

Hypertension During Pregnancy May Affect Cardiovascular Health

Women who experience hypertension during pregnancy face an increased risk of heart disease and hypertension later in life, according to a new study led by **Dr. Kristian Filion** of the Centre for Clinical Epidemiology at the LDI.

Among 146,748 women with a first pregnancy and a follow-up of approximately four-and-a-half years, 997 were diagnosed with cardiovascular disease and 6,812 developed hypertension. Compared with women without hypertension during pregnancy, those with hypertension during pregnancy had a 2.2-times higher risk of developing cardiovascular disease and a 5.6-times higher risk of developing hypertension after pregnancy. Subsequent pregnancies did not appear to influence these associations.

“This study highlights the need for long-term follow-up of women with a history of hypertension during pregnancy to provide early management of risk factors for cardiovascular disease,” said Sonia Grandi, PhD candidate at McGill University and lead author of the study, published in [Paediatric & Perinatal Epidemiology](#).



Frailty and the risk of cardiac surgery for elderly patients

As a cardiologist who sees many elderly patients, **Dr. Jonathan Afilalo** has a practical concern for frail individuals suffering from heart disease. He has undertaken extensive research into how frailty impacts surgical outcomes, and how best to measure frailty in order to arrive at the best treatment plan for his patients.

His most recent paper on the subject, published in the [Journal of the American College of Cardiology \(JACC\)](#), looked at seven different frailty scales to predict how elderly patients will recover from transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR) procedures.

A clinical study of more than 1,000 patients, with a median age of 82, revealed that frailty is a major risk factor for death and disability following both procedures. The research, known as the FRAILTY-AVR Study, was undertaken at fourteen centres and led from the Jewish General Hospital.

“Because there is no clear consensus among clinicians on how to objectively evaluate frailty, we compared different measures of frailty,” Dr. Afilalo explains. “The scale that we developed, called the Essential Frailty Toolset (EFT), proved to be the strongest predictor of outcomes.”

The EFT consists of a four-item scale that measures:

- Lower-extremity weakness
- Cognitive impairment
- Anemia (hemoglobin)
- Serum albumin.

“We use these measures to help us tailor therapy for the individual patient to enhance their recovery after the acute procedure and for quality of life one or two years afterward,” he said. “The vast majority of patients survive these procedures, but begin to decline over the ensuing months, largely because of their frailty and deconditioning. Very frail patients may be better suited to less invasive treatment approaches, or may require more pre- and post-operative rehabilitation and nutritional supplementation. A multi-disciplinary approach is vital to optimize patient care, including a concerted effort by physiotherapists, nutritionists, geriatricians, cardiologists and cardiac surgeons.”

Francois Mercier recruited for research in blood stem cells and oncology

Dr. Francois Mercier has joined the Division of Hematology at the JGH as an attending physician and the LDI as a principal investigator in blood cancers.

He spent the past seven years on a research fellowship at Harvard University and Massachusetts General Hospital where he worked on understanding how blood stem cells regenerate and mutate to form leukemias.

Dr. Mercier is pursuing a clinical study to employ single cell RNA sequencing on cell samples taken from patients with acute myeloid leukemia (AML) in order to distinguish between the cells of those patients who respond favourably to certain drug therapies as opposed to those who do not. This work is supported by a grant from the Leukemia and Lymphoma Society of Canada.

“With DNA sequencing, we know that AML involves fewer genetic mutations, by several orders of magnitude, than other cancers,” he said. “Despite identifying the mutations, our treatment plans have not changed drastically in many years, so this is a fertile field for research”



As well, he is employing the revolutionary gene editing technology CRISPR to see whether splicing genes associated with AML can eliminate the disease.

Leukemia frequently recurs after going into remission. The suspicion is that a reservoir of the cancer remains at undetectable levels even after it appears to have been eliminated. Evidence suggests that leukemic cells are, like blood cells, a kind of stem cell that is capable of regenerating itself. In order to eradicate the disease entirely, the stem cell that is the progenitor for the cancer must be eliminated. Exploring how to accomplish this task is among Dr. Mercier’s lines of inquiry.

New insight on drug resistance in lymphoma

Peroxisomes are organelles within cells whose major function is to break down long chains of fatty acids. Once thought to be a vestigial organelle, their absence or mutation is associated with rare congenital pediatric neurological disorders, including Zellweger syndrome, that result in early death. **Dr. Wilson Miller’s** lab has discovered that peroxisomes are over-expressed in lymphomas that have developed resistance to the histone deacetylase inhibitor (HDACi) Vorinostat, which is used to treat persistent or relapsed disease. These findings were recently published in [Cell Death & Differentiation](#).

“Peroxisomes are metabolic organelles, which are under-studied in cancer. Peroxisomes are known to play a role in reactive oxygen species (ROS) modulation, but their role in drug sensitivity and resistance in cancer has never been examined,” said Dr. Sonia del Rincon, Project Director at the LDI and co-corresponding author on the paper. “We observed that peroxisomes are enriched in cells that have become resistant to Vorinostat. Michael Dahabieh, a PhD candidate in our lab, discovered that knocking down peroxisomes sensitized lymphoma cells to the cytotoxic effects of Vorinostat, but also overcame resistance to the drug.”

This discovery is being applied to melanoma and breast cancer to determine how broad the role of peroxisomes is in resistance to cancer therapies, and its potential as an approach to circumventing resistance.

Suppression of the expression of peroxisomes may enhance sensitivity to anti-cancer treatments, whereas in pediatric peroxisomal disease, the therapeutic imperative is to increase their presence. “Our experiments did not cause a complete knock-out of peroxisomes. Although clinical studies have not yet been started, we hypothesize that potential loss of peroxisome function will not negatively impact the adult immune system, which is where peroxisomes play an ongoing role.” Dr. del Rincon adds, “It is agreed that the discovery that peroxisomes play a role in malignant cells is a very exciting and uncharted area for study.”

Dr. Amel Hamdi, a postdoctoral fellow in Dr. Prem Ponka’s lab, has been awarded a Postdoctoral Fellowship Award by the Faculty of Medicine at McGill for the 2017-18 academic year.



Advocacy for Science

A group of scientists from the Lady Davis Institute, McGill University and the University of Montreal participated in a meeting with the federal Minister of Science, the Hon. Kirsty Duncan, in order to express support for stable and sufficient funding for scientific research.

“Our concern is that declining funding will not only compromise our current efforts to fulfill Canada’s potential in biomedical research, but has a cascading effect,” deplored **Dr. Volker Blank**, a cancer researcher at the LDI who initiated and organized the meeting. “What ground we lose today will affect coming generations of scientists. Our institutions will hire fewer trainees, our best researchers will have to seek opportunities elsewhere and, consequently, we will produce less innovative and impactful results.”

Historically, Canada has been an international leader in health sciences, making major contributions in cancer research, stem cell biology, brain function, and infectious diseases – all areas of interest at the LDI. Canada stands to provide better health outcomes for its population by growing its scientific resources and ensuring that ongoing research is funded without interruption, which can be disastrous in forcing the abandonment of projects that take years to bring to fruition.

Dr. Blank was inspired to seek a meeting with the Minister upon discovering that several other

researchers happen to live in the federal riding of Brossard-Saint-Lambert. He reached out to his local Member of Parliament, Alexandra Mendes, who, after a first meeting, set up the encounter with Minister Duncan, which also involved other researchers from the LDI, including principal investigator Dr. Koren Mann, and trainees Laura Hulea, Michael Dahabieh and Jesse Hudson.

“I was pleased to see that the Minister was very interested in what we had to say and was very receptive to our presentation,” said Dr. Blank. “She appreciated that research is at a critical juncture at which we must decide whether we continue to be a globally competitive knowledge-driven country with superior scientific training and output, or run the risk of decline.”

The uncertainties of the funding environment are of concern to all Canadian scientists. One of the motivations for meeting with the Minister was to establish a dialogue in a forum wherein scientists would be heard in the political arena. Dr. Blank came away satisfied that the government appreciates the need to support research.

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Recipients of the 2017 LDI / TD Bank Scholarship:

- Emma Fowler, a Master's candidate in Dr. Mark Basik's lab, working on biomarkers of chemoresistance in breast cancer;
- Yi Lian, a PhD candidate in Dr. Laurent Azoulay's group, studying a drug interaction study between proton pump inhibitors and androgen deprivation therapy in prostate cancer;
- Sahil Sharma, a PhD candidate in Dr. Marc Fabian's lab, researching a novel neuronal translational repressor; and
- Kaiqiong Zhao, a PhD candidate in Dr. Celia Greenwood's group, developing methods for analysis of DNA methylation data.

The scholarship supports and extends the research profile of the student and the research capabilities of the supervisor. The LDI is grateful to TD Bank for supporting the JGH Foundation's capital campaign and our mission to advance health research.

Dr. Volker Blank has been promoted to full Professor in the Department of Medicine at McGill University.

Danielle Rice, a PhD candidate in clinical psychiatry being supervised by Dr. Brett Thombs, has been awarded the prestigious **Vanier Canada Graduate Scholarship**. Her project is "Making accurate depression screening and assessment a reality for Canadians: using individual patient data meta-analysis to personalize risk estimates."

"The aim is to ensure that people with depression are accurately identified and provided access to the treatment they need," she said. "There is a lot of mixed evidence on the effectiveness of depression screening, so it's important to have an approach that will allow us to identify those who stand to benefit most from screening protocols. Using large data samples, we hope to identify the characteristics of people who are most likely to experience depression."

Targeting dementia with electrical stimulation

Dr. Howard Chertkow, Scientific Director of the Canadian Consortium for Neurodegeneration in Aging (CCNA) and Director of the Bloomfield Centre for Research in Aging at the LDI, and his team have published the results of a "proof of principal" pilot study of transcranial direct current stimulation (tDCS) therapy in patients with dementia in [Alzheimer's & Dementia: Translational Research & Clinical Interventions](#).

"Treatment options for dementia are limited, as is the effectiveness and durability of the few options we have available," he said. "Thus far, pharmaceuticals that target chemical elements of the brain have proven disappointing. We are looking at electro-magnetic stimulation to target the illness through the brain's electrical impulses."

Ten patients with two forms of dementia: anomomic Alzheimer's disease – a variation wherein loss of language skills, as opposed to memory, is the primary symptom – or fronto-temporal dementia – where tau proteins affect the language centres of the brain, were targeted in this study, which was sufficiently promising to warrant further study. Using a double-blind cross-over design, patients were tested on their picture naming capacity over a series of ten thirty-minute sessions of tDCS or sham stimulation. When subjects received the real stimulation, they showed noticeable improvement that lasted at least two weeks (and up to two months).

"The tDCS is able to lower the threshold at which neurons function," explains Dr. Carlos Roncero, a post-doctoral fellow working with Dr. Chertkow at the LDI, "thereby enabling more neurons to fire more easily, which represents increased brain function."

Not only are the patients' picture naming abilities measurably improved, but family members report positive changes in behaviour that coincide with the treatment.

"This trial is the first of any therapy attempted to show demonstrable improvements for patients with fronto-temporal dementia," said Dr. Chertkow. "We are now working to specify the parameters of the therapy, carry out larger clinical trials, and to determine whether it is robust enough to be offered in a manner comparable to dialysis, where patients receive tDCS some number of times per month."

While not envisioned as a cure, if it could improve a variety of important symptoms it may enable families to keep loved ones at home longer, which would improve the patient's quality of life while lessening the burden on the health care system.

Upcoming Grants and Awards Deadlines

September 12, 2017	CIHR Foundation Operating Grant 2017-18 Stage 1
September 15, 2017	CIHR Project Grant Fall 2017 Full Application
September 15, 2017	CCSRI Impact Grants Full Application
October 10, 2017	FRQS Chercheurs-bourisiers/cliniciens Junior 1, 2, & Senior Full Application
October 10, 2017	FRQS Chercheurs-boursiers de mérite Full Application
November 1, 2017	NSERC Discovery Grant Full Application
March 1, 2018	FRQS Étudiants-chercheurs étoiles

SAVE THE DATE : Thursday November 2, 2017 8:00 am—5:00 pm

Inaugural annual symposium in memory of Dr Mark Wainberg (1945-2017)

The challenge of emerging and complex infectious diseases: honouring
a champion

Featuring:

Dre Françoise Barré-Sinoussi, Nobel Laureate Institut Pasteur, Paris, France

« HIV translational science: from the first ARVs to the hope of a cure »

Dr Gerald Friedland, Yale University

« Confronting HIV and TB from the Bronx, NY to Tugela Ferry KwaZuluNatal, South Africa and Beyond »

Dr Myron Cohen, University of North Carolina Chapel Hill

« Treatment as prevention, lessons from HIV »

Ron Rosenes

« Mark Wainberg as a passionate HIV community advocate and ally »

Dre Marina Klein, McGill University Health Centre

« Towards Elimination of Hepatitis C Virus in HIV Infected Populations »

Dre Catherine Hankins, McGill University Health Centre

« HIV science to action: knowledge translation for lasting impact »

Dr Matthias Götte, University of Alberta

« Management of newly emerging infections- Lessons learned from HIV »

Location: JGH Block Amphitheatre, 3755 Cote-Ste-Catherine

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