On 13 September two young scavengers in Goiânia, Brazil, removed a stainless steel cylinder from a cancer therapy machine in an abandoned clinic, touching off a radiation accident second only to Chernobyl in its severity. On 18 September they sold the cylinder, the size of a 1-gallon paint can, to a scrap dealer for $25.

At the junkyard an employee dismantled the cylinder and pried open the platinum capsule inside to reveal a glowing blue salt-like substance—1400 curies of cesium-137. Fascinated by the luminescent powder, several people took it home with them. Some children reportedly rubbed it on their bodies like carnival glitter—an eerie image of how wrong things can go when vigilance over radioactive materials lapses.

In all, 244 people in Goiânia, a city of 1 million in central Brazil, were contaminated. Four people have died, including the 6-year-old niece of the junkyard dealer. Two are in guarded condition, and about 15 others remain hospitalized in Goiânia and Rio de Janeiro. The eventual toll, in terms of cancer, is estimated to be hundreds or even thousands.

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had treated the victims of the Chernobyl accident. They arrived in Rio on or near 7 October; Trexler, an environmental specialist, immediately left for Goiânia.

The medical team found the 20 most seriously irradiated victims had received doses ranging from 100 to 800 rads, reports Ricks, who is director of REACTS. Nineteen of the 20 had radiation-induced skin burns, from minor to major. And all 20 patients were internally contaminated, which meant that they were being continually irradiated from the cesium that they had inhaled or accidentally ingested. The patients themselves were radioactive.

Radiation destroys the most rapidly dividing cells of the body—the cells of the skin, hair, gastrointestinal tract, and bone marrow. Because the bone marrow gives rise to the blood cells, including those of the immune system and the platelets that staunch bleeding, radiation victims are susceptible to infections and hemorrhaging. But unless the dose is exceedingly high, the bone marrow can recover; the challenge is to keep the victims alive until that happens. At exceedingly high doses, bone marrow damage is irreversible, and bone marrow transplants may be the only recourse. Transplants, however, are risky and are useful only in rare cases in which other organs are not severely damaged and a matched donor is available.

The Brazilian physicians ruled out transplants for the Goiânia victims. Rather, the first task was to attempt to rid their bodies of cesium. For this, they administered Prussian blue, an iron compound that binds with cesium, aiding in its excretion. The problem in this case was the substantial delay—at least a week—from initial exposure to treatment. By that time much of the cesium had moved from the bloodstream into the tissues, where it is far more difficult to remove. As a result, the patients are still contaminated, but the levels of cesium have been reduced, reports Ricks. The patients were also treated with antibiotics as needed to combat infections and with cell infusions to prevent bleeding, Ricks says.

When Ricks and Lushbaugh left at the end of a week, with the understanding that they would return, six patients were seriously ill, and four or five were expected to die. Since then four have died. The Argentinian, Jimenez, stayed an additional 4 or 5 days; the Soviet hematologist is reportedly still in Brazil.

At the same time, government workers were scouring Goiânia for traces of the glowing powder, using helicopters equipped with radiation detectors to identify the hot spots. They have turned up contaminated furniture, cars, buses, money—and five pigs. Much of the powder soaked into the soil, which is being scooped up into concrete-lined drums. Some houses and buildings are still dangerously radioactive and may have to be destroyed. What cannot be decontaminated is being dismantled and put into concrete-lined drums for disposal as nuclear waste.

Reports vary about how thorough the decontamination efforts have been and whether all the scattered cesium has been found. According to the Nuclear Energy Commission, the contamination is confined to a 2000-square meter area, very close to a small stream. So far, no signs of contamination have been found in either the stream or the river it flows into. Cleanup is expected to take until at least March.

The ultimate fate of the tons of radioactive waste from the accident remains to be determined. Brazil does not have a permanent nuclear waste disposal site; the drums of waste from the accident are being stored temporarily at a surface site some 30 kilometers from the city until a permanent site can be found.

Meanwhile, local health officials continue to offer radiation monitoring. To date, about 78,000 people have reportedly been screened, along with many of their possessions and their pets.

The circumstances surrounding Gale's activities are somewhat more difficult to piece together, as his account differs from those of Brazilian officials. Gale spoke with Science on 6 November but is now traveling in Argentina and could not be reached for further comment.

Gale arrived in Brazil on 17 October, where he spent about 10 days. On 2 November, in a front-page article that sparked the current furor in Brazil, the New York Times reported that Gale saved the lives of two of the most severely irradiated victims through the use of an experimental drug, granulocyte-macrophage colony-stimulating factor, or GM-CSF. The article describes how Gale received his invitation to go to Brazil while he was attending a meeting in West Germany. He collected a supply of the recombinant drug, a hematologic growth factor, from Behring, a West German pharmaceutical company, alerted the medical team that treated the victims of Chernobyl, and flew on to Rio, supported again, as he was at Chernobyl, by Armand Hammer of Occidental Petroleum.

Then in an exacting procedure, Brazilian doctors working under Gale's guidance administered the drug to six patients who otherwise would have died, the article said. (GM-CSF was given to two additional patients after he left.) A little more than a tenth of a pint was injected directly into the vena cava in a continuous infusion over 24 hours. Four who were extremely ill died, two recovered. Gale attributed their survival to the experimental therapy, which has never been tried on radiation victims before. Gale told Science that the story reported in the New York Times is accurate.

GM-CSF is one of a family of hormones that stimulate the bone marrow to produce white or red blood cells. GM-CSF specifically stimulates neutrophils and monocytes, the white blood cells that kill microbes. GM-CSF is not approved for medical use in the United States or Brazil, but is undergoing clinical trials here to determine its usefulness in boosting white cell production in patients with suppressed bone marrow (Science, 1 May, p. 517).

A similar story appeared in the 16 November Time, with the same photograph that appeared in the newspaper showing Gale, in mask and gown, standing by the bed of one of the accident victims. "We are living in a new age of medicine," Gale is quoted as saying. "When it comes to these disasters, all the handbooks on treatment will have to be rewritten."

Brazilian officials were reportedly taken aback to learn of the New York Times article, which engendered a flurry of trans-Atlantic calls among Brazilian authorities, the American Medical Association, and the IAEA. "It has caused a lot of gastritis," says Ricks, who is in regular contact with Brazilian Navy doctors and nuclear commission. Ricks will be returning to Brazil in December.

Brazilian officials say, contrary to Gale's account, that they did not invite him. In
fact, Gale's offer of assistance after the accident was respectfully declined because bone marrow transplants, Gale's area of expertise, were not indicated, says Luis Arrieta, executive director of the Nuclear Energy Commission.

According to Arrieta and Brazilian press accounts, Gale was invited by a Brazilian friend of his, Daniel Tabak of the National Bone Marrow Transplantation Center in Rio. "It was a personal invitation, not a government invitation. He came on a tourist visa," says Arrieta. Tabak then escorted Gale to the hospital and introduced him to the director, Admiral Amiha Burlah.

But Gale insists that the government invited him. "I was invited by the Navy, which I consider the government, by Admiral Burlah," Gale told *Science*. "I was invited by the person handling the treatment." In a second conversation that day, Gale said, "someone from the hospital called me, I'm not sure who it was."

"I don't know who invited him. I did not invite him," Burlah told *Science*. "He came to the hospital and we were introduced."

There is some question about how the decision to use GM-CSF was made and how large a role Gale played. Gale, who brought the drug with him and arranged for additional supplies to be sent, has described his role as pivotal.

Burlah, who is in charge at the Navy hospital, says that Gale was one of several doctors offering their advice. "He gave his opinion, as did other doctors." The decision to use the drug was a group one, Burlah says, and Gale was in the hospital "only a few days."

The Brazilian equivalent of the Food and Drug Administration, is now investigating Gale's role and whether proper experimental protocols were followed. No one suggests that the experimental treatment harmed the patients, but there is some question about whether it helped.

"We are in trouble with our agency, like your FDA," Arrieta concedes. "The agency is concerned that it is not exactly normal to use a new drug without prior approval. But of course it was an emergency and the medical team was probably not thinking about it," Arrieta says. Gale was reprimanded by the National Institutes of Health in 1985 for using an experimental protocol on cancer patients without receiving approval of the UCLA Human Subjects Protection Committee or informed consent of the patients (*Science*, 1 August 1986, p. 513).

Gale seems to be oblivious to the controversy. "My presence was requested, so I can't see why they would be unhappy about GM-CSF. I wouldn't think they would be unhappy because two people lived. We are trying to save victims of a radiation accident—the specific technique is irrelevant." He told *Science* that he followed appropriate FDA procedures for using an investigational drug, including obtaining approval from the head of the hospital, Burlah, and from the institutional review board, as well as the informed consent of patients.

Gale told *Science* he was returning to Brazil for a couple of weeks. Neither Burlah nor Arrieta knew anything of his return. "As far as I know he is not coming back on an official invitation," says Arrieta.

At this stage it is difficult to tell whether Brazilian officials are more concerned about the experimental treatment or about Gale's grandstanding before the press, which they say does a disservice to the other doctors involved and violates their own desire for confidentiality. The Navy doctors had agreed not to discuss medical data with the press until the results could be properly evaluated.

Brazilian officials also clearly resent some of Gale's remarks to the press. "Gale said the first medical team did not have the right profile and that we were late to call for his assistance," Arrieta says. "We never called for his assistance." Moreover, Gale's comments "do not say much for the other medical team," which Arrieta says performed superbly. "Of course we welcome Dr. Gale's help. But we do not welcome his intervention in the decisions we made."

The American Medical Association (AMA) is also looking into the matter. "We are concerned about some aspects of the incident," says AMA's William Hendee. "We are trying to find out as much information as we can to see that nothing has been misrepresented." Hendee emphasizes that AMA is not investigating Gale but is gathering information on the medical care of the radiation victims, including Gale's activities.

"We are interested in new types of therapy and results and in the accurate reporting of those results. We want to see if what is stated to be the effect [of the experimental therapy] can be documented. I don't know how you can say that the two Brazilians who did not die were saved by the treatment."

Gale concedes that the two patients might have survived without the drug. "Two of the people are alive. Without a random trial you can't say why. They had an abrupt reversal, the white blood count went way up. The major effect of the drug is to elevate the white blood count. So it is very likely the drug."

Whether the drug actually enhanced recovery or improved survival is difficult to judge without more information, others working with GM-CSF say. The drug has been used on only about 150 patients in clinical trials, though early results are encouraging and to date it seems to have few toxic effects. Theoretically, several say, GM-CSF could be useful in treating radiation victims who have some responsive bone marrow left. However, questions remain about the long-term effects of this hormone. Nor is it clear whether GM-CSF alone
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, 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 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.

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. "Improvement 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 Peter Drake of Kidder Peabody.

LESLIE ROBERTS

Leslie Roberts was the science editor of Science magazine. She has also written for the New York Times and the Los Angeles Times. She is the author of several books, including "The/Great Inventions of the 20th Century."