

HEALTH

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Can we limit stroke damage?

Because every second counts, patients in a novel study will be treated before they reach the hospital.

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Times Staff Writer

Stroke patients throughout Los Angeles County who dial 911 are becoming part of a first-of-its-kind study designed to determine whether a low-cost, common mineral can protect the brain from damage.

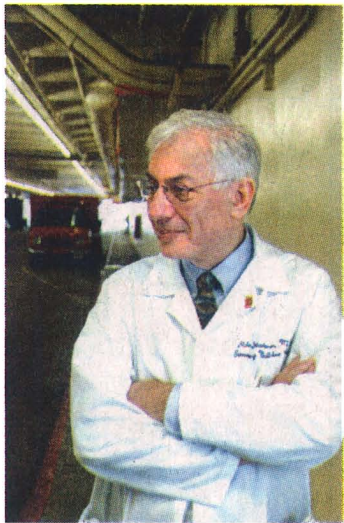
Los Angeles County paramedics in mid-January started screening patients for participation in the planned three-year study, which would allow emergency personnel to administer a specially prescribed solution to patients being transported to any hospital in the county for further treatment. The study is expected to involve nearly 1,300 people before it concludes.

The treatment under study is called "Fast-Mag," named for magnesium sulfate. Researchers believe this mineral might slow the chemical process that can kill 12 million brain cells per minute during an untreated stroke, leading to long-term disability and death. They aim to test whether a rapid increase in a stroke victim's magnesium sulfate level — delivered within two hours of the appearance of symptoms — can reduce the often-devastating effects of such a "brain attack," during which the blood supply to the brain is partially cut off.

Magnesium sulfate is found in most leafy green vegetables and is naturally present in healthy humans. But the experimental Fast-Mag treatment would quickly double a patient's normal blood level of the mineral and would keep it at that elevated level for roughly 24 hours. Used for 75 years in the treatment of preeclampsia, a complication of pregnancy, the dose of magnesium sulfate under study has been shown to be extremely safe. Its most common — and severest — side effect, suffered by 5% to 10% of patients, is a sudden flush of warmth to the cheeks.

In the last decade, dozens of costly stroke treatments have failed, and others have proven less effective than hoped, according to experts in the field. "If this is found to be beneficial, you have a drug that might help, and there's no cost issue," said Dr. Marc Eckstein, medical director of the Los Angeles Fire Department.

UCLA's \$16-million study breaks new ground in two respects. It is the largest and most comprehensive medical study to be undertaken in the Los Angeles emergency medical system, researchers said. All 69 hospitals in L.A. County are expected to participate in the study, as well as 3,000 paramedics working for 32 agencies — from the tiny Montebello Fire Department to the much larger L.A. County Fire Department.



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SLEUTH: Dr. Sidney Starkman is one of UCLA's chief researchers in magnesium sulfate treatment for strokes.

It is also the first study to initiate stroke treatment, in all cases, in the first two hours after symptoms appear. Stroke researchers now consider that narrow window of time to be the most promising opportunity to limit stroke's debilitating effects on the brain. "Time is brain," said Dr. Sidney Starkman, one of the study's chief investigators. If treatment, including brain protection agents, can be started within two hours of a stroke's onset, he adds, "there's going to be brain to save."

Researchers said that the sheer scale and diversity of the population that lies within the study's area could establish its findings quickly as relevant across the country — and possibly the world. Los Angeles County's demographic melting pot is expected to draw subjects into the study that reflect the wide range of people affected by stroke, said Dr. Jeffrey L. Saver, director of UCLA's stroke team and a principal investigator of the study. Even if Fast-Mag is not a success, adds Saver, the establishment of a such a large re-

search structure could make the county a crucible in which the next generation of stroke treatment is forged.

Half of those who participate in the study will receive a placebo — an ineffective saline solution — and the others will get the magnesium sulfate solution. To assess the effectiveness of the experimental treatment, researchers will compare how well participants in each group are functioning three months after their stroke.

The study's first three volunteer participants — all women who were brought to UCLA Medical Center since late January after suffering a stroke — have since been released from the hospital, said the study's coordinators.

For Marcia Ross, a 74-year-old Westwood resident who suffered a stroke on Jan. 29, participation was an easy decision. Ross knew that she might end up getting a useless placebo but calculated that, as a study patient, "I knew I'd get extra attention." She added that she and her husband "are both firm believers in legitimate research ... the only way you know is if you try it on people," she said.

The county's 3,000 paramedics, each of whom has undergone three hours of initial training to help carry out the trial, will be critical to its completion. Once a paramedic has identified a patient as suffering acute stroke, the patient is asked whether he or she is interested in learning more about the trial. If so, the paramedic dials an on-call study investigator, who discusses the study (currently in English or Spanish) with the patient or a legal stand-in. If the patient's consent is given, the paramedic hangs a small intravenous bag provided by those conducting the study and begins the infusion.

In the heat of a medical emergency, brokering the consent process can be unwieldy and distracting for a paramedic, said Eckstein, who called it "the main bone of contention" he has heard from some of the 750 paramedics he oversees. But Dr. William Koenig, medical director of the Los Angeles County Emergency Medical Services Agency, said most of those involved are intrigued enough by the study's prospects that they are willing to shoulder the extra work.

"I think paramedics reflect the frustration of the medical community in general," said Koenig. "We have been frustrated by the fact that oftentimes by the time a patient seeks treatment it's too late, and that many of the treatments available are very limited."

Each year in Los Angeles County, 15,000 to 25,000 residents suffer a stroke, which is the leading cause of disability among adults nationwide and the third leading cause of death. As few as half dial 911 to seek emergency medical services, and many call or show up at an emergency room after suffering many hours of symptoms, when damage to brain cells has become extensive and difficult to reverse.

The UCLA study will accept subjects only if they are treated first by paramedics, and only if the emergency medical team arrives on the scene and receives a patient's consent within two hours of the time that stroke symptoms first appeared. The study also will exclude patients younger than 40 or older than 95, in a coma, or with unusually high or low blood pressure, kidney disease or recent head trauma. Those who have had a stroke within the previous 30 days also will not be admitted.

Upon arrival at the hospital, participants in the trial are to receive any standard treatment for stroke that physicians normally provide, as well as a continuing dose of magnesium sulfate for the first 24 hours.

UCLA researchers hope that, if it is found to help reduce the size and severity of a stroke, magnesium sulfate could become part of an arsenal of new stroke treatments. In 1996 the FDA approved tissue plasminogen activator, or t-PA, a drug that must be administered in a hospital within three hours of a stroke's onset. But the drug, which is difficult and risky to administer, has been found effective in only one in eight patients.

The UCLA Fast-Mag study is being conducted under a \$14-million grant from the National Institutes of Health. Drug companies have little interest in the expensive process of developing or testing a stroke treatment based on magnesium sulfate, because the widely available mineral compound could not be patented and would not likely result in profits.

The NIH agreed to fund the project in 2003 after animal studies found that magnesium sulfate proved to be a powerful protector of brain tissue under assault from stroke.

As the study progresses, its sponsors say, it could also become unusual in another way, drawing in some subjects who may be unable to understand or communicate their agreement to participate. This departure from the normal practice of seeking explicit consent from a potential subject or a legal stand-in is permitted after a complex and controversial process. Saver said his team "would reluctantly have to consider" seeking the special waiver required only if the normal consent process failed to bring sufficient numbers of subjects into the study.

Warning signs of a stroke

If you notice one or more of these symptoms in yourself or someone you are with, call 911 immediately or get to a hospital right away:

- Sudden weakness or numbness of the face, arm or leg, especially on one side of the body (the most common sign of stroke).
- Sudden confusion; trouble speaking or understanding.
- Sudden trouble seeing with one or both eyes.
- Sudden trouble walking; loss of balance or coordination.
- Sudden, severe headache with no known cause.

Source: American Stroke Assn.



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VOLUNTEER: Marcia Ross, 74, with the paramedic who helped her, Steve Stern, was one of the first participants in the stroke study.