

Groundbreaking Canadian stroke study ‘unprecedented in scope’

Registry reveals who suffers a stroke, where, when and why

The world’s most ambitious study ever of stroke patients is well ahead of target and already providing an early snapshot of stroke and stroke care in Canada.

Just six months after its launch, 3,282 stroke patients have been enrolled in the Registry of the Canadian Stroke Network, more than half the 6,000 patients organizers hope to have signed-on in the first year. Twenty-one participating hospitals are now enrolling patients and have begun collecting data.

“Things are really moving along nicely,” says CSN investigator Dr. Frank Silver, a University of Toronto professor of neurology who is overseeing the project with Dr. Stephen Phillips of Dalhousie University.

While the project is still in its early days, a preliminary analysis of 492 patients for whom researchers have complete data reveals:

- 22% of strokes were evident when the patient woke up; the stroke was recognized in one in five patients on awakening;
- 58% of stroke victims were male;
- hemorrhagic strokes, which occur when a blood vessel in or around the brain ruptures, accounted for about 20% of all strokes, while the remainder were ischemic strokes (caused by a blood clot in an artery in the brain);



Just six months after its launch, about 3,300 stroke patients have been enrolled in the Registry of the Canadian Stroke Network.

- about 40% of patients arrived at hospital by ambulance;
- 25% of patients arrived at the emergency room within two hours of the onset of stroke symptoms; 43% of patients arrived within five hours of their stroke.

“That’s bad, because we want patients to get to hospital a lot faster than that,” Dr. Silver says.

Treatment with the clot-busting drug t-PA can dramatically lower the risk of a patient being left with irreversible brain damage following a stroke, but it must be used within three hours of when a stroke begins to be used safely.

In the preliminary analysis, only 7% of patients received t-PA.

See **REGISTRY** on page 2

Inside

Brain repair research holds promise **3**

First three hours post-stroke ‘critical’ **5**

Telestroke brings patients within ‘electronic arm’s length’ of specialists **7**

Canadian Stroke Network study probes affect of stroke on patients and families **9**

Core facility saves time, money for researchers **10**



Réseaux de centres d'excellence
Networks of Centres of Excellence

Registry: World's richest stroke database

Continued from page 1

Dr. Silver said that number was slightly better than what researchers expected they would find, given that earlier studies have found that only about 3% to 5% of stroke patients receive t-PA, but he still said it should be much higher.

"We'd like to see the number closer to 10% or 15%, so we've got our work cut out for us," Dr. Silver says.

The registry is unprecedented in its scope. Previous registries were much smaller and usually involved only one or two hospitals.

The Canadian registry, by comparison, will involve 24 hospitals across the country, including large tertiary-care teaching facilities and community hospitals. Three northern Ontario hospitals will also participate through the Telestroke project. (See Telestroke story on page 7).

The information collected will include how long it took patients to reach hospital after a stroke, how quickly they were investigated, how soon they were seen by rehabilitation specialists and whether patients who received different kinds of care had better outcomes.

The data will allow investigators to identify variations in how stroke patients are managed between provinces – and between hospitals – and feed that information back to hospitals and health ministries. For example, researchers plan to calculate a hospital's average "door to needle" time – the time it takes staff to administer medication from the moment a stroke patient comes through the emergency room doors.

"We're not planning to name hospitals, but we will be feeding confidential information back to that hospital and compare their outcomes to pooled outcomes from other hospitals. We'll be able to show them graphically, and with statistics, their outcomes as compared to



Patients enrolled in the Registry will be followed for 10 years.

five similar hospitals in the region," Dr. Silver says. "It's a very powerful feedback loop to improve care."

In addition, patients will be tracked for up to 10 years using a "linkage study", which allows investigators to link patients to provincial government databases that track admission and discharge information from Canadian hospitals.

Dr. Silver stressed that the data collected is completely anonymous and stripped of any identifying information, so there is no breach of privacy to patients.

"But it will mean that we can see exactly what kind of care the patient received over the next 10 years, and how many times that patient was re-admitted to hospital with other problems. No one else has ever been able to do this to this degree."



The Canadian Stroke Network

David Scott, Chair, Board of Directors

Dr. Antoine Hakim, CEO and Scientific Director

Dr. Paul Morley, Deputy Scientific Director,

Katie Lafferty, Executive Director

Cathy Campbell, Newsletter editor

Sharon Kirkey, Writer

Contact us at:

451 Smyth Road, Ottawa, ON, K1H 8M5

Tel: 613-562-5696

Fax: 613-562-5403

Email: csn@uottawa.ca

Website: www.canadianstrokenetwork.ca

Publication Mail Agreement Number
40609522

The contents of this newsletter may be reprinted or used on radio or television without permission. However, a credit is requested. In print, please send a copy to the Canadian Stroke Network.

Brain repair research holds promise

Network seeks key to reversing stroke damage

Researchers with the Canadian Stroke Network are working on ways to achieve the once unimaginable: reverse brain damage due to stroke by harnessing the brain's own extraordinary ability to repair itself.

Investigators are uncovering intriguing clues into the brain's capacity to replace dead neurons with fresh new cells, as well as the role genes play in coaxing brain cells to regenerate and form new connections with neighboring cells.

The work promises to one day lead to an entirely new approach to the treatment of stroke, from preventing and limiting damage to actually restoring lost brain function.

And it is challenging long-held scientific dogma that humans are born with a finite number of neurons, and that once these brain cells die or are damaged as a result of an injury such as a stroke, they are lost for good.

Doctors know that stroke survivors can make improvements in abilities such as dressing, walking or washing for up to two years following a stroke, says Dr. Antoine Hakim, Scientific Director of the Canadian Stroke Network.



Research will lead to an entirely new approach to the treatment of stroke, from preventing and limiting damage to actually restoring lost brain function.

Neurologists have shown that some return of function can occur up to five years after a “brain attack.”

“Why is this happening? Some of it may be compensation, not true repair but just learning to ‘get around’ the deficit.” True brain recovery, Dr. Hakim says, means the function that was lost returns.

“If you just start with the fact the brain has mechanisms to return lost function after stroke, then the conclusion must be that either those dead neurons are replaced by fresh neurons, or the neighbors learn to do new tricks they couldn’t do before. It turns out the answer is both.”

A human embryo has early versions of neurons called neuronal stem cells that can develop to take up different functions in the brain. For a long time scientists believed that soon after birth

these matured and connected into a fixed network, and the genes that once allowed them to be flexible or “plastic” in the embryo were turned off for good.

“We thought wrongly, until three years ago, that as adults, once a neuron died we had lost the ability of getting new neurons. It turns out that’s not true,” Dr. Hakim says. “There is this incredible ability for new cells to be born and to be directed and grow to their destination.”

University of Calgary scientist Sam Weiss was one of the first to discover stem cells, the master cells that have the ability to grow into other cell types, in the brains of adult mice in 1992; his team is now nourishing stem cells with molecules called growth factors and testing ways to get the cells into injured areas of the brain in lab animals.

Small reservoirs of stem cells have also been discovered in the adult brain. Researchers believe these reserve supplies remain dormant in the brain after birth but are activated after a stroke. Yet only about 1% or so survive to become new neurons. Researchers with the Stroke Network are trying to understand why.

“In the setting of a stroke, can we manipulate these stem cells to move more rapidly, survive in a more controlled way, talk to their neighbors in a more efficient way, do it faster and do it sooner?” Dr. Hakim asks. “We don’t know, but we are beginning to understand how to manipulate stem cells and how to manipulate the environment for repair.”

The ultimate goal would be to develop therapies that would mobilize and somehow pilot a patient’s own neuronal stem cells to the damaged areas of the brain immediately following a stroke.

See REPAIR on page 4

Repair: New therapies on the way

Continued from page 3

It may also be possible one day to inject or transplant stroke patients with stem cells harvested from other areas of their body, such as their bone marrow or even skin. Freda Miller and her team at McGill University's Montreal Neurological Institute recently succeeded in capturing stem cells from the skin of adult mice as well as a human scalp that were capable of growing into brain cells, including neurons.

Meanwhile, Dr. Hakim and other Canadian Stroke Network scientists are looking at the cascade of genetic reactions that occur immediately after a stroke, research that could one day open the door to gene therapy to treat stroke.

"When a stroke happens, the brain is rejuvenated, it goes back in time to when it was just developing, and all the genes that used to be there when the brain was just a baby come back."

"We're looking at these genes sequentially over time after a stroke and what we are learning is just what turns on. More than 200 genes turn on 10-fold; many more turn on five-fold. We're talking about an incredible amount of activity in the brain around the area of injury."

But while some of the genes switch on, others are suppressed. Understanding more about these genetic stop and start commands, and how to switch them on and off, could lead to new treatments to limit or even reverse stroke damage.

While much of what lies hidden in the brain's "black box" remains a mystery, new therapies for brain repair and regeneration could be ready for clinical trials within two years.



Already, CSN researchers have found that physiotherapy appears to activate some of the development proteins that used to exist in the brain.

"Physiotherapy just makes the brain more ready for recovery," Dr. Hakim says. Recently, researchers in Toronto and the U.S. have discovered that giving amphetamines after stroke along with physiotherapy results in improved and faster recovery for patients.

Physiotherapy is also essential in getting healthy neurons to sprout new communication lines in order to take over for their stroke-damaged neighbors. "We don't know how or why, but we know the re-training is absolutely crucial. The curve of recovery is going to look very different if the patient gets, or doesn't get, physiotherapy," Dr. Hakim says.

While much of what lies hidden in the brain's "black box" remains a mystery, he believes new therapies for brain repair and regeneration could be ready for clinical trials within two years.

"It's coming that soon. And the Canadian Stroke Network wants to be first."

Canadian Stroke Network Board of Directors

Dr. Antoine Hakim, MD, PhD, University of Ottawa

Paul Morley, PhD, National Research Council

Katherine Lafferty, BSc, MBA

David. W. Scott, (Chair of the Board of Directors) Q.C., Borden Ladner Gervais LLP

The Right Honorable Ramon J. Hnatyshyn, Gowling Lafleur Henderson LLP

William G. Tholl, CEO, Canadian Medical Association

Gerald McDole, President and CEO, AstraZeneca Canada

George Jackowski, PhD, Chief Scientific Officer and Vice-Chair, SYN-X Pharma Inc.

Frank Nieboer, Stroke Recovery Association of Alberta

Louise Nieboer, Stroke Recovery Association of Alberta

Joy Calkin, PhD, Deputy Chair, Extencicare Inc.

Susan Crocker, Corporate director

Brian Field, MBA, Executive Vice-president, Interdev Technologies

Arthur J. Carty, PhD, President, National Research Council Canada

Dr. H.J.M. Barnett, MD University of Western Ontario

Dr. Alastair Buchan, MD, PhD, University of Calgary

Dr. Gregory Del Zoppo, Scripps Research Institute

Dr. Richard Riopelle, MD, PhD, McGill University

Howard Alper, PhD, Vice-Rector, Research, University of Ottawa

Eniko Megyeri-Lawless, Networks of Centres of Excellence

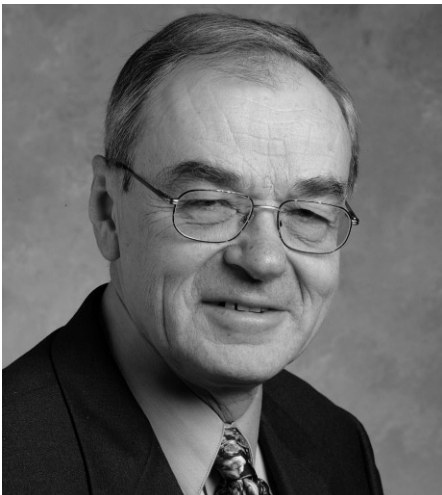


Stroke is a medical emergency and its victims need to seek immediate medical attention.

First three hours post-stroke ‘critical’

When it comes to stroke, “time is brain.” The faster a person gets to hospital, the greater the chance of surviving a stroke and escaping devastating brain injury.

So what should you not do if you suddenly experience a strange numbness in one arm, or droopiness on one side of your face? Do not go back to bed and wait to see if it gets better in the morning. Do not finish folding the laundry. Do not leave a message on your doctor’s answering machine and wait for her to call back when the office opens.



Dr. Vladimir Hachinski

Treatments exist today that, if administered within three hours of the onset of symptoms, can dramatically reduce the risk of serious disability, or death from stroke.

Yet studies show that more than half of stroke victims fail to get to hospital soon enough to benefit.

A large part of the problem is that fewer than 30 per cent of Canadians even recognize the symptoms of stroke, such as a sudden numbness or weakness of the face, arm or leg or sudden difficulty speaking or walking.

But doctors say it is not enough to know the warning signs. It’s crucial that stroke victims get to a hospital or health-care facility that has the staff and equipment needed to administer rapid treatment. That means having an emergency plan in place before a stroke strikes.

“For a patient who suffers a stroke, the first thing is to recognize the symptoms as potentially something happening in the brain that could have permanent consequences,” says Dr. Vladimir Hachinski of the University of Western Ontario, one of the leaders of stroke prevention research for the Canadian Stroke Network.

“You have to find a way to transport yourself to a health-care facility. The health-care facility has to recognize this is an absolute emergency and they have to have the staff and physical infrastructure to manage the patient,” Dr. Hachinski says.

“When all these things happen, we have a drug. The goal is to get the patient to that drug.”

It was Dr. Hachinski who coined the term “brain attack” for stroke – as a way of making the condition understandable to patients and emphasizing the urgency of receiving medical attention.

Stroke is the third leading cause of death in Canada and the number one cause of long-term disability in Canadians. Every year, 50,000 Canadians suffer a stroke, 60 per cent of whom will be left with some form of disability.

It doesn’t have to be that way.

Until about a decade ago, no emergency treatment existed for stroke. Today, the clot-busting drug t-PA, or tissue plasminogen activator, can restore blood flow to the brain and substantially limit neurological damage due to stroke.

See **CRITICAL** on page 6

Critical: ‘It’s important to be proactive’

Continued from page 5

But it has to be administered quickly – within three hours of the onset of symptoms – and to the proper patients. About 80 % of strokes are ischemic strokes, which occur when a blood clot forms in an artery supplying a region of the brain. Administering t-PA intravenously can dissolve or lyse those blood clots, restoring blood flow to the brain. Canadian Stroke Network researchers are now exploring giving t-PA directly into an artery within six hours of a stroke. But about 20% are hemorrhagic, caused by a ruptured blood vessel in the brain. Giving clot-busting drugs to patients whose brains are bleeding would cause even further damage.

Dr. Hachinski says that is why it is crucial for stroke victims to get to hospitals that are equipped with CT scans, which can determine the type of stroke they have suffered, as well as staff available 24 hours a day to administer the scans. In addition, the hospital should have emergency personnel experienced in using t-PA.

“Most emergency rooms that have CT scans can give t-PA to stroke patients,” Dr. Hachinski said. “Most physicians accept that this is an effective therapy and are learning how to evaluate the CT scan before giving this drug to appropriate patients.”

That has made it all the more important for stroke patients to get to hospital quickly. Dr. Hachinski says people at high risk for stroke, including those with a family history of stroke or known risk factors such as high blood pressure, diabetes or obesity, should have an



The symptoms of stroke:
Sudden numbness or weakness of the face, arm or leg, especially on one side of the body; sudden confusion, trouble speaking or understanding; sudden trouble seeing in one or both eyes; sudden dizziness, loss of balance or coordination or trouble walking; sudden severe headache with no known cause.

emergency plan in place. “Remember this: 30 % or more of stroke patients are not going to be able to speak, or understand language.” People at high risk of stroke who live alone should have access to a medical alarm system, or work out in advance an emergency response with a neighbor or relative.

In addition, people should know the location of the nearest hospital that is set up to receive and rapidly treat a stroke patient. “It is worthwhile for patients who know that they’re at risk to call their hospital and ask: Do you have a stroke person on-call for strokes

at all times? Do you have a CT scan? Are you able to give t-PA?,” Dr. Hachinski said. If the closest hospital isn’t equipped to deal with a stroke, people could contact other hospitals within a 45- to 60-minute drive of their home.

But the most important step is to know the signs of stroke. Call 9-1-1 or seek immediate medical attention if you experience one or more of the following symptoms: Sudden numbness or weakness of the face, arm or leg, especially on one side of the body; sudden confusion, trouble speaking or understanding; sudden trouble seeing in one or both eyes; sudden dizziness, loss of balance or coordination or trouble walking; sudden severe headache with no known cause.

Sometimes the symptoms can disappear within minutes. But these “mini-strokes”, which are known as transient ischemic attacks and are caused by a temporary decrease or blockage of blood flow to the brain, should be taken just as seriously, because they can be a precursor to a full-blown stroke.

With stroke, every minute counts. “It’s important for people to be proactive,” Dr. Hachinski says.

Telestroke brings specialists within an ‘electronic arm’s length’ of patients

A 69-year-old retired miner arrives at a Sudbury hospital unable to move his arm; his speech is slurred and he can’t make sense of what everyone around him is saying. The emergency room doctor quickly determines the man has suffered a stroke, but he’s not certain whether it’s safe to inject the patient with the powerful clot-buster, t-PA.

Within minutes, a stroke specialist from Toronto is “virtually” transported to the patient’s bedside. Using sophisticated two-way video conferencing equipment, the neurologist reviews the brain scans taken of the patient lying on a hospital bed 400 kilometres away. He asks the man to hold up his arm and to move his eyes from side to side; he talks to the patient’s family members and then discusses offline with the emergency doctor how best to proceed.

Scenes like this will soon be played out in three northern Ontario communities under an innovative program designed to save lives and reduce permanent severe disability due to stroke.

The Telestroke program will connect stroke patients at Sudbury Regional Hospital, North Bay General Hospital and Thunder Bay Regional Hospital with stroke specialists at the Toronto Western Hospital and Sunnybrook and Women’s College Hospital in Toronto.

“We don’t have the human resources to put stroke specialists in all remote hospitals, but this is a way to bridge that disparity between urban and rural centres by bringing the stroke experts to the smaller hospitals in a virtual sense.”



Prompt treatment is critical when it comes to stroke. The longer it takes to diagnose and treat a “brain attack”, the greater the neurological damage, and the more brain function that is likely to be sacrificed.

The pilot project, which is expected to go “online” in early April, will put stroke specialists no further than an electronic arm’s length away from emergency doctors in the three remote communities, day or night, says Dr. Frank Silver, of the Canadian Stroke Network.

“One of the biggest problems with health care is that there is not uniform access to care. People in bigger urban centres tend to get more sophisticated care than smaller centres. We don’t have the human resources to put stroke specialists in all these hospitals, but this is a way to bridge that disparity by bringing the stroke experts to the smaller hospitals in a virtual sense.”

The CSN has partnered with the NORTH network, an organization established to promote telemedicine in Ontario, to test the program in Canada.

Prompt treatment is critical when it comes to stroke. The longer it takes to diagnose and treat a “brain attack”, the greater the neurological damage, and the more brain function that is likely to be sacrificed.

While t-PA has become the standard treatment for ischemic strokes, which occur when a blood clot lodges in an artery in the brain, blocking blood flow and starving the brain of oxygen, it must be administered within the first three hours of the start of a stroke. In addition, because t-PA can make hemorrhagic strokes even worse, doctors have to be certain the stroke is ischemic and not hemorrhagic before administering the clot-busting therapy.

See **TELESTROKE** on page 8

Telestroke: Expanding access to advanced care

Continued from page 7

Having a stroke specialist electronically transported to the patient's bedside can help rural doctors who may be uncomfortable using t-PA make the most appropriate treatment decision.

Under Telestroke, portable stroke "carts" will be installed in the emergency rooms of the three northern medical centres. Each cart includes teleconferencing equipment, a high-quality video camera, television monitors, microphone and electronic stethoscope.

According to Dr. Silver, here's how it would work: Protocols have been put in place in each rural hospital to help emergency staff rapidly assess whether a patient is having a stroke and might be a candidate for t-PA. If the patient meets the criteria for the intravenous medication, the emergency physician will call CritiCall, the Ontario government's 24-hour emergency referral program. The operator will connect the physician with an on-call stroke specialist at one of the two participating Toronto hospitals.



Dr. Frank Silver

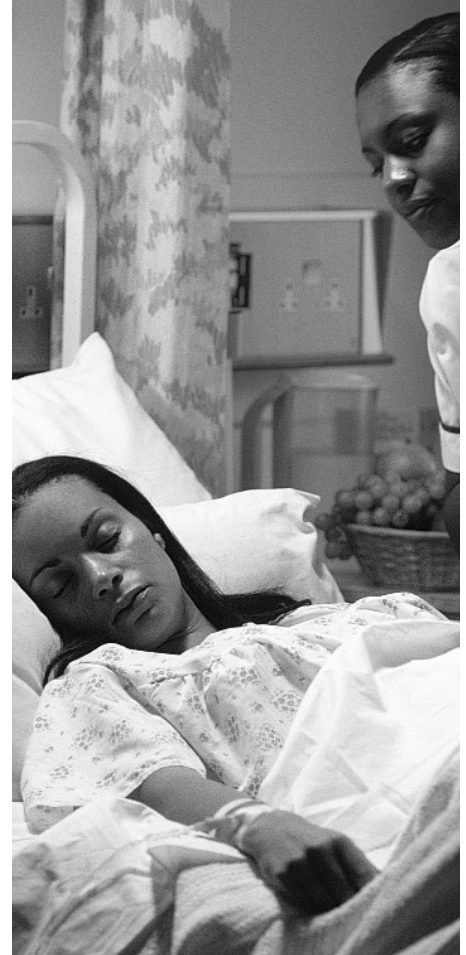
Whether the consulting doctor is at home or work, sophisticated computer software will allow the specialist to simply switch on a laptop computer and read the patient's CT scans "to see if there is any reason, based on the scan, that the patient may not be a candidate for t-PA," explains Dr. Silver, an associate professor of neurology at the University of Toronto. "If everything looks fine, but I want to talk to the patient to clarify some of the findings, I'll tell the emergency physician to activate the 'Intern' – portable teleconferencing equipment for medical applications produced by Tandberg. The mobile unit allows two-way, real-time video and audio communication between the physician and patient.

"The patient will be able to talk to me directly and see me on the TV monitor, and I'll be able to see them. I can explain to the patient and the family what's involved in the treatment, what the risks and benefits are, and then make the final decision with the emergency physician whether to treat with t-PA or not."

A second "tele-radiology" project will link a hospital in Stratford with radiologists in London, Ont., who will be on-call to provide expert interpretation of CT scans of patients in Stratford.

The installation of the Telestroke network, including the high-speed connections between participating hospitals, is expected to be completed by April. The Canadian Stroke Network is also providing support for local nurse co-ordinators in each remote centre to oversee the system.

"If we can show that we get buy-in from the northern doctors, that patients are happy and that we are actually expanding the access to advanced stroke care to



Having a stroke specialist electronically transported to the patient's bedside can help rural doctors make the most appropriate treatment decision.

these distant communities, then hopefully we can get support from government to fund us on a much larger scale," Dr. Silver says.

"The patient will be able to talk to me directly and see me on the TV monitor, and I'll be able to see them. I can explain to the patient and the family what's involved in the treatment, what the risks and benefits are, and then make the final decision with the emergency physician."

‘Our lives changed overnight’

Stroke Network study probes affect of stroke on patients and families

Celia Turnbull is struggling to come to terms with a sudden reversal in family roles neither she nor her mother wanted.

Celia’s 78-year-old mother, Sara, recently suffered a stroke that has left the once dynamic and exceptionally independent Montreal woman weak, disoriented and dependent on her daughter.

“Our lives changed overnight,” says Celia, a mother of four. “It’s like nothing we’ve ever dealt with.”

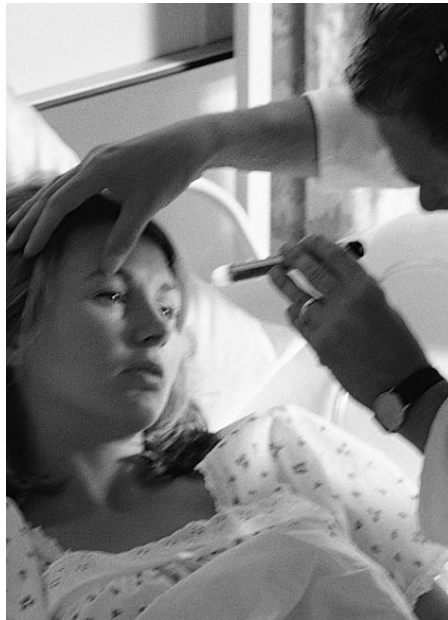
This year in Canada, about 50,000 people will sustain a stroke. Of those who survive, up to 60 per cent will be left with varying degrees of disability, making stroke the leading cause of adult disability in Canada.

But surprisingly little research has been done on the quality of life of stroke survivors – and even less on how stroke affects the lives of the spouses, adult children or parents who take care of them.

A novel Canadian Stroke Network study now underway will change that. Headed by Dr. Sharon Wood-Dauphinee, of McGill University’s School of Physical and Occupational Therapy, the study will explore the physical, emotional and social impact of stroke on survivors and their caregivers.

Stroke doesn’t just affect an individual. It touches an entire family. While 75% of stroke patients eventually return to the community, “this return is dependent upon a caregiver, usually a family member who is prepared to look after them,” Dr. Wood-Dauphinee says. “And it’s a major, major commitment.”

With the incidence of stroke in Canada expected to soar over the next seven



With the incidence of stroke expected to soar as baby-boomers age, the toll on caregivers will grow.

years as baby boomers age, the toll on caregivers will only grow.

But much of the research on the impact of caregiving has focused on the psychological consequences. In particular, depression has been studied, but there are many other effects, such as loss of free time, changes in relationships or finances.

In addition, most of the care-giving literature is related to Alzheimer’s, a disease with a far different course. “With Alzheimer’s, you see a person begin to deteriorate, and it’s a long process, so that the caregiver makes small changes in their lifestyle over a few years,” Dr. Wood-Dauphinee says. “In stroke, you’ve got somebody who is relatively healthy one day, and is paralyzed the next.”

The study will look at how stroke affects a patient’s basic activities of daily living, such as dressing, personal hygiene and the ability to move around independently, as well as the impact on their emotional well-being and their roles as spouses or

parents. For caregivers, researchers will explore the stresses on family members suddenly thrust into the role of nurse and housekeeper, from the physical demands – helping people dress or move around – to the psychological, such as learning how to cope with a loved one who suddenly may be prone to violent outbursts, or who can’t communicate properly.

Further, the study will explore the factors that can ultimately lead to a family’s painful decision to institutionalize a loved-one with stroke – and what can be done to intervene and help keep stroke survivors at home.

There are not only negative impacts of caregiving, Dr. Wood-Dauphinee stresses. “People have identified that there are things that are positive about providing care, in terms of how people feel about themselves and their relationship with their loved-one. Most of the literature has to do with the burden of caregiving. What we’re trying to say is that there are positive aspects as well, and if you’re going to talk about the quality of life of caregivers then you have to investigate both.”

Investigators will also look at whether technology in the form of assistive devices and technical aids actually increases independence and improves a stroke patient’s quality of life.

Two hundred people with stroke and their caregivers will be recruited from centres in Montreal, London and Toronto and followed for one year.

“I think enhancing quality of life is the final goal of health care,” Dr. Wood-Dauphinee says.

“We’re all trying to get patients and caregivers back to as productive lives as they had before, to the extent that it’s possible.”

See FAMILIES on page 10

Unique lab helps researchers save time, money

A unique Ottawa laboratory is turning a common cold virus into microscopic cargo carriers to shuttle healthy DNA into cells – and helping top Canadian stroke researchers explore the enormous potential of gene therapy in the process.

The Adenovirus Core Facility is constructing customized viral vectors or messengers for use in gene therapy projects. The facility uses a disabled adenovirus – the virus that causes the common cold – to deliver healthy copies of genes into cells to replace faulty or missing genes.

Established two years ago, initially with a Canadian Foundation for Innovation new opportunities grant to Ruth Slack and David Park, the facility produces vectors for researchers at cost, and has now expanded to provide the service to members of the Canadian Stroke Network.

“Since producing this vector can be difficult and costly for individual laboratories, the core facility saves Canadian researchers a great deal of time and expense, because it’s streamlined to generate large quantities of these vectors,” says Dr. Slack, a professor in the department of medicine and department of cellular and molecular medicine at the University of Ottawa.

“This is a delicate operation, and it takes training to do it well,” adds Dr. Antoine Hakim, Scientific Director of the Canadian Stroke Network.

The Adenovirus Core Facility is constructing customized viral vectors or messengers for use in gene therapy projects.

“The question was: ‘Why force all the labs across the country to learn this technique? Why don’t we offer it to them at cost?’ ”

Defective or mutated genes cause many diseases. Gene therapy aims to deliver a healthy copy of a missing or misfiring gene into the abnormal cells and restore normal function.

But finding an effective way to get these repair genes to where they are needed has been a challenge. Researchers have been experimenting with different viruses engineered to act as a kind of gene-delivery van. The adenovirus, in particular, is being used because of its ability to infiltrate a wide range of cells.

The Ottawa facility uses a disabled adenovirus that is “replication defective”, meaning it can’t reproduce and cause infection, as a gene-delivery tool.

Lab manager Steve Callaghan, who operates the facility along with his technician, Sean Sebastien, is “highly experienced” in producing the vectors, Dr. Slack says. “Steve also keeps up to date with the latest technology and constantly improves the vectors provided to users.”

Investigators send a DNA fragment of the gene they want engineered into an adenovirus vector. The facility then constructs the vector, purifies the recombinant virus and grows large preparations of the virus.

The adenovirus is being used in a number of gene therapy projects. Researchers are using it in the delivery of the hormone leptin for the treatment of obesity, as well as a gene delivery system for neurons.

“Expressing genes in neurons is notoriously difficult, and an adenovirus engineered to deliver the gene of interest serves as an efficient system, and relatively safe method,” Dr. Slack explains.

The facility has generated more than 100 vectors in the last year for CSN investigators alone, and receives new requests daily.

The viruses are being used to explore the molecular mechanisms that regulate neuronal cell death, or to block cell death using “pro-survival” genes that keep cells alive. The viruses are being tested in cell cultures and also in lab animals used in stroke studies.

“The response has been excellent,” Dr. Slack says. “The facility provides high quality reagents to CSN laboratories at minimal cost, and greatly facilitates research projects involving the use of these vectors.”

Families: ‘It was really worth it’

Continued from page 9

Dr. Wood-Dauphinee recalls the phone call she recently received from a man whose wife died a few weeks ago following a stroke. “He kept her home for two-and-a-half years. He said it was really worth it, but that it would have

been so much easier if he had had a break every now and then. He couldn’t get any respite, he couldn’t get any relief.”

“These are the kinds of things we’re trying to get a handle on.”

Investigators in the *Understanding Health Related Quality of Life (HRQL) Post-Stroke: A Study of Individuals and Their Caregivers* are Sharon Wood-Dauphinee (Montreal), Nancy Mayo (Montreal), Angela Cheung (Toronto), Jane Garland (London), Jeff Jutai (London), Mark Bayley (Toronto)