

**Statement of Eugene L. Saenger, M. D.
Before the House Judiciary Committee
Subcommittee on Administrative Law and Governmental
Relations
April 11, 1994
Cincinnati, Ohio**

E.L. Saenger, M.D.

**April 11, 1994
Page 1**

SUMMARY

Several important points are presented summarizing our work:

- a. One purpose of the study was the treatment of patients with far advanced cancer for whom the goal was the relief of pain, shrinkage of cancer and improvement in well being.**
- b. A second purpose was to study the systemic effects of radiation on the patient.**
- c. Treatment was given only if benefit to the patient was anticipated.**
- d. Patients were chiefly from the Cincinnati General Hospital. Selection was made only based on the presence of advanced cancer and where no other therapy was considered to be as or more efficacious than that currently available chemotherapy. Race, IQ, or socioeconomic standing were not selection factors.**
- e. Treatment was paid for by Cincinnati General Hospital and the National Institutes of Health. No Department of Defense funds were used for treatment or patient care or decisions regarding therapy or patient reimbursement.**
- f. Patients were told that the treatment might help them and were cautioned that it might not. Some patients chose not to be treated.**
- g. There was nothing secret about our work. There was nothing secret as to its being conducted. There was nothing secret about the findings obtained.**

E.L. Saenger, M.D.

**April 11, 1994
Page 2**

I am Eugene L. Saenger, M. D. of Cincinnati. It is a privilege for me to speak before this distinguished sub-committee of the Judiciary Committee of the U.S. House of Representatives to present a summary of our work on the treatment of far advanced cancer and the effects of wide field radiation therapy, work which I was privileged to direct and the results of which I am proud. The participation and support of the highly qualified physicians, allied scientists and associated health professionals is gratefully acknowledged. My Curriculum Vitae is attached. (See Appendix 1)

I am a graduate of Walnut Hills High School, Harvard College, 1938, cum laude and University of Cincinnati, College of Medicine 1942. My training in Radiology was at Cincinnati General Hospital completed in 1945. I am a Diplomate of the American Board of Radiology and the American Board of Nuclear Medicine.

My major appointments at University of Cincinnati College of Medicine include rising from Assistant Professor of Radiology to Professor of Radiology from 1949-1987 and Professor Emeritus since then. I was the founder and director of (what continues today) the Eugene L. Saenger Radioisotope Laboratory from 1950 to 1987. I was Radiology Therapist at Children's Hospital from 1947 to 1987.

I have given over 40 guest and invited lectures in the U.S. and elsewhere. I have received the De Hevesy Nuclear Pioneer Award of the Society of Nuclear Medicine and the Gold Medal of the Radiological Society of North America and the Daniel Drake Award of the University of Cincinnati College of Medicine, these being the highest honors of these organizations.

My consultant appointments to my government encompass both domestic and international service, and include among others requests from the Department of Justice; Department of Energy; Environmental Protection Agency; Department of Health and Human Services; National Institutes of Health; Department of Defense; Food and Drug Administration; International Atomic Energy Agency; Oak Ridge Affiliated Universities; Surgeon General of the Air Force; the U. S. Public Health Service and numerous government administered hospitals. Additionally, I was proud to serve my country as an officer in the United States Army, attaining the rank of Major prior to my honorable discharge.

My principal appointments at the University of Cincinnati College of Medicine range from Assistant Professor of Radiology in 1949 rising to Professor, and from 1987, the rank of Professor Emeritus. I am a member of 29 medical and scientific societies and the Founding President of the Society for Medical Decision Making. In addition to being an honorary member of the National Council on Radiation Protection and Measurement (NCRP), I delivered the Sixth Lauriston Taylor Lecture--the highest honor of this organization. The NCRP is an organization chartered by Congress that develops recommendations for radiation safety used by Federal Agencies for protection of the public.

E.L. Saenger, M.D.

**April 11, 1994
Page 3**

With my colleagues, I am the author of 187 publications in the scientific literature, the majority being in refereed journals.

I. Introduction

Several important points are presented summarizing our work:

A. One purpose of the study was the treatment of patients with far advanced cancer for whom the goal was the relief of pain, shrinkage of cancer and improvement in well being.

B. A second purpose was to study the systemic effects of radiation on the patient.

C. Treatment was given only if benefit to the patient was anticipated.

D. Patients were chiefly from the Cincinnati General Hospital. Selection was based only on the presence of advanced cancer and where no other therapy was considered to be as or more efficacious than then available chemotherapy. Race, IQ, or socioeconomic standing were not selection factors.

E. Treatment was paid for by Cincinnati General Hospital and the National Institutes of Health. No Department of Defense funds were used for treatment or patient care or decisions regarding therapy or patient reimbursement.

F. Patients were told that the treatment might help them and were cautioned that it might not. Some patients chose not to be treated.

G. There was nothing secret about our work. There was nothing secret as to its being conducted. There was nothing secret about the findings obtained.

II. What Was The Purpose of The Total Body Irradiation (TBI)/Partial Body Irradiation (PBI) Study:

The primary goal of the study was to improve the treatment and general clinical management by increasing, if possible, survival of patients with advanced cancer and palliation of symptoms. (Palliation is treatment directed at relief but not cure.) In addition, observations and laboratory tests were carried out to seek effects of radiation on cancer patients and on the changes that could be ascribed to radiation.

The palliative effects of TBI were considered to be at least equal to and very likely to be superior to the chemotherapy available in the period from 1960 - 1970. Also the treatment methods

E.L. Saenger, M.D.

April 11, 1994

Page 4

were thought to be less stressful to the patients than chemotherapy then in use, especially in terms of initial symptomatology following administration of the dose, as for example, the painful mouth ulcers from methotrexate and 5-fluorouracil, drugs used at that time.

The background for this project originated in my observations over the prior 20 years that cancer patients treated with radiation might be benefitted by a more careful evaluation of the effects of this kind of treatment on the total patient.

It seemed to me at that time that the approach to the total management of the cancer patients receiving radiation therapy was not as well studied as was that of the same patient who would be treated surgically. In addition, the effect on the cancer patient of doses of radiation given through large fields in relation to systemic effects was not being adequately considered, even though much work was being done on the radiation effects on the tumor and its immediate substrate.

The scientific indications that these goals might be achievable were based on two levels of evidence one from animal studies and one from human studies.

a) Animal studies indicated better tumor regression when total body irradiation was preceded by localized radiation than when localized radiation therapy was given alone both for lymphoma and carcinoma in mice.

b) Studies in human beings: Human studies for treatment of far advanced solid tumors prior to 1960 suggested the value of TBI. It was employed in several American centers and internationally. Treatment was given with success in relieving pain, shrinking tumors and, in some cases, prolonging survival. (See Appendix 2)

A major reason that we could begin TBI and PBI resulted from several important developments. The cobalt 60 teletherapy unit was installed at General Hospital in 1958, the first in Ohio. Harold Perry, M. D. was the first full time radiation therapist at our hospital. He had come from Memorial Sloan Kettering Cancer Center in New York Hospital and was familiar with TBI and PBI techniques and indicators. James G. Kereiakes, Ph.D., a physicist, joined the Department of Radiology in 1959. He calculated the doses, dose rate and distribution of radiation.

I believed that there could be implications from this treatment for well individuals exposed to radiation under other circumstances. In 1958, I submitted an unsolicited application to DOD because there had been no studies on the metabolic effects of radiation and funds were available. This proposal was reviewed by J. A. Isherwood, M. D. for the Army Medical Research and Development Command. He made the following comments: "Any correlation of tumor response to total dose of irradiation by such means as proposed in this project would be of great value in the field of cancer. In addition if by some means such as those proposed accurate knowledge of the total dose of radiation received could be determined it would be of inestimable value in case of atomic disaster or nuclear warfare." (See Appendix 3)

E.L. Saenger, M.D.

April 11, 1994

Page 5

III. The Study

A. Typical of medical investigations, this study progressed through phases. These phases are defined as follows:

Phase I studies are to determine whether the treatment is toxic.

Phase II is to determine in patients without controls but with measurable disease, whether the treatment is effective. Our studies included Phase II.

Only then are Phase III studies with controls and ideally with randomization conducted to determine therapeutic values. Although a Phase III study was proposed, we did not reach this level.

B. Patient selection: Patients were not recruited. Patients were referred for consideration for this form of therapy mostly from the Tumor Clinic (outpatient) and the Tumor Service (in-patient). I was not involved in patient selection or in determination of extent of therapy or dosage. These decisions were made solely by the attending physicians, internists and surgeons, and by radiation therapists. There were 24 patients entered into the study who were not given TBI or PBI. Some were rejected because it was thought that the patient would not benefit. Several patients and their families declined treatment.

1. Eligibility for therapy was spelled out in our 1962 document to DOD:

- a. There is a reasonable chance of therapeutic benefit to the patient.
- b. The likelihood of damage to the patient is not greater than that encountered from comparable therapy of another type.
- c. The facilities for support of the patient and complications of treatment offer all possible medical services for successful maintenance of the patient's well being.

2. Race was not a factor in selection--only the type of cancer and its extent. A statistical analysis, done only after the program was terminated, confirmed that the patients in this study did not differ from the patient population of Cincinnati General Hospital.

3. IQ was not a factor in patient selection.

IV. Informed Consent

As in selection of patients, informed consent for therapy was obtained by the attending physicians.

E.L. Saenger, M.D.

April 11, 1994

Page 6

In the 1940's and 1950's informed consent was verbal except for the general brief informed consent required by the hospital from all patients to be hospitalized irrespective of the treatment to be administered.

In this project, the purpose and actual treatment and the possible outcomes were discussed with the patient and often included family members.

In April 1965, the use of written informed consent, both for radiation and bone marrow harvesting and reinfusion, were developed by this project. These forms clearly indicated that risks of treatment were discussed. At that time, DHEW and DOD did not require written informed consent. As a result of a number of helpful suggestions from the University of Cincinnati Faculty Research Committee, several revisions to the form were made between 1967 and 1971 (See Appendix 4). Furthermore, this written informed consent that we developed preceded any written requirements of the University of Cincinnati Medical Center by two (2) years.

One criticism of our work stemmed from the instructions to the attending personnel not to inquire concerning nausea, vomiting and diarrhea in the first few days after treatment. We were particularly interested in the frequency of these manifestations. Since both nausea and vomiting could be induced by suggestive questions, we requested that no questions be asked as to how the patient felt. This restriction did not in any way restrict the administration of drugs such as Compazine to relieve symptoms. This care is amply documented in patients' charts. Of interest is that after treatment 39 patients (44%) had no nausea and vomiting, that 23 (27%) had symptoms for three (3) hours or less and that 12 patients (14%) had symptoms for six (6) hours or less. These responses are comparable to chemotherapy at the time, e.g., methotrexate, 5-fluorouracil and Chlorambucil.

V. Funding

As noted earlier, most costs of treatment were paid by Cincinnati General Hospital. An estimate of the expenditures for direct patient care for about 3,804 days at about \$114 per day with some additional cost estimates gave a total calculated amount of \$483,222. There were no professional costs or physician fees for patient care.

Some funding was obtained from the NIH. Some patients were maintained on the General Clinical Research Center of Cincinnati General Hospital; this unit was supported by NIH. The protocols and records of each patient so hospitalized were submitted to the NIH and approved. In addition, several of the Post Graduate Fellows supported by the Radiation Training Grant of the National Institute of General Medical Sciences (NIH) participated in some phases of the DASA program.

DOD funding was utilized solely for observation of patient symptoms and signs and for the extensive laboratory tests (See Appendix 5). DOD funds had no relation to choice of dose, choice of patient or patient care, in any way. No patient was compensated or reimbursed or paid for

E.L. Saenger, M.D.

April 11, 1994
Page 7

treatment. A Congressional General Accounting Office audit documented all of this in 1972. The total DOD contract for FY 1960 through FY 1971 was \$671,482.79.

VI. Success of the TBI study

Mortality. In the group of patients who received radiation, there were three categories in which there were enough patients to compare with other patients of the Cincinnati General Hospital treated differently or with comparable groups reported in the refereed medical literature. The cancers were those of the breast, lung and colon. The death rates were comparable to those treated by other means.

An important question is whether radiation was the factor leading to the early death of a patient. These patients had far advanced cancers which were growing exponentially. In the course of the disease, patients received chemotherapy and/or localized radiation therapy both before and immediately after TBI or PBI. For these reasons, it is not possible to identify a single form of treatment or the rapid growth of cancer as being the single contributing cause of death. It most likely would be the rate of growth of the cancer itself.

There were 20 cases in which patients survived longer than one year. Except for the one patient with Ewing's tumor who remains alive after 25 years, the longest survivor lived 9 years. Two other relatively long survivors lived five years.

Palliation was successful with relief of pain in 31% of patients. Some decrease in tumor size occurred in 31% and an increase in well being was found in 30%. No change was observed in 31%. (In some patients there was more than one indication of improvement; thus the percentages exceed 100%). (See Appendix 6).

Because of radiation induced hematological depression, autologous bone marrow storage and reinfusion began in 1964. With improvement in technique to include harvest of the marrow under general anesthesia and replacement immediately after TBI it became possible to avoid the characteristic depression of the white blood cells in five patients. This promising development was stopped at the time of termination of the contract.

VII. Review by Others

A. Faculty Research Committee. Our protocol was submitted to this newly formed committee in March of 1966. Provisional approval was given in 1967 with recommendations for review of therapeutic efficacy, bone marrow infusion as a supportive measure and some revision in the study design. At no time was the project disapproved by the Faculty Research Committee as it received exhaustive and critical reviews.

B. The ad hoc Committee of the University of Cincinnati (the Suskind Report) undertook a complete review of the TBI project. Among the findings were that Phase III studies should be initiated with better criteria for the determination of palliative effects and

E.L. Saenger, M.D.

April 11, 1994

Page 8

that bone marrow transplantation be pursued. The study was judged to be adequate for support of the critically ill patients because of the development of skilled team management especially with the help of the psychiatrist and psychologist coupled with home visits.

C. American College of Radiology. At the request of Senator Mike Gravel, the American College of Radiology formed an expert committee of Dr. Henry Kaplan, Chairman of Radiology at Stanford University, Dr. Frank Hendrickson, Chairman of Radiation Therapy at Rush-Presbyterian Hospital, Chicago and Dr. Samuel Taylor, III, a medical oncologist at Rush-Presbyterian Hospital, Chicago. This distinguished group made two visits to our hospital. Their major findings were as follows:

1. The project is validly conceived, stated, executed, controlled and followed up.
2. The process of patient selection based on clinical considerations conforms with good medical practice.
3. The records, publications and patient follow-up are voluminous and commendable.
4. The procedure used for obtaining patient consent is valid, thorough and consistent with the recommendations of the National Institutes of Health and with the practice of most cancer centers.
5. Should this project come before the Senate or one of its committees in some fashion, we would urge your support for its continuation. (See Appendix 7)

D. At the request of Senator Edward Kennedy, the Government Accounting Office reviewed the accounts of the Cincinnati General Hospital to determine whether there had been any intermingling of DOD funds used for patient care, since we had pointed out from the start of our work that no DOD funds would be used for this purpose.

An excerpt from the letter dated May 26, 1972 from the Comptroller General to Senator Kennedy follows: "Concerning the contract with the University of Cincinnati, officials of the Defense Nuclear Agency stated that the cost of radiation treatment and patient care had not been borne by their agency. They stated also that funds of the Defense Nuclear Agency had been used only to pay for supplementary laboratory analyses of patients who had received whole body irradiation in order for the Defense Nuclear Agency to gain information in areas that were relative to national defense." (See Appendix 8)

E. National Institutes of Health (DHEW). D.T. Chalkley, Ph.D., Chief, Office for Protection from Risks, Office of the Director NIH, was very supportive of our work. In a letter copied to Senators Nunn and Talmadge, he comments that "It is to be regretted that this incident has halted what promised to be a very significant addition to our armamentarium against metastatic cancer." He also wrote directly to Senator Nunn pointing out that "...the patients were treated individually for the diseases they had." (See Appendix 9)

F. Secrecy. This study received widespread publicity in the early 70's. We responded to all questions about it at the time including at an open press conference. The study

E.L. Saenger, M.D.

April 11, 1994
Page 9

resulted in numerous unclassified presentations at open medical meetings and in published papers and reports (See Appendix 10).

VIII. Total Body Irradiation & Partial Body Irradiation Since 1971

It is apparently a common misunderstanding that the use of TBI/PBI as a therapeutic agent has been discontinued. In the period from 1970 to the present there have been major changes in the use of TBI and PBI (See Appendix 2). Doses have risen from the low levels of 100-300 rad TBI and up to 300 rad PBI used by us from 1960 to 1970. Doses now range from 600 to 1200 rad in single or divided doses of TBI and with sequential HBI in these same dose ranges.

Fractionation has replaced single large doses (1200 rad) because of the complication of radiation pneumonitis. Among the solid tumors treated during these two decades have been cancer of breast, prostate, lung, colon and some sarcomas.

At the University of Cincinnati Department of Radiation Oncology beginning in 1979, TBI and PBI were administered to adults and children for leukemias, lymphomas, cancers of breast and prostate and neuroblastoma. Non-malignant diseases treated included aplastic anemia and congenital anomalies.

E.L. Saenger, M.D.

April 11, 1994
Page 10