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NEWS AND COMMENT

The Krebiozen Case: What Happened in Chicago

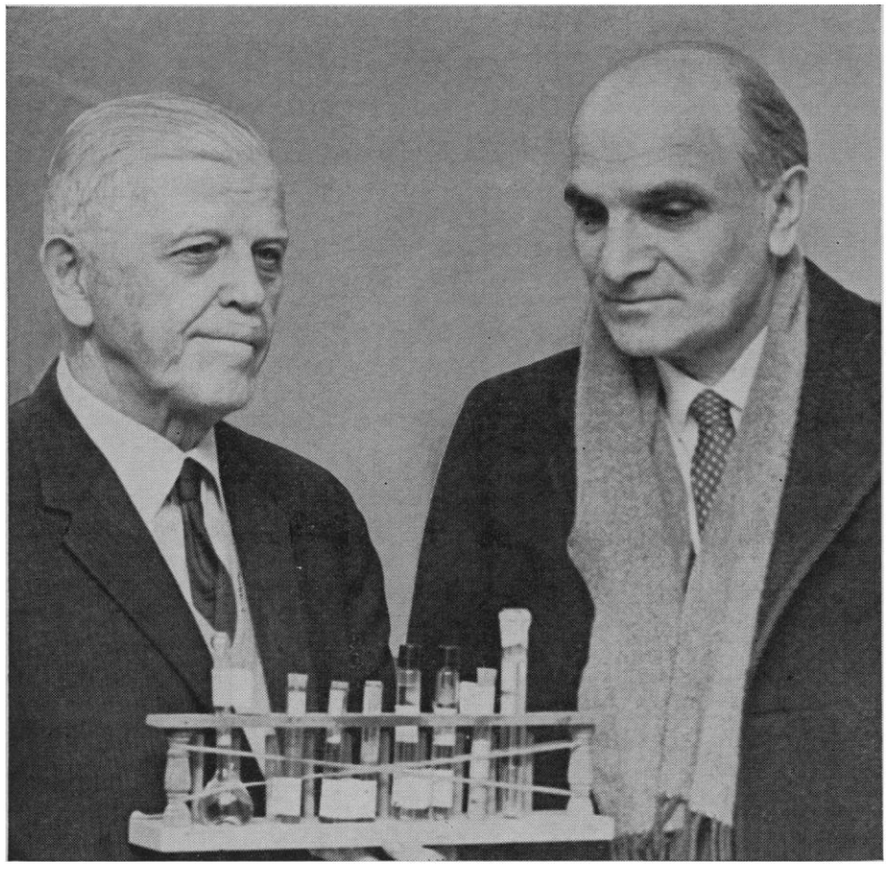
Chicago. The main question left standing in the Krebiozen case after 15 years of controversy and a 9-month criminal trial ending in acquittal for all the principals is how so many people could spend so much time on a problem so limited and come up with so little. The federal government prosecuted Andrew Ivy, Stevan Durovic, and two of their associates, Durovic's brother Marko and a Chicago physician, William Phillips, with all the zeal of the crusaders pursuing infidels. But, despite the government's efforts, the record is thin and full of contradictions. Immediately after the trial the Food and Drug Administration and the American Medical Association issued statements stressing that the verdict in no way altered their scientific judgment that the alleged anticancer agent is therapeutically worthless. Whether the public will accept that view, however, is open to doubt. As a challenge to public policy, the question of Krebiozen is plainly not yet settled.

To understand what happened at the trial it is important to realize how badly the government wanted to win the Krebiozen case. The passion was generated in part by certain characteristics of the Food and Drug Administration, in part by the peculiar intractability of the Krebiozen problem. The FDA has long had difficulty maintaining its scientific capability and in navigating the tricky shoals of drug regulation. But it has been unfailingly proud of its record against quackery: the agency is happiest when it is left to the fight against frauds.

In the case of Krebiozen, the FDA had much at stake. Throughout the 1950's, while Krebiozen, already controversial, was being distributed as an experimental drug, the agency took the position that the problem belonged in other hands. But in 1963 it became engaged in a full-scale investigation of the drug. FDA's involvement began as an effort to help the National Cancer Institute gather data on Krebiozen-treated patients to determine whether a long-sought official test of the drug seemed indicated (*Science* 21 June, 28 June, 5 July, 1963). It soon spread into an ambitious campaign to reconstruct all aspects of the drug's clinical, financial, and chemical history.

By the fall of 1963, FDA had reached its scientific conclusions. The Krebiozen powder, the agency announced, had been identified by several chemical tests as creatine. The contents of Krebiozen ampules were identified as mineral oil, with minute amounts of two other substances, amyl alcohol and 1-methylhydantoin, found in ampules shipped in 1963. FDA's chemical analysis was soon supported by the findings of the National Cancer Institute that Krebiozen "does not possess any anticancer activity in man."

These announcements had two effects. First, they put FDA's scientific reputation on the line: if Krebiozen were ever demonstrated to be something other than creatine, the agency, fighting hard for a progressive image, would find itself aligned instead with all the discredited reactionaries in the history of science. Second, no bureaucracy is sensitive to ambiguity, but the findings completely obliterated whatever appreciation of the complexities of the Krebiozen mystery FDA officials had previously been able to muster. From then on, they treated it as an open-and-shut case. If Krebiozen was creatine, it was obviously fraudulent. If it was fraudulent, the men marketing it were not erring scientists but crooks.



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Andrew Ivy (left) and Stevan Durovic after the Krebiozen trial.

If they were crooks, they could be treated as crooks.

From that point on, everything the government did had one result: to elevate the stakes. Interstate shipment of Krebiozen was already prohibited under the terms of new drug regulations that went into effect in the summer of 1963. But the drug was still available in Illinois, and the government wanted to close down the supply lines once and for all. Accordingly, they decided on a splashy criminal trial, a risky procedure usually entered upon only reluctantly because the government is barred from appealing an adverse verdict. In October 1964 the Justice Department, which prosecutes such cases for the government, went to a Chicago grand jury and obtained a massive 49-count indictment charging conspiracy, mail fraud, mislabeling, and making false statements to the government; conviction could have cost Ivy and Durovic several hundred thousand dollars and put them in jail for over 100 years. Another government move reinforced the mood: the setting of an unprecedented bail of $500,000 for each of the Durovic brothers. (This was later disallowed by a judge who let them go without bail.) By the time of the trial, which began in the spring of 1964, it was clear that the government's position was that it was dealing with vicious desperadoes. And the government believes it.

Although the details of the government's case are overwhelmingly complex, the underlying thesis was simple: Krebiozen never existed. In his closing argument to the jury, government prosecutor Arthur Connelly read aloud the Anderson fairy tale "The Emperor's New Clothes." The analogy pleased the prosecution for several reasons. The substance, Krebiozen, was as invisible as the Emperor's clothes. The Food and Drug Administration became the innocent child who admitted that the clothes could not be seen, while the populace was admiring them and the chamberlains were lifting the train above the ground. And, best of all, the errant weavers had actually gone through the motions, working away at empty looms, "burning sixteen candles so that people might see how anxious they were to get the Emperor's new clothes ready. They pretended to take the stuff off the loom. They cut it out in the air with a huge pair of scissors, and they stitched away with needles without any thread in them." The prosecution contended that that was the story of Krebiozen. The government did not deny that Durovic had processed horses at a plant in Rockford, Illinois (horses injected with an extract of *Actinomyces bovis* are said to be the source of Krebiozen), nor that his Chicago laboratory contained a variety of scientific instruments. But, said the prosecution, "those were the looms, those were the shuttles." According to Connelly:

> . . . You have the story here of the two swindlers who come from Argentina. They said they had the secret stuff in a vial. They said they dissolved it in mineral oil so no one could see it, and they thought no one could find whether it was there by any other means.
>
> They met the emperor, the man who considered himself to be the greatest of all scientists; a man who considers his opinions beyond question, beyond any question by any one. He provided these two swindlers with the rooms, and the other trappings to put the scheme over. The emperor cast in his scientific reputation. Without it, not a nickel's worth of this stuff could have been sold.
>
> Almost from the very first, if not from the very first, the emperor knew, or must have known, that this stuff didn't exist.
>
> When the skeptical asked to see the secret powder, the swindlers and the emperor himself made excuses and charged that those who doubted were prejudiced and motivated by ideas of themselves taking the profit from the secret stuff.
>
> Then came the little boy, the Food and Drug Administration, who knew that if the stuff existed as the swindlers and the emperor claimed, that it at least ought to be visible in the amounts that they claimed it was in these ampules. . . . When finally the time came when the stuff could no longer be sheltered by excuses, claims of unfairness, it turned out not to be a beautiful, unique fabric at all. It was a common chemical and the shots offered as the great treatment for cancer were mineral oil.
>
> Even when presented with overwhelming scientific evidence, even when their own chemist identified the stuff as creatine, the swindlers and the emperor persisted.
>
> Why?
>
> In 1950–1951 because they hoped to sell the secret stuff to Abbott, or Lilly Laboratories for millions. For this they falsified the result of clinical trials, as well as the truth about the stuff.
>
> From 1956 until today because mineral oil at prices from $9.50 to $95.00 per ampule was making them rich from frantic cancer patients grasping for a straw of hope.

The government's position was plainly extreme. Subtler hypotheses, perhaps, could have explained as many if not more of the facts that months of investigation uncovered. But the FDA lacks affinity for subtlety. The agency's

investigation had led it to the conclusion that, for essentially circumstantial reasons, Durovic could not have produced Krebiozen by the method he claimed, at the time he claimed, or in the amounts he claimed. These circumstantial considerations, stressed heavily during the trial, were reinforced by the chemical analysis and by the medical findings that the patients had not benefited. FDA came to its position naturally and honestly. But as a strategy it was a poor choice.

The prosecution kept repeating that, except for the fraud and conspiracy counts, the body of the charges—alleged violations of the food and drug laws—could be decided without reference to the efficacy (or the existence) of Krebiozen. Strictly speaking, that was true. The false-statement charges, for instance, included a statement in a letter from Durovic to the National Cancer Institute in 1961 in which he stated that Krebiozen could be produced for the government for $170,000 a gram. The statement was false, the government said, because, since Krebiozen is creatine, it would cost 30 cents a gram and "even if Krebiozen could be produced by the method allegedly used . . . it would cost about $8000 per gram. . . ." Demonstration of the falsity of the statement inevitably involved the demonstration that Krebiozen was creatine, which in turn involved extensive testimony on the chemistry that had clear implications for the efficacy of the substance. Some of the other charges, however, simply claimed that the defendants violated laws governing investigational drugs by shipping Krebiozen across state borders on a mail-order basis without the experimental follow-up the law requires, and that the motive was commercialization, not experimentation.

If the government had omitted the fraud charges and concentrated on the drug-law charges, the outcome of the trial could conceivably have been different; the government had by no means failed to do its homework on these points. But once the two became entangled, it was humanly impossible to separate them. If the jury had any doubts about Krebiozen's chemistry or efficacy, it was inevitable that they would view the other charges as relatively petty. As one juror commented to a Chicago newspaper after the trial, "There was no proof that Krebiozen wasn't worth anything . . . we did not want to destroy Krebiozen." Other jurors remarked that they had been impressed by the government's evidence that the Durovics had made money and wanted to convict them of something, but that the charges were so intertwisted it could not be done.

Ivy's reputation also affected the jury. The government alleged that an "unusual activity in his bank account" in recent years explained his involvement with Krebiozen. (Ivy said he was lucky in the stock market.) But the jurors found it hard to believe: "Ivy's reputation is known all over," one remarked after the trial. "I don't think a man would throw away 50 years of work for humanity and just dump it overboard."

The government's case seems to have suffered both from being too intricate to follow and too simple to be believed. The details of the Krebiozen case just don't add up, the government said. The Krebiozen story is impossible. But it is also "impossible" to lose a hydrogen bomb. The jury was simply not convinced.

A Reasonable Doubt

A federal jury, before returning a verdict of guilty, is supposed to be convinced of guilt "beyond a reasonable doubt." The defense saw to it that the jury would have doubts. One of the most discomfiting features of the Krebiozen trial is that the prosecution and the defense did not necessarily address themselves to the same issues. The prosecution leaned heavily, for instance, on its claim that Durovic did not ever purchase enough ether or benzene to process horse blood in the way he contended he did. The defense argued that he purchased more than the government claimed, and that his laboratory equipment enabled him to reuse the materials. Who is right? There are a thousand such details left dangling in the 20,000-page record of the Krebiozen trial.

For the most part the defense concentrated not on the details of the business end of the operation but on refuting the government's claims that Krebiozen and creatine are identical and that the drug possesses no anticancer activity. The scientific conflicts involved are far beyond the capacity of any layman to arbitrate, and no attempt will be made to do so here. But it is a fact that the conflicting testimony heard would have made any jury hesitant about conviction. And the question that has troubled the scientific community for years remains: is Krebiozen a fraud so flawless in its execution that it defies convincing exposure? Or is it a scientific conflict so profound that the tools of 1966 are not adequate to deal with it?

What Next?

The government is taking its defeat on Krebiozen as a major disaster. Officials close to the case believe the government's evidence was complete and its conclusions logical. They attribute their defeat to the emotionality of the issue and the popularity of Andrew Ivy. They believe that the jurors were moved also by testimonials from patients, both on the witness stand and in the galleries which were always filled with Krebiozen loyalists. "We were doomed from the beginning," one official commented. "It wouldn't have made any difference what we said or did." Privately, government officials are grumbling about the jury system and questioning the capacity of the jurors—none of whom had more than a high school education—to deal with so complicated an issue.

The government's evaluation of the trial is not necessarily wrong. But the jury system is here to stay, and the government chose the forum. If officials believed a jury competent to vote for conviction they also must believe it competent to vote for acquittal. If they believe it incompetent, they should have avoided a criminal trial.

What the government will actually do when its wounds are healed is another question. Practically speaking, there is little to be done. FDA officials have made it clear that the agency will under no circumstances interpret the verdict as a mandate for a federally sponsored test of Krebiozen. But barring some new provocation by the Krebiozen forces—such as an open renewal of interstate shipment—the government can take no further action. The state government of Illinois has for several years been attempting to find a way to ban Krebiozen distribution there and has concluded that it could only be accomplished through special legislation. The prognosis for such an effort is poor—it would be exceedingly unpopular—and, therefore, the most likely prospect is for continued distribution of Krebiozen to patients who live in, or come to, Illinois.

As for the Krebiozen forces, they are elated but exhausted and, temporarily at least, are planning to make no moves. Ivy has a $392,000 libel suit pending against George Stoddard, former president of the University of

Illinois, which is expected to be brought to court shortly. Durovic, who was hospitalized for a time during the trial, was reported this week to have gone to Paris to be treated for a kidney ailment, and both brothers are now facing charges by the Internal Revenue Service that they each owe the government several hundred thousand dollars in back taxes. Outside the immediate camp, Krebiozen patients, always an effective lobby, are reported to be trying to interest some third party, such as organized labor, in the possibility of sponsoring a test, and the movement of constituents is also sending some ripples through Congress. But the mood is strangely desultory. Can it be, after all these years, that the Krebiozen case will end not in fanfare, but in a fizzle?

—ELINOR LANGER

Albert Thomas: Late Congressman Who Supervised NSF Budget Had Witty Views on Science and Politics

In the political councils that deal with basic research, no individual during the past 15 years was more influential than Albert Thomas, the Texas congressman who died last month. As chairman of the Independent Offices Appropriations subcommittee, Thomas conducted virtually a one-man reign over the budget of the National Science Foundation, from the creation of the Foundation in 1950 through the approval of the budget now in effect. Thomas came slowly to the conviction that the federal government should assume the responsibility for supporting basic research. At times he could be ruthless with the NSF budget and the officials who appeared before him in defense of it; he could also be quite paternalistic in advising the NSF to steer away from what he considered to be political pitfalls. But in either case he was one of the saltiest and wittiest commentators on relations between science and government. Following are some Thomas remarks drawn from the hearings he conducted annually on the NSF budget and a few words on the situations that elicited them.

In 1955, NSF sought funds for what was described as a study "to find out whether it is worthwhile to pursue research in a particular area and to what extent." Said Thomas:

"You know what the answer is before you make the study. . . . The upshot of your report is going to be that it is worth the money and that there should be more spent. So why not let's just take the cost of that economic report and spend it on basic research. . . ."

That same year NSF defended its programs on the grounds that they were reviewed by scientists who functioned as "expert witnesses"; to this Thomas replied:

"I have never heard of anyone calling in an expert witness . . . unless he was to testify favorably to those calling him."

Thomas regularly put his witnesses through the mill, but occasionally he would relent and offer a bit of friendly advice, as he did a few months later when funds were being sought for the International Geophysical Year.

"We may argue a little bit with you . . . but if you argue back, why, we might soften up a little bit. . . ."

However, like any congressman, Thomas did not take kindly to what he considered to be usurpation of his prerogatives. When the White House announced the IGY prior to the appropriation of $28 million that was needed, Thomas said to NSF Director Alan T. Waterman:

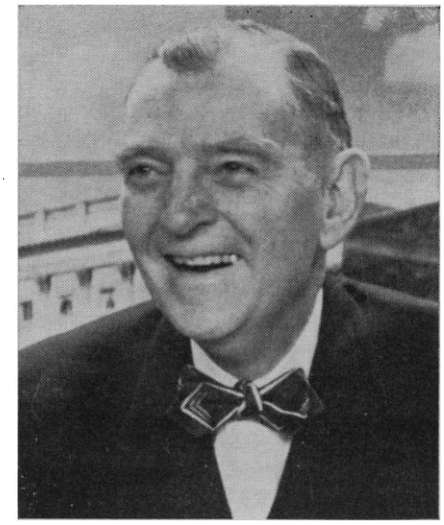
"Now I am going to jump on you in a nice way. . . . Doctor, we were just wondering if the Congress had anything to do with this program. If it was all settled at the White House, we were wondering why you came over here . . . it is all over with, all except the little item of $28 million; is that what you want?"

Thomas seemed to have a particularly warm relationship with Detlev Bronk, who would appear before him in his capacity of chairman of the National Science Board, the top advisory board of NSF. Bronk, one of the leading multiple-hat-wearers in the scientific community, drew this introduction from Thomas in 1958:

"President of the Rockefeller Institute for Medical Research, and president of about 10 other organizations."

Two years later, when Lloyd Berkner, one of the organizers of the IGY, appeared before the committee, Thomas greeted him with great praise, and then added:

"The last time you were here, you walked out with $20 million for a new laboratory."



Albert Thomas

The annual appearance before Thomas was never a pleasurable experience for NSF officials, a fact of which Thomas was clearly aware, for in 1960 he said, as Waterman was about to explain the budget:

". . . our able and sturdy friend, Dr. Waterman . . . you take a lot of punishment, but you are able to roll it off."

Thomas regularly cautioned NSF on the perils of rapid growth and the risk of political embarrassment in underestimating the ultimate cost of big projects. In connection with the Green Bank Radio Astronomy Observatory, where the costs eventually were far in excess of the estimates, he warned NSF officials to watch their pennies, and added:

"I am talking sense to you, whether you agree or disagree."

In 1961, when Thomas asked an NSF official about the duration of the Foundation's program for computers, the answer was, "We think this is with us for a long time." Replied Thomas:

"Oh, doctor, you give us such unexpected answers."

When NSF officials cited letters showing that the scientific community was desperately in need of federal support, Thomas referred them to the budgetary concerns of his constituents. To Waterman in 1962:

"Read some of our mail, doctor."

In support of the Antarctic research program, witnesses told Thomas of the research effort there, including wind velocity measurements. Replied Thomas: