



October 2019

## Chair's Column

### Highlights:

#### Introducing Our Researchers

*Dr. John Byrne  
Dr. Charles de Mestral  
Drs. Matthew Doyle,  
Thomas Forbes, Cristina  
Amon  
Dr. Kathryn Howe  
Dr. Graham Roche-Nagle  
Dr. Mohammad Qadura*

*The 2020  
K. Wayne Johnston  
Lecturer will be  
Dr. Gilbert Upchurch  
from the University of  
Florida*

I'd like to welcome you to the 2019/20 academic year and the return of our newsletter ... Toronto Pulse!

Last year was busy and productive and this year is shaping up to be even more so. 2018/19 saw the continuation of our busy Visiting Professor Program and culminated in our Graduation & Research Day. The highlight of Research Day was our 8<sup>th</sup> Annual K. Wayne Johnston Lecturer, Professor A. Ross Naylor from Leicester, U.K.

We also had an intensive external review by Dr. Elliot Chaikof from the Beth Israel Deaconess Medical Center and Harvard University. Dr. Chaikof met with many faculty and trainees and commended our Division for many of the things that we are doing well and, most importantly, pointed out many areas of potential improvement. We know we can do better, and we will! Remember, "Be Happy, But Never Content!"

The coming 2019/20 year will see Visiting Professors from the University of Michigan (Dr. Matthew Corriere), the University of Manitoba (Dr. April Boyd) and Duke University (Dr. Cynthia Shortell) visit us. Dr. Gilbert Upchurch, Chair of the Department of Surgery at the University of Florida will join us in early May as the 9<sup>th</sup> K. Wayne Johnston Lecturer.

The culmination of the academic year will be the return of the Society for Vascular Surgery Vascular Annual Meeting to Toronto in June 2020. This marks the end of a 15 year period when VAM did not stray from inside the United States.

We're looking forward to welcoming the vascular surgery world to Toronto and will kick off VAM week with a welcome reception at the Hockey Hall of Fame. Wouldn't it be great if this coincided with the first Toronto Maple Leaf Stanley Cup victory since 1967? One can only hope!

The theme of this issue of Toronto Pulse is to introduce you to some of our researchers. All the researchers in our Division were asked to give a brief description of their academic program and to answer the question "How can others be involved?". I'm sure you'll be interested and intrigued by their specific areas of investigation and the breadth of academic productivity within our Division, ranging from basic science to engineering to quality improvement to clinical outcomes research and health systems research and beyond!

I'm impressed every day with the passion and drive of these academic vascular surgeons. I'm sure you will be too. Enjoy.



Thomas L. Forbes, MD

## Dr. John Byrne\*

\*Dr. Byrne is a Blair Early Career Professor in Vascular Surgery at the University of Toronto and a Society for Vascular Surgery Wylie Scholar

### Investigation into the pathogenesis of aortic aneurysm and dissection

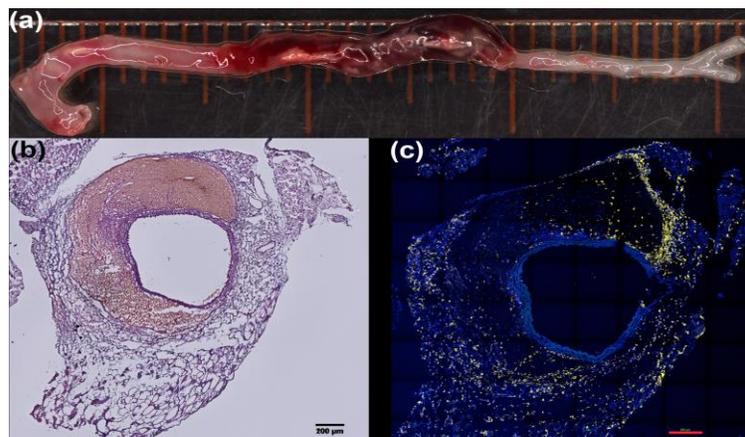
I am interested in understanding the biology driving aortic aneurysm and dissection, more specifically the role of the immune system and how different populations of macrophages participate in the disease process. In the laboratory we reproducibly create aortic aneurysm and dissection in mice using Angiotensin-2 (see figure). Whilst mouse models are not exact recreations of human disease, they are useful to investigate the disease processes that drive development of AAA. This circumvents the limitations of investigating aneurysm growth in humans: biopsy of small aneurysms is clearly not practical, and tissue samples from AAA patients undergoing surgery reveal less information about the pathology that got them to surgical threshold size. We have discovered that two newly discovered populations of macrophages differentially contribute to AAA, one contributing to maintenance of aortic integrity and the other worsening the disease process. My ongoing research is aimed at understanding what determines the phenotypic differences in these macrophage populations, how they are functionally distinct, and whether they are responders to tissue injury, or drive the disease process. Future research will examine the role of cigarette smoke exposure in mice and how this causes AAA, as this will be more relevant to the AAA patients we see clinically.

### How can others be involved?

Translating bench discoveries to the clinic ultimately requires human tissue/blood samples. We are fortunate at UHN to have a cardiovascular program level Biobank at an advanced stage of development. Having local champions at each University of Toronto site to drive Biobanking at other sites will enhance our ability to create a critical mass of clinical data and specimens for future research. I also welcome colleagues with interesting ideas that could be explored in a laboratory setting, in particular in the laboratory mouse, and also those with expertise that might be relevant to AAA research, to reach out and collaborate.

### More from the lab ...

Figure legend. (a) Whole aorta from mouse treated with Angiotensin-2. Orientation: aortic arch on left side of photo, iliac bifurcation on right side of photo. Specimen shows aortic aneurysm and dissection in the middle (suprarenal aorta). (b) Hematoxylin and eosin stain of mouse aneurysm demonstrating intramural hematoma within elastin layers. (c) Immunofluorescence image of same aorta in (b) demonstrating intense accumulation of macrophages (stained yellow).



## Dr. Charles de Mestral

### Turning the Rising Tide of Amputations due to Peripheral Artery Disease and Diabetes

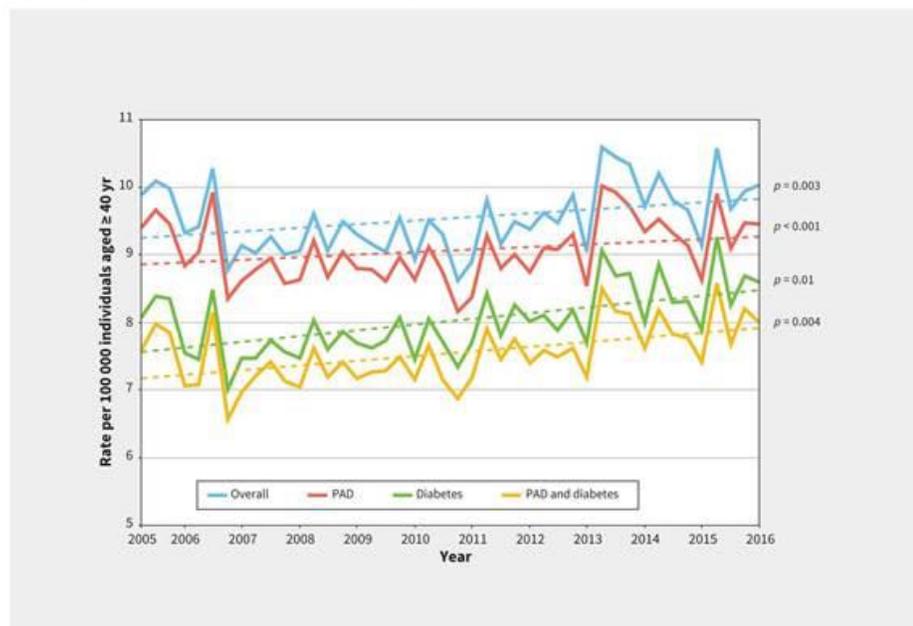
Affecting one in ten Canadians, PAD and diabetes are frequently synergistic. Care of patients with cancer, cardiac disease, trauma or organ transplantation is optimized through regional care networks and centers of excellence in many parts of Canada. However, care of a person at risk of amputation from PAD and diabetes remains disjointed, if not outright neglected. My collaborators and I are using Canada and Ontario's rich administrative "big" health data coupled with health provider surveys and patient interviews in order to produce key deliverables with which to inform strategies to reduce amputation. The overarching goal of my research program is to clarify the clinical and economic evidence-basis for integrated amputation prevention efforts in PAD and diabetes across Canada.

### How can others be involved?

- (1) If you know of, or collect, unique data on patients with diabetic or PAD-related foot complications these may be linkable to population-based health records in order to provide better insight into patients' clinical course and the effectiveness of prevention efforts.
- (2) I would also appreciate receiving your insight (by email, by phone or in person at city-wide rounds) into any unique regional challenges or success stories relating amputation prevention in Toronto, Ontario or elsewhere in Canada (e.g. clinic structure, diabetes pathways, programs targeting specific patient groups, etc.).

### More from the lab ...

*Rising Rate of Major or Minor Lower-extremity Amputations Related to Diabetes and PAD in Ontario*



Hussain et al. CMAJ 191 (35) E955-E961

## Drs. Matthew Doyle, Thomas Forbes, Cristina Amon

### CAVE – Centre for Applied Vascular Engineering

Our lab sits at the interface between vascular surgery, mechanical engineering and biomedical engineering. We are currently working on two research projects related to postoperative complications of endovascular aneurysm repair. In Project 1, we are looking at the impact of fenestrated endovascular aneurysm repair on renal artery hemodynamics by comparing flow-related indices before and after repair using computational fluid dynamics modelling (Fig. 1a). We are also looking at the impact of modelling assumptions and respiratory motion on renal artery hemodynamics. In Project 2, we aim to study the biomechanics of thoracic endovascular aneurysm repair and specifically the interactions between the mechanical properties of the stent graft and the mechanical properties of the aorta that lead to the formation of the “bird-beak” configuration, which increases the potential for type Ia endoleaks. We aim to determine the optimal stent graft properties that minimize or eliminate the presence of a bird-beak in specific patients. To do so, we are developing personalized computational solid mechanics (finite element) models of delivery and deployment of stent grafts in the thoracic aorta (Fig. 1b).

### How can others be involved?

We are interested in any relevant cases, including those of patients who have developed impaired renal function through bridging stent fracture or thrombosis, as well as cases with severe bird-beak configuration that went on to develop type Ia endoleaks or were converted to open repair.

### More from the lab ...

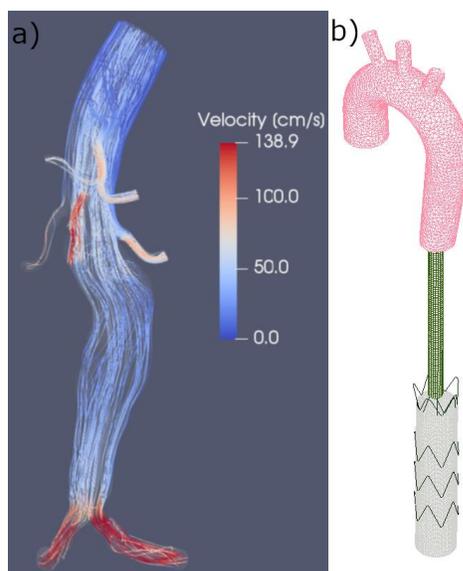


Fig. 1. Blood flow streak lines in a post-fenestrated endovascular aneurysm repair patient (a) and initial set-up for stent graft deployment simulations in thoracic endovascular aneurysm repair (b)

## Dr. Kathryn L. Howe

### How cells in atherosclerotic plaque communicate good and bad signals to cause disease – finding biomarkers and new therapeutic targets

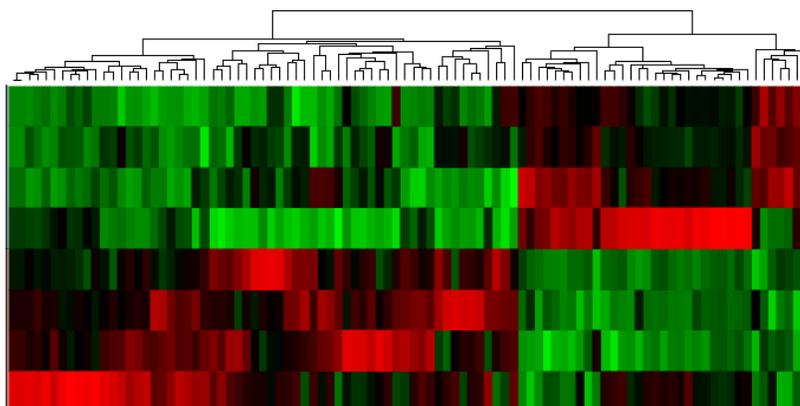
With mentorship from Dr. Jason Fish who is an expert in microRNA and vascular biology, I have been given physical bench space in the beautiful MaRS building. My work is focused on a new and exciting field of cell communication called extracellular vesicles (EVs). These nano-sized packages of information contain select “cargo” that are released into the bloodstream (i.e. blood-borne biomarkers) and into the vessel wall milieu (i.e. affecting plaque progression). We have been looking at the different contents of EVs released by endothelial cells to better understand how these messages are delivered in the setting of inflammation and importantly, how they can be exploited to determine biomarkers or therapeutic targets. Alongside these studies, we have already begun collecting carotid plaques from operative cases and isolating EVs in order to compare the difference in cargo content between asymptomatic and symptomatic patients. Ultimately, these studies will help us design ways to identify the patients at risk of stroke *before* a clinical event occurs.

### How can others be involved?

- 1) Participation in a biobank (SMH has one through Dr. Qadura and we are working to get our protocol passed at Sunnybrook with the help of Dr. Kayssi)
- 2) Ensure patient data is also collected (amit.rungta@uhn.ca is a great point of contact if you want to know more)
- 3) Clinic referrals to the UHN for asymptomatic patients that are willing to join the biobank (Dr. Wooster has kindly been doing so for the past year – thank you!)
- 4) Become a bench researcher – join Sneha Raju and the Fish trainees for an amazing journey into the field of microRNA communication in atherosclerosis
- 5) Find donors keen to fund our work! Stroke affects everyone at some point. Let's find a better way to prevent this terrible disease.

### More from the lab ...

Cool heatmap....stay tuned! (unpublished data)



## **Dr. Graham Roche-Nagle**

### **Quality of care in Vascular Surgery**

**Body composition as a biomarker in Advanced Endovascular interventions:** To evaluate the association between body composition and clinical outcomes in patients undergoing trans catheter aortic valve implantation (TAVI) and complex endovascular Aneurysm repair (cEVAR).

**Mobile Phone-Based Telemonitoring of Blood Pressure and Symptom Control to Optimize Management of Acute Aortic Dissections**

The objective of our study is to investigate of the feasibility of using a highly automated and user-friendly mobile phone-based telemonitoring system to optimize management of patients following acute type A and type B dissection.

**Optimizing pre-operative hemoglobin levels to reduce post-operative complications and mortality.**

To delineate the relationship between pre-operative anemia and post-operative complications including mortality using VQI data.

### **How can others be involved?**

I am happy to collaborate with anyone who is interested.

### **More from the lab ...**

**SVS**

**VQI**

**VASCULAR QUALITY INITIATIVE**

## **Dr. Mohammad Qadura\*\***

\*\*Dr. Qadura is a Blair Early Career Professor in Vascular Surgery at the University of Toronto

### **Combating Aspirin Resistance**

Antiplatelet therapy, such as aspirin, is a major pillar in the treatment of several atherosclerotic diseases such as peripheral arterial disease and carotid arterial stenosis. However, it has been reported that up to 30% of patients suffer from 'aspirin resistance' - a phenomena where aspirin fails to prevent clinical atherothrombotic events. These "aspirin resistant" patients are at a fourfold increased risk of non-fatal and fatal cardiovascular, cerebrovascular, or vascular events while taking aspirin in comparison to their aspirin sensitive counterparts.

Therefore, we are working on utilizing light transmittance aggregometry in a way that can be used to personalize antiplatelet medication and dosage among high-risk patients with advanced atherosclerotic disease. If successful, each individual patient receives the optimum dosage/medication, ensuring that the antiplatelets are effective for everyone. Our protocol is a simple algorithm that can be achieved at the bedside. This project has the potential to provide several clinical and economic benefits to our patients, healthcare system, and society at large. Appropriate medical management with aspirin and rapidly achieving aspirin sensitivity is anticipated to result in reduced adverse cardiovascular outcomes. Furthermore, we also expect that our algorithm will drastically decrease the time needed for patients to achieve adequate ASA induced platelet dysfunction.

### **How can others be involved?**

Others can be involved in a variety of ways, especially other scientists and trainees. Our lab is very willing to collaborate with other surgeons and scientists in this project. They can help immensely in areas such as patient recruitment, providing expertise etc. Similarly, trainees can help out in a number of ways. For instance, they can help by running some of the experiments, seeking patient consent, statistical analysis, and more. Should you be interested in collaborating or working with me, please don't hesitate to reach out!

## We welcome your support

*K. Wayne Johnston Lecture in Vascular Surgery* – This is held annually at our Research Day and gives our faculty and residents the opportunity to learn from a world leader in our specialty.

*Division of Vascular Surgery Chair's Fund* – This fund allows for continued support of our residency and fellowship programs, research support and continuing medical education and professional development.

Donations can be made online at [donate.utoronto.ca/surgery](https://donate.utoronto.ca/surgery) or by cheque to:

The Office of Advancement  
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## Contribute to our Newsletter

Story ideas, articles, photos or comments are welcome for upcoming issues, please send them to [vascular.admin@utoronto.ca](mailto:vascular.admin@utoronto.ca) or [thomas.forbes@uhn.ca](mailto:thomas.forbes@uhn.ca)

Moving, or do you know someone else who would like to receive this newsletter? Please let us know.

## Upcoming Events & Meetings

- |               |   |
|---------------|---|
| Oct 29, 2019  | U of T Vascular Surgery City-Wide Rounds, University Club of Toronto<br>Visiting Professor – Dr. Matthew Corriere, University of Michigan |
| Jan 16, 2020  | U of T Vascular Surgery City-Wide Rounds, University Club of Toronto<br>Visiting Professor – Dr. April Boyd, University of Manitoba       |
| Mar 10, 2020  | U of T Vascular Surgery City-Wide Rounds, University Club of Toronto<br>Visiting Professor – Dr. Cynthia Shortell, Duke University        |
| Mar 31, 2020  | Abstract Submission Deadline for Research Day   |
| Apr 30, 2020  | U of T Vascular Surgery Graduation & Research Day Dinner  |
| May 1, 2020   | U of T Vascular Surgery Research Day<br><i>9<sup>th</sup> Annual K. Wayne Johnston Lecturer – Dr. Gilbert Upchurch</i>                    |
| May 8, 2020   | U of T Department of Surgery Gallie Day   |
| June 17, 2020 | Reception – U of T Welcomes SVS to Toronto!   |
| June 17 2020  | SVS Vascular Annual Meeting (VAM)<br>Toronto, ON  |

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