



HEALTH & SCIENCE

Stroke care's window of opportunity: Emerging responses

The traditional view of who has strokes and how they can be treated is changing.

By [Kathleen Phalen Tomaselli](#), *AMNews* correspondent. June 18, 2007.

John Murphy was no weekend warrior. The 47-year-old had been running four-minute miles for years. So when he had difficulty seeing out of one eye at mile 23 of his second Chicago Marathon, he thought, "That's weird." He stopped at a water stop, convinced it was "a dehydration thing," and went on to finish in his usual "Johnny Go-Go" style.

The Austin, Texas, resident says his hamstring had been bugging him for weeks. That's why he got on the floor to stretch later that evening, but then he couldn't get up. "I was horribly embarrassed when someone said to call an ambulance."

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Murphy was diagnosed with an ischemic stroke from a dissection in his carotid artery -- a finding physicians did not discover until the wee hours of the next morning. "Initially I was admitted to general medical versus neurological," he says.

Stroke has long been associated with the 65-and-older population, and symptoms in younger patients often go undetected for hours or days as valuable intervention minutes vanish.

For Murphy, the window for the clot-dissolving drug, tissue plasminogen activator, or tPA, had closed, leaving few options to treat this runner who suddenly was partially paralyzed.

"When a clot blocks a blood vessel and stroke occurs, blood is cut off completely to a small group of cells, and they die almost immediately," says Jeffrey L. Saver, MD, professor of neurology at the University of California, Los Angeles, who quantified and timed the brain damage that occurs during a stroke. "Surrounding that is a larger region of cells that suffers moderately reduced blood flow, a situation [the brain] can tolerate for a short period. This gives us a brief window of opportunity to intervene and save the threatened brain."

Who has strokes and why?

Every three to four minutes someone in the U.S. dies from stroke. Annually, more than 700,000 people have a stroke, and more than one third are younger than 65. "We see 40-year-

olds with stroke every day," says David C. Hess, MD, professor and chair of the Dept. of Neurology at the Medical College of Georgia in Augusta. "It's a myth that everybody who has a stroke is old."

The classic, one-size-fits-all idea of symptoms also is not always reality.

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Stroke presents differently, especially in younger patients, says Jan Flewelling, stroke outreach program coordinator for the Eddy Scurlock Stroke Center at the Methodist Neurological Institute in Houston. She spends time educating paramedics, first responders, physicians and the community about stroke and the importance of early intervention.

"It depends on the part of the brain affected," she adds. "If it hits the back of the brain, the symptoms may be blurred vision, or the balance center may mean dizziness. It's important to get a detailed description of onset."

Take the 47-year-old woman who came to the emergency department the day after Christmas with drastic and immediate onset of vertigo and vomiting. "They thought it was a sudden gastritis," Flewelling says. "She had thrown a clot to her balance center, but they were a day and a half chasing tummy trouble."

Causes, too, may vary, especially in younger patients, says Larry Goldstein, MD, professor of medicine and director of the Stroke Center at Duke University in Raleigh, N.C. He chairs the American Heart Assn.'s Stroke Council. "In children, it could be clotting abnormalities. Women who recently gave birth are at increased risk."

Dissections of the carotid and vertebral arteries now are seen as relatively common causes, particularly in younger age groups. "These tears can come from vigorous exercise programs, head and neck manipulation from a chiropractor, auto accident," says Richard L. Harvey, MD, a physiatrist at the Center for Stroke Rehabilitation at the Rehabilitation Institute of Chicago, where Murphy received care. "The inner lining of one of the arteries to the brain tears and forms a clot."

Still, several studies have shown that nearly 50% of arterial dissections have no apparent associated injury. In the 65-plus population, strokes are mostly due to traditional cardiovascular-related problems. But in younger patients, strokes are from many maladies -- structural abnormalities, clotting disorders, heart valve problems and atrial fibrillation.

In the first second of an ischemic stroke, 32,000 brain cells die.

One of the most common factors contributing to the occurrence of ischemic stroke is patent foramen ovale or PFO, a flap or a valve-like opening between the chambers of the heart. When pressure is created inside the chest -- coughing, sneezing or straining during a bowel movement -- the flap can open and blood can flow in either direction, bypassing the lungs' filtering system. If small clots are present, they can pass through the left atrium and lodge in the brain, causing a stroke.

And what about migraine-associated stroke? Or those associated with pregnancy, hormone replacement, diabetes, smoking, birth

control pills, cocaine and methamphetamine use?

"Family docs are going to see this stuff," says Thomas J. Weida, MD, professor in the Dept. of Family and Community Medicine at the Milton S. Hershey Medical Center in Hershey, Pa. "I had an unusual case, a 55-year-old woman with left-sided numbness," he says. "She went to the ER, but her CT scan was normal." Since Dr. Weida had known the woman for 15 years, he thought something was wrong and sent her to a neurologist.

"She had antiphospholipid antibody syndrome, and it was giving her a hypercoagulable state," he says. "This was one of those things that could have been a major stroke. Basically, if it doesn't follow a usual pattern, look a little bit harder. We always need to be vigilant."

Treatment and a golden window

Salvaging brain tissue often means getting help in the first three hours -- the golden window for tPA. Not always an easy proposition, especially for first responders or rural community hospitals. Before tPA can be administered, the patient must be evaluated with a CT scan to rule out brain hemorrhage, and that often means transferring to a regional hospital or stroke center.

A new trend, telestroke care, connects neurologists with health care professionals in the field through Web-based medicine. Take Medical College of Georgia's Remote Evaluation of Acute Ischemic Stroke -- REACH -- program, which links nine rural hospitals within a 100-mile radius to the medical center. This telemedicine program transmits real-time patient videos to MCG neurologists for immediate diagnosis. Physicians can see patients via a secure feed, review the CT scan online, evaluate physical signs and symptoms, download medical history data from the participating hospital and send back instructions.

Most strokes in people 65 and older are due to cardiovascular problems.

"In the past, patients weren't able to get treated in time, community hospitals used to transfer stroke patients here, but missed out on the window," Dr. Hess says. "Now we get therapy started -- it's drip and ship," he says. "We started in 2003 with one hospital and have expanded to nine."

One of the bigger changes in acute stroke care is brain imaging, says Anthony J. Furlan, MD, associate director of the Cleveland Clinic's Cerebrovascular Center. "Most hospitals do routine CT in acute stroke to rule out brain hemorrhage," he says. "With new imaging of tissue, we can see [if it is] salvageable." In particular, Dr. Furlan is referring to diffusion and perfusion MRI, which shows the ischemic penumbra, the tissue surrounding the damaged core. "A patient comes in say, five hours into symptoms, they may still have time, tissue may still be at risk."

In addition, combination therapies such as IV tPA and intra-arterial mechanical devices to remove a clot are the trend, Dr. Hess says. Such devices like the MERCI (mechanical embolus removal in cerebral ischemia) coil, are delivered through the groin by catheter to the clot. The coil is twisted into the clot and it grabs it the same way a corkscrew grabs a cork.

"Two-thirds of the time we are able to re-establish normal blood flow," says Ronald Benitez, MD, chief of endovascular neurology at Overlook Hospital in Summit, N.J. "We have up to eight hours with the MERCI device."

Robotic treadmills, vampire bats and pit vipers

Marathon runner Murphy's stroke may have surpassed the treatment window. Nonetheless, the Rehab Institute of Chicago's Prime of Life program got him moving again. "There's a group of younger stroke survivors who have different needs," Dr. Harvey says. "They often don't have chronic physical problems and can tolerate more intensive therapy."

There was no doubt for Murphy. He wanted to return both to competitive running and his high-level marketing position.

Still, it wasn't easy. "When I took my first steps, I fell flat on my face," he says. "They taught me how to walk in four days."

Murphy attributes his rapid progression to body-weight supported training. A parachute-like device held him over a treadmill, which forced him to take steps. While he continues to deal with spasticity, Murphy recently ran a 5K, raising \$11,000 for the American Stroke Assn. And he keeps asking for more from his brain. "I'm still not where I want to be, but there's this new technique for noninvasive brain stimulation," he says, referring to the work of a Brazilian scientist.

Also, an investigational device -- Northstar Stroke Recovery System -- uses cortical stimulation to help patients regain use of arms and hands by applying electrical impulses during rehabilitation. Currently in a multicenter phase III trial, the device is similar to a pacemaker and is implanted near the shoulder, says Mark Huang, MD, an RIC attending physician.

Other therapies are in the pipeline, too.

The anticoagulating properties of vampire bat saliva could be harnessed in the form of desmoteplase, a drug that may offer a three-to-nine hour window. Also, Viprinex or ancred, a clot-dissolving drug made from the venom of the Malayan pit viper, may help ischemic stroke patients within six hours of symptom onset.

"The downside to all these drugs is bleeding," says David Chiu MD, medical director of the Eddy Scurlock Stroke Center in Houston. He is involved in several of these trials. "We are hoping the new ones may be less so."

Another investigational drug containing microscopic bubbles combined with saline could improve the breakdown of clots in the brain when combined with ultrasound and tPA. After microbubbles are injected, a series of high-energy pulses from an ultrasound cause the bubbles to burst, breaking the clot. And research might show that ultrasound improves the effects of tPA.

"For so many decades, stroke was thought of as largely untreatable," Dr. Chiu says. "Today there's tremendous promise. And we hope new therapies will be available in the next few years that might extend the window beyond six to nine hours and even 24 hours."

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ADDITIONAL INFORMATION:

Stroke facts and findings

- Among adults ages 20 and older, the prevalence of stroke in 2004 was an estimated 5,700,000.
- Each year about 700,000 people experience a new or recurrent stroke.
- Stroke is a leading cause of serious, long-term disability in the U.S.
- The median time from a person's stroke onset to their emergency department arrival is between three and six hours.
- On average, every 45 seconds someone in the United States has a stroke.
- Each year, about 46,000 more women than men have a stroke.
- Women are more likely to have a stroke if they are diabetic, pregnant, menopausal, on hormone therapy, or if they have hypertension or migraines.
- A woman who has migraines with visual disturbance has a 70% greater risk of stroke.
- Blacks have almost twice the risk of first stroke compared with whites.
- Stroke accounted for about one of every 16 deaths in the U.S. in 2004.
- Among people ages 45-64, 8% to 12% of ischemic strokes and 37% to 38% of hemorrhagic strokes result in death within 30 days, according to the National Heart Lung and Blood Institute's Atherosclerosis Risk in Communities study.

Sources: American Heart Assn., the Stroke Council, Centers for Disease Control and Prevention

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No time to lose

In a study, Jeffrey L. Saver, MD, professor of neurology at the University of California, Los Angeles, quantified and timed the brain damage that occurs during a stroke. Among his findings:

- In the first second of an ischemic stroke, 32,000 brain cells die.
- In the first minutes, 1.9 million neurons, 14 billion synapses and 7.5 miles of myelinated fibers are gone.
- Every minute the brain is deprived of oxygen, 2 million more nerve cells die.
- At three hours, the golden window begins closing for the administration of the clot-busting drug tPA (tissue plasminogen activator), known to reduce long-term disability.
- After 10 hours, the brain loses 1.2 billion neurons, 8.3 trillion synapses and 4,470 miles of myelinated fibers.
- Brain tissue the size of 1.5 ping-pong balls is irretrievably lost if a typical stroke runs its course.

Source: *Stroke: Journal of the American Heart Association*, December 2005

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Weblink

A stroke scale and stroke toolbox from the National Institute of Neurological Disorders and Stroke, in pdf (www.ninds.nih.gov/doctors/nih_stroke_scale.pdf)

American Stroke Assn. (www.strokeassociation.org)

"Guidelines for the Early Management of Adults with Ischemic Stroke," abstract, *Stroke*, April 12 (stroke.ahajournals.org/cgi/content/abstract/38/5/1655)

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