No more Pain

Krembil researchers are on a mission to cure arthritis.
Incidents of arthritis have ballooned, and it’s only going to affect more people in the future. Here are some numbers — about arthritis and University Health Network’s Arthritis Program — to put things into perspective.

350 million
People living with arthritis around the world — it’s a leading cause of disability (Global OA Network)

$35 billion +
Cost of arthritis, injuries and musculoskeletal-related diseases to the Canadian healthcare system (Canadian Institutes of Health Research)

50%
Canadians living with arthritis who are under 65 (Arthritis Society)

20 years
until the number of Canadians living with arthritis increases by 50% (Arthritis Society)

6 million
Canadians currently living with arthritis (Arthritis Society)

UHN’S ARTHRITIS PROGRAM

80,000+
Patients treated annually

1,200+
Joint replacement procedures performed every year

150,000+
Tissue samples
from ankylosing spondylitis, lupus, osteoarthritis and psoriatic arthritis — in Krembil’s arthritis biobank, one of the largest of its kind in North America

Researchers at the Krembil Research Institute were the first to discover microRNA tissue biomarkers associated with psoriatic arthritis

LARGEST MULTIDISCIPLINARY ARTHRITIS RESEARCH PROGRAM IN CANADA, integrating medical, surgical and basic science aspects of arthritis

Number of international research networks studying arthritis that are headquartered at Krembil

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THE STATISTICS ARE STAGGERING, AND THEY’RE GETTING WORSE

One in five adult Canadians is currently living with arthritis, a painful, debilitating chronic health condition that affects the mobility of joints and bones. By 2040, that number is expected to rise by 50 per cent, affecting nearly a quarter of our population.

These shifting demographics currently leave our aging population with increasing levels of disability, which in turn limits earning potential in the most productive years, affects relationships with family and friends, and even impacts mental health. Arthritis hits us where it hurts the most.

This is a crisis, and we at the Krembil Research Institute are on the front line. It’s time to invest in our future, by empowering scientific research, so that we can help more people, sooner.

University Health Network’s (UHN) Arthritis Program, based at Toronto Western Hospital, incorporates rheumatology, orthopedics, hand and osteoporosis programs under one roof. The program has evolved with the changing needs of our society.

We have assembled a team of the world’s most innovative arthritis clinicians and researchers. We have given them the tools, the resources and the support they need to push the boundaries of discovery and to translate those discoveries into advanced patient care.

New technologies — such as sophisticated imaging and biological profiling with immune and inflammatory markers, as well as predictive analytics and artificial intelligence — allow us to diagnose patients earlier, customize their treatment and track their progress in real time.

This interdisciplinary approach helps us to break down silos in order to speed up progress. Our quest for answers has led us to discover, innovate and improve patient care for those who need it most.

It’s patients like Jill Miller, Susan Rivers and Everton Williams, all living with arthritis, who are helping to drive the program’s success. We are driven by a passion to make a difference in their lives — to diagnose them earlier and provide them with effective treatments, to help them better manage their symptoms and improve their mobility. Ultimately, we want to help them achieve productive and fulfilled lives, free of pain and disability.

Today, there is no cure for arthritis, but we’re envisioning one for tomorrow.

Let’s all work together to make this dream a reality.
Osteoporosis’ effect on astronauts

Krembil researchers are helping NASA come up with better bone strength guidelines

By Wendy Haaf

Bone becomes weak, which is what happens in osteoporosis. (Weight-bearing exercise, like walking, builds the bricklayers to keep working, which is why low gravity causes bone loss.)

Typically, doctors use what’s called dual X-ray absorptiometry to measure bone density, but it can’t “see” whether the framework inside the bone is sturdy or spindly; soundly or shoddily constructed. However, high-resolution peripheral quantitative computer tomography (HR pQCT), which uses low-dose CT and sophisticated software, can provide information about a bone’s structure, says Dr. Cheung.

Scanning may be a better way to evaluate astronauts, as you need both bone structure and mineral content to determine bone strength, she says. HR pQCT is sensitive enough to monitor whether bone loss treatments, such as medication, work in space flight.

Recently, NASA incorporated Dr. Cheung’s recommendations into their guidelines for evaluating bone integrity—which are more important than ever with the advent of long-duration missions. So, thanks to Dr. Cheung and her colleagues, astronauts and osteoporosis patients alike will benefit from this research, and can be more confident about their future bone health.

EVERTON WILLIAMS HAD ALWAYS WANTED to become a professional football player. But at 24, just as he was finishing university, he tore the ACL, ligament in his knee. Williams, an offensive lineman, missed training camp for Canadian Football League prospects that year, but then signed with the Hamilton Tiger-Cats, crediting early intervention, including knee reconstruction surgery, for helping him recover months ahead of schedule. “It’s like brand new,” he says.

Williams is one of about 5,000 people in Ontario who undergo ACL repair each year. Some do so because non-surgical treatments haven’t sufficiently restored normal function; others, like Williams, are athletes intent on resuming sports and want to avoid further joint damage. “Surgical intervention prevents knee buckling, and secondary damage to knee joint structures that can occur with pivoting and twisting motions associated with sport,” explains Dr. Jase Chahal, an orthopedic surgeon and Krembil Research Institute clinician scientist. He adds that people of all ages and activity levels can benefit from ACL surgery if non-operative care isn’t effective.

Currently, Dr. Chahal is investigating whether leg position during surgery affects patient outcomes. If it does, then health professionals may be able to customize the surgical and rehabilitation process to each individual. “With an appropriate treatment program including surgery and physiotherapy, athletes like Everton can recover from their injuries and continue to play competitive sports at the highest levels,” explains Dr. Chahal.

Williams is just one of many players, including Tom Brady and Kyle Lowry, who haven’t missed a step post-surgery. “I’m feeling great and looking forward to getting back in the game,” he says.

Meet your future researchers

Soon-to-be scientists come to Krembil to train

Promising trainees come to Krembil from around the world to study with top scientists and physicians, and participate in leading-edge arthritis research. Here are four early-career researchers who are already on their way to becoming superstars in the field.

RESEARCH GOAL

Current therapies for osteoarthritis only ease symptoms like pain; our goal is to develop a disease-modifying tool that can stop cartilage destruction. In obesity, which is the number-one risk factor for osteoarthritis after aging, fat cells release harmful inflammatory molecules that can target the joints. I’m looking at the influence of obesity on osteoarthritis, specifically whether a molecule that we previously found is present at high levels in the joint fluid of people with advanced-stage osteoarthritis and contributes to joint destruction.

KEY ACCOMPLISHMENTS

Found a common link between obesity and osteoarthritis—abnormalities in the production of a molecule that contributes to cartilage destruction.

RESEARCH GOAL

My goal is to understand spondyloarthritis in order to develop more effective treatments. In this type of arthritis, which starts when people are in their 20s or 30s, you get destruction of joints in the spine and limbs, but you also get fusion of the joints. The drugs we have now reduce symptoms, but they don’t prevent joint fusion.

KEY ACCOMPLISHMENTS

Discovered that an immune cell involved in inflammatory bowel disease plays a role in spondyloarthritis and pinpointed a potential target for treatment—a specific type of white blood cell.

RESEARCH GOAL

I’m working on finding a new therapeutic target in ankylosing spondylitis. Ankylosing spondylitis has two main features—inflammation and abnormal bone formation in the joints of the spine. Currently, we don’t have a disease-modifying tool that can stop cartilage destruction.

KEY ACCOMPLISHMENTS

Co-discovered a small molecule that is now being tested as a prospective treatment for osteoarthritis in the spine and knees.

RESEARCH GOAL

About 30 per cent of patients with psoriasis will eventually develop psoriatic arthritis. I’m looking at whether the skin microbiome—the community of bacteria on the surface of the psoriatic lesions—could be involved in triggering psoriatic arthritis.

KEY ACCOMPLISHMENTS

Found an association between the diversity of skin bacteria on psoriatic lesions and inflammation severity, as well as a link between microbiome diversity and a gene that predisposes people to psoriasis.

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Osteoarthritis afflicts one in six Canadians – and the painful disease is only going to affect more people in the future. Scientists at the Buchan Arthritis Research Centre at Krembil Research Institute are hoping to stop it before it starts.

By Sarmishta Subramanian

When Jill Miller competed at the Pan American Masters Weightlifting Championships in Orlando, Fla., in late May 2019, hoisting an 88-lb barbell over her five-foot-two-inch frame, people watching would never have guessed she was due in a Toronto operating room five weeks later, for surgery on her arthritic right knee. Miller, who is 68 years old, has a high pain threshold. She could weather the tightness in the joint, but she also describes sudden pangs of “a knife-like pain.” During the operation to repair her meniscus – the C-shaped disk of cartilage that cushions the knee and that breaks down in arthritis – her surgeon removed seven floating fragments of bone, adding up to some 13.5 centimetres. These fragments would get stuck in her joint, locking it. “A lot of the time it wouldn’t hurt,” Miller recalls. “But when one of those pieces of bone shifted, eewwww!”

And that was the good knee. Diagnosed with arthritis in 2012, Miller had the same surgery on her left knee last year – top of cortisone shots, an injection of stem cells taken from her lumbar area and platelet-rich plasma to trigger healing. She shouldn’t even have been walking, her orthopedic surgeon, Dr. Darrell Ogilvie-Harris, at Toronto Western Hospital, told her. Four days after her July surgery, she was off the anti-inflammation drugs. Within a couple of weeks, she had returned to her gym in Collingwood, Ont., where she would gradually work up to her usual level. Walking long distances is challenging, and it still hurts to travel up and down stairs, but in late July she was in Peru, refereeing a weightlifting championship. “If I wasn’t a bit of a Pollyanna,” Miller admits, “I couldn’t do any of this. I wake up in the morning and it hurts.”

A LURKING EPIDEMIC

Miller is as typical as she is exceptional. One in six Canadians suffer from osteoarthritis (OA). By 2035, it will be one in four. In OA, the cartilage that cushions the bones in the body’s joints degenerates, leaving them to grind against each other. Knees, hips and spines are all common sites, but OA can hit elbows, shoulders, even thumbs and toes.

Age-related changes to joint function – cartilage becoming brittle, the loss of muscle mass – make people more susceptible, but typically there is also a genetic predisposition or another factor such as obesity, a sedentary lifestyle or repeated injury.

Millions of Canadians live with OA – most of whom are not athletes like Miller. It lurks in many more, who may not yet feel its telltale signs: pain or stiffness in the joints, swelling and crackling sounds. By the time there is a diagnosis through X-ray or MRI, the disease has progressed, and the loss of mobility may eventually demand surgery, perhaps the replacement of a hip or knee. There is no way to reverse its damages; treatments only ease the pain.

However, as game-changing research from Krembil shows, long before this point, there are hints of OA at the cellular level: certain molecules, called microRNAs, float undetected in joint tissue cells. As they increase, they wear down cartilage. If those molecules can be detected so disease can be averted in the first place, it could transform lives. Early detection – and a treatment that modifies the disease, rather than just addresses the symptoms – is the Holy Grail among researchers. And the Arthritis Program at University Health Network is making significant headway.

In 2016, a team led by Dr. Kapoor, and included spinal surgeon Dr. Raja Rampersaud and rheumatologist Dr. Akihiro Nakamura, identified two significant microRNA molecules in tissue samples of patients with osteoarthritis, long-time weightlifter Jill Miller continues to train and compete.
OA of the spine. If DNA molecules contain the cell’s genetic blueprint, RNA molecules are the messengers that translate that genetic information into protein production. MicroRNAs are tiny RNAs; they regulate gene expression by silencing or activating certain genes. With funding from the Campaign to Cure Arthritis, Dr. Kapoor’s team identified two microRNAs by studying the tissue of patients with mild, moderate and severe arthritis biospecimen biobank, one of the world’s largest, with some 150,000 tissue and fluid samples.

One molecule, microRNA 181-5p, proved promising; the worse the osteoarthritis, the higher its levels were. To learn why, the researchers conducted a series of patient-cell studies and pre-clinical studies. “We started to understand the molecule is produced in the cartilage, but breaks down the cartilage,” says Dr. Kapoor. Production is triggered by “an inflammatory sort of insult” to the cartilage - that is, injury, a pathological trigger or repeated strain. “And massive production of this molecule starts to damage the cartilage.”

This is what Miller would have been feeling when she went to her doctor with knee pain, as well as pain in her back and legs following an injury. That led to a diagnosis of arthritis of the back and knee. By the time she saw Dr. Ogilvie-Harris in Toronto, her back issues had improved greatly thanks to intensive physiotherapy and her own training – but she still had pain and loss of motion in the left knee.

THE ATHLETE’S DILEMMA

Miller has faced both the reward and risk associated with intensive sports: almost three decades of Olympic-style weightlifting have kept her healthy and fit. But being an athlete might have made her more vulnerable to OA due to injuries, including a partial tear of her ACL. As a past team physician for the Toronto Maple Leafs, Dr. Ogilvie-Harris has had many patients tear an ACL and end up with OA later in life. Some researchers, including Dr. Kapoor’s lab, are pursuing ways to restore or regenerate the cartilage eroded by arthritis. In the three years since identifying microRNA 181-5p, the team has developed a blocker that relies on “anti-sense technology,” which essentially disables the molecule. The blocker has a comb-like structure that locks onto the molecule, preventing it from functioning. The hope is to one day inject it into patients’ joints. If it works, it will be the first treatment for OA that halts its progression. It has been effective in pre-clinical studies.

The Kapoor lab’s researchers, in conjunction with their orthopedic colleagues, are also working on a diagnostic blood test. “If you have a biomarker that can tell you that you are either at risk or you have osteoarthritis,” says Dr. Kapoor, “it’s like having a glucose test [for diabetes].” A blood test could also help doctors determine whether a surgical approach or physiotherapy, for instance, is best. To help develop this test, one molecule, microRNA 181-5p, proved promising; the worse the osteoarthritis, the higher its levels were. To learn why, the researchers conducted a series of patient-cell studies and pre-clinical studies. “We started to understand the molecule is produced in the cartilage, but breaks down the cartilage,” says Dr. Kapoor. Production is triggered by “an inflammatory sort of insult” to the cartilage - that is, injury, a pathological trigger or repeated strain. “And massive production of this molecule starts to damage the cartilage.”

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By Wendy Haaf

Davis, epidemiologist and Krembil senior scientist, explains their symptoms through exercise and education. Dr. Aileen Denmark can help people with osteoarthritis (OA) improve.

International program GLA:D (Good Life with osteoArthritis: Denmark) can help people with OA improve their symptoms through exercise and education. Dr. Aileen Davis, epidemiologist and Krembil senior scientist, explains.

By Wendy Haaf

Learning to move improves OA

International program GLA:D (Good Life with osteoarthritis: Denmark) can help people with osteoarthritis (OA) improve their symptoms through exercise and education. Dr. Aileen Davis, epidemiologist and Krembil senior scientist, explains.

Q: WHAT IS GLA:D? Aileen Davis: We’ve long known that patient education, exercise and weight control can prevent or at least slow the progression of symptoms and functional problems experienced by people with hip and knee osteoarthritis. GLA:D Canada is a community-based, supervised, targeted program that incorporates these elements. It was developed in Denmark, and in partnership with Bone and Joint Canada we’ve brought it to Canada, and moved it from a research project into a national clinical program.

Q: HOW DOES PATIENT EDUCATION HELP? A: We spend a lot of time educating people about this paradox that, while it can hurt to be active, in the long run, exercise improves pain. We can help people learn how to manage their pain, and help them understand how much pain during and after exercise is OK. They then lose the fear of damaging their joints and feel more comfortable exercising.

Q: WHY IS EXERCISE IMPORTANT? A: When people have pain, they unconsciously change the way they move. That decreases muscle strength, and it can change joint alignment, which increases stress on the joints. Doing the right exercises can ease the load on the knee or hip by strengthening the muscles that support it. We also work on keeping people’s joints properly aligned during activities, like getting out of a chair and going down stairs.

Q: HOW WELL IS THE GLA:D PROGRAM WORKING? A: GLA:D has been implemented in more than 150 clinics across Canada, and results indicate that people are achieving a reduction in pain intensity of about 33 per cent, and have improved function and quality of life. That’s a huge benefit for people.

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October 23, 2018, is a date Craig Burgen won’t soon forget. The 48-year-old industrial mechanic was in the midst of a repair, removing a massive eight-foot steel roller at the Woodbridge, Ont., plastic sheeting company where he works, when one side of it slipped and came down on his left hand like a guillotine. His thumb was severed between the two knuckles, left to hang perilously from a small piece of skin. “I held my thumb in my right hand and it was like getting out of a chair and going down stairs,” recalls Burgen.

Craig Burgen is thrilled to be back at work after nearly losing his thumb in a workplace accident.

“Felt like I was going to be in good hands, so I spoke,” he says, reflecting on the experience. “You don’t realize how much you need your thumb until you don’t have use of it anymore.”

“Hand injuries are extremely common, sending more Canadians to the emergency room annually than any other cause. In Ontario alone, research suggests that there are more than 100,000 cases of traumatic hand injuries every year — including fractures, dislocations and amputations. These injuries can be life-changing. Arthritis, for example, is extremely common in hand-injury patients and can cause long-term health consequences, even if the damaged joint was treated properly. As well, many patients find themselves struggling with mental health and addiction issues after a traumatic hand injury, according to research conducted by Dr. Heather Baltzer, a hand surgeon and interim director of the Hand Program, and a clinician investigator at Krembil. “Hand trauma is an unrecognized public health issue that has a profound impact on the patient, limiting the ability to carry out activities of daily living,” she says. In an attempt to shed more light on hand trauma and improve patients’ lives, Dr. Baltzer and other researchers are looking at the economic burden of hand and wrist injuries, how

In good hands

Bridging research with her clinical work, Dr. Heather Baltzer is treating more patients with severe hand injuries than almost any other doctor in Canada.

By Tamara Saltov
different delivery-of-care models affect patient outcomes, and whether preventive measures such as improved workplace safety standards could reduce the incidence of hand injuries.

Using population health data, Dr. Baltzer identified two-million emergency department (ED) visits in Ontario for hand trauma over the past decade, with 500,000 being repeat visits. More than a third of surgical hand trauma patients access mental health and addiction services after their surgeries, compared to 10 per cent of the general population. The average length of an ED visit due to hand trauma is two and a half hours, which translates into over 1,300 hours of ED health care per day. That may be contributing to emergency room congestion.

For Burgen, recovery is ongoing. He's back in the machine shop and has been in physiotherapy since January, but many everyday tasks, such as doing up zippers, buttons and spreading butter on toast, are challenging. In July, nearly nine months after his accident, he had a second surgery to help regain the sensation on the inside of his thumb where it meets the index finger. A third surgery, yet to be scheduled, will improve movement of his thumb, as the joint has become scarred and stiff.

Burgen is grateful for the care he's received from Dr. Baltzer and the rest of the team at Toronto Western Hospital, and he's doing what he can to help with his recovery. "I'm trying to lead a more stress-free life," he says. "That's music to Dr. Baltzer's ears, who wants nothing more than to help her patients live their best lives, both through her actions as a clinician and as a researcher. "When someone has had part of their hand function taken away, and I can give it back to them, that's an excellent feeling," he says."

"One of the biggest challenges we face is the length of recovery, which in certain cases can be in excess of six months to a year, and the fact that patients require a lot of post-operative care and therapy to restore motion and strength," says Dr. Ryan Paul, an orthopedic surgeon in the hand surgery group at Toronto Western Hospital. That includes battling stiffness after surgery, as well as the emotional fallout from experiencing a trauma and loss of dexterity. "Even small deficits are really felt because we use our hands so frequently," he explains.

In response to these challenges, Toronto Western Hospital's Hand Program has set up a pilot project to help patients through the recovery process. A psychologist and pain management team screen patients to see who might benefit from additional treatment, such as group therapy or other mental health and addiction services. "The more we can identify individual needs, the better their outcomes will be," says Dr. Baltzer. "For Burgen, recovery is ongoing. He's back at work in the machine shop and has been in physiotherapy since January, but many everyday tasks, such as doing up zippers, buttons and spreading butter on toast, are challenging.

By the time Burgen arrived at the hospital, he was starting to feel a lot of pain. Within about 10 minutes, before it could really take hold, the nurses hooked him up to an IV with a morphine drip. "Next thing I knew, I'm waking up in my hospital bed in my room with my arm suspended," he says. "What seemed like no time at all to Burgen was more than six hours of surgery performed by Dr. Baltzer and her team. They started by thoroughly cleaning his hand and wound, which was still gory from the machinery he had been handling, then spent about an hour finding and tagging the tiny blood vessels in his thumb and hand they would need to reattach. "We put a very fine suture – a little blue stitch – in each one at the start, so we could easily see them later when we've been in surgery for hours," says Dr. Baltzer.

Next was an hour of what she calls heavy work, or fixing the bones with wires, plates and screws, so they had a stable base on which to do the delicate repair of nerves, arteries and veins. After about 40 minutes of repairing tendons, which allowed the thumb to bend, they moved on to the nerves and arteries. Some of the blood vessels, which are only 0.5 millimetres in diameter, had parts that were crushed, so those parts needed to be removed to open up blood flow. They used high-magnification microscopes and micro-equipment – forceps, dilators and sutures finer than a piece of hair – to perform the painstaking work, one of the reasons why hand surgeries take as long as they do.

Another hour was spent harvesting a vein from Burgen's arm to replace a segment of a badly damaged artery in his hand. It took one hour to set the vein, allowing blood to flow into his thumb. "I wasn't sure how it was going to go, but his thumb pinked right up," says Dr. Baltzer. Finally, they closed the skin and handaged his hand.

Staff had to check Burgen's circulation every hour in the days following the surgery to make sure his thumb was getting enough blood. If circulation was poor, they would have to return to the operating room, since fingers can only last about six to 12 hours without adequate blood supply.

Thankfully, that didn't happen, and he was released – with his thumb intact – a week later. But leaving the hospital wasn't the end of the story for Burgen, nor is it for most patients who undergo hand surgery.
Back pain breakthrough

Nearly everyone feels back pain at some point, with many experiencing chronic pain. Krembil Research Institute researchers hope that new tools and tests can alleviate, if not eliminate, the suffering.

By Wendy Glauser

ABOUT SIX YEARS AGO, Aki Tanaka felt her first pangs of back pain. It was intermittent at first, with water aerobics, Pilates and visits to physiotherapists helping to keep the pain at bay. Over the next few years, though, things worsened. By 2016, she needed a walker and had to bend forward slightly when she moved. If she stood for too long, she’d feel a stabbing pain in her back and especially down her leg. Tanaka also had to give up her job as an engineer at a non-profit organization and said goodbye to gardening, her passion. She couldn’t even help her university-aged sons settle into their new homes. “There was a lot of lying down,” she says. “I was in my sixties, but my life was like I was in my eighties. It felt like my life had been stolen from me.”

Then, in the fall of 2016, a breakthrough. She was referred to the Inter-professional Spine Assessment and Education Clinic (now called the Rapid Assessment Clinic), which was launched in 2012 by a team at UHN led by Dr. Raja Rampersaud, an orthopedic surgeon and clinician investigator at Krembil, to help pain sufferers get assessed and treated faster. After several tests, she finally received a long-awaited diagnosis: osteoarthritis (OA) and spondylolisthesis in the lower back. One of the vertebrae in Tanaka’s spine had slipped over the bone below it, which made her spine unstable and pinched her nerves.

Doctors think age and osteoarthritis caused the muscles supporting the spine to wear down, allowing the disc to slip. In 2017, Dr. Rampersaud surgically stabilized her spine, and Tanaka soon started feeling like her old self again. “By about a year, I thought, ‘Wow, this is pretty good,’” she recalls.

Although Tanaka’s situation is less common, debilitating back pain unfortunately is not. In any given year, one in three people will experience life-altering back pain. While the problem can disappear with time, exercise and posture improvement, many people can’t shake the pain no matter what they do. In a study published in early 2019, Dr. Mayilee Canizares from Dr. Rampersaud’s research team looked at data from 13,000 Canadians over a 16-year period and found that almost half of these people reported back pain to a practitioner at least once. Of those, nearly 20 per cent said their back pain continued to persist, while almost a third said their pain, whether occasional or persistent, worsened over time.

While it’s clear that back pain is a major issue among Canadians, it’s often an invisible struggle. Worse still, back pain, which can be caused by severe forms of arthritis, has received little research attention. A review done by Dr. Anthony Perruccio, a scientist at Krembil, found that at major North American public health and epidemiology conferences, less than one per cent of the tens of thousands of studies that have been presented focused on musculoskeletal issues, “even though musculoskeletal conditions, like osteoarthritis, are among the most common chronic conditions and the leading cause of disability in the population,” he says. With more than 20 per cent of Canadians living with arthritis – a number this is expected to grow – more research is critical, says Dr. Perruccio.

Fortunately, Krembil researchers are facing this growing problem head on. They’re trying to find ways of predicting the types of back pain that are likely to be persistent or worsen over time. That way, clinicians can pinpoint who would benefit the most from specialized diagnostic tools and early treatment. Drs. Perruccio and Rampersaud have studied how factors like age, sex, and severity of pain and disability relate to different patterns of back pain – whether it’s back-dominant or leg-dominant, intermittent or constant. By identifying differences between subgroups of patients with back pain, researchers hope to be able to develop more personalized treatment plans.
and quality of life,” she explains.

Passalent and colleagues found that screening patients for axial spondyloarthritis—a particularly painful type of inflammatory arthritis that affects the back—by physiotherapists with advanced training can speed up the diagnosis by three years. In her research, physiotherapists conducted a comprehensive assessment including a detailed history, a physical exam and appropriate investigations. They would then refer those they suspected of having spondyloarthritis to a rheumatologist who specializes in the disorder.

According to Passalent’s study, these physiotherapists are comparable to rheumatologists in accurately identifying patients with axial spondyloarthritis.

While early and accurate diagnosis is always important, it’s especially critical in axial spondyloarthritis, where the immune system attacks the ligaments and tendons around the spine over many years, leading to swelling that can erode the bone and cause it to grow back abnormally. As Dr. Rampersaud puts it, “We want to identify patients earlier so we can actually do something to prevent some of the chronic destructive changes that can happen in the joints and bones.”

It’s also important to treat pain early because it can snowball and affect other areas of health, including sleep and mood. Due to inactivity, patients with arthritic back pain also have a potentially higher likelihood of dying or ending up in a nursing home, says Dr. Rampersaud.

It’s been two years since Tanaka’s surgery, and her pain is no longer dictating her life. She can now laugh and talk with her 99-year-old mother at her nursing home; before her surgery, her visits were limited to daytime. “I cultivate milkweed, and it’s a favourite home for caterpillars that will become beautiful butterflies,” she says. It’s a fitting metaphor for Tanaka, who is now spreading her wings, after what seemed like an impossibly long wait.

Nestled inside Toronto Western Hospital sits one of the country’s most revolutionary rehab clinics: Altum Health.

The clinic, which is headquartered at the hospital but also has satellite clinics across Ontario, is focused on early intervention and an integrated delivery of care.

Unlike in the past, when a patient might receive care from a single practitioner, people who come to Altum Health can be seen by a variety of specialists, such as physiotherapists, chiropractors and massage therapists who work together to come up with a highly tailored treatment program for that person. That team approach helps patients receive better, and often more effective, care. “A lot of patients come for back pain assessment and find that a good course of physiotherapy can fix their problem,” explains Dr. Rajiv Gandhi, an orthopedic surgeon at Toronto Western Hospital and medical director of Altum Health.

When it comes to surgery patients, Altum Health provides “prehab” before an operation and then rehab after it, because “the stronger you are going into surgery, the faster you recover,” says Dr. Gandhi. Once it’s over, Altum’s surgeons and specialists will create a detailed recovery plan. “Patients feel a sense of confidence knowing that all of their health providers are on the same page, and they’re talking to each other and learning from each other,” he says.
It’s a young person’s problem, too

Most people don’t realize arthritis affects thousands of teenagers and young adults. Here’s why that matters and what Krembil Research Institute scientists are doing about it.

By Elizabeth Chorney-Booth

When Rivers first met Dr. Robert Inman, a rheumatologist and medical director of the Arthritis Program at University Health Network, as well as a researcher at the Krembil Research Institute, 20 years ago, she was struggling. She had started attending university, but she couldn’t climb stairs or walk more than short distances, and her medical team had a hard time finding drugs that worked without causing unacceptable side effects, such as nausea, headaches and dizziness. Rivers withdrew from her friends and found it difficult to pay attention in class because it hurt to sit. It worked without causing unacceptable side effects, such as nausea, headaches and dizziness. Rivers was referred to a rheumatologist, who diagnosed her with ankylosing spondylitis (AS), a form of arthritis that triggers inflammation of the vertebrae, causing severe pain. If it goes untreated, AS can also cause permanent damage to the spine, limiting mobility.

“My first reaction to the diagnosis was, ‘I’m not crazy,’” says Rivers, now 38. “It was something this whole time.”

When Rivers graduated from high school in Parry Sound, Ont., she had spent nearly half her life in often debilitating pain. The sporadic stiffness and aching she’d experienced as a child had grown more frequent, and Rivers could no longer ignore it or shake it off. “I felt old, but I wasn’t old,” she says. “It was very frustrating.

At the age of 18, Rivers was referred to a rheumatologist, who diagnosed her with ankylosing spondylitis (AS), a form of arthritis that triggers inflammation of the vertebrae, causing severe pain. If it goes untreated, AS can also cause permanent damage to the spine, limiting mobility.

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IMPACT ON THE YOUNG

Rivers is far from alone in her story. Dr. Nigil Haroon, co-director of the Spondylitis Program at Toronto Western Hospital and a scientist at Krembil, says that spondyloarthritides – a group of inflammatory diseases that impact the joints, along with the sites where tendons and ligaments attach to bones – affects just over one per cent of the population, or more than 300,000 Canadians, nearly all of whom get it when they are between 15 and 40.

People are usually surprised by the diagnosis. But young people suffer from a variety of arthritis types – rheumatoid arthritis has similar occurrence rates as AS, and osteoarthritis, which is typically associated with aging, can also affect the young. Dr. Haroon hopes that by educating the medical community about recent advances in diagnosing AS, especially in primary care, this may help to reduce wait times for patients to receive a diagnosis.

Some of the signs of AS include morning stiffness that improves with activity and nighttime pain that interrupts sleep. The trouble is those symptoms can also point to other, more easily explained ailments, which means physicians often don’t consider a diagnosis of AS and refer to a rheumatologist.

Another complicating factor is that AS comes with no obvious physical signs of inflammation in the back, making it harder to diagnose than, say, rheumatoid arthritis, which produces visible swelling of the joints. There are some telltale clues, however, such as inflammation in the eye or inflammation in the gastrointestinal tract, which could represent an inflammatory bowel disease such as Crohn’s disease, says Dr. Inman.

This is all related, because Crohn’s and eye inflammation are, like AS, rooted in a patient’s immune system. Rheumatologist and Krembil researcher Dr. Vinod Chandran specializes in what’s called psoriatic arthritis – a form of arthritis that is either preceded or accompanied by psoriasis, a chronic skin disease that causes itchy scales to form on the skin. Such autoimmune issues are often hereditary, though they might manifest with differing symptoms, which means primary-care physicians should delve into a patient’s family history in search of similarities.

“You could also see patients in a family where one person has psoriasis, another has Crohn’s disease and a third person has ankylosing spondylitis,” Dr. Chandran explains. “They’re all in the same family of diseases.”

Dr. Chandran wants to identify blood markers and develop a blood test to help diagnose psoriatic arthritis.

After my treatment started, I improved so much, I thought I was cured. I could even jump on the trampoline with my sister’s kids.”

Susan Rivers
Arthritis Program patient

Susan Rivers was just 10 when she experienced “growing pains.” It turned out to be a form of arthritis, which she’s learned how to manage over time.

Dr. Vinod Chandran (centre) and his team are hoping to identify a blood marker that can help diagnose psoriatic arthritis.

EARLY-ONSET ARTHRITIS

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THE IMPORTANCE OF EARLY DIAGNOSIS

Anything doctors can do to diagnose a young patient faster will impact their quality of life. According to Dr. Inman, studies show that AS patients experience back pain for an average of five years before getting a diagnosis. It’s not just five years of pain, either: AS and other forms of early-onset arthritis often cause significant fatigue, and many patients—like Rivers—experience depression as they watch their peers build careers and have families. “It certainly impacts patients’ recreational activities and has a very significant impact on work productivity,” Dr. Inman says.

Typically, AS is diagnosed with an X-ray that shows changes in a patient’s sacroiliac joint in the pelvis, but new research has shown an MRI can confirm an AS diagnosis before those changes even start happening. That’s crucial, because Dr. Inman is seeing evidence that early diagnosis can slow down the progression of the disease, which can cause significant disabilities as patients age. If left unchecked, chronic arthritis of the spine can cause the spine to fuse together, meaning patients end up with very limited mobility and a deformed posture.

Fortunately, there are treatments available. Exercise and physiotherapy, along with anti-inflammatory drugs, can help alleviate symptoms. Krembil researchers are also studying the use of biologic drugs that work to slow the progression of the disease. Dr. Haroon published a landmark study in 2018 that showed drugs that target a molecule in the blood called TNF can decrease the chance of AS progression by 50 per cent.

But there’s a short window of opportunity for achieving optimum results, says Dr. Haroon. The potential to slow progression is at its highest if treatment is started within the first few years of symptoms appearing. Dr. Haroon hopes that, one day, AS can be stopped altogether. “My lab is studying a molecule that can drive both inflammation and bone formation,” he says. “If we are successful in blocking this molecule, we hope we can directly block both spinal fusion and inflammation in AS patients.”

All of this is great news for patients like Rivers. Through a clinical trial with Dr. Inman, she was able to find a biologic drug that alleviated many of her symptoms with no significant side effects. “After my treatment started, I improved so much, I thought I was cured,” she says. “I could even jump on the trampoline with my sister’s kids. I could work more hours and make money, rather than depending on my family to help.”

There have been hiccups: In 2007, UHN’s Dr. Rod Davey performed a double hip replacement because Rivers’ joints were already damaged so much that she could feel bone grinding on bone. But she recovered quickly, thanks in part to her age, and in the intervening years she has gone from a young woman struggling with chronic disease with little hope for a pain-free future to an active person who is able to fully participate in work and family life.

Where once Rivers needed assistance to perform routine physical tasks, she now has two jobs—working in administration at the front desk of a local hospital and as a part-time waitress. Her condition hasn’t disappeared, but finding the right treatment means she can look forward to a good quality of life for years to come. “I never thought children could get arthritis,” says Rivers. “It turns out, that’s what I had this whole time.”

“Studies show that ankylosing spondylitis patients experience back pain for an average of five years before getting a diagnosis. Many experience fatigue and depression.”

Dr. Robert Inman
Medical director, UHN Arthritis Program

If we can catch arthritis earlier in patients, then ultimately, we should be able to cure it.”

Drs. Igor Jurisica and Christian Veillette hope to improve treatments and eventually stop arthritis from developing in patients. How? With data and analysis

By Bryan Borzękowski
For Drs. Igor Jurisica and Christian Veillette, AI isn’t just a buzzword.

The two have been using AI and machine learning algorithms to analyze arthritis-related information and create rich data sets, which will help doctors diagnose arthritis earlier and treat the disease more effectively.

Q: DR. JURISICA, YOU BEGAN YOUR CAREER USING PREDICTIVE ANALYTICS FOR CANCER RESEARCH. WHAT DREW YOU TO FOCUS ON ARTHRITIS?
CV: When I did my PhD, I had access to a good amount of data – many patients had a large amount of data, and the collection continues to expand in numbers and richness. It’s really incredible to have access to such a wealth of high-quality data. You don’t have as much data with cancer, and especially not longitudinal samples from the same patient.

Q: WHAT’S THE BENEFIT OF INCORPORATING AI INTO MEDICINE?
CV: One of the main reasons for incorporating AI into medicine is to create efficiencies in order to help patients get better faster. In 2007, when I joined University Health Network, I was involved in getting rid of all paper-based outcomes, such as the questionnaires people filled out in the clinic, and creating an electronic platform. This is one example of how using AI can help create an infrastructure, which allows you to capture data that you can then use to help drive decisions.

Q: AI ISN’T NEW IN MEDICINE, BUT IT’S EVOLVED. WE NOW HAVE HIGHER-RESOLUTION IMAGES, USING VISUALIZATION AND SIMULATION TO MAKE MORE ACCURATE OUTCOME PREDICTIONS. WHEN I DID MY PHD, I HAD ACCESS TO 700 PATIENT SAMPLES FROM AN IN VITRO FERTILIZATION CLINIC. AT THAT TIME, THIS WAS CONSIDERED A HUGE DATA SET FOR MACHINE LEARNING ALGORITHMS. NOW, WE HAVE HUNDREDS OF HIGHLY CHARACTERIZED PATIENT SAMPLES WITH TENS OF THOUSANDS MORE DATA POINTS, AND HUNDREDS OF CLINICAL PARAMETERS AND LAB MEASUREMENTS. IN OUR ARTHRITIS DATA INTEGRATION PORTAL (ADIP), WE HAVE MORE THAN 10,000 PATIENT SAMPLES.

Q: HOW ARE YOU USING ALL OF THAT DATA?
CV: We participate in multiple collaborations where the data and our algorithms help us understand a complex spectrum of diseases. And we use it in our own studies to look for new treatments for arthritis, such as repurposing existing drugs for other diseases and modifying lifestyle factors specific to each patient, to increase their response to the treatment. For example, we use these data to predict a novel treatment for osteoarthritis, and we expect we’ll be able to validate it using pre-clinical models and eventually translate that into the clinic.

Q: ON THE CLINICAL SIDE, THE DATA IS HELPING US WITH THE PREDICTION OF PATIENT OUTCOMES. SO, BASICALLY, WE’RE SAYING, “THIS PERSON HAS THIS PER CENT CHANCE OF HAVING A GOOD OUTCOME,” OR “THOSE ARE THE MODIFIABLE FACTORS, SUCH AS EXERCISE, SURGERY OR THERAPEUTICS, THAT WE SHOULD CHANGE IN ORDER TO IMPROVE THEIR CHANCE OF HAVING A SUCCESSFUL OUTCOME.” THAT’S WHERE WE’VE STARTED TAKING THE DATA WE’VE BEEN Capturing FROM THE BIOPAN AND FROM THE CLINIC, AND WE’RE NOW ABLE TO BRING THAT FULL CIRCLE INTO ACTUALLY MAKING AND ASSISTING WITH DECISIONS.

Q: ARE THERE ANY RISKS TO ALL OF THIS DATA COLLECTION AND ANALYSIS? HOW DO YOU MAKE SURE YOU’RE DOING IT RIGHT?
CV: If you don’t do it properly, you can come up with incorrect decisions or predictions. One thing we’ve learned is that integration across the team – having that clinical information and clinical knowledge paired with technical, analytic knowledge – is key to mitigating those risks and not generating erroneous results.

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Living with lupus

Krembil researchers have studied lupus for half a century. They’re now looking at new ways of treating, and potentially stopping, this debilitating disease.

By Anna Sharratt

Liz Attfield’s lupus nearly prevented her from having a child. Her daughter, Molly, is now eight years old.

Rheumatologist Dr. Dafna Gladman wants to help lupus patients get the treatment that works best for them.

A potentially fatal disease

Many people don’t realize how serious lupus can be. It can cause severe joint pain, skin lesions, extreme fatigue and organ damage, as well as fatal strokes and heart attacks. In fact, it is one of the leading causes of death in young women. New treatments and medications are sending the condition into remission, giving new hope to patients.

Krembil’s researchers are working to identify biological molecules in blood and urine that may predict how lupus will develop. They’re looking at ways to deliver earlier treatments.

This summer, Liz Attfield hopped into her car and drove for two hours to Muskoka, a cottage community north of Toronto. The Rolling Stones were playing a rare outdoor show, and she wasn’t going to miss it. However, attending a concert under the blazing sun and with thousands of other people isn’t easy for Attfield. She suffers from lupus erythematosus, a chronic autoimmune disease in which the body can attack the joints, skin, kidneys, blood cells, brain, heart and lungs.

Indeed, the event led to a flare-up. “I was outside all weekend – and the sun isn’t good for lupus,” she says. “I only have so much energy, and I have to be careful about expending it.”

As one of the 35,000 Canadians who have lupus – it usually strikes between the ages of 15 and 44 – Attfield is well versed in pain management. She’s been dealing with symptoms since she was 14. “I had gone trick-or-treating and I could barely walk up the stairs,” says the now 44-year-old marketing and fundraising executive.

Since she was diagnosed at age 17, Attfield has been treated by Dr. Murray Urowitz, director of the Lupus Clinic at Toronto Western Hospital and a senior scientist at the Krembil Research Institute. She has received corticosteroids and drugs to suppress her immune system, which have effectively controlled the disease.

Still, life with lupus has challenges. Attfield never thought she could have a child, as lupus patients have high-risk pregnancies. “I knew there was a chance I wouldn’t be able to keep the pregnancy,” she says. “That was the hard part.”

And she did have trouble conceiving. Fortunately, in 2011, she delivered a healthy baby girl. “She was three weeks early,” recalls Attfield. “But I had a great medical team. I am so grateful for my daughter.”

We understand much more about lupus than we did 10 years ago, but this complicated disease requires a tailored approach.

Dr. Dafna Gladman
Senior scientist, Krembil Research Institute

The disease of many faces

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Krembil’s researchers are working to identify biological molecules in blood and urine that may predict how lupus will develop. They’re looking at ways to deliver earlier treatments to help reduce irreversible organ damage, and they’re gathering information related to the long-term health complications, such as premature cardiovascular disease, osteoporosis, bone damage and cognitive impairment.

However, lupus presents differently in every patient. Examining a patient’s genetic, environmental and lifestyle factors can help predict which organs could be impacted and how responsive the disease may be to different treatments. “We understand much more about lupus than we did 10 years ago,” says Dr. Dafna Gladman, a rheumatologist and senior scientist at Krembil. “But this complicated disease requires a tailored approach.”

Dr. Dafna Gladman wants to help lupus patients get the treatment that works best for them.
function could possibly halt the disease's progression. Dr. Wilner's studies into the immune basis of lupus also extend into other systemic autoimmune rheumatic diseases, such as scleroderma and Sjögren's syndrome.

Dr. Sindhu Johnson is director of UHN's scleroderma clinic. Dr. Johnson is also playing a leadership role globally in defining criteria that enable doctors to accurately classify such rheumatic diseases.

A unique multidisciplinary Sjögren's syndrome clinic has been established by Dr. Arthur Bookman. This clinic provides one-stop care for this autoimmune disease, incorporating experts from rheumatology, dentistry, ENT and ophthalmology.

MORE DATA, BETTER OUTCOMES

Dr. Zahi Touma, a clinician investigator with Krembil, has enrolled more than 300 lupus patients into a screening program that uses computer questionnaires and performance-based tests to detect cognitive changes, such as a decline in memory and thinking speed, attention and planning abilities. Another platform, PROMIS (Patient-Reported Outcomes Measurement Information System), will help doctors assess the different aspects of a patient's quality of life, explains Dr. Touma.

This data has led to many advancements in lupus research over the past 20 years, and will help doctors better understand how the disease progresses and how different treatments might work on specific patients. This can allow for a more personalized treatment regimen, adds Dr. Urowitz.

There's also been significant progress in treating pregnant lupus patients, like Attfield. Researchers have found that patients have the best chance for success when they're clinically inactive before getting pregnant, if they're put on the right medications and if they're monitored regularly. The Lupus Clinic has so far helped more than 450 patients have healthy babies. "This is why we do what we do," says Dr. Urowitz.

Attfield is happy that her lupus hasn’t defined her life. “I’ve had a successful career, and I have my daughter,” she says. “I think I’ve done a pretty good job of having a normal life.”

FOR MORE THAN FOUR DECADES, University Health Network’s Arthritis Program has been a global leader in arthritis-related research and treatments. Naturally, it’s taken years of hard work by numerous medical and scientific teams working together with patients and volunteers to get to this point. “It has involved many champions over the years,” says Dr. Mohit Kapoor, research director of the Arthritis Program.

The program has taken a multidisciplinary approach to research, education and clinical care, with a focus on orthopedics, rheumatology, hand and osteoporosis. This “complete approach,” as Dr. Kapoor puts it, has been a recipe for success. “One day we will stop arthritis in its tracks.”

The Campaign to Cure Arthritis, started in 2011, has been instrumental in fast-tracking discoveries and accelerating their translation to improve care for patients. Philanthropy has played a huge role in the success of the Arthritis Program. Every full-time doctor in the program has pledged a donation to the Campaign to Cure arthritis.

Their dedication has inspired hundreds of people living with arthritis and their loved ones to donate generously to the program, too. “These donations help us to continue our work as world leaders in arthritis research, education and patient care,” says Dr. Kapoor. “We are so grateful.”

Dr. Murray Urowitz leads the Lupus Clinic at Toronto Western Hospital.

Dr. Joel Witner hopes that by stopping specific proteins from disrupting immune function, she can prevent lupus' onset.

5 million
People worldwide who have a form of lupus
(Lupus Foundation of America)