

# NCI May Evaluate “Alternative Therapy”

*OTA drawing up a protocol as part of congressionally assigned report on “unorthodox” cancer therapies*

THE CONGRESSIONAL Office of Technology Assessment (OTA) is currently drawing up a protocol for a clinical trial on “immuno-augmentative therapy” (IAT), an “alternative” cancer therapy developed by Lawrence Burton, a former cancer researcher who runs a clinic in the Grand Bahamas. The National Cancer Institute (NCI) has indicated willingness to fund such a study.

There is no scientific evidence concerning the safety or efficacy of IAT. Burton is the only practitioner of the treatment, which involves the injection of blood serum fractions to enhance the immune function of cancer sufferers. Several years ago government tests showed that samples of Burton’s sera were contaminated with a variety of pathogens. The American Medical Association says that “The known risks posed to recipients of this ‘treatment’ clearly outweigh the unproven claims of effectiveness even for this often desperately ill population of patients.” The American Cancer Society says it has found “no evidence” that IAT treatment “results in objective benefit. . . .”

Why is the government going to sponsor clinical research on this treatment? The answer, according to Roger Herdman, director of the OTA’s health and life sciences division, is Congress asked for it. In 1986, at the initiative of Representative Guy V. Molinari (R-NY), 36 congressmen and 3 senators requested that OTA examine the evidence of IAT’s efficacy and develop a protocol to evaluate it. At the behest of Representative John Dingell (D-MI)—who is also on the OTA board—OTA was asked to make this part of a broader assignment, a report on “unorthodox” cancer therapies. The IAT evaluation is to be a “case study” for the report, which is due out at the end of this year.

According to an NCI spokesman, the institute has long been willing to fund such a study if it is approved by the NCI’s board of scientific counselors and if uncontaminated samples of Burton’s serum could be obtained. Maryann Roper, a pediatric oncologist at NCI who is consulting with OTA on the project, says NCI is cooperating “for the same reason as we did the laetrile study a few years ago.”

The laetrile study, however, was initiated under rather different circumstances. Charles G. Moertel of the Mayo Clinic, who headed that study, points out that in the late 1970s, when the study began, the use of laetrile had become “a major national social-medical issue.” The substance had been legalized in 27 states and sales and production were booming. Laetrile—which in 1978 the NCI estimated had been used by 75,000 Americans—“was being used as frequently as any cancer chemotherapeutic agent,” says Moertel. Furthermore, there were serious concerns about the toxicity of amygdalin, the substance from apricot pits from which laetrile is derived.

IAT, by contrast, has been used on only about 3000 people. Only one person—Burton—knows the details of the treatment. IAT was legalized in two states—Florida and Oklahoma—in the early 1980s, but

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## ***There is no objective evidence that IAT works.***

Florida rescinded the law after the Bahamian government closed down the clinic temporarily in 1985.

Molinari became interested in IAT when a group of Burton’s patients protested the closing of the clinic. In 1986 he held a hearing in New York at which Burton testified at length. Molinari subsequently was instrumental in getting it reopened.

The Bronx-born Burton, 62, has a doctorate in experimental zoology from New York University. For 9 years an oncology researcher at St. Vincent’s Hospital in New York, he developed his treatment theory on the basis of research with fruit flies and mice, from which he isolated blood factors that he claimed showed anticancer activity on human cells. According to Burton’s testimony at the 1986 hearing, his funding at St. Vincent’s was eventually withdrawn and he was “blackballed” by journals (he has not had anything published since 1963). He left in 1974 to set up his own research foundation in Great Neck, New York, and in 1977

moved to Freeport, Grand Bahamas.

IAT is based on beefing up a patient’s immune system with the intramuscular injection of protein fractions from dead tumor cells and blood pooled from cancer patients and healthy donors. Burton claims that four proteins, a “blocking protein,” a “deblocking protein,” a “tumor antibody,” and a “tumor complement,” mediate the immune system’s response to tumors. The initial treatment requires about 4 weeks of residence in the Bahamas, with frequent testing and treatment, at a cost of about \$5000 for the first month and \$500 a week thereafter.

Burton does not claim to cure cancer and does not supply any data with which to assess the benefits of treatment other than a chart showing that more than 50% of most of the cancers he treats show long-term remissions.

Burton got into trouble in 1985 after the NCI examined some samples submitted by Burton patients and found them contaminated with bacteria and hepatitis B antigen. Gregory A. Curt of NCI reported that “all of the treatment materials were dilute blood proteins, in which the major component was albumin,” and that “all fractions were devoid of the components described as being essential to activity.” The Centers for Disease Control tested other samples following reports of abscesses at injection sites and found they were contaminated with a variety of bacteria and fungi. Later, a laboratory in Tacoma, Washington, found samples contaminated with hepatitis B antigen and HTLV-III antibodies. There is, however, no evidence that anyone has contracted AIDS from the therapy.

The OTA has appointed an eight-member “IAT working group” to advise it on the design of the protocol, and several OTA staff members, including study director Helen Gelband, an epidemiologist, visited Burton’s clinic last year to make preliminary arrangements for a study. Working group member Craig Henderson, head of the breast cancer program at the Dana-Farber Cancer Center in Boston, says a rough draft of the protocol still awaits review by the NCI and the Food and Drug Administration.

Negotiations have been time-consuming because Burton is reportedly difficult to deal with—despite the fact that he has often expressed interest in having the NCI test his therapy. Donald Gleason, a retired Minneapolis pathologist who is on the working group, says there is not much detailed information to go on: “Burton is so secretive about the whole method it’s very difficult to formulate a clinical trial.” Burton has agreed to participate in the study only if the methodology meets with his approval. He has declined to participate in the working group

and relays his views through his attorney.

The IAT trial would involve about 100 patients, including controls. All will be patients for whom conventional treatment is judged ineffectual. The types of cancer have not been settled, but leading candidates are non-Hodgkin's lymphoma and a solid tumor such as colon cancer. The serum will be prepared on site according to Burton's specifications. But the rationale for treatment decisions will remain his secret. Patients will be tested daily and the results will be transmitted to Burton, who will transmit back daily requirements on the types, amounts, and frequency of dosages.

Members of the working group are not supposed to talk about the protocol—"OTA is very concerned that controversy might knock this out before it gets a fair test," says Roper of the NCI. One person with deep misgivings about the project is Moertel, director of the laetrile study. When asked about it by *Science*, he said the "public social need" for such a study had not been demonstrated, and that "we cannot go chasing around after every funny quack treatment . . . somewhere you have to draw the line." Moertel also said he would be "shocked" if Burton were allowed to dictate any of the terms of the study and that allowing him to keep certain information proprietary was "absurd."

The plans have attracted an irate response from Wallace I. Sampson, professor at Stanford School of Medicine and a founder of the National Council Against Health Fraud. He contends that any publicity will only increase the demand for and hustling of this "fraudulent" treatment. He says IAT promoters will never accept negative results, and that if the study should, by a statistical "blip," show positive results, it would take a large number of negative studies to disprove it. He also observes that "no dubious or 'unorthodox' treatment has ever been shown to be effective."

Herdman, a former vice president of Memorial Sloan Kettering Cancer Center, manfully defends the study: "we're basically in it to show that a clinical trial of an unorthodox cancer treatment can be designed." Robert Makuch, a Yale University biostatistician on the working group, concurs that a trial of IAT will be valuable as "a case example of how alternative therapies should be considered and evaluated—a model for other ones that may come down the pike." Herdman adds that interest in unconventional therapies is a strong strain running through American culture, and that the issues raised by this sort of thing need to be confronted. "It doesn't help to take an uncompromising attitude."

■ CONSTANCE HOLDEN

## Lower Radiation Effect Found

Human beings appear to be less susceptible to the genetic effects of the radiation of atomic bomb blasts than people have feared. "There isn't any good news coming out of atomic war, but the genetic consequences may not be as great as we thought at one time," says James Neel of the University of Michigan Medical School in Ann Arbor.

This conclusion is the most recent finding of the long-term study that has been exploring how the radiation unleashed by the atomic bombs dropped on Hiroshima and Nagasaki at the end of the World War II affected the survivors of the blasts and their children. Now conducted under the aegis of the Radiation Effects Research Foundation in Hiroshima, the study is in its 43rd year and is the largest single source of data on the consequences of human exposures to radiation.

The new analysis compared several indicators of genetic damage in the children of men and women who had been exposed to radiation from the bomb blasts and in the children of comparable individuals who had not been exposed. Among the indicators measured were congenital malformations, stillbirths and newborn deaths, childhood cancers, various chromosomal defects, and protein changes that could have resulted from specific gene mutations.

There were no significant differences in any of these individual categories between the children of exposed and nonexposed individuals, says Neel, who reported the results at the XVIth International Congress of Genetics, which was held in Toronto from 20 to 27 August. Combining all of the data, however, indicated that the Hiroshima and Nagasaki radiation caused a small increase in genetic damage.

Using this information, Neel and his colleagues, William Schull of the University of Texas Health Science Center in Houston and the Radiation Effects Research Foundation and Akio Awa, Chiyoko Satoh, Masanori Otake, Hiro Kato, and Yasuhiko Yoshimoto, all of the Foundation, calculated that the "doubling dose," the amount of radiation required to produce mutations equal in number to those occurring spontaneously in human beings, is in the range of 145 to 255 rems—or roughly four times higher than the doubling dose projected from studies of mice.

In other words, people may be substantially less sensitive to the genetic effects of radiation than mice. "I feel reasonably confident at this time that man is not more sensitive to radiation than the mouse, and there is a good chance that he is less sensitive," Neel says.

The impact that this conclusion might have on government standards for radiation exposures—always a contentious area—is unclear as the data have just been released. It might conceivably mean that a loosening of standards is warranted, although the issue is sure to be controversial. Moreover, radiation increases the cancer risk of exposed populations, and this factor will also have to be considered. The Hiroshima-Nagasaki data on radiation and cancer are currently undergoing a reevaluation, according to Neel.

An earlier analysis of the Hiroshima-Nagasaki data, which was published 7 years ago, also pointed to the possibility that the genetic consequences of radiation could be lower than expected. Since then, however, the radiation exposures in the two Japanese cities have been recalculated. Although the resulting changes might have altered the doubling dose estimates, the current work, which used the new exposure estimates and also includes an additional 8 years of data, nevertheless confirms and extends the previous findings.

The question then concerns whether the calculated differences in mouse and human susceptibilities to radiation reflect true biological differences between the species or merely differences in the experimental methods used to assess the susceptibilities. Neel points out, for example, that one of the prominent methods used in mice may have overestimated radiation's ability to cause mutations in that animal.

But human beings may also have more effective ways of protecting against radiation damage than mice. All species, including mice and men, have enzymes that can repair the damage caused to DNA by radiation and chemicals. As Neel points out, "In humans, the interval from birth to reproduction is on average 25 times longer than it is for the mouse. It would make evolutionary sense if we had evolved smarter repair enzymes." It may be possible to test this hypothesis by determining the ability of radiation to cause mutations in comparable genes of the two species, Neel suggests.

■ JEAN L. MARX