After the battle, tPA declared a winner

A "clot-busting" drug approved last week by the federal government is expected to help salvage the quality of life enjoyed before a heart attack, and even life itself in some cases — good news for the one out of every four or five people in the United States who will someday experience a heart attack.

Called tissue plasminogen activator (tPA), the genetically engineered protein performed well in recent clinical trials, dissolving clots in 71 percent of patients if injected intravenously within six hours of a heart attack. Data presented in Anaheim, Calif., at this week's annual meeting of the American Heart Association suggest that quick use of the drug also allows the heart to retain its blood-pumping capabilities, thus promoting a more complete recovery.

In announcing the approval, Food and Drug Administration Commissioner Frank E. Young said the approval marks "a new era of pharmaceutical development" based on biotechnology. But FDA enthusiasm didn't come easily for the drug's manufacturer, Genentech, Inc., of South San Francisco.

The drug ran into a regulatory roadblock last May when an FDA advisory panel recommended against its approval. At the time, the panel's position was denounced by some scientists, who said tPA would help prevent major cardiac damage in many of the 800,000 U.S. patients each year who suffer their first heart attack. An FDA spokesman says researchers in the United States and Australia recently provided the additional data that helped convince the FDA of tPA's safety and efficacy.

Although clots in arteries are thought to be the cause of damage in about 80 percent of heart attack cases, the panel had concluded that it was unclear whether tPA's clot removal led to actual health benefits. Two of the recently submitted studies looked at functional improvement of the left ventricle, a heart chamber that pumps blood through the body. If heart muscle is damaged when a clot blocks this ventricle's supply of blood, circulatory problems occur.

To test ventricular function, scientists at Johns Hopkins University in Baltimore used dyes injected into the hearts of several hundred post-heart-attack patients. Some received tPA within four hours of the attack, and all had their ventricular function measured during a 10-day period. Results reported this week indicate that the control group's function worsened over time, while that of tPA-treated subjects improved significantly. A second study in Australia gave similar positive results, says Genentech Vice President James Gower.

Among the questions raised by the FDA panel in May was the possibility of unwanted bleeding caused by the dissolving of clots that are somehow protective. An enzyme naturally produced in the body in minute amounts, tPA specifically binds to the protein fibrin in all clots and converts the blood protein plasminogen to plasmin — which in turn "eats away" the clots. Early clinical trials suggested that tPA treatment may unbalance this feedback process, leading to internal bleeding and the possibility of stroke in some patients. But the lower, currently recommended doses do not increase the risk of bleeding in the brain, says Burton E. Sobel of Washington University School of Medicine in St. Louis, who has coordinated several tPA studies (SN: 1/17/87, p.42). He says intracranial bleeding occurred in only 0.4 percent of the 3,300 patients given the lower doses. This, he adds, is comparable to the incidence seen in heart attack patients not receiving any of these so-called fibrolytic agents.

Ironically, tPA may prove useful in preventing severe strokes. This potential use is the focus of two ongoing studies in the United States, says John F. Rothrock of the University of California at San Diego. Although he says it is doubtful that tPA will benefit most milder cases of "transient ischemic attacks" caused by too little oxygen in the brain, he considers the drug "the most exciting therapy [for severe strokes] at this point."

There are, however, patients in whom tPA should not be used, such as those with a high risk of hemorrhaging. FDA guidelines also call for caution in treating pregnant women and patients over age 75. The drug's usefulness, says Sobel, requires educated physicians and patients who promptly call for medical help.

Cost is another factor. Genentech estimates the cost of a single treatment at $2,000, about 10 times that of the well-established fibrolytic agent called streptokinase. A week prior to tPA's approval, FDA approved intravenous administration of streptokinase, a faster method than the previous approach of injecting it into the heart. Yet streptokinase has its own disadvantages: Derived from bacteria, it can cause allergic reactions and cannot be given as frequently as tPA in cases of recurrent attacks.

With tPA hailed as a speedy and highly specific drug that can be mass-produced through genetic engineering, a crowd of biotech companies are at work on their own versions of the protein. In October, Integrated Genetics, Inc., of Framingham, Mass., announced that mice could be custom-designed to secrete human tPA in their milk.

The bottom line, says Sobel, is that tPA can reduce mortality after a heart attack from the 9 to 11 percent seen with nonfibrolytic treatments to 5 percent or less, "a truly astonishing change."

— D.D Edwards

Solar cells that work in the dark

Immerse a sliver of semiconducting material in an electrically conducting chemical soup and the result is a photoelectrochemical cell capable of converting sunlight directly into electrical or chemical energy. Recently, a group of researchers in Israel constructed a single device that combines photoelectrochemical conversion and electrochemical storage. The final product is a solar cell that includes the equivalent of a built-in storage battery. The storage system allows the cell to draw on energy stored during daylight hours so that it continues to generate electricity even at night.

In the cell, developed by Stuart Licht and his colleagues at the Weizmann Institute of Science in Rehovot, the light-absorbing electrode is a single crystal of the semiconductor cadmium selenide telluride. This light-sensitive electrode and its companion counter-electrode are immersed in an aqueous polysulfide solution. A permeable membrane separates the photoelectrochemical cell from the storage part of the device, which consists of a tin-sulfide electrode dipped in an alkaline sulfide solution.

Light shining on the cadmium selenide telluride electrode starts a chain of events that forces electrons to flow in a wire joining the photoelectrochemical cell's two electrodes. The photoelectrochemical half of the device produces more than a volt of electrical potential at a respectable solar conversion efficiency of 11.8 percent. At the same time, part of the generated current is used to convert tin ions into tin metal in the storage half of the device. In darkness or below a certain level of light, the storage unit delivers power by converting tin back into tin ions. The net result is that the cell continues to work at an overall efficiency of 11.3 percent regardless of the light level.

"It's a wonderful system in its simplicity," says Licht, who is presently at MIT. "There's no electronic switching. There's no computer control. It's just a chemical system that stores energy and spontaneously releases it when it's needed." Licht provides a detailed description of the chemistry involved in this and similar photoelectrochemical cells in the Nov. 12 NATURE. "This is the first chemical description of how these cells work," he says.

Photoelectrochemical cells are potentially more versatile than solid-state photovoltaic devices because they can generate fuels and other useful chemical products in addition to producing electricity. "These are still in the future," says Licht, "but they're being worked on."

— I. Peterson