovation and impact of Lawson research across many different areas. Normally released in the spring, we chose to hold distribution as our focus quickly shifted to keeping everyone safe.

During the initial wave of the pandemic, our hospital-based research activity was drastically reduced to essential studies only. I want to acknowledge the tremendous effort and support of our staff, researchers and learners through this unprecedented challenge. The character and quality of our team here at Lawson is second to none.

It became evident early on as the pandemic unfolded that urgent research related to COVID-19 was needed. Several research groups here in London quickly mobilized, seeking to better understand the SARS-CoV-2 virus and investigate the prevention, diagnosis and treatment of the resulting disease. Several studies on the long-term effects of COVID-19 and the pandemic are also underway. You will find some examples of our research on the next page.

Lawson excels in rapid response research, and our researchers have always focused their efforts on the most pressing needs in health care.

I would like to thank our community who continue to help flatten the curve, and also contribute to research through the COVID-19 response funds of London Health Sciences Foundation, Children's Health Foundation and St. Joseph's Health Care Foundation.

Sincerely,

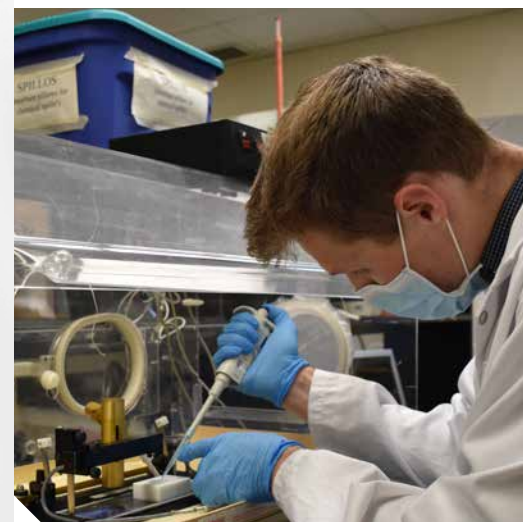
Dr. David Hill, Scientific Director

UNDERSTANDING COVID-19: LAWSON'S RAPID RESEARCH RESPONSE

Visit lawsonresearch.ca to learn more about our COVID-19 research.



Researchers unravel three mysteries of COVID-19 by profiling the body's immune response to the virus, predicting how severe a patient's illness will become, and providing evidence for why some patients develop life-threatening blood clots



Researchers trial the use of exogenous surfactant for treatment of COVID-19 respiratory failure



New device being trialed to reduce COVID-19 infection risks and demand for invasive ventilators



Researchers launch clinical trial to test specialized dialysis as a treatment for COVID-19



Multiple studies aim to understand the pandemic's impact on Canadian health care workers



Researchers test rapid diagnosis using artificial intelligence and lung ultrasound

EASING SOCIAL SYMPTOMS OF A CRUEL DISEASE

London researchers explore first-of-its-kind treatment for frontotemporal dementia

Seven years ago, Ray Jacobs was diagnosed with frontotemporal dementia (FTD) when he was just 63 years old. One of the less common forms of dementia, FTD causes the frontal and temporal lobes of the brain to shrink and lose function.

Looking back, his wife Linda realizes there were personality changes long before they had a diagnosis – as far back as 14 years. “The three years before the diagnosis were the hardest because I knew something was changing, but it seemed more psychological than dementia-related.”

There are many subtypes of the illness with behavioural variant FTD being the most common. Symptoms include disinhibition, apathy, loss of sympathy and empathy, compulsive or ritualistic acts such as examining objects by the mouth, and dietary changes. Each person’s experience differs depending on which areas of their brain are affected.

“The MRI scans in patients with FTD are striking,” says Dr. Elizabeth Finger, Scientist at Lawson and Neurologist at St. Joseph’s Health Care London specializing in FTD. “Specific parts of the frontal or temporal lobes stop functioning and can shrink dramatically. Right beside those affected brain regions, we have other parts that are functioning normally.”

Many people with FTD also have thinning of the cingulate cortex, a part of the brain that’s important in initiating behaviours. When the cingulate isn’t functioning, the person becomes very apathetic. “Even though the individual could have a conversation, wash the dishes or read a book, they don’t,” adds Dr. Finger, also an Associate Professor at Western University.

Dr. Elizabeth Finger is a neurologist and researcher specializing in frontotemporal dementia. She is leading the first clinical trial using oxytocin to treat symptoms related to empathy and apathy for people who suffer from this disease.





“It felt like my husband became a different person. He had always been dependable and logical. He started making erratic decisions and was not able to see anyone else’s viewpoint. It was like I was living with a stranger,” shares Linda Jacobs.

People with this type of dementia are usually unaware of the changes or chalk them up to memory trouble. “In the clinic we have people who’ve had a complete change in personality and yet they can’t see it. The affected frontal and temporal regions are critical for regulating behaviour and emotion,” explains Dr. Finger.

As a result, some become resistant to care and support. The disease is not well recognized and often misdiagnosed. It can take an average of five years before a clear diagnosis is made.

Ray didn’t have any awareness of the changes, and didn’t understand the concern. “He just didn’t get it,” remembers Linda.

FTD can also hinder the ability to consider other people’s wellbeing, needs and emotions.

Relationships can be severely impacted and loved ones alienated.

Over time, Linda and Ray started to have some

confrontational discussions. Ray, who loved working, lost his job. He soon experienced depression and started to drink more. Convinced something wasn’t right, Linda encouraged him to see a doctor.

“He’s had language trouble from the start. He would forget the words for things and fit in other words instead,” says Linda. “The doctor showed him a picture of an elephant and he didn’t have a word for it.”

When they received the diagnosis, the loss of brain function was visible in the MRI.

Linda remembers how the doctor explained to Ray that he had a disease in his brain, and that he’ll have trouble making decisions and it will affect many things. “He never quite understood.”

Ray was happy but had difficulty relating to people. “We would

be out and he would say something completely inappropriate, like his social filter was gone. People showed a lot of grace when they understood why, but there was embarrassment and shame.”

There are no treatments for dementia symptoms related to empathy and apathy. This has been the focus of Dr. Finger and her team’s research.

In the early 1990s, researchers identified differences in social behaviour in mammals related to levels of the hormone oxytocin. Oxytocin is thought to have an important role in social behaviour, acting as a neurotransmitter in our brains.

There was an explosion of studies showing that acute doses of oxytocin increased behaviours such as social recognition, pair

bonding, nest building and grooming while decreasing anxiety. For people with autism, oxytocin improved reaction to social cues, processing of facial expressions and cooperative decision-making.

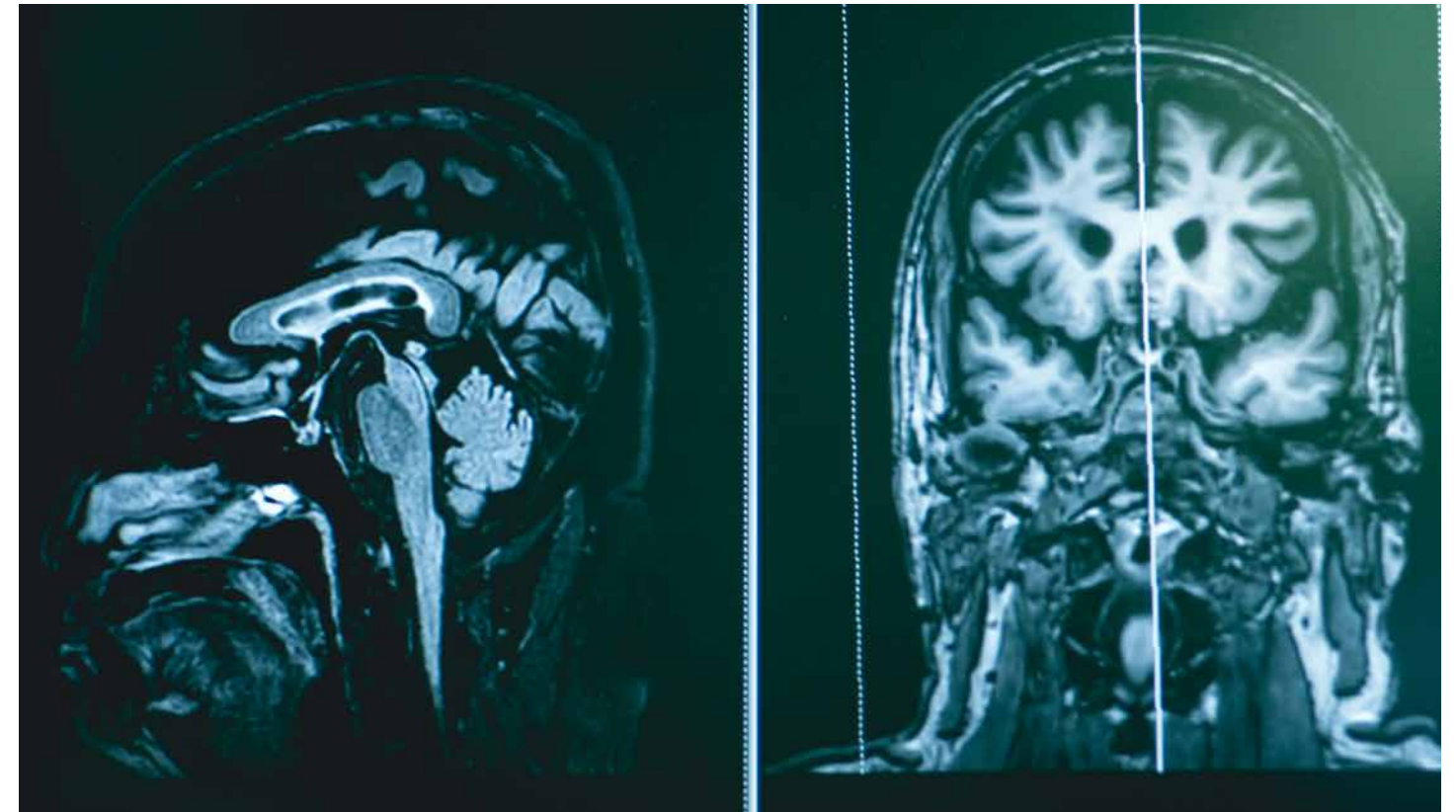
Dr. Finger’s team conducted the first oxytocin clinical trial for treating symptoms of FTD, with patients at St. Joseph’s. It was a crossover study where each participant was given the drug and a placebo.

Oxytocin was administered as an intra-nasal spray. After getting the dose, participants looked at facial expressions and were asked to describe the emotions they saw. Caregivers rated their loved one’s behaviour that evening.

The results showed that oxytocin lessened recognition and processing of fear and anger expressions. This could be linked to reduced threat detection that allows for more positive social interactions. Caregivers also reported more social behaviour afterwards.

“We moved on to a second study focusing on safe and effective dosing,” says Dr. Finger. “Again, we saw improvement

“It’s a rotten and cruel disease. It affects so many parts of someone’s life and their loved ones,” says Dr. Finger. “We finally feel we can improve quality of life and are gathering proof that it’s not hopeless.”



With frontotemporal dementia, MRI scans show a striking loss of brain function. Instead of appearing as white, entire regions of the brain are dark in the images. Those parts of the frontal or temporal lobes stop functioning and shrink dramatically.

in behaviours and the changes were directly related to apathy and indifference. About half of the patients who had oxytocin saw improvements in these areas, compared to no changes at all after placebo.”

Encouraged by these initial findings, the team sought more objective results. At Roberts Research Institute, they measured brain activity, using fMRI, in participants who were given a single dose of oxytocin and then asked to watch and imitate expressions. “We could clearly see in the scans that oxytocin increased brain activation in the frontal and temporal regions.”

Dr. Finger’s team is now leading the FOXY Trial, a Phase II multi-centre clinical trial of oxytocin for empathy deficits and apathy in FTD, with participating sites across North America. The study will take several years to complete.

FOXY is a crossover study designed to also look at dosing schedules. With chronic dosing over time, oxytocin can lose its effectiveness in some participants.

“We are testing a variety of ways to measure apathy and empathy, and we have several secondary measures to put those results into context to decide whether to proceed to a Phase III trial,” explains Dr. Finger.

One of those important measures is caregiver experience and burden. Maybe the patient is improving, but does that translate to better outcomes from the caregiver’s perspective?

“It’s a rotten and cruel disease. It affects so many parts of someone’s life and their loved ones,” adds Dr. Finger. “We finally feel we can improve quality of life and are gathering proof that it’s not hopeless.”

Ray has been in long-term care for the past year. He was no longer safe at home due to wandering and obsessive eating of inedible objects.

“Ray’s communication and recognition of family is rarely evident. Most of our seven grandchildren have few memories of Ray without dementia, but they enjoy visiting him with their parents,” shares Linda.

“Our retirement has not been what we might have hoped for, but I am grateful for the support of family, friends and community resources throughout our journey. You learn quickly with FTD that you must develop patience, a thick skin and a good sense of humour if you’re going to survive. And most importantly, you must ask for help. I’m still learning.”

Ray and Linda were involved in a number of clinical trials including those testing the oxytocin spray. These are small but important pieces of the larger puzzle. “It made me feel like at least what we’re going through may have some value down the road. This is painful and not what either of us would have chosen. But, if there’s a glimmer of hope that our contributions will make a difference, it helps me accept this difficult journey.”

FIGHTING WEAR AND TEAR

Improving outcomes for patients with hip and knee implants

Every day, John LeFeuvre tries to get in at least 7,000 steps, tracked by his Fitbit.

“I have the competitive nature of a sportsman,” explains John, a 74-year-old retired special education teacher. “The Fitbit spurs me on.”

John wears a Fitbit as part of a Lawson research study. The device tracks his activity levels following a hip replacement surgery at London Health Sciences Centre’s (LHSC) University Hospital.

“It was inevitable. I played a fair amount of sports when I was young, everything from football to basketball to hockey. It’s great when you’re young, but you pay for it when you’re older.”

John’s hip replacement was performed using a new surgical technique called a muscle-sparing approach, which holds promise in leading to a faster recovery.

To assess whether activity and function is improved with this technique, a team of Lawson researchers are using technology like Fitbits and wearable sensors. The sensors are custom-programmed to capture data on a patient’s mobility and function. They’re being used with hip replacement patients to assess fall risk.

“We’ve come a long way with artificial joints, but we want to advance even further,” says Dr. Matthew Teeter, Lawson Scientist. “Our research focuses on developing tools to speed patient recovery, improve function and make implants last longer.”

HARNESSING TECHNOLOGY

The different tracking measures being used in various studies are giving researchers and clinicians a clearer picture of the patient’s experience and the success of their implanted device.

“Surgeons need more accurate measures of a patient’s hip or knee function to decide on the best surgical techniques,

We’ve come a long way with artificial joints, but we want to advance even further.

set targets for recovery and innovate with new ideas,” explains Dr. Teeter, who is also an Assistant Professor at Western University. “Our wearable sensors provide these measures.”

The sensors, programmed in-house by PhD candidate Riley Bloomfield, capture a total of 55 measurements from the upper and lower leg, including multiple angles, velocities and speeds. Through artificial intelligence (AI), the research team is harnessing the complex sets of data to predict patient outcomes.

The sensors are worn by patients below and above each knee as they perform a timed-up-and-go (TUG) test – a routine clinical test that involves getting up from a chair, walking three metres, returning and sitting back down. The faster a patient completes the test, the better their function.

Wearable sensors take the TUG test to a whole new level. The sensors provide a vast amount of data that is transmitted to a mobile app.

“While the original TUG test gives us a prediction of function, it doesn’t measure complexities. It doesn’t tell us whether the patient’s knee is stiff or how it’s bending for example,” says Dr. Brent Lanting, Orthopaedic Surgeon at LHSC and Associate Scientist at Lawson. “The sensors provide much more information.”



Following a hip replacement, John Lefeuvre (right) is participating in a number of research studies with his orthopaedic surgeon, Dr. Brent Lanting (left).

In an initial study, the wearable sensors were used with 68 knee replacement patients to assess function before surgery. The data was put into an AI algorithm which identified two groups of patients.

“We weren’t sure why the machine identified these two groups,” explains Dr. Teeter. “We didn’t tell the computer what to do; we simply asked it to make sense of the data.”

Patients continued to perform the tests at regular follow-up appointments and the difference between the two groups soon became clear. Function did not improve following surgery for the majority of patients in the first group while most in the second group experienced significant improvements.

“These findings are critically important. Using data from wearable sensors, a machine was able to predict which patients would improve and which patients would not,” says Dr. Teeter.

The team hopes this research can help personalize care for different groups of patients, communicate expectations and inform health care funding decisions.

“By predicting how a patient will respond after surgery, we will better understand what each patient needs in terms of surgical techniques, length of hospital stay, pain management and physiotherapy,” says Dr. Lanting.

They hope to collect even more data by combining the sensors with patient-reported outcomes like pain. They will also compare function ability against actual activity levels from the Fitbits. Specific groups of patients will be further classified with AI, studying whether recovery differs by implant choice, surgical technique or patient factors like age, sex and BMI.

RETRIEVING THE IMPLANT

The team is also working to improve implant design to reduce the need for revision surgeries.

Revision surgeries involve replacing an implant when it wears down or fails due to age, material defects or infection.

“Implants are lasting longer, but people are also living longer and many patients are younger at the time of surgery,” says Dr. Teeter. “With higher rates of obesity and more patients wanting to remain highly active, implant failures remain an issue.”

Dr. Teeter studies recovered implants at Lawson’s Implant Retrieval Laboratory located at LHSC’s University Hospital. The facility is one of only two in Canada and houses more than 4,000 recovered hip and knee implants.

Each implant is examined in an attempt to understand why it failed. They construct ‘wear maps’ by scanning each implant with micro-CT imaging and then visually reconstructing it. The map shows where and how badly the implant has worn down. Researchers can look at corrosion, fractures and cracks under the surface.

“Each implant on its own doesn’t tell us much. But when we’re able to look at groups of them, meaningful patterns emerge,” explains Dr. Lanting. “Our goal is to improve implant design by understanding the effects they have on failure mechanisms and patient outcomes.”

“Lawson has a unique collaborative environment,” adds Dr. Teeter. “There are scientists, surgeons, coordinators, assistants and trainees who are all very keen on research. We bring different disciplines together to develop technological innovation that can be applied directly to patient care.”

Together, they are painting a brighter future for people like John, who views this research as vital. “I’m happy to participate. If you can do something to help future patients, I think it’s a citizen’s obligation.”

Orthopaedic surgeon, Dr. Brent Lanting (left), and Lawson Scientist, Dr. Matthew Teeter (right), are collaborating to improve outcomes for hip and knee replacement patients.



CROSS COLLABORATION

With expertise in orthopaedic and microbiome research, Lawson Scientists are collaborating to better understand infections in hip and knee implants.

“Implant infection is a long-standing problem that can be devastating and difficult to treat. Oftentimes it’s not clear whether an implant is infected or not,” says Dr. Matthew Teeter. “Loosening is a primary cause of failure and there’s a growing theory that those implants are actually infected.”

He is collaborating with Dr. Jeremy Burton to test this theory. They are conducting DNA analysis on implants as soon as they are removed from patients who need revision surgery. The implants, even those not thought to be infected, will be studied for signs of bacteria. The team will then look at whether certain regions are more prone to infection than others and analyze the damage in Lawson’s Implant Retrieval Laboratory.

The goal is to provide clinicians with more tools to diagnose and treat infections in the future.

To learn more about Dr. Jeremy Burton’s research, read “Drugs vs. bugs” on page 28.

STUDENT SPOTLIGHT

MICHELLE SOLOMON



Michelle Solomon has completed a portion of her training at Parkwood Institute, part of St. Joseph's Health Care London, with Dr. Cheryl Forchuk, Lawson Scientist. She is working towards a PhD in Nursing Leadership in Health Promotion and Advanced Nursing Practice at Western University.

MY RESEARCH

For people between the ages of 15 to 24, suicide is the leading cause of death. Previous research shows that spiritual coping helps to reduce depression and suicide rates.

Spiritual coping is the use of beliefs, attitudes or practices to help reduce the emotional distress caused by stressful events of life, helping to give the suffering meaning and make it more bearable.

People who have bipolar disorder are more at risk of suicide compared to other psychiatric diagnoses. My research focuses on spirituality among youth who have bipolar disorder to learn how they define and experience spirituality during their illness.

Traditional pharmacotherapy-based treatments have limited effectiveness on quality of life for chronic and complex illnesses such as bipolar disorder; therefore, a more holistic approach to treatment is important. I want to look at a psychosocial intervention like spirituality to help people manage their symptoms. Spirituality is a universal concept and something that many can relate to. Focusing on spirituality, rather than religion, is more inclusive allowing us to study the impacts for people with diverse cultures, religions, beliefs and backgrounds.

PARTNERING WITH PATIENTS

For mental illness, the initial care often happens in hospital. We see this as an

important time when health care providers, social workers and researchers – with the patient – contribute and work together. The person experiencing a mental health challenge can be under a lot of stress, and we want them to feel comfortable knowing that they are receiving the best care with evidence to support it.

My research will involve interviewing youth who live with bipolar disorder and asking them questions about their spiritual health. I hope that by interviewing youth, they will teach us more about how we can better facilitate spiritual health.

THE NEXT STEP

I would like to continue developing my program of research. From there, I want to network and build a team of people who share my research interests. I would love to collaborate with people internationally to meet the mental health needs of youth around the world.

EMPOWERING YOUNG SCIENTISTS

To those interested in working in health research, my advice is to take good care of yourself, have hobbies outside of health research and maintain a balanced lifestyle.

As a scientist, always stand for what you believe in and work well as a team because research is very collaborative.

UNLOCKING THE CODE OF RARE DISEASES

DNA is the molecular code for all life on Earth. The human genome is made up of approximately 25,000 protein-coding genes, and many more non-coding sequences that control the expression of these genes. The amount of information contained in our genome is so vast that our understanding of genetic determination is far from complete.

Dr. Bekim Sadikovic is an Associate Scientist with Lawson and Head of the Molecular Genetics Division at London Health Sciences Centre (LHSC). “Even though our knowledge has exploded in the last decade, we are just scratching the surface of what there is to know about our DNA,” he cautions. “We have the capability to sequence human genomes in a single day, but we are limited by our ability to interpret the clinical impact of this information.”

Many diseases and their potential therapies are studied at a population level. With a large number of people affected, discoveries and improvements are more likely. But what about diseases that are rare? Or those that have a high degree of variability among individuals?

This is where genetic profiling can make a difference.

Jacob Seltzer (middle) was diagnosed with a unique neuroblastoma at just five months old. He stands with his mother, Jennifer Seltzer (left), and father, Adam Seltzer (right).



PAEDIATRIC ONCOLOGY RESEARCH

Approximately 20 per cent of children diagnosed with cancer do not respond positively to treatment. While many other areas of cancer research have made great progress, in the last three decades the needle has barely moved for our smallest and most vulnerable patients. Incidences of childhood cancer continue to go up.

Very few breakthroughs have been made impacting the treatment of childhood cancer, but it's not for lack of trying. Existing drugs and their various combinations have been tested. Still, many children are not recovering.

Dr. Alexandra Zorzi is an Associate Scientist at Lawson and Chief of Paediatric Oncology at Children's Hospital, LHSC. “I often tell families that I loathe statistics. We can cite that the cure rate of a particular cancer is 80 per cent, but in reality, there is only one child in front of us with their own story,” she shares.

Dr. Zorzi is part of a research network known as PROFYLE – Precision Oncology for Young People. PROFYLE is a Canadian initiative that brings together the country's top scientists, clinicians and experts, all with a united goal of understanding childhood cancers, finding cures and improving outcomes for affected kids and their families. The initiative is supported by The Terry Fox Foundation and locally by the Fight Like Mason Foundation.

JACOB'S STORY

Jacob Seltzer was born in May 2018. His parents, Jennifer and Adam, felt everything was developing normally until a family member noticed a small bump on Jacob's belly. It seemed like nothing to worry about, but they soon noticed that it was growing.

Jacob's family physician referred them to Dr. Zorzi. After multiple tests, they were able to determine what was going on with the odd mark under the skin.



Dr. Alexandra Zorzi studies pharmacogenomics for childhood cancer.

Jacob's bump was the visible outward sign of a neuroblastoma – a type of cancer that develops from immature nerve cells, and is most commonly found in the adrenal gland near the kidneys. Inside, it was invading his bones, organs and bone marrow. He was only five months old.

Neuroblastomas in infancy typically respond well to conventional treatment. After Jacob started his treatment, Dr. Zorzi closely monitored the results of his physical exams, scans and tumour markers secreted in his urine. After four months, nothing was changing. Dr. Zorzi knew this neuroblastoma was different.

Unlocking the genetic code of Jacob's cancer helped Dr. Zorzi and her team find the key that would rewrite the story for Jacob and his family.

As a PROFYLE collaborator, Dr. Zorzi was able to send a sample to a lab in Toronto, where they sequenced the genome of the tumour. Now knowing the DNA profile of the tumour, experts were able to determine that he had a mutation in the gene that codes for anaplastic lymphoma kinase (ALK). This mutation causes cells to divide uncontrollably, resulting in cancer.

Precision and personalized medicine is now a reality, and many targeted drug therapies exist for multiple diseases. “It is bittersweet that paediatric cancers represent only one per cent of all cancer diagnoses in Ontario. Due to the rarity of these diseases, they do not receive the same attention or the same funding and drug development as, for example, adult lung cancer,” says Dr. Zorzi.

It turns out that the same ALK mutation is commonly found in the tumours of lung cancer patients, with a targeted medicine already developed for adults.

“By understanding the genomic landscape of Jacob's tumour, we were able to make the case that this drug could help him and received compassionate access. We were cautious, because this drug has not been thoroughly tested in children. Given the alternatives we were facing, it was our best option,” explains Dr. Zorzi.



Researchers discovered that Jacob's tumour has the same genetic mutation commonly found in adult lung cancer.

Today, Jacob's lab tests show almost no trace of the cancer and his scans have normalized. "We feel so fortunate to have been assigned Dr. Zorzi as our doctor. She's one of the best out there and she has connections to other experts. This research has changed our lives. Jacob can do normal things now, like visit with family and friends. Before, the risk of infection was too high," says Jennifer.

DEINTENSIFYING CANCER TREATMENT

Dr. Anthony Nichols, a Lawson Scientist and Chief of Head and Neck Surgical Oncology at LHSC, focuses his research on improving outcomes for patients with head and neck cancer.

Head and neck squamous cell carcinoma (HNSCC) is the fifth most common cancer worldwide. The disease, as well as its treatment, has a profoundly negative impact on the patient's quality of life due to physical disfigurement and difficulty speaking and swallowing.

Approximately 25 per cent of HNSCC cases are caused by oral infection with the human papillomavirus (HPV) and tend to respond well to treatment. Most HPV-negative tumours are caused by smoking, but one third of these patients are non-smokers.

"Having the genetic profile of these tumours can help inform physicians on how their patient's disease will respond to treatment, and in many cases a less intense cancer treatment can be used effectively."



Dr. Anthony Nichols studies genomic markers and their association with head and neck cancer treatment outcomes.

Dr. Nichols and his team conducted a genomic analysis of HPV-negative tumours to determine the connection between smoking and cancer recovery. They discovered that two genes, NSD1 and COL1A11, were more frequently mutated in heavy smokers. Surprisingly, they found that patients carrying the NSD1 mutation experienced significantly better outcomes when compared to those carrying the non-mutated gene. These findings were later validated in a cohort of patients at LHSC.

"Having the genetic profile of these tumours can help inform physicians on how their patient's disease will respond to treatment, and in many cases a less intense cancer treatment can be used effectively," says Dr. Nichols.

BEYOND THE GENOME

Part of Dr. Sadikovic's research concentrates on diagnosing extremely rare, heritable diseases. Children with developmental delay are commonly referred to the Medical Genetics Program at LHSC for genome sequencing. The medical team must then attempt to determine which of the 25,000 genes is responsible for the condition. For some, there are no genetic abnormalities detected.



Dr. Bekim Sadikovic studies genomic markers associated with rare, heritable diseases.

Many people believe our genes determine our destiny, but there's another layer, the epigenome, that controls the expression of our genes – whether a gene is turned on or off. The patterns of genes being turned off can now be tested, facilitating the diagnosis of previously unsolved cases of congenital abnormalities.

"Families may spend years going through repeated tests and exams, hoping for a diagnosis. This process is very hard on them and is costly for our health care system," explains Dr. Sadikovic.

While there are still limited treatment options for many of these conditions, a diagnosis can help physicians better predict the course of the disease, allowing families to plan more accurately for the future.

"It is important for everyone to understand the other layers of life that contribute to the observable characteristics of our genes. It's not about our particular collection of genes, it's the different ways those genes are expressed and the environment we are exposed to."

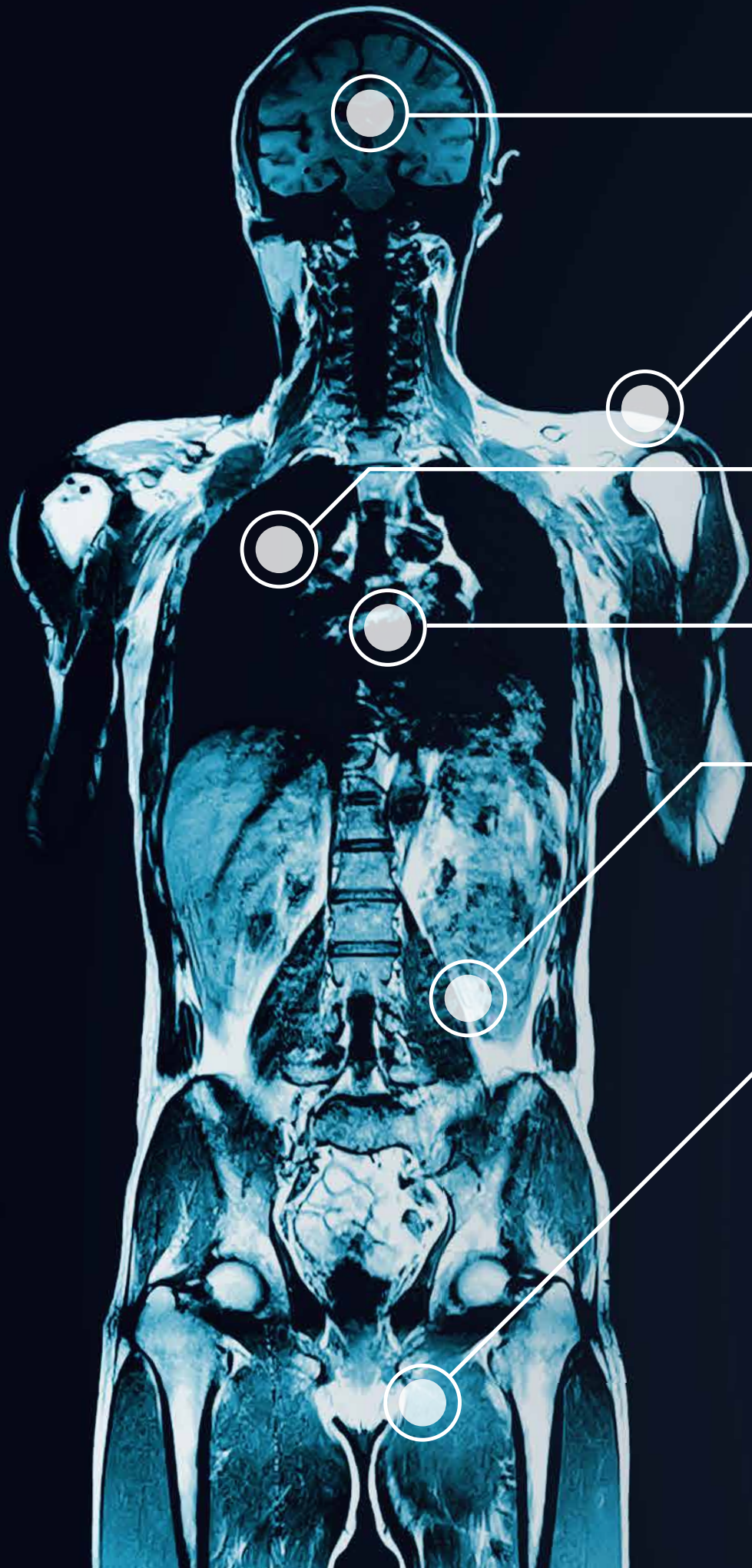


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BRAIN

fMRI is being used to better understand and diagnose mental illnesses

KNEE, HIP, SHOULDER

Radiostereometric analysis is used to measure joint implant migration, wear and kinematics

BREAST

Researchers are developing a photoacoustic hand-held probe for tumour detection during breast conserving surgery

HEART

Cardiac functional MRI provides a non-invasive way to image heart muscle activity, detecting heart disease

KIDNEY

CT perfusion is being used to improve treatment outcomes by measuring blood flow to the kidneys during dialysis

GROIN

New PET scan tracers are being tested for early detection of prostate cancer in men.

For women, 3D ultrasound provides a more clear and accurate picture, helping to guide surgical treatment for gynaecological cancer.

LONDON IS A GLOBAL LEADER IN IMAGING RESEARCH

Advanced hybrid imaging platforms, including MRI and CT, are being used to drive discoveries and innovation in areas such as cardiology, neurology, metabolic disease and cancer.

Cyclotron and radiochemistry facilities provide essential resources for this research. The newly emerging technologies of photoacoustics, optical spectroscopy and bioelectromagnetics are also being studied to improve health care.

Lawson is home to brilliant scientists and state-of-the-art-technology, where medical imaging is improving our health and well-being – from head to toe.

THE EVIDENCE ON MEDICAL CANNABIS

A promising black box

Cannabis is quickly gaining momentum as a wellness trend with people touting its many medicinal properties. But is there enough data to support the hype?

Dr. Dwight Moulin, Scientist at Lawson, Professor at Western University and the Earl Russel Chair of the Western Pain Program, is a leading expert in the area of pain management. He answers some common questions to shine a light on the evidence for medical cannabis.

WHAT ARE CANNABINOIDS AND HOW ARE THEY BEING USED?

There are hundreds of different chemicals in the cannabis flower, yet only a few have ever been studied. The most well-known is delta-9-tetrahydrocannabinol (THC), the main psychoactive compound. Cannabidiol (CBD) is another major constituent of the plant. Both act on cannabinoid receptors in the body.

THC is considered a painkiller. It's analgesic mechanism of action is similar to opioids, but THC can offer relief without side effects like constipation and respiratory depression. CBD has a completely different way of producing effects in the body.

WHAT EVIDENCE DO WE HAVE?

We have many trials testing THC for pain relief, especially for people with nerve or neuropathic pain. CBD may be analgesic as well, but we don't have any published clinical trials of CBD use in humans for pain relief. We have very compelling testimonials suggesting benefit and some studies are underway. It's a huge gap.

WHY DO WE NOT HAVE MORE RANDOMIZED CONTROLLED TRIALS?

Trials using THC are often of short duration with small numbers of participants. Even when the attempt is made for a double blind study, the euphoria and drowsiness from THC makes blinding difficult – the participants tend to know if they've taken THC and it can alter the data.

Medical cannabis use has focused almost entirely on THC for the last five to 10 years, but more attention is being given to CBD. People started noticing strains high in CBD were helping them with pain or other conditions, and the anecdotes are now overwhelming.

Because these are natural products, there are fewer incentives for industry to pay for the trials and patent a formulation. Researchers have to look elsewhere for funding.

ARE WE AWARE OF RISKS RELATED TO CANNABIS USE?

We believe that smoked cannabis carries increased risk to the lungs; although, short term studies have not shown adverse effects. While we don't recommend smoking cannabis, smokers can reduce the risks to the lungs by vaporizing at lower temperatures or they can switch to ingested oils, edibles and capsules.

About 10 per cent of people who use cannabis are at risk of developing an abuse disorder. The greater the feeling of euphoria the drug provides, the more likely a person gets addicted. The risk of addiction with nicotine is much higher at 50 to 60 per cent.

When THC is used under the age of 25 by predisposed individuals it can increase the risk of psychosis. That's something we are quite concerned about. Psychiatrists are seeing more and more psychosis, including schizophrenia, in individuals who used cannabis at younger ages, and we are seeing the same through many observational studies.

DO WE KNOW ENOUGH ABOUT THE HEALTH BENEFITS AND POTENTIAL HARM?

An exciting potential benefit is that cannabis may be used as an opioid-sparing technique. That is, it can be used in place of opioids to relieve pain. It has fewer side effects than opioids and is handled well by most people. Cannabis has no risk of respiratory depression – no one's ever died from an overdose. Across the border in states where recreational cannabis has been legal for many years, they've seen the incidence of opioid-related deaths going down. The trade-off is that there is a modest increase in impaired driving.

Overall, we are confident that medical cannabis can be prescribed safely and despite some of the limitations, we have reasonable evidence for THC as a painkiller. We don't know enough about CBD yet because we don't have the data.

WHAT ARE SOME OF THE MOST COMMON USES RIGHT NOW?

The most common use is pain management, for both acute and chronic pain such as arthritis, nerve

pain, headaches and migraines. Cannabis may also be beneficial for people with inflammatory bowel disease. CBD is being used for some forms of intractable epilepsy and a major area of focus is using CBD for relieving symptoms of post-traumatic stress disorder (PTSD) and anxiety, as well as for athletes with post-concussion syndrome.

WHAT ARE THE NEXT STEPS?

We are still investigating dosing of medical cannabis and how much CBD to give with THC. Right now we use low amounts and go from there to see how each individual reacts. The real limitation is that cannabis is expensive and some people don't get the full benefit because they can't afford it.

We don't want people smoking it and ingested cannabis can take one or two hours to kick in, making accidental overdoses more likely. Administering it under the tongue is being explored, which could be a great option because it bypasses the liver and goes directly to the arteries, brain and spinal cord.

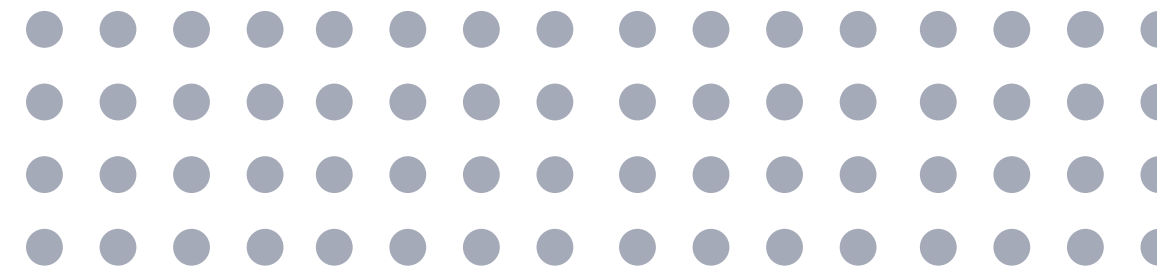
We need short-term randomized controlled clinical trials that are blinded, along with long-term pragmatic studies to look at the efficacy and safety over time. I do expect some clinical trials on CBD to come out soon but it will probably be a few years before we have solid information. Right now CBD is almost a black box, and we are relying on testimonials.

We have very compelling testimonials suggesting benefit and some studies are underway. Right now scientific evidence on CBD is almost a black box.

Dr. Dwight Moulin is a leading expert in the field of pain management. He has published extensively on the role of opioid analgesics in the management of chronic pain and done studies on medical cannabis for pain management.



Cool Science



Spinal cord stimulation brings back mobility to patients with Parkinson's

Dr. Mandar Jog and his team were the first in the world to implant a stimulator device on the spines of Parkinson's patients, helping them walk again. They have found that stimulating signals that move from the body towards the brain can greatly improve movement. The stimulator is an efficient and cost-effective therapy, with the patients in the clinical trial experiencing much better quality of life.



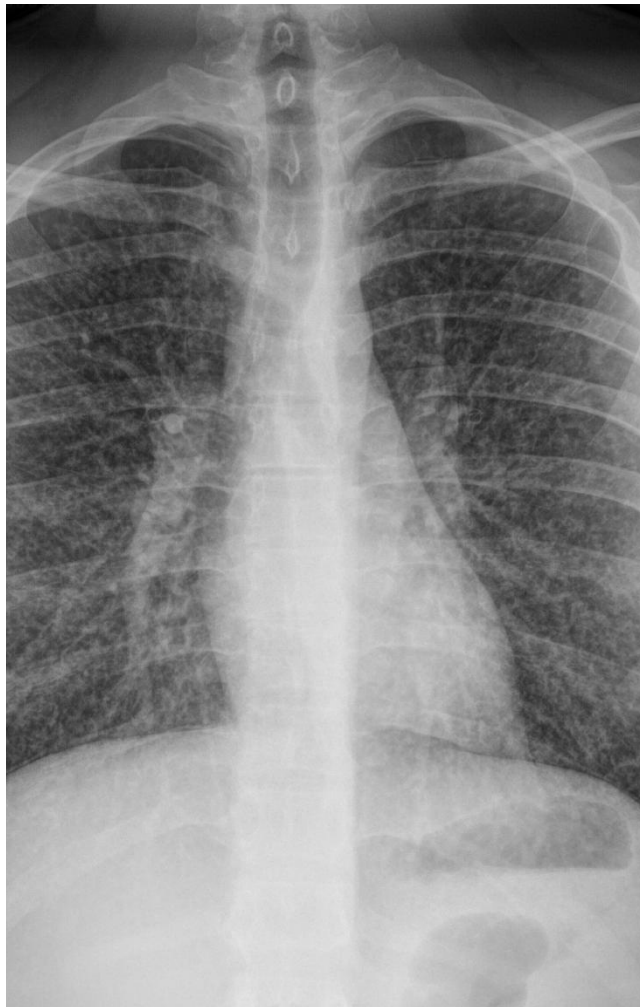
Neuro Course: Online Cognitive Behavioural Therapy

To improve outcomes for patients with neurological disorders who are also experiencing mental health challenges, Drs. Swati Mehta (pictured left) and Eldon Loh (pictured right) are studying an internet-delivered cognitive behavioural therapy program called The Neuro Course. This therapy teaches skills to self-manage mental health symptoms. Those living in remote areas can access the course online and it removes the traditional barriers of face-to-face approaches.

New device for feeding tube insertion

In collaboration with medical device company CoapTech LLC, Lawson researchers are the first in the world to trial a new method of feeding tube insertion. By combining magnets and ultrasound, the PUMA-G System allows feeding tubes to be inserted at the bedside rather than needing specialized imaging or endoscopy suites. Unlike traditional methods, the PUMA-G System allows physicians to see the space between the skin and the stomach, minimizing the risk of puncturing other organs.





Vaping can cause life-threatening lung disease

Lawson researchers published the first reported case of vaping-related lung injury in Canada. The case describes a new type of vaping-related lung injury that appears similar to 'popcorn lung,' a condition seen in microwave popcorn factory workers exposed to the chemical diacetyl. After ruling out other causes in the previously healthy teen, the team suspects flavoring in vaping products as the culprit.

Air pollution associated with adverse birth outcomes

Researchers in London have found that pregnant women exposed to higher amounts of sulfur dioxide are 3.4 times more likely to have a low birthweight baby and two times more likely to have a preterm birth. The study suggests that toxic air enters the placenta after traveling through a pregnant woman's lungs and blood stream. The research team is now working on identifying clusters or 'hotspots' of exposure that can help inform future health promotion interventions.



Stopping discharges to homelessness

For some people, the experience of homelessness starts with a hospital discharge. The No Fixed Address (NFA) strategy has proven successful in providing people with critical support when they have been discharged from hospital and are re-integrating into the community. With a study funded by the Government of Canada's Homelessness Partnering Strategy and led by Dr. Cheryl Forchuk, the expanded NFA strategy reduced discharge to homelessness by half for medical patients at LHSC.

Women face poorer outcomes following aortic surgery

In the largest study of its kind, a research team led by Dr. Michael Chu found that women experience poorer outcomes following aortic surgery when compared to men. Women are 40 per cent more likely to experience a complication, 90 per cent more likely to experience a stroke and 80 per cent more likely to die. The study highlights the importance of better screening for heart conditions in women and taking a different approach when treating female patients with aneurysms.



Transitional support program empowers youth with diabetes

In the first multicenter randomized controlled trial of its kind, teams from across Ontario led by Lawson researchers found that young patients with Type 1 diabetes benefit significantly if they have a transitional plan when moving from paediatric to adult care. Those assigned a transition coordinator attended more care visits, were more satisfied with their care and better managed their diabetes on a daily basis, while suffering less distress and emotional burden. The program has the potential to ease young adults into being able to comfortably navigate the health care system on their own.

SERVING THOSE WHO SERVE

Members of the Canadian Armed Forces and retired Veterans represent a distinct population when it comes to understanding mental health. Researchers in London are working closely with military members to better understand their needs and explore tailored treatment options.



Major Ronald Miller, Canadian Armed Forces Veteran and research participant at the MacDonald Franklin OSI Research Centre.

The MacDonald Franklin Operational Stress Injury (OSI) Research Centre, located at Parkwood Institute, part of St. Joseph's Health Care London, is an international leader in research on military and Veteran mental health. The primary mission of the Centre is to improve the mental health and well-being of this distinct population through clinical and neuroscience research.

Closely connected to the OSI Research Centre, St. Joseph's OSI Clinic offers specialized services for Veterans, active military members, RCMP and family members experiencing mental health challenges as a result of military service.

Military members experience trauma and injury in a way that most civilians will never know. In the line of duty, they may perform, witness or fail to prevent acts that conflict with their own deeply held moral standards. This adds another layer of complicated feelings and emotions, known as moral injury, that researchers are just beginning to understand.

Moral injuries are on the rise among members of the Canadian Armed Forces, and research shows that those exposed to these events are at a higher risk of developing post-traumatic stress disorder (PTSD). The OSI Research Centre is investigating patient perceptions of confidentiality around disclosing moral injuries to mental health professionals.

"We have a duty to honour the service of our military personnel and Veterans and take care of them if they're injured," says Dr. Don Richardson, Lawson Associate Scientist, Scientific Director of the OSI Research Centre and Lead Physician at the OSI Clinic. "They may not disclose certain details, due to mistrust or a perceived lack of confidentiality, and knowing this helps us serve them better."

Dr. Richardson's work also looks at comorbidities of PTSD and how they can be used as predictors of treatment outcomes. It's common for persons with PTSD to also show symptoms of depression. Research has shown that in military or combat-related PTSD, rates of comorbidity are higher than in the general population, and they tend to have more severe symptoms. This can complicate treatment and make recovery more challenging.

Military personnel by nature have a desire to help and improve situations. They will often seek help when they need it and want to participate in research. Even if it might not help them directly, they hope it will help future Veterans and others.

The research team has been measuring changes in the brain that occur with PTSD, using fMRI technology. It's helping researchers and clinicians to identify new subtypes of PTSD and their unique symptoms.

Researchers at the OSI Research Centre are investigating many other areas of mental health, including gender differences in symptom profiles, the impact of sleep on suicidal ideation, sexual health in persons with depression and PTSD, and understanding recovery from the perspective of Veterans and their family members.

As Dr. Richardson explains, "a clinician may determine that a person is recovered because they meet some target on a scale, but when we speak to Veterans and their significant others, they may have a different perspective."

Much of what we know about treating PTSD has come from the Veteran population, but researchers are learning more about how other types of trauma can lead to PTSD for civilians. What is learned in the context of Veteran's mental health can improve care for others.

"Military personnel by nature have a desire to help and improve situations. They will often seek help when they need it and want to participate in research. Even if it might not help them directly, they hope it will help future Veterans, and others."

When patients come through the clinic, they can provide consent for their data to be used for research purposes. Because this research is integrated within the OSI Clinic, there is strong collaboration and results can be translated into care quickly.

The MacDonald Franklin OSI Research Centre's Advisory Council includes Veterans and spouses of Veterans. "We want to ensure that the OSI Research Centre is meaningful for the individuals we're trying to help," says Dr. Richardson. "A Veteran might have a question about their symptoms or treatment, and we can help formulate that into a research question."

For Dr. Richardson and his colleagues, it is an honour to have so many Veterans participating in research. "We do our best to return the favour by making sure our research is driven by the interests of Veterans."



Dr. Don Richardson studies the assessment and treatment outcomes of Veterans and Canadian Armed Forces members with PTSD.

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Dr. Michael Silverman
Medical Director,
Infectious Diseases Care Program
St. Joseph's Health Care London

DRUGS VS. BUGS

Harnessing the microbiome to improve treatments

From ibuprofen to chemotherapy, everyone has taken medication at some point in their life. But why do some people respond differently than others? Could our microbiome play a role?

The human microbiome consists of all the microorganisms on the inside and outside of our bodies, including bacteria, viruses and yeasts. While the majority of microbes reside in our gut, research is revealing their presence in other areas such as the skin, urogenital tract and breast.

“It’s no surprise that the human microbiome has huge potential to influence our health,” says Dr. Jeremy Burton, Lawson Scientist. “It outnumbers other cells in our body 10 to one.”

Interest in the human microbiome has been growing and researchers are now starting to learn its importance in relation to pharmaceutical drugs. With potential to modify everything from immune reaction to properties of the drug itself, it may be the key to improving a patient’s response to therapy.

The majority of drugs are taken orally, making their way through the intestinal tract where they often spend a long time in contact with billions of microorganisms. Even those that are administered in other ways, such as intravenously, may come into contact with microbes at other sites.

“Our microbes have huge potential to metabolize drugs and therefore modify their activity and alter their effects,” explains Dr. Burton, who is also the Miriam Burnett Chair in Urological Sciences at Lawson and Western University.

Since everyone has a different microbiome, drug responses may vary drastically by individual.

In their lab located at St. Joseph’s Hospital, part of St. Joseph’s Health Care London, Dr. Burton and his team are working to learn more about microbiome-drug interactions and how the microbiome can be harnessed to make drugs safe and effective for every patient.



Dr. Seema Nair Parvathy (above) works with Drs. Michael Silverman and Jeremy Burton in Lawson’s fecal transplant research laboratory. Dr. Silverman’s team is one of the first to administer fecal transplants using specially-prepared oral capsules.



Dr. Jeremy Burton is researching the ways in which the human microbiome interacts with prescription drugs. The goal is to harness the microbiome to make drugs safe and effective for every patient.

An unexpected consequence

In one study, the team partnered with Dr. Joseph Chin, Associate Scientist at Lawson and Urologist at London Health Sciences Centre (LHSC), to examine how a prostate cancer drug called abiraterone interacts with the gut microbiome.

Prostate cancer growth is stimulated by testosterone, which belongs to a group of hormones called androgens. Abiraterone decreases androgen production in an effort to stop the growth of prostate cancer. It is used in combination with another drug called prednisone which helps to reduce side effects.

“Abiraterone works for many patients, but not all,” says Dr. Burton. “We studied the drug’s interaction with the microbiome to see whether it provided any new insights.”

They discovered that patients’ microbiome changed drastically after taking abiraterone.

Bacteria in the gut were metabolizing the drug and, while androgen-producing organisms decreased, an organism called Akkermasia began to thrive. Akkermasia is a microbe associated with positive metabolic control and better health.

“We know that abiraterone turns off androgen production, but it has other positive effects that we couldn’t explain,” adds Dr. Burton. “Are these positive effects influenced by the microbiome?”

The team also examined the interaction of prednisone with the gut microbiome and found something very surprising. Bacteria can utilize prednisone and turn it into androgen-like compounds.

“This is an important finding as it may explain why treatment fails for some patients. With the body being starved of androgen, is the bacterial population stepping up to produce it and driving the growth of prostate cancer?”

Using poop to make drugs more effective

Another way the microbiome impacts our response to medication is through its influence on our immune system.

With the rise of immunotherapy drugs in cancer treatment, Lawson researchers are conducting Phase I clinical trials to see whether the microbiome can be modified through fecal microbial transplants (FMT) to improve treatment outcomes and prevent side effects.

Immunotherapy drugs stimulate the immune system to attack cancer. While they can significantly improve survival outcomes, they are not always effective and can cause severe immune reactions.

“We know the gut microbiome influences immunity from an early age. It makes sense that a healthy gut could improve response to immunotherapy and prevent side effects,” explains Dr. Burton.

Imaging the microbiome

There’s growing interest in analyzing a person’s microbiome using their poop, but researchers suspect this is not representative of what happens further up the digestive tract. Instead, Dr. Jeremy Burton is collaborating with Dr. Donna Goldhawk, Lawson Imaging Scientist, and her graduate trainee, Sarah Donnelly, to visualize a person’s gut microbiome using magnetic resonance imaging (MRI). This is based on unique MRI signals emitted by gut bacteria.

“Some microbes in the gut send very interesting signals. We’re working to develop targeted imaging agents to see bacteria in real-time,” says Dr. Burton.

Eventually, MRI could be used to see how a person’s microbiome changes after taking a probiotic or having a fecal transplant.

The potential of poop

Dr. Michael Silverman, Lawson Associate Scientist and Chair/Chief of Infectious Diseases at Western University, St. Joseph’s and LHSC, is a pioneer in the field of fecal transplants. He was one of the first in the country to use fecal transplants in the treatment of patients with *Clostridium difficile* (*C. diff*). His team is also one of few delivering fecal transplants for select conditions using specially-prepared oral capsules.

“Fecal transplants have saved the lives of countless patients with recurrent *C. diff*,” says Dr. Silverman. “We’re now starting to see its potential for the treatment of other diseases.”

In addition to cancer immunotherapy, Drs. Silverman and Burton are studying fecal transplant for multiple other conditions including non-alcoholic fatty liver disease and multiple sclerosis (MS).

He is collaborating with a team of researchers that includes Dr. Michael Silverman, a pioneer in the field of FMT. Fecal transplants involve collecting stool from a healthy donor, preparing it in a lab and transplanting it to a patient. The donor's microbiome is transplanted so that healthy bacteria can colonize in the patient's gut.

We know the gut microbiome influences immunity from an early age. It makes sense that a healthy gut could improve response to immunotherapy and prevent side effects.

The team is the first in Canada to study fecal transplants to improve outcomes in melanoma patients treated with anti-PD1 immunotherapy drugs. Dr. John Lenehan, Associate Scientist at Lawson and Oncologist at LHSC, hopes that fecal transplants can alter the microbiome and ensure more patients respond.

In another trial, the team is studying fecal transplants with stage IV renal cell carcinoma patients who are treated with a combination of two immunotherapy drugs called ipilimumab and nivolumab. These drugs have significantly improved survival outcomes, but approximately half of patients experience severe immune-related side effects like inflammation of the bowel, lungs and skin. Side effects can become so severe that patients need to stop treatment.

Study participants will undergo a fecal transplant before their first immunotherapy treatment and two supportive fecal transplants with smaller dosing before their second and third treatments. Dr. Ricardo Fernandes, Lawson Associate Scientist and LHSC Oncologist, hopes this will bolster the microbiome and reduce immune-related side effects so patients can stay on treatment.

"We're one of the first in the world to study fecal transplants in cancer patients. These studies are as cutting-edge as it gets," notes Dr. Saman Maleki, Lawson Scientist specializing in cancer immunotherapy.



Drs. Michael Silverman (left) and Jeremy Burton (right) are collaborating to study fecal transplants in the treatment of a variety of diseases.

The future of microbiome therapy

For Dr. Burton, these studies are just the beginning of exploring the relationship between pharmaceuticals and the microbiome.

In the future, highly-specific antibiotics could be developed that only target bacteria involved in the growth of cancer. Instead of using fecal transplants, the growth of beneficial organisms could be boosted by powerful prebiotics and probiotics.

"We need to undertake one of the largest paradigm shifts to ever occur in medicine. Every drug needs to be reevaluated for its effects after interaction with the microbiome."

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



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



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