On March 26, 1951, at a conference in the Drake Hotel in Chicago, Dr. Andrew C. Ivy startled the world of science by announcing a new treatment for cancer. It was called Krebiozen. Twenty of the first 22 patients he himself had treated with it, said Doctor Ivy, had experienced an ‘‘improvement in their general condition . . . and a regression of the cancer.’’ Coming from someone of Doctor Ivy’s standing—he was then a world-renowned professor of physiology at the University of Illinois School of Medicine in Chicago—this pronouncement stirred a wave of excitement and hope. But from the outset the affair had a great many mysterious and troubling aspects.
Discoverer of the substance was Dr. Stevan Durovic, a refugee Yugoslav physician, whose production method was only sketchily outlined at the meeting. Since Doctor Durovic was not fluent in English, Doctor Ivy explained for him that Krebiozen was obtained from horse blood after the horse's "cell network had been stimulated." The end product was a white powder.

Soon after the Drake meeting, Doctor Ivy told reporters that Doctor Durovic had refused to reveal details of the Krebiozen process and formula because he did not want Iron Curtain countries to benefit. "He despises communism," Doctor Ivy declared, "because he was deplored by communism in Yugoslavia." In addition, Doctor Ivy said, Doctor Durovic's brother, Marko, had invested more than $1,000,000 in Krebiozen development and wanted to recoup his investment.

"I think his position is proper," Doctor Ivy said. "Too many discoverers have died in the poorhouse." Because of this refusal to reveal Krebiozen's formula the American Medical Association branded it a "secret remedy." The end product was a white powder.

Within recent months two agencies of the Federal Government—the National Cancer Institute and the Food and Drug Administration—have issued statements to the effect that Krebiozen is ineffective in the treatment of cancer. The National Cancer Institute, a unit of the Department of Health, Education and Welfare, had appointed a committee of 24 leading medical authorities to examine Krebiozen case records and determine whether Government-sponsored clinical trials should be undertaken.

The committee, after scrutinizing the records of 504 treated patients, stated last October 16, "It is the unanimous opinion of the Review Committee that Krebiozen is ineffectual as an antitumor agent. In a very small number of patients, tumor regressions of varying degrees were seen during Krebiozen treatment. The validity of these regressions is subject to question for several different reasons. It is the opinion of the committee that the nature, degree and number of effects noted are what one might expect in any large random sample of cancer patients. The committee strongly recommends that no clinical trial of Krebiozen be undertaken."

A month earlier another damaging blow against Krebiozen had been struck by the Food and Drug Administration. A chemical analysis of Krebiozen powder supplied by Doctor Durovic showed it to be a creatine, a common amino acid derivative "plentifully available from meat in the ordinary diet... and a normal constituent of the human body."

The FDA also declared that in its sampling of ampuls of Krebiozen in liquid form, shipped prior to 1960, it found nothing but mineral oil. Samples from 1963 in its possession contained, in addition to mineral oil, "minute amounts" of amyl alcohol and a creatine derivative different from that identified in the powder.

"It is impossible to conceive that creatine... could be of any value in treating human cancer... This chemical was tested some time ago against animal tumors in the routine cancer chemotherapy screening program of our institute and was found to be ineffective, even in high doses."

Government action finally came—only after 13 years of uncertainty. Within recent months two agencies of the Federal Government—the National Cancer Institute and the Food and Drug Administration—have issued statements to the effect that Krebiozen is ineffective in the treatment of cancer. The National Cancer Institute, a unit of the Department of Health, Education and Welfare, had appointed a committee of 24 leading medical authorities to examine Krebiozen case records and determine whether Government-sponsored clinical trials should be undertaken.

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At the University of Illinois but resigned as vice president for medical affairs at the University of Illinois itself. Dr. Harold Diehl, then dean of the University of Minnesota Medical School and new vice president of the American Cancer Society, said the evaluation at his school brought dismal results. "We got Krebiozen very early," he said, "enough for thirty patients. We had no preconceived prejudices. We carried out the test with an air of optimism. Many of us knew and respected Doctor Ivy. But Krebiozen did absolutely no good. There were similar results in other institutions where it was tried, including the Mayo Clinic, the Lahcy Clinic and the University of Illinois itself."

Gradually, as test results came in from a variety of institutions, the famed Doctor Carlson himself became distrustful about his former star pupil. One night in the early 1950's Doctor Carlson invited to his home Doctor Ivy and a number of other leaders in Chicago medicine. Doctor Carlson, according to one of the participants at the meeting, pleaded with Doctor Ivy to "get out of this Krebiozen mess." It simply did not work.

Doctor Ivy's attitude toward his former mentor and toward the other physicians assembled was: I do not need your advice. I know what I am doing.

In 1953-54 a special committee of the Illinois State Legislature investigated the whole affair, concluded that both Doctor Ivy and Doctor Durovic were "men of good character" and that neither Doctor Stoddard nor the A.M.A. had conspired against Doctor Ivy. During the committee's hearing, Doctor Ivy adamantly defended his stand: "I was not duped. . . . Other people were duped as it normally does with both commercial and experimental drugs."

"I sat beside Doctor Carlson at some of the Illinois legislative hearings," says the A.M.A.'s Doctor Howard. "At one session I glanced toward him, the world's greatest physiologist, and tears were rolling down his cheeks. He kept repeating, 'Why is Ivy talking this way? Why is Ivy talking this way? It's not true. It's not true.'"

A major force in keeping the Krebiozen affair going has been Senator Douglas, the Illinois Democrat. He is a longtime friend of Doctor Ivy. They taught together years ago at the University of Chicago. Very early in the Krebiozen affair, Senator Douglas sponsored a private bill to obtain United States citizenship for the Durovics. "As I recall, the Yugoslav quota to the U.S. was filled, and the Durovics had only temporary visitors' permits," Senator Douglas says. "I knew that Senator Brien McMahon of Connecticut had received Krebiozen [he later died of cancer], and I called him to get his support for the private bill. Others helped and it passed relatively quickly." Now just how deeply Senator Douglas feels about Doctor Ivy is revealed in the following excerpt of a 1951 meeting of officers of the Krebiozen Research Foundation. In the minutes, Senator Douglas is quoted as having said:

"At this point, I want to make one thing clear, and I hope it sticks, and that is this: that whatever I do, I am doing for our Doctor Ivy, who in my estimation is a man deserving of the greatest respect and cooperation from all of us. As a matter of fact, were it not for Doctor Ivy, I would be very skeptical of the whole damn thing."

This loyalty resulted in Senator Douglas's putting pressure on both the FDA and the National Cancer Society to conduct what he called a "fair test" for Krebiozen. Senator Douglas states flatly that the FDA test which found Krebiozen to be creatine was not competent and that even the numerous scientists who carried out the test did not agree on Krebiozen's chemical composition. Further, he says that the NCI study of patient treatment results was biased and overlooked many pertinent facts of patient improvement.

"In addition, the FDA has been spreading rumors to the effect that a vast fortune has been made from Krebiozen," says Senator Douglas. "This is sheer nonsense. It was given away until 1954, and after that, I'm told, the Krebiozen Foundation has received donations for only about one third of the ampuls distributed in the U.S.

"The medical profession sometimes errs. This is a matter of historical fact. But when it makes up its mind and takes a stand, it can distort and be cruel merely to save face. Nothing that has happened in the past twelve years has made me lose confidence in Doctor Ivy's honesty, competence or integrity."

Among other Krebiozen supporters is U.S. Rep. Roland Libonati of Chicago, also a longtime friend of Doctor Ivy. According to Doctor Stoddard, Libonati had a part in forcing his resignation from the University of Illinois after Stoddard criticized Doctor Ivy. Libonati is a fascinating individual, a lawyer who in the past represented underworld characters and who was a known Capone associate.

Quite apart from such official supporters of Krebiozen, however, the Government's longtime role in the affair was to remain largely inactive. For years federal agencies did little to inquire into the production process of Krebiozen or to analyze its ingredients. One reason, as Government sources point out, was that Doctor Durovic refused until 1960 to provide definitive information on the production or to furnish an adequate sample of Krebiozen powder from which Government chemists could make an independent analysis. Another reason was that federal laws applied to the testing and sale of drugs, but Krebiozen was not formally sold. From 1951 to 1954 the drug was shipped to patients without the Government's really attempting to classify it at all, or to police its production—as it normally does with both commercial and experimental drugs.

Then in 1954 Mrs. Oveta Culp Hobby, Secretary of Health, Education and Welfare, ruled that Krebiozen was a "biologic product," which meant it would have to be licensed by the Division of Biologies Standards. But Doctors Ivy and Durovic never applied for such a license and therefore the Division never inspected Promak Laboratories in Chicago, where Krebiozen was being put into ampuls. It never sought to determine the purity of Krebiozen, or its efficacy in treatment, both of which it is charged to do under federal regulations.

Why Krebiozen was classified as a biologic—as are vaccines, antitoxins and blood products—no one seems to know.
SENATOR DOUGLAS: "HISTORY IS REPLETE WITH PERSECUTIONS OF THE MEDICAL DISCOVERER."

In any event, Doctor Ivy argued before the Public Health Service that Krebiozen was in fact not a biologic but a hormone and belonged under FDA regulation, which was at that time less stringent than the regulation of biologies. Under FDA rules then in force a drug manufacturer could distribute an experimental product in what even the FDA's chief counsel, William Goodrich, refers to as "loose fashion." The producer had only to prove his medicine was nontoxic, not that it was efficacious. In other words, a drug which could not cure anyone of anything was perfectly legal so long as it did not harm the patient. This loophole probably prevented a showdown on Krebiozen for more than five years.

It was not until 1963 that these loopholes were closed by the Kefauver-Harris amendments to the FDA regulations. The late Sen. Estes Kefauver and his committee had investigated the drug industry. And the thalidomide disaster, in which a sleeping pill deformed thousands of unborn babies, emphasized the need for better controls on drug testing.

The Krebiozen Research Foundation submitted a plan of investigation last June to conform to the new regulations, but withdrew it the following month. The FDA therefore ruled that Krebiozen could no longer be shipped outside the state of Illinois. As of last month a small group of patients and relatives were still traveling to Illinois from other states to obtain Krebiozen, but Doctor Durovic said Krebiozen supplies were dwindling.

Thus in fuel not a biologic but a hormone of its membership. Such a case is that of George Friedman, a 49-year-old engineer who died of cancer last August 10. His wife, Mrs. Laine Friedman, of Flushing, N.Y., a charming and articulate woman, is chairman of the Cancer Survivors on Krebiozen of Queens. "It is from these people that a group called the Cancer Survivors on Krebiozen draws the bulk of its membership."

Such a case is that of George Friedman, a 49-year-old engineer who died of cancer last August 10. His wife, Mrs. Laine Friedman, of Flushing, N.Y., a charming and articulate woman, is chairman of the Cancer Survivors on Krebiozen and a tireless worker on behalf of the drug. She led the march on the White House last year, carried a sign imploring the late President Kennedy to "save our lives—we need Krebiozen." She was arrested because she approached too close to the White House, was mistreated by the police, she cried, and was released.

Here is Mrs. Friedman's story concerning her late husband:

When in the spring of 1961 he began to have persistent trouble with his digestion, his wife persuaded him to see a surgeon at the New York Hospital-Cornell Medical Center. Although tests by an internist proved negative, an exploratory operation was performed. "After the operation," Mrs. Friedman related, "the surgeon called me with the horrible news. George was riddled with stomach cancer. 'How much time does he have?' I asked. 'I'm not a good judge of time,' he told me. 'Maybe a month or so.' "

"The doctor told me to take George home, make him comfortable and tell him he had cancer so that he could wind up his affairs. I thought it over and decided to tell George nothing. Instead I resolved to fight this thing, this cancer. That was in the spring of 1961." Mrs. Friedman asked the American Cancer Society and several doctors about Krebiozen and was told it was worthless. Nevertheless she persuaded a neighborhood doctor to give it to her husband, although he, too, said it was worthless. He would give it, he told Mrs. Friedman, "only for your psychological well-being."

Mr. Friedman received his first injection of Krebiozen in July, 1961. "His condition began immediately to pick up," Mrs. Friedman recalls. "His appetite increased. He was able to walk around and do simple gardening once again. He literally came back to life. He stayed on an even keel for months, returned to work and periodically went to the hospital for a stomach tap, to remove the fluid causing the distension."

As time went on, Friedman learned that he was on Krebiozen, joined his wife in the fight to save it from "Government persecution." Last June Friedman went into a steep decline.

On the morning of August 10, his wife recalls, "he got up, made his own breakfast, had lunch and said that he felt uncomfortable. I gave him an enema and he said he would rest in bed. He got into bed, stayed there a while and suddenly said, 'There's a drum in my head.' Then he stared straight ahead and died quietly a half hour later. Krebiozen kept him alive and made his death a peaceful one. There is no doubt of that in my mind."

Because of Mrs. Friedman's prominence in the Krebiozen movement, the FDA investigated the case. It obtained a
pathological specimen of Friedman's cancer and sent it to the Armed Forces Institute of Pathology, Washington, D.C.

The AFIP finding, which has never before been made public, is clearcut. George Friedman had what pathologists refer to as a "lazy tumor." Its growth rate could not be accurately predicted. It might have killed him in a few weeks, a few months or a few years. Some patients with this type of tumor have been known to survive for extremely long periods.

More generally, medical authorities attribute the seeming benefits of Krebiozen to a number of causes. Says Gilbert Goldhammer, chief of FDA's regulatory division, "The mere fact that you announce a drug as beneficial against cancer will cause countless people to use it and claim that it has saved their lives. These people, some of whom have cancer and some of whom do not, are so eager for a 'cancer cure' that they will attribute real therapeutic value to anything, even distilled water."

"It is a fairly common experience for late-stage cancer patients [labeled as terminal]," says NCI's Doctor Endicott, "to show what are often interpreted as beneficial results. Most often these results are said to involve decrease of pain, improvement of appetite and ability to walk around. This apparently is what has been reported by Krebiozen patients. But they probably would have gained the same effect from anything else offered to them as a cancer therapy—anything from snake oil to blinking lights."

**Clamor for a "fair test"**

As for Krebiozen's disproving a doctor's prediction of a patient's death, Doctor Endicott warns that cancer is extremely unpredictable, and no doctor can accurately foretell its course. In addition, he points out that many of the advanced-stage patients taking it have also received conventional types of treatment—surgery, radiation or chemotherapy. If their lives have been prolonged, he says, it is because of these standard therapeutic measures, not because of Krebiozen.

Throughout the tumultuous 13-year history of the Krebiozen affair, the drug's proponents have clamored for a "fair test of Krebiozen" on known cancer patients. Indeed, several senators have joined Senator Douglas in drafting a resolution calling for such a test.

"We will not perform a test on a worthless substance," answers Doctor Endicott. "For three years I felt like the little Dutch boy with his finger in the dike out there in front of God and everybody else. At that time, I was alone trying to cope with this Krebiozen situation."

"Now we have absolute proof that Krebiozen is of no value in the treatment of cancer. How can anyone ask that a test be performed on such a substance, that we deny patients all other known forms of treatment and give them only Krebiozen? With known, effective forms of treatment, about thirty-three percent of all cancer patients can be cured for five years or longer. If we tested Krebiozen, we would be sacrificing that thirty-three percent. Would you want to be a patient in such a test? A Krebiozen test on patients would be immoral. For any physician to participate in such a test would be unethical to say the least. The Senate resolution demands that we carry out a test which I consider almost a criminal act."

Who is ultimately responsible for perpetuating the Krebiozen affair? Dr. William Stewart, of Health, Education and Welfare, believes "the basic responsibility rests on the backs of the doctors who injected Krebiozen into their patients."

"If doctors had the attitude through the years of 'show me how this works, tell me what it is,' Krebiozen never would have happened," he maintains.

Last summer, after the NCI report on Krebiozen failures in patients, Doctor Endicott said, "Krebiozen, from a scientific point of view, is a closed matter," But Doctor Durovic steadfastly rejects that statement.

"Last September," he says, "I wrote to Mr. Celebrezze [Secretary of Health, Education and Welfare], stating that we would produce a new batch of Krebiozen with FDA people present. I was saying to him in effect, you can hang me with my own rope if I am wrong about Krebiozen. But the FDA refused. The FDA's plan, of course, is to harass us to such an extent that we will abandon Krebiozen."

"I will never do that. I am not going to drop Krebiozen. I believe in it. It helps patients. Krebiozen represents thirty-three years of my life's work. I hope we can get the help to win this fight. I believe we will win—because of the power of human justice."

Doctor Ivy is equally vehement.

"I'm going to keep going. I'm going to continue my work. This isn't Russia. Here the creative scientist is free."

Is the Krebiozen affair dead? Not by a long shot.