

# Chez nous

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## The sky is not the limit

Team of astronauts help researchers study chronic pain and sleep

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# The sky is not the limit

By Maureen McCarthy

**W**hen Dr. Pablo Ingelmo, Director of the Edwards Family Interdisciplinary Centre for Complex Pain at the Montreal Children's Hospital (MCH), was asked to take part in a new research project, he knew immediately it was the opportunity of a lifetime. The reason? The research would be part of an upcoming space mission.

"The knowledge we have about pain in space and the relationship between microgravity and pain is so minimal that it's almost non-existent," he says.

It was easy to recruit his colleagues for the study. "All of them are so knowledgeable about their specific areas of pain research but this opportu-

► Above: Mark Pathy training for his upcoming Axiom Space Ax-1 mission to the International Space Station.

nity is so different that everyone quickly agreed to take part in it.”

Like Dr. Ingelmo and his colleagues, Dr. Evelyn Constantin and her team are also conducting research as part of the upcoming space mission. Dr. Constantin has spent her career studying sleep in children, and as a Senior Clinician Scientist at the Research Institute of the McGill University Health Centre (RI-MUHC) and Director of Pediatric Sleep Medicine at the MCH, she has developed a unique research program with inter-professional collaborations to explore sleep issues in children with chronic conditions, including neurodevelopmental disabilities and metabolic conditions. The space mission is providing her the opportunity to study sleep in a completely new environment.

#### **THE AX-1 MISSION: READY FOR TAKE-OFF**

Montrealer Mark Pathy, a long-time supporter of The Children’s Foundation and member of its Board of Directors and its Unexpected Ways to Heal campaign cabinet, is part of a four-person team taking part in Ax-1, a space mission organized by Houston-based Axiom Space. It will be the first fully private mission to visit the International Space Station (ISS).

► Dr. Evelyn Constantin in one of the MCH Pediatric Sleep Medicine polysomnography rooms, where children can undergo overnight sleep studies to record their sleeping and breathing patterns.

The four astronauts have been training at NASA’s Johnson Space Center in Houston and will conduct approximately 25 experiments while onboard the ISS to gather critical data in human research, life and physical sciences, technology demonstrations, and Earth observation, with the goal of expanding the applicability of research into microgravity, the condition in which people or objects appear to be weightless.

#### **THE PAIN MANAGEMENT RESEARCH TEAM**

The change in gravity in space affects the human body in ways that aren’t fully understood yet. To date, only two studies have been conducted on pain experienced by astronauts specifically,

and both showed that microgravity in space can heighten the pain perception in 50 per cent of astronauts.

“In order to understand why 50 per cent of astronauts experience pain, we must first understand why the other 50 per cent don’t,” explains Dr. Ingelmo. “We are not looking just for the abnormalities in people who have pain, but we want to understand why some people, even after an insult like microgravity, get better. Our hope is that the information we collect will advance our research to help people here on earth.”

For the pain management component of Ax-1’s research, Dr. Ingelmo assembled a team of experts including **continued >**





Dr. Luda Diatchenko, Dr. Jean Ouellet, Svetlana Komarova, PhD, Lisbet Haglund, PhD, and Maryse Fortin, PhD, whose affiliations include the MCH, Shriners Hospital for Children, McGill University's Faculty of Medicine and Health Sciences, the Alan Edwards Centre for Research on Pain, the RI-MUHC, and Concordia University.

Marie Vigouroux, Clinical Research Coordinator in the Chronic Pain Service at the MCH, Eric Zimmerman, a psychology student at McGill University, and Kacper Niburski, an anesthesia resident at University of British Columbia, round out the team.

#### **APPROACHING THE QUESTIONS FROM MULTIPLE PERSPECTIVES**

The pain researchers are trying to answer three main questions, broken down into six different experiments: Can a short trip to space change pain sensation? Can a short trip to space influence genomic processes of bone physiology and inflammation in response to pain? How does a short trip to space affect bones, muscles and ligaments?

The Ax-1 astronauts will go through a series of tests before and after the space flight, which include questionnaires, blood tests, MRIs, and measuring their pain thresholds. The researchers will then compare the results from before the space flight to right after the flight, then three months later to determine if there are any changes to the astronauts' bodies.

The researchers assembled by Dr. Ingelmo have expertise in a range of subjects including spinal pain, genetic mechanisms of pain, bone cell and tissue pain,



► Dr. Pablo Ingelmo

intervertebral disc degeneration and pain, and musculoskeletal spine imaging and rehabilitation.

"The novelty of our project is that we're trying to answer the questions from different perspectives in a single project so in reality, it's six studies in one," says Dr. Ingelmo. "Because we will share the data in this study, we are going to get answers faster."

#### **THE CONNECTION BETWEEN POOR SLEEP AND POOR HEALTH**

Dr. Constantin and her research team are leading another experiment being

conducted on Ax-1 related to sleep in space and the microbiome. The human gut microbiome comprises trillions of microorganisms, and the early childhood years are critical to establishing a healthy microbiome. Poor sleep is associated with abnormal gut microbiome, and is linked to a number of diseases, including obesity and asthma, and increased cardiometabolic risk, such as experiencing a cardiovascular event or developing diabetes.

The Ax-1 astronauts are helping Dr. Constantin and her team by providing data from the space mission.

"We are trying to understand if the unique environment of the space mission can affect the astronaut's microbiome, and if the space environment creates any association between sleep, cardiometabolic risk factors and their microbiome," says Dr. Constantin. "And since space travel can lead to jetlag, we are also studying the astronauts' sleep quality and quantity to describe the changes in sleep and circadian rhythm."

All these factors will be studied before, during and after the space flight.

Research has shown that the quality and quantity of astronauts' sleep are impacted during spaceflight, however the effects of a space shuttle environment and microgravity on sleep, microbiome and cardiometabolic factors have not yet been determined, and few studies have assessed sleep in space using

objective sleep measures. This research represents the first study in space travel to assess the associations with sleep and microbiome at the same time, using objective medical devices to measure sleep.

### **CIRCADIAN RHYTHM AND SOCIAL JETLAG**

One of Dr. Constantin's current research projects involves assessing sleep, diet and the microbiome in children, the first study of its kind in pediatrics.

"We are looking at the associations between sleep and glucose [sugar] intake, and measuring the child's microbiome via stool samples," explains Dr. Constantin. "We're doing nutritional intakes with the children, assessing the quality and quantity of their sleep and looking at any associations with their microbiome."

Another of Dr. Constantin's studies is looking at preschool-aged children's circadian rhythm, which is the body's internal sleep/wake clock, and a newer concept called social jetlag, the discrepancy between a child's sleep patterns on weekdays compared to weekends. Dr. Constantin hopes to gather information from the space mission on social jetlag.

"I'm interested to know if the changes in sleep patterns and environment between earth and space can also create this social jetlag entity, which will help us to gain further understanding about social jetlag and circadian rhythms," she says.

For the space mission, each of the astronauts will keep a sleep diary, answer sleep-related questionnaires, [continued >](#)



► From left to right: Reza Sharif-Naeini, PhD, Director, Alan Edwards Centre for Pain Research, McGill University, Lisbet Haglund, PhD, Associate Professor of Surgery, McGill University, Pablo Ingelmo, MD, Anesthesiologist and Director, The Edwards Family Interdisciplinary Centre for Complex Pain at the Montreal Children's Hospital, and Svetlana Komarova, PhD, Associate Professor, Faculty of Dentistry, McGill University.

and wear an actigraph wristband, which measures sleep: it records motion when the person is awake, and non-motion when they're asleep.

"By wearing the actigraph a few weeks before the mission, then during and after, we hope to get a sense of their usual sleep habits, duration and quality to see if the space environment changes that in any way," says Dr. Constantin.

The astronauts will also have blood work done at various intervals and their cardiometabolic risk factors will be determined through measuring body mass index, waist circumference, blood pressure, heart rate, and oxygen saturation among others. The research study will also look at stool microbiome diversity.

#### **A FULL CIRCLE: FROM CLINICAL PEDIATRIC WORK TO RESEARCH AND BACK**

Dr. Ingelmo says his co-investigators regularly share their findings with each other and the important clinical work being done in the Edwards Family Interdisciplinary Centre for Complex Pain at the MCH often incorporates research produced at the RI-MUHC and the Alan Edwards Centre for Research on Pain, which is world-renowned.

"What makes this project so interesting is that a pediatric hospital is leading research that we hope will lead to the development of new technology and treatments not just for children but for adults as well."

Dr. Ingelmo says Mr. Pathy and his fellow astronauts are doing a great service by taking part in the pain research and sleep research. Dr. Ingelmo and his team plan to incorporate the information collected from the astronauts into animal models, which may then lead to applications in humans and eventually new treatments.

"They're giving us their time before, during, and after the space mission to help us produce data to create new models of analysis for helping people with complex pain. We're really grateful for their commitment to our study and in particular to the Montreal Children's Hospital."

Dr. Constantin is enthusiastic about what lies ahead. As just one example, she cites the microbiome data they will collect.

"I think any new research in microbiome is novel," she says. "We're working and collaborating on this with the McGill M14 Microbiome Research Centre, which has done some space research, but a prospective study like this, which looks at information before, during and after the space mission, is unique."

"What we learn about the astronauts' microbiome in space, in such a structured environment, will help us understand more about the links between a child's microbiome and their sleep and overall health. The more we know about the microbiome, whether on earth or in space—it's just an interesting new concept to assess the possibility of the microbiome being a snapshot of your cardiometabolic risk."

Dr. Constantin's co-investigators on the study are Drs. Patricia Li, Nicholas Brereton, Emmanuel Gonzalez, Ken Dewar, and Elise Mok, whose affiliations include the MCH, the Child Health and Human Development Program at the RI-MUHC, the Department of Biology at Université de Montréal, the Canadian Centre for Computational Genomics (C3G) based at McGill University, and the Department of Human Genetics at McGill University. In addition, Marie Vigouroux, Clinical Research Coordinator on this study, has been instrumental in helping move the project forward. ❁



► The astronauts will wear actigraph wristbands before, during and after the space mission to measure their sleep habits, duration and quality.





## Ventilation: when a different idea helps to heal

By Christine Bouthillier

*Sometimes the best results come from thinking outside the box. Neonatologists Wissam Shalish and Guilherme Sant'Anna proved it when they used a type of ventilation called NIV-NAVA (non-invasive neurally adjusted ventilatory assist) in a way that had never been done before in Quebec, sparing their two-month-old patient from undergoing open-heart surgery.*

**S**ia Terhzaz Senica was born prematurely at 25 weeks on March 18, 2021. She had to be resuscitated at delivery and was suffering from respiratory problems for which she needed a breathing tube. She developed a pneumothorax, a collapsed airway, blood in her lungs due to their immaturity and had to be quickly transferred to the Neonatal Intensive Care Unit at the Montreal Children's Hospital (MCH), where she was intubated.

Intubation is typically not recommended for too long, as it can damage the vocal cords and irritate the airway.

"I was told that Sia might not be able to talk and that she might develop oral aversion, the feeling of disgust when something is put in your mouth, like food," says her mother, Tanja Senica.

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► Above: Sia's first family picture with her parents, Tanja Senica and Samih Terhzaz, at six days of age. It was her first time being held.

After each attempt to extubate, Sia would immediately show signs of significant breathing difficulties, which prompted the need to reintubate her.

"When this happens, you suspect that something is blocking the trachea," explains Dr. Shalish.

Dr. Sam Daniel, Director of the Otolaryngology - Head and Neck Surgery Department at the MCH, performed a bronchoscopy, a procedure in which a camera is inserted down the throat to the trachea so that doctors can look into the lungs and airways.

Dr. Daniel discovered that Sia had severe tracheomalacia; when she was upset, her trachea collapsed, preventing her from breathing, which upset her even more... A vicious circle that needed to be stopped.

### INNOVATION TO THE RESCUE

The status quo was not an option. The family was provided with two choices: leave Sia on a breathing tube even though she was uncomfortable, which also meant more scarring, or perform open-heart surgery to move her aorta so it would not compress her trachea.

Still eager to avoid those avenues, Drs. Shalish and Sant'Anna decided to discuss Sia's condition with a colleague at Columbia University, in New York, with extensive experience in difficult respiratory cases. They came up with a third option: using the NIV-NAVA.

This device pushes air through the child's nose in a way that is perfectly synchronized to their breathing and needs by using a catheter with a sensor that

detects the movements of the diaphragm. Whenever Sia's trachea collapsed and she became agitated, the machine responded immediately by providing additional pressure to keep the trachea open, thereby ending the vicious circle.

The NIV-NAVA is frequently used on infants, but had not been traditionally applied for cases of tracheomalacia. For Sia, the positive effects of the NIV-NAVA were evident quite quickly.

"She was miserable on other ventilation modes. With the NIV-NAVA she was much more comfortable. When she became upset, she calmed down faster,

and her oxygen levels were better," indicates Dr. Shalish.

The device didn't cure Sia, but it bought her the time she needed to heal. She stayed on the NIV-NAVA for five weeks. She was then placed on oxygen on July 3, 2021.

"That was my expected delivery date. I was told I could try to breastfeed her. Everyone was skeptical, but she latched on like she had always done that. Everyone cried that day," says Tanja.

### GREAT PROGRESS

Sia was finally able to return home with oxygen after four and a half months in



► Sia is now 7 months old corrected age and almost a year old actual age.



the hospital. During that time, her trachea grew and the problem resolved itself. Three months later, she no longer needed oxygen. She continues to do physical exercises with a physiotherapist and an osteopath.

Sia seems to be developing normally. She has started to eat solid food and according to her parents, she has strong vocal cords!

"We will be forever grateful to Dr. Shalish and Dr. Sant'Anna for trying something different and for believing in our daughter," Tanja concludes. ✨



► Sia is now well and clearly happy!

### **MOM IS HOSPITALIZED TOO**

Tanja Senica's postpartum period was not a restful one, to say the least. While her daughter Sia had to be admitted to the MCH's Neonatal Intensive Care Unit (NICU), Tanja herself was also dealing with health issues.

Suffering from several cardiac dysfunctions since birth, the young woman gave birth in the Intensive Care Unit at the Royal Victoria Hospital. As a result, she had to stay on ECMO (extracorporeal membrane oxygenation) as a precaution after the birth of her daughter. Tanja was not able to visit her baby for the first 48 hours.

"Was I afraid for my child? That's an understatement," the mother emphasizes.

### **BACK AND FORTH**

Eight days after giving birth, Tanja was discharged. Back home, however, she was having trouble breathing, sleeping and eating, thinking it was typical for a C-section recovery. She returned to the emergency room five days later to find out that she had a stomach ulcer from the naproxen painkillers. She underwent an emergency procedure.

Tanja also developed a rupture of the uterine C-section incision which became severely infected and she had to take antibiotics. She got ascites, which is an accumulation of fluid in the abdomen. As a result, the pacemaker she had had under her ribs since she was five years old, which was no longer functioning, had to be closely monitored for fear of bacteria attaching to it; it was later removed and replaced with a new one. The young woman spent the entire month of April 2021 in the hospital.

"Except when I was too weak or had just had a procedure, I went to see Sia. I would put her on me as much as I could, but it was difficult because of my own IV lines," she says.

In May 2021, Tanja's ascites had still not resolved and she had to be hospitalized again. She finally had open-heart surgery in June. She was discharged from the hospital 10 days later... to move to the NICU with her daughter.

Thankfully, the whole ordeal is now over and the family is quietly recovering at home, from both physical and emotional challenges. ✨



# Heart malformations: a message to give hope

By Christine Bouthillier

**B**orn with a congenital heart defect, twins Camille and Alexie Poirier lived the first months of their young lives on a roller coaster, undergoing several interventions. Now over a year old, they are doing well. During Heart Month in February, their parents and doctors are sharing their story to encourage families who are going through the same challenges.

Camille and Alexie were born at the Anna-Laberge Hospital in Châteauguay. Camille needed assistance breathing and was transferred to the

Montreal Children's Hospital (MCH) on the first day for investigation of a heart murmur.

On arrival, Dr. Adrian Dancea, Head of the MCH Cardiology Division, immediately identified a congenital heart malformation in Camille called pulmonary atresia, a blockage in the valve that separates the heart and the lungs.

"Since they were identical twins, I thought Alexie might have a defect as well, so I requested a transfer," he says.

► Above: Camille and Alexie Poirier



It turned out to be a good idea, because Alexie happened to have pulmonary stenosis, a blockage similar to her sister's, but less severe.

"The diagnosis was a big shock, but we were very well looked after," testifies Sonia Nadeau, the twins' mother. "The MCH is like the National Hockey League of health care... I have never seen a hospital with staff so well equipped to respond to patients. I really liked the multidisciplinary aspect of care."

"We felt we were in good hands. For that, we will be eternally grateful to the team," adds Jean-Philippe Poirier, the girls' father.

#### CHALLENGES TO OVERCOME

At just one month old, Alexie had to undergo a cardiac catheterization – a procedure in which a thin, flexible tube is guided through a blood vessel to the heart – to open the valve with a balloon catheter. She was discharged after a month in the hospital.

For Camille, it was more complicated. A first catheterization showed that her condition was not suitable to treatment by catheter. Dr. Pierre-Luc Bernier, a pediatric cardiac surgeon at the MCH, had to operate on her at one month of age to open the valve and insert a shunt, which creates an additional passageway that helps blood flow to the lungs.

A few months later, Camille went through a second heart catheterization to see if she still needed the shunt. It turned out that the blood flow to the lungs no longer depended on it. During a third procedure, days later, Dr. Dancea blocked it with a small metal plug.

"If we leave it open, the lungs can become congested and the heart is under greater stress," says Dr. Bernier.

It was at seven months of age that the baby was finally able to go home.

"With COVID-19, the sisters did not see each other often and could not be near each other. The first thing Alexie did when Camille came home was pull her hair!" recalls Sonia, laughing. "Now they sit across from each other and talk, but I don't know what they say to each other..."

#### A LIFETIME OF FOLLOW-UP

Despite spending the first seven months of her life in a hospital bed, Camille has almost caught up on the developmental delays she experienced. However, the twins will need a lifetime of medical follow-up.

"This is always the case with such significant heart defects. Camille will need to be seen every six months, while Alexie will come in once a year," explains Dr. Dancea.

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► Camille and Alexie Poirier with their parents, Jean-Philippe Poirier and Sonia Nadeau, during a follow-up visit at the MCH.

## By the numbers

- In Canada, 1% of children are born with congenital heart defects.
- About 40% of these defects will be treatable without intervention.
- In twins, the genetic component increases the risk that both will be affected by a malformation.

Sources: *Fondation En cœur* and Montreal Children's Hospital.

► The Nadeau-Poirier family, with Drs. Adrian Dancea (left) and Pierre-Luc Bernier (right).

It's not impossible that Camille will need another operation, but nothing is planned at this time, adds Dr. Bernier.

"I hope that parents who are going through the same thing will read our story and see that there is hope. We've come through this and have reached some normalcy," says Jean-Philippe.

Both Dr. Dancea and Dr. Bernier thanked the entire cardiology team and the parents for their collaboration.

"We know it's not easy, especially with another child at home, but Sonia and Jean-Philippe have always been

there. Such an alliance relationship is very much appreciated," mentions Dr. Bernier.

"We would like to say, with all our heart, thank you to all the staff from far and near who took care of our daughters, even today. We would also like to thank our moms who, as soon as they were allowed, came to Camille's bedside, as well as our families who were with us in thought. Finally, we will be eternally grateful to nurse Monique Paquette, who took care of Camille like her own child. She went above and beyond the call of duty and will always be an important person to us," concludes Sonia. ❄



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