



UNIVERSITY OF OTTAWA
HEART INSTITUTE
INSTITUT DE CARDIOLOGIE
DE L'UNIVERSITÉ D'OTTAWA

THE BEAT™

A COMPENDIUM OF INFORMATION ABOUT THE UNIVERSITY OF OTTAWA HEART INSTITUTE

HIGHLIGHTS

“We often see parents who are concerned about a remaining child after a son or daughter has died suddenly from unexplained causes.”

– Dr. Michael Gollob, Director of the Inherited Arrhythmia Clinic, UOHI
(from *Canada's First Cardiac Autopsy Guidelines for Unexplained Sudden Deaths*, pages 1–2)

For individuals diagnosed with a cardiac rhythm disorder, such as a family member of a sudden cardiac death victim, there are preventive treatment options.

(from *Some Facts About Sudden Cardiac Death*, page 3)

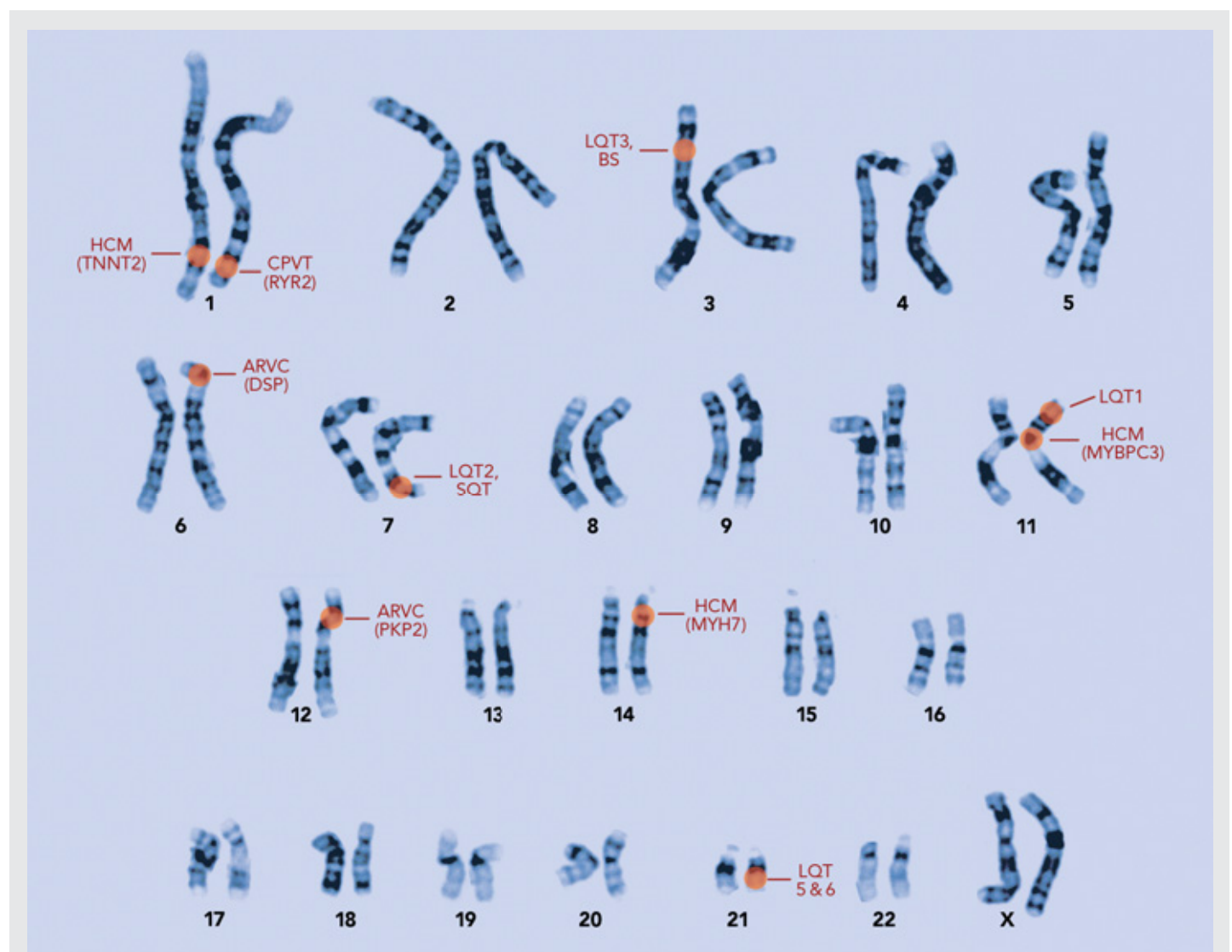
“Usually it’s a young person who wants to take a picture of it to put on their Facebook page. Adults are just happy to be alive. It’s not something that life has prepared you for – to look at your own heart. It’s a measure of our medical technology and how far we’ve come.”

– Dr. John Veinot,
Director of Anatomic Pathology, UOHI
(from *Cardiac Pathology: Answering Questions of the Heart*, pages 3–4)

“The survey results suggest that Ontario appears to be among the best in the world in blood pressure management.”

– Dr. George Fodor,
Head of Prevention and Rehabilitation Research, UOHI
(from *Taking Control of High Blood Pressure*, pages 4–5)

Canada's First Cardiac Autopsy Guidelines for Unexplained Sudden Deaths



Some genes associated with sudden cardiac death: This image of human chromosomes shows the genes known to be responsible for several inherited conditions that can cause arrhythmias. The name of the condition is followed by the gene abbreviation, indicated in parentheses. See page 3 for full condition names. Often, more than one gene can be associated with a disorder, or different genes can be associated with variations of a disorder. This is the case with Long QT Syndrome. (Adapted from a Mayo Medical Laboratories image)

IN THIS ISSUE

- P. 1–2** Canada's First Cardiac Autopsy Guidelines for Unexplained Sudden Deaths
- P. 3** Some Facts About Sudden Cardiac Death
- P. 3–4** Cardiac Pathology: Answering Questions of the Heart
- P. 4–5** Taking Control of High Blood Pressure
- P. 5–6** “Living Legend” Explores Hormones in the Heart and Promotes Science in Argentina

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The sudden death of a young person always comes as a shock. When the cause of a death remains undetermined, even after autopsy, surviving family members can be left frustrated and looking for answers. They may also be left with a serious, unidentified health risk.

Ontario has recently introduced cardiac autopsy guidelines to help diagnose sudden deaths and to facilitate the genetic screening of family members, when appropriate. Initiated by the University of Ottawa Heart Institute (UOHI) and developed in partnership with the Office of the Chief Coroner of Ontario, these guidelines provide the country's first standardized protocol for investigating unexplained cardiac deaths in people under 40. They also specify how to safeguard genetic material to identify family members who may be at risk for the same condition.

In recent years, incidents of sudden cardiac death in young athletes have been widely reported in the media. As many as 100 youths aged 18 and under die each year in Ontario from no apparent cause that

can be determined by standard autopsy. Often, these deaths occur in otherwise healthy individuals who have exhibited no prior symptoms.

Julie Rutberg, a Heart Institute genetic counsellor and part of the team that helped develop the guidelines. “We can’t identify all causes, but we can diagnose

As many as 100 youths aged 18 and under die each year in Ontario from no apparent cause that can be determined by standard autopsy.

Many of these deaths are the result of cardiac arrhythmias – problems with the electrical functioning of the heart. A standard autopsy will find nothing wrong with the heart because these often inherited conditions may leave no physical traces in the cardiac tissue. This is where the ability to do a genetic autopsy becomes critical.

“We now can genetically test for a variety of arrhythmia conditions,” said

20 to 30 per cent, and that number grows every year.”

The Guidelines for the Investigation of Sudden Cardiac Death do two things. First, they specify a standard protocol for examination of the heart. These procedures are more extensive than those employed in a standard autopsy. This is to exclude conditions that may leave evidence in the organ tissue but would otherwise go undetected.

(continued on page 2)

(Canada's First Cardiac Autopsy Guidelines for Unexplained Sudden Deaths, continued)

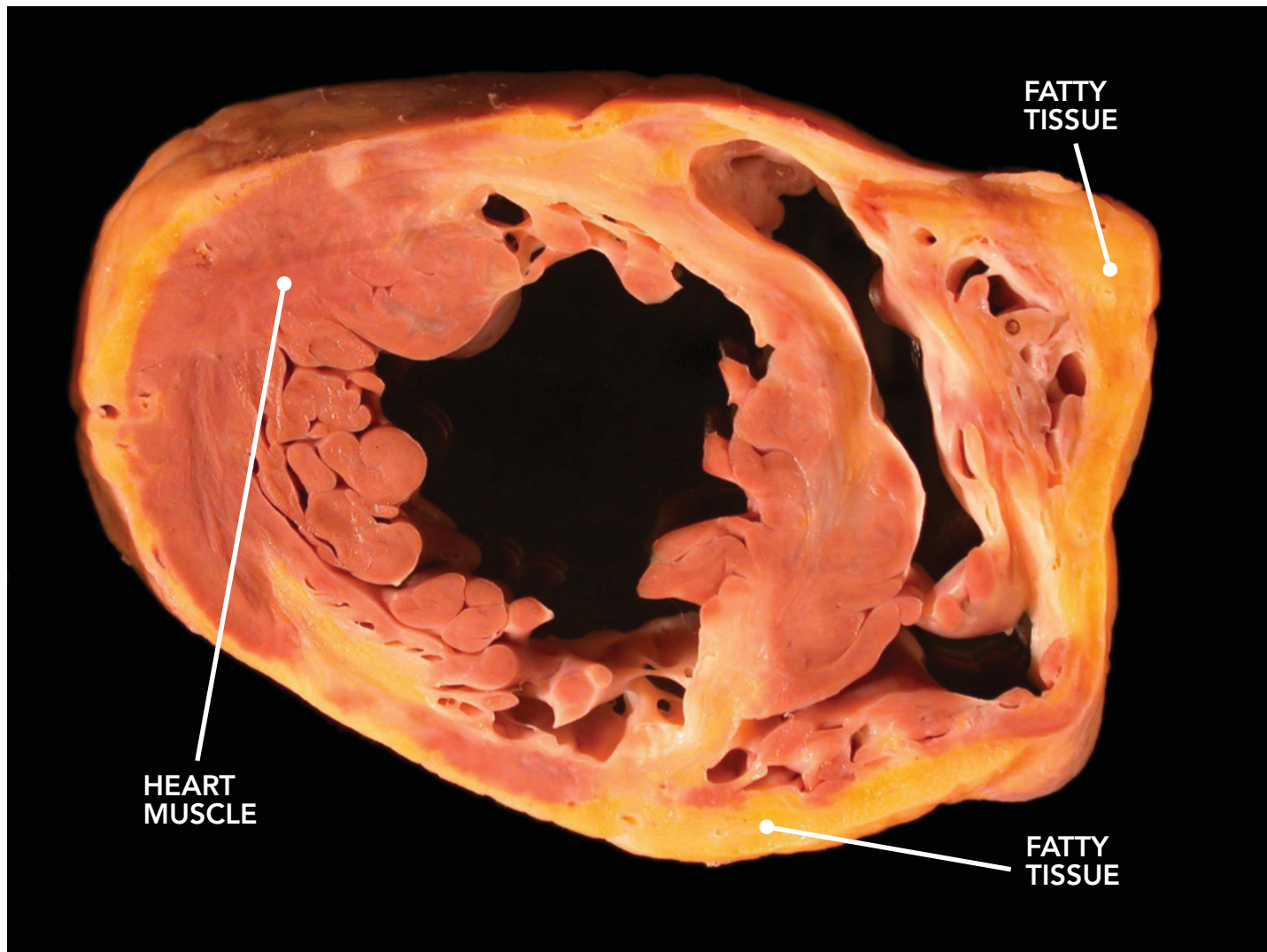
An example of such a condition is arrhythmogenic right ventricular cardiomyopathy (ARVC), sometimes the result of an inherited genetic abnormality. As the name suggests, ARVC affects the right ventricle, but often only the left is examined during a standard autopsy. Ruling out ARVC at autopsy means family members don't have to undergo potentially costly and time-consuming screening for this condition.

Second, the guidelines provide direction to pathologists on tissue collection and storage. Samples from autopsy are generally chemically preserved. Frozen tissue provides a better source of DNA for extraction and subsequent genetic screening, also known as molecular autopsy.

Dr. John Veinot is the Heart Institute cardiac pathologist to whom these difficult cases are often referred. According to Dr. Veinot, the capability to genetically test for inherited cardiovascular diseases has become available only in the last five years. "For many years, all I could do was recommend that the family undergo standard tests and that their EKGs be reviewed by a specialist. Now, with our genetics labs and Inherited Arrhythmia Clinic, the Heart Institute is right at the forefront of this."

The process to develop the autopsy guidelines began with the case of a family whose 21-year-old daughter had died suddenly. In this instance, the autopsy had not been definitive and the mother and a sister of the deceased exhibited potentially relevant symptoms. The family pushed hard to get an answer in the young woman's death, driven by their concern for other family members. In this case, the autopsy had not included a detailed assessment of the heart.

If a genetic defect is identified in one family member, it's likely that others carry that same defect. Two years after the death, the deceased and her mother were diagnosed by the Heart Institute's Inherited Arrhythmia Clinic with Long QT Syndrome. This is an inherited abnormality in the heart's electrical function. Seven other family members eventually underwent genetic screening for the life-threatening condition, and one was diagnosed with it.



Heart cross-section exhibiting ARVC: This heart, taken from a Heart Institute transplant patient, shows advanced ARVC (arrhythmogenic right ventricular cardiomyopathy). The salmon-coloured tissue is healthy heart muscle, while the yellow areas are fat deposits indicative of ARVC. It is this fatty tissue that interferes with the electrical signalling of the heart and can cause arrhythmias. Less advanced cases are often only evident in the right ventricle and can be missed by standard autopsies.

"We often see parents who are concerned about a remaining child after a son or daughter has died suddenly from unexplained causes," said Dr. Michael Gollob, Director of the Inherited Arrhythmia Clinic and the Arrhythmia

relatives, but second-degree relatives as well – cousins, aunts, uncles, nieces."

Dr. Gollob is an international authority on genetics and arrhythmia. His landmark research findings include identifying

Initially setting its sights on eastern Ontario, the Heart Institute involved representatives from the Ottawa Hospital and the Children's Hospital of Eastern Ontario in working with the coroner. Supportive beyond expectations, McCallum suggested that the issue should be addressed province-wide. And so began an 18-month process of development and review.

Ruling out ARVC at autopsy means family members don't have to undergo potentially costly and time-consuming screening for this condition.

Research Laboratory. "If the cause of death was an inherited condition, this can potentially affect not just first-degree

a genetic basis for atrial fibrillation, a common form of irregular heartbeat, and evidence that Canadians at risk for sudden cardiac death may be misdiagnosed and receive treatment for other symptoms. His work has led to a Heart Institute program for molecular autopsy, genetic screening and genetic counselling in support of families whose genetic makeup will affect their future cardiac health.

As the first of their kind in Canada, and possibly North America, the guidelines are drawing attention from other provinces. Dr. Martin Gardiner of Dalhousie University is the President of the Canadian Heart Rhythm Society. "I'm pleased with the initiative Ontario has taken in this matter," said Dr. Gardiner. "Based on their lead, this is an issue that the Society will be taking up to determine how it can influence jurisdictions across the country to follow suit."

Now in place, the cardiac autopsy guidelines offer coroners and pathologists another avenue for diagnosing what had been potentially unexplainable deaths. "As part of our public health mandate,



Dr. Michael Gollob

"If the cause of death was an inherited condition, this can potentially affect not just first-degree relatives, but second-degree relatives as well – cousins, aunts, uncles, nieces."

- Director, Inherited Arrhythmia Clinic and Arrhythmia Research Laboratory, University of Ottawa Heart Institute
- Cardiac Electrophysiologist, University of Ottawa Heart Institute
- Assistant Professor, Division of Cardiology, Faculty of Medicine, University of Ottawa
- Research interests: the genetics of inherited arrhythmia syndromes leading to sudden cardiac death, the genetic basis for atrial fibrillation, and models of human arrhythmogenic diseases

"With our genetics labs and Inherited Arrhythmia Clinic, the Heart Institute is right at the forefront."

– Dr. John Veinot,
Director of Anatomic Pathology, University of Ottawa Heart Institute

It was the difficulty of assessing familial risk that spurred the Heart Institute team to approach Andrew McCallum, the then coroner for eastern Ontario, now Chief Coroner for the province. "They reached out and said we would like to form a working arrangement with you in order to identify people with families who might be at risk," said McCallum.

this is an important step in identifying and protecting families at risk," said McCallum. Ontario's coroners want to provide definitive answers whenever possible. In the case of sudden cardiac death, their motto is particularly appropriate: *We speak for the dead to protect the living.*

Some Facts About Sudden Cardiac Death

Roughly 50,000 Canadians are living with an inherited heart rhythm disorder – and many are unaware of it.

Most sudden cardiac deaths occur in the elderly, but 1 to 2 per cent occur in young people, aged 40 years or less. Of these, about one-third are designated as unexplained deaths because autopsies find no physical cause. Such “negative” autopsy results are often due to the deceased having suffered from some form of cardiac arrhythmia that left no identifiable traces in the heart tissue.


These conditions that affect the electrical signalling of the heart are most likely inherited genetic disorders. This means that other family members could be at risk. Based on incidence rates, roughly 50,000 Canadians are living with an inherited heart rhythm disorder – and many are unaware of it. Often, a fatal incident can be the first sign of a problem, because these conditions may exhibit no symptoms.

Some of the genetic causes of sudden cardiac death in the young include:

- ARVC (arrhythmogenic right ventricular cardiomyopathy), also known as ARVD (arrhythmogenic right ventricular dysplasia) – A usually inherited deterioration of the muscle tissue of the right ventricle that results in arrhythmias.
- BS (Brugada Syndrome) – A genetic rhythm disorder that can cause ventricular fibrillation and sudden cardiac arrest.
- CPVT (catecholaminergic polymorphic ventricular tachycardia) – A calcium channel disorder in the heart muscle, resulting in problems with electrical signalling and irregular heartbeats, especially during exercise.
- FHCM or HCM (familial hypertrophic cardiomyopathy) – A thickening of the heart muscle that reduces cardiac function.
- LQT (Long QT) Syndrome – A prolonged electrical recovery phase (QT interval) of the heartbeat that can result in rapid, chaotic beats. Can be inherited or caused by various medications or other medical conditions.
- SQT (Short QT) Syndrome – A shortened QT interval that can result in life-threatening arrhythmias.

Researchers are rapidly gaining an understanding of the genetic basis for these disorders. For instance, a team in St. John's recently identified the gene responsible for a type of ARVC prevalent in Newfoundland.

For individuals diagnosed with a cardiac rhythm disorder, such as a family member of a sudden cardiac death victim, there are preventive treatment options. Drug therapies, including beta blockers, can help prevent arrhythmias in some patients. Another approach, in certain cases, is an implantable cardioverter-defibrillator. This device, similar to a pacemaker, monitors the heart and delivers electric shocks when an arrhythmia is detected.

When an inherited disorder is a possibility, genetic counselling becomes an important part of clinical care. Genetic counsellors are medical professionals with expertise in genetics as well as in psychology and counselling. Their role is to educate patients and family members about genetic disorders and the risks of inheriting or transmitting them. They also provide counselling about the associated health and lifestyle implications, such as recommendations for restricting certain types of physical activity. 

Cardiac Pathology: Answering Questions of the Heart

Pathology may be a behind-the-scenes activity, but that doesn't mean it all has to happen behind the microscope. As Director of Anatomic Pathology at the University of Ottawa Heart Institute, Dr. John Veinot is active across the organization. But it's his expertise as a cardiac pathologist that makes him a rare breed. There are only a few such specialists in Ontario and less than a dozen in all of Canada.

Autopsy referrals regularly come to him from across Ontario, and others from as far away as British Columbia and Newfoundland. Sometimes it's not clear what form a referral will take. Usually he receives slides or tissue samples. Other times a box arrives with a whole heart in it.

That's when the investigation starts. Pathology is about solving the question of what is wrong with a patient, whether alive or deceased. To arrive at a diagnosis, the pathologist sifts through the evidence, which can include blood, tissues, patient histories, and surgical, anesthesiology and nurses' notes.

“The heart has it all. It has surgical pathology and autopsy pathology; it has diseases of young people and diseases of old people. It's our number one killer,” said Dr. Veinot. “A teacher of mine used to say, ‘Every heart is like a Christmas present. You never know what's inside until you open it up and have a look.’ If you want to spend your time doing something worthwhile, the heart is a good organ to focus on.”

Yet most patients don't realize that it's often the doctor they don't see who

diagnoses their illness. The classic example is of a surgeon who takes a biopsy and then comes back to the patient and tells him that he has a certain condition. The patient assumes, quite reasonably, that the

Forty to fifty per cent of autopsies provide new information about the prior health of the deceased.

surgeon made the diagnosis. He doesn't realize that his tissue sample was given to a pathologist who ran one or a number of tests, interpreted the results, and then informed the surgeon of the diagnosis. The pathologist is a bit like a speechwriter who doesn't get credit for the speech.

“In a way, I really have three jobs,” Dr. Veinot said. “I have my patient care job, my education job, and my research job. But I think of myself as a doctor first and foremost.” Though he rarely meets his patients face to face, he doesn't feel any less a part of the continuum of care. In the case of a death, he might be the last doctor to see a patient, and it's his job to provide the final diagnosis, to determine the cause of death. Just as often, he may make the first diagnosis of a patient's condition, and the patient receives treatment based on his findings.

Even within medicine, pathology can be misunderstood. Some think of pathologists

as dead people's doctors, or that doctors become pathologists because they aren't good with people. “That's a stereotype,” Dr. Veinot said. “I have always enjoyed working with patients and their

families. I didn't go into pathology to get away from that.” In fact, he tries to involve himself in patient care as much as possible. One of the things he enjoys most about working at the Heart Institute, apart from being at the epicentre of cardiac care, education and research, is the close, interactive relationship he has with clinicians.

Autopsy pathology is an equally important part of the job, though. Forty to fifty per cent of autopsies provide new information about the prior health of the deceased, and they are often the only way to determine the cause of death. Autopsy pathology also plays an important public health role in identifying diseases, determining when and how surviving family members and others should be screened, and clarifying the efficacy of treatments so that improved care can be provided to others in the future.

It was Dr. Veinot's expertise in cardiac autopsy pathology that involved him in

the Heart Institute's initiative to develop guidelines for Ontario coroners in cases of unexplained deaths in people under 40. These guidelines will help ensure that cases are referred to a cardiac pathologist when appropriate.

As for being a doctor for dead people, he can recall times when he showed colleagues a cross-section of heart tissue, and they asked him how the patient died. He was able to tell them that the patient wasn't dead, but got a new heart. “For years, I've been privileged to be a part of the cardiac transplant team. As part of that process, I can be involved with a patient for a period of years,” he said. “They may never know that I exist, but I know their patient cases and follow them through the whole course of their care.”

That course begins with helping the transplant committee assess the diseases of transplant candidates and their eligibility to receive a scarce new heart. Following a transplant, he examines the old heart. “Did the patient have the disease we thought they did? Or was it something else? Is it something inherited that the family should be screened for? Is it a disease that could come back in the new heart? These are the questions I need to answer.” The patient will then undergo periodic biopsies over the following years, which Dr. Veinot examines to look for signs of rejection or recurring disease.

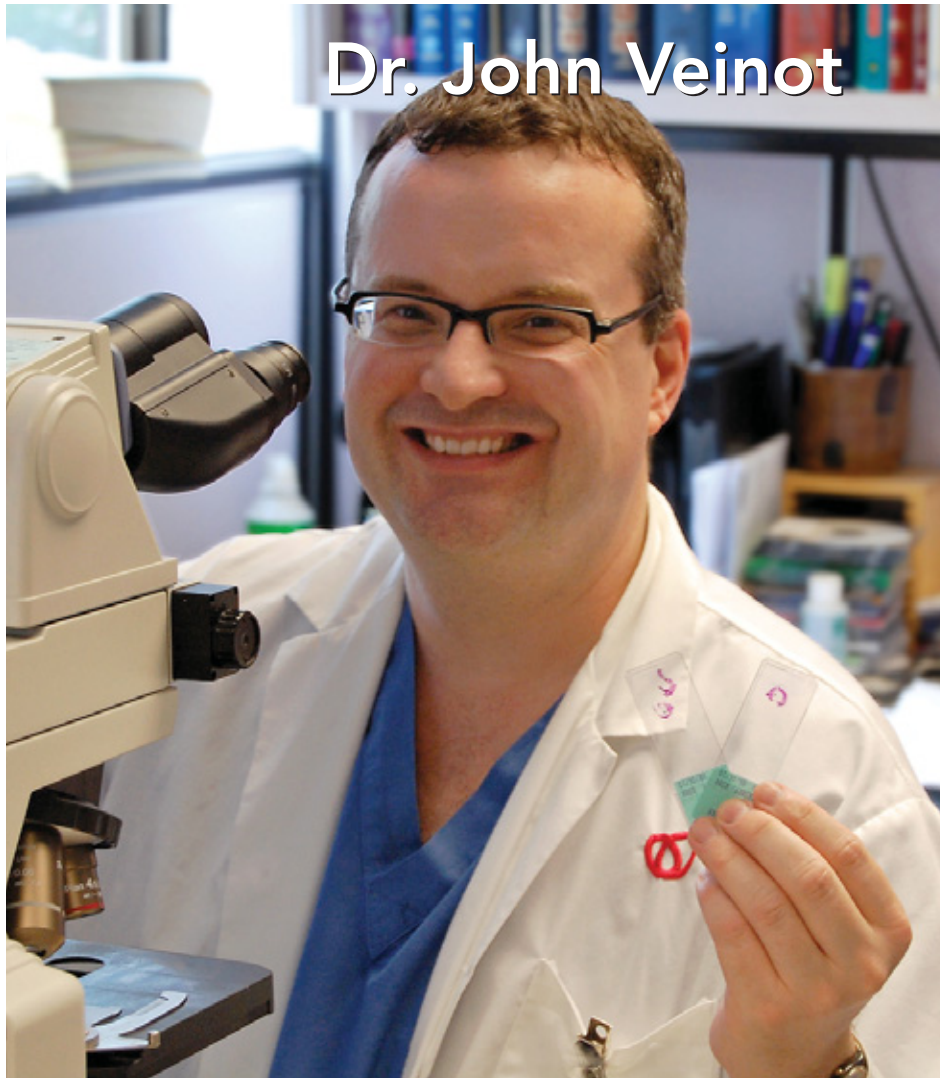
Sometimes, a transplant patient will want to see his or her old heart. “Usually it's a young person who wants to take a picture of it,” he laughs, “to put on their Facebook *(continued on next page)*”

(Cardiac Pathology: Answering Questions of the Heart, continued)

page. Adults are just happy to be alive. It's not something that life has prepared you for – to look at your own heart. It's a measure of our medical technology and how far we've come."

As an educator, Dr. Veinot is a member of the Faculty of Medicine at the University of Ottawa, where he teaches medical students, cardiology residents, cardiac surgery residents and cardiac nurses, among others. He does a good deal of research pathology as well, looking at rat and mouse hearts. "Pathologists," he says, "are in a good position to do translational medicine because pathology is grounded in the basic sciences and basic anatomy. But we're also doctors and we can apply the research to real patients, living and dead. We see the full spectrum of animal and human tissues."

As someone with a foot in the research, clinical and education aspects of medicine, he appreciates the way the Heart Institute integrates all three. This is a perspective he likes to share with science graduate students. Putting the human face of the patient on basic research puts it in context. When you know what you are working towards, the science becomes more meaningful. 🐾



Dr. John Veinot

"The heart has it all. It has surgical pathology and autopsy pathology; it has diseases of young people and diseases of old people. It's our number one killer. If you want to spend your time doing something worthwhile, the heart is a good organ to focus on."

- Director of Anatomic Pathology, University of Ottawa Heart Institute
- Professor, Department of Pathology and Laboratory Medicine, Faculty of Medicine, University of Ottawa
- Attending Staff Pathologist, Ottawa Hospital, Civic Campus
- Special interests: cardiac and vascular pathology, coronary artery restenosis and atherosclerosis, cardiac transplantation and medical education 🐾

Taking Control of High Blood Pressure

Two-thirds (66 per cent) of Ontarians with high blood pressure are being successfully treated, says an extensive province-wide survey conducted by University of Ottawa Heart Institute researchers.

The figures show substantial improvement compared with the 1992 Canada Heart Health Survey, when 12 per cent were treated and successfully controlled in Ontario and the figure was 13 per cent across Canada overall. Currently in Canada, the

"Clearly, both physicians and the public are paying greater attention to prevention. Good blood pressure management means we are keeping people healthy and out of hospital longer," Dr. Leenen added.

"This is one of the real success stories in Canadian cardiovascular medicine," said Dr. Fodor. "The survey results suggest that Ontario appears to be among the best in the world in blood pressure management."

flip side of the figures shows that nearly 34 per cent of Ontarians with high blood pressure still do not have it under control. This translates into 500,000 middle-aged and older Ontarians who remain unnecessarily at risk for heart disease.

These survey results represent only an initial analysis of an extensive amount of data. The figures show that blood pressure treatment and management in Ontario progressed across all age groups and in both sexes, and is fairly similar across major ethnic groups.

In Ontario, high blood pressure was prevalent in 21 per cent of all participants; 24 per cent of males and 19 per cent of females. These figures are virtually identical to results in the 1992 national Heart Health Survey.

Of the 2006 Ontario population with hypertension, 66 per cent were successfully treated and had their blood pressure under control. Another 15 per cent were being

treated but their blood pressure was not controlled, and 19 per cent were not being treated at all.

Rates of high blood pressure are substantially higher in the United States based on the most recent study in 2003–2004, known as the National Health and Nutrition Examination Survey (NHANES). The American rates were 20 per cent higher in the 60–79 age group and 5 per cent more in the 20–39 group. But these rates may be related to measurement of blood pressure by physicians. This can cause white-coat hypertension, so named for people measured with higher blood pressure while visiting a physician because they feel more anxious at the time.

In Ontario's \$1.2 million study, the team tested a total of 2,551 participants aged 20 to 79 in regions throughout Ontario beginning in August 2005. Measurements for blood pressure, height, weight, waist/hip circumference, arm circumference

Two-thirds of Ontarians with high blood pressure are being successfully treated.

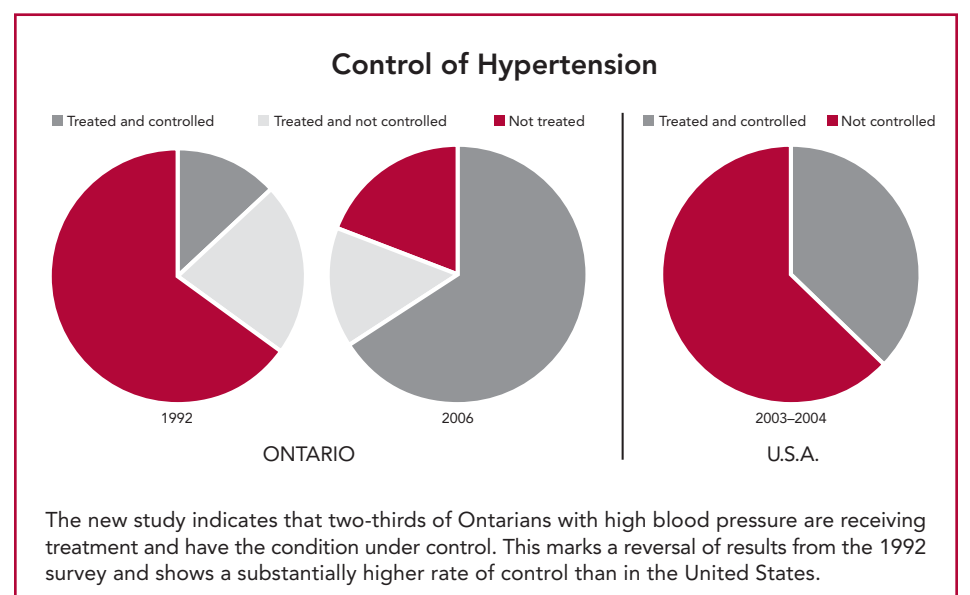
definition of hypertension or high blood pressure is more than 140 mmHg for systolic pressure or more than 90 mmHg for diastolic pressure. High blood pressure is a major risk factor for stroke, heart attack and death from heart disease.

"The survey results have shown us a dramatic change in the landscape in the management of high blood pressure," said cardiologist Dr. Frans Leenen, who holds the Pfizer Chair in Hypertension at the Heart Institute. Both he and cardiologist Dr. George Fodor, who is the Heart Institute's Head of Prevention and Rehabilitation Research, were principal investigators in the study. Their work on hypertension is recognized internationally.

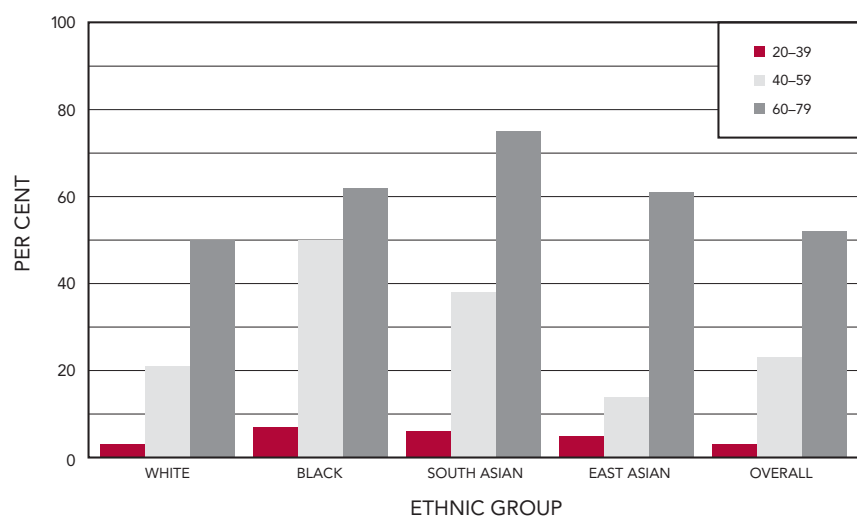
The Heart Institute study is the most comprehensive assessment of high blood pressure in Canada in 15 years. A community-based cross-sectional study, it was especially aimed at three prevalent groups in Ontario for which there is virtually no quality information: East Asians, South Asians and blacks.

Overall, 52 per cent of people aged 60 and older exhibited high blood pressure. The prevalence of high blood pressure in this age group has not declined since 1992. Given the growing population of older Canadians, this represents a significant health risk.

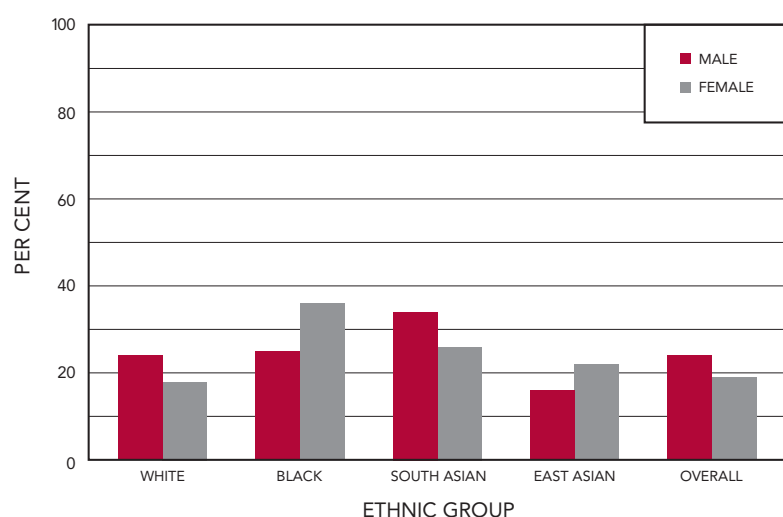
While management of blood pressure in the population has certainly improved, the



Prevalence of Hypertension by Age Group



Prevalence of Hypertension by Gender



When the Ontario findings are looked at by ethnic group, several variations are apparent. Black and East Asian women exhibit higher rates of hypertension than do men in those groups. The opposite is true for white and South Asian women. The data also show that blacks and South Asians are much more likely to develop hypertension earlier in life, and that South Asians aged 60 to 79 have the highest incidence of all groups measured.

and Body Mass Index (BMI) were taken. BMI measures weight in relation to height, correlated with body fat. The number is widely used to indicate health risks, and in this survey, high blood pressure was associated with a higher BMI.

The sample of households where interviewers selected participants was drawn from municipalities and areas in the 2001 Census for health regions covering 94 per cent of Ontario's population. The responses of participants were weighted to the population of Ontario adults (roughly 8 million at the time). Weighting the data enables analysts to draw conclusions for the entire population rather than just the sample that was collected.

The rate of people in Ontario whose high blood pressure was under control was 66 per cent, compared with 37 per cent in the U.S. found in the NHANES study. Research shows treatment and control rates have improved in the U.S., but the extent of improvement was much better in Ontario – and by extension in Canada. “Whereas in the early '90s, the United States system appeared to perform better, subsequent improvements in the detection and treatment in Ontario appear to be more substantial,” the Heart Institute research found.

The Heart Institute study was supported by the Heart and Stroke Foundation of Ontario. The research team partnered with the Statistical Consultation Group at Statistics Canada for its expertise in working with surveys with a large database. The proportion of participants in different ethnic groups was chosen to ensure that the survey results represented Ontario's diverse ethnic groups.

Findings from the Ontario study also show:

- Diabetics accounted for 7 per cent of the Ontario population, and 50 per cent of these had high blood pressure.

- Blacks and South Asians were three times more likely to have high blood pressure than whites.

- Both systolic (the upper number) and diastolic blood pressure appeared to have decreased substantially in different age groups. The highest drop, 20/10 mmHg, was seen in the 60–79 age group. These lower figures could be a reflection of lower prevalence of high blood pressure or better management.


- High blood pressure was present in 24 per cent of males and 19 per cent of females overall.

- A significant difference in ethnic groups was observed in the 40–59 age group, where the rate of blood pressure was highest among blacks but lowest among East Asians.

- By gender, South Asian and white men tend to have a higher incidence of high blood pressure compared with women from the same ethnic background.

- Among blacks, females have 36 per cent prevalence compared with 25 per cent in males.

- Blacks and South Asians in the 20–39 age group are more than twice as likely as whites to have hypertension.

High blood pressure is a major risk factor for premature disability and death from heart disease. Studies estimate that in the 40–69 age group, a difference of 20 mmHg in usual systolic blood pressure is associated with a two-fold difference in the death rates for stroke and heart disease. The World Health Organization estimates that at least 50 per cent of heart disease and 75 per cent of strokes are caused by high blood pressure. People with high blood pressure also have significantly higher rates of heart failure, kidney disease and diabetes. 

“Living Legend” Explores Hormones in the Heart and Promotes Science in Argentina

While his face might not appear on trading cards, Dr. Adolfo de Bold is something of a superstar. The Director of the Cardiovascular Endocrinology Laboratory at the University of Ottawa Heart Institute (UOHI) has had a long and distinguished career that includes one of the landmark discoveries in cardiovascular physiology.

Outside of the lab, he continues to distinguish himself by encouraging youth in his native Argentina to pursue careers in science. His dedication to this cause recently led him to establish a foundation to broaden the effort.

In 1981, Dr. de Bold discovered atrial natriuretic factor (ANF), a hormone produced in the atria of the heart. He found that, through ANF, the heart is able to regulate blood pressure, blood volume, and the growth of cardiovascular tissue.

Argentina has produced three Nobel Prize winners in medicine – a tradition of excellence that could be lost due to declines in the educational system.

This groundbreaking work revealed that the heart has an endocrine function and opened up an important new area of research. Science papers stemming from the discovery of ANF now number in the tens of thousands from around the world, and associated diagnostic and therapeutic tools are in use today.

The significance of Dr. de Bold's achievements can be measured in the number of prestigious awards and honours that have come his way. These include the World Congress of the World Society of Cardio-Thoracic Surgeons naming him a “living legend” for his contributions to medicine, and the Heart and Stroke

Foundation placing the discovery of ANF at the top of its top 10 list of research achievements of the last 50 years.

Born and raised in Parana, Argentina, Dr. de Bold was the product of an excellent educational system that drew heavily on models found in Europe. In 1968, he came to Canada to pursue his graduate studies at Queen's University, where he eventually joined the faculty and conducted the research that led to the ANF discovery. He then joined the Heart Institute, where he has spent the bulk of his career.

In the years since leaving Argentina, he has returned many times. It was on these visits that he saw how government instability and poor administration have led to a decline in the country's educational system and, increasingly, a lack of focus among students. Argentina

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("Living Legend" Explores Hormones in the Heart and Promotes Science in Argentina, continued)

has produced three Nobel Prize winners in medicine, and Dr. de Bold doesn't want this tradition of excellence to be lost.

During his visits, he began giving talks to high school students, encouraging them to pursue careers in science and medicine. At the same time, he stressed the importance of dedication and hard work in achieving one's professional goals.

"The response of the kids is just incredible, the depth of the questions they ask. They have left behind their teachers

in terms of information. They absorb the concepts I give them like sponges," says Dr. de Bold. "I talk about what is required here in Canada to get into medicine. When I tell them how we go about business here, they immediately understand."

There are two traditions in science, he explains: the northern European approach, as seen in Canada, and the Mediterranean approach, practiced in Argentina. "Both are equally rigorous," says Dr. de Bold. "For both, two plus two equals four, but how you get to that is

where the difference lies." He sees the northern European approach as more disciplined and competitive, and the Mediterranean more humanistic and creative, but less adept at developing the systems to support and encourage scientific research.

He hopes, through his Foundation for Education in Science, to expose students to the northern European scientific tradition and fuel their competitive spirit. Established just last year, the foundation will sponsor talks by visiting scientists

for youth in the upper secondary grades. This will target students at the time they are starting to make decisions about their careers.

Back in the lab, Dr. de Bold has been pursuing several lines of research related to hormones produced by the heart. One involves the basic secretion mechanisms of brain natriuretic peptide (BNP), another hormone closely related to ANF and a standard marker for cardiovascular disease. It's possible that the process by which BNP is manufactured could be unique.

Another area of research is the function of BNP at the systemic level. ANF and BNP are, in many ways, nearly identical. They respond similarly to circulatory changes and produce similar circulatory effects. Stored together in the heart, the hormones share the same receptor.



Adolfo de Bold, PhD

"Both [the northern European and Mediterranean approaches to science] are equally rigorous. For both, two plus two equals four, but how you get to that is where the difference lies."

- Director, Cardiovascular Endocrinology Laboratory, University of Ottawa Heart Institute
- Professor of Pathology and Laboratory Medicine and of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa
- Fellow of the Royal Society of Canada, the Royal College of Physicians and Surgeons, the American Society for the Advancement of Science, the International Society for Heart Research, and the American Heart Association; and Officer of the Order of Canada
- Selected awards: Gairdner Foundation International Award, Royal Society of Canada McLaughlin Medal in Medical Research, International Society for Hypertension Research Achievement Award
- BSc (Clinical Biochemistry), MSc and PhD (Experimental Pathology)
- Research interests: heart inflammation and cardiac endocrine function, pharmaceutical applications of atrial natriuretic factor (ANF) and brain natriuretic peptide (BNP) 🌀

"The response of the kids is just incredible, the depth of the questions they ask."

– Adolfo de Bold, PhD, Director, Cardiovascular Endocrinology Laboratory, University of Ottawa Heart Institute

Anything that alters hemodynamics alters the levels of ANF and BNP. But sometimes there can be a change in BNP levels without a change in hemodynamics. One cause of this is the inflammation associated with acute rejection following cardiac transplants. It's possible that other inflammatory conditions may also alter BNP. The causes and mechanisms of these changes need to be better understood.

ANF, like insulin, breaks down very quickly after release. Dr. de Bold's lab is developing an analog of ANF whose effects could last for days rather than mere minutes. This would prove highly useful not only in the treatment of acute heart failure, but also in support of the remodelling of the heart following myocardial infarction. Based on progress achieved thus far, the lab has applied for a patent. This project was conceived and is managed by Dr. de Bold's wife, Mercedes, who has worked alongside him for more than 40 years.

It's clear that Dr. de Bold practices the dedication and hard work he encourages in the students that attend his presentations. In his dual roles of scientist and ambassador of science, he still has much to contribute to our knowledge of the heart and to the future ranks of researchers and medical professionals. 🌀