TIME is

Causes, imitators & prehospital measures of stroke

By Ian Greenwald, MD, & J. Keith Hall, MD

PHOTO CRAIG JACKSON

BRAIN

Case 1: A 60-year-old male is purchasing a car at a dealership when he suddenly collapses in the showroom. As the salesman attempts to assist the customer into a chair, he notices that the patient is awake and looking around, but moving only the left side of his body. His speech is difficult to understand. A coworker arrives to help and dials 9-1-1. The emergency medical dispatcher determines this was likely an acute neurological or cardiovascular emergency and sends a first response engine and an ALS ambulance.

First responders arrive on scene, place the patient on supplemental oxygen and obtain an initial set of vital signs. Pulse: 64; RR:14; BP: 194 / 90. An ALS unit arrives on scene a few minutes later, initiates a KVO IV, obtains a blood sugar of 112 gm / dL and assesses the patient using the Cincinnati Prehospital Stroke Scale (see sidebar, p. 29). As they initiate emergent transport, they contact medical direction for permission to bypass the closest community hospital and transport the patient to the designated stroke referral center. Their request is granted, and 15 minutes later they arrive at the university hospital, where the patient is transferred to a hospital stretcher. As the paramedics give their report, the patient is assessed by the physician and nursing staff and taken directly to the CT scanner.

Case 2: A 42-year-old female is standing in line at a bank when she collapses and has a witnessed, five-minute convulsive episode. Bank security personnel arrive at the woman's side two minutes after she begins convulsing and call for an ambulance. They place the woman in the recovery position. As they await ambulance arrival, the woman appears confused and makes several attempts to stand up. She doesn't appear to be able to move her right leg.

A BLS crew arrives and finds the patient confused with a large hematoma on her forehead. She has no spontaneous movement of her right side but is able to follow simple commands involving her left side. The crew immobilizes the patient and obtains an initial set of vital signs. Pulse: 88; RR: 18; BP: 146 / 84; 99% oxygen saturation on room air. As they initiate transport to the emergency department (ED), the providers assess the patient using the Cincinnati Prehospital Stroke Scale. They arrive in the ED, report to the staff and turn over patient care.

Objectives

- Identify patients who might benefit from fibrinolytic therapy following stroke.
- Describe causes of stroke.
- List conditions that may mimic stroke.

Glossary

Aphasia: Loss of ability to speak.
Ataxia: Deficit in muscular coordination.
Coagulopathy: Disorder that inhibits the blood's ability to coagulate.
Dysarthria: Difficult or poorly articulated speech.
Embolism: Condition in which a foreign object (an embolus) travels in the bloodstream until it lodges in a vessel, blocking circulation.
Thrombosis: Condition in which a clot of platelets or other cell elements (a thrombus) attaches to the interior of a blood vessel, blocking circulation.

History of stroke management

Because the clock starts ticking when a patient first experiences symptoms, and EMS providers are often the first health-care professionals to examine the patient, EMS plays a pivotal role in facilitating the prompt and appropriate treatment of stroke patients. However, historically, many EMS authorities believed no prehospital interventions would help an acute stroke patient. In fact, in the not-so-distant past, many EMS systems considered "stroke" calls such a low priority that units would routinely respond without lights and siren. A widely held notion was that simply "nothing could be done for these patients."

Supplemental oxygen, blood glucose determination to exclude hypoglycemia and supportive care were the mainstay of our treatment for stroke patients. In fact, patients who suffered a stroke would often be briefly admitted to the hospital in an effort to find an underlying cause of the stroke but then quickly sent to rehab to recover as much function as possible with physical, occupational and speech therapy.

Recently, large international studies investigating the use of different therapies for acute ischemic strokes and new innovations in neurological imaging have led to a tremendous change in the prehospital and ED approach to the stroke patient. Currently, the pendulum has swung, and stroke patients are approached and managed with the same high awareness of time sensitivity as myocardial infarction.

FIGURE 1: **Hemorrhagic & Ischemic Stroke**

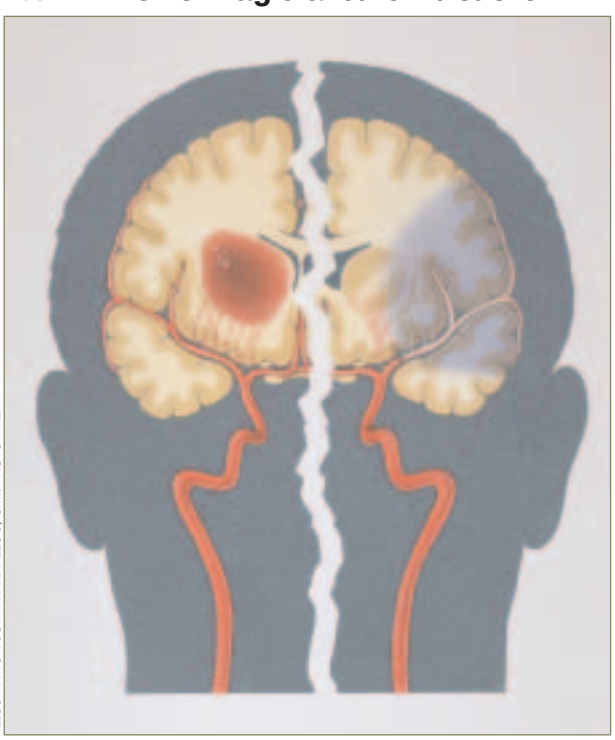


ILLUSTRATION JOHN KARAPELOU, CMI/PHOTOTAKE

Hemorrhagic stroke (left) and ischemic stroke (right) both result in the lack of oxygenated blood to the brain and the eventual death of involved brain tissue.

Anatomy & physiology of stroke

A stroke can be generally defined as the death of brain tissue. Two distinctly different events can lead to or cause a stroke. The common result of these two very different types of strokes—hemorrhagic and ischemic—is the lack of delivery of oxygenated blood to brain tissue and the ensuing death of brain tissue (see Figure 1, opposite).

Differentiating the type of stroke is a vital distinction that is made in the ED. The type of stroke can be definitively diagnosed only after viewing images of the brain, most commonly obtained via CT scan technology. The modern-day treatment for an acute stroke is based on the rapid identification and treatment of the underlying cause of the stroke.

Roughly 70% of all strokes are caused by the occlusion of a blood vessel in the brain; these are the so-called *ischemic* or *dry* strokes. They're typically the result of the embolism or thrombosis of atherosclerotic plaque, often from the carotid artery. If part of plaque breaks off, it can travel up into the cerebral circulation and lodge in a blood vessel in the brain. Because the occluded blood vessel can't supply the brain tissue with oxygenated blood, the brain tissue becomes starved and dysfunctional. The result is clinically manifested as neurological deficits, e.g., weakness or paralysis in an extremity, dysarthria, aphasia and / or ataxia. Often little to no deterioration in consciousness occurs unless specific parts of the midbrain or brainstem are involved.

Non-traumatic hemorrhagic strokes, usually the result of chronically elevated blood pressure or **coagulopathy**, can vary significantly in size. Small hemorrhagic strokes can present similarly to ischemic strokes, whereas large hemorrhagic strokes commonly have signs of significant neurological deficits early, followed by profound deterioration in mental status. Often, signs of elevated intracranial pressure (e.g., vomiting) can develop. Hospital treatment for hemorrhagic strokes includes medical management of blood pressure and blood glucose, and the correction of any pro-bleeding abnormality. Intracranial pressure monitoring devices may need to be placed for prevention of secondary brain injury from swelling.

FIGURE 2: **Circulation of the Brain**

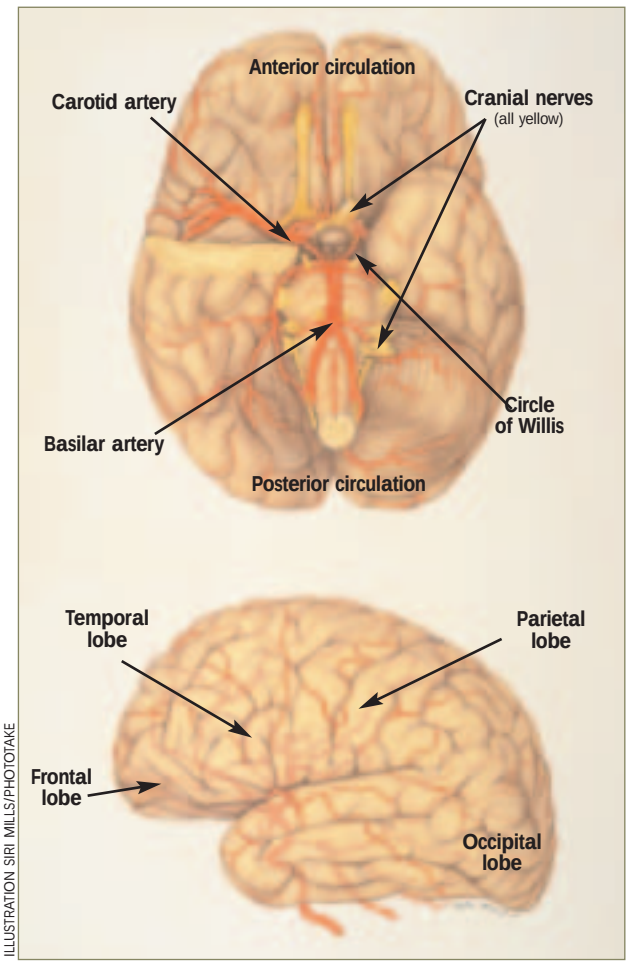


ILLUSTRATION SIRI MILLS/PHOTOTAKE

Via the carotid artery, the anterior circulation supplies the majority of the brain's blood supply. Posterior circulation supplies blood to the cerebellum and brainstem via the basilar artery. The two circulations share blood flow in the Circle of Willis.

Cerebral circulation is divided into anterior and posterior circulation "systems," with posterior communicating arteries on both sides of the brain connecting the two (see Figure 2). The anterior circulation supplies the majority of the brain's blood supply. Originating from the carotid system and consisting of three major branches, the anterior circulation includes the ophthalmic artery supplying the optic nerve and retina (ischemia here causes sudden-onset one-sided blindness), and the anterior and middle cerebral arteries that supply the frontoparietal and the anterotemporal lobes of the brain. These areas of the brain are responsible for major motor, sensory and speech functions.

The posterior circulation of the brain is supplied by two vertebral arteries that merge to become the basilar artery, which has a series of branches that supply the cerebellum and brainstem. Ischemia of the posterior circulation usually causes ataxia, vertigo and / or dysarthria.

Signs & symptoms of stroke

Occlusion (from an embolus) or disruption (from a hemorrhage) of an artery to a specific region of the brain causes decreased or total lack of function of that portion of the brain. As described, different parts of the brain control motor function, sensation, speech, vision, balance, etc. If the lobe of the brain that controls movement of the right arm is involved, the patient will have decreased or no function of that extremity.

All patients exhibiting potential stroke symptoms should be treated as if they were having a stroke, until proven otherwise.

The complexity of the blood supply and the motor and sensory distribution of the brain create an almost endless number of clinical exam findings that can be present after a stroke.

It's important to assess the patient's deficit in comparison with their function before the acute event. This comparison requires historical data from the patient or a bystander. If a patient can't lift an arm or a leg, is this a new finding or a worsening of a preexisting problem? The general symmetry of the human body also allows one side to be compared with the other. Does the patient normally have equal strength or sensation in both arms? Patients with previous strokes or other neurological conditions can be difficult to diagnose with a new finding of a neurological deficit.

The use of a quick and accurate diagnostic tool, such as the Cincinnati Prehospital Stroke Scale, will help prehospital personnel rapidly identify potential stroke patients. The Cincinnati Prehospital Stroke Scale requires the EMT or paramedic to ask the patient to show their teeth (or smile), to have the patient close both eyes and hold both arms straight out in front of them for 10 seconds (pretending to catch rain drops), and then to ask the patient to repeat the phrase, "You can't teach an old dog new tricks." If the patient manifests any facial drooping with smiling, arm drift, slurring of words, or uses the wrong words or is unable to speak, they have possibly suffered an acute stroke. Other prehospital stroke screening scales can also be used.

Stroke mimics

To complicate matters, a host of medical conditions mimic stroke, including diabetes, seizures and head injuries. From a prehospital perspective, it's important to consider these, but be mindful that such diagnoses (except hypoglycemia) are made in the ED. All patients exhibiting potential stroke symptoms should be treated as if they were having a stroke, until proven otherwise.

Prehospital glucose determination is vital in patients with acute neurological deficits for three reasons. First and foremost, severe isolated hypoglycemia can by itself cause stroke-like symptoms. These symptoms are generally reversed with the administration of dextrose. If left untreated, profound hypoglycemia can lead to permanent neuronal cell death. Hypoglycemia can also lead to a seizure, which is frequently associated with a post-ictal state that is a stroke mimic.

Second, for patients suffering a stroke, serum blood sugar extremes can potentially increase the size and severity of the stroke. Blood sugar should be normalized to maximize the potential for a good outcome.

Last, elevated blood sugars can lead to a host of electrolyte,

fluid and pH abnormalities that can lead to altered levels of consciousness. This effect can be confused for a stroke-like state as well.

Still other diagnoses can present with stroke-like deficits. Certain migraine headaches can be associated with acute and significant neurological deficits. These deficits generally resolve when the migraine abates. Interestingly, a variant of this condition exists when a patient experiences a "migraine" without head pain but with neurological deficits. This condition would be impossible to definitively identify in the field and often requires an extensive evaluation by a neurologist. The hallmark of the condition is resolution of the neurological deficits with medications used to treat migraines.

Additionally, following grand mal seizures, patients usually experience a post-ictal period. This period can vary significantly in duration and is usually marked by a global alteration in the patient's mental status. A subset of patients will experience a condition known as Todd's paralysis during the post-ictal phase. This unilateral paralysis can last up to a day (although it generally resolves sooner).

Patients typically don't experience a seizure with an acute stroke. One-sided paralysis after a seizure should prompt the astute prehospital provider to check glucose (to rule out hypoglycemia as a cause of the seizure) and check the patient for a

PHOTO RAUL TORRES

Check glucose levels to rule out hypoglycemia as a cause of a seizure with one-sided paralysis.

seizure disorder MedicAlert bracelet or necklace.

Other less common stroke mimics include certain central nervous system (CNS) disorders (e.g., brain abscess, meningitis), electrolyte abnormalities and traumatic brain injuries. Any patient with an acute neurological deficit following trauma should be immobilized and transported to the closest appropriate facility.

Prehospital care

Once the diagnosis of acute stroke is suspected, the prehospital management of the patient becomes of paramount importance. As with the general approach to all patients, the ABCs should be first assessed to ensure that no immediate intervention is required.

PHOTO JEFFREY MAYES

First assess ABCs and then progress to oxygen, IV access and cardiac monitoring as indicated—without delaying transport.

Blood glucose determination to exclude hypoglycemia as the cause of symptoms should be performed along with vital sign measurements. Low blood glucose levels should be treated accordingly.

In patients for whom you suspect acute stroke, do not treat elevated blood pressure in the field. Acutely lowering blood pressure in patients with an ischemic brain insult can worsen and expand the area of brain that is lacking adequate blood flow.

Probably the most critical prehospital action for possible acute stroke patients is obtaining an accurate and expedient history from the patient and bystanders. In this current era of fibrinolytic therapy for acute ischemic stroke, the most important aspect of the history that must be accurately confirmed is the exact time of the onset of symptoms. Because in-hospital therapy for stroke patients is guided largely by the duration of the patient's symptoms, fibrinolytic therapy must be given inside a three-hour window from the onset of the patient's symptoms in order to be both effective and reasonably safe. With advanced neurological imaging and specialty consultation, patients with symptoms within a six-hour window can also be considered candidates.

It's imperative that prehospital personnel confirm with the patient (and/or witnesses) the exact time that the symptoms began because they are often the only providers who will have access to reliable historians within the time window of therapeutic intervention. Prehospital personnel should use time markers (e.g., noting that a certain TV show was airing when the symptoms began) to help identify the exact time that the symptoms began or the last time the patient was seen at their neurologic baseline.

Other aspects of the patient's history to collect include previous transient ischemic attack (TIA) or stroke, head trauma, use

of anticoagulants, recent surgery, recent bleeding, hypertension, seizure at the onset of symptoms and/or history of cancer (brain cancer or otherwise). It's critical to ascertain these clinical history points because they are potential contraindications for certain stroke therapies. On-scene history collection should take no longer than 10 minutes; most of the historical data can be obtained on the way to the hospital. Beyond glucose determination on scene, transport delays should not be accepted. In the patient experiencing a stroke, *time is brain*.

On the basis of assessment findings, clinical care should include oxygen, IV access and cardiac monitoring without delaying transport. Depending on the patient's protective airway reflexes and length of transport, definitive airway control (such as intubation) may be required.

Pay close attention to prevention of hypoxemia and large fluctuations in end-tidal CO_2. Many EMS agencies that use rapid sequence induction (RSI) protocols have specific drug combinations for patients with a suspected brain injury (whether secondary to trauma or a medical cause). The use of different drug combinations is outside the scope of this article, but current research indicates outcome is mostly tied to prevention of hypotension, maximizing oxygen delivery and near-normal CO_2 levels.

Early communication with medical direction is recommended to determine the most appropriate receiving facility and to ensure the necessary personnel are ready to begin assessment soon after the patient arrives in the ED. EMS agencies faced with long transport times should discuss with their medical directors the use of aeromedical assets to transport acute stroke patients.

New developments

With the advent of fibrinolytic therapy in acute stroke, not only has the prehospital on-scene time and history taking become paramount, but the early notification of and transport to the appropriate emergency facility have also increased in importance.

Acute stroke care is a multidisciplinary effort that relies heavily on prehospital communication with hospital-based emergency medical providers and specialized "stroke teams" of CT technicians, neuroradiologists and neurologists. Early notification of receiving facilities allows for the mobilization of both hospital emergency services and these specialized stroke teams and may make the difference in a patient receiving a brain-saving therapy within the window of efficacy or not.

Current research suggests it's both safe and more effective to give fibrinolytics within a three-hour window for a certain subset of patients. Additionally, the NINDS rt-PA stroke study (in 2000) showed that fibrinolytics given at one hour after the onset of acute stroke symptoms is four times more effective than if given at three hours. Given this data, prehospital and emergency provider roles in expediting the evaluation and transport of potential stroke patients are taking on even greater emphasis.

An exciting new area of treatment and research for "clot-busting" fibrinolytic therapy has been the advent of intra-arterial administration of tPA. This involves placing a catheter in the femoral artery and using a guide wire and IV contrast dye, advancing the catheter to the area of the clogged artery in the brain. The tPA is then infused directly to the affected vessel. Less tPA is required compared with system administration through a peripheral IV. The smaller dose of directly infused tPA is associated with less systemic side effects. Early studies also suggest it can be safely administered outside of the three-hour time window for systemic tPA. Ongoing stud-

Cincinnati Prehospital Stroke Scale

According to the American Stroke Association, a study by researchers at the University of North Carolina–Chapel Hill School of Medicine has shown a version of the following Cincinnati Prehospital Stroke Scale test (used by health-care professionals to detect initial stroke symptoms) was correctly administered by laypeople 96% of the time.

	Normal	Abnormal
Facial Droop	Both sides of face move equally	One side of face does not move at all
Arm Drift	Both arms move equally or not at all	One arm drifts compared to the other
Speech	Patient uses correct words with no slurring	Slurred or inappropriate words or mute

Source: www.strokecenter.org

Have the patient smile or show their teeth so you can watch for facial droop.

PHOTOS A.J. HEIGHTMAN

Have the patient close both eyes and hold both arms out straight in front (pretending to catch rain drops) for 10 seconds to determine arm drift.

ies are attempting to define the actual time window for the safe and effective usage of this therapy.

Another development on the horizon for the emergency management of acute stroke patients is the designation of stroke centers. Much like the current practice of triaging major trauma victims to designated trauma centers, The Brain Attack Coalition (www.stroke-site.org) has proposed and developed criteria for emergency centers to be named "Stroke Centers of Excellence." These stroke centers must demonstrate the ability of their facilities and personnel to provide excellent and expedient care to victims of acute stroke.

Neuroimaging, the process of obtaining pictures of the brain, is also rapidly evolving. CT scanners have become faster and provide more detailed images of the brain. MRI technology is now being used in the acute setting, and stroke specialists are studying how the use of images obtained by MRI is changing ED management of stroke patients. Specifically being researched is the use of tPA in a subset of patients who have had symptoms for greater than three hours but have minimal evidence of tissue swelling on MRI.

Despite these advancements, most patients who suffer a stroke aren't eligible for much treatment beyond simple aspirin therapy, even in designated stroke centers, either due to delayed presentation or contraindications.

A typical stroke patient is admitted to the hospital, where

Quick-Thinking EMS Crew Saves Young Life

One afternoon, 28-year-old Heather Williams of Paola, Kan., suddenly became ill, vomited without explanation and then went to the kitchen to make a sandwich. When she spread peanut butter on the counter instead of the bread, her husband called 9-1-1.

"It was weird. I didn't have a headache, I couldn't feel anything, and I could hardly stand," says Williams.

When Miami County (Kan.) EMS paramedics Mark Dozier and Frank Burrow arrived, they tested Williams using the Cincinnati Prehospital Stroke Scale. Her right arm was limp, her speech was slurred, and her movements were uncoordinated, indicating stroke.

Bypassing a local hospital that wasn't equipped to handle what they suspected was a massive stroke, Dozier and Burrow called a LifeNet medical helicopter to fly Williams to Saint Luke's Hospital, site of the Mid America Brain and Stroke Institute, in Kansas City, Mo.

In Saint Luke's, neurologist Michael Schwartzman, DO, assessed Williams. By this time, she was mute, paralyzed on her right side and could only occasionally respond to simple commands. Williams was given an aspirin suppository to thin her blood, a cerebral angiogram to locate the clot and a shot of the clot-busting drug tPA in her carotid artery to dissolve the obstruction that had almost completely blocked the vessel.

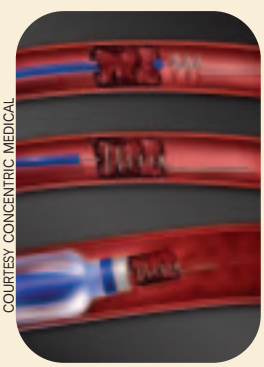
But time was running out. When given intravenously, tPA is effective in treating strokes up to about three hours after one begins. And when injected into the clot itself, as in Williams' case, tPA is effective for up to about six hours. However, it had been almost that long since Williams had her stroke. And her clot was so large it could take up to two hours to dissolve.

"A massive stroke involving a clot as large as Heather's is often fatal," says Marilyn Rymer, MD, medical director, Saint Luke's Mid America Brain and Stroke Institute. "And it's a myth that a stroke like hers can't happen to someone so young."

Clearly, Williams needed a miracle. Fortunately, one was on hand.

Saint Luke's is one of only five hospitals in the country originally selected to test a revolutionary corkscrew-shaped mechanical device, called the Merci Retrieval System, that removes brain clots. Unlike intravenous tPA, the only current FDA-approved treatment for ischemic stroke, the instrument can remove a clot almost immediately on contact.

Merci Retrieval System



COURTESY CONCENTRIC MEDICAL

A clot is pierced, threaded like a corkscrew and suctioned through the catheter.

Neurointerventional radiologist Thomas Grobelny, MD, threaded the catheter-like Merci Retrieval System through Williams' groin up to the affected artery. Then he pierced the clot and twisted it out like a cork from a wine bottle.

The treatment worked, and, within 24 hours, Williams was conscious and alert, and could follow simple commands. Within 48 hours, she started talking.

A few days later, she went home–able to walk, talk and use both sides of her body. "Some people who have massive strokes are in the hospital for six months," Williams said. "I went home in six days."

Eighteen months after her stroke, Williams is self-sufficient and back at work, with minimal impairments. She sometimes struggles with her speech and reading big words, but she can drive and plans to attend nursing school. Doctors expect an almost complete recovery.

Schwartzman is quick to point out that when someone shows signs of a stroke, they need treatment immediately. The decision by paramedics Dozier and Burrow to take Williams to the stroke center at Saint Luke's was critical to her outcome.

"When someone's having a stroke, it's our protocol to take them to Saint Luke's because of [the hospital's] advanced treatment capabilities," says Dozier. "I'm convinced that taking [Heather] there definitely saved her life."

"Strokes kill brain cells," says Schwartzman, "So lost time equals lost brain tissue. Immediate treatment after a stroke can not only reduce the chance of major impairments, it can mean the difference between living and dying."

–A.J. Heightman

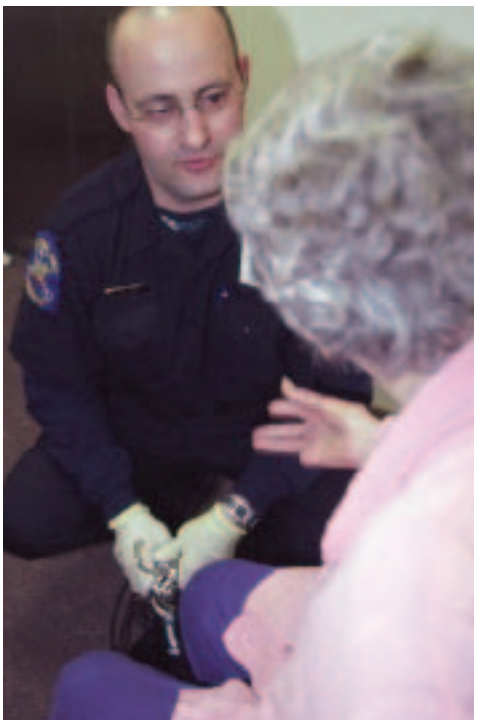


PHOTO CRAIG JACKSON

Limit on-scene history collection to 10 minutes and obtain supplemental information during transport.

blood glucose is normalized and tightly controlled and chronic hypertension is treated. (Acute hypertension in the setting of a stroke is not treated and often resolves on its own.) An investigation is launched into the cause or etiology of the stroke (e.g., a blood clot in the heart or atherosclerotic plaque in the carotid artery) is identified and treated as appropriate.

Soon after admission, patients begin rehabilitation to attempt to regain lost neurological function. This process is the current state of affairs for the vast majority of stroke patients. But for those patients (or their families) who recognize their symptoms early and are treated and transported by knowledgeable prehospital care providers, hospital treatment and outcome may be very different.

Case follow-up

Case 1: For the male who suffered an acute neurological event, EMS providers arrived on scene, determined normal blood glucose, assessed vitals and obtained a rapid but detailed history. The crew initiated transport to the closest appropriate hospital and provided plenty of "heads-up" time to the hospital for gathering the stroke team in advance of the patient's arrival. The CT scan showed no evidence of bleeding in the brain, and the patient was therefore a candidate for tPA therapy. The tPA was administered at 90 minutes after symptom onset, and the patient recovered significantly from his neurological deficits. The admitting diagnosis was acute ischemic stroke.

Case 2: Following her seizure, the patient had one-sided paralysis. This condition gradually improved during the first 30 minutes after ED admission. She later relayed a history of epilepsy. Hospital staff ordered a head CT, which was normal. Two hours later, the patient's Dilantin (phenytoin sodium) level was noted to be increased, and she was discharged home, symptom-free. The discharge diagnosis was Todd's paralysis following grand mal seizure secondary to preexisting epilepsy. JEMS

Ian Greenwald, MD, is an assistant professor in the Department of Emergency Medicine at Emory University, Division of Prehospital and Disaster Medicine. Dr. Greenwald is the medical director of Rural/Metro Ambulance, North Georgia Operations. He received his residency training in Emergency Medicine at the University of Pittsburgh and his medical degree from the University of Vermont.

J. Keith Hall, MD, is a third-year resident in Emergency Medicine at Emory University. He's a graduate of Emory University School of Medicine and has a bachelor's from the University of South Carolina—Columbia.

This continuing education activity is approved by the Center for Emergency Medicine, an organization accredited by the Continuing Education Board for Emergency Medical Services (CECBEMS), for 1.5 hours credit for First Responder, Basic and Advanced providers. If you have any comments regarding the quality of this program and/or your satisfaction with it, please contact CECBEMS by mail at CECBEMS, 5111 Mill Run Road, Dallas, TX 75244; by phone at 972/387-2862; by fax at 972/716-2007; or by e-mail at lsibley@cecbems.org.

Stroke Stats

- 750,000 new or recurrent strokes occur in the United States every year.
- Stroke is the third leading cause of death and the leading cause of adult disability.
- Someone in the United States has a stroke about every 45 seconds, and someone dies of one about every three minutes.
- 22% of men and 25% of women under age 65 who have an initial stroke will die within a year.
- 14% of people who survive a first stroke or mini-stroke will have another within a year.
- 35–40% of strokes occur in people under age 65.
- Blacks have almost twice the risk of first strokes as whites.
- 40,000 more women than men have a stroke.
- The estimated cost of strokes in 2004 was $53.6 billion.

Sources: Saint Luke's Hospital's Mid America Brain and Stroke Institute and the American Heart Association.

Resources

- Dion JE: "Management of ischemic stroke in the next decade: Stroke centers of excellence." *Journal of Vascular and Interventional Radiology.* 15(1 Pt 2):S133–S141, 2004.
- Fulgham JR, Ingall TJ, Stead LG, et al: "Management of acute ischemic stroke." *Mayo Clinic Proceedings.* 79(11):1459–1469, 2004.
- Marler JR, Tilley BC, Lu M, et al: "Early stroke treatment associated with better outcome: The NINDS rt-PA stroke study." *Neurology.* 55(11):1649–1655, 2000.
- Tintinalli JE, Kelen GD, Stapczynski JS (editors): *Emergency Medicine: A Comprehensive Study Guide, 6th ed.* McGraw-Hill Professional, 2004.