BRAIN ATTACK COUNTERATTACK

Stroke, which strikes 50,000 Canadians each year, is the most prevalent cause of brain disability, but it's also preventable. That's why researchers, who have made great advances in treatment, are executing an earlier line of defence: prevention

"It was like a miracle."

That's how Richard Westwood describes what happened the evening of January 24, 2009.

Mr. Westwood was watching hockey on television when he called out to his wife Lois in the next room of their North York condominium. She didn't answer. He went to check on her and found she couldn't speak. Worried she might be having a stroke, he called 911, and within a few minutes the fire department arrived, followed by an ambulance.

The paramedics recognized it was a stroke—Mrs. Westwood's entire left side was paralyzed—and transported her directly to Sunnybrook's Regional Stroke Centre, bypassing the nearest hospital emergency departments. A computed tomography (CT) scan showed a clot had blocked blood flow to her brain. The Sunnybrook stroke team quickly administered a clot-busting drug called tissue plasminogen activator (tPA) that began to dissolve the clot. Feeling returned to her foot, then limbs, about two hours later.

After a night of careful monitoring, Mrs. Westwood regained all movement in her left side, and another CT scan showed the clot was gone. A few days later she was home, fully recovered.

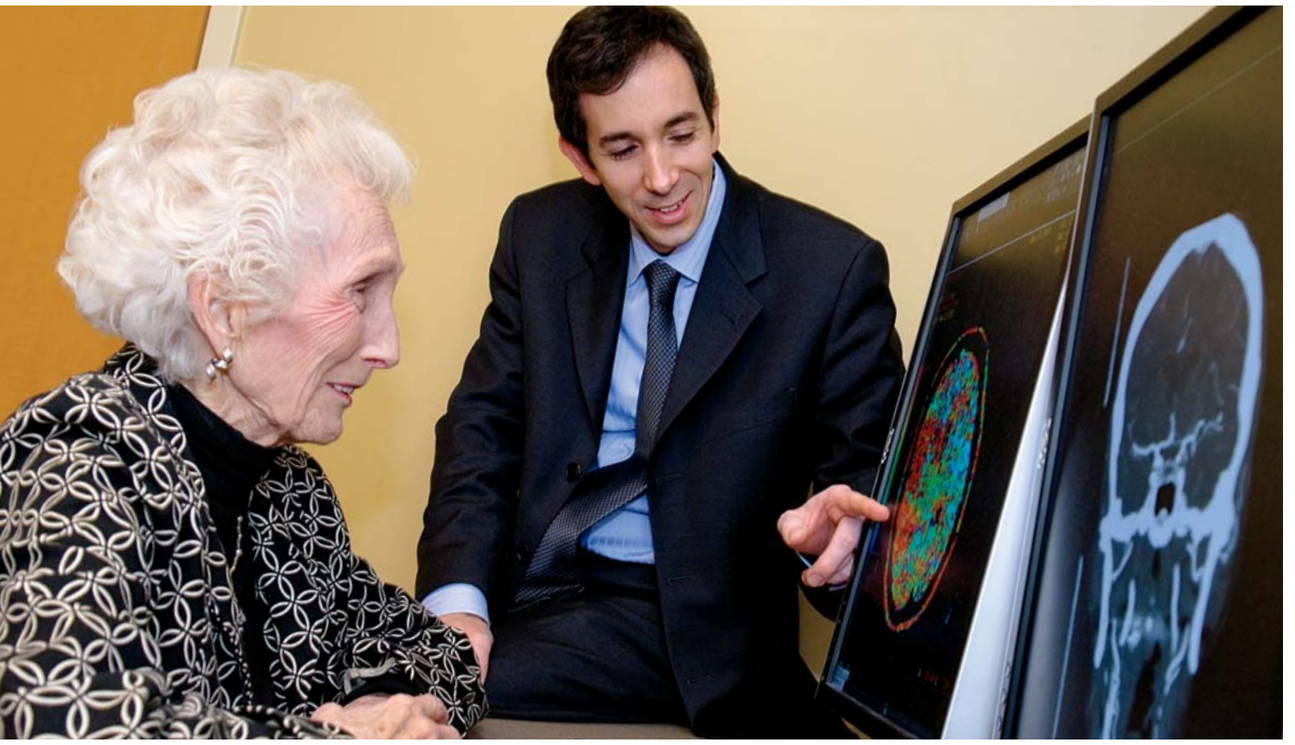
On the phone from her home nearly one year later, the month after her two great-granddaughters visited from California and a day after her twice-weekly carpet-bowling outing, Mrs. Westwood was upbeat.

"I'm doing very well. I have pretty much everything I could want," she said.

Mrs. Westwood's treatment success was part of a Toronto-wide Code Stroke protocol, implemented by the Ontario government in 2005 to speed acute stroke patients to a Regional Stroke Centre for initial management. The protocol addressed the problem of limited accessibility to tPA, which at the time was not reaching many patients because not all hospitals offered this therapy, and there has been a three-hour post-stroke time window in which it must be delivered.

"It's an important initiative," says Dr. David Gladstone, director of the regional stroke prevention clinic at Sunnybrook, who was called in to treat Mrs. Westwood in the emergency department the night of her stroke. "When it works well, tPA can reverse the signs and symptoms of a stroke within minutes. But timing is critical—the faster tPA can be administered, the greater the chance of a good outcome."

In 2009, Gladstone, a scientist at Sunnybrook Research Institute and assistant professor in the department of medicine at the University of Toronto, published a paper in the journal *Stroke* that examined the initial success of the Code Stroke protocol at Sunnybrook. Gladstone and his colleagues found that Sunnybrook treated four times as many patients with tPA immediately after the protocol was launched compared to the same time period the previous year,



LOIS WESTWOOD AND DR. DAVID GLADSTONE

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thereby achieving one of the highest stroke treatment rates in North America. Delays between stroke onset and drug administration also decreased significantly.

Gladstone says he is hopeful that this type of stroke protocol can be sustained, but meanwhile he's making strides in another area of stroke research: prevention. "Prevention is much better than a cure, especially when dealing with stroke," he says.

Noting that stroke has reached "epidemic" proportions—it's now the world's second-leading cause of death and the most common cause of neurological disability among Canadian adults—Gladstone says that the societal burden of stroke will worsen in the coming years without a major shift toward optimizing prevention strategies.

Of particular concern for Gladstone in effecting that change is improving the diagnosis and treatment of atrial fibrillation, a common condition in which the heartbeat can become sporadically irregular, and which is one of the biggest risk factors for stroke. Up to one in three strokes is "cryptogenic," meaning of unknown cause, but Gladstone believes many of these strokes are related to undetected, intermittent atrial fibrillation.

He is therefore leading a multicentre, cross-Canada, randomized controlled trial called EMBRACE that will investigate a new diagnostic strategy to detect atrial fibrillation in patients who have had an unexplained stroke or mini-stroke. Patients will wear a heart-monitoring device attached to a soft belt, which will check for arrhythmias for 30 days continuously. Gladstone says he suspects it will be more effective than the standard one- or two-day monitoring approach now used. "If we can improve the early detection of atrial fibrillation in this high-risk population, then more patients will receive appropriate blood-thinning medication, and more strokes, deaths and disability will be prevented," he says.

In 2009 Gladstone published another study in *Stroke* examining the use of anticoagulant medication in more than 500 patients known to have atrial fibrillation who were admitted to Ontario hospitals with a stroke. The data, based on the Registry of the Canadian Stroke Network, showed an alarming number of patients had not been prescribed anticoagulant medication, which works by preventing the blood from clotting. Among those who were taking warfarin—an anticoagulant proven to lower stroke risk by 64%—three-quarters were "subtherapeutic," meaning levels of the drug in their system were insufficient. Overall, only one in 10 patients in the study were taking adequate anticoagulant therapy at the time of their stroke.

"Older studies from other countries had also demonstrated this problem of an underuse of warfarin for patients who would benefit most from it," says Gladstone. "We thought that by now the situation would have improved, but sadly it has not."

There are many reasons why doctors don't prescribe warfarin despite its proven benefits. It can lead to bleeding side effects, and even when a patient is a good candidate a physician's single bad experience with someone who has hemorrhaged can create a powerful psychological deterrent. As well, warfarin is prone to food and drug interactions, and it requires frequent blood-level monitoring, a responsibility that not all doctors or patients want.

Gladstone is hopeful that a new class of blood-thinning drugs under development may be safer and easier to prescribe than warfarin for some patients. "If the newer drugs are proven safe and effective, they could help solve one of the biggest care gaps in stroke prevention."

Meanwhile, Gladstone—whose grandmother suffered a stroke related to atrial fibrillation before warfarin or tPA were available—stresses the importance of anticoagulant management with patients and their health care practitioners. "Nearly every week in the hospital we see patients admitted with a disabling stroke related to atrial fibrillation that might have been avoided or lessened in severity if only they had been taking appropriate preventative medication. We must correct this practice gap," he says.

That message got through to Mrs. Westwood, who has atrial fibrillation and who has now maintained preventive anticoagulation with warfarin since her stroke. "Dr. Gladstone told me to always take it, and never let anyone tell me not to take it unless there's a really good reason," she said of the medication, before driving to her physician's office for a blood-level test.—Jim Oldfield

Gladstone's work is funded by the following: Heart and Stroke Foundation of Ontario Centre for Stroke Recovery, Canadian Stroke Network, Sunnybrook department of medicine and University of Toronto department of medicine.