Navigating the Shortage of Medical Isotopes

The University of Ottawa Heart Institute has taken steps to ensure that the care of patients at Ottawa hospitals—and not just cardiac patients—would be protected during the resulting [isotope] shortage.

“Heart failure is a growing burden with substantial health care costs that we can reduce through prompt intervention.”

— Christine Straubers, Advanced Practice Nurse, Cardiac Telehealth, UOHI

(from Navigating the Shortage of Medical Isotopes, page 1)

All diseases are thought to have some sort of genetic predisposition. However, most of the predisposition to cardiovascular disease is thought to be caused by the contribution of many genes.

(from The Heart Institute Hosts “Genes and the Heart” Symposium, page 4)

The University of Ottawa Heart Institute went on alert in December 2007 with the shutdown of a 50-year-old Canadian nuclear reactor that produces medical isotopes to diagnose and treat patients in Canada and around the world.

Since then, the Heart Institute has taken steps to ensure that the care of patients at Ottawa hospitals—and not just cardiac patients—would be protected during the resulting shortage. When the unscheduled shutdown of the so-called NRU reactor hit in May 2009, researchers and staff at the cardiac imaging facility were ready. In fact, the Heart institute’s leading cardiac imaging specialists were invited to Parliament Hill to discuss their experience with MPs at the Commons Health Committee on June 18.

The Heart Institute has been commended by other experts in the nuclear imaging field on its advanced planning and initiatives to solve shortages that have forced many hospitals across the country to postpone tests while increasing wait times for cancer patients.

With notice of the reactor shutdown in mid-May, the Heart Institute quickly switched away from the nuclear reactor-produced tracer called technetium-99m and moved to another tracer, thallium-201. Purchasing thallium-201 helped preserve the dwindling stock of the cheaper more effective technetium-99m, necessary for some cardiac tests.

As well, an Institute team of chemists, medical physicists and other allied researchers was already producing another promising alternative medical isotope, rubidium-82, for Positron Emission Tomography (PET) scans. Canada’s National Cardiac PET Imaging Centre is located at the Heart Institute. The PET Centre conducts critical diagnostic imaging by injecting traceable radioisotopes that last only a few hours but which light up when scanned to reveal blood flow and blockages in and around the heart.

Rubidium-82 is a very short lived tracer and is regarded as a more accurate medical isotope. It is also considered safer because it exposes patients to less radiation. Just how safe, accurate and useful it will prove to be is what scientists at the Heart Institute are currently investigating. Rubidium-82 is made at the Heart Institute in a small generator, about the size of a miniature refrigerator, for use almost immediately in patients.

The Heart Institute also supplies the Ottawa area with alternative isotopes for tests to diagnose cancer. This supply project is part of a national consortium project.

(continued on page 2)

PARTICIPATE IN THE BEAT READER SURVEY AND GET A CHANCE TO WIN!

Ten survey respondents will win their choice of a $50 donation in their name to their favourite charity, or a Heart Institute gift package containing our very own T-shirt, baseball cap and water bottle. Chances are good that you will find it five minutes very well spent.

Complete the survey at www.ottawaheart.ca/surveybeat, and thanks in advance for your valued participation.
Heart Health in the House of Commons

The following are excerpts from testimony before the House of Commons Health Committee, which met on June 18, 2009 to hear expert witnesses discuss the consequences of the reactor shutdown at Chalk River, Ontario.

Two leading specialists from the Heart Institute were invited to give testimony about their experience in this matter. They were Dr. Terrence Ruddy, Chief of Cardiology and Director of Nuclear Cardiology, and Dr. Rob Beanlands, Chief of Cardiac Imaging and Director of the National Cardiac PET Centre.

Dr. Beanlands:

First and foremost, I think the main goal for all of us is for the care of our patients to be given in a timely manner and for this timely care to be provided to the best of our abilities.

There are already some initiatives in place to evaluate some long-term solutions. There’s a plan for a workshop and a program to look at some of these very seriously in the fall, and we’re very pleased to be part of that initiative.

We heard about medium-term solutions from the Minister of Health earlier this week, when she spoke about the CIHR [Canadian Institutes of Health Research] grant program to try to look at alternatives to technetium.

Short-term solutions are things that we are doing on-site in the Heart Institute. For example, in cardiac imaging in our facility we have switched to a tracer called thallium, which can be used quite reliably to image the blood flow in the heart. We also have acquired—a scanner that uses less technetium.

That’s a new technology. We also have access to PET imaging for blood flow agents, and we do PET imaging of the heart as well, so we have been able to adapt with those situations.

In addition, our staff is working extremely hard. Many of them are coming in on the weekends to help deal with the situation.

“The staff are working extremely hard. Many of them are coming in on the weekends to help deal with the situation.”

– Dr. Rob Beanlands, Chief of Cardiac Imaging and Director of the National Cardiac PET Centre, UOHI

Heart Health in the House of Commons

of research organizations approved by Health Canada to produce medical isotopes for regional distribution and includes the Heart Institute. The reason: the Institute has its own cyclotron. A cyclotron produces short-lived non-nuclear medical isotopes by aiming a stream of accelerated protons at a target substance.

The search for alternative isotopes is a serious endeavour for Canadian medical scientists. The federal government announced in June a contribution of $6 million through the Canadian Institutes of Health Research (CIHR) and the Natural Sciences and Engineering Research Council of Canada (NSERC) for research to replace technetium-99m in medical imaging procedures. The funding announcement was made at the Heart Institute by Health Minister Leona Aglukkaq to support the production and clinical testing of alternative isotopes. It is expected the funds will be available for competing proposals beginning October 11.

The funding announcement was continued to be given in a timely manner and for of our patients is waiting significantly

The Heart Institute is substituting the medical isotope Thallium-201 as a perfusion agent in PET scanning owing to the current shortage of Technetium-99m. In a typical perfusion imaging test, which measures blood flow to the heart muscle, patients undergo two scans—one at rest and one at stress following a period of physical exercise. The two isotopes are compared below.

**Technetium-99m**
- Base agent, added to a pharmaceutical known as technetium-bearing tracer
- Two injections required
- Injection given before rest scan, then again before stress test
- Procedure lasts about 4 hours
- The half-life of the agent is no longer in the blood, is 6 hours.

**Thallium-201**
- Stand-alone agent, ready for injection
- Single injection
- Injection given only at stress test and not again at rest scan
- Procedure lasts about 5 hours
- The half-life is 72 hours, which means it takes about 12 days before the agent is no longer in the blood.

Anyone planning to travel (and passing through a scanner at an airport, for example) should ask for a note from their doctor.

Dr. Terry Ruddy, Chief of Cardiology and Director of Nuclear Cardiology, explains to Health Minister Leona Aglukkaq how the Heart Institute’s advanced equipment helps improve cardiac diagnosis. The minister was at the Heart Institute to announce a $6-million federal contribution to research into alternative isotopes.
longer than they were before the Chalk River reactor shut down.

I should add that in the Heart Institute, we are also helping with the production of sodium fluoride. This is thanks to the foresight of Dr. Sandy McEwan [Special Adviser on Medical Isotopes to the Minister of Health]...the University of Alberta team, and the McMaster University group as well. We worked with them to submit a proposal to Health Canada, which was rapidly reviewed and approved.

We will now be ready to provide sodium fluoride as an alternative in bone-scan imaging in Ottawa. We’ll supply it to the Ottawa Hospital. The Heart Institute will also provide access to our cameras so that the patient overload at the Ottawa Hospital, we’ll be able to do some on our system as well.

I think one of the key things here is that we are working together within the city and with the Ottawa Hospital. The University of Ottawa [Heart Institute] is also working with the other cyclotron facilities across the country and with the nuclear medicine community to try to find solutions for the problem we now face.

I should add that we were recently at the Society of Nuclear Medicine meeting, and many of my colleagues in the cardiac imaging field commended us on the initiatives that we’ve taken already to solve this. We’re proud of that. I think we’ve been working together very well to try to achieve that.

Dr. Ruddy: I am also head of nuclear medicine at The Ottawa Hospital, so I look at business from both ends.

In the cardiac world we’re doing well. It’s more or less business as usual, but not exactly. When we switch to thallium from the technetium compound, we’re actually using a compound that has a less favourable symmetry and less favourable imaging characteristics. It’s adequate, but sort of borderline adequate. It’s a Band-Aid solution that works okay, but something you wouldn’t really want as a long-term solution.

So we need either our technetium compounds restored in a way that we can count on them, or we need to go into PET imaging to a greater degree. Technetium-labelled compounds for cardiac imaging are adequate or borderline adequate compared to PET. PET diagnostic accuracy is much greater in cardiac disease than SPECT technetium compounds. You can look at this as an opportunity to move more toward PET. That means more PET cameras across Canada and more development of cyclotrons so we can use a superior alternative to technetium, get away from the concern about technetium, and actually have better diagnostic imaging.

To offset future shortages, having more PET cameras across the country would be very desirable. It would also be very desirable for the bone scans that are at risk with our technetium shortage.

We made a decision to switch all our cardiac scans over to thallium, as well as to utilize the PET scanner for perfusion imaging, or blood flow imaging. That would allow us to enable our sister hospital, The Ottawa Hospital, where most of the cancer imaging is done, to do more bone scans.

* * *

Dr. Ruddy: So it isn’t a crisis; it’s a problem. The crisis is that this is a recurrent problem. We need a long-term solution. Either the MAPLEs [nuclear reactors] get turned on—that would be a good long-term solution—or get into PET in a big way and build PET centres at another 10 or 20 sites, which is more money. We could take the operating costs now for SPECT cameras and move them into PET so that the financial hit wouldn’t be that hard. We’d actually end up with a better clinical solution for our patients. We’d end up with PET across the country. That would be tremendous.

Dr. Beanlands: With the previous shutdowns we became aware that there could potentially be future problems, so we planned for this and we prepared ourselves and our staff for this type of eventuality.

The other issue is distribution. There’s a lot of imbalance in the way it’s being supplied in different jurisdictions. It’s an example of how we as a community take our leadership, we look forward to solving a lot of these problems as we go forward. Nuclear medicine is certainly an important community, but there are also cardiology patients and oncology patients who are being affected. These specialties also need to be engaged in the process, and I’m pleased to hear that this will be happening.

We’ve heard advice about having a special committee to look at MAPLEs. Would it be helpful to have some other mechanism to help coordinate access in the short term?

Dr. Beanlands: I think the issue is really a balance between providing more supply and providing alternatives. The supply needs to be available or increased in some way.

Conservative MP Patricia Davidson: If there were three things you thought we should be doing as a Health Committee towards making recommendations, what would your top three be to move forward in the short term?

Dr. Ruddy: I think the answer is more PET. Right now we’re at about 75 per cent of the technetium that we had, say, a year ago. We’re able to cope with that because we switched cardiac studies from technetium to thallium, so at 75 per cent we’re holding our own.

Thallium is not as good as technetium. Having greater access to PET would also be a solution. For every patient who has a PET scan or a thallium scan, that’s one less patient who needs to have a technetium scan. So all of these are solutions. I also still think that the medium- and long-term solutions cannot be ignored in this balanced approach. We must have some medium-term solutions for new things that come along, and longer-term solutions.

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Conservative MP Tim Uppal: Can you indicate how we’re doing globally compared to other countries?

Dr. Rob Beanlands: In terms of the cardiac field, at the recent Society of Nuclear Medicine meeting, certainly there were comments made about how—at least in the cardiac imaging realm—we’ve been able to manage this both at the Heart Institute but also nationally, in terms of being able to switch over to thallium. Many American centres haven’t used thallium for a long time and they’re looking to us for guidance in terms of how to make that switchover in their departments. So we’ve been an example that we should be proud of.

It’s an example of how we as a community have been able to work together to try to solve some of these problems. Certainly, with Dr. McEwan’s leadership, we look forward to solving a lot of these problems as we go forward.

Dr. Beanlands: It’s an example of how we as a community have been able to work together to try to solve some of these problems. Certainly, with Dr. McEwan’s leadership, we look forward to solving a lot of these problems as we go forward.
Telehealth Supports Heart Failure Patients while Saving Money

Leaving the hospital can be unnerving—medications to take, symptoms to monitor, lifestyle changes to make. The result? Patients can feel very alone. But for heart failure patients at the University of Ottawa Heart Institute, that’s not the case.

“Patients tell us that they love the ongoing connection,” says Christine Struthers, Advanced Practice Nurse for Cardiac Telehealth.

The connection Struthers is talking about is a home telehealth monitoring program that is helping to keep people healthy and out of hospital while saving money. “Heart failure is a growing burden with substantial health care costs that we can reduce through prompt intervention,” she explained. “A very common problem is compliance among patients who leave hospital then stop taking their medication.”

The program has cut hospital readmissions for heart failure patients in the six-month period after discharge from 69.4 per cent to 48.8 per cent, saving up to $12,000 for each patient safely diverted from an Emergency Department visit, re-admission and hospital stay.

Most important, says Struthers, who was instrumental in starting the program, is that the program enables patients to participate in their own care. “They really need to change their way of thinking. There’s a whole new idea about diet, including avoiding salt or processed foods, new medications, they need to monitor their weight daily. We professionals make it seem very easy, but it’s really not.”

To help patients make the transition from hospital to home, they are discharged from the hospital with home monitors that transmit pulse, weight, blood pressure, blood sugar and other important indicators over an ordinary phone line to a central station at the Heart Institute. Patients transmit the data each day for three months, along with answers to questions about things like shortness of breath. If they gain more than two pounds in a day or five pounds in a week, if they report waking up at night short of breath or if there is any other questionable answer, a nurse contacts them. The program also focuses on making resources available on subjects such as how to start a walking program or how to eat out in a restaurant safely.

The telehealth program strives to broadly address patient care by coordinating with the health care providers within the patient’s primary care team. “We work with family physicians to develop plans for medications, dosage increases, etc.,” says Struthers. “These are challenging, complex patients; sometimes the practitioners need help. This part of the program isn’t as well known as the patient connection, but it’s an equally important part.”

The program now supports more than 1,200 patients across the country and includes satellite sites in 31 hospitals in the Ottawa region.

The monitoring program is unique in that it is a hospital-led program (usually telehealth is part of the home-care system) and is being used for chronic disease management, instead of for acute care, such as surgical recovery. Also unique is the way it integrates three programs: the monitoring program itself; telemedicine, which permits consultation with specialists over the phone or via videoconference; and the interactive voice response (IVR) system, which provides ongoing distance care on a less-intense basis than the monitoring program.

“The goal is to promote self-care by patients, by giving them the tools to manage their own health and the resources to go to when they need help,” says Struthers. “They feel in control of their health. And hospital space is reserved for the necessary work that can only be done onsite.”

The Heart Institute Hosts “Genes and the Heart” Symposium

In June, the University of Ottawa Heart Institute was privileged to host “Genes and the Heart,” one of seven symposia held around Canada to celebrate the 50th anniversary of the Gairdner Foundation. Since 1959, the Foundation has presented the Gairdner International Award each year to a handful of international biomedical scientists nominated by their peers and selected through a rigorous selection process.

In his opening remarks at the symposium, Foundation President and Scientific Director, Dr. John Dirks, explained that the Awards were established “with the goal that they would eventually lead to the cure of diseases, such as coronary artery diseases, and alleviate human suffering by curing those diseases.”

Nearly 100 researchers have received the Gairdner International Award since its inception, and 71 of these awardees have gone on to win the Nobel Prize. Two former Gairdner awardees spoke at “Genes and the Heart” —Dr. Robert W. MacLennan of the University of Toronto and Dr. Jack Hirsh of McMaster University.

The two awardees were joined by invited guest speakers Dr. Duncan Stewart, CEO, Scientific Director and Senior Scientist of the Ottawa Hospital Research Institute, and keynote speaker Dr. Robert Roberts, CEO of the University of Ottawa Heart Institute and Director of the Institute’s Ruddy Canadian Cardiovascular Genetics Centre. The Heart Institute is proud to have been part of the Gairdner Foundation’s 50th anniversary celebrations and to aid in its goal of supporting and disseminating leading edge biomedical science. What follows is a summary of each of the “Genes and the Heart” presentations.

The First Common Genetic Risk Factor for Coronary Artery Disease

Dr. Roberts spoke on the discovery of the first common genetic risk factor for heart disease, discovered at the Heart Institute in 2007. His keynote address traced the search for genetic risk factors for cardiovascular disease back almost 20 years, to what he termed the “golden age” of single-gene disorder discovery. Although single-gene disorders predisposing a person to disease are rare—occurring in less than one-tenth of 1 per cent of the population—they are relatively easy to pinpoint. The discovery of a single-gene disorder requires only two things. The first is a family with 10 to 12 members identified as being affected with a particular disorder. The second is genetic linkage analysis technology, which uses 100 known genetic markers on the human genome to pinpoint the location of the responsible
What is Heart Failure?

Contrary to popular belief, heart failure is not a disease, but a chronic condition characterized by periods of stability interspersed with periods of deterioration, often acute. “Heart failure” is what happens after a series of “insults” to the heart that damages the heart muscle. When that happens, the heart can’t pump as efficiently. As a result, fluid builds up in the lungs, abdomen or legs.

Heart failure is most often caused by previous heart disease, including heart attacks or hardened arteries that result in a build-up of scar tissue. In younger people, heart failure can be caused by a virus or can be a congenital defect, since birth. The usual symptom of heart failure that sends people to their doctors or to the hospital is shortness of breath.

Heart failure is considered among the most challenging, complex forms of heart disease, requiring intensive treatment and frequent follow-up. This is, in part, why the telehealth program at the Heart Institute has been so effective. The condition is associated with substantial mortality, morbidity and health care costs. The goal of treatment is to eliminate symptoms through medication and lifestyle changes, such as lowering salt intake.

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Genome-wide association studies search for these variations in single units of DNA, called single-nucleotide polymorphisms (SNPs). Modern gene chip technology allows researchers to study half a million of these SNPs at a time, greatly reducing costs compared to genetic linkage analysis. Using case-control studies (which compare people with and without a disease) and gene chip technology, scientists at the Ruddy Canadian Cardiovascular Genetics Centre discovered the first common SNP that contributes to susceptibility to heart disease independent of any other known risk factor, such as blood pressure or diabetes.

This SNP, called 9p21, has since been verified in seven independent populations, and has also been shown to contribute to the risk of anxieties, indicating that it may cause a defect in the walls of blood vessels. The Heart Institute team is working hard to uncover the function of this area of the genome. Knowing the function of the gene will give researchers a target for developing treatments.

Types of stem cells under study for cardiac repair include endothelial precursor cells harvested from the blood, mesenchymal stem cells from the bone marrow or fat tissue, and myoblasts from the muscle. Cell-enhancement strategies use gene-transfer technology to engineer the stem cells to express proteins that may improve their post-transplantation number and function. A safety study called the PHACET Trial showed promising results for recovery of heart function after the infusion of endothelial precursor cells engineered to express an enzyme called endothelial nitric oxide synthase. This treatment is now being tested in a multicentre, randomized double-blind clinical trial called the EnACT-AMT trial at sites including the Heart Institute.

Can We Separate Bleeding from Clotting?

Dr. Jack Hirsh discussed the challenges faced in developing new antithrombotic drugs for the prevention of blood clots.

Other current activities include Genetics Centre participation in the international CARDioGRAM project, the goal of which is to find up to 80 per cent of the common genetic variants contributing to coronary artery disease.

Mending a Broken Heart with Stem Cells

Dr. Duncan Stewart spoke on the cutting-edge technology of using stem cells for the repair of heart tissue after a heart attack. Early clinical studies indicate that the approach can indeed work. Results have shown a 2 to 1 per cent increase in global ejection fraction (the amount of blood pumped out of the heart with each beat). This is similar to the improvement seen in randomized controlled trials of thrombolytic (anti-clotting) drugs.

An important question in the field is whether these results can be improved, through better patient selection for treatment, or by using different types of stem cells, changing the dose and timing of therapy, or enhancing stem cell function before treatment.

Gairdner Speakers: Esteemed speakers at the “Genes and the Heart” symposium included, from left to right, Dr. Duncan Stewart (Ottawa Hospital Research Institute), Gairdner Laureate Dr. Jack Hirsh (McMaster University), Dr. John Dirks (Gairdner Foundation), Gairdner Laureate David H. MacLennan, PhD (University of Toronto), and Dr. Robert Roberts (President & CEO, University of Ottawa Heart Institute).

The first gene for Wolf-Parkinson-White syndrome, which predisposes people to deadly arrhythmias, was discovered by a Dr. Roberts-led team using genetic linkage analysis. They went on to discover 12 genes used to identify the gene itself.

For example, the discovery of mutations in the gene that produces the protein LINC00768, which is working hard to uncover the function of this area of the genome. Knowing the function of the gene will give researchers a target for developing treatments.

Cardiovascular diseases and their complications are the leading cause of global mortality. Identifying the causes of these diseases is important to improve or develop treatments. For example, researchers understand the physiology of many cardiovascular diseases and improve or develop treatments. For example, the discovery of mutations in the gene that produces the protein LINC00768, which is working hard to uncover the function of this area of the genome. Knowing the function of the gene will give researchers a target for developing treatments.
And not having to order duplicate tests or medications, reducing their workload.

Additional diagnoses, test results or information that used to be kept in multiple silos—medications, lab results, clinic letters, just as they always were—is complete, physicians can simply adapt to it. The visit is over, and a copy is appended to the patient's electronic health record.

The Patient Database Management System (PDMS) brings together comprehensive clinical records of all cardiology patients seen at the Institute, without placing any additional burden on caregivers. Physicians simply dictate their clinic letters, just as they always have done. But rather than the traditional tape-based Dictaphone, they use a digital voice recorder. Once finished, they simply place the recorder in its cradle. The letter is then automatically transferred to a central repository and transcribed. A copy is sent to the referring physician, and a copy is appended to the patient's electronic health record.

The benefits of PDMS are easy to see. Information that used to be kept in multiple silos—medications, lab results, clinic letters—is consolidated in one place, instantly available to practitioners in most Ottawa hospitals. In this way, physicians can simply adapt the previous clinic letter to incorporate additional diagnoses, test results or medications, reducing their workload. And not having to order duplicate tests means more efficient use of resources and money saved.

The system also enhances patient safety, as all relevant information, including potentially life-threatening allergies, is always available. And, if a patient goes to the emergency department of any Ottawa Hospital campus, the physician can call up his or her health records within seconds, reducing potential delays in care.

Producing the system in-house has been significantly less expensive than a commercial solution. Development costs are only one quarter of the estimated $300,000 to $750,000 for commercial software.

Today, PDMS is used for all outpatient records in Cardiology and Cardiac Rehabilitation at the Heart Institute, improving patient care and outcomes. Dr. Davies credits involving his fellow cardiologists along the way with ensuring the system is used.

“I listened to them and adapted the system to how they practice, rather than asking them to change,” said Dr. Davies. “As a result, there’s been 100 per cent adoption of PDMS. It’s a win-win situation for doctors and patients.”

The success of PDMS has been recognized beyond medical circles in the IT world. The system has been named a 2009 Laureate in the Computerworld Honors Program in the health care category. It also received the 2008 Health Innovation Award from the Ottawa Centre for Research and Innovation (OCRI).

The developers now have plans to take PDMS further. First in line is a move to fax server technology, enabling the system to fax authenticated letters directly to referring physicians. This will save money, as letters won’t have to be printed, placed in envelopes and mailed. And, adds Dr. Davies, it’s much faster.

“Someone who comes for an appointment from an outlying town in the region won’t even be home yet before his physician has the results of his visit,” he says.