

would be sufficient in radiation cases, as it works on only certain types of white blood cells, or whether a "cocktail" of several hematologic growth factors would be needed.

"Questions do remain about these drugs, but I would view it as a rational maneuver in lethally irradiated patients," says Grover Bagby of the University of Oregon. "Radiation cases are serious, so with the reality of impending doom, it seems reasonable."

"GM-CSF potentially has a role in radiation cases. Maybe it could help if other alternatives were not available. It depends on what he did and how he did it," says Jerome Groopman of the New England Deaconess Hospital, who recently conducted a clinical trial with 16 AIDS patients. However, Groopman and others say that the use of the hormone in this particular case cannot be evaluated without information on the radiation dose each patient received, how much of the hormone was administered, how it was administered, or the white counts before and after treatment.

Meanwhile, in Rio and Goiânia the federal police are wrapping up their investigation into who is to blame for leaving the cancer therapy machine unattended for 2 years. The owners of the clinic who abandoned the machine have been charged with criminal negligence, the *Washington Post* reports. But which agency is to blame for the slipshod monitoring—and who is in charge of monitoring the 109 other radiotherapy machines in use in Brazil—is the subject of sharp debate.

Brazil's Nuclear Energy Commission is under attack, but it denies that it has responsibility for routine monitoring. The agency is responsible for licensing all radiation sources in the country and for the disposal of all radioactive waste, says Arrieta, but the monitoring of these devices is a responsibility shared by the nuclear commission, the Ministry of Health, and the Ministry of Labor. "In the past that has not been clear. Now, following this unfortunate accident, it is clear," he says.

The nuclear agency's monitoring consists of reviewing periodic reports, filed by the users, detailing the dosimetry of the operators and the calibration of the machine. Energy officials have said that federal and state health officials are in charge of routine inspections. Health officials maintain that they do not have inspection staff.

Last week the Brazilian press reported that indictments for manslaughter were being prepared against officials in both the federal Nuclear Energy Commission and the state. Those reports could not be confirmed. And the citizens of Goiânia continue to worry. ■ **LESLIE ROBERTS**

## New Data Clinch Heart Drug Approval

By early December, hundreds of heart attack victims in the United States will have a better chance of survival because a powerful new clot-dissolving drug recently approved by the Food and Drug Administration will be available in many hospitals across the country. The drug, a tissue plasminogen activator (TPA), is also the first major product of the biotechnology industry and is expected to generate at least a half billion dollars in sales for Genentech, Inc., its manufacturer, by the early 1990s.

"This will significantly modify the way we practice cardiology," says Eugene Braunwald, chief of medicine at Harvard's Beth Israel and Brigham and Women's hospitals. At least 80 percent of the heart attacks suffered by 1.5 million Americans each year are triggered by blood clots plugging coronary arteries.

TPA is an enzyme naturally present in the body in minute amounts. With the help of

This month, FDA approved Activase after new clinical data were submitted, said agency commissioner Frank Young at a press conference on 13 November. New data came from clinical trials conducted at Johns Hopkins, in Australia, and from a multicenter study coordinated by the National Heart, Lung, and Blood Institute. Robert Temple, director of FDA's Office of Drug Research and Review, who was among those in May who wanted more clinical information, says now that data "are impressive." Researchers from the heart institute sponsored study, which is headed by Braunwald, reported in a letter in the October issue of the *Journal of the American College of Cardiology* that Activase did not cause undue intracranial bleeding at the doses recommended by Genentech. Bleeding occurred in less than one-half of 1% of the patients tested at the recommended dosage.

The Hopkins and Australian data showed that the drug did improve heart function, according to Robert Bonow, chief of nuclear cardiology at the heart institute. In the studies, which included about 140 patients each, researchers measured the volume of blood ejected by a patient's heart after treatment with the drug. The Hopkins data showed that the patients' left ventricles were able to pump more blood after the drug was administered. "The preservation of left ventricular function is the most important determinant of survival after a heart attack," Bonow said in an interview.

The new data were reviewed and approved by an ad hoc advisory committee, which included Bonow, Eugene Passamani, another top investigator at the heart institute who coordinates the multicenter TPA trials, and two members of the FDA advisory committee. As recently as 2 September, the ad hoc committee voted not to approve the drug until more data were examined.

The crucial factor in Activase therapy is that a patient be treated with the drug as soon as possible after the onset of an attack, according to cardiologists. The drug will be available primarily in hospitals and must be administered intravenously. A single treatment will be priced roughly about \$2000, says Robert Swanson, Genentech's chief executive officer.

When Genentech failed to win approval in May for Activase, there was much speculation that the company would lose a lot of ground to other competitors. But little, if any, damage has occurred in 5 months, say David Manyak, a Merrill Lynch analyst, and Peter Drake of Kidder Peabody. ■

**MARJORIE SUN**



**Approving smiles.** FDA chief Young, center, with Genentech's Swanson, left, and Snyderman.

genetic engineering, scientists can now produce the substance in quantity by modifying mammalian cells. The version of the drug approved last week is marketed by Genentech under the brand name Activase.

In late May, an FDA advisory committee rocked the cardiology community, Wall Street, and patients by voting not to approve the drug and requested more clinical information (*Science*, 3 July, p. 16). Although the data showed Activase to be a potent clot-dissolver, committee members and some FDA officials questioned the appropriate dosage because some patients, who had been treated with high levels suffered bleeding in the brain. Committee members also were not persuaded that the drug actually improved a patient's heart function. Braunwald and other cardiologists believed, however, that the drug should have been approved.