Fulfilling the Promise

Speed Is Essential When Treating Stroke

A stroke can leave a once-vital adult unable to speak, lift a coffee mug, or walk unassisted. Each year, more than 780,000 Americans suffer strokes. Stroke causes more serious long-term disabilities than any other disease and is the third-leading cause of death in this country. While a stroke can occur at any age, the risk of stroke more than doubles each decade after age 55.

There are two types of stroke. The more common ischemic stroke is caused by a clot or a narrowing of the arteries that blocks a vessel supplying blood to the brain, a hemorrhagic stroke is caused by bleeding into or around the brain.

With support from the National Institutes of Health (NIH), principally through the National Institute of Neurological Disorders and Stroke (NINDS), scientists at U.S. medical schools and teaching hospitals are studying the genetics of stroke and stroke risk factors, and discovering new and better ways to help the brain repair itself and restore important functions. Their efforts have helped identify manageable risk factors and resulted in development of the only FDA-approved therapy for treating stroke that maximizes the potential for patient recovery. Because of this groundbreaking research, deaths from stroke have dropped more than 60 percent since the 1970s.

As in many neurological diseases, advances in treatment depend on an improved understanding of the underlying basic science. NINDS-funded basic research on the regulation of brain blood flow, brain cell death and protection, blood brain barrier, brain metabolism, inflammation, and the brain’s mechanisms of repair after injury inform our present and future patient studies. Some recent findings from NIH-supported research follow.

Risk and Prevention

The most important known risk factors for stroke are hypertension, heart disease, diabetes, and cigarette smoking. Researchers are studying these and other risk factors, including how genetics may play a role, to improve prevention. Finding ways to prevent a recurrence is also a critical research goal.

- Using magnetic resonance imaging, researchers at Boston University School of Medicine found that 10 percent of midlife adults had experienced a stroke without knowing it, raising their risk for future strokes and memory loss. The 2008 study showed that atrial fibrillation, or irregular heartbeat resulting in pooling of blood in the heart’s two upper chambers and formation of blood clots, doubles the risk of a silent stroke.

- The Ischemic Stroke Genetics Study, whose lead researchers were at Wake Forest University School of Medicine, revealed in 2006 that individuals who suffer a stroke are more likely to have a severe one if they have a sibling who had a stroke.

- Aspirin is equivalent to warfarin (marketed under the brand name Coumadin) in preventing subsequent strokes, according to a 2005 study conducted at 59 medical centers. Researchers at Emory University School of Medicine who led the study also discovered that aspirin causes fewer and less serious side effects, costs less, and is easier to use.
• Fiber consumption may lower stroke risk and severity, according to a 2008 observational study by researchers at Massachusetts General Hospital. Of people who had recently had a stroke, those with the highest fiber intake had the best recovery outcomes.

• Exercise reduces the risk for stroke and other diseases, according to a 2004 study at Johns Hopkins University School of Medicine. Even a moderate program of physical exercise lowers risk factors such as high blood pressure, elevated blood glucose levels, abdominal fat, and high cholesterol levels.

• Results of the 2003 African American Antiplatelet Stroke Prevention Study, a large, multicenter trial led by researchers at Rush Medical College, showed treatment with aspirin is as effective as the anticoagulant agent ticlopidine in preventing recurrent stroke. African Americans have about twice the risk of experiencing a stroke as whites.

Emergency Treatment
Stroke is treated with medications and sometimes surgery. Treatment is most effective when administered as soon as possible after stroke onset, before irreparable brain damage occurs. NIH-funded research advances have transformed the outlook for stroke patients.

• Since 1996, t-PA (tissue plasminogen activator) has been the only FDA-approved therapy for acute ischemic stroke. The drug, when administered within three hours of ischemic stroke onset, breaks down blood clots and can greatly improve a patient’s chance for a full recovery. In the 1980s, University of Cincinnati College of Medicine scientists led the first multicenter t-PA studies in the United States and established a protocol for quick diagnosis and treatment for stroke victims.

• A 2006 review of the economic benefits of phase 3 clinical trials by the University of California, San Francisco Medical Center found that the trial which indicated t-PA could prevent brain damage if used within the first three hours after a stroke had an estimated net benefit of more than $6 billion over 10 years.

• The leukemia drug Gleevec (also known as imatinib) may improve stroke treatment, according to a 2008 study conducted with mice. The international clinical study, led by researchers at the University of Michigan Medical School, revealed that Gleevec reduced the bleeding caused by t-PA, and allowed for the administration of t-PA after the three-hour treatment window.

• Injection of a gene called kallikrein after the onset of stroke in rats protects against ischemic brain injury by inhibiting cell suicide and inflammation and promoting growth of new blood vessels and nerves in the brain, according to 2006 research conducted by the Medical University of South Carolina College of Medicine.

Stroke Recovery
NIH-supported scientists are looking for new, more effective ways to aid brain repair following a stroke. Recent advances in imaging and rehabilitation have shown that the brain can rewire itself to compensate for a function lost as a result of a stroke. Researchers have found that after a stroke, a secondary wave of damage results from inflammation and toxic chemicals created by dying brain cells. They are working to develop neuroprotective agents that prevent this damage.

• Stroke patients who have lost use of one arm can regain significant function through a special training program, according to a 2006 multicenter study led by researchers at the Emory University School of Medicine. Constraint-induced movement therapy, which restrains the unaffected arm, effectively trains the patient to use the affected hand and arm.

• A 2007 randomized study at the Indiana University School of Medicine showed that a management program called “AIM” improved outcomes in patients with post-stroke depression. Thirty-nine percent of patients had complete remission from depression after 12 weeks of treatment. AIM consists of three steps: activating stroke survivors and their families to understand and accept depression diagnosis and treatment, initiating antidepressant medication, and monitoring treatment effectiveness.

For more information about how medical schools and teaching hospitals are fulfilling the promise of medical research, go to www.aamc.org/research/ftp.