Drug Wards Off Sickle-Cell Attacks

Federal officials announced this week the first drug therapy that prevents the painful attacks of sickle-cell anemia, an inherited blood disorder that in the United States afflicts mostly blacks of African descent.

Claude Lenfant, director of the National Heart, Lung, and Blood Institute (NHLBI) in Bethesda, Md., called it "the first effective treatment for this serious illness."

The huzzahs for the drug, hydroxyurea, stem from data collected in an NHLBI-sponsored, multicenter test of its effectiveness. Although scheduled to continue until May 1995, the drug trial was called off on Jan. 14, after a group of independent scientists determined that interim results offered compelling evidence of the drug's value. NHLBI's decision to halt the study means that physicians can now offer all patients the option of hydroxyurea treatment.

Investigators at 21 medical centers across the United States began the trial by recruiting 299 people with moderate to severe sickle-cell disease. All the volunteers were age 18 or older and had experienced at least three sickle-cell crises in the year prior to enrollment. Half the recruits received hydroxyurea; half got an inactive substance, or placebo.

The interim results revealed a dramatic benefit from drug therapy. Daily treatment with hydroxyurea reduced by half the number of sickle-cell episodes.

People with this disorder suffer periodic attacks in which their red blood cells form a characteristic crescent shape. An abnormal hemoglobin, or pigment, in these cells lies at the root of the problem. After releasing the oxygen they carry, hemoglobin molecules are supposed to remain separate. But in sickle-cell anemia, they form rigid rods that prevent the red blood cell from remaining pliable.

These sickle-shaped cells then clog the body's small blood vessels and block the distribution of life-giving oxygen, an exceedingly painful event that can cause organ damage.

Until now, doctors had to rely on palliatives such as painkillers and blood transfusions to treat symptoms of the disease. But these measures didn't attack the underlying problem.

"The patients treated with hydroxyurea also required about 50 percent fewer blood transfusions during the study," noted study chairman Samuel Charache of the Johns Hopkins University School of Medicine in Baltimore. In addition, the drug significantly reduced a complication of the disease in which patients develop severe chest pain and fever, he said.

Researchers don't fully understand why hydroxyurea works. But they suspect it boosts the body's supply of fetal hemoglobin, a type of hemoglobin produced by fetuses and newborns that does not form stiff rods inside red blood cells. Normally, adults make only tiny amounts of this variation of hemoglobin.

The Food and Drug Administration has already approved the drug as a treatment for polycythemia vera, a disease in which the body makes too many red blood cells. Thus doctors can now prescribe hydroxyurea for their patients even though the compound has yet to pass FDA muster specifically as a treatment for sickle-cell disease.

However, researchers offered patients a warning. "Hydroxyurea is not a cure," Charache says. "It has beneficial effects, but they last only as long as the patient continues to take the prescribed dose."

They also caution that not every sickle-cell patient should get the drug, which can cause serious side effects.

"Hydroxyurea is a cytotoxic agent," Charache says, noting that it has been linked with leukemia in some polycythemia vera patients. In addition, the trial collected data only on adult patients. For now, scientists advise against giving the powerful medication to children. — *K. Fackelmann*

Mapping stormy weather in the ionosphere

Solar outbursts can roil Earth's ionosphere, rapidly changing the distribution of electric charge at high altitudes. In turn, these disturbances can damage orbiting satellites, disrupt radio communications, and cause harmful surges in electric power lines.

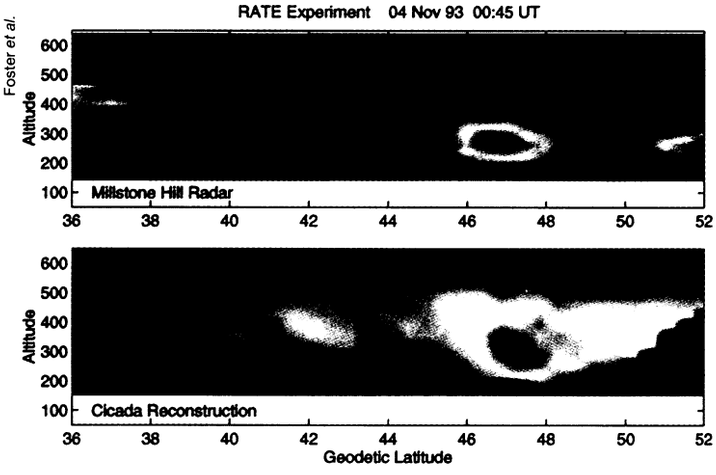
Although researchers have long used radar to study storms and other features of the ionosphere, they have lacked the tools needed to monitor and map it on a regular basis. A recent experiment has now furnished important data that will help scientists develop and refine a novel technique for producing global "weather" maps of the ionosphere.

Known as radio tomography, the technique involves the reconstruction of the three-dimensional distribution of ionospheric electric charge from its effect on radio signals sent from orbiting navigation satellites to ground-based receivers. It requires the same kind of mathematics used in medical tomography to construct three-dimensional X-ray images of biological tissue.

"Radar systems are too costly to build and run to do long-term, global monitoring of the upper atmosphere," says John C. Foster of the MIT Haystack Observatory in Westford, Mass. Radio tomography offers a relatively inexpensive way of achieving such coverage.

To test the validity of ionospheric radio tomography, Foster, Vyatcheslav E. Kunitsyn of Moscow State University, Evgeny D. Tereshchenko of the Polar Geophysical Institute in Murmansk, Russia, and their coworkers set up a joint experiment to see how well tomographic reconstructions stack up against radar measurements. The project, called the Russian-American Tomography Experiment (RATE), also allowed them to compare rival mathematical schemes for constructing the images.

Over a 10-day period beginning Oct. 29, 1993, the researchers used pairs of portable radio receivers at various locations in North America to monitor signals from radio beacons aboard the Russian Cicada and U.S. Transit satel-



Both radar observations (top) and a Russian tomographic reconstruction based on radio signals from a Cicada satellite (bottom) delineate key features of dramatic fluctuations in the concentration of charged particles in the ionosphere.