RADIATION EXPERIMENTS CONDUCTED BY THE UNIVERSITY OF CINCINNATI MEDICAL SCHOOL WITH DEPARTMENT OF DEFENSE FUNDING

HEARING

BEFORE THE

SUBCOMMITTEE ON ADMINISTRATIVE LAW AND GOVERNMENTAL RELATIONS

OF THE

COMMITTEE ON THE JUDICIARY HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRD CONGRESS

SECOND SESSION

APRIL 11, 1994

Serial No. 67

Printed for the use of the Committee on the Judiciary

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RADIATION EXPERIMENTS CONDUCTED BY THE UNIVERSITY OF CINCINNATI MEDICAL SCHOOL WITH DEPARTMENT OF DEFENSE FUNDING

MONDAY, APRIL 11, 1994

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON ADMINISTRATIVE LAW
AND GOVERNMENTAL RELATIONS,
COMMITTEE ON THE JUDICIARY,
Cincinnati, OH.

The subcommittee met, pursuant to notice, at 10 a.m., in courtroom 2, room 822, U.S. Post Office and Courthouse, Fifth and Walnut Streets, Cincinnati, OH, Hon. John Bryant (chairman of the subcommittee) presiding.

Present: Representatives John Bryant and David Mann.

Also present: Representative Rob Portman.

Staff present: David Naimon, assistant counsel; Nichole Jenkins, assistant counsel; and Ray Smietanka, minority counsel.

OPENING STATEMENT OF CHAIRMAN BRYANT

Mr. BRYANT. Good morning, ladies and gentlemen and distinguished guests. The subcommittee will come to order.

The House Judiciary's Subcommittee on Administrative Law and Governmental Relations meets today in Cincinnati to take testimony concerning the whole and partial body of radiation experiments conducted in Cincinnati General Hospital and the University of Cincinnati Medical Center between 1960 and 1991, and partially funded by the Department of Defense.

This subcommittee has jurisdiction over compensation for claims against the Federal Government based on the Federal Government's wrongdoing and considered previous compensation legislation such as the Civil Liberties Act of 1988, which compensates Japanese-Americans who were in internment camps during World War II, and the Radiation Exposure Compensation Act of 1990, which compensates the residents who lived downwind from a Nevada nuclear test site and participated in those tests by the Government.

On February 2, 1994, the subcommittee held a hearing examining the issue of Government-sponsored experiments performed on humans who did not give informed consent to the experiments, including separate tests involving radiation, mustard gas, LSD, and other chemical agents.

The allegations regarding the Cincinnati radiation experiments are very serious. If they are true, these human experiments could be the most egregious that have been brought to light yet.

Our task is to examine these tests, determine whether the subjects gave informed consent to participating in such tests, and what harm resulted from the tests, and whether compensation is appropriate.

I would like to thank Congressman David Mann, a member of this subcommittee, for bringing the Cincinnati radiation experiments to the subcommittee's attention. I commend Congressman Mann's commitment and persistence for bringing these experiments to the forefront of the Congress and to the attention of the Clinton administration.

I know he also has worked closely with the working group established by President Clinton to ensure these experiments get serious examination as part of that group's consideration.

The subcommittee would also like to welcome Rob Portman to this subcommittee. While he is not a member of this specific subcommittee and the Judiciary Committee does not allow nonmembers to question witnesses at committee hearings, as chairman I think it is appropriate in this instance for Congressman Portman to sit with the subcommittee based on his extensive involvement with this issue. I think Congressman Portman's involvement in this hearing is an unusual case and it does not set a precedent for future subcommittee or committee policies elsewhere.

The subcommittee expects to be involved in the human testing issue for some time to come. Today's hearing is just a step in that process. It does not focus on any particular legislation, which has not yet been written by this subcommittee. We expect to have more hearings before we consider whether to legislate in this area, and we will be working closely with the Clinton administration in fashioning an appropriate response.

We appreciate the presence today of all of our witnesses and commend them for their preparation. We realize that with so many witnesses there will be limited time for making statements and answering questions today. However, additional materials and answers may be submitted at a later date.

I am informed that I said 1960 through 1991 while referring to those experiments. As everyone knows, it was 1960 through 1971.

I would like, before concluding my statement, to say a very profound thank you to Judge Webber for the use of his courtroom. I would also like to give thanks to Betsy Brockmeyer for all of her logistical development in making this possible.

At this time, I recognize Congressman Mann.

Mr. MANN. Thank you, Mr. Chairman. Welcome to Cincinnati. We are proud that you are here and I am proud to serve on your subcommittee. I enjoy very much working with you and I admire your leadership.

I think this is an important hearing. As you know, I have been working on this subject for some months now, as this entire community has been focused increasingly on the experiments that occurred between 1961 to 1971. I hope this hearing will cast new light and help focus the issue as this subcommittee takes up the question of compensation.

I too would like to thank the witnesses who have agreed to testify today. My heart goes out to all of the family members of the patients we will be discussing during this hearing. I know that reliving the illnesses of your loved ones some 20 years ago has brought you real pain. Three of you will sit at the witness table today. But I know many more of you would have liked to share your stories.

I would like to ask unanimous consent, Mr. Chairman, that all the written statements submitted to the subcommittee, whether by witnesses or otherwise, be included in the record for today's proceedings.

Mr. BRYANT. Without objection, so ordered.

Mr. MANN. I would like to voice my appreciation for all witnesses other than family members who will be participating today, including Dr. Saenger.

What we know to date, Mr. Chairman, is that some 87 patients received whole or partial body radiation. We know the patients involved were diagnosed with various forms of cancer believed to be terminal.

We also know while they may have consented to the treatment, many or perhaps all of them were unaware of the Department of Defense interest in their conditions and many or perhaps all were unaware of the potential side effects of the radiation.

We also know that written consent forms were not used until the mid-1960's.

But let's get to the heart of the matter. We also know that the original University of Cincinnati proposal to the Pentagon, the contract between the University of Cincinnati and the Pentagon, and the first five reports about the project from the University of Cincinnati to the Pentagon all describe the purpose of the project in terms only of the Pentagon's needs, particularly its need for biological tests of radiation exposure, and not in terms of therapy for patients.

Each of the first five reports covering the period from February 1960 to April 1967 label the project as "metabolic changes in humans following total body irradiation."

The term "therapeutic efforts" does not even become a part of the title of the reports to the Pentagon until 1968 when the title becomes "Radiation Effects in Man: Manifestations and Therapeutic Efforts."

It is also important to understand and keep focused on the fact that this project was conducted while the contract with the Pentagon and while the Pentagon's money continued. Whole body radiation under this project neither preceded nor outlived the Pentagon's contract.

The two primary issues that I believe we need to resolve, Mr. Chairman, are, first, did the patients knowledgeably consent to the experiments? And by "knowledgeably," I mean were they fully informed of all the facts and circumstances and possible consequences to them and funding.

And second, was this type of treatment appropriate for the types of illnesses suffered by the patients? By this I mean, absent the $8,000 or $10,000 per patient provided by the Department of De-

fense, would whole body radiation have been an appropriate medical therapy for these patients?

If we find the answer to any of these questions is "no," then I believe we have no choice but to conclude that the radiation experiments were simply wrong and that the Government owes a huge apology to the victims, their families, and the Nation.

Again, Mr. Chairman, I appreciate the hard work you and the staff have put into preparing for this hearing and I look forward to the testimony here today. Thank you very much.

[The opening statements of Messrs. Bryant and Mann follow:]

OPENING REMARKS

REP. JOHN BRYANT, CHAIRMAN

SUBCOMMITTEE ON ADMINISTRATIVE LAW
AND GOVERNMENTAL RELATIONS

HEARING ON RADIATION EXPERIMENTS CONDUCTED BY THE
UNIVERSITY OF CINCINNATI MEDICAL SCHOOL WITH
DEPARTMENT OF DEFENSE FUNDING

GOOD MORNING LADIES AND GENTLEMEN AND DISTINGUISHED GUESTS. THE SUBCOMMITTEE WILL COME TO ORDER. THE HOUSE JUDICIARY COMMITTEE'S SUBCOMMITTEE ON ADMINISTRATIVE LAW AND GOVERNMENTAL RELATIONS MEETS TODAY IN CINCINNATI TO TAKE TESTIMONY CONCERNING THE WHOLE AND PARTIAL BODY RADIATION EXPERIMENTS CONDUCTED AT CINCINNATI GENERAL HOSPITAL AND THE UNIVERSITY OF CINCINNATI MEDICAL CENTER BETWEEN 1960 AND 1971 AND PARTIALLY FUNDED BY THE DEPARTMENT OF DEFENSE.

THIS SUBCOMMITTEE HAS JURISDICTION OVER COMPENSATION FOR CLAIMS AGAINST THE FEDERAL GOVERNMENT BASED ON THE FEDERAL GOVERNMENT'S

WRONGDOING, AND CONSIDERED PREVIOUS COMPENSATION LEGISLATION, SUCH AS THE CIVIL LIBERTIES ACT OF 1988, WHICH COMPENSATES JAPANESE-AMERICANS WHO WERE IN INTERNMENT CAMPS DURING WORLD WAR II, AND THE RADIATION EXPOSURE COMPENSATION ACT OF 1990, WHICH COMPENSATES THE RESIDENTS WHO LIVED DOWNWIND FROM THE NEVADA NUCLEAR TEST SITE AND THE WORKERS WHO PARTICIPATED IN THOSE TESTS OR MINED URANIUM FOR THE GOVERNMENT.

ON FEBRUARY 2, 1994, THE SUBCOMMITTEE HELD A HEARING EXAMINING THE ISSUE OF GOVERNMENT-SPONSORED EXPERIMENTS PERFORMED ON HUMANS WHO DID NOT GIVE INFORMED CONSENT TO THE EXPERIMENTS -- INCLUDING SEPARATE TESTS INVOLVING RADIATION, MUSTARD GAS, LSD AND OTHER CHEMICAL AGENTS.

THE ALLEGATIONS REGARDING THE CINCINNATI RADIATION EXPERIMENTS ARE VERY SERIOUS. IF THEY ARE

TRUE, THESE HUMAN EXPERIMENTS COULD BE AMONG THE MOST EGREGIOUS THAT HAVE BEEN BROUGHT TO LIGHT YET.

OUR TASK IS TO EXAMINE THESE TESTS, WHETHER THE SUBJECTS GAVE INFORMED CONSENT TO PARTICIPATING IN SUCH TESTS, WHAT HARM RESULTED FROM THE TESTS, AND WHETHER COMPENSATION IS APPROPRIATE.

I WOULD LIKE TO THANK CONGRESSMAN DAVID MANN, A MEMBER OF THIS SUBCOMMITTEE, FOR BRINGING THE CINCINNATI RADIATION EXPERIMENTS TO THE SUBCOMMITTEE'S ATTENTION. I COMMEND CONGRESSMAN MANN'S COMMITMENT AND PERSISTENCE IN BRINGING THE ISSUE OF THESE EXPERIMENTS TO THE FOREFRONT IN THE CONGRESS AND THE ADMINISTRATION. I KNOW HE ALSO IS WORKING CLOSELY WITH THE HUMAN RADIATION INTERAGENCY WORKING GROUP ESTABLISHED BY PRESIDENT CLINTON TO ASSURE THAT THESE EXPERIMENTS GET SERIOUS EXAMINATION AS PART OF THAT GROUP'S CONSIDERATION.

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THE SUBCOMMITTEE ALSO WOULD LIKE TO WELCOME CONGRESSMAN ROB PORTMAN TO THIS SUBCOMMITTEE HEARING. WHILE CONGRESSMAN PORTMAN IS NOT A MEMBER OF THE JUDICIARY COMMITTEE OR THIS SUBCOMMITTEE, AND THE JUDICIARY COMMITTEE'S POLICY DOES NOT ALLOW NON-MEMBERS TO QUESTION WITNESSES AT COMMITTEE HEARINGS, I THINK IT IS APPROPRIATE IN THIS INSTANCE FOR CONGRESSMAN PORTMAN TO SIT WITH THE SUBCOMMITTEE, BASED ON HIS EXTENSIVE INVOLVEMENT WITH THIS ISSUE. I THINK CONGRESSMAN PORTMAN'S INVOLVEMENT IN THIS HEARING IS AN UNUSUAL CASE, AND I DO NOT INTEND FOR HIS INVOLVEMENT TO BE A PRECEDENT FOR FUTURE SUBCOMMITTEE OR COMMITTEE HEARINGS.

THE SUBCOMMITTEE EXPECTS TO BE INVOLVED IN THE HUMAN TESTING ISSUE FOR SOME TIME TO COME. TODAY'S HEARING IS JUST A STEP IN THE PROCESS, AND DOES NOT FOCUS ON ANY PARTICULAR LEGISLATION. WE EXPECT TO HAVE MORE HEARINGS BEFORE WE CONSIDER WHETHER TO

LEGISLATE IN THIS AREA, AND WILL BE WORKING CLOSELY WITH THE CLINTON ADMINISTRATION IN FASHIONING AN APPROPRIATE RESPONSE.

WE APPRECIATE THE PRESENCE TODAY OF ALL OUR WITNESSES AND COMMEND THEM FOR THEIR PREPARATION. WE REALIZE THAT WITH SO MANY WITNESSES THERE WILL BE LIMITED TIME FOR MAKING YOUR STATEMENTS AND ANSWERING QUESTIONS TODAY. HOWEVER, ADDITIONAL MATERIALS AND ANSWERS MAY BE SUBMITTED AT A LATER DATE.

I NOW RECOGNIZE CONGRESSMAN DAVID MANN TO MAKE AN OPENING STATEMENT.

CONGRESSMAN PORTMAN, WOULD YOU LIKE TO MAKE AN OPENING STATEMENT?

NEWS from
Congressman David Mann
First District — Ohio

The Statement of
The Honorable David Mann
April 11, 1994

Mr. Chairman, I would like to thank you for agreeing to convene this hearing today. As you know, I have been working very hard to uncover the facts with regard to the radiation tests performed at Cincinnati General Hospital in the 1960s and 1970s and I believe that this hearing will help to uncover evidence previously unknown and put some logical order to the information already available to us.

I would like to thank the witnesses who have agreed to testify before us today. My heart goes out to all of the family members of the patients we will discuss during this hearing. I know that reliving the illnesses of your loved-ones some twenty years ago has brought you real pain. Three of you will sit at the witness table today, but I know many more of you would have liked to share your stories. I would like to ask for unanimous consent that all of the written statements submitted to the Subcommittee and our offices be included in the record for today's proceedings.

I would also like to recognize and voice my appreciation for witnesses who will present their candid views of the radiation studies, Dr. Egilman, Dr. Stephens, and Dr. Cox. I would like to thank Dr. Soper from the Department of Defense for presenting testimony on the DOD record retrieval process and President Steger for his testimony on the University's efforts to help investigate this matter. And I would like to thank Dr. Saenger for his willingness to present his views on the radiation experiments and to answer the many questions this Subcommittee will pose.

What we know to date, Mr. Chairman, is that some 87 patients received whole and partial body radiation in experiments funded in part by the Department of Defense. We know that the patients involved were diagnosed with various forms of cancer believed to be terminal. We also know that while they may have consented to the treatment, many or perhaps all of them were unaware of the Department of Defense interest in their conditions and many or perhaps all were unaware of the potential side effects of the radiation. We also know that written consent forms were not used until the mid 1960s.

(over)

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But lets get to the heart of the matter. We also know that the orginial University of Cincinnati proposal to the Pentagon, the contract between U.C. and the Pentagon and the first five reports about the project from U.C. to the Pentagon all describe the purpose of the project in terms of the Pentagon's needs -- particularly its need for a biological test of radiation exposure -- and not in terms of therapy for patients. Each of the first five reports (covering the period from February 1960 to April 1967) labeled the project as "Metabolic Changes in Humans Following Total Body Irradiation". "Theraputic Efforts" do not even become a part of the title of the reports to the Pentagon until 1968 when the title becomes "Radiation Effects in Man: Manifestations and Theraputic Efforts."

Note also that this project was conducted while the contract with the Pentagon and the Pentagon's money continued. Whole body radiation under this project neither preceeded nor outlived the Pentagon contract.

The two primary issues that I believe we need to resolve, Mr. Chairman, are (1) Did the patients knowledgeably consent to the experiments? And, (2) Was this type of treatment appropriate for the types of illnesses suffered by the patients. By this I mean, absent the $8,000 - $10,000 per patient in Department of Defense funding, would whole body radiation have been an appropriate medical therapy?

If we find that the answer to either of these questions is "no" then I believe we have no choice but to conclude that the radiation experiments were SIMPLY WRONG and that the government owes a huge apology to the victims, their families and the nation as a whole!

Again, Mr. Chairman, I appreciate the hard work you and your staff have put into preparing for this hearing. I believe that the testimony we hear today will enable us to craft a fair and just compensation bill in the weeks and months ahead. Thank you.

Mr. BRYANT. Mr. Portman.

Mr. PORTMAN. Mr. Chairman, thank you for coming to Cincinnati to hold this important hearing and also for including me as a panelist. As you noted, I am not a member of the subcommittee; however, I do have a long commitment to this issue. I have been heavily involved in the issue for the past several months, and also the issues impact the people who live in my district. In particular, some of the patients involved lived in what is now the Second District of Ohio. Many of the family members, including at least one who will be testifying here today, currently live in the district I represent.

This matter has a long but unfortunately incomplete history of public scrutiny. There remain unanswered questions that relate not only to the critical aspect of how people and their families were treated, but also the role of the Federal Government in conducting such experiments on human beings.

Although there are many issues that will be addressed by the various parties involved, in my mind, there are two cardinal issues that we, as Federal officials, can and must address. The first is the appropriateness of the Federal Government compensating the victims and their families. If it is determined that the patients involved were not clearly informed in accordance with the standards for informed consent in force at the respective times of the experiments, or that these experiments became vehicles primarily for testing, not treatment, then compensation, in my view, would be appropriate.

This is so especially in light of the many potential legal barriers to recovery, including the statute of limitations under the Federal Tort Claims Act, sovereign immunity, and possible immunity of Government contractors.

Chairman Bryant's subcommittee has jurisdiction over the compensation issue, and I understand that there is some precedent for compensation when the facts so merit it. Because I am not on the subcommittee or committee, I will not have the opportunity to vote upon this issue at the committee level.

I believe that the second issue from the Federal Government's standpoint is one of disclosure—disclosure by the Department of Defense and the Cincinnati General Hospital and all others involved—of all relevant information concerning these cases.

In addition to reviewing the merit of compensating potential victims, I believe the Government and the Government contractors have an obligation to be fully forthcoming, to admit mistakes if mistakes have been made, and to ensure that safeguards are put in place with respect to any experiments that may be conducted today or in the future.

The issues of full disclosure and safeguards may not be directly related to this forum. However, I have particular interest in these issues, and the Government Operations Committee upon which I serve has been exploring the possibility of having additional hearings on those two issues.

Finally, I am here to listen and to continue to learn as much as I can about what happened two and three decades ago. This is not a court of law; we are not here to press charges. We are also not here to politicize what is a sensitive and emotional topic.

I view our role as factfinders who want to ensure that the Federal Government acts responsibly and fairly with respect to the patients and their families, to the investigators and to the DOD officials involved in the study.

I commend all of the witnesses for being here today. I commend you for agreeing to testify and very much look forward to your testimony.

Thank you, Mr. Chairman.

[The prepared statement of Mr. Portman follows:]

1

STATEMENT OF HONORABLE ROB PORTMAN

SUBCOMMITTEE ON ADMINISTRATIVE LAW AND GOVERNMENTAL RELATIONS

APRIL 11, 1994

Mr. Chairman, first, let me thank you for coming to Cincinnati to hold this important hearing and for including me as a panelist. Although I am not a member of the Subcommittee, the issues addressed here impact many people who live in the District I represent. In particular, some of the patients involved lived in what is now the Second District and many of the family members - including some we will be hearing from today - are my constituents.

This matter has a long, but unfortunately incomplete, history of public scrutiny. There remain unanswered questions that relate to not only the critical aspect of how people and their families were treated, but also the role of the federal government in supporting such experiments on human beings.

Although there are many issues that will be addressed by the various parties involved, in my mind, there are two cardinal issues that we <u>as federal officials</u> can and must address.

2

The first is the appropriateness of the federal government compensating the victims and their families. If it is determined that the patients involved were not clearly informed in accordance with the standards for informed consent in force at the respective times of the experiments, or that these experiments became vehicles primarily for testing not treatment, then compensation, in my view, would be appropriate. This is so especially in light of the many potential legal barriers to recovery, including the statute of limitations under the Federal Tort Claims Act, sovereign immunity, and possible immunity of government contractors. Chairman Bryant's subcommittee has jurisdiction over the compensation issue, and I understand that there is some precedent for compensation when the facts so merit it. Because I am not on the subcommittee or committee, I will not have the opportunity to vote upon this issue at the Committee level. However, I would have the chance to consider any proposal for compensation on the Floor of the House of Representatives.

I believe the second issue from the federal government's standpoint is one of disclosure -- disclosure by the Department of Defense and the Cincinnati General Hospital and all others involved -- of all relevant information concerning these cases. In addition to reviewing the merit of compensating potential victims, I believe the government and the government contractors

have an obligation to be fully forthcoming, to admit mistakes if mistakes have been made, and to ensure that safeguards are put in place with respect to any experiments that may be conducted today or in the future. The issues of full disclosure and safeguards may not be directly related to this forum. However, I have particular interest in these issues, and the Government Operations Committee upon which I serve has been exploring the facts of the UC cases and the possibility of holding hearings on disclosure of government information and safeguards.

Finally, I am here to listen - and to continue to learn as much as I can about what happened 2 and 3 decades ago. This is not a court of law; we are not here to press charges. We also are not here to politicize a sensitive and emotional topic. I view our role as fact finders who want to ensure that the federal government acts responsibly and fairly with respect to the patients and their families, to the investigators and to the DOD officials involved in the study.

I commend all of the witnesses who have agreed to testify before us today and very much look forward to their testimony. Thank you Mr. Chairman.

Mr. BRYANT. At this time we would invite to come to the witness table the first three witnesses on our panel.

First, Joseph Larkins, survivor son; Gloria Nelson, survivor granddaughter; and Katherine Hager, survivor daughter.

We would ask that each of you, as well as all of the witnesses who come behind you, limit your statement to 5 minutes in order that we might ask you questions and have time for all the witnesses to speak.

I will begin on my left with Mr. Larkins. Mr. Larkins, thank you very much for coming here today. Please proceed.

STATEMENT OF JOSEPH LARKINS, SURVIVOR SON

Mr. LARKINS. All right. Well, my name is Joe Larkins. I am 52 years old now. My father, Willard Larkins, passed away in 1971. At that time, I was 30. My family consisted of myself, an older sister, and my parents. When my father passed away he and my mother were in the process of raising a grandchild, my sister's son. Neither of my parents were well educated, but my father was hard working and honest. If Cincinnati General Hospital and the doctors therein had been honest, there is, of course, the possibility that my father could have lived for several more years. Instead, he went from a fairly able-bodied, middle-aged father, and husband to a premature death caused by an experiment. My father did not know that he was being used as a guinea pig; my mother did not know; as his children, we were not informed of the procedures to be used or of the risks involved.

I feel as though Dr. Saenger and the other doctors involved, if you will, knew that the high levels of radiation which they administered to these patients had the very real probability of being fatal. Oh, how right that is! My father was very much a family man, yet these people killed him as surely as if they had put a gun to his head and pulled the trigger themselves. These doctors left my mother, with no job skills, to raise a grandchild as best as she could. My mother lived until 1983, but she was a broken woman after my father's premature and unexpected death.

I know that my father knew that something was very wrong with the treatments being given to him at Cincinnati General. He even asked me, "Son, what are they doing to me? They're trying to kill me." That is how bad the pain he endured after the treatment was. He suffered so needlessly.

What really gets me about this situation is the fact that the Pentagon contracted with these doctors and this hospital to test the effects of radiation on the human body. Everyone realizes that Cincinnati General Hospital, now the University of Cincinnati Hospital, treated many low-education, low-income patients. I guess they felt that in some way the fact that these patients were not rich, upper class citizens gave them the right to experiment with their bodies without informed consent. Not so. I feel sure these physician-researchers were well paid for their part, and it would be very interesting to know the types and dollar amounts of the grants given to Cincinnati General by the Federal Government. I feel sure that all parties, with the exception of the poor, unsuspecting patients and their families, were well compensated.

But since when, in our society, does one man or even a group of them, have the right to play God?

A very good example of this is our 20th century "assisted-suicide doctor." This man is contacted by terminally ill patients who wish to end their own lives with dignity and choose, by their own volition, not to suffer needlessly for years. These people make the decision to die in peace, yet our great judicial system, along with the medical community, brought this compassionate physician up on charges.

The differences in these deaths and the death of my father are that my father did not choose to die—someone else made that decision for him without consulting or informing him, and they were amply compensated for it.

I feel that the price they should be required to pay to the families of the people they killed should be exceedingly high. I also feel that the Federal Government should be named as a coconspirator in this case, because that is exactly what it was, a conspiracy.

No person—and I emphasize "no" person—would willingly consent to a treatment with any degree of fatality involved. People, both you and I, simply value life too much. I think that is the big thing here, the patients were not informed. I know that behavior of this sort would not be tolerated by the medical community today.

But then again, this entire mess was surrounded by a thick veil of secrecy on both the doctors' part and on the part of Cincinnati General Hospital. It is still being closely guarded and kept under yet another veil of secrecy to this very day by the University of Cincinnati, in that they have yet to provide the medical records of the patients involved in this experiment—but they have, as of now. At the time of this statement they were not—in the entirety, to the next of kin immediately.

They are hedging to save their own skin. I was promised my father's complete medical file over a month ago; as of this writing, I have nothing. But like I said, we do have them now.

I only hope that you, the congressional committee, see fit, as members of the human race, to break this matter wide open here and now and award just compensation to the families of the victims. I feel that the physicians involved and also the Federal Government, the Pentagon, should pay; and also I beg you to strip any and all of the doctors involved of all their medical credentials that they hold. If justice prevails in this matter—and I have faith that it will—a strong message will be sent to our government officials and the private physicians, to whom people entrust their lives and the lives of their loved ones, that behavior of this sort will simply not be tolerated, that justice will, in fact, be both swift and severe.

I pray that a situation such as this will never again be faced by a group of people. If this statement to you, the congressional committee, does anything to help in the name of justice, then my father's death and the sorrow and hardships that his family faced, will not have been completely in vain.

Thank you.

Mr. BRYANT. Thank you, Mr. Larkins.

Ms. Nelson.

STATEMENT OF GLORIA NELSON, SURVIVOR GRANDDAUGHTER

Ms. NELSON. Amelia Jackson, patient number 67.

On October 21, 1966, after being discharged from General Hospital, Ms. Jackson was a very weak, ill woman. She was unable to take care of herself properly and depended on the family for all of her basic needs. She experienced bleeding from her rectum, loss of appetite, nausea, vomiting, weight loss, and was in constant pain. Her condition never improved.

Within a few weeks, she was readmitted to General Hospital. The family was informed she should be transferred to Drake Hospital. Ms. Jackson indicated she was afraid and want to return home. She was transported home, where she was loved and cared for by us until she died on March 25, 1967.

The family of Amelia Jackson would like for this committee to know that for the entire 163 days after receiving the irradiation, her condition continued to deteriorate. We feel that the 100 rads of partial-body irradiation administered to her was cruel, and didn't help her condition in any way. It is our belief that she may have lived longer if this experiment had not taken place.

A doctor is someone you trust. His job is to do everything in his power to alleviate your pain and suffering. However, this was not the case. She was always crying, moaning, groaning, and in excruciating pain. Ms. Jackson was used to further Dr. Saenger's professional goals. It was purely an ambitious and callous act. Neither Ms. Jackson nor the family was informed or consented to her being used in an experiment conducted by Dr. Saenger, and funded by the Department of Defense. There has clearly been a coverup by means of the Government, General Hospital, Dr. Saenger, and the city of Cincinnati. We cannot believe that they consented to such atrocities to be financed by the Government utilizing the Jacksons' and the family's taxpaying dollars.

Mr. BRYANT. Thank you, Ms. Nelson.

Ms. Hager.

STATEMENT OF CATHERINE HAGER, SURVIVOR DAUGHTER

Ms. HAGER. To the total body radiation subcommittee and whom it may concern:

In January 1994, I began noticing articles in The Cincinnati Enquirer regarding total body radiation experimentation done on cancer patients in the 1960's at Cincinnati General Hospital. Since I knew my father, Joseph Mitchell, was treated at that hospital for cancer during that period of time, I contacted Linda Reeves at the Cincinnati Enquirer. After a brief discussion with Linda, it was determined that my father had indeed been involved in the total radiation experimentation as patient No. 51, the first patient to be identified. From this point, my husband and I, along with the assistance of the news media, attempted to piece together any records available regarding my father's treatment at the hospital.

In October 1963, my father was diagnosed with lung cancer in the right lung, and was admitted to Cincinnati General Hospital. Surgery was scheduled for November 1963. Although there is no notation of this scheduled surgery in his medical records, we have a letter which was written by my father to my sister detailing the

planned operation. For some unknown reason, the surgery was canceled on the day it was scheduled to take place, with no explanation. The surgery was never rescheduled. Instead, my father was given a schedule of dates to return to the hospital for cobalt treatments. At this point, I asked the doctor why the surgery was canceled. He told me he was too weak for surgery and decided to opt for the cobalt treatments instead.

In reality, my father was not in a weakened state at that time, but was in relatively good health, still working, and living a normal life. It wasn't until the cobalt treatments started that my father began to go downhill. After 35 days of treatments, my father was so weak that he had to retire from work and move closer to my family so we could help care for him.

In early 1965, my father was again admitted to Cincinnati General Hospital with severe chest pains. It was at this time he was subjected to the total body radiation, 150 rads. He immediately started on a drastic downhill spiral. After much suffering, my father died on July 14, 1965, 74 days after the total body radiation.

Since total body radiation had not been performed on cancer patients at Cincinnati General Hospital prior to the Government funding of 1960, I feel that my father, along with other cancer patients, were handpicked and used in total body radiation, not as a treatment for cancer, as they had been told, but as a coverup for a study performed for the Department of Defense to determine possible effects on soldiers in nuclear warfare.

It might be noted that at the time my father died, two of my brothers were in the U.S. Air Force, one in Vietnam in the war zone. The Red Cross had to locate him and bring him home for the funeral. Both brothers have since retired from the Air Force. Isn't it ironic that two of my brothers were serving this country in the military, while at the same time the Government was sponsoring experiments which shortened or ended their father's life?

I would like to read the little note that my father sent to my sister, which was written November 2, 1963.

DEAR ISABELL: I am very sorry, honey; I need your help. First, I am going to have an operation, first part of the week. The doctor is not giving out the right news to the family. It is going to be a long, serious operation. I will be about two months here, and it is very serious. Only a 50/50 chance to come through, as all I have left is half a lung. So therefore I ask you to do all you can to help mom as much as possible, while I am in here.

I can tell you more when I see you again, but please do not take it to heart. I am trusting everything will turn out okay, which is doubtful. See you soon.

Love,

DAD.

Thank you very much.

Mr. BRYANT. Thank you, Ms. Hager.

Mr. Larkins, let me start with you by asking, when did you or your representative request your relative's records from the University of Cincinnati?

Mr. LARKINS. A little over a month ago.

Mr. BRYANT. Have you received them yet?

Mr. LARKINS. Yes, I finally got them today.

Mr. BRYANT. Did you make the same request, Ms. Nelson?

Ms. NELSON. Yes.

Mr. BRYANT. And have you received them also?

Ms. NELSON. Yes, I received them Friday.
Mr. BRYANT. How long ago did you make the request?
Ms. NELSON. Over a month ago.
Mr. BRYANT. A month ago.
Ms. Hager, did you request the records?
Ms. HAGER. Yes, I did. But I don't think we have all of them. We got some, but I still think there are more there.
Ms. NELSON. Same here.
Ms. HAGER. You feel so, too?
Ms. NELSON. Yes. They are not all there.
Mr. BRYANT. When did you get yours, Ms. Hager?
Ms. HAGER. When did we receive ours, Bob?
Mr. BOB HAGER. Approximately 3 weeks ago.
Mr. BRYANT. Sir, would you identify yourself?
Mr. BOB HAGER. I am Mr. Hager, Catherine's husband.
Mr. LARKINS. Can I say something else?
Mr. BRYANT. Yes, Mr. Larkins.
Mr. LARKINS. When we were going through my dad's files, we found charts from 1971, December. He died in June of 1971. I would like to know how that can be.
Mr. BRYANT. Did you find anything else unusual?
Mr. LARKINS. The signatures on half of the papers are not his. A couple of them are, but not all of them.
Ms. NELSON. The signatures on my grandmother's papers, they are not hers either.
Mr. BRYANT. You say they are not?
Ms. NELSON. No.
Mr. BRYANT. Does it purport to be her signature, but it is not her writing?
Ms. NELSON. Right. And also I found documents in my grandmother's records that were originally made out for someone else. That person's name is scratched out. Her name put in and a different number put in.
Mr. BRYANT. Can you tell us, Mr. Hager, what type of harm your relatives suffered from the radiation treatment that was not a normal result of cancer treatment?
Mr. Larkins—I am sorry; I spoke the wrong name—what type of harm did your father suffer from radiation treatment that was not a normal result of cancer treatment?
Mr. LARKINS. Well, I guess the fact—just the way he went downhill. He was hoping to get well, but he was telling me, deep down, I guess that he knew, like I said, that something was wrong. He didn't know what. He wasn't getting no better. He was getting worse.
Mr. BRYANT. I should say obviously we don't expect you to know what is the normal result of cancer, since you are not a doctor. But in terms of a layman's observation. Mrs. Nelson.
Ms. NELSON. My grandmother lost over 30 pounds after she had her radiation treatments, within a 3-month period.
Mr. BRYANT. Ms. Hager.
Ms. HAGER. My father was burnt pretty bad after he had his total body radiation. He had it on May 1. I think he came home—he had it on May 1. He came home on May 8, 1965, he came home, and we had to take care of him. He was bedridden. We had to give

him baths. The Red Cross had to come and take him back and forth to the hospital every day. A nurse came every day and took a blood test from his finger.

I mean, he was just—he couldn't eat. He couldn't sit up. He had to—whatever came out of him, whatever kind of spittle came out of him, we used to have to save that and take it back to the hospital.

Mr. BRYANT. OK. Let me ask you a question.

You spoke in your testimony about the fact that your father's surgery was called off, and instead he was given cobalt treatments. After 35 days——

Ms. HAGER. He had 35 days of cobalt treatment plus the whole body radiation also.

Mr. BRYANT. But the whole body radiation took place about 2 years later; is that correct?

Ms. HAGER. That is correct.

Mr. BRYANT. And the letter from your father was dated 1963, implying that you——

Ms. HAGER. That was the first surgery he was supposed to have, that they did not give him. They had him prepared for surgery that day, and the nurse come in the same day and said—they started taking the things off of him.

I said, what are you doing? And she said, they canceled the surgery. He is not going to have surgery today.

And I said, well, who do we talk to to find out what is going on? And she said, you will have to get a hold of his doctor.

We sat there all day and no doctor came into the room to talk to us to explain anything.

Mr. BRYANT. Mr. Mann.

Mr. MANN. I want to thank each of you for taking the time to be with us. I know that it is not easy going over a sad chapter in your life. And it is of immense value to us.

Mr. Larkins, were you or any member of your family ever present when the radiation treatment, the radiation experiments were discussed with your father by any of the doctors at the hospital?

Mr. LARKINS. No, sir; I wasn't.

Mr. MANN. Did he ever talk with you about the radiation that he was going to have administered to him?

Mr. LARKINS. He didn't talk to me about it, but he talked to me after. I was out there a couple of times after his treatments. That is the one time he asked me what they were trying to do with him. He received 300 rads of the radiation. I understand he got the most of anybody.

Mr. MANN. Do you know why he asked the question that way, what are they trying to do to me?

Mr. LARKINS. I think he was scared that he was dying from it.

Mr. MANN. Was he suffering in a particular way at that point that led him to make that comment?

Mr. LARKINS. To me, he was suffering all over. I mean, he was just hurting all over. He didn't know what to think about what was going on. He wanted to get well, but I guess that is what he had in the back of his mind, was that eventually he would get well, but he didn't. He was only 55 years old, 3 years older than I am now.

Mr. MANN. Ms. Nelson, your grandmother, how old were you when she died?

Ms. NELSON. I was 20.

Mr. MANN. Were you or any other family members present when the proposed treatment was discussed with her?

Ms. NELSON. No. We didn't even know that she had the treatment until I had read that in the Enquirer, and we pieced together—and the date of her death, and the condition of her cancer and all that. That is when we found out that this was my grandmother. All they had was H.A.

Mr. MANN. So there was no discussion that they had with any member of the family, that you are aware?

Ms. NELSON. No.

Mr. MANN. Did she ever say anything about the radiation?

Ms. NELSON. She never said anything about the radiation nor did she say anything about the three cobalt treatments she received, that I found in her records.

Mr. MANN. Basically, she was doing what the doctors recommended to her?

Ms. NELSON. Right. She didn't know any better.

Mr. MANN. Ms. Hager, your father, in his treatment, did you or any member of the family—were you present when the doctors were explaining what they were proposing?

Ms. HAGER. No. The doctors never told us anything. The only thing the doctor told me was when I went out there, when they canceled the surgery, I made an appointment to go out there and talk to the doctor, and all he told me was that they wanted to build him up and make him a little stronger. He was only 5-foot-2 and weighed 116 pounds. He was doing this normal work every day, and I mean, you know, you listen to what the doctor says and you don't question it.

So I figured, well, maybe they want to fatten him up a little bit more than 116 pounds to do the surgery they wanted to do; and he said, we are going to go with the cobalt treatment, and we are going to let it go at that for now.

And that is the only—that is the only time I met with the doctor on any of this. And I used to go with him when he would go get his treatments; I was there every time with him. They would take him away from me; I would sit in the hall, and then they would come out and say, well, your dad is a little sick for a while; we are going to hold him for a little bit, then we can release him and come home.

Him and I rode the bus together. But they never let you go back and see what they did; they made you sit in the hall and wait.

Mr. MANN. Did he ever express concern to you about what was happening to him or wondered whether——

Ms. HAGER. No. He trusted the doctor. He trusted the doctor. Whatever the doctor said, that is what he did, because he thought the doctor was going to make him better.

Mr. MANN. Which doctors do you have contact with? Do you remember the names?

Ms. HAGER. Sir, I wish I could remember. I asked for the doctors in charge. Whoever they gave me, I have no idea.

Mr. MANN. Did you ever meet Dr. Saenger?

Ms. HAGER. Sir, I couldn't tell you. I don't know if I did or not.
Mr. MANN. Dr. Silberstein.
Ms. HAGER. Like I said, I couldn't tell you.
Mr. MANN. Dr. Aron.
Ms. HAGER. I have no idea.
Mr. MANN. Dr. Horowitz.
Ms. HAGER. I have no idea. I met one doctor at one time. I don't know who it was.
Mr. MANN. Mr. Larkins, do you remember meeting any of those doctors, the names I just gave?
Mr. LARKINS. No. I think I remember seeing Dr. Saenger, but I never met him. The only people I talked to was like nurses and orderlies, sometimes.
Mr. MANN. Where did you see Dr. Saenger?
Mr. LARKINS. In the tunnels and General Hospital.
Mr. MANN. Did you talk to him?
Mr. LARKINS. No. He was pointed out to me by someone else.
Mr. MANN. Pointed out to you as what?
Mr. LARKINS. As the doctor in charge.
Mr. MANN. Ms. Nelson, do you recall meeting any of the doctors?
Ms. NELSON. Never saw any of the doctors, never talked to them. Whenever I went with my grandmother to the hospital, there were just the nurses around.
Mr. MANN. Thank you, Mr. Chairman.
Mr. BRYANT. Mr. Portman.
Mr. PORTMAN. Thank you, Mr. Chairman.
Thank you all for being here today. It takes a lot of courage to do what you are doing. It is difficult, I know, to talk about it. I just have a few questions.
Mr. Larkins, first, my question to you is really whether you know whether your father knew anything about the military study that was going on. Did he ever talk about that?
Mr. LARKINS. He never knew anything about that. Me and my dad were pretty close, and I think he would have talked to me about it. He probably would have said, hey, man, they have got the Government on us, and they are really going to do some good action. They really did.
Mr. PORTMAN. How did you and your mother first learn about the military aspect of the study?
Mr. LARKINS. In the paper, when it first started to come out this year.
Mr. PORTMAN. This year?
Mr. LARKINS. Yes.
Mr. PORTMAN. On the consent side, did your father ever talk about the various options he had before him? Do you know if he was apprised of the risks and benefits——
Mr. LARKINS. The only thing he ever told me was, "they have got their treatment schedule for me; they have got another treatment schedule for me." That is all he would say.
Mr. PORTMAN. So in terms of whether he consented to the treatment in an informed way, do you know whether he was told what the risks and benefits of the treatment were?
Mr. LARKINS. I don't think he was. He was kind of like me, or I guess I am like him. I want to know what is facing me. He would

have told me, Joe, I have got chances of dying. We would have talked about it. He didn't say nothing like that.

He said, they have got another treatment scheduled for me. They are going to use me again. That is one time he said that, "They are going to use me again." What he meant at that time, I didn't know.

Mr. PORTMAN. At the end of your testimony you talked about the compensation issue. I just wondered if you could give us a sense of what you might think just compensation would be in this case.

Mr. LARKINS. Bring him back, but I know that is not possible.

I have no idea, but I think it should be something just. I have no idea what to say.

Mr. PORTMAN. Thank you again for being here and for your statement.

Ms. Nelson, your grandmother, Mrs. Jackson, went through a tough time. You gave us a lot of good information.

Just in terms of getting the dates straight, you mentioned she was discharged in 1966. When did she first become involved in the radiation experiments; do you know?

Ms. NELSON. In October 1966.

Mr. PORTMAN. October 1966? OK. Again, do you believe that she understood the risks involved and the benefits involved in the treatment that she received?

Ms. NELSON. No. If she was told anything about it, she didn't understand it.

Mr. PORTMAN. Did she?

Ms. NELSON. She was illiterate. She couldn't read or write.

Mr. PORTMAN. Did she ever talk to you or other family members about it?

Ms. NELSON. She never mentioned it. We never knew anything about it until we read it in The Enquirer. That is when we were first informed of it.

Mr. PORTMAN. And in terms of the Government's role, the Department of Defense's role, did she ever bring that up, or did you have any inkling of that?

Ms. NELSON. She never talked about any of that. We never heard anything about any of that until we read about it in The Enquirer.

Mr. PORTMAN. So it was not until this year that you had any inkling of that?

Ms. NELSON. That is right.

Mr. PORTMAN. Thank you.

Ms. Hager, do you know whether your dad was ever told about the existence of a military study?

Ms. HAGER. No. He had two sons in the military, and I am sure if he had been told, he would have told us. He told me just about everything he signed. He told me just about everything that they did to him. Him and I were very close right at the end, and he told me pretty much of what was going on. He knew nothing of this at all.

Mr. PORTMAN. He knew nothing of the DOD involvement?

Ms. HAGER. Of the Government being involved. He knew nothing of that. I am sure if they would have come and talked to him and told him that, you know, Mr. Mitchell, you are not going to live, maybe a couple of more months or so, and they would have ex-

plained this to him, he might have said, well, you know, go ahead and do it. But with him not knowing, no.

He was a man that loved his wife and he loved his family, and he would have wanted to spend as much time as he had left with his—with my mother. Because he hated—did he not want to leave her behind. That was his one main thing of getting better; is he did not want to leave her behind.

Mr. PORTMAN. Just one specific question. It relates to the letter he wrote to your sister, Isabell. He says in the letter that the doctor is not giving out the right news to the family. Chairman Bryant talked about the timing of this. I understand this is in relation to the initial operation that never took place. But how did you read that? Does that mean that he thought the doctors were trying to mislead the family, or that the doctors just didn't have good news for the family concerning his condition?

Ms. HAGER. What he didn't know was the doctors were not telling the family anything. The doctors did not tell us about the operation that he was going to have. The doctors never told us anything. This letter that my sister showed me, she showed me the week we had the meeting with David Mann. I knew no idea of this letter. I could have told him, dad, the doctors are not telling the family nothing. We know nothing. They are not keeping us informed at all.

I asked the nurse every night I left his room, I would make it a point to go to the nurse's station and say, if my father gets worse, please call me, no matter what time, call me, because I want my mother there, and I want to be there. We lived 10 minutes from Cincinnati General Hospital. I never received one phone call, nothing.

When my dad passed away, my brother made a trip to the hospital. He found him in a private room. When we left him the night before, he was in a ward. We left him; they let me stay there that night until 9:30, quarter to 10, to be with him. When my brother went back the next day, he was in a private room. He said, my father was in a private room—my dad was in a private room. I said, your dad has never been in a private room.

But they moved him when they know that he was dying. But they never picked up the phone and they never called me to let me know that my dad was dying. And I begged them to let me know.

Two days before he died, he begged me to bring him out of that hospital. He said, they are not doing what is right with me. Take me home. And the nurse pulled me aside and said, just agree with your dad, go along with what your dad said, because he can't go home. And I had to leave him.

They didn't do what was right by my dad and by any other patient that was in there connected with this treatment. They were wrong. They know they were wrong. And it is about time they stand up and they say they were wrong.

Mr. PORTMAN. Thank you, Ms. Hager.

Mr. BRYANT. On behalf of the subcommittee, I would like to thank each of you for coming forward and giving us a personal angle on this whole matter and taking the time to take off in the middle of the week and come up here and let the subcommittee see exactly how this has impacted your individual families.

I thank each of you for being here.

Mr. BRYANT. At this time we would like to ask the second panel to come forward, which consists of Dr. Gordon K. Soper, Principal Deputy to the Assistant to the Secretary for Atomic Energy in the Department of Defense; Dr. James Cox, professor of radiotherapy, M.D. Anderson Cancer Center, and chairman, Radiation Therapy Oncology Group; and Dr. Joseph Steger, president of the University of Cincinnati.

Dr. Steger, you are also accompanied by Mr. Stan Chesley, correct?

Mr. STEGER. Yes.

Mr. CHESLEY. I am here as counsel, Mr. Congressman, Congressman Bryant, just here as an assistant, to assist Dr. Steger in any way I can.

Dr. Soper, please proceed.

Mr. BRYANT. Dr. Soper, can we begin with you?

STATEMENT OF DR. GORDON K. SOPER, PRINCIPAL DEPUTY TO THE ASSISTANT TO THE SECRETARY FOR ATOMIC ENERGY, DEPARTMENT OF DEFENSE

Mr. SOPER. Thank you very much, Mr. Chairman, members of the subcommittee. I am Gordon Soper and I represent the Department of Defense at this hearing.

With me are two of my colleagues from the Department of Defense. Capt. Robert Bumgarner, Medical Corps, U.S. Navy, is the Director of the Armed Services Radiobiology Research Institute and is an expert in military medicine. It may also be useful to hear from Col. John Fraser Glenn, who is an expert on the Federal, Department of Defense, and Army's rules on human use experimentation.

You have already commented on the extensive effort the administration is conducting to uncover the facts surrounding past radiation experiments. I can only tell you, the Department of Defense pledges to you our unqualified commitment to a thorough and complete search of all of the records.

My purpose today is to provide you with a summary of the role that the Department of Defense played in the human radiation studies conducted at the University of Cincinnati from 1960 to 1972. My report to you is based upon reports, files and documents that we have been able to locate from wide and varied sources.

Most of the official Department of Defense records were retired and then destroyed long ago as part of the normal regulatory instructions for disposal of contract files. And as such, what I am going to tell you or summarize for you is not newly uncovered information.

The entirely unclassified University of Cincinnati studies have been extensively reported in the open literature. They have been a subject of peer review, review by the American College of Radiology, congressional hearings, and as all of you know, a series of news articles starting as far back as 1971; all of these reviews have in one way or another addressed the Department of Defense's involvement.

Now these studies will be further reviewed by a blue ribbon advisory committee on human radiation experiments, which was just

recently established by President Clinton. This committee is composed of eminent scientists, physicians, legal experts, and medical ethicists; and their purpose is to advise and guide the Government on the larger questions of ethical and scientific standards of any Government-sponsored experiments which involved the intentional exposure of humans to ionizing radiation.

A major goal of what we have been doing in DOD is to retrieve as many of the records as we possibly can of all DOD involvement in human experimentation, particularly that of the University of Cincinnati, and to provide a complete record of this to the advisory committee for their review.

I would like to give you a brief summary of the Department of Defense support to this research, and for those of you who are interested, a more detailed chronology is attached to my submitted testimony.

As you all know, in September 1958, Dr. Eugene Saenger of the Department of Radiology, University of Cincinnati College of Medicine, as the principal investigator, submitted what was called an unsolicited proposal to the Research and Development Division of the Army Surgeon General's Office; and as you have already stated, the application proposed to research metabolic changes in humans following total body irradiation, so that we could develop a simple urine or blood test to detect how much radiation an individual had received.

This unsolicited proposal was reviewed over the next year within the Department of Defense, and the available remaining documentation reveals that at least five Army Medical Corps officers reviewed the proposal and recommended approval of the contract application.

In October 1959, staff elements of what we call the Defense Atomic Support Agency recommended that they negotiate a contract with the University of Cincinnati for the study. So in early 1960, I think it was the first of January 1960, a contract was entered into between the Defense Atomic Support Agency, now called the Defense Nuclear Agency, and the University of Cincinnati board of directors.

The contract provided $25,058 for the initial study, and over the contract period—there were three separate contracts—between 1960 and 1971, a little more than $650,000 was spent on this effort.

Let me say just a few words about the reason for the Department of Defense involvement. The search for a biological marker of radiation exposure was one steadfast aim of the University's research for the Department of Defense over the life of these contracts. And I will also say that the results of the research contributed in a general way to a better understanding of the influence of radiation exposure on the combat effectiveness of military personnel, and it provided a more suitable method for diagnosis, prophylaxis and treatment of radiation effects on the nuclear battlefield, a very fearful possibility at that time.

Department of Defense funds were used for laboratory studies and psychological and psychiatric tests of cancer patients that received this whole or partial body radiation for treatment of their disease. No Department of Defense funds were used for direct pa-

tient care, nor did the Department of Defense play any part in patient selection or their choice of treatment.

The University of Cincinnati submitted 10 reports to the Department from 1961 to 1972; they are a part of the record. I have provided a copy of these reports to your offices along with other relevant documents in our possession.

Certainly, in reviewing these materials, Mr. Chairman, we at DOD can understand the controversy that arose in the early 1970's and continues to this day. Some of the records, as Congressman Mann said, especially from the viewpoint of 30 years later, are troubling and raise understandable concerns. Examples include statements in the University's early progress reports to the DOD that only nonradiosensitive tumors were selected for the research which some see as an indication of nontherapeutic purpose.

Some see the inadequacy of the informed consent procedures. On the other hand, for example, in 1972 the American College of Radiology concluded that the research was validly conceived and carried out, the patient selection conformed with good medical practice, and that consent procedures complied with applicable standards.

We in the Department do not at this point seek to resolve these apparent contradictions. Our main focus, Mr. Chairman, is to compile as complete a record as we can, make it available to the President's Advisory Committee and to the public for their study.

Today, DOD-supported research is governed by the so-called common rule—the Federal Policy for Protection of Human Subjects—and a copy of this regulation is attached to my statement. DOD is a full partner in the Government's commitment to this standard.

Under these regulations, today, a proposal like that from the University of Cincinnati in 1958 would require much more supporting documentation and justification to be considered for funding support by the Department of Defense.

During the course of these hearings, perhaps I could have the opportunity to expand upon this point more thoroughly.

So, Mr. Chairman, I have given you a very top-level summary of what we know so far. We are continuing to track down further information.

We sincerely appreciate the openness of the University of Cincinnati in sharing with us their records. We appreciate the local press sharing their records with us also. This hearing will also be a contribution to the knowledge-gathering process.

We agree, in the Department of Defense, with the need to air once again the issues surrounding this early chapter of our Government's human use research. Our sincere goal is to pull together as complete a record as we can of our involvement and provide it to the President's Advisory Committee for their detailed study and ultimate release to the public.

Thank you for your attention, sir.

Mr. BRYANT. Thank you.

[The prepared statement of Dr. Soper follows:]

STATEMENT
OF
GORDON K. SOPER, PRINCIPAL DEPUTY
ASSISTANT TO THE SECRETARY OF DEFENSE
FOR ATOMIC ENERGY
BEFORE THE
SUBCOMMITTEE ON ADMINISTRATIVE LAW
AND GOVERNMENT RELATIONS
CINCINNATI, OHIO
APRIL 11, 1994

Mr. Chairman and Members of the Subcommittee, I am Gordon Soper the Principal Deputy in the Office of the Assistant to the Secretary of Defense for Atomic Energy. I am here to support your request of March 24th to conduct hearings on radiation experiments performed by the University of Cincinnati Medical School which were funded in part by the Department of Defense(DoD).

If I may, Mr. Chairman, I'd like to provide a prelude to my testimony in order to put our efforts into context. Since early January, when the White House called for the formation of a senior level Interagency Working Group to coordinate the government-wide effort to uncover the nature and extent of any government sponsored experiments on individuals involving intentional exposure to ionizing radiation, the Department of Defense has been engaged in an extensive effort to discover the facts surrounding DoD sponsored human radiation experiments.

It goes without saying that the Department takes this action seriously, that it has the complete support of Secretary Perry and that we pledge to you our unqualified commitment to a thorough and complete search of all available records and the full public release of the pertinent information in those records. As Dr. Harold Smith, the Assistant to the Secretary of Defense for Atomic Energy, and the DoD focal point for this action, testified to you at your February 2 hearing on this subject, the retrieval of records is a discovery process requiring time intensive "detective work"--we are well into that process now and beginning to make excellent headway. I would be glad to take any questions that you might have regarding the Interagency Working Group process and the results we have obtained so far.

With that as background, I'd like to provide you with as complete a report as I can on the role that the Department of Defense played in the human radiation experiments conducted at the University of Cincinnati College of Medicine from 1960-1972 which were led by the principal investigator, Dr. Eugene L. Saenger, MD. My report to you is based on documents, reports and files that we have thus far been able to locate from wide and

varied sources--some of the official Department of Defense records were destroyed long ago as part of the normal regulatory instructions for disposal of contract files.

What I am going to report to you is really not newly uncovered information. The entirely unclassified University of Cincinnati studies have been previously reported in ten technical reports, 17 publications, and 26 presentations at scientific meetings; they were the subject of peer reviews at the University of Cincinnati; discussion of this work appears in the Congressional Record in 1971 and 1972; they were the subject of a report by the Comptroller General of the United States in 1972 for Senator Edward Kennedy, Chairman of the Senate Health Subcommittee; they were the subject of a separate investigation in a report by the American College of Radiology in 1972, at the request of U.S. Senator Mike Gravel; and they were--and continue to be--the subject of news articles in the press and other media reports.

In addition, Mr. Chairman, these studies will be further reviewed by the Advisory Committee on Human Radiation Experiments which just recently established by President Clinton. This Committee is composed of eminent scientists, physicians, legal experts and medical ethicists. Its purpose is to advise and guide the government on the larger questions of ethical and scientific standards of any government sponsored experiments which involved the intentional exposure to ionizing radiation. Specifically, as stated in the Executive Order issued by President Clinton in January: "The Advisory Committee shall consider whether (A) there was a clear medical or scientific purpose for the experiments; (B) appropriate medical follow-up was conducted; and (C) the experiments' design and administration adequately met the ethical and scientific standards, including standards of informed consent, that prevailed at the time of the experiments and that exist today." A major goal of DoD's "detective work" regarding the University of Cincinnati research is to provide a complete record for review by the Advisory Committee.

Next I want to run through a brief chronology of this research, based on the record compiled to date, focusing on the Department of Defense sponsorship.

In September, 1958 Dr. Eugene L. Saenger of the Department of Radiology, University of Cincinnati College of Medicine, as the principal investigator, submitted an unsolicited research proposal to the Research and Development Division of the Army Surgeon General's Office. The research proposal was initiated by the University of Cincinnati and not solicited by the Department of Defense. The application proposed to research metabolic changes in humans following total body irradiation for the purpose of determining whether the presence of amino-aciduria in

humans after radiation would provide a reliable biological marker of radiation exposure. Restated less technically, the original goal was to try to develop a simple urine test to detect the amount of radiation exposure. The University of Cincinnati requested approximately $25,000 for the first year and $21,000 for two subsequent years. The proposal stated that Dr. Saenger was at that time also conducting pediatric cancer research funded by the National Institutes of Health, and preparing a Handbook on Medical Aspects of Radiation Accidents, under contract from the U.S. Atomic Energy Commission.

This unsolicited proposal was reviewed over the next year within the Department of Defense. Available documentation reveals that at least five Army Medical Corps officers reviewed the proposal. They recommended approval of the contract application. In October 1959 staff elements of the Defense Atomic Support Agency (DASA) recommended that DASA negotiate a contract with the University of Cincinnati for the study of the metabolic changes in humans following total body irradiation.

At that time a need existed within the Department of Defense to be able to determine the biological, statistical and clinical features of radiation injury. This was based on the requirements of our military commanders in the field to predict the outcome of human exposure to ionizing radiation, to predict the number of persons requiring hospitalization and to estimate the decrement in work capacity after radiation exposure on a nuclear battlefield. Remembering the context of the late 1950's, where fallout shelters were common in homes and schools and superpower tensions dominated public affairs, this was a real possibility of that time. Furthermore, such information would aid civil defense authorities in their efforts to combat the effects of nuclear explosions on the civilian population. I believe the fairly recent Chernobyl nuclear power reactor explosion underscores the importance of being able to ascertain radiation exposure effects and also understand its impact on a subject population.

So, in early 1960, a contract (DA-49-146-XZ-029, dated 1 January 1960) was signed between DASA and the University of Cincinnati Board of Directors. The contract provided $25,085 for the study. This contract, with supplements and modifications, funded the study through February, 1964. Another contract (DA-49-146-XZ-315) carried the research until April, 1969. The final contract (DASA-01-69-C-0131), effective May, 1969, funded the research until March, 1972 when the University of Cincinnati refused DASA's offer for additional contract funding. Through 1971, the DoD spent $651,482.79 on this research.

While the search for a biological marker of radiation exposure was one steadfast aim of the University's research effort over the life of the contract, the goals of the Department of Defense were to also understand better the influence of

radiation on the combat effectiveness of troops and to develop more suitable methods of diagnosis, prognosis, prophylaxis and treatment of radiation injuries. In order to obtain this information, the Department of Defense provided funds for laboratory, psychological and psychiatric tests to assess the effects of varying doses of whole and partial body irradiation for the treatment of cancer patients. No funds were paid to the University of Cincinnati for direct patient care nor did the Department of Defense play any part in patient selection or choice of treatment.

The University of Cincinnati College of Medicine submitted ten reports to the Department of Defense from 1961 through 1972 in accordance with the terms of the contract. I have provided the committee a copy of these ten reports as well as a number of other relevant documents that we have in our possession. Attachment 1 to my statement is a chronology summarizing major parts of the record compiled to date.

In reviewing these materials, we at DoD can understand the controversy that arose in the early 1970's, involving the University community, the press, and the Congress, and that which has reemerged this year, regarding this research. Some of the records, especially from the viewpoint of 30 years later, are troubling and raise very understandable concerns. Examples of these include statements in the University's early progress reports to the effect that only patients with non-radiosensitive tumors were selected for the research, which some see as evidence of a non-therapeutic purpose, and that symptoms and side effects were not described to the patients, which some see as evidence of the inadequacy of the informed consent procedures. On the other hand, for example, the 1972 peer review of the American College of Radiology, carried out at the request of Senator Mike Gravel, concluded that the research was validly conceived and executed, that the patient selection conformed with good medical practice, and that consent procedures complied with applicable standards. We at DoD do not at this point seek to resolve these apparent contradictions. Rather, our sole focus regarding this task is to compile a complete record and to make it available to the President's Advisory Committee and to the public.

Before concluding my statement, I want to address the constraints which the Department of Defense imposes on human subject experiments today and how we would respond to an unsolicited proposal, like the 1958 proposal from the University of Cincinnati College of Medicine, for experiments in which humans would participate.

Formal DoD policy for the protection of human subjects in research date back to at least 1953, when a then TOP SECRET Memorandum was sent to the Secretaries of the Services from Secretary of Defense C.E. Wilson, titled "Use of Human Volunteers

in Experimental Research". This memorandum authorized the voluntary participation of military personnel and civilian employees in DoD conducted research for atomic, biological and chemical warfare defense and established specific standards for informed consent, minimization of risk of harm to subjects, and other matters.

Over the years, more detailed procedures were established, including incorporation in 1991 of the 1974 Department of Health and Human Services regulations for the Protection of Human Subjects, 45 C.F.R. Part 46.

Today, DoD-supported research is governed by the so-called "Common Rule"--the Federal Policy for the Protection of Human Subjects--which is part of DoD regulations at Title 32, Code of Federal Regulation, Part 219. A copy of this regulation is attached to my statement. DoD is a full partner in the government's commitment to this standard and has further defined its human use regulation in DoD Directive 3216.2, "Protection of Human Subjects in DoD Supported Research," January 7, 1983 and Department of Defense Guidance for Assurance of Compliance with the Federal Policy for the Protection of Human Subjects, June 10, 1993.

Under these regulations, a proposal like that from the University of Cincinnati would require much more supporting documentation and justification to be considered for funding. This includes the following:

1. The therapy itself, separate from the research, would require more information on the possible benefits and the known side effects.

2. Several local committees (specifically, scientific, radiation and Institutional Review Boards, or IRBs), would have to review the proposed research protocol package, with proposed consent forms, before DoD would review the proposal for acceptance.

3. It would be required that the sponsor's Institutional Review Board be made up of people from diverse backgrounds, including non-scientific perspectives, who could objectively and fully assess the proposal.

4. The IRB record would have to document that the research design is sound, that risks to subjects are minimized, that the selection of subjects is equitable, and that, if applicable, special protections have been adopted for any vulnerable groups mentioned.

5. A written consent form signed by the patient/subject would be required for participation in the research. This

consent form would require an explanation of the proposed therapy, all procedures and studies to be performed, and all expected outcomes and side effects in laymen's terms. The consent form must also state that the patient has been counseled about all of the above, and space provided for the patient to sign stating this has occurred and that the patient understands it.

6. The protocol would be required to justify withholding radiation in the control group of patients if such radiation therapy were the standard of care for the cancer each patient had.

7. The investigator would be required to give a more in depth description of the known and suspected risks and the intended benefits of the research for the subject.

In other words, Mr. Chairman, we believe we have in place a set of guidelines for human use experimentation that will preclude 30 years from now, hearings like we are conducting today.

So in summary, Mr. Chairman, the DoD received from the University of Cincinnati College of Medicine in 1958 an unsolicited proposal, which resulted in a contract from 1960 to 1971 supporting a human radiation experiment. DoD played no role in the selection of subjects, decisions regarding treatments, or the day-to-day conduct of the research. DoD received a series of reports describing the research results, none of which were ever classified. Data that we obtained from the University of Cincinnati studies were used to enhance our knowledge about the biological response to nuclear warfare--knowledge that we all hope will never have to be put to use. We well understand the controversy regarding this research, but make no effort at this time to resolve apparent contradictions in the voluminous record compiled to date. Our goal is to compile a complete record for the use of the President's Advisory Committee and ultimate release to the public.

That concludes my prepared remarks. I would be happy to take your questions.

CHRONOLOGICAL SUMMARY -- DASA/DNA REPORTS

1. General Observations:

a. Dr. Saenger submitted ten reports to DASA/DNA from 1961 through 1972 in accordance with the terms of his contract.

b. The reports provide a means to trace the expansion of the research's scope, increased sophistication of techniques, and ambitiousness of future plans. The reports were similar in that they stated the purpose of and criteria for the research, research structure and techniques, how the work was conducted, the results of the experiments, observations and analysis of the data, plans for future study, and individual case histories of patients observed during the reporting period.

2. General information about DoD sponsorship of radiation experiments at the University of Cincinnati 1960-1971.

1958 In September, 1958 Dr. Saenger submitted an unsolicited research application to the Research and Development Division of the Army Surgeon General's Office. The application proposed to research metabolic changes in humans following total body radiation for the purpose of determining whether the presence of amino-acidura in humans after radiation would provide a reliable biological marker of radiation exposure. Dr. Saenger requested approximately $25,000 for the first year and $21,000 for two subsequent years.

1958-1959 Over the next year the proposal was reviewed within the Defense Department and a contract negotiated. Available documentation reveals that at least four Army Medical Corps and one Medical Service Corps officer reviewed the proposal. They recommended the contract application be approved. In October, 1959 the Defense Atomic Support Agency's (DASA) Deputy Chief of Staff, Weapons Effects and Test requested, thru the Chief, DASA, the Contract Management Branch, Directorate of Logistics negotiate a contract with the University of Cincinnati for the study of the metabolic changes in humans following total body radiation.

1960 In early 1960 a contract (DA-49-146-XZ-029, dated 1 January 1960) was signed between DASA and the University of Cincinnati Board of Directors. The contract provided $25,085 for the study. This contract, with supplements and modifications,

funded the study through February, 1964.

The first contract stated the technical scope of the research was "to study the phenomen of amino-acidura following irradiation, a condition which has been reported in humans and animals, to clarify some of the mechanisms responsible for amino-acidura and to determine whether it is a practical biological test of radiation exposure." The search for a biological marker of radiation exposure was one constant of Dr. Saenger's research effort over the next decade.

1961 On 28 February 1961 the Cincinnati project's contract was modified for the first time. The contract was modified to establish a new date for work completion to provide additional time for research on amino-aciduria following irradiation; amended the technical scope of the work to meet additional objectives of the government; provided additional funds to meet research requirements under the amended scope of work; altered portions of the contract to bring the contract in accordance with Armed Services Procurement Regulations that became effective subsequent to the signing of the original contract. The contract amount increased almost $30,000 from $25,000 to $54,000 and the length of the project was extended from February, 1961 to April, 1962. The scope of the work was expanded by three requirements: a breakdown of desoxyribonucleic acid and is derivatives in patients receiving total body radiation; DNA studies on patients who received partial irradiation and radiomimetic chemotherapeutic agents; and preliminary determination of appropriate psychometric tests.

1961 In June, 1961 the contract was modified for the second time. An additional $650 was allocated to use the technical services of a French authority on radiobiology at a Whole Body Radiation Conference to be held by DASA at the University of Cincinnati in October, 1961.

1962 In April, 1962 the project's contract was modified for the third time. The contract total was increased approximately $39,000 to $94,400. The project completion date was extended to April 30, 1963. The scope of work was also further expanded. Three additional objectives were added. Additional studies were to be made of--increasing the upper range of radiation dose to 150-200 rad,

and single doses of nitrogen mustard or other radiomimetic drug using .4mg/kilo. The following tests were to be conducted for 9 days post-treatment--urinary taurine for correlation with leukocyte count, BAIBA in urine, Kynurenic and xanthurenic acids, deoxycytidine, DNA fragments in urine, et al, xanthine and hypoxanthine in urine, urinary phosphate, and glutathione. The test were to be done over a 30 day period--routine electrophresis, immunoelectrophoresis, quantitative precipitin studies, serum urea nitrogen and/or serum creatine once weekly, urinalysis once weekly and as needed, routine hematology, and completion of the manuscript of the DASA Conference on Total Body Irradiation of October, 1961.

1963 On April 1, 1963 the contract was modified for the fourth time. The contract was extended through April 30, 1964. Funding was increased $40,000 to $134,56. The scope of the work was further amended. Test to be conducted over a 30 day period between March 1, 1962 and February 28, 1963 were to be: (1) routine electrophesis, (2) immunoelectrophesis, (3) quantitative precipitin studies, (4) serum urea nitrogen and/or serum creatine once weekly, (5) urinalysis once weekly or as needed, and (6) routine hematology. During the same year the following tests were to be conducted over a 42 day period included 3,4,,5,6 and chromosome cultures of peripheral blood.

1964 Contract DA-49-146-XZ-315 came into effect and funded the research from February, 1964 to April, 1969.

1965 Ralph C. Rursiek and Dr. Eugene L. Saenger wrote a letter, dated May 17, 1965, to Director, Defense Atomic Support Agency, ATTN: STMD requesting that NWER No. 03.009 be funded at an estimated cost of $45,000 for FY65. The overall objective was to study various phenomena of desoxyribonucleic acid breakdown and other abnormalities following whole or partial body irradiation of human beings. Fifteen patients were to be studied. The project intended to study patients for 5-14 days prior to irradiation and for as long as possible after to evaluate clinical hematological and psychological changes. Investigation of the metabolism and urinary excretion of deoxycytidine was to be continued. Bone marrow was also to be stored prior to

irradiation. All serum was to be sent to Dr. Luzzio at Fort Knox.

1967 In 1967 a member of the University of Cincinnati research team, Dr. James G. Kereiakes, attended an Atomic Energy Commission sponsored conference at Oak Ridge, Tennessee. A purpose of the conference was to refine the dosimetric aspects of whole and partial body irradiations being used by the medical community to treat leukemia and widely disseminated cancers. The aim of the conference was to standardize the dosimetry being used to report patient dose. Information developed at the conference revealed 1,835 patients at about 35 institutions had received whole or partial body irradiations for the palliation or treatment of cancers. The use of radiation was widely spread and acknowledged as an effective modality.

1969 The final contract (DASA-01-69-C-0131), effective May, 1969 funded the research until March, 1972 when the University of Cincinnati refused DASA's offer for additional contract funding.

1971 Dr. Eugene L. Saenger wrote a letter, March 22, 1971, to Dr. Robert Loind, DASA, Attn: STMD. The cover letter with attachments forwarded the projects proposal for FY 73. The proposal requested $70,000 for a study entitled "An Appraisal of Human Studies In Radiobiological Aspects of Weapons Effects". A six page description of the study's philosophy, the role of future human research in relation to the remainder of the radiobiology program, specific areas of endeavor (eight--clinical evaluation, metabolic effects, behavioral effects, dose response studies, partial body studies, prognosis, therapeutic methods, use of healthy volunteers), and future plans regarding funding.

1960-1971 Through 1971 DoD ultimately spent over $650,000 on Dr. Saenger's endeavors which treated 85 adults whole- or partial-body radiation. Three children with localized Ewing's tumor were also treated with whole-body radiation. DoD funds were provided for laboratory, psychological and psychiatric tests to assess the effects of varying doses of whole and partial body irradiation. No funds were paid to the University of Cincinnati for direct patient care.

3. Report Summaries

1960-1961

The report for the first research period (February 19, 1960 to October 31, 1961) was DASA 1422 Supplement, which was entitled Metabolic Changes in Humans Following Total Body Irradiation. This title was used for the reports through 1967. The report provides a detailed itemization of the investigations and study projects. The aim of the studies was "to obtain new information about the metabolic effects of total body and partial body irradiation so as to have a better understanding of the acute and subacute effects of irradiation in the human." During this period ten patients received total body irradiation in doses that ranged from 16 to 150 rads. Patients were selected for the study were those with "proven metastatic or far advanced cancer...in relatively good nutritional status, i.e., able to maintain their body weight....[and] have normal hematological values." An explanation of one of the study's technique stated "the patient is told that he is to receive treatment to help his sickness. There is no discussion of subjective reactions resulting from the treatment. Other physicians, nurses and ward personnel are instructed not to discuss these aspects with the patient." The remainder of report discussed on-going studies, clinical observations, dosimetry, and other study techniques supplemented with tables and patient case histories.

1961-1963

The second report, DASA 1422 reported on the research from November, 1961 to April, 1963. Ten patients were treated with total body radiation in doses that ranged from 150-200 rad during the report period. The study's statement of aims was identical to that of the previous report except that it was expanded. The added aim stated "This information is necessary to provide knowledge of combat effectiveness of troops and to develop additional methods of diagnosis, prognosis, prophylaxis and treatment of these injuries." Patient selection criteria was more refined. In addition to those already stated new criteria was that "patients with lymphoma [were] excluded...Patients with solid neoplasms not radiosensitive are sought." The technique reported previously remained in use. Verbal consent of the patients was obtained prior to treatment.

One of the issues the researchers encountered involved complications in trying to determine the

effects of radiation. the report stated "Physicians assess patient to be certain that the underlying disease can be evaluated. Thus, there was difficulty in selection of patients for assessment of radiation effects because of underlying disease. Patients previously treated by radiation or chemotherapy were excluded because previous treatment confounded the response to radiation in several early patients."

Throughout the narrative and near the conclusion with the researchers thoughts on "Human Effectiveness Following Whole-Body Irradiation". Several of their observations included:

"Marked hematological changes occur generally between the 25th and 35th day following exposure. Maximum recovery to be obtained generally requires about 100 days."

"Human beings recover slowly and are quite sensitive to radiation with multi-system involvement."

"Prodromal acute effects such a nausea, vomiting, anorexia, and lassitude are of the duration hours. Intermediate effects such as hematologic complications are to be conceived of in weeks."

"A previous dose of radiation does influence the incidence of acute effects. Therefore the incidence of 'combat effectiveness' will be significantly increased on re-exposure of an individual."

"...individuals with previous exposure to radiation will be less tolerant of subsequent exposures. hence troops previously exposed to 150-300r of whole body radiation will tend to show more combat ineffectiveness in the prodromal period than will those who are unexposed."

"This field of investigation has obvious important implications. Breakdown of DNA has long been implicated as the fundamental biochemical change of radiation and there is an impressive literature bearing on this point...The observation cited above of decrease of DOC after the administration of protective agents indicates the possibility of the use of specific prophylactic agents for the protection of humans in nuclear warfare."

A final observation was offered on future study:

"It is our opinion that human radiation studies need to be expanded.
We propose to establish facilities for withdrawal, storage, and reinfusion of autologous bone marrow. As indicated elsewhere in this report we have encountered significant hematological difficulties with a dose range of 200-325r. Therefore, to proceed with higher doses, we feel the need to protect our patients even if we might sacrifice their value for hematological evaluation after 2-3 weeks since the hematological effects are well documented. Once this technique has been developed as a support procedure we then anticipate increasing doses to higher levels."

Tables, figures and case histories rounded out the report.

1963-1964

DASA 1633 was the report submitted for the period May 1, 1963 to February 29, 1964 during which six patients were treated with total body radiation doses between 100 to 150 rad. The aims of the study remained as previously reported. "Normal renal function' was added to patient selection criteria. The technique to limit subjective reactions treatment was unchanged. Proposals for human study expanded on the previous report's discussion of autologous bone marrow reinfusion. The report stated:

"Storage and reinfusion of autologous bone marrow will be accomplished in the facility which has been established...The purpose of marrow storage and reinfusion is to protect subjects who receive doses in excess of 150 rad in the event of bone marrow failure. We hope to utilize doses between 200-300 rad."

Tables and case histories once again accompanied the report.

1964-1966

DASA 1844 covered not only the study years 1964 to 1966 but also provided a summary of the first six years of the experiment. Midway through the decade the aims of the project were stated as:

"This program is designed to obtain new

information regarding the metabolic, physiologic, immunologic, hematologic, and biochemical effects of TBR and PBR in human beings. It will then be possible to understand better the influence of radiation on combat effectiveness of troops and to develop more suitable methods of diagnosis, prognosis, prophylaxis and treatment of radiation injuries. It is our belief that information concerning radiation effects in the human being can be determined as well or better in these subjects as in the laboratory animal even though the characteristic of cancer must be kept in mind in the evaluation of the data."

On page 2 the aims were once again addressed in terms of the original scope of the study:

"A major objective of these studies has been a search for a suitable biological indicator of radiation dose in human beings....At this time the urinary excretion of deoxycytidine seems to be promising as a biological indicator."

Another aim was stated on pages 2 and 3.

"Psychological and psychiatric testing has been started in 14 patients....This approach will provide information on another important parameter of combat effectiveness of troops."

Later in the report an aspect of the psychiatric evaluation is further discussed.

"One of the most difficult aspects of radiation injury requiring evaluation is that of performance decrement. This term is loosely used but in our laboratory it is defined as any decrease in ability to carry out assigned tasks."

Patient selection criteria was more specific:

"Patients with metastatic or incurable neoplasms are given whole partial body radiation for palliative treatment of their disease. Patients for the studies described in this report are selected from patients treated as described above providing that they satisfy the following criteria:

1. The patients have solid tumors. Patients with lymphoma are excluded.
2. Relatively good nutritional status

(ability to maintain weight).
3. Normal renal function
4. Stable hemogram in the control period."

Twenty three additional patients were treated during the research period between 1964 and 1966. Of these patients 13 received total body radiation treatments with dosages between 25 and 150 rads. Partial body radiation doses between 100 and 300 rads were used in the treatment of 10 patients.
The technique to "isolate" patients from discussions of subjective reactions remained the same.

Discussion of hematology stated:

"Since severe hematological depression was found in most patients who expired, autologous bone marrow storage has been performed for 13 patients. In only two patients has infusion been carried out. The method is being refined so as to include filtration prior to infusion. Although we have not encountered morbidity...filtration appears to decrease the probability of incidence of pulmonary emboli."

Accompanying the 35 page report were 122 pages of tables, and case histories of the all patients treated to date.

1966-1967

DASA 2179 described the treatment of four patients between May 1, 1966 and April 30 1967. Of the four patients treated one received total body radiation (150 rad) while the other three received partial body radiation doses in the range of 100-200 rad. Aims, patient selection criteria, and technique remained as previously reported. Three accomplishments were reported. The first involved "the completion of an infusion filtration system for reinfusion of autologous stored human bone marrow." As a result of the development the researchers stated "Since this instrumentation will make infusion of marrow a safer and more easily controlled procedure we feel that earlier infusion to prevent the hematological depression from radiation should be investigated." The text noted that the methods were described in a paper presented in Paris, France which cited DASA support.
The second accomplishment was the "perfection

by Dr. I-Wen Chen of a new, much improved method for the determination of deoxycytidine (CdR) in urine from humans and from rats."

The third involved "the growth of two strains of phage on synthetic culture medium." This development made it "possible to titrate antibody production in experimental animals and man before and after irradiation."

Future plans included the evaluation of "alterations in antibody production and /or destruction in human beings due to radiation." Observations of this nature on "the effects of radiation exposure will yield a better understanding for military planning and triage."

Tables, figures, and case histories supplemented the text.

1967-1968

The report for the period May 1, 1967 to April 30, 1968 was DASA 2168. The report's title changed to Radiation Effects in Man: Manifestations and Therapeutic Efforts. Reports carried this title for the remainder of research. This report recounted the treatment of seven patients. Four patients were treated with total body radiation doses between 100 and 200 rad. Three patients were treated with lower body partial body radiation doses of 200 to 300 rad. The report's forward noted "these studies were performed in conformation with the 'recommendations guiding doctors in clinical research' as stated in the Declaration of Helsinki of the World Medical Association (1964). Reported aims, criteria and techniques were as previously reported. Updated information from the psychiatric-psychological team noted "the number of patients who have been evaluated by the psychiatric-psychological team now totals 20." Hematology research continued. The researchers reported "seven patients received autologous bone marrow transfusions at completion of DADA 2168. Guidelines for quantity of marrow cells to be infused for successful transfusion and bone marrow protection were developed."

Case histories and tables provided additional information.

1968-1969

The research over the period between May 1, 1968 and April 30, 1969 was the subject of DADA 2428. Eight patients were treated during this period. Total body radiation doses of 100-200 rad were given to six patients. Two patients were treated with 200-300 rad doses of partial body radiation.

Once again the forward noted that the studies conformed to the recommendations of the Declaration of Helsinki. Aims and goals remained unchanged. In the field of hematology the report stated "success has finally been obtained in autologous marrow infusion which will permit us to employ higher doses of radiation in the coming year. Several new biological dosimeters are under evaluation." Tables and case histories accompanied the report.

1969-1970

DASA 2599 reported on the research based on observations of twelve patients between May 1, 1969 and April 30, 1970. The recommendations of the Declaration of Helsinki were once again noted. A presentation by Dr. Edward B. Silberstein on the team's earlier work and the data contained in this report at the IAEA-WHO Conference in Paris on 24 June 1970 was reported.

During this period six patients were treated with doses of 100-230 rad of total body radiation. The other six patients received partial body radiation doses between 150 to 300 rad. Regarding these patients the report stated "Most of the patients had inoperable metastatic carcinoma which was not amenable to conventional chemotherapy. Nevertheless, these patients were all clinically stable, many of them working daily. Several of the subjects, apparently tumor free and clinically normal after regression of regionally irradiated tumors (Ewing's tumor), received prophylactic whole body radiation."

Hematological work, specifically related to biological dosimetry, was discussed. Several biological dosimetry issues were discussed.

"We are pursuing this goal at whole-body radiation doses up to 250 rad with even higher doses planned with the support of marrow autotransfusions and laminar-flow 'sterile' rooms. Large-volume partial-body irradiation is also being performed to learn more about the efficacy of chromosome aberrations as a radiation dosimeter in the more frequent situation of inhomogeneous exposure. With a linear accelerator, we hope to study the effects of various dose rate <u>in vivo</u> as well."

As for the continued research into the utility of deoxycytidine the report noted "deoxycytidinuria appears to be related to general

tissue catabolism from several causes, including radiation. Other problems in using urinary CdR include variations in excretion due to race (57) and age (63)." [Note: Numbers in () are bibliographic reference numbers.]

Tables and case histories were included with the report. Table XII provided "a summary of demographic and other pertinent data...for the entire group of 36 patients" observed since the start of testing.

1970-1971

DNA 2751T was the report for the period May 1, 1970 to April 30, 1971. Eight patients underwent treatment. Three received total body radiations dosages of 100-200 rad. Five underwent partial body radiation with doses of 300 rad. The research aims were restated.

"The University of Cincinnati studies in radiation effect in man continues as a carefully integrated effort to maximize clinical, psychiatric, therapeutic, biochemical, and theoretical approaches to whole and partial therapeutic irradiation as given for palliation of certain selected cancers."

To achieve these aims "the methods of applying radiation have remained essentially the same since the inception of these studies."

Acknowledgement was made of guidance provided.

"The nature of the specific projects undertaken in our laboratories reflects the consideration of many of our faculty and the thoughts and problems of the other DNA conferences organized over the past several years by Col E.J. Huycke. Valuable interchange of ideas have been stimulated by visitors from Department of Defense laboratories who give our staff a more practical insight into military problems than we might otherwise have."

Future plans were described.

"Many of the new directions in our investigation stem from concurrent advances in cytogenics, organ transplantation, bio-chemical aspects of molecular biology, and clinical aspects

of cancer therapy."

"A renewed interest is manifested in chromosome aberrations as being eventually an index of 'effective radiation dose,' particularly since almost all exposures encountered in nontherapeutic circumstances will have varying degrees of nonuniformity of dose rate and dose distribution."

"As an outgrowth of our needs to afford maximum protection to patients receiving doses in the LD_{50} range, some new technical advances have been developed in bone marrow transfusion in patients."

Regarding biological dosimetry the report stated:

"Yet in severely burned individuals deoxycytidine ((deoxycytidine excreted in urine)) occurs late (in 2 to 4 weeks) and in the several patients studied the levels seemed directly related to the extent and depth of the burn. Radiation induced deoxycytidinuria when found occurs within 2-3 days and then disappears. Additional studies may suggest this test as a way of differentiating relative contribution of these two modalities of injury."

The usual tables and case histories supplemented the narrative.

1971-1972

The final report in the series was DNA 3024F which was to be for the period April 1, 1971 to March 31, 1972. However, its was really a summary of the entire research effort and was a "scientific communication presented at the meeting of the American Roentgen Ray Society in Washington on 3 October 1972." It was further noted that "this report has been accepted for publication in the American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine."

As stated in this report the research were "to improve the treatment and general clinical management and if possible the length of survival of patients with advanced cancer. Systemic effects of radiation therapy have been given particular attention in our work."

The issue of informed consent was addressed.

"All patients gave informed consent in

accordance with directives of the Faculty Research committee of the University of Cincinnati College of Medicine and those of the National Institutes of Health. The use of formal informed consent forms in this study antedated the above requirements by two years. The project is reviewed and approved regularly by the above committee."

The report noted that "patients become eligible for this form of treatment if they have advanced cancer for whom cure could not be anticipated....Chief among the reasons for elimination was an indication in the pretreatment phase that some risk from wide-filed radiation might ensue or that another method of treatment was considered preferable."

From an analysis of radiation mortality "one can identify eight cases in which there is a possibility of the therapy contributing to the mortality."

A comparison is later made between times of death of those that entered the study and received radiation treatments, and those that entered the study and did not receive radiation treatments. From this comparison the report noted:

"Fisher's exact probability test yields a p value of 0.16, indicating that there is no difference between the two groups. Therefore, one may conclude that in other patients described, the effect of whole- and partial-body radiation therapy was less important in contributing to death than was the extent of disease in these patients. Another interpretation would be that a physician selecting far advanced cancer patients for a given treatment would have about the same degree of difficulty in selecting any form of treatment for these very ill patients."

Tables and figures accompanied the report as did a section entitled "Thermography as a Radiobiological Dosimeter".

1971-1972 Issues arise that lead to the termination of the contractual relationship between DNA and the University of Cincinnati.

Project Chronology
October 1971 - January 1973

October 8, 1971 -- An article appeared in *The Washington Post*, "Pentagon Has Contract to Test Radiation Effect on Humans", by Stuart Auerbach and Thomas O'Toole that prompted the subsequent governmental investigations of the Cincinnati project.

October 11, 1971 -- Dr. Eugene L. Saenger, Dr. Clifford G. Grulee, Dean of the University of Cincinnati College of Medicine, and Dr. Edward A. Gall, Vice President of the University of Cincinnati and Director of the University of Cincinnati Medical Center, were present at a press conference the subject of which was the impending Senate and Government Accounting Office (GAO) investigations of the conduct of the Cincinnati project.

October 11, 1971 -- A follow up article appeared in *The Washington Post*, "Pentagon's Radiation Experiments Defended". The article featured Dr. Saenger explaining the process of patients selection and Department of Defense (DOD) funding of the project.

Mid-October 1971 -- DOD developed a Fact Sheet on the Cincinnati project that discussed its contractual arrangements with the University of Cincinnati. A copy of the Fact Sheet was later entered into the Congressional Record on December 15, 1971 as an attachment to a letter from the Assistant Secretary of Defense (Legislative Affairs) to Senator Robert Taft, Jr.

November 10, 1971 -- Senator Mike Gravel wrote a letter to Dr. Robert W. McConnell, President of the American College of Radiology (ACR) requesting the ACR to conduct an evaluation of the Cincinnati Project.

November 12, 1971 -- Dean Clifford G. Grulee appointed an Ad Hoc committee to review the "whole-body radiation study" which Dr. Eugene L. Saenger had been conducting at the University of Cincinnati Medical Center. The Ad Hoc committee, chaired by Dr. Raymond Suskind, Director, Environmental Health, University of Cincinnati, was made up of eleven members and was charged with reviewing the scientific content, methodology, and data treatment of this study, as well as other aspects which the committee deemed appropriate. All eleven committee members were professors at the University of Cincinnati. Ten committee members were medical doctors and one was a Ph.D. in Physiology.

December 6, 1971 -- Mr. Ellis R. Mottur, Science Adviser to the Senate subcommittee on Health, Senate Committee on Labor and Public Welfare and Dr. Caper, both of Senator Kennedy's staff interviewed Dr. Edward B. Silberstein, University of Cincinnati Medical Center, Dr. Eugene L. Saenger, and others at Cincinnati General Hospital.

December 6, 1971 -- Dr. Robert S. Daniels, Professor and Director, Department of Psychiatry, University of Cincinnati, wrote a letter

to Dr. Raymond Suskind. The letter forwarded a list of question to Dr. Suskind for inclusion in a "our [Ad Hoc Review Committee] report on 'Total Body Radiation' project".

December 7, 1971 -- Mr. Ellis R. Mottur of Senator Kennedy's staff requested the opportunity to conduct interviews with surviving project subjects.

December 7, 1971 -- Dr. Eugene L. Saenger wrote a letter to Dr. Raymond Suskind, which discussed the impending arrival of the ACR Committee to review the project.

December 13, 1971 -- The subject of interviewing patients was broached in a letter from Senator Edward Kennedy, acting in his role as Chairman of the subcommittee on Health, Senate Committee on Labor and Public Welfare, to Dr. Warren Bennis, President University of Cincinnati.

December 17, 1971 -- Dr. Eugene L. Saenger wrote a letter to Dr. Charles Barrett, Department of Surgery, University of Cincinnati Medical Center. The letter details Dr. Saenger's objections and concerns about providing patients to be interviewed.

December 20, 1971 -- Dr. Eugene L. Saenger authored "Comments on Differences Between Therapeutic and Non-Therapeutic Investigation". Dr. Saenger generally defended his research and methods by citing legal and medical opinions. He then went on to refute specific allegations that relate to DoD funding, informed consent techniques (Dr. Saenger made the point that since 1968 patients were told the information gained might be of use on the battlefield), follow-up, alleged contributory effects of radiation to patient deaths, racial composition of study group, and the below average intelligence level of the project subjects.

December 21, 1971 -- Dr. Eugene L. Saenger wrote a letter to Dr. Edward A. Gall. The letter was a response to Dr. Gall's request that Dr. Saenger identify patients that might be suitable for interviews by Mr. Mottur.

January 1972 -- The Ad Hoc Review Committee chaired by Dr. Raymond Suskind of the University of Cincinnati communicated its report to the Dean of the College of Medicine concerning Dr. Saenger's project. The Report contains seven sections,two of which are pertinent to DOD involvement; Section IV Financial Support of Program and Section V Informed Consent and Human Rights.

In Section IV it is reported that the request for financial support for the project was initiated by the University of Cincinnati. The systematic investigation of whole body radiation did not begin until the project was funded by the Defense Atomic Support Agency (DASA). Through March 1972 DASA had granted $651,483, 13% to 15% of the budget of the Radioisotope Division. Section IV also details the breakdown of expenditures. There is no evidence that the DASA funding was made contingent on work, ideas,

or suggestions proposed by DASA and that all the information reported to DASA was kept unclassified and publicly available. The work was also carried out by the University researchers with complete scientific freedom.

In Section V it was stated that the procedures for informed consent followed by Dr. Saenger's partial and whole body radiation project reflected the process characteristic of the University of Cincinnati and the nation. As the idea of informed consent developed nationally in the 1960's from informal, oral, and non-specific to formal, written, and more detailed, Dr. Saenger's project appropriately updated their procedure for informed consent to meet the more stringent levels required for good medical research.

January 3, 1972 -- The ACR responded to Senator Mike Gravel's request to conduct an inquiry into the whole-body radiation therapy project supervised by Dr. Eugene L. Saenger. The ACR Report concluded that the Cincinnati project was validly conceived, stated, executed, controlled and followed up. The process of patient selection was based upon clinical considerations and conformed with good medical practice. The procedures for obtaining patient consent was valid and consistent with the recommendations of the National Institutes of Health and with the practice of most cancer centers. The ACR Report indicated procedures for obtaining informed consent were likely performed better than the average institution because of the volume of projects generated by the medical facility and the quality of the people involved. ACR urged Senator Gravel to support the projects continuation. The ACR Report also noted that DOD funds were used to support the laboratory and psychological studies, but not the treatment or the care of the patients. The ACR Report discusses at length the subject selection procedures and notes that in both race and IQ the group is representative of the patients served at Cincinnati General Hospital. The ACR Report also agreed with Dr. Saenger that ". . . it seems reasonable to continue [whole-body radiation] therapy for the gravely ill individual since this method of treatment is less elaborate and with no greater risk than many present forms of chemotherapy."

January 11, 1972 -- Senator Edward Kennedy wrote a letter to Dr. Warren Bennis in reference to the University's refusal to identify patients to be interviewed by the committee. The Senator pointed out that some patients appeared in a documentary produced by National Education Television in September, 1971, and it was difficult to understand why the University allowed them to appear on TV and not before a Senate Subcommittee. Senator Kennedy stated that the University's decision was unfortunate because "the most crucial element in the inquiry is the patient's perception and understanding of the experiments in which they were participating..."

January 19, 1972 -- Dr. Edward A. Gall wrote a letter to Senator Kennedy responding to the Senator's January 11, 1972 letter. Dr.

Gall stated that names were provided to NET with the consent of the patients but points out that the situation had subsequently changed. In response to the Senator's request the University was sending letters to surviving patients to ask them if they would give their consent to being questioned by representatives of the subcommittee. He said that experts were consulted and they were of the opinion that any such questioning may have led to some unfavorable medical implications. Dr. Gall also asked the Senator if he would consent to a meeting with senior university officials.

January 21, 1972 -- Mr. Ellis R. Mottur wrote a letter to Dr. Edward A. Gall requesting copies of the letter (with names omitted) sent to patients or parents of surviving patients asking if they would consent to interviews.

January 25, 1972 -- Dr. Edward A. Gall wrote a letter to Mr. Ellis R. Mottur, Science Adviser, Senate Committee Labor Public Welfare, that forwarded the requested copies of letters sent to patients or parents to request interviews.

February 4, 1972 -- In a letter to Dr. Robert W. McConnell Senator Mike Gravel indicated his displeasure with the results of the ACR Report released on January 3, 1972. Senator Gravel felt the report was deficient in relevant information and poorly organized. The Senator pointed out the ACR report "confirms that the patients were not thoroughly informed about the extra discomfort, the military aspects, or the possible lethal effects."

February 4, 1972 -- Mr. Myrton Tom Stewart and Mr. Robert Murphy of the General Accounting Officer (GAO) met with Dr. Eugene L. Saenger. Dr. Saenger was asked nine questions: when did the project start; did he approach DoD or vice versa [he approached]; how were parts of research funded; where were Federal funds used, etc. In response to question 4 which asked about the use of federal funds for patient care, Dr. Saenger replied that "[n]o DOD funds under these contracts were at any time used for payment of patient days in any hospital. DOD funds were used for technical help, support of a biochemist, physicians, physicists and for psychological and psychiatric studies." In response to question 6 which asked if treatments were given for the benefit of the patients or DOD, Saenger responded, "that in all cases the treatment was given for the palliation of cancer of the patients and information for the Dod was a byproduct."

February 16, 1972 -- Dr. Warren Bennis wrote a letter to Senator Kennedy referring to meeting with the Senator and Ohio Governor Gilligan on February 24, 1972. Dr. Bennis included a copy of the Ad Hoc Review Committee's report, and advised the Senator that Dr. Gall would be responding within a few days to the Senator's request for an evaluation of the report by the Junior Faculty Association. The letter concluded with the promise that he was willing to cooperate with the Subcommittee in any way consistent with the health and legal rights of the patients.

February 17, 1972 -- Dr. Edward A. Gall wrote a letter to Senator Edward Kennedy which provided a copy of the Ad Hoc Committee Report and other documentation. Regarding the Junior Faculty Report, Dr. Gall wrote that since the Ad Hoc Committee report addressed the points raised by the Junior Faculty Association he considered the Ad Hoc report "a complete and authoritative response." He also informed the Senator that they had received responses from all the surviving patients and the parents of the children treated regarding interviews. All responses had declined to be interviewed. Dr. Gall further expounded on the point made in his January 19, 1972 letter that two cancer experts (not local and not associated with the University) had given as their opinion that there would be unfavorable medical implications if patients were interviewed.

February 17, 1972 -- Dr. Edward A. Gall wrote a letter to Dr. Warren Bennis forwarding the consultant opinions from the two cancer experts. Dr. Gall noted they were in concurrence with their own physicians about the undesirability of subjecting the patients to interviews.

February 22, 1972 -- Mr. Cyril W. Kupferberg, Chair of Radiation Response Team, wrote a letter in response to an individual who requested to know if a family member was part of the experiment that was reported to DoD. The individual was not a subject of Dr. Saenger. The letter included attachments - University of Cincinnati Guideline for releasing medical information on deceased patients, an authorization for release of information form, and an example of a "Consent for Special Study and Treatment" form.

March 31, 1972 -- The Cincinnati project contract number DASA-01-69C-0131 expired. The University of Cincinnati had earlier indicated that it did not want to continue conducting research under this contract with the Defense Nuclear Agency.

July 5, 1972 -- Dr. Eugene L. Saenger wrote a letter to Dr. Edward A. Gall. The three page letter appears to be Dr. Saenger's response to an article published in the *Cincinnati Post* on April 25, 1972. Dr. Saenger's response focuses on several points: University procedures for seeking Federal grants/contracts, issues associated with seeking DoD funds for research in FY 74 and the terminating of research utilizing FY 73 funds.

August 1, 1972 -- Several pieces of correspondence relating to the Cincinnati project were entered into the *Congressional Record*, including a letter from the Comptroller General of the United States to Senator Edward Kennedy summarizing the results of the GAO investigation of DOD policy regarding the protection of humans used in medical research projects and DOD responses to questions from Senate staffers concerning DOD policy relative to human experimentation policies and procedures. The letter from the Comptroller General indicated that DOD policy was set forth by DOD Instruction 5030.29, dated May 12, 1964. Instruction 5030.29 states that "The Department of Defense assumes full responsibility

for the protection of humans involved in research under its sponsorship whether this involves investigational drugs or other hazards." The letter also states, "[c]oncering the contract with the University of Cincinnati . . . [DNA] stated that the cost of radiation treatment and patient case had not been borne by their agency. They also stated 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."

The questions from Senate staffers focused on (1) the level of human experimentation funded by DOD, (2) what authorization was needed to conduct human experiments, (3) the adequacy of information given to prospective subjects and (4) were there differing standards applied to military personnel than to civilians. DOD responded to question one that only a very small portion of its medical R&D budget was given to human experimentation. In response to question two DOD stated that although there was no standardized authorization process, all human experimentation was guided by DOD instructions and service regulations and instructions. In response to question three DOD stated that informed consents was a primary ethical and legal requirements for all DOD use of human volunteers. In response to question four DOD responded that in terms of supervision, volunteering, informed consent and freedom to terminate there was no difference.

January 11, 1973 -- Mr. Lawrence Elish released a 26 page paper titled, "Legal Rights of Human Subjects in the University of Cincinnati Whole-Body Radiation Study", that examined the legal and ethical implications of the Saenger experiments.

DEPARTMENT OF DEFENSE

IMPLEMENTATION OF THE

"COMMON RULE" --

FEDERAL POLICY FOR THE

PROTECTION OF HUMAN

SUBJECTS

32 C.F.R. PART 219

PART 219—PROTECTION OF HUMAN SUBJECTS

Sec.

AUTHORITY: 5 U.S.C. 301; 42 U.S.C. 300v-1(b).

SOURCE: 56 FR 28012, 28021, June 18, 1991, unless otherwise noted.

§ 219.101 To what does this policy apply?

(a) Except as provided in paragraph (b) of this section, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may

be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the federal government outside the United States.

(1) Research that is conducted or supported by a federal department or agency, whether or not it is regulated as defined in § 219.102(e), must comply with all sections of this policy.

(2) Research that is neither conducted nor supported by a federal department or agency but is subject to regulation as defined in § 219.102(e) must be reviewed and approved, in compliance with § 219.101, § 219.102, and § 219.107 through § 219.117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

(i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

(ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:

(i) The human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(4) Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

(i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(c) Department or agency heads retain final judgment as to whether a particular activity is covered by this policy.

(d) Department or agency heads may require that specific research activities or classes of research activities conducted, supported, or otherwise subject to regulation by the department or agency but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

(e) Compliance with this policy requires compliance with pertinent federal laws or regulations which provide additional protections for human subjects.

(f) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(g) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research.

(h) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the FEDERAL REGISTER or will be otherwise published as provided in department or agency procedures.

(i) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Protection from Research Risks, Department of Health and Human Services (HHS), and shall also publish them in the FEDERAL REGISTER or in such other manner as provided in department or agency procedures.[1]

[56 FR 28012, 28021, June 18, 1991, as amended at 56 FR 29756, June 28, 1991]

§ 219.102 Definitions.

(a) *Department or agency head* means the head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

(b) *Institution* means any public or private entity or agency (including federal, state, and other agencies).

(c) *Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

(d) *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

(e) *Research subject to regulation*, and similar terms are intended to encompass those research activities for which a federal department or agency

[1] Institutions with HHS-approved assurances on file will abide by provisions of title 45 CFR part 46 subparts A-D. Some of the other Departments and Agencies have incorporated all provisions of title 45 CFR part 46 into their policies and procedures as well. However, the exemptions at 45 CFR 46.101(b) do not apply to research involving prisoners, fetuses, pregnant women, or human in vitro fertilization, subparts B and C. The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or nonresearch in nature (for example, Wage and Hour requirements administered by the Department of Labor).

(f) *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains

(1) Data through intervention or interaction with the individual, or

(2) Identifiable private information. *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. "Private information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

(g) *IRB* means an institutional review board established in accord with and for the purposes expressed in this policy.

(h) *IRB approval* means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

(i) *Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(j) *Certification* means the official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

§ 219.103 Assuring compliance with this policy—research conducted or supported by any Federal Department or Agency.

(a) Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Protection from Research Risks, HHS, and approved for federalwide use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the Office for Protection from Research Risks, HHS.

(b) Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance approved as provided in this section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to fed-

erally supported or conducted research shall at a minimum include:

(1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself. This requirement does not preempt provisions of this policy applicable to department- or agency-supported or regulated research and need not be applicable to any research exempted or waived under § 219.101 (b) or (i).

(2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

(3) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head, unless in accord with § 219.103(a) of this policy, the existence of an HHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Protection from Research Risks, HHS.

(4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(5) Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval.

(c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.

(d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval.

(f) Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived under § 219.101 (b) or (i). An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by § 219.103 of this Policy has been reviewed and approved by the IRB. Such certification must be submitted with the application or proposal or by such later date as may be prescribed by the department or agency to which the application or proposal is submitted. Under no condition shall research covered by § 219.103 of the Policy be supported prior to receipt of the certification that the research has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

(Approved by the Office of Management and Budget under control number 9999-0020)

[56 FR 28012, 28021, June 18, 1991, as amended at 56 FR 29756, June 28, 1991]

§§ 219.104—219.106 [Reserved]

§ 219.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

§ 219.108 IRB functions and operations.

In order to fulfill the requirements of this policy each IRB shall:

(a) Follow written procedures in the same detail as described in § 219.103(b)(4) and, to the extent required by, § 219.103(b)(5).

(b) Except when an expedited review procedure is used (see § 219.110), review proposed research at convened meetings at which a majority of the

members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

§ 219.109 IRB Review of Research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with § 219.116. The IRB may require that information, in addition to that specifically mentioned in § 219.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with § 219.117.

(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Secretary, HHS, has established, and published as a Notice in the FEDERAL REGISTER, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the FEDERAL REGISTER. A copy of the list is available from the Office for Protection from Research Risks, National Institutes of Health, HHS, Bethesda, Maryland 20892.

(b) An IRB may use the expedited review procedure to review either or both of the following:

(1) Some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk,

(2) Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in § 219.108(b).

(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

(d) The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

§ 219.111 Criteria for IRB approval of research.

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already

being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by § 219.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by § 219.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

§ 219.112 Review by institution.

Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

§ 219.113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.114 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

§ 219.115 IRB records.

(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show at-

tendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members in the same detail as described is § 219.103(b)(3).

(6) Written procedures for the IRB in the same detail as described in § 219.103(b)(4) and § 219.103(b)(5).

(7) Statements of significant new findings provided to subjects, as required by § 219.116(b)(5).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of in-

formation shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) Public benefit of service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and

(2) The research could not practicably be carried out without the waiver or alteration.

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.117 Documentation of informed consent.

(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

(b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by § 219.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A short form written consent document stating that the elements of informed consent required by § 219.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the

oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.118 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under § 219.101 (b) or (i), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the department or agency.

§ 219.119 Research undertaken without the intention of involving human subjects.

In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted, by the institution, to the department or agency, and final approval given to the proposed change by the department or agency.

§ 219.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

(a) The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency through such officers and employees of the department or agency and such experts and consultants as the department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

(b) On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

§ 219.122

§ 219.121 [Reserved]

§ 219.122 Use of Federal funds.

Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

§ 219.123 Early termination of research support: Evaluation of applications and proposals.

(a) The department or agency head may require that department or agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the department or agency head finds an institution has materially failed to comply with the terms of this policy.

(b) In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragarph (a) of this section and whether the applicant or the person or persons who would direct or has have directed the scientific and technical aspects of an activity has have, in the judgment of the department or agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to federal regulation).

§ 219.124 Conditions.

With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.

Mr. BRYANT. Dr. Cox.

STATEMENT OF JAMES D. COX, M.D., PROFESSOR OF RADIOTHERAPY, M.D. ANDERSON CANCER CENTER, AND CHAIRMAN, RADIOTHERAPY ONCOLOGY GROUP

Dr. COX. Mr. Chairman, I am James Cox, a physician involved in the treatment of patients with cancer and clinical research dealing with radiation oncology and other cancer treatments.

My remarks will center on cancer treatments in the 1960s, the use of total body irradiation in cancer treatment, including the Cincinnati project, the status of clinical trials for the treatment of cancer during the period in question, and the evolution of informed consent.

The treatment of patients who were found to have cancer in the 1960s was centered on the use of surgical removal or radiation therapy, which were the only known means to cure cancer. The drugs available to treat widespread cancer in patients at that time were minimally affected by current standards. Virtually all cancer treatments considered standard in the early 1960s had evolved without formal clinical trials.

Patients whose spread of cancer was beyond local regional tumors were considered incurable. The aim of treatment of such patients was to alleviate symptoms without any expectation of prolonging the patient's life.

Faced with the choices of doing nothing and administering local palliative treatments, or attempting experimental treatments, patients frequently wished to do something unproven rather than doing nothing.

Radiation therapy was known to produce predictable responses in most forms of cancer, and it was often curative—is often curative for Hodgkin's disease, cervical cancer, advanced cancer of the mouth, throat, et cetera. Its limitation was that it could be applied only to local or regionally advanced tumors. Total body irradiation had been used with some success in the treatment of patients with chronic leukemias and lymphomas.

It was reasonable to hypothesize that total body irradiation might have some benefit in widely disseminated cancer of other types. Enthusiasm for total body irradiation increased as the technology evolved to reinfuse bone marrow to overcome potentially lethal bone marrow depletion.

Published data from the University of Cincinnati indicate that the total body irradiation trials were undertaken to determine the tolerance and effectiveness of this treatment in several types of cancer. The total body irradiation doses differed range from 100 to 200 rads and were not considered in the range that would cause death. All but three patients had advanced cancer not considered curable by local regional treatments.

Total body irradiation was given as an adjunct to three children considered at extremely high risk to the threat of metastasis.

The study at the University of Cincinnati went under several levels of review by the National Institutes of Health, the editors of scientific journals. In addition, a special review, already alluded to, by Dr. Henry Kaplan of Stanford University, Frank Hendrickson in

Chicago, was requested by the American College of Radiology in response to an inquiry by Senator Mike Gravel in 1972.

Clinical trials which compared experimental treatments to standard treatments for patients with cancer were begun in the United States only in the mid-to-late 1950s. As these studies evolved, the concept of informed consent evolved. Formalization of informed consent by the National Institutes of Health was begun in the 1960s, and has continued to evolve to this day.

In a 1973 publication of the Cincinnati studies by Dr. Saenger and colleagues, a statement is included which says,

> All patients gave informed consent in accordance with the directives of the Faculty Research Committee of the University of Cincinnati College of Medicine and those of the National Institutes of Health. The use of formal, informed consent forms in this study antedated the above requirements by two years.

In conclusion, radiation therapy is an important part of the armamentarium of physicians in the care of patients with cancer. Because of its effectiveness in the treatment of local regional tumors, whole body irradiation has been the subject of research for decades. At present, total body irradiation followed by bone marrow transplantation is considered a standard part of the treatment of many patients with leukemia, lymphoma and Hodgkin's disease, and it is under investigation still for other diseases.

In the era prior to the establishment of bone marrow transplantation to support such treatment, lower, sublethal doses of total body irradiation were explored for patients with advanced cancers as a possible alternative to no treatment or to treatment with cytotoxic chemicals or hormones.

The University of Cincinnati's studies of total body irradiation conducted between 1960 and 1971 were based on a reasonable hypothesis were conducted and reported in the scientific literature in a manner consistent with other clinical investigations, and seem to have used the accepted standards of informed consent for that period.

One might judge them harshly from a perspective 20 years later, but they were reviewed and repeatedly approved by peers of the investigators at the time the studies were conducted.

Thank you.

Mr. BRYANT. Thank you.

[The prepared statement of Dr. Cox follows:]

SUBCOMMITTEE ON ADMINISTRATIVE LAW AND GOVERNMENTAL RELATIONS

COMMITTEE ON THE JUDICIARY

HOUSE OF REPRESENTATIVES

SUMMARY STATEMENT OF JAMES D. COX, M.D.

Radiation therapy is an important part of the armamentarium of physicians in the care of patients with cancer. Because of its effectiveness in the treatment of local-regional tumors, whole body irradiation has been a subject of research for decades. At present, total body irradiation followed by bone marrow transplantation is considered a standard part of treatment of many patients with leukemia, lymphoma, and Hodgkin's disease, and is under investigation for myeloma and cancer of the breast. In the era prior to the establishment of bone marrow transplantation to support such treatment, lower (sublethal) doses of total body irradiation were explored for patients with advanced cancer as a possible alternative to no treatment or treatment with cytotoxic chemicals or hormones. The University of Cincinnati studies of total body irradiation, conducted between 1960 and 1971 were based on a reasonable hypothesis, were conducted and reported in the scientific literature in keeping with clinical investigations of that period, and seem to have used the accepted standards of informed consent for that period. One might judge them harshly from a perspective 20 years later, but they were reviewed and repeatedly approved by peers of the investigators at the time the studies were conducted.

SUBCOMMITTEE ON ADMINISTRATIVE LAW AND GOVERNMENTAL RELATIONS
COMMITTEE ON THE JUDICIARY
HOUSE OF REPRESENTATIVES
BIOGRAPHY OF JAMES D. COX, M.D.

PRESENT TITLE & AFFILIATION:	Professor of Radiotherapy Hubert L. and Olive Stringer Chair in Oncology in Honor of Sue Gribble Stringer Coordinator, Interdisciplinary Program Development The University of Texas M.D. Anderson Cancer Center Houston, Texas 77030
BIRTH DATE & PLACE:	July 16, 1938; Steubenville, OH
OFFICE ADDRESS:	The University of Texas M.D. Anderson Cancer Center Interdisciplinary Program Development (Box 312) 1515 Holcombe Boulevard Houston, Texas 77030 (713) 792-2260
EDUCATION:	
Undergraduate:	1960, Kenyon College, Gambier, OH
Graduate:	1965, University of Rochester School of Medicine and Dentistry, Rochester, NY
POSTGRADUATE TRAINING:	
1963 - 1964:	Fellow: Clinical Oncology and Therapeutic Radiology, Penrose Cancer Hospital, Colorado Springs, CO
1965 - 1966:	Intern: (mixed with major in Medicine), University of Chicago, Chicago, IL
1966 - 1969:	Resident: Therapeutic Radiology, Penrose Cancer Hospital, Colorado Springs, CO
1969 - 1970:	Fellow: Therapeutic Radiology, Institute Gustave-Roussy, Villejuif, France

SPECIALTY BOARDS:

1966: Diplomate, National Board of Medical Examiners

1971: American Board of Radiology (Therapeutic Radiology)

MILITARY SERVICE:

1970 - 1972: Major, US Army, Walter Reed General Hospital, Washington, DC
Honorable Discharge

ACADEMIC & PROFESSIONAL APPOINTMENTS:

FACULTY:

1972 - 1974: Assistant Professor of Radiology
Georgetown University Hospital
Washington, DC

1974 - 1977: Associate Professor of Radiology
Medical College of Wisconsin

1977 - 1982: Professor of Radiology
Medical College of Wisconsin

1982 - 1985: Professor and Chairman
Department of Radiation Oncology
Medical College of Wisconsin

1985 - 1988: Professor and Chairman
Department of Radiation Oncology
Columbia University College of Physicians and Surgeons

1988 - 1992: Professor of Radiotherapy; Vice President for Patient Care and Physician-in-Chief, The University of Texas M.D. Anderson Cancer Center

1992 - : Professor of Radiotherapy; Coordinator, Interdisciplinary Program Development, The University of Texas M.D. Anderson Cancer Center

LOCAL:

Texas Radiation Advisory Board

1992 -Present: Member

NATIONAL:

National Cancer Institute (NCI)

1972 - 1974: Visiting Physician, Medicine Branch

1983 - 1987: Cancer Research Manpower Review Committee, Division of Extramural Activities

1987 - 1991:	Board of Scientific Counselors Division of Cancer Treatment
1987 - Present:	Committee of Clinical Trials Cooperative Group Chairs
1990 - 1993:	Chairman, Committee of Clinical Trials Cooperative Group Chairs
	American Society for Therapeutic Radiology and Oncology (ASTRO)
1985 - 1986:	President
1986 - 1987:	Chairman, Board of Directors
	American College of Radiology (ACR)
1981 - 1987:	Chairman, Committee of Radiotherapeutic Research and Development
1981 - 1987:	Steering Committee of the Council
1987 - 1993:	Chancellor
1987 - 1993:	Chairman, Commission on Radiation Oncology
	Radiation Therapy Oncology Group (RTOG)
1981 - 1987:	Vice Chairman for Research Strategies
1987 -Present:	Chairman, RTOG
	American Board of Radiology (ABR)
1979 - 1989:	Subcommittee for Written Examination in Radiation Oncology
1981 -Present:	Examiner, Oral Examination in Radiation Oncology
	Veterans Administration Lung Group (VALG)
1974 - 1979:	Chairman, Radiotherapy Committee Executive Committee
	Council of Radiation Oncology Committee Chairpersons (CROCC)
1978 - 1980:	Member

EDITORIAL BOARDS:

1981 -Present:	Editorial Consultant: AMERICAN JOURNAL OF CLINICAL ONCOLOGY CANCER CHEST INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY, BIOLOGY, PHYSICS JOURNAL OF CLINICAL ONCOLOGY NEW ENGLAND JOURNAL OF MEDICINE

1985 -Present:	Editor, INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY, BIOLOGY, PHYSICS
1990 -Present:	Site Editor for Rapid Communications Section, INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY, BIOLOGY, PHYSICS
1990 - Present:	Editorial Board, LUNG CANCER

HONORS & AWARDS:

1960:	AB: Magna Cum Laude, Phi Beta Kappa
1965:	MD: With Honor
1983:	Fellow of the American College of Radiology (FACR)
1984:	Robert Fowler Fellow of the Anti-Cancer Council of Victoria, Australia
1985:	President: American Society for Therapeutic Radiology and Oncology (ASTRO)
1986:	Sixth Isadore Lampe Lecture University of Michigan
1987:	International Guest Lecturer, 30th Anniversary, Department of Radiology, Hiroshima University Medical School
1988:	Honorary Member, Belgian Association for Radiation-Oncology
1989:	W. G. Cosbie Lecture, Royal College of Physicians and Surgeons of Canada
1992:	Gillies Memorial Lecture, The University of Iowa
1992:	William Caldwell Memorial Lecture, The University of Wisconsin
1992:	Hubert L. and Olive Stringer Chair in Oncology in Honor of Sue Gribble Stringer
1993:	Annual Oration in Radiation Oncology, Radiological Society of North America
1994:	Invited Lecturer, 7th International Symposium of the Foundation for Cancer Research.

In addition, Dr. Cox is the author of 212 peer-reviewed journal articles, book chapters, and books. Copies of the bibliography are available upon request.

SUBCOMMITTEE ON ADMINISTRATIVE LAW AND GOVERNMENTAL RELATIONS

COMMITTEE ON THE JUDICIARY

HOUSE OF REPRESENTATIVES

PREPARED STATEMENT OF JAMES D. COX, M.D.

The following comments are submitted at the request of Congressman Jack Brooks, Chair, House of Representatives Committee on the Judiciary. They pertain to hearings on radiation experiments performed by the University of Cincinnati Medical School. My formal remarks will center on:

1) Cancer treatment in the 1960's;

2) The use of total body irradiation in cancer treatment, including the Cincinnati project;

3) The status of clinical trials for the treatment of cancer during the period in question and the evolution of informed consent.

Status of Cancer Treatment During the 1960's

The treatment of patients who were found to have cancer in the 1960's was largely centered on the use of surgical removal or radiation therapy. Such treatments were the only known means to cure cancer. Hormonal therapy and systemic cytotoxic chemotherapy were undergoing investigation: with rare exception, such systemic treatments were used with palliative

intent or to retard progression of uniformly fatal diseases. The drugs available to treat widespread cancer in patients in the 1960's were minimally effective by current standards. Cancer of the bronchus or the colon infrequently responded to the available drugs, and breast cancer was only slightly more responsive.

Virtually all standard cancer treatment in the 1960's evolved by clinical applications of best known therapies without formal clinical trials. Standard surgical procedures for cancer such as radical mastectomy, laryngectomy, resections of the large bowel, stomach and esophagus had not been tested in formal clinical trials. Similarly, radiation therapy considered standard, such as that for cervical cancer, had not been studied in clinical trials, but had proven to be curative over several decades.

Patients whose tumors had spread beyond local-regional means of treatment (surgery and radiation therapy) were considered incurable. The aim of treatment of such patients was to alleviate symptoms such as pain, bleeding and obstruction of natural passages. Such palliative treatments were not undertaken with an expectation of prolonging the patient's life. Faced with the choices of doing nothing, administering local palliative treatment, or attempting highly experimental unproven treatments, the patient would frequently express a desire to do something unproven rather than doing nothing.

Total Body Irradiation in Cancer Treatment

The responsiveness of tumors to ionizing radiations demonstrated soon after the discovery of x-rays by Roentgen in 1895 resulted in a steady increase in the use of such treatments. By the early 1950's, high-energy photons became available for cancer treatment with Cobalt 60 teletherapy units, betatrons, and linear accelerators, and the use of radiation therapy expanded rapidly.

Radiation therapy was known to produce predictable responses in most forms of cancer and was often curative for Hodgkin's disease, cervical cancer, advanced cancer of the mouth, pharynx (throat) and larynx (voice box), etc. Its limitation was that it could be applied only to local or regionally advanced tumors. Total body irradiation had been used with some success in the treatment of patients with strikingly radioresponsive diseases such as chronic and acute leukemias and lymphomas. It was reasonable to hypothesize that total body irradiation might have some benefit in widely disseminated cancer.

Even greater enthusiasm for total body irradiation as a component of cancer treatment developed as the technology to remove, store and reinfuse bone marrow to overcome the potentially lethal effects of high-dose systemic treatment was explored. E. Donnall Thomas, M.D., of the University of Washington, was awarded the Nobel Prize in Physiology and Medicine in 1990 for pioneering treatments which included total body irradiation with doses so high as to

be lethal were it not for bone marrow transplantation.

Published data from the University of Cincinnati indicate that the total body irradiation trials were undertaken as phase I (to determine maximum tolerated dose) and phase II (to determine anti-tumor effect with specific diseases). The total body irradiation doses delivered ranged from 100 to 200 rads and were carefully calculated and measured. The trials involved three major forms of cancer--carcinoma of the colon, bronchus and breast. All but three patients had advanced cancer not curable by local-regional treatments. Total body irradiation was given as an adjuvant to local irradiation for three children with Ewing's sarcoma of the bone (considered at extremely high risk for the presence of distant metastasis). The treatment team consisted of radiation oncologists, two specialists in internal medicine and a medical physicist.

The University of Cincinnati project underwent several levels of peer review. In addition to concurrence with the protocol by the participating members of the team, the studies were reviewed by the Faculty Research Committee of the University of Cincinnati College of Medicine. They also underwent review by the National Institutes of Health, editors of scientific journals, and a special review by Drs. Henry Kaplan of Stanford University, Frank Hendrickson of Chicago's Presbyterian St. Luke's Hospital, and Samuel Taylor, III, of the Presbyterian St. Luke's Hospital at the request of Robert W. McConnell, President, American College of Radiology, in response to a request by Senator Mike Gravel in 1972.

Cancer Clinical Trials and Informed Consent

The history of medicine is filled with clinical experiments undertaken with the intent to benefit individual patients or all mankind. Clinical trials which compared experimental treatments to standard treatments for patients with cancer were begun in England in the 1940's and in the mid to late 1950's in the United States. Seventeen clinical cooperative groups were established in 1956 with funding from the National Cancer Institute. The conceptual framework leading from phase I (toxicity) to phase II (efficacy) to phase III (comparisons with standard treatment) was first formalized in the early 1960's at the National Cancer Institute.

As studies in these cancer clinical cooperative groups evolved, the concept of informed consent evolved. Prior to 1965, patients enrolled in clinical trials were obviously asked to consent and such consent was usually documented in the medical record; formalization of this process began in the 1960's and has continued to evolve to the present time. Current standards include a description to the patient of the experimental treatment offered, specifics risks that such treatment might entail, statements to the effect that all risks are not fully understood and unexpected effects might occur, the possible benefits to the patients and society as a whole, and the express willingness of the physicians to treat the patient outside the protocol with the best standard treatments if the patient declines participation. It is now customary to provide the patient written information (usually two or three pages long); to let the patient keep a copy of this information

so he or she may discuss it with family or friends; and, after opportunities for questions, to ask the patient to sign a consent form. The patient always has the right to withdraw from investigational treatment at any time, and to receive the best standard care.

In a 1973 publication of the Cincinnati studies by Eugene L. Sanger, et al ("Whole Body and Partial Body Radiotherapy of Advanced Cancer", American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine. Vol 117; 670-685), the following statement is included: ***All patients gave informed consent in accordance with the directives of the Faculty Research Committee of the University of Cincinnati College of Medicine and those of the National Institutes of Health. The use of formal, informed consent forms in this study antedated the above requirements by two years.***

Summary

Radiation therapy is an important part of the armamentarium of physicians in the care of patients with cancer. Because of its effectiveness in the treatment of local-regional tumors, whole body irradiation has been a subject of research for decades. At present, total body irradiation followed by bone marrow transplantation is considered a standard part of treatment of many patients with leukemia, lymphoma, and Hodgkin's disease, and is under investigation for myeloma and cancer of the breast. In the era prior to the establishment of bone marrow transplantation to support such treatment, lower (sublethal) doses of total body irradiation were

Mr. BRYANT. Mr. Steger.

STATEMENT OF JOSEPH STEGER, PRESIDENT, UNIVERSITY OF CINCINNATI, ACCOMPANIED BY STANLEY M. CHESLEY

Mr. STEGER. Thank you, Mr. Chairman and members of the committee. I am Joseph A. Steger, president, University of Cincinnati. Stan Chesley has joined the University as an adviser, not really assistant, and he is former chairman of our board, and more than willing to help in this instance.

I appreciate the opportunity to have a chance to present the actions taken by the University of Cincinnati relative to the whole body radiation studies conducted at the then General Hospital some 20 to 30 years ago.

There have been some seven independent investigations of these studies mostly 20 to 30 years ago, when the current University was asked by the press and the families to supply documents or records, we began voluntarily to compile immediately all of the records we had relative to the study. It was a very complicated task. The records were not in one place. The records were in written forms, some were written, some were microfiche. And much of it, in order to copy it, we had to send to the State of Washington, to a special company that then took the microfiche and turned it into printed documents.

Although we did this, we still had in our archives or we found some 11,233 pages of documents—all of which we have made public. We have made them public in terms of the press, in terms of inquiries, in terms of Government officials; and we will continue to make anything we find public.

The patient records, however, we have not made public. They are being, however, given to the families. I apologize if it has taken a long time. Most of them are on microfiche, and it took us several months to get the microfiche into print.

With the help of Senator Glenn and Congressman Mann, we secured the original DOD contract, which we did not have.

At the same time that we were undertaking to locate and reproduce documents, we began—again, voluntarily—to search for the patients' families, some 88 families. As of this date, we have located 38 surviving relatives, and we are still trying to locate 50 other patients' close relatives. We will continue to do so until we have exhausted different search techniques to find these families.

We have also established a hot line so that people could check to see if they or a relative had participated in the studies. We have handled over 2,857 calls and cross-checks with the records to ascertain if any of the inquirers or their relatives had been in the study. Obviously, few had.

We also feel a societal obligation to the surviving relatives. Although we are no longer the same entity under which the studies were conducted, we have offered social work support and/or pastoral counseling, should the families wish.

As a public entity, we shall continue to cooperate in any way we can to provide information, should we uncover any additional documents. At this time, we are fairly certain, in the sense of 90 to 100 percent, that we do not have any other documents that have not been reported, because we have contacted the departments in the

studies, we have gone through all our archives, we have contacted every individual associated with the studies, and as far as we are concerned, we cannot find any other documents.

Thank you for allowing my testimony. I shall be glad to answer any of your questions. We will continue to cooperate in any way we can.

Mr. BRYANT. Thank you.

[The prepared statement of Mr. Steger follows:]

TESTIMONY

COMMITTEE ON JUDICIARY

SUBCOMMITTEE ON ADMINISTRATIVE

LAW AND GOVERNMENTAL RELATIONS

APRIL 11, 1994

MR. CHAIR, MEMBERS OF THE COMMITTEE, I AM JOSEPH A. STEGER, PRESIDENT, UNIVERSITY OF CINCINNATI.

I APPRECIATE THE OPPORTUNITY TO HAVE A CHANCE TO PRESENT THE ACTIONS TAKEN BY THE UNIVERSITY OF CINCINNATI RELATIVE TO THE WHOLE BODY RADIOTHERAPY STUDIES CONDUCTED, AT THE THEN GENERAL HOSPITAL, SOME TWENTY TO THIRTY YEARS AGO.

THERE HAVING BEEN SOME SEVEN INDEPENDENT INVESTIGATIONS OF THESE STUDIES MOSTLY 20 TO 30

YEARS AGO, WHEN THE CURRENT UNIVERSITY WAS ASKED BY THE PRESS AND THE FAMILIES TO SUPPLY DOCUMENTS OR RECORDS, WE BEGAN TO COMPILE IMMEDIATELY ALL THE RECORDS WE HAD RELATIVE TO THE STUDY. MUCH TO OUR SURPRISE, ALTHOUGH IT WAS A COMPLICATED TASK, WE STILL HAD IN OUR ARCHIVES OR WE FOUND SOME 8,200 PAGE OF DOCUMENTS--ALL OF WHICH WE HAVE MADE PUBLIC. AND WITH THE HELP OF SENATOR GLENN AND CONGRESSMAN MANN, WE SECURED THE ORIGINAL D.O.D. CONTRACT.

AT THE SAME TIME THAT WE WERE UNDERTAKING TO LOCATE AND REPRODUCE DOCUMENTS, WE BEGAN A SEARCH FOR THE PATIENTS' FAMILIES (SOME 88 FAMILIES). AS OF THIS DATE, WE HAVE LOCATED 38 SURVIVING RELATIVES AND WE ARE STILL TRYING TO LOCATE 50 OTHER PATIENTS' CLOSE RELATIVES.

WE ALSO ESTABLISHED A HOT LINE SO THAT PEOPLE COULD CHECK TO SEE IF THEY OR A RELATIVE HAD PARTICIPATED IN THE STUDIES. WE HAVE HANDLED OVER

1,000 CALLS AND CROSS CHECKS TO ASCERTAIN BY PATIENT RECORDS (OF THESE 1,000 SOME CALLS) IF ANY OF THE INQUIRERS OR THEIR RELATIVES HAD BEEN IN THE STUDY--OBVIOUSLY FEW HAD.

WE ALSO FEEL A SOCIETAL OBLIGATION TO THE SURVIVING RELATIVES. ALTHOUGH WE ARE NO LONGER THE SAME ENTITY UNDER WHICH THE STUDIES WERE CONDUCTED, WE HAVE OFFERED SOCIAL WORK SUPPORT AND/OR PASTORAL COUNSELING SHOULD THEY WISH.

WE AS A PUBLIC ENTITY SHALL CONTINUE TO COOPERATE IN ANY WAY WE CAN TO PROVIDE INFORMATION SHOULD WE UNCOVER ANY ADDITIONAL DOCUMENTS. AT THIS TIME, WE ARE 90% CERTAIN THAT WE DO NOT HAVE ANY OTHER DOCUMENTS THAT HAVE NOT BEEN REPORTED.

THANK YOU FOR ALLOWING MY TESTIMONY. I SHALL BE GLAD TO ANSWER ANY OF YOUR QUESTIONS.

Mr. BRYANT. Dr. Soper, in your written statement, you said one of the reasons the Department was interested in the experiments was to understand the influence of radiation on combat effectiveness. Why couldn't the Department fund an experiment using its own healthy servicemen as opposed to innocent civilian cancer patients that were used in these studies?

Dr. SOPER. I can't, Mr. Bryant, give you a direct answer to that. I know that in developing the types of criteria for battle, whether it is on a conventional, a chemical, or a nuclear battlefield, information is gathered from many sources—from animal studies, for example, and I think, also from studies with people in uniform and civilian members of the Department of Defense.

This information that we obtained from the University of Cincinnati, sir, was one part from many different sources. We put together those manuals that perhaps are offensive to some, but those manuals are required by the commander on a nuclear battlefield to fight in a hostile environment. Like it or not, that is the business I am in; and I am doing that the best that I can. All the members of the Department of Defense are.

Mr. BRYANT. Did the Department of Defense carry out any such experiment on healthy servicemen?

Dr. SOPER. I will have to answer that, for the record, I don't know of any.

[The information follows:]

Our record search is still ongoing, but to date we have not discovered any such experiments.

Dr. SOPER. Let me say, I do know of other experiments besides the Cincinnati experiments that were done, reported in the literature, having to do with total body irradiation, as Dr. Cox pointed out—that contributed to our overall data base. But, I do not know the answer to your specific question.

Mr. BRYANT. If the Department received a proposal for such an experiment on healthy servicemen, would it have been funded?

Dr. SOPER. There are a series of protocols through which funding for human-use experiments must pass. The rules for that in the Department of Defense started as early as 1953, with a then top secret memorandum from Secretary of Defense Charles Wilson to the Secretaries of the military services, which outlined in some specific detail the rules for human-use experimentation of healthy soldiers and civilian members.

Mr. BRYANT. The Department did not pay $651,000 up front for the experiments. Rather, it paid $25,000 for the initial contract, and then increased the amount for close to 10 years as the contract was renewed and modified?

Dr. SOPER. Yes, sir.

Mr. BRYANT. Before approving the contract or its modifications, did the Department of Defense officials inquire as to the potential harm being caused to patients being administered such high doses of radiation?

Dr. SOPER. I don't know the answer to that. The available surviving records do not show any such inquiry. I have a few of the documents, I think you have them as well, that have survived, these many years; and the approval process in the Department of De-

fense is, as far as that documentation is concerned, rather superficial.

Let me be more specific. I have been able to find nothing in the records of specific questions sent back to the University of Cincinnati with regard to informed consent or patient selection criteria. It was our purpose to use the information from the psychological and psychiatric tests and blood and urine tests.

Mr. BRYANT. Did the project officer monitor the effect on patients as part of his responsibilities?

Dr. SOPER. There is no indication that the project officer, what we call the contracting officer's representative, (COR) did so. As a matter of fact, some of the records suggest that the University commented on the fact that they had total scientific freedom with respect to their work.

Now, I was a contracting officer's representative at the Defense Nuclear Agency for much of my career, sir, and I was responsible for and expected to do exactly that, be a contracting officer's representative, ask the technical questions and ensure that the American taxpayer was getting what he paid for.

That is not to say that it wasn't done, there is just nothing in the record. If you are interested, we have made repeated attempts at locating a nondestroyed file. As I said, as part of the normal contract destruction process that occurs by law 6½ years after the contract is terminated, the file is destroyed. We have called people that we have known, we have tried to locate somewhere in someone's desk drawer a contracting officer's representative (COR) file that would give us some indication of that.

Now, there is no indication either that there was or there wasn't influence by the contracting officer's representative.

Mr. BRYANT. Are any of the project officers alive? Isn't anybody around that was involved?

Dr. SOPER. The gentleman at the Defense Nuclear Agency, the senior official, is dead. At least two of the people whose names appear on the forms about which I just spoke have died. I spoke with another gentleman on the telephone the other day in preparation for this hearing, and his recollection of involvement was of no help.

The contracting officer at the Defense Nuclear Agency, while still living, is medically impaired and is not able to contribute. So we have tried.

Mr. BRYANT. My time has expired.

Mr. Mann.

Mr. MANN. Thank you, Mr. Chairman. I want to pursue first the line that is similar to what Mr. Bryant has been pursuing. I read with some care the original proposal by Dr. Saenger, the original contract, the periodic reports that were sent to the Department of Defense; and nowhere can I find any evidence that anybody at the Pentagon or with the Government had the least bit of concern about where the patients were coming from, what the consequences to them might be of the administration of whole body irradiation that was being reported from the Pentagon perspective at great length and great detail insofar as the various parameters that were being used in the study.

I mean, didn't somebody at some point ask at least in their own mind, I wonder who these people are and what else is happening to them?

Dr. SOPER. Congressman Mann, I agree with what you are saying. There is nothing in the file that has remained that suggests that that was done. That is not to say it wasn't. But I can find nothing, either.

Mr. MANN. You make the point in the attachment to your statement that the title of the report was changed in 1968, whereas previously the report had talked totally about metabolic changes, now we are talking also about therapeutic efforts.

Do you have any knowledge of the reason for that title change?

Dr. SOPER. No, I do not. I do note it, however.

Mr. MANN. To your knowledge, were whole body radiation experiments of the kind that the Pentagon paid for conducted at the University of Cincinnati either before or after the period of the contract with the Pentagon?

Dr. SOPER. There is reference in the file to experiments at the Sloan-Kettering Cancer Research Institute at the University of Baylor School of Medicine, and at the M.D. Anderson Clinic, I believe. There are those references in the file of related whole body irradiation experiments as contributory to Department of Defense needs.

And after that, I do not know of any. Perhaps we can call Captain Bumgarner in a moment.

Mr. MANN. Did any of that work involve Dr. Saenger or any of his personnel?

Dr. SOPER. No, I don't think the work at Sloan-Kettering or at M.D. Anderson did. Dr. Saenger's work is referenced, along with others, in military documents that relate to military radiobiology.

Mr. MANN. Can you tell us how often in the 1950s an unsolicited proposal such as Dr. Saenger's would have come to the Pentagon?

Dr. SOPER. I don't know, but I will give you my experience beginning at the Defense Nuclear Agency in 1972, primarily a research and development organization funded by 6.2 money, if that means anything—it was primarily research and development funds. A significant portion—that is, better than 10 percent of the work that was done in the early 1970s when I was there—was done as a result of unsolicited proposals.

The Department came under criticism by Members of Congress and others that there was an indication that these weren't unsolicited, perhaps they were solicited unsolicited proposals. So it normally happened that the contracting requirements were tightened up.

There is no indication, sir, that this was a solicited unsolicited proposal.

Mr. MANN. Are you aware of any other studies similar in the overall purpose or scope to the one that we are looking at today, that was funded by the Department of Defense at any time?

Dr. SOPER. Yes, I believe mention is made of the work at Sloan-Kettering and M.D. Anderson. I have information on that. I will provide that for the record.

[The information follows:]

We have identified several studies supported by the Department of Defense in which radiation effects on humans were studied.

In our records there are three reports that cover research conducted at Sloan-Kettering Institute for Cancer Research in New York during the 1950's and early 1960's. The work at Sloan-Kettering exposed patients with widespread cancer to low-level doses of total body irradiation to study post-irradiation syndrome in humans and to evaluate the effects on the modification of tumor response.

In the early to mid-1950's research at M.D. Anderson Hospital in Houston, Texas evaluated the systemic and clinical effects induced in 263 cancer patients by whole body x-irradiation with nominal air doses of 15r to 200r. Another study was conducted at the Baylor University College of Medicine, also in Houston, from 1954 to 1964. This research studied the effect of total body irradiation on the immunologic tolerance of bone marrow and homografts of other living tissue. A third study in Texas during the same general time period (1956 to 1962) was conducted by the University of Texas to study the effects of total body irradiation and local irradiation on the metabolism of the hematopoietic system in humans.

Another study we have identified was conducted from 1960 until 1963 at the University of Southern California. The research was conducted to observe the effect in humans of 250-300r of total body irradiation. Also, from 1972 to 1976 at the Armed Forces Radiobiology Research Institute, leukemia patients were treated with total-body irradiation to ablate their bone marrow so that a bone marrow transplant could be done to cure their leukemia.

I want to reiterate that this is current information and that our record search continues.

Mr. MANN. Those were DOD-funded?

Dr. SOPER. Yes, they were. In fact, supported by the Defense Atomic Support Agency.

Mr. MANN. For the same question, developing a biological indicator to indicate——

Dr. SOPER. Yes.

Mr. MANN. Let me get the timing. That was before or after or during the UC—1960 to 1971?

Dr. SOPER. I have a report here on the work at Baylor University College of Medicine. It is the final report for February 1, 1963, to January 31, 1964, entitled "The Effect of Total Body Irradiation on Immunologic Tolerance of Bone Marrow and Homographs of Other Living Tissue, Tables and Charts Therein."

I also have a paper by M.D. Anderson Hospital Tumor Institute, entitled "Systemic and Clinical Effects Induced in 263 Cancer Patients by Whole Body Irradiation with Nominal Air Doses of 15 to 200 Rads."

Mr. MANN. What hospital did you say it was? What institution did you say it was?

Dr. SOPER. Radiology Department, University of Texas, M.D. Anderson Hospital Tumor Institute, TX. This was done for the Department of Radiology, School of Aviation Medicine, U.S. Air Force.

As part of the record, I have, and I think I gave it to you or at least I hope I did, a memorandum of November 12, 1958, from Lt. Col. Arthur Sullivan, Assistant Chief of Biophysics and Astronautics. The Saenger proposal has received favorable comment from Colonel Maupin, Colonel Isherwood, Colonel Hutgerhang, I think he died, and Colonel Cox. In the opinion of the undersigned, the work being done by Dr. Collins at Baylor and the Sloan-Kettering Institute, who are working with humans——

Mr. MANN. I know Sullivan's name. I don't think I have that particular document. I would like to have it. I guess, expanding on Mr. Bryant's question, would any of those five people be alive and be able to offer information to us?

Dr. SOPER. We are trying to track those people down. I think Dr. Sullivan, we found, died a month or so ago. But we are still trying to track those people down, sir.

Mr. MANN. Finally, Dr. Soper, you mentioned there was a 1953 top secret document that set forth specific standards for informed consent. Is that something you can now—I assume that is not still classified.

Dr. SOPER. It is not. It was unclassified in 1975 or 1979.

Mr. MANN. Have you had the occasion to ponder whether the informed consent procedures that were used in this particular project meet the standards in that memorandum?

Dr. SOPER. Good question. I have it here, and I will search for it if you don't have it, the memorandum from the Secretary of Defense, Mr. Charles Wilson, in 1953, was specifically for human use of military people, in uniform, and Department of Defense civilian workers, and it did not speak to the issue of contracted studies like the work here at the University of Cincinnati.

Mr. MANN. Could you give us a flavor of what information would be given to a member in uniform, the serviceman, before an experiment?

Dr. SOPER. Yes, if I can find it.

Mr. MANN. OK.

Dr. SOPER. The copy I have here is dated February 26, 1953; it was declassified, I can't read when it was, 1975; and it speaks to a number of criteria. The voluntary consent of the human subject is absolutely essential, and it gives three very specific subparagraphs with respect to the criteria for voluntary consent.

The experiment, that was number A, B, the experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature. C, the number of volunteers used shall be kept to a minimum.

I will go through the others if you wish.

Mr. MANN. If you could, give us a copy of that for the record.

Dr. SOPER. Of course.

[The information follows:]

C O P Y

SECRETARY OF DEFENSE
Washington

26 Feb 1953

MEMORANDUM FOR THE SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE

SUBJECT: Use of Human Volunteers in Experimental Research

1. Based upon a recommendation of the Armed Forces Medical Policy Council, that human subjects be employed, under recognized safeguards, as the only feasible means for realistic evaluation and/or development of effective preventive measures of defense against atomic, biological or chemical agents, the policy set forth below will govern the use of human volunteers by the Department of Defense in experimental research in the fields of atomic, biological and/or chemical warfare.

2. By reason of the basic medical responsibility in connection with the development of defense of all types against atomic, biological and/or chemical warfare agents, Armed Services personnel and/or civilians on duty at installations engaged in such research shall be permitted to actively participate in all phases of the program, such participation shall be subject to the following conditions:

a. The voluntary consent of the human subject is absolutely essential.

(1) This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by

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which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

(2) The concept of the human subject shall be in writing, his signature shall be affixed to a written instument setting forth substantially the aforementioned requirements and shall be signed in the presence of at least one witness who shall attest to such signature in writing.

(a) In experiments where personnel from more than one Service are involved the Secretary of the Service which is exercising primary responsibility for conducting the experiment is designated to prepare such an instrument and coordinate it for use by all the Services having human volunteers involved in the experiment.

(3) The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

b. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

c. The number of volunteers used shall be kept at a minimum consistent with item b., above.

d. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

e. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

f. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur.

g. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

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h. Proper preparation should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

i. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

j. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

k. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

1. The established policy, which prohibits the use of prisoners of war in human experimentation, is continued and they will not be used under any circumstances.

3. The Secretaries of the Army, Navy and Air Force are authorized to conduct experiments in connection with the development of defenses of all types against atomic, biological and/or chemical warfare agents involving the use of human subjects within the limits prescribed above.

4. In each instance in which an experiment is proposed pursuant to this memorandum, the nature and purpose of the proposed experiment and the name of the person who will be in charge of such experiment shall be submitted for approval to the Secretary of the military department in which the proposed experiment is to be conducted. No such experiment shall be undertaken until such Secretary has approved in writing the experiment proposed, the person who will be in charge of conducting it, as well as informing the Secretary of Defense.

5. The addresses will be responsible for insuring compliance with the provisions of this memorandum within their respective Services.

/signed/
C.E. WILSON

Copies furnished:
Joint Chiefs of Staff
Research and Development Board

Mr. MANN. Finally, in this round, Dr. Soper, there came a point in time when, as I understand it—maybe we will have more detail later—the project at UC had multiple funding sources in terms of the dollars that were necessary to treat the patients. At some point in the 1960s, before the project ended, NIH, at least for a period, declined to offer funding based on some moral issues, that is somebody else's characterization.

Was the Pentagon aware of that refusal by NIH at the time?

Dr. SOPER. At the time, the records don't show that they were or they weren't. I am in contact with HHS. Part of the interagency working group has allowed senior members of each one of the Departments to meet together on a very regular basis and talk seriously about these issues, and the senior official at HHS is researching that for us. I hope to have an answer to that question.

Mr. MANN. Mr. Chairman, I have other questions, but I will wait to the second round.

Mr. BRYANT. Mr. Portman.

Mr. PORTMAN. Thanks, Mr. Chairman.

Dr. Soper, thank you for the help you have provided me and my staff over the last couple of months. I know our dialogue will continue.

Dr. SOPER. I hope so.

Mr. PORTMAN. I really want to echo some of the concerns the chairman raised in terms of the efforts you are making to contact people who were directly involved at the time. It sounds as though you have made some efforts, and we have talked about that. I would just hope that we would redouble those efforts now, to try to find out as much as we can about what the DOD role was, how much oversight there might have been or not have been. The records, as you indicate, are very sparse in that regard.

That is an issue that I know this subcommittee, as well as the Congress as a whole, is intensely interested in.

With regard to documentation between the Cincinnati General Hospital and DOD, let me ask you, was there any evidence, particularly in the documents from the earlier years, that the radiation proposed to be administered to patients was expressly designed to treat cancer?

Dr. SOPER. Quite to the contrary. I think the information that you see in the early documentation—the first reports, I have their numbers—clearly does not state treatment of cancer as a part of the reports. As I said early, those earlier reports, for those of us who are looking at them for the first time, are certainly troubling.

And, as I have talked about this issue with medical ethicists in the Department of Defense and other places—my younger brother is a radiologist and I have talked with him about this—is open for interpretation.

It is one element that I hope the advisory committee, that is made up of ethicists and radiologists like those that are here at the table today, will look at and come to a view on. Perhaps it was just a badly written report. I can't judge; I am not qualified to judge that.

Mr. PORTMAN. Getting back to the documents for a moment, how about the 1958 proposal from the University to the DOD with regard to this issue?

Dr. SOPER. There is certainly an early indication that we have an appraisal of human studies and the radiobiological aspects of weapon effects. The word weapon appears. The report was written by Dr. Saenger and Dr. Friedman. It was prepared for the Defense Atomic Support Agency.

The date I have here is November 14, 1962, and this is an appraisal, I presume at that time, of the work that is being performed by the Department of Defense. They talk about the adequacy or the inadequacy of animal data. And it says,

> Nevertheless it is essential to consider further well-planned studies in patients as long as the following criteria are fulfilled: There is a reasonable chance of therapeutic benefit to the patient; the likelihood of damage to the patient is no greater than that encountered from comparable therapy of another type; and 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.

So this, Mr. Portman, is in 1962, written word from a Department of Defense-supported document written with Department of Defense funds, that speaks to the therapeutic issue associated with these experiments. It is the earliest one that I can find on the record.

Mr. PORTMAN. This is not directly related to the then General Hospital situation? This was a general document with regard to DOD-funded projects?

Dr. SOPER. Oh, no. This was supported by DOD. This was work, an appraisal of the work, that they were performing, prepared for the Defense Atomic Support Agency under contract; and the number of the contract was one of the three contracts that the Department of Defense had with the University of Cincinnati.

Mr. PORTMAN. You mentioned earlier that you were a contracting officer's representative yourself in a previous life?

Dr. SOPER. Yes, sir. I would like to go back.

Mr. PORTMAN. It is too late.

Dr. SOPER. Yes, you are right.

Mr. PORTMAN. I would like to ask you a general question, and that is, should there have been more oversight, from what you have been led to believe, from the discussions with people and from the documents?

Dr. SOPER. Absolutely. It is the responsibility of the contracting officer's representative. You don't raise your hand and swear to that, but one of the tenets of doing a good job at the Defense Nuclear Agency, or the Defense Information Systems Agency, or the CIA, or any agency in representing taxpayers' money is to be an informed buyer. I took courses early on in my career that told me how to be a good COR, what to ask for, and what to expect in response.

Mr. PORTMAN. Let me ask you then a follow-up question. This is something that I found very unusual in looking through the documents.

Should there not have been a DOD report at the conclusion of this study? Should there not have been a DOD report at the conclusion of the study in 1971?

Dr. SOPER. Let me ask for clarification. Do you mean when the contract was terminated, a report by the Department of Defense

saying, we, the Department of Defense, spent $650,000 of your money, this is what we got for it A, B, C?

Mr. PORTMAN. Exactly. I am not aware of the existence of any such report.

Dr. SOPER. I am not either. The information we paid for appears throughout radiobiology and military medical radiobiology literature. So it was used extensively in preparing documents like I have before me regarding military radiobiology, et cetera.

Mr. PORTMAN. Do you find it unusual that there was not a report at the end of the study?

Dr. SOPER. It is a good question. I am now trying to think in my career, whether or not each contract that ended, ended with a report, and the DOD provided a report on this as to what we got or didn't get. I am not sure that wouldn't have been the norm. I think that would not have been the norm.

Mr. PORTMAN. Not have been the norm?

Dr. SOPER. No, sir.

Mr. PORTMAN. One final question, Mr. Chairman, and that is simply, are there any documents out there of which you are aware, classified or unclassified, that DOD has not yet disclosed?

Dr. SOPER. Oh, let——

Mr. PORTMAN. Of which you are aware.

Dr. SOPER. There are no documents of which I am aware, classified or unclassified, that aren't going to be a part, that are not, or will be a part of the record retrieval process and the documents that we submit to the advisory committee for their review. The advisory committee, by the way, is meeting for the first time on April 21 and 22. I am expected to brief them on the results of the DOD record retrieval process, I believe this will be a major element.

Mr. PORTMAN. One follow-up, then, to that. Are you saying then that the working group or the advisory committee to the working group may receive documents that this subcommittee does not receive, or the public does not receive?

Dr. SOPER. No. No.

Mr. PORTMAN. When you say——

Dr. SOPER. What I am saying is that the process through which we are going, this interagency working group, is open. It has been advertised as intensive and providing a view into the cold war experimentation, good or bad, sir, we will provide to you, as well as to the advisory committee, the records that we find.

Mr. PORTMAN. Thank you.

Mr. BRYANT. Dr. Soper, I think it is important to pursue this question about the NIH. Apparently, the National Institutes of Health was asked to fund experiments, and they refused to do so because of the moral concerns; at least that is what the indications are.

Was it your testimony that the Department of Defense did not know about that refusal?

Dr. SOPER. I do not know the answer, specifically. I think we did not, but if I can leave it at that, I think we did not—and I am researching that—I will supply that answer for the record.

[The information follows:]

The University of Cincinnati Ad Hoc Committee Report of January 1972 noted that a proposal entitled Protection of Humans with Stored Autologous Marrow was

submitted to NIH in 1966 or 1967 by Dr. Ben Friedman, one of Dr. Saenger's research colleagues. The report further noted that the application was not approved and that reason for this decision was not disclosed. Our efforts, and consultations with HHS and NIH, have not revealed additional information on this matter. However, documents provided by the University of Cincinnati do reveal that during this same time period Dr. Saenger had three research contracts with HEW (two) and NIH (one).

Mr. BRYANT. Dr. Cox, you talked about the peer reviews that took place regarding all this activity, including one sought by the American College of Radiology. Were they aware that the National Institutes of Health had refused to participate in experiments based upon moral concerns?

Dr. COX. Not to the best of my knowledge.

Mr. BRYANT. Were you aware of it before this morning?

Dr. COX. I was not.

Dr. SOPER. May I ask a question?

Mr. BRYANT. Yes.

Dr. SOPER. Is this NIH refusal, does that appear in the written record for the first time in the University of Cincinnati ad hoc committee report? I mean, I have a copy of that.

Mr. BRYANT. Yes, that is correct. That is exactly where it appears.

Dr. SOPER. Thank you.

Mr. BRYANT. We are seeking more information from the National Institutes of Health about it. They have not yet constructed their response.

Dr. Cox, your statement quotes a 1973 article by Dr. Saenger saying that all patients gave informed consent to the radiation experiments. Do you have any evidence as to whether the statement in the article is accurate?

Dr. COX. I have no corroborating evidence.

Mr. BRYANT. Did the individuals in these experiments have cancers that would benefit from radiation treatment?

Dr. COX. Many of them, as expressed by one of the earlier family members, suggested that local irradiation was used for some of the patients, and even suggested from, I believe, maybe a 2-year period, 2-year interval to the time when the total body irradiation was given that it may have been of benefit. So the local radiation that was given to these patients would very likely have been of benefit.

The total body irradiation was experimental, and was presumably undertaken on the hypothesis that it might have been a benefit to patients for whom no other systemic treatment was available.

Mr. BRYANT. We understood that portion of your testimony. Some of this was—as you testified, was experimental, and ill patients with very little hope of survival were willing to undergo the tests.

Let me ask you, what types of cancer were radio sensitive or were known to be radio sensitive at the time?

Dr. COX. A wide variety. The exception were those that were not considered radio sensitive. However, they required high doses to produce control of the disease, and such high doses could only be given locally. They could not be given to the entire body. So the question was, could lower doses be of some benefit if given to the whole body, and that was the hypothesis.

Mr. BRYANT. What types of cancers are radio resistant?

Dr. COX. The ones that are relatively radio resistant are certain tumors of bone, cartilage, and soft tissues. Most of the rest are considered sensitive or moderately radio sensitive. Some are exquisitely radio sensitive—the leukemias, lymphomas, Hodgkin's disease; there is a long list. The others are of intermediate radio sensitivity and require higher doses.

Mr. BRYANT. I guess my question is whether the individuals that were the subject of these experiments had cancer which might logically be assumed to have been sensitive to radiation treatment, based upon what you knew at the time.

Dr. COX. The published information indicates that the studies were being done, the whole body irradiation and half-body irradiation studies were being done—were being done for diseases where the tumors were considered intermediate radio sensitivity, not extremely radio sensitive. See, there is a gradation from extremely radio sensitive to pretty radio resistant, and these were intermediate. They are curable, when local treatments—where radiations can be given and the tumor is only localized, so in that sense they are sensitive.

You are asking a very difficult question from a radiation biology perspective.

Mr. BRYANT. Are colon, lung and breast cancer radio resistant or radio sensitive?

Dr. COX. When they are localized and treated with radiation therapy alone, they are curable. They can be eradicated permanently. When they have spread widely, the doses are usually considered such that you couldn't give them for the whole body.

But they were investigating that. That was exactly the subject of the study in the 1960s.

Mr. BRYANT. I think the logical extension of that is, would it not, therefore, be unreasonable to assume that perhaps whole body radiation at an acceptable level might have an impact on them if they had spread?

Dr. COX. Exactly.

Mr. BRYANT. The radiology report states that patients were not specifically informed that the partial financial support, this is for the experimentation, came from the Department of Defense. The patients were told that support came in part from a national agency.

The question of the source for support of a project is not construed by the American College of Radiology committee or most medical investigators as being relevant to the issue of informed consent. That is all in the quote.

With the standard of informed consent, is the patient told what agency is funding the experiments he or she may be taking part in?

Dr. COX. They may or may not be told which agency is funding the experiments. I don't really believe that it is a standard part of most informed consent, because for clinical investigations—because the approval process is one that is independent of the funding source. The approval process within any institution, and in adherence with the NIH guidelines, is independent. It is in each institution and is independent of the funding source. That is what drives the informed consent.

Mr. BRYANT. Mr. Mann.

Mr. MANN. Thank you, Mr. Chairman.

Dr. Cox, my understanding of the way that the project was organized is that the Pentagon dollars were used for laboratory work that had to do with the things the Pentagon was interested in. And patient care and cost of administering radiation and so forth were paid from separate sources.

So I guess the question is, if this was an appropriate experimental therapy from a medical perspective, could it have been done without the Pentagon funding? In other words, if the lab work is purely to support what the Pentagon is interested in, why were they merged together; and would it have been appropriate to proceed without any Pentagon involvement, and on the same budget? You wouldn't need the Pentagon dollars if my hypothesis is correct.

Dr. COX. I can't really speculate on the thinking at the time. I can say that the support for clinical research is very meager. Even from the National Cancer Institute at the present time, there is an average of $50 per new patient diagnosed each year to support clinical research. So investigators usually either do it on their own with institutional support, or they may seek any number of opportunities to get funding if such funding might be available.

And it usually, if there is any outside support, it comes from multiple sources, but it only covers a very tiny amount of the cost. So my guess is, based both on what was going on then and what I know now, the experiments probably would have been done much as they were; maybe not all those measurements of interest to the Department of Defense might have been made, but I think the total body irradiation experiments would have been done anyhow.

Mr. MANN. That is not the way it was done. It was done coincidentally, timewise, with the contract with the Pentagon. Obviously, the question that we are all struggling with is, would it have happened without the Pentagon dollars and what was driving the research?

Your statement closes with this sentence, "One might judge them harshly from a perspective of 20 years later, but they were reviewed and approved by peers and directors at the time the studies were conducted." Are you one of those that would judge them harshly from a 1994 perspective?

Dr. COX. With the evolution of informed consent between that time and now, I think we would bend over backwards to be much more clear in what is made available to the patients and their families. I think we would provide written information to them before they were ever asked to give informed consent to describe the experiment, and let them take such information home and discuss it with anyone that they wish.

I think we would provide them with repeated opportunities to discuss this with anyone they wish, including the referring physician, including any other physicians. That is pretty much the standard of today.

That was not the standard at that time. And so in that sense I think, sure, we would not do informed consent today anything like what they did then, like what we did then. The half-body irradia-

tion experiments are going on right now in exactly the same way, with NCI funding.

So I think there is little question that those would not be considered out of the ordinary by current standards.

The total body irradiation experiments would only be done nowadays with the help of bone marrow support, either bone marrow transplants from other individuals or from other family members or from the patient's own blood, or more modern techniques to use peripheral blood stem cells.

So we would not undertake those studies of whole body irradiation now without having the supportive structure to assure us that the bone marrow would be reconstituted. But high-dose, otherwise lethal, therapy is given now, now with doses far above anything that was given to these patients, with bone marrow rescue; and it is not always successful.

And those are the nature of the clinical experiments that are going on.

Mr. MANN. Some of that work now is in the experimental category?

Dr. COX. Yes, sir.

Mr. MANN. In the later years of this project it did, as I understand, involve bone marrow transplants, typically by taking marrow before the irradiation from the patient and reinserting it, whatever the proper term is.

You have reviewed the ACR, American College of Radiology, report from 1972. Do you agree with what that report says?

Dr. COX. I have no reason to disagree. Nothing else has come to my attention that would cause me to change the opinion which was rendered by Drs. Kaplan, Hendrickson, and Taylor at that time.

Mr. MANN. Do you have any professional relationship with Dr. Saenger, just for the record?

Dr. COX. No.

Mr. MANN. Dr. Steger, we appreciate your presence, and I guess I want to make sure I understand exactly what the stance is of the University of Cincinnati today.

Obviously, you made very clear that you are making every effort to be as completely forthcoming with the documents as possible. I think that is important. There are those in the community who are saying that it is appropriate for someone to say we are sorry. And the question is, what responsibility is the university assuming for a judgment today on the appropriateness of using 1960s values and standards of what was done at the University of Cincinnati?

Mr. STEGER. Well, there are certainly two sides of the story, when you read the evidence and listen to witnesses. Unfortunately, we are under litigation, so I really can't respond to that other than to say I think that the university would like to see investigations done—that you are doing, that outsiders are doing—because we are suspect, frankly. And so we invite you to answer that question; we invite other groups to study and answer the question.

And that is the stance we are taking. I think it is the only one we can take.

Mr. MANN. Thank you.

Mr. BRYANT. Mr. Portman.

Mr. PORTMAN. Thank you, Mr. Chairman.

Dr. Cox, thank you for coming to Cincinnati. We appreciate your perspective as an expert on oncology and also radiation therapy from a very distinguished medical institution.

I would really like to build on the earlier questions with regard to informed consent. I think you answered very well what today's standards are. I think you answered less well what the standards were in place at the time of the experiments.

You said in your testimony that they seemed to have used the appropriate standards of informed consent, in response to questions from my colleague. You mentioned that you thought that standards had evolved significantly, as they surely have. I just wonder if you could fill us in a little further as to what the standards actually were in 1960 or in 1966, or indeed in 1971.

Dr. COX. Well, the standards underwent an evolution during that time, not only in terms of clinical experiments, such as this one, but in terms of what one told the patient that was being treated with standard therapy.

There was literature in the early 1960s from prestigious universities that defended the idea of not telling the patient they had cancer at all because it would harm them. In sophisticated institutions in other countries, that is still the standard today.

So there was an evolution in what you told cancer patients about their disease and of course about their treatment. In the middle 1960s, the National Institutes of Health quite appropriately, even at that time we thought appropriately, demanded, because most of us advocated complete honesty with patients all along, advocate that if they were to be involved in clinical research, that we tell them everything that we could about the experimental treatment about what they had, about what benefits they might receive, and about what benefits mankind might gather from such treatments.

More and more and more, those demands have become increasingly arduous, but the basics of them were there, and it was really more a matter of how you documented them. And so what we told patients then, in my experience, was not profoundly different.

The degree to which it was documented for the medical record and for such hearings as this has become far more rigorous.

Mr. PORTMAN. With regard to whole body radiation, you spoke earlier about the fact that it continues to be used today at doses higher even than doses which were administered in this experiment. Going back to the 1960s again, which is the relevant time period for our inquiry, was whole body radiation at that time thought to actually be helpful either in curing cancer or to reduce the symptoms related to the cancer?

Dr. COX. Yes.

Mr. PORTMAN. And that obviously would include the Ewing sarcoma, as you talked about earlier, and would include the cancers in your discussion with Chairman Bryant that are more subject to metastasism, spreading throughout the body, but would that also be true with all the cancers in this study, to your knowledge?

Dr. COX. No. I don't think I could answer yes to the fact that they would—that that would be considered the standard at the time. That was what was being experimented. What was done, standard treatment, was mostly with leukemias, lymphomas, especially chronic leukemias, acute leukemias of childhood.

The other types of cancers, such as total body irradiation would be considered investigational.

Mr. PORTMAN. With regard to the doses that were given in the 1960's, do you believe that those were at the appropriate level? You had mentioned earlier some levels that you deemed to be nonlethal versus lethal.

In your study of this matter, do you believe the doses given were appropriate?

Dr. COX. The doses given, I believe, were probably selected because they were the highest doses that could be given without bone marrow support, as I described, that would not be lethal. So the doses that were administered that I have read would be considered sublethal.

But they were as high as one could hope to achieve for tumors that were not exquisitely radio sensitive. So it seems to me that they were reasonable doses for the experiments that were done.

Mr. PORTMAN. Thank you, Dr. Cox.

Mr. Steger, again, thank you for being here today. Earlier, we heard from Gloria Nelson that her grandmother's name may not have been correctly signed. In other words, it might not have been her grandmother's signature on some of the forms.

I have not had an opportunity to look at all the patient records. I understand those records have now been released to family members that have been identified.

But do you have any procedure in place to be sure there is not any tampering with the existing records, such as they are?

Mr. STEGER. Yes. We have formed a particular group that are now the custodians of all the records surrounding the whole body radiation studies, and they are now kept in one place under lock and key and only one individual, myself, essentially can release those. So that I would hope that they are currently very well protected.

Mr. PORTMAN. University Hospital is a teaching hospital, a research hospital, well-known throughout the country. It seems to me one of your jobs is to provide information, research, data, and so on, to agencies like the Department of Defense from time to time.

You have another job, which is to treat patients. And I guess my general question for you is whether in looking at the facts in the record from 1960 to 1971, the then General Hospital, do you think that General Hospital became too concerned with the providing of information and not concerned enough with the treatment of the patients at the time?

Mr. STEGER. Well, again, since we are under litigation, I can't answer that question.

Mr. CHESLEY. Let me just volunteer as a former chairman of the board of the university. There has been, just as Dr. Cox has talked about, an evolution. The evolutionary aspect of the university, since the days when it was Cincinnati General Hospital, under the city of Cincinnati as a municipal university, has been a miracle as far as evolution.

I am not taking anything away, but from my role as chairman of the board for 5 years and on the board of trustees for 9 years, just what I saw as far as the movement forward toward the 21st

century relative to that institution and the medical complex has been phenomenal.

It is very, very difficult to compare back, Congressman Portman, and I think it is an excellent question, it is almost impossible to compare back to what it was like in the 1960s as far as a teaching university, which it was, as compared to today, where it is one of the real crown jewels in this community and a crown jewel regionally as one of the finest medical complexes in the country, irrespective of the fact that we are in litigation, the university is in litigation.

I think it is very significant that here is a defendant, I am usually on the other side, a defendant in litigation coming forward, which we have, the university in the last month or so, and put all of the documents forward on a volunteer basis when it was not in any way required, because I believe, Dr. Steger believes that that is the role of this teaching university, which is that information which we have, at least from an archives standpoint, must go forward to the public and be put.

In response to the question on the signature, we will look into that because all of the patient records are on microfiche, so if there is a different signature on that medical record of those unfortunate individuals that would have been contemporaneous when that document was put on microfiche. And we want to take a look at it.

I am glad—I forgot which one of the women it was—brought it forward to our attention so we can take a look at it and find out what the facts are.

Mr. PORTMAN. Thank you for that commitment and thank you for that explanation.

I really have no further questions.

Thank you, Mr. Chairman.

Mr. BRYANT. Dr. Steger or Mr. Chesley, either of you who wish to respond, one of our purposes, of course, our essential purpose in this hearing, is to determine if we have inherited responsibility for actions that might have been illegal or wrong from the previous generation of leadership, that require us, in order to show good faith, to compensate people for damage that might have been done to them.

It would be helpful if you could tell us the nature of the litigation you are involved with right now.

Mr. CHESLEY. Let me respond. I have purposely stayed out of any aspect of the litigation. I happen to be, by job description, an attorney, but in this role I am an adviser, I like to call myself his assistant.

We, the University of Cincinnati, has been sued in a number of cases, I believe there are presently pending three class actions, none of those classes have been certified, and a class action, as you know, Mr. Chairman, means that there are lawyers who are suggesting that they represent all of the victims and all of the claims, and that may very well end up being.

So the way we are looked at it in the university is that the University of Cincinnati at present is a defendant on behalf of every person, whether they have individual counsel or are a participant as part of a class. So theoretically, that is 88 claims against the University of Cincinnati. The same claimants have also brought

lawsuits against Dr. Saenger, he and his counsel can speak about that, and the other 8 or 10 physicians and professionals who were part of that original team.

That litigation is presently pending here in the United States District Court. I believe it is three separate lawsuits, if that is of help to you.

Mr. BRYANT. And what have they alleged?

Mr. CHESLEY. They have alleged violation of—and I think one of the—two of the plaintiffs' lawyers are here. They can probably speak clearer about it. As I say, I am not counsel for the university. It is my understanding that they have alleged violation of civil rights. They have alleged violation of medical malpractice claims and sundry other claims of conspiracy, fraud, and so forth that are all encompassed.

One of the significant claims bringing it into the Federal Court was the violation of the individual's civil rights.

Do I not know—and maybe counsel can speak as to whether or not the Department of Defense is presently a defendant in those lawsuits. I would ask if you would speak to one of the attorneys that are here and they could—I know there is someone here, I know Mr. Newman is here. He represents some of the plaintiffs, and he is seated right behind some of the people that testified, and maybe they could give you more specificity or in the alternative, I think the best thing to do is to see to it that we get this panel a copy of the present lawsuits that are pending, we can get that for you today.

Mr. BRYANT. Obviously my wheels are turning about whether or not these individuals are going to receive the most thorough possible hearing in a Federal courtroom, and therefore, having this entire matter adjudicated without this committee having to look at it.

Mr. STEGER. I believe what you and Congressman Mann and Congressman Portman are doing is very, very important. It may have other issues over and above when a lawsuit will or will not be heard what the facts are, and an opportunity to have all sides aired.

Unfortunately, litigation, while it is very, very complete, in the final potential resolution, it is slow in going forward, and these are issues that I think you are bringing together with President Clinton's admission that are issues that I think are important for the university to be brought forward.

I think it is very important for us to be able to say, we are here to cooperate irrespective of the litigation, irrespective of the lawsuit, and we will continue that cooperation with Congress, the interagency commissions, President Clinton's commission.

Mr. BRYANT. Very well.

Finally, Dr. Cox, the severest critics of this entire matter remain—the ones on the next panel are those who have been critics for a very long time. I am looking at the peer reviews that took place here and wondering, how should we view these peer reviews of the actions of 20, 30 years ago?

Are they dispositive of the issues of responsibility here? Should they be read as a clear approval of what went on in terms of having given the patients adequate information, and any other elements of responsibility or not?

Dr. COX. I can say that I believe the only way of being fair is to judge them by the standards of the time, not the standards of today. To do otherwise would be to treat them unfairly.

To judge cancer treatments of the time by the standards of today would be to judge them unfairly. We have evolved. Medicine has evolved and the process of informed consent has evolved.

Mr. BRYANT. You mentioned the studies reviewed by the Faculty Research Committee of the Cincinnati University College of Medicine.

I think it is fair to say we might set that aside, inasmuch as they are, I would think, an interested party.

Dr. COX. I would take exception to that, sir. I believe that that is the title for what we would now call the Institutional Review Board, and that that is a standard part of the review process.

As a matter of fact, key to the review process to this day. So I was interpreting that as being a specific term for the general term of what we would call the IRB or Institutional Review Board, and that is absolutely critical to this, but the standards have changed relative to the IRB today relative to what they were then.

Mr. BRYANT. I agree we should stick to the standards at the time in judging everybody's intent at the time. You say they were also reviewed by the National Institutes of Health. We have now found that apparently they refused to participate in this. Is that relevant?

Dr. COX. I took that from the footnote to Dr. Saenger's paper of 1973, where it said that this was supported in part by the Department of Health and Human Services. I don't know any other agency that would have supported it in whole or in part except NIH at that time.

Mr. BRYANT. What do you mean by support?

Dr. COX. I——

Mr. BRYANT. You mean help pay for the research?

Dr. COX. I assumed that is what it meant. Is it possible that the NIH approved and supported this for a period of time and then withdrew its support?

I don't know the answer to that, but I was just going by what was included in the publication. You will have to ask others.

Mr. BRYANT. We are asking others, but this reference that you made on page 4 of your testimony, and is in the list of things which you characterize as peer review.

My question is, if this matter underwent peer review by the National Institutes of Health, it is a fair question for us to ask how it could be that they did not participate. There is indication they didn't participate, and at the same time came back and gave this a clean bill of health in the peer review process.

Dr. COX. I made that statement based on this quote from Dr. Saenger's paper of 1973: "Supported in part by USPH RR–5408, NIH General Research Support Grant of the College of Medicine in Cincinnati." Maybe the grant was through the University in a broad sense and not specifically to this project. But it would have undergone review by NIH as a part of the review of the University of Cincinnati's grant from NIH.

Mr. BRYANT. Have you seen a review of this that went back to judge whether or not it was handled in a proper way?

Dr. COX. No.

Mr. BRYANT. So I wonder if it is appropriate that you list it under peer review in your testimony here. Perhaps you are just assuming they would have reviewed it if they had a role in it, and now we doubt that they even had a role in it.

Dr. COX. I am just taking it from the publication that is—that is where that came from. I took it from the quote in the publication by Dr. Saenger's report, Dr. Saenger and colleague's report from 1973.

Mr. BRYANT. Let's go to the one conducted by the American College of Radiology at the request of Senator Gravel in 1972.

Would that have taken place over the telephone? Would that have been everybody exchanged written data and read it over in their office, or would that mean a visit to Cincinnati? What would that mean?

Dr. COX. From the report that I have, which I really only have two documents that serve as background for this, one is Dr. Saenger's paper, the one is the report from Drs. Kaplan, Hendrickson and Taylor, through the American College of Radiology, to Senator Lavelle.

In that report, they indicate that they first had a preliminary meeting in Chicago, and after that paid a site visit to the University of Cincinnati and reviewed records, discussed with a wide variety of people here, and did that which we would consider standard for a site visit today and they did it in the context, as they wrote, of what they would consider a study section or a peer review at NIH at that time.

So they were approaching it as if they were peer reviewers, as they would review any grant that had been submitted to them for review at NIH. They were all experienced reviewers. So they both reviewed the documents and they paid a site visit.

Mr. BRYANT. Any further questions?

I would like to thank all the panelists, particularly Dr. Soper and Dr. Cox who traveled a long way, and Dr. Steger and Mr. Chesley for taking your time in coming forward and helping us in this inquiry.

Thank you very much.

At this time, the committee would invite the third panel to come forward, which consists of Dr. David Egilman, clinical assistant professor, Department of Community Medicine, Brown University; and Dr. Martha Stevens, professor of English at the University of Cincinnati.

We thank both of you for being here today. As with the other witnesses, we ask you to hold your opening statement to five minutes so that we might go right to the questions.

We will start on the left of the committee, Dr. David Egilman.

STATEMENT OF DAVID EGILMAN, M.D., CLINICAL ASSISTANT PROFESSOR, DEPARTMENT OF COMMUNITY MEDICINE, BROWN UNIVERSITY

Dr. EGILMAN. Chairman Bryant, committee members, thank you very much for inviting me here. I am a private physician, practicing in Braintree, MA. I am on the faculty at Brown University.

I teach a course on the development of medical and scientific knowledge and history of the 20th century that includes the issue of the development of ethical standards during that time.

For 10 years or so, I have been trying to get the research funded by our Government on its own citizens that was performed here and at other institutions for purposes of military research investigated. I appreciate this opportunity today.

I want to begin first by responding to a question that was asked of the previous panel. Dr. Cox was asked whether or not he could find confirmatory evidence of informed consent in the 1973 paper. Well, there is some evidence on page 678.

It says,

> The acute radiation syndrome develops in stages. In the prodromal stage, nausea and vomiting of a transient nature occur. These complaints are not discussed with the patient before treatment.

The comments I make are not a retrospective look at the 1960's by 1970's standards or 1980's standards or 1990's standards. They are rather a look at the 1960's and 1970's by the standards of the 1890's, the 1940's, and the 1950's. As I begin with comments of physicians who reviewed this research for the University of Cincinnati, on the faculty of the University of Cincinnati, at the time the work was going on, that will be clear.

Dr. Gall, first in 1966, in a letter, stated that the informed consent form was inadequate. Dr. Shields, also writing about the informed consent form, in 1967, wrote "I believe a 25 percent mortality is too high." He also made a small comment about the adequacy of the therapy for cancer. "All patients should be informed not only that a risk exists, but of a one in four chance of death within a few weeks of treatment."

Evelyn Hess, writing in 1969, stated "The acceptability of our general consent form for human volunteers participating in research was questioned."

Dr. Thomas Gaffney, in 1967, wrote:

> The applicants have apparently already administered 150 to 200 rads to some 18 patients with a variety of malignancies and to the researcher's themselves' satisfaction, have not found a beneficial effect. In fact, as I understand it, they found considerable morbidity associated with this high dose of radiation. Why is it now logical to expand this study? Its current design will not yield meaningful data. The study should not be done.

Dr. Gaffney was on the faculty of the University of Cincinnati reviewing these experiments. But the ethical standards were known and established long before, with reference to this type of an experiment.

In 1950, Dr. Hamilton wrote describing similar work to Dr. Shields Warren, and said that this type of experiment had a little bit of the Buchenwald touch.

My father was at Buchenwald. I can assure you by 1950 it was well known what it meant to say that an experiment had a little of the Buchenwald touch.

The subjects were uneducated, had poor education, low IQs, and many had brain dysfunction because of their disease. They were unable to give informed consent. Rose Strom was diagnosed as resectable sarcoma in April 1970. She received a course of chemotherapy.

Chemotherapy was given for colon cancer in this time period. It was and still is to date palliative therapy for colon cancer. She was readmitted to the CGH on December 14, 1970.

According to Mrs. Strom's records, at 2 p.m. on that date, she received 10 milligrams of morphine IM, intramuscularly. Also at 2 p.m. she signed a consent form for radiation. She was then irradiated.

This was immediately followed by nausea and vomiting that lasted for 3 hours. She vomited repeatedly for 3 days. Antinausea medicine was withheld until the staff noted she was depressed to the point of crying and that she said, "I am so sick."

Withholding therapy for nausea and vomiting is not then nor is it now part of normal cancer treatment.

The researchers knew that informed consent was the standard of the day. As you have heard in the paper we read, they claimed they received informed consent. Despite that fact, only six of the first three patients received any information on the nature of the experiment, and none were informed of possible risks. If their published papers correctly report their failure to advise their patients about the possible experimental risks, their stated conclusion that they received informed consent is surely wrong.

The researchers were aware of informed consent requirements. They said they met the informed consent requirements of the Helsinki Code published in 1962. Similar experiments were rejected by one of the researcher's colleagues and when advised of the research in 1966 when it was suggested that the same thing be done at Oak Ridge University.

Oak Ridge researchers said, we are hesitant to treat these cancers because we believe there is so little chance of benefit to make it questionable ethically to treat them. Lesions that require moderate or a high dose of local therapy for benefit or are actually radio-resistant such as gastrointestinal cancer, just to help Dr. Cox, are not helped enough by total body irradiation to justify the bone marrow depression that is induced.

The argument that these experiments were appropriate from the ethical standards of the 1960s lack both scientific and historic accuracy.

In addition, cancer therapy was not the purpose of this research. Previous research had already been done. In 1942, it was published, "Little or no benefit follows its use," that is radiation, whole body radiation, "in the treatment of generalized carcinoma or sarcoma."

That is the kind of cancer in this study. "In no patient was there evidence that total body irradiation affected disease, 1965." In the kinds of cancers in this study.

Cancer therapy was not the purpose of the research. The researchers themselves described the purpose of the research: "To provide knowledge of combat effectiveness of troops." In real medical research, in real therapy, treatment for nausea and vomiting is provided. In military research in the U.S. experiments, it was denied until the patients had severe nausea and vomiting.

In real research, in real cancer therapy, psychologic and peer counseling is provided. In this work, in this military research, in

these U.C. experiments, patients were intentionally psychologically isolated.

In real medicine, in real radiation therapy, the radiation is given slowly and from many directions to improve effect and reduce side effects. In military research, in these experiments, the radiation was given fast and unidirectional, in the words of the researchers, because that was the radiation of military interest.

On February 9, 1971, Mr. Willard Larkins was noted to either have a lymphoma or adnocarcinoma of the colon. According to the hospital notes written by Dr. Aron and Dr. Rau, if he had a lymphoma, radiation would be indicated, while if an adnocarcinoma chemotherapy would "probably be in order."

On February 19, Mr. Larkins was found to have adnocarcinoma and Dr. Rau said, "Radiotherapy was definitely out of the picture and the patient may be a candidate for 5FU." 5FU is chemotherapy.

Five days later, he got the radiation. He never got the chemotherapy. There were four or five informed consents signed in Mr. Larkin's chart for surgical procedures. There was no informed consent signed for radiotherapy like this.

This was 1971, well into the period where people claim all the patients signed informed consents, well into the period when people claim the standard was a signed informed consent should be given.

Who was responsible? I think we find here we still have a problem. The fact that the representatives of the ACR, admittedly apparently from an institution that did similar work, could still come here and claim that this work was appropriate means that we have a problem in the medical community in this country. It is a problem that is a current problem. It is not an old problem.

The fact that there is an attempt to let you think that this was in some way not previously found to be inappropriate therapy means we have a problem in this country.

It is in the medical community. The fact that the University of Cincinnati's report reported almost everything I said and then said they had no problem means that there is a problem at the University of Cincinnati and at other universities. The fact that NIH denied the funding and then didn't tell anybody it was because of ethical reasons means we have a problem.

Thank you.

Mr. BRYANT. Thank you.

[The prepared statement of Dr. Egilman follows:]

BROWN UNIVERSITY Division of Biology and Medicine
DEPARTMENT OF COMMUNITY HEALTH

Statement to Congress, Subcommittee on Administative law and Governmental Relations, April 11, 1994 by David S. Egilman MD, MPH, 759 Granite Street, Braintree, Massachusetts.

Chairman Bryant, Subcommittee Members, Good Afternoon

My name is David Egilman. I am a physician. I am primarily a practicing doctor in Braintree, Massachusetts. I am also a member of the faculty at Brown University. In that role I teach and conduct research on the history of the development of medical knowledge in the 20th century.

I want to thank the Subcommittee for inviting me here to speak. For almost ten years I have tried to raise my voice about some of the experiments conducted by our Government on its own citizens, and I am grateful for this opportunity today.

I would like to begin by reviewing some contemporaneous comments of the colleagues of the University of Cincinnati (UC) researchers. There is little that I can add to these, however some still defend these experiments so I will endeavor to explain the bases of the criticisms later in my comments.

"It is not certain from the [consent form] narrative whether the patient is advised that no specific benefit will derive to him and that there are, indeed risks involved in the procedure proposed." - Edward Gall MD, May, 1966

"I believe a twenty-five percent mortality is too high." All patients should be informed not only that a "risk exists" but of, "a 1 in 4 chance of death within a few weeks" of treatment - George Shields MD, 1967

"The applicants have apparently already administered 150-200 rads to some 18 patients with a variety of malignancies and to their satisfaction have not found a beneficial effect. In fact, as I understand it, they found considerable morbidity associated with this high dose of radiation. Why is it now logical to expand this study?

Even if this study is expanded, its current design will not yield meaningful data. ... It will be difficult if not impossible to observe a beneficial effect in such a small sample containing a variety of diseases all of which share only CANCER in common.

This gross deficiency in design will almost certainly prevent making meaningful observations. When this deficiency in experimental method is placed next to their previously observed poor result and high morbidity with this type of treatment in a 'variety of neoplasms' I think it is clear that the study as proposed should not be done.

I have the uneasy suspicion, shoed up by the revised statement of objectives, that this revised protocol is a subterfuge to allow the investigators ... to test the ability of autologous marrow to 'take' in patients who have received high doses of total body radiation. This latter question may be an important one to answer but I can't justify 200 rad total body radiation simply for this purpose, 'even in terminal case material'. - Thomas Gaffney MD - 1967

..."the acceptability of our general consent form for human volunteers participating in research was questioned" - Evelyn Hess MD - 1969 commenting on the reason for rejection of two grant applications by the National Institutes of Health.

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In my statement I will cover four areas.

1. What were the experiments?

The whole body radiation (WBR) experiments conducted at the University of Cincinnati (UC) were designed to provide information to the military. They were not in any way cancer treatment or palliation. Some of those studies resulted in the deaths of their subjects.

2. Were the experiments conducted according to the ethical standards of their time?

The answer to this question is a firm no.

3. Why did these experiments occur and continue over a considerable period of time? Why did it take until 1994 for these activities to reach the national consciousness?

There was a lack of oversight and we are all responsible.

4. We must do our best to right past wrongs and prevent this from happening again.

I would argue that this necessitates taking several long and short-term steps, including the following:

A. We must document and assess what happened.
B. Those harmed should receive compensation.
C. Appropriate actions should be taken against researchers who acted improperly.
D. We must establish permanent mechanisms to assure that this type of experiments will not occur again.

In my opinion, they could occur again, they may occur again, and we need to establish a system of checks and balances to assure that hearings such as these are not held again. Never again.

The University of Cincinnati Experiments 1961-1972

A. Ethics and Informed Consent

On November 28, 1950, Dr. Joseph Hamilton wrote a letter to Shields Warren MD, Director Division of Biology and Medicine, The Atomic Energy Commission (AEC) concerning the ability of irradiated soldiers to function. (AEC) researchers wanted to determine the dose that might limit a soldier's "capacity to execute intricate tasks for which physical well being is essential." He discussed the difficulties of performing such a research study, and suggested that "For both politic and scientific reasons, ... it would be advantageous to secure what data can be obtained by using large monkeys such as chimpanzees which are somewhat more responsive than lower mammals." If the research was to be done on humans, Dr. Hamilton predicted that "those concerned in the (AEC) would be subject to considerable criticism, as admittedly this would have a little of the Buchenwald touch... The volunteers should be on a freer basis than inmates of a prison. At this point, I haven't any very constructive ideas as to where one would turn for such volunteers should this plan be put into execution."

Despite Hamilton's "political" sensitivity to a possible adverse public reaction to this research, the DOD funded studies similar to those described in his letter. Eugene Saenger MD and his fellow researchers at the University of Cincinnati conducted these experiments between 1960 and 1971. In all researcher irradiated 88 cancer patients during those years. Dr. Saenger and coworkers published some of their findings in 1969 in the Archives of General Psychiatry. The article was titled, "Total and Half Body Irradiation, Effect on Cognitive and Emotional Processes."

Cancer therapy was not the purpose of this research. Recently some defenders of this work have stated that the experiments met the ethical standard of their day. This is not true.

As they say, the devil is in the details. In their 1969 paper the researchers stated, that preirradiation analysis of the experimental subjects revealed that the researchers would have had difficulty in obtaining true informed consent from the study participants. "Relevant intellectual characteristics of the patient sample were as follows: a low-educational level (ranging from 63 to 112 on the full-scale of the Wechsler-Bellevue which has a mean of 84.5), and a strong evidence of cerebral organic deficit in the baseline (preradiation) measure of most patients." Thirteen of sixteen subjects were "Negro," three were White.

These researchers like others involved in similar experiments funded by the DOE and NASA, selected the most vulnerable of our citizens as subjects, the poor, the mentally and emotionally impaired, and African-Americans. UC researchers knew or should have known that their patient population was incapable of giving informed consent even if had they were informed of the experimental risks (which they were not). The UC researchers did not give the subjects all the facts on the side effects of the radiation. Therefore, if the patients consented to the experiments, the consent was not informed. According to the UC investigation of this research (Suskind report) a review of 27 of 33 patient charts between 1960-1964 **did not contain any notation that the patients were informed about anything.** Six of the patient charts contained information indicating that the patient "was informed about the nature of the treatment and its possible benefits." The patient charts did not contain any notation on the risks of the experiments. It must be assumed from comments of relatives of survivors and the lack of notation that 27 of 33 patients received little or no information of the risks. The researchers own contradictory statements about informed consent provide the best evidence that they violated the ethical and moral standards of both the sixties and the nineties.

UC researchers in their 1969 research paper revealed these contradictory elements themselves. The report included both of the following statements: "In each case the patient was advised that the therapy might be beneficial to him but that it was experimental in nature. Informed consent was obtained in all cases." And, "There was no discussion with the patient of possible subjective reactions resulting from the treatment. Other physicians, nurses, technicians and

ward personnel were instructed not to discuss post irradiation symptoms or reactions with the patient. This precaution was carefully followed so as to standardize and minimize 'iatrogenic' factors in influencing whatever subjective reactions the patients might have to radiation." Iatrogenic means doctor induced. The researchers claim they did not tell the patients about the possible side effects because this information could have induced nausea and vomiting in the patients. This is further evidence that the study was a study of the side effects of radiation not of the treatment of cancer. It is obviously impossible to obtain informed consent without giving information on the side effects of the treatment.

In response to a junior faculty report critical of the research, the UC researchers claimed that they had informed the patients of the risks involved and the possibilities of complications. They even produced a consent form allegedly used and signed by every adult patient in the study from 1965 onward. However, in addition to the detailed information on the lack of informed consent presented in the 1969 paper a 1973 publication that outlined the study methods stated specifically that the researchers did not tell the patients of the severe nausea or vomiting that could result from therapy. The researchers clearly understood that informed consent represented the standard of the day. They felt obligated to include a statement on informed consent in the paper they published. Did they lie about receiving informed consent from the patients when the story broke or did they lie about not giving them information required to receive informed consent in their published papers? If their published papers correctly report their failure to advise patients about the possible experimental risks, their stated conclusion that they received informed consent is surely wrong. Having failed to provide informed consent, (how could their patient population possibly give informed consent?) they had to lie about it when the experiments became public. There is no better evidence that they violated their own and our own ethical and moral standards.

The researchers were so aware of the importance of informed consent that they stated they received it from the participants in the experiment even though it is clear they did not.

In 1966 Saenger and Lushbaugh (in charge of studies of WBR at Oak Ridge funded in part by NASA), combined the results of their WBR research and published a joint paper. The paper reported the amount of radiation it took to kill half of the recipients. That same year, a review panel of the AEC suggested that Oak Ridge conduct experiments similar to those conducted by UC researchers. In reviewing a suggestion that patients with carcinoma of the breast, gastrointestinal tract, and urogenital tract should be treated by total body irradiation, the panel made the following statement: "These groups of patients have been carefully considered for such therapy, and **we are very hesitant to treat them because we believe there is so little chance of benefit to make it *questionable ethically* to treat them. Lesions that require moderate or high doses of local therapy for benefit, or that are actually resistant (gastrointestinal tract) are not helped enough by total body irradiation to justify the bone marrow depression that is induced.** Of course, in one way these patients would make good subjects for research because their hematologic responses are more nearly like those of normals than are the responses of patients with hematologic disorders." (Emphasis added) The argument that these experiments were appropriate from the ethical standards of the 1960's lacks both scientific and historic accuracy.

In their 1967 report to the DOD, UC researchers said that they followed ethical standards as set forth in Declaration of Helsinki. Again, this is not true. The Declaration clearly states:

I. (4) Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subjects or to others.

III. (2) The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.

III. (3) ...the responsibility for clinical research always remains with the research worker; it never falls on the subject, even after consent is obtained.

There is no question that the research failed to meet the ethical standards of the late 1940's as expressed in the first part of the Nuremberg code, "The voluntary consent of a human subject is absolutely essential." The code states that the subjects must have sufficient understanding of their situation, and must be capable of making an informed decision as to their participation in the research. The research conducted by UC researchers did not meet this standard established for prisoners of War.

Informed consent was the ethical standard of Dr. Saenger's day, and was the medical standard since the 1890s. On April 8, 1899, an editorial in the Journal of American Medical Association asserted that "the rule of conduct in this matter is for the physician to put himself in the patient's place with all his natural feelings and desires. **Even consent on the part of the subject can not justify an experiment that needlessly puts his health or life in peril, or diminish the responsibility of the one who performs or permits it.**" (Emphasis added)

The legal importance of informed consent was established in 1914, when Justice Cardozo wrote that, "Every human being...has a right to determine what shall be done with his own body and a surgeon who performs an operation without his patient's consent commits an assault for which he is liable in damages." Schloendorf v. Society of New York Hospital, 211 NY 125 (1914).

The courts again clearly stated the standard of informed consent in 1960. This decision stated that, "A man is master of his own body .... A doctor may well believe that ... treatment is desirable or necessary, but the law does not permit him to substitute his own judgment for that of the patient by any form of artifice or deception." Natanson v. Kline, 350 P 2d 1093 (Kansas 1960). Deception is precisely what occurred. "The patient is told that he is to receive treatment to help his disease," wrote the authors in another DOD report, despite the fact that they selected patients with non-treatable cancers for the experiments. The researchers denied some of the patients potentially effective treatments.

The human experiments which Dr. Hamilton discussed in his 1950 letter, and which Dr. Saenger designed in Cincinnati, were an atrocious example of medicine gone wrong.

B. Cancer therapy was not the purpose of this research.

Researchers tested the efficacy of whole body irradiation in the 1930's-50's at several centers, including Memorial-Sloan Kettering in New York City. WBR was not useful in the treatment of solid tumors. Researchers found that the so-called "non-radiosensitive cancers" such as those that UC researcher irradiated, were unresponsive to whole-body radiotherapy. The medical utility of this study was suspect and disguised, and as a result the research resulted in the deaths of at least eight, and probably more than twenty of the participants.

In a separate article titled "Whole Body Radiotherapy of Advanced Cancer," Dr. Saenger et al., wrote, "If one assumes that all severe drops in blood cell count and all instances of hypocellular or acellular marrow at death were due only to radiation and not influenced by previous therapy, then one can identify 8 cases in which there is a possibility of the therapy contributing to mortality." Suskind states that up to 19 may have died as a result of the radiation.

In 1905, Dessauer first used irradiation of the entire body for purposes of the experimental therapy of disease. Physicians used whole-body irradiation for treatment of a wide variety of benign conditions including asthma, migraine, and arthritis (Scott 1940) reports of adverse effects from radiation (Brues 1955, Furth and Lorenz 1954) quickly narrowed the use of the treatment to metastatic tumors.

Physicians conducted a set of clinical trials of whole-body irradiation for cancer out at Memorial Sloan-Kettering in New York from 1931 through the 1940's. These trials involved high total dose irradiation given over a period of days. Physician designed the low-dose rate irradiation to minimize side-effects such as radiation sickness and bone marrow suppression. Low-dose rate irradiation exposed the cancer cells to radiation during the entire cycle of cell division in order to irradiate each cell at the most vulnerable stage in its division. Physicians published progress reports of the experiments performed at Memorial in 1932, 1934, and 1942. The reports were in agreement with other literature from that time. The technique of whole-body irradiation showed some promise with leukemias and lymphomas, but "little or no benefit follows its use in the treatment of generalized carcinoma or sarcoma." (Emphasis added) (Medinger and Craver 1942). In the same study, Medinger and Craver explained why the therapy did not work on carcinomas (the type of cancer selected for the UC experiments): "The results in these generalized carcinoma cases were discouraging. The reason for this is quickly apparent. Carcinomas are much more radioresistant than lymphomatoid tumors, and by total body irradiation the dose cannot be nearly large enough to alter these tumors appreciably." The reason the dose cannot be large enough is that a dose that will kill the tumor will also kill the patient.

Later studies found similar results. Jacobs and Marasso reported in 1965 on 52 patients treated with whole-body irradiation when "other modalities had failed or could not be employed." They found that in patients with radioresistant tumors, "In no patient was there evidence that total-body irradiation affected the disease." (Emphasis added) In contrast to the Memorial Hospital studies, these studies administered the radiation at higher doses, and much more rapidly.

Interestingly Dr. Aron, one of the UC researchers and a member of the UC committee that investigated the appropriateness of this work in the early 1970's, recently stated, "In Cincinnati, the patients' disease had spread throughout their bodies, and most were given a life expectancy of six months. The effect of the study was a short prolongation of their lives. All who had the treatment have died of their cancers. They lived an average of fifteen months after the radiation exposure." If this was therapy and it worked, why did the researchers stop it when it became public? Did the researchers stop the experiments because they became public? If the radiation did not help, the subjects, who lived an average of 15 months after being irradiated, were not really suffering from terminal cancer. They were not. The researchers reported that until they were irradiated most of the patients were in, "relatively good health." Suskind's report indicated that the researchers excluded terminal patients from the study, "Some of the reasons for patient rejection included advanced stage of malignancies leading to disorientation, stupor, and/or coma, and terminal advanced malignant disease in which the life expectancy was only a few weeks." (pg. 27) At least nine and probably more than twenty subjects died as a result of the experiment.

The studies at the University of Cincinnati began and continued after the medical literature clearly reflected that whole-body irradiation was inappropriate. UC researchers knew about the acute and chronic toxicity of whole-body irradiation; they knew that only leukemias and lymphomas responded to the treatment; they knew that radioresistant tumors would require a dose that would be lethal to the patient in order to affect the tumor. In the literature review of the paper by UC researchers in 1973, the authors cite the study by Medinger and Craver, and note that "thirty-five patients with advanced carcinoma and sarcoma were included in this series". UC researchers preferentially selected patients with tumors that were not treatable by whole-body irradiation (cancer of the colon, breast, and lung) and then told the patients that they would receive therapy for their disease.

It is important to note that the ill-effects of successful irradiation consist of symptoms from the radiation and from the widespread destruction of the tumor cells (which release cellular chemicals and cause symptoms from the body's effort to remove the dead tumor cells). Irradiating patients with radioresistant tumors allowed the investigators to state that the symptoms the patients experienced were caused by the radiation and not by the effects of tumor destruction. This is the reason the patients with radioresistant tumors received high dose rate

irradiation. The experiment mimicked the effects of nuclear war on soldiers. The purpose of the experiments was as described in the researchers reports to the Department of Defense, "These studies are designed to obtain new information about the metabolic effects of total body and partial body irradiation so as to have a better understanding of the acute and subacute effects of irradiation in the human....The long-term program envisions carrying out the various observations at dose levels of 100 to 150, and 300 rad. Eventually doses up to 600 rad are anticipated." **These doses were potentially and were in fact lethal. Other physicians established decades before the UC researchers conducted these experiments. A dose of 250 rads would kill up to 50% of those who received it. A 600 rad dose would kill almost everyone who received it.**

The treatment methods

An examination of the treatment methods reveals much about the true purpose of the experiments. Patients received treatment in a sitting position with legs raised, and head tilted slightly forward. This position mimics that of a soldier in a protective fetal position. The powerful single doses resembled the dose rate of a nuclear blast. "Whenever possible unidirectional radiation will be attempted since this type of exposure is of military interest," the researchers wrote in 1969. This was not the way radiation physicians used in therapeutic applications. Physicians give real therapy slowly and from as many different directions as possible to minimize side effects and maximize efficacy.

In addition, the UC researchers denied the patients treatment for nausea and vomiting. This was apparently so anathema to the hospital staff used to caring for patients that the researchers had to create a special form to ensure that the doctors, nurses and other personnel would not perform their usual function of caring for sick patients. This form instructed hospital staff not to ask about the symptoms and signs of radiation poisoning. "DO NOT ASK THE PATIENT WHETHER HE HAS THESE SYMPTOMS," the form said. The form went on to instruct the staff to record the time, duration and severity of these symptoms. The researchers offered no treatment.

From another DOD report we find that the researchers sought to psychologically isolate the patients, "There is no discussion of possible subjective reaction resulting from the treatment with the patient. Other physicians, nurses, technicians and ward personnel are instructed not to discuss post-irradiation symptoms or reaction with the patient. This 'isolation' is carried out carefully so as not to influence any objective reactions of the patient which might be attributable to radiation." Patients resided in the psychiatry unit instead of the tumor ward, "The environment is far more attractive and there are no other patients receiving radiation therapy with whom the patient can exchange experiences." What manner of cancer treatment seeks to psychologically isolate patients and deny them treatment for nausea and vomiting?

II. Assessing Responsibility

In my opinion the responsibility for these experiments rests on many shoulders. These include: the government agencies that funded them and failed to provide adequate ethical safeguards; the Congress which failed to provide adequate oversight; the researchers who violated their Hippocratic oaths and their sacred trust with their patients; the universities which failed to provide adequate oversight of their researchers; the journals that published the work without comment, or review of the ethical issues that the research raised.

The research conducted by UC researchers was clearly unethical and resulted in the deaths of many of the irradiated patients. Dr. Stephens revealed this information to the public in 1971. Dr. Thomas Gall brought this information to the attention of University personnel in 1966.

We must address several if we are to assure ourselves that similar experiments will not occur in the future.

1. If the research was wrong and people knew it was wrong when it was done, why wasn't it stopped sooner? In fact, the Suskind committee suggested that the research should continue in a modified form.

2. Why was there no outcry, apology or thorough investigation after the research became public?

There are several answers to these questions.

1. There was a lack of appropriate oversight by the University.

There are several reasons for this.

A. No one likes to admit they made mistakes or apologize.

B. Dr. Saenger and his colleagues were well known and respected. It is hard to criticize the powerful and famous. Dr. Mossman, head of the Health Physics Society, told me at the last Congressional hearing that he would not criticize Dr. Saenger because he was a "big man."

C. Physicians do not like to criticize their peers especially if they work at the same institution.

D. The University ignored the timely criticisms of is own faculty. (letters by Drs. Gaffney and Gall - 1967)

E. The University allowed the research to continue from 1966-1971 without the approval of its own human subjects review board established in March 1966. The UC research review board granted a protocol limited to WBR and bone marrow transplantation provisional approval in May 1967. The approval granted in 1967 was provisional and requested that three modifications be made to the original protocol. A final revised protocol was not approved until August 1971. The experiments continued during this entire period.

F. At least two of the researchers were members of the University committee (Suskind report) that investigated the research. The UC burdened the researchers with the evaluation of their own work. This is a clear conflict of interest and a situation that is not likely to result in an objective evaluation of the research. (See below)

G. The University chose to attack the messenger by using McCarthyite tactics against the critiques of the research. This has continued to date.

7. There was lack of appropriate oversight by the Medical Community

a. The United States Senate requested that an "outside review" be carried out by the American College of Radiology (ACR). Dr. Robert McConnell a "long time fishing partner" of Dr. Saenger conducted this "review". In his report to the Senate Dr. McConnell noted that Dr. Saenger was a member of the American College of Radiology. He neglected to mention his personal friendship with the principle investigator or the fact that Dr. Saenger was at the time of the investigation a member of five different committees of the American College of Radiation, including the Commission on Radiological Units, Standards, and Protection, the Committee on Research and Development in Nuclear Medicine, the Commission on Public Health, the Subcommittee on Nuclear Medicine Technology, and the Committee on Efficacy. Prior to the investigation Saenger also served as a member of the Subcommittee on Radiological Aspects of Disaster Planning. These relationships constituted a conflict of interest and a situation that is not likely to result in an objective evaluation of the research.

b. Two UC researchers were members of the UC committee that reviewed the research for the University. This is an obvious conflict of interest.

c. The Ohio board of medical licensure has to date not investigated any of the physicians involved in this series of experiments.

d. The Cincinnati Medical Society has not investigated this series of experiments.

3. There was lack of appropriate oversight by the Congress.

Senator Taft vigorously obstructed a potential Senate investigation.

4. There was lack of appropriate oversight by the Department of Defense.

Who reviewed this work while it was conducted? Is there a current investigation of this research?

5. Were there violations of Medicare or Medicaid rules?

If it is true that the DOD only funded researcher salaries, overhead and travel money then public funds paid for these experiments.

6. The press failed in its oversight role.

The press, the last link in the chain that must protect our citizens from its government failed to cover the story. The press permitted the uncontroverted comments of the researchers and universities to stand alone as reports on these experiments.

7. The previous investigations were inadequate and filled with conflict of interest problems.

It is important to consider the University's evaluation of these experiments (Suskind report). When these experiments again reached the public consciousness this year, the University claimed the review agencies had found the experiments to be ethical and appropriate. It is my opinion that the reviews were inadequate and wrong. Nonetheless the University, the researchers, and the DOD have used the reviews to protect themselves from scrutiny. The reviews were part of an organized effort to mislead the public about the research. A careful

examination of the Suskind report reveals the inadequacies of the University's analysis of the radiation experiments and the unethical nature of the experiments themselves.

a. What were the objectives of the study?

The only protocol that preceded the experiments indicates that the purpose was to provide, "information [that] is necessary to provide knowledge of combat effectiveness of troops and to develop additional methods of diagnosis, prognosis, prophylaxis and treatment of these injuries." (pg. 1 DOD report 1963)

After the research was publicly criticized, the researchers claimed the DOD protocol was an add-on to a cancer treatment program. A cancer treatment protocol was produced in 1966 and approved on August 9, 1971. Perhaps because UC researchers never implemented any protocol while the study was conducted, friendly reviewers have had differing conclusions about the purpose of the experiments.

The ACR stated that the experiment was a Phase I study of the toxicity of whole body radiation in humans. American College of Radiology: "The committee viewed the project as it was designed -- as a clinical investigation of a modality for the care of cancer patients with extensive and incurable disease. Phase one investigations follow basic animal work and always precede randomized clinical trials which may or may not be justified on the basis of the first human applications." (pg. 3)

Suskind found the experiment to be a Phase II cancer study of the efficacy of treatment. Suskind's report states that the hazards of whole body radiation were well established before the UC studies were started, "the hazard [bone marrow suppression] is well documented in the available literature and the dose relationship to side effects well understood." (pg. 9) Suskind then states that the study was some type of Phase II study of the efficacy of bone marrow transplant and radiation. However, of the 87 patient's treated only 13 received a bone marrow transplant. In addition, Suskind notes, "The committee, however, was unable to find any written protocol in which the purpose of the study was to determine palliative effects of whole body radiation until...1967."(pg. 14) He latter notes, "No plan for a systematic study of palliative effects was made." (pg. 64)

Only the researchers' own words fully explain the experiments. They explained that the purpose was military. Only this purpose explains the experimental design, that included psychological isolation, organized denial of treatment for nausea and vomiting, and no plan for analysis of cancer palliation or treatment efficacy. Since treatment was not the intent of the study there was no need to organize the study so that treatment outcomes could be evaluated.

b. Was there a need to test whole body radiation for cancer treatment?

Suskind reviewed the prior studies of WBR to try to see if physicians had conducted adequate Phase II trials prior to the UC experiments. They report universal failure. "Medinger and Craver (1942) - Results were described as discouraging in this group of patients 'except for transient relief of pain in a few cases'." Jacobs and Marasco (1965) - 11 of 16 "died within one month of treatment; the remaining 5 having survivals of 1-1/2, 2, 3, 4, and 9 months. The statement suggesting the need for further evaluation of this form of treatment refers most probably to the radiosensitive, widespread neoplasms rather than the results in the 16 patients with radioresistant cancers." (pg. 10-11) In addition, Suskind could not find anyone else performing similar experiments, "Although whole body radiation is widely used for many forms of radiosensitive tumors, no information is available to the committee which indicates that this form of treatment is used elsewhere in radioresistant, disseminated or localized cancers as used at the University of Cincinnati." (pg. 12)

Suskind notes that in 1966, "This proposal received a critical internal review and was submitted to the NIH in an application for a research grant. The application was not approved and the reasons for this decision were not disclosed." (pg. 42) This was not true. In 1969, Evelyn Hess MD, the chairwoman of the faculty committee on research wrote that NIH had rejected two research grants because, "the acceptability of our general consent form for human volunteers participating in research was questioned."

Suskind concluded that, "The Phase II criteria for whole body radiation were not adequately satisfied at the time the original protocol was designed in 1960 and evidence for its effectiveness was incomplete. The results which were available for interpretation were not encouraging. Hence, the need for mounting a Phase II study at that time was indicated." (pg. 11)

If, after reviewing the dismal results of previous studies examining WBR use for radioresistant tumors and faculty criticisms of the WBR experiments at UC, Suskind really thought another study was necessary, there is something fundamentally wrong with the way UC researchers evaluate medical treatment and research needs. This is perhaps a more important area of investigation than the original studies themselves.

It may indicate that there is still a problem in this area at UC today. If the University authorities cannot recognize that the WBR experiments were wrong and apologize to the community, how can the community trust them to evaluate current experimental programs?

c. Quality of care

Suskind: "The thoroughness of the psychological support is apparent from the report of the psychological staff." (pg. 28)

DOD report: "There is no discussion of possible subjective reaction resulting from the treatment with the patient. Other physicians, nurses, technicians and ward personnel are instructed not to discuss post-irradiation symptoms or reaction with the patient. This 'isolation' is carried out carefully so as not to influence any objective reactions of the patient which might be attributable to radiation." (pg. 4)

If denial of treatment for nausea and vomiting and psychological isolation is good quality of care perhaps there is a current problem at UC in this area as well.

d. Ethics

Suskind: "Patients and families were not informed about the possibility of transient nausea and vomiting since such symptoms may be induced by suggestion. Typically, such side effects can occur a few days after treatment." (pg. 50)

Suskind: "Were there patients, whose IQ was subsequently determined to be 75 or below, who signed the consent form themselves?

Yes there were ten patients. There was no reason to believe that they did not understand the conditions of the project. The Committee also questions the significance of the scores of intelligence tests in this group of patients who were dying of far advanced cancer." (pg. 51) It was precisely these IQ scores that formed part of the basis for the DOD cognitive effects research.

Suskind: "Informed consent should be obtained as it is now. Revisions of the consent forms should be considered in relation to the use of the phrase 'sound mind and body'. The procedure for withdrawal from the project should be improved." (pg. 56)

If it is Suskind's (and the University's) opinion that sick patients with IQ's less than 75 who are not told about side effects like nausea, vomiting and a 25% death rate within weeks of treatment can provide informed consent there is a serious problem at the University.

e. Research quality

Suskind noted, "It is uncertain whether this study and similar studies reported in the medical literature are truly comparable in all major factors that influence survival, such as selection of patients and ancillary medical management. Therefore, the significance of comparisons of survival rates is doubtful, unless marked differences are found."(pg. 59)

"Since the manner in which the data on palliative effects was developed was inadequate, no conclusions can be drawn from them." (pg. 66)

Despite these comments Suskind concluded, "Since the Committee cannot at this time rule out a positive effect of whole body radiation, a well-designed study to compare whole body radiation with other forms of therapy is necessary if the investigator wished to continue." (pg. 66)

Is this the current type of analysis UC uses to evaluate research and researchers?

III. Why did this happen?

That's a list of who but the answer to why this occurred is a more subtle and important issue. Our population views the United States as a unique country, and it is. It is uniquely democratic; these hearings are an example of that. It is my belief that we in the United States have a certain belief in the infallibility of our own history and our own behavior. We tend to believe that our actions could only have good intentions. I am afraid this is not so. We have at times done the wrong thing for the wrong reasons just as many other countries have done. The history of medical science, replete with the use of certain marginalized groups in our society for harmful experimentation, offers some examples of repugnant actions performed in this country. Perhaps these experiments will serve as a turning point and provide us with a fresh look at ourselves. A look that recognizes that the United States is the greatest country on earth but also recognizes that it is not an infallible country. That not everything we have done has been with good intentions or with good results, and therefore we, like other countries, must remain vigilant of our government, and our citizens and our companies. We must continue to maintain and buttress our system of checks and balances to assure us that these types of experiments will never go on again.

IV. What should be done?

A. Short term

1. The University should apologize.

2. The victims or their families should be compensated.

3. State Medical boards should investigate.

4. Criminal investigations should occur.

5. A single Congressional investigation should occur.

6. The DOD should investigate their role and oversight procedures

7. Medicare and Medicaid agencies should investigate the possible use of patient care funds for research.

8. The Association of Occupational and Environmental Clinics should provide an independent non-governmental evaluation of all of the DOD, NASA and DOE research.

B. Long term

1. Medical review boards must be composed of >50% independent and unrelated researchers and lay people.

2. Medical journals should have ethical reviewers.

3. NIH must inform appropriate authorities when they find that a research project violates ethical standards. Their silence must stop.

Some people have asked why I am here. To paraphrase Thoreau, the question should not be why am I here, but why aren't other responsible parties here? It is every physician's duty to speak out when medicine goes wrong.

To quote from Pastor Niemdler about the Holocaust:

"In Germany the Nazis came for the communists, and I did not speak up since I was not communist.
Then they came for the Jews, and I did not speak up since I was not a Jew.
Then they came for the trade unionists, and I did not speak up since I was not a trade unionist.
Then they came for the Catholics, and I was a Protestant so I did not speak up.
Then they came for me, and by that time no one was left to speak up.

Thanks

My wife Helene, my students, my staff, my friends at NIOSH, Mitch Singal, and Bill Halperin, and my friends, particularly Mike Donahue.

Contemporaneous comments of colleagues

"It is not certain from the (consent form) narrative whether the patient is advised that no specific benefit will derive to him and that there are, indeed risks involved in the procedure proposed." - Edward Gall MD, 1966

"I believe a twenty-five percent mortality is too high." All patients should be informed not only that a "risk exists" but of, "a 1 in 4 chance of death within a few weeks" of treatment - George Shields MD, 1967

Contemporaneous comments of colleagues

"The applicants have apparently already administered 150-200 rads to some **18 patients** with a variety of malignancies and to their satisfaction have not found a beneficial effect. In fact, as I understand it, they found considerable morbidity associated with this high dose of radiation. **Why is it now logical to expand this study?**

Even if this study is expanded, **its current design will not yield meaningful data**. ... It will be difficult if not impossible to observe a beneficial effect in such a small sample containing a variety of diseases all of which share only CANCER in common.

This gross deficiency in design will almost certainly prevent making meaningful observations. When this deficiency in experimental method is placed next to their previously observed poor result and high morbidity with this type of treatment in a 'variety of neoplasms' I think it clear that **the study should not be done.** - Thomas Gaffney MD - 1967

Contemporaneous comments of colleagues

...."the acceptability of our general consent form for human volunteers participating in research was questioned" - Evelyn Hess MD - 1969 commenting on the reason for rejection of two grant applications by the National Institutes of Health.

Overview

1. First I will the describe the whole body radiation (WBR) experiments that were conducted at the UC. These were designed to provide information to the military. They were not in any way cancer treatment or palliation. Some of those studies resulted in the deaths of their subjects.

2. Secondly, I will address the question of whether the experiments were conducted according to the ethical standards of their time. The answer to this question is a firm no.

3. Third, I think we should consider why these experiments were allowed to occur and continue over a considerable period of time. Why did it take until 1994 for these activities to reach the national consciousness?

4. Fourth, we must do our best to right past wrongs. We must accurately assess responsibility for these studies if we are to address my final concern: how can we prevent this from happening again? I would argue that this necessitates taking several long and short-term steps, including the following:

A. We must document and assess what happened.
B. Compensation should be provided to those who were harmed.
C. Appropriate actions should be taken against researchers who acted improperly.
D. We must establish permanent mechanisms to assure that this type of experiments will not occur again.

The University of Cincinnati Experiments 1960-1972

a. Ethics and Informed Consent

On November 28 1950 Dr. Joseph Hamilton wrote a letter to Shields Warren MD., Director Division of Biology and Medicine, The Atomic Energy Commission (AEC).

(AEC) researchers wanted to determine the dose that might limit a soldier's "capacity to execute intricate tasks for which physical well being is essential." Hamilton discussed the difficulties of performing such a research study, and suggested that "For both politic and scientific reasons, ... it would be advantageous to secure what data can be obtained by using large monkeys such as chimpanzees which are somewhat more responsive than lower mammals."

If the research was to be done on humans, Dr. Hamilton predicted that "those concerned in the (AEC) would be subject to considerable criticism, as admittedly this would have a ***little of the Buchenwald touch***... The volunteers should be on a freer basis than inmates of a prison. At this point, I haven't any very constructive ideas as to where one would turn for such volunteers should this plan be put into execution."

The University of Cincinnati Experiments 1960-1972

a. Ethics and Informed Consent

2. Selection of subjects

   a. Uneducated - average 4th grade
   b. Low intelligence - average IQ 84 (many mentally retarded
   c. Brain dysfunction (did not know how to follow instructions)
   d Patients with tumors that were ***resistant*** to radiation therapy.
   e. "They must be in relatively good nutritional status and with a stable hemogram. "
   f. 54 of 88 patients African-American

These researchers, like others involved in similar experiments funded by the DOE and NASA, selected the most vulnerable of our citizens as subjects, the poor, the mentally and emotionally impaired, and African-Americans.

The University of Cincinnati Experiments 1960-1972

a. Ethics and Informed Consent

1) Patient population was incapable of giving informed consent.

2) Patient population not informed of the experimental risks.

The University of Cincinnati Experiments 1960-1972

a. Ethics and Informed Consent

3. Researchers were aware of informed consent requirements-

a. **Researchers claimed - patients informed of the risks and complications.**

b. **Researchers reported - Only 6 of first 33 patients received any information on the nature of the experiment**

c. **Researchers claimed - they received informed consent in the paper they published.**

d. **Researchers reported - they did not tell the patients of the risks.**

If their published papers correctly report their failure to advise patients about the possible experimental risks, their stated conclusion that they received informed consent is surely wrong.

There is no better evidence that they violated their own and our own ethical and moral standards.

The University of Cincinnati Experiments 1960-1972

a. Ethics and Informed Consent

3. Researchers were aware of Informed consent requirements

a. Researchers were aware of the Helsinki code

The Declaration states:

(4) Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subjects or to others.

II (2) The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.

II (3) ...the responsibility for clinical research always remains with the research worker; it never falls on the subject, even after consent is obtained.

The University of Cincinnati Experiments 1960-1972

a. Ethics and Informed Consent

4. Researchers were aware research was "questionable ethically"

a. Similar experiments were rejected in 1966.

"The suggestion is made that we should treat carcinoma of the breast, gastrointestinal tract, and urogenital tract by total body irradiation. These groups of patients have been carefully considered for such therapy, and **we are very hesitant to treat them because we believe there is so little chance of benefit to make it *questionable ethically* to treat them. Lesions that require moderate or high doses of local therapy for benefit, or that are actually resistant (gastrointestinal tract) are not helped enough by total body irradiation to justify the bone marrow depression that is induced."**
(emphasis added)

The argument that these experiments were appropriate from the ethical standards of the 1960's lack both scientific and historic accuracy.

The University of Cincinnati Experiments 1960-1972

b. Cancer therapy was not the purpose of this research.

1) Result of previous research - Dismal

a) **"little or no benefit follows its use in the treatment of generalized carcinoma or sarcoma."** (emphasis added) (Medinger and Craver 1942).

"The results in these generalized carcinoma cases were discouraging. The reason for this is quickly apparent. Carcinomas are much more radioresistant than lymphomatoid tumors, and by total body irradiation the dose cannot be nearly large enough to alter these tumors appreciably."

b) **In no patient was there evidence that total-body irradiation affected the disease." [with radioresistant tumors]** (emphasis added) (Jacobs and Marasso 1965).

A dose which will kill the tumor will also kill the patient.

The University of Cincinnati Experiments 1960-1972

b. Cancer therapy was not the purpose of this research.

2. The Researchers themselves described the purposes of the experiments in their reports to the Department of defense.

The purpose was, " to provide knowledge of combat effectiveness of troops and to develop additional methods of diagnosis, prognosis, prophylaxis and treatment of these injuries."

The University of Cincinnati Experiments 1960-1972

b. Cancer therapy was not the purpose of this research.

Issue	Real Medicine	Military Research
TREATMENT FOR NAUSEA AND VOMITING	PROVIDED	DENIED
PSYCHOLOGICAL AND PEER COUNSELING	PROVIDED	PATIENTS PSYCHOLOGICALLY ISOLATED
DOSE RATE	SLOW	FAST
DOSE DIRECTION	MULTI-DIRECTIONAL	UNI-DIRECTIONAL

What manner of cancer treatment psychologically isolates patients and deny them treatment for nausea and vomiting?

The University of Cincinnati Experiments 1960-1972

C. Assessing Responsibility

1. Government agencies that funded them and failed to provide adequate ethical safeguards - DOD, ?Medicare and Medicaid.

2. Congress failed to provide adequate oversight.

3. Researchers violated their trust with their patients.

4. Universities failed to provide adequate oversight.

5. Journals that published the work without comment failed to provide adequate oversight.

6. NIH refused to fund the work on ethical grounds kept silent.

The University of Cincinnati Experiments 1960-1972

D. Explaining the continuance of the experiments in the face of ethical questions

1. There was a lack of appropriate oversight by the University.

2. There was lack of appropriate oversight by the Medical Community

a) ACR The fishing buddy reviewer

b) The Ohio board of medical licensure

c) The Cincinnati Medical Society

The University of Cincinnati Experiments 1960-1972

D. Explaining the continuance of the experiments in the face of ethical questions

3. **There was lack of appropriate oversight by the Congress**

Senator Taft vigorously obstructed a potential senate investigation.

4. **There was lack of appropriate oversight by the Department of Defense.**

Who reviewed this work while it was being conducted? Is there a current investigation of this research?

5. **Were there violations of medicare or medicaid rules?**

If it is true that the DOD only funded researcher salaries, overhead and travel money then public funds paid for these experiments.

6. **The press failed in its oversight role.**

Permitted the uncontroverted comments of the researchers and universities to stand alone as reports on these experiments.

The University of Cincinnati Experiments 1960-1972

D. Explaining the continuance of the experiments in the face of ethical questions

7. Previous investigations inadequate, filled with conflict of interest, incomplete research and bizarre analysis.

The Reviewers' views:

a) What were the objectives of the study?

i) The ACR - phase I study of the toxicity of whole body radiation in humans.

ii) Suskind -phase II cancer study of the efficacy of bone marrow transplant and radiation.

iii) The UC researchers stated purpose was ignored.

b) Was there a need to test whole body radiation for cancer treatment?

i) Suskind reviewed the prior dismal studies of WBR

ii) Suskind found that no one else anywhere in the world is doing this.

iii) Suskind found that in 1966 NIH rejected the proposed research

Suskind concluded, "the need for mounting a Phase II study at that time was indicated."

If the University authorities cannot recognize that the WBR experiments were wrong and apologize to the community, how can the community trust them to evaluate current experimental programs?

The University of Cincinnati Experiments 1960-1972

D. Explaining the continuance of the experiments in the face of ethical questions

7. The previous investigations were inadequate and filled with conflict of interest problems, incomplete research and bizarre analysis.

c) Quality of care

Suskind: "The thoroughness of the psychological support is apparent from the report of the psychological staff." (pg. 28)

DOD report: The patients were psychologically isolated and denied treatment for nausea and vomiting.

If denial of treatment for nausea and vomiting and psychological isolation is good quality of care perhaps there is a current problem at UC.

The University of Cincinnati Experiments 1960-1972

D. Explaining the continuance of the experiments in the face of ethical questions

7. The previous investigations were inadequate and filled with conflict of interest problems, incomplete research and bizarre analysis.

d)Ethics

Suskind: "Patients and families were not informed about nausea and vomiting.... Typically, such side effects can occur a few days after treatment." (pg. 50)

Suskind: Patients, with IQ's 75 or below [mentally retarded] can "understand the conditions of the project" and provide informed consent.

If it is Suskind's (and the University's) opinion that sick patients with IQ's less than 75 who are not told about side effects like nausea, vomiting and a 25% death rate within weeks of treatment can provide informed consent there is a serious problem at the University.

The University of Cincinnati Experiments 1960-1972

D. Explaining the continuance of the experiments in the face of ethical questions

7. The previous investigations were inadequate and filled with conflict of interest problems, incomplete research and bizarre analysis.

e) Research quality

Suskind noted, ..." the significance of comparisons of survival rates is doubtful, unless marked differences are found."(pg. 59)

"Since the manner in which the data on palliative effects was developed was inadequate, no conclusions can be drawn from them." (pg. 66)

Despite these comments Suskind concluded a modified study could continue. (pg. 66)

Is this the current type of analysis UC uses to evaluate research and researchers?

V. What should be done?

A. Short term

1. The University should apologize.
2. The victims or their families should be compensated.
3. State Medical boards should investigate.
4. Criminal investigations should occur.
5. A single Congressional investigation should occur.
6. The DOD should investigate their role and oversight procedures.
7. Medicare and Medicaid and the city should investigate the diversion of patient care monies to research.
8. There should be an investigation by the Association of Occupational and Environmental clinics.

B. Long term

1. Medical review boards must be composed of >50% independent and unrelated researchers and lay people.
2. Medical journals should have ethical reviewers.
3. NIH should abandon its a code of silence.

Thanks

My wife Helene, my students, my staff, my supervisors at NIOSH, Mitch Singal, and Bill Halperin, and my friends particularly Mike Donahue.

ERRATA

The University of Cincinnati Experiments 1960-1972

On page 4, paragraph 3, line 6 the sentence should read: "In reviewing a suggestion that patients with carcinoma of the breast, gastrointestinal tract, and urogenital tract should be treated by total body irradiation, the Oak Ridge researchers made the following statement..."

Mr. BRYANT. Dr. Stephens.

STATEMENT OF MARTHA STEPHENS, Ph.D., PROFESSOR OF ENGLISH, UNIVERSITY OF CINCINNATI

Dr. STEPHENS. I have been somewhat disappointed that we couldn't hear from more family members. I would like to look at some of the medical charts.

The family of the people who spoke to us today suffered. I think everybody that was in these experiments suffered. They were made sick for several days—intensely, usually. Many had to go into the hospital for this treatment. They were taken out of their homes, called up, told to come to the hospital for this treatment.

No matter how long they lived after the radiation, they suffered. The doctors tell us in fact that it can take up to 100 days to recover from whole body or partial body radiation. For those who didn't die directly of the radiation, nevertheless they all suffered, were made ill, possibly were sicker than they would have been for up to 100 days, the ones that lived that long.

Now, we did not hear this morning from any of the so-called short survivors, and we must remember that there were at least eight people who died directly of radiation. We can document this from the doctors' reports. They give us the blood scores for those patients. These patients died within 40 days. We know that they suffered from bone marrow failure. And when that happens, you are wide open to infection. Infection swoops down and takes you away because you have no white and red blood cells to fight it with.

Thus, I wish we could have heard from a lot more families. Let's remember this: 26 people died within 60 days. Their lives were almost certainly hastened by radiation.

As the years went on, the doctors stopped telling us what the blood scores were, because they were no longer studying what was happening to the blood scores. They had already found out that with 200 rads of radiation, you have a good chance of dying of it. They knew what would happen, and they kept on doing it.

So we don't know, for all of those 26 people—that is, until we study the medical records which we have only recently gotten and which Dr. Egilman now is studying and others will be studying—we don't know exactly how all of them died. I am sure we will find that many more than eight also suffered severe bone marrow depression.

The question has been raised, were these patients terminal? My view is, many were not what we would in common parlance today call terminal. Early on in the experiments, a woman was irradiated who had had cancer of the tongue. She was given a high dose of radiation that she might have died from. She was submitted to that lethal risk, but she recovered.

You usually either die or begin to get better within about 40 days of having total body radiation.

She survived. She got very sick, but she survived. She lived after that over 5 years. In fact, we don't know the date of her death. I don't think she could be considered terminal at the time she received this high, possibly lethal dose of radiation.

I have been particularly interested in one patient, No. 090, because of those 26 patients who died between 6 and 59 days after

they were irradiated, she is the shortest survivor of all. She lived only 6 days after her radiation. She was an 80-year-old African-American woman who lived in Hillsboro, OH.

I did not know until last Friday when I went to a meeting of the families in attorney Bob Newman's office that her family have been identified. I had wondered all of these years who they were. I didn't know her name. Her name is Margaret Bacon. Here is what happened to her. First I should say that we have heard a good bit about bone marrow transplantation and whether this could have helped protect the people who were receiving the higher doses in the later years of the project. It wasn't even tried until mid-way through the project, and at that time, even, it was experimental. The doctors were not sure they could make it work.

So Margaret Bacon had an operation to have her bone marrow removed so that it could then be replaced after her irradiation, to give her a chance of her bone marrow recovering. On the operating table—and this was a severe, serious operation, to have your bone marrow removed, it was another ordeal that people had to go through, it took up to 2 hours with general anesthesia—on the operating table or shortly thereafter she suffered a stroke.

She still was irradiated that very day, at 2. They probably did not know that she had suffered a cerebral accident. We read in her patient history, she was shammed, that is, given fake radiation to "see whether that would have any psychological effects, on June 2, 1969. On June 4, bone marrow was aspirated from the posterior and anterior sternum with ease.

At approximately 2 in the afternoon, the patient received 150 rads midline tissue dose total body irradiation.

She experienced only mild nausea and vomiting. Following irradiation, the bone marrow was infused. The patient tolerated the procedure well. No fever, chills, were noted.

On June 9, 1969, the patient was noted to have left sided facial weakness. This is just a few days later. Suggestive of a cerebral vascular accident.

On June 10, the next day, six days post TBR, she expired.

In that same report that the doctors submitted, which contains this history, we read as follows.

The second death (patient 090) was anesthesia related. Four days, they say here, after the procedure, that is, the bone marrow aspiration.

I could read—maybe I will have a chance later on, to look at these statements from her family, her nephew, her great niece and her great nephew, who appeared at our meeting on Friday, and they have submitted to you three statements.

They, like the others, do not know anything of an experiment being carried out on their aunt.

If I may return to the question of informed consent, there is no evidence of any kind of consent for the first 5 years, written, oral, otherwise. There is no evidence that has ever been put forward. When consent forms were introduced—and after all we do have these, I saw them years ago, we do have the consent forms—none of them ever stated the real risk to the patients, that is, none said to the patient, "You may die of this treatment, do you really wish to have it?" None ever said that.

I have two recommendations I would like to make, if there is time.

Mr. BRYANT. You might summarize them so we can begin to ask questions.

Dr. STEPHENS. Maybe I will save those. Can I save those?

Mr. BRYANT. Very well.

Thank you very much.

[The statement of Dr. Stephens follows:]

Statement for House Judiciary Committee -- Martha Stephens

Q. How did you first find out about the radiation project at U. C.?

A. In the fall of 1971 I was starting my fifth year in the University of Cincinnati English Department. I was thirty-four, an Assistant Professor.

When I first began to look into these experiments, I had no idea anyone had died of the radiation. In the corridor of McMicken Hall one day, a friend in the department, Dave Logan (now the director of Prospect House, an alcohol treatment center in Cincinnati), showed me a brief report from the *Village Voice* about experiments being done at U. C. for the Defense Department, using poor cancer patients. The reporter was questioning whether or not the patients knew they were in an experiment; he said some were being irradiated over their whole bodies and were suffering nausea and vomiting for several days afterward.

This was all we knew when a group of us in the Junior Faculty Association decided we should look into the matter. We were living in the tail-end of the sixties, after all, not long after the bombing of Cambodia and so on, and we should remember that many Americans had developed a profound distrust of everything that issued from the Defense Department.

I had a research leave coming up in the winter, with time to study this issue, and I went over to see Edward Gall, who was then director of the Medical Center. I remember visiting him several times and trying out various arguments on him to try to get information; he was courteous, but for quite a while nothing was forthcoming from him. I remember his saying that the files on the project were long and complicated and would not mean much to people who were not doctors. He said, "I'm sure you wouldn't want them all." I said, "We do though. We would like to see them all. If everything is all right, as you say, Dr. Gall, and we have no reason to doubt your word, then perhaps it would be useful to have a campus organization clear up the matter." One day I went back over to his office and there was a large pile of documents on his desk. These papers were copies of the typescript reports the doctors were sending to the DOD, and I would later find that they told a tragic and terrible tale. Even now, I do not know why Gall surrendered these papers to me, and I later realized I was quite possibly the first person outside the Medical School and the Defense Department to see them.

This set of documents that has now been copied and re-copied in Cincinnati and elsewhere.

I drove back over to McMicken Hall that day, and I sat out on the campus drive, up on our hill with its beautiful lawn stretching down to Clifton Avenue, and pulled these papers out on my lap to see what I had. I saw that individual patient histories were attached to the backs of each of the nine reports, and I began reading these histories. I read for about an hour, and when I got out of the car, it was as if I could hardly recognize what was around me. Everything I saw looked different to me.

I was used to reading in plays and novels about tragic deaths, full of pity and sorrow, but I was not used to *this* pity, *this* sorrow. I felt that these experiments had to be stopped, and of course in due time they were stopped.

Over that Christmas holiday, I spread these papers out late at night over my dining room table, after our children were put to bed, and I wrote a summary of what had happened to the eighty-seven individuals that had been irradiated. I wrote about how they died.

I presented my findings to a meeting of the Junior Faculty Association on January 14, and the group decided to have a press conference, and this we did on January 26 of 1972. I feel now, as I look into the whole matter again, that our report was actually a conservative one. My friends in the JFA had gone over with me every sentence of it. We knew it had to be clear and it had to be right. I introduced a number of qualifying phrases, everywhere we had the least idea that an assertion could be challenged. Today I would not be as hesitant; but at that time it was as if I could hardly believe myself what I was putting down on paper. Still, this report told all the basic truths of the case; it told the truth, and it examined every possible argument the doctors could use to justify what they had done.

In some ways it is even more astonishing to me today to reflect on what transpired and to image up the whole scene from the point of view of the patients that were used. Even now, after so much discussion of these fellow citizens of ours, we don't know all their names or where they lived, what they did for a living, what they personally went through, the ways in which their loved ones suffered -- as they themselves waited helplessly for word of this or that from doctors and nurses that usually could not be found, or stood at bedsides in crowded wards, often *dirty* wards, as various hospital users of those years have testified.

These families I'm speaking of have been [illegible] — the invisible people inhabiting all our debates and discussions about this project. I'm thinking, for instance, of a man with

stomach 3
cancer who, after his irradiation, never came back to the hospital, bore his painful disease without help, as far as we know, not willing to be treated again after such an experience. I think of an eighty-year-old African American woman, "M. B.," who had lung cancer and suffered a stroke on the operating table in 1969, having her bone marrow aspirated in preparation for her irradiation. She died six days afterwards -- "an anesthesia-related death," as the doctors themselves describe it. Did she volunteer to be in an experiment that might end her life?

Q. How many patients died?

We know that at least 8 patients died of bone marrow failure as a direct result of radiation; for these patients the doctors provide the blood scores that allow us to document these cases of classic radiation injury. Then there were cases like that of M. B. mentioned above. Some of the histories, however, tell more than the others; in the later period, blood scores are no longer being studied and we are not generally told how much bone marrow depression existed at time of death. But there are altogether 26 individuals who died within 60 days of being irradiated and whose deaths were almost certainly hastened by radiation. For some of these short survivors we need to see their full hospital charts and follow-up in the clinics and hospitals to know exactly how they died.

Q. Were these cancer patients terminal? Were they people expected to live only a few months, as the medical school has said?

The patients who survived the radiation often lived several years. One woman with cancer of the tongue was irradiated in 1961 and lived at least five years after the radiation. We in fact do not know when she died.

A later group of subjects were chosen specifically because they were in relatively good shape, were not elderly, and could be interviewed in their homes or workplaces about coming in for this "treatment." They were working, eating normally, with good blood counts. Definitely not bed-ridden, extremely feeble, or about to die.

Q. Who were the doctors?

It was not a question of one or two or three individuals performing a deadly rite that very few other doctors knew about. A project that goes on for eleven years and involves the screening and consideration of at least 111 patients had to be known to a great many people. There were *thirteen doctors* on this team over the years, co-authoring the reports and publications, and many more who assisted in various ways

and were sometimes closely involved, in the complex testing of irradiated subjects for mental functioning, for instance. Then we have the doctors who were staffing the Tumor Clinic at the hospital and willing to hand over patients to the chief investigator and his associates, as well as staff at several other hospitals; at least three subjects were "recruited" from Drake, to use the doctors' term, and three youngsters with Ewing's sarcoma were brought over as "volunteers" from Children's.

Though Dr. Bernard Aron has been put forward by the Medical School as if he were an uninvolved or neutral spokesman, he was himself a member of the team for the final two years of the project. This doctor also served on the Medical School's internal review which cleared the project of any wrong-doing.

In general, I believe we do not expect to have the individual who is in the defendant's box also sitting on the jury.

Where in fact does the complicity begin and end? *The American College of Radiology did not find anything offensive in these trials and in fact termed them "heroic."*

What should we think about the long list of important medical journals which published the findings of these doctors over the years? How did their editors and readers regard the deaths they learned about in these reports? What were the attitudes of the local hospital authorities, the state licensing board?

Why did the review committees at U. C. fail?

In Cincinnati, it can also be said, not one m. d. in the Medical School came forward to offer help to the faculty group studying the project in 1971, or simply to examine their results with an independent eye, though one research biologist did consult with our group -- anonymously.

No doctor in the greater medical community of the town openly expressed any doubts about what had been done.

This is that wider complicity that should alarm us more than anything else, and here in 1994 -- when things are supposed to be "better" -- the same situation exists. *No doctors coming forward.* I believe it is correct to say that no reporter here in town has been able to find a single local doctor to examine what our faculty group found.

In 1985 an m. d. working here for NIOSH got in touch with me about this project and examined some of the medical histories in my home one night. Since then this individual, David Egilman, has attempted to draw attention to these trials; he bears out the findings of the JFA and has publicly explained the state of medical knowledge about whole body radiation for cancer as it existed at the time of the U. C. tests. He finds

no reason for the doctors to have believed that radio-resistant tumors such as most of their patients suffered from could have been helped by the "treatments" administered; the doses given, as deadly as they proved to be for many subjects, were not high enough to reduce tumors or stop the spread of cancer.

Q. Why did the Medical School succeed in drawing a curtain over this whole affair in 1972? If the case against the doctors was as clear as it sounds, why was there not a lawsuit from subjects or a criminal investigation?

One needs to understand the role of the media in Cincinnati (and in many other American towns). When the JFA press conference took place, the *Washington Post* sent a reporter and the *New York Times*. A crew came from CBS. Our report was entered into the *Congressional Record* by Senator Kennedy. But there was no real coverage in Cincinnati -- no way for any of the subjects or their families to know what had taken place. No one here broached the words "radiation death."

The Medical School was never compelled to acknowledge any wrong-doing, and yet there was a tacit acknowledgement that such work could no longer be tolerated, for after all the project was stopped. No patient was irradiated after the fall of 1971, even though in the report that would prove to be their last to the DOD, the doctors had announced their plans for more experiments in the year to come.

Q. Was there a cancer study being carried out using these patients?

There was no publication or report on cancer study during the eleven years of the project.

No design for a cancer study was ever produced during the actual course of the experiments, although a study on cancer was issued after the fact and as a result of public revelations. There is no reference to an ongoing cancer project in the DOD reports. There is no evidence of close follow-up by the team of the patients who survived more than 60 days. When the team had completed its radiation-injury tests, it seemed to have no more interest in the patients or their cancers.

If there was a cancer project, who were the doctors, where is the design, by whom was it funded, what were its results and how were they being reported?

Q. Didn't some people at the university object to what you and your group were doing, feeling that the activities of your medical colleagues were none of your business?

A. Of course. But surely events like these are *everyone's* business.

The people who used General Hospital were mostly Cincinnati working people; the great majority of them we now know were paying taxes; they were helping to pay the salaries of those of us in the JFA, and the salaries of the doctors. They were helping to fund this public hospital, not to mention the U. S. war machine of those days (as they do today). One can say that their taxes helped to pay the salary of Ohio Governor John Gilligan, who came, not to their defense, but to the defense of the Medical School and assisted in the cover-up. Gilligan convinced Senator Kennedy to drop U. C. from the hearings on human experimentation which followed the U. C. revelations and those about Tuskegee (where beginning in the thirties men in Alabama with syphilis were denied treatment for their whole lifetimes, and many died of syphilis-related disease or became insane).

I grew up among ordinary working people. My father worked for the railroads; my mother had only an eighth grade education. Many of us in the JFA were individuals who tended to side with common people against leaders and experts who wanted to control everything. I think people like ourselves are still hoping that we in the U. S. can grow into a true democracy, that common citizens will take the lead and assume control over their own society.

We are a class-ridden country, and actually it should not surprise us when our class conflict results in grievous actions like those of the U. C. doctors, actions, that is, of one potent and protected class against another that is powerless. It was a question here of a conflict between wealthy doctors and administrators -- in a public institution insulated against public accountability -- and common working people who could not afford doctors of their own choosing.

Q. What changes should come out of these revelations?

A. First of all, surely it ought to occur to us that if we had had national health insurance of a single-payer kind, that is, of the Medicare type that allows people to choose their own doctors, these fellow citizens of ours would not have been trapped in a public hospital with nowhere else to turn.

We need to see who is going to medical school. Is it only the children of the wealthy? often the children of doctors, whose incomes, after all, are within the top one or two percent of U. S. incomes? There should be a public examination of all our admission practises around the country and the way that medical schools are funded and how doctors are trained.

We ought to know, finally now, that we *must* have ordinary citizens of all walks of life well represented on medical boards, hospital boards, university boards and so on.

In the same year (1972) that the U. C. radiation project was first exposed, a group called the People's Health Movement was attempting to change the way the General Hospital Board was formed. It was asking for a city amendment that would allow for common people to be elected to the board; many hospital workers were involved in this struggle, and a massive petition drive was launched to place an amendment to this effect on the ballot, but the city fathers saw to it that citizens were never able to vote on this measure.

We need common citizens on the hospital board today and on the Board of Trustees of the university. At present the U. C. board is made up largely of wealthy business-people and attorneys.

We need to struggle in every way we can to alter the general class-ism and elitism of our medical system (and indeed of our whole society). I believe we could have good doctors, *better* doctors in fact, without the need to have doctors who are rich and powerful. Possibly in time we will even come to recognize that medicine for profit is not such a good idea anyway and that it doesn't have to be this way. Perhaps our current health care crisis and the recognized need for universal access to humane medicine will lead to some of the changes we need.

Q. Didn't we need, during the Cold War, to protect ourselves from our enemies abroad, and wasn't that why the U. C. doctors decided to do what they did?

A. Aside from the fact that the Cold War was -- as I see it anyway, and as more and more Americans are coming to realize -- largely an invention of those who wanted to benefit from the arms race, we might ask this: *if sacrifices were necessary, why could not the investigators have experimented on other doctors . . . or on themselves?*

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Mr. BRYANT. The Chair recognizes itself for 5 minutes.

Dr. Egilman, in your experience did any of these patients have cancers that would benefit from cancer radiation treatment?

Dr. EGILMAN. In some cases, if treated locally, some of them had cancers that were radioresistant to whole body radiation but would have responded to some local radiation, so that not all of the radiation they got was inappropriate. Only the whole body radiation they received was inappropriate.

The three Ewing's cases got what was thought to be correct care at the time, and there were other studies on that.

The total body radiation applied to the rest of the patients was inappropriate and had been tested before in the 1940s and 1950s and was known to be inappropriate and not to work.

The possibility of using bone marrow replacement was an interesting possibility, but, of the 88 patients, it was only tried on 13. So it is hard to argue that the approach to cancer therapy using bone marrow replacements was the reason this study was done. And in those 13 it was universally a failure.

I don't think you wait until 13, until you have stopped doing the work. I think one or two or three should be more than enough if it is a cancer treatment examination.

Mr. BRYANT. I guess you are saying the sum total of your lengthy study of this matter and your concern for 20 years about this matter, the essence of it is that there was no informed consent, first; is that correct?

Dr. EGILMAN. That is correct.

Mr. BRYANT. Because of illiteracy?

Dr. EGILMAN. No. In part because of their mental status. Not only were they illiterate, but they also were ill. They could not follow simple instructions.

For the military part of the experiment that related to the psychological testing, normally the questionnaire was self-administered. These patients could not fill out the self-administered questionnaire as part of the psychological testing. It had to be administered by the investigator. So they were not able to follow simple instructions because of their—for a variety of reasons.

Mr. BRYANT. Second, they weren't fully informed, I think you said, that they might die—there was some chance they might die within a few weeks.

Dr. EGILMAN. It was recommended at the time that that is what the informed consent form said.

Mr. BRYANT. But it didn't say that?

Dr. EGILMAN. It didn't say anything about any risk.

Mr. BRYANT. You said it was recommended at the time. Who recommended that?

Dr. EGILMAN. That recommendation was by Dr. Shields in 1967.

Mr. BRYANT. And who is he?

Dr. EGILMAN. He was a University of Cincinnati physician, a reviewer of the research.

Mr. BRYANT. Is there a record——

Dr. EGILMAN. He wrote a letter. That is in his letter.

Mr. BRYANT. Is there any indication of why they chose not to include his advice and follow his advice and include that information in the consent form?

Dr. EGILMAN. The research protocol was not finally approved at the University of Cincinnati until 1971, in August. There was a progressional approval given in 1967 but no final protocol was approved until 1971. The research was allowed to continue without approval, as far as I could tell, reading Dr. Suskind's evaluation.

Mr. BRYANT. This is a little harsh, but it seems to be your conclusion that they also carried out radiation tests on these individuals in order to obtain information for the Defense Department that were not therapeutic, that did not hold a promise of curing these people. Is that accurate?

Dr. EGILMAN. Curing, for sure. They never even thought that a cure was a possibility. At best, it was thought—the best they can argue now was to reduce the size of the tumor and reduce pain. That is a hard argument because, as Dr. Suskind noted, there was never a protocol written to evaluate the effect of the therapy on palliation. There was never a study protocol to look at the effect of this therapy on what they now claim was the purpose.

Mr. BRYANT. When you say palliation, you mean reduction of pain?

Dr. EGILMAN. It means reduction of pain. Or reduction of size of the tumor, et cetera. Or life expectancy. All that was done in retrospect. This 1973 paper was a retrospective after the study was criticized by Dr. Stevens.

Mr. BRYANT. In the medical community, does the lack of such protocol lead to the absolute conclusion that was not the intent of their work at the time?

Dr. EGILMAN. I don't know. Only a mind reader could know what was absolutely in their mind. I think that it wouldn't have been viewed as reasonable research. If there is no way to evaluate the question because there is no protocol for evaluating palliative effects, how can you say it was research to look at the effects of palliation?

That was Dr. Suskind's comment. The University's own analysis of the project said that there was no protocol that would allow one to evaluate the effects on palliation. What they tried to do was, when it was criticized, is they went back and quickly tried to put the data together.

Mr. BRYANT. You are asserting—I am not going to put words in your mouth; I am just trying to boil it down here—that basically they did military research on people who didn't know what was happening to them. That was not done for the benefit of the patient but for the benefit of the Defense Department, is that what you are saying?

Dr. EGILMAN. That is what they say. And I am agreeing with them. That is what they said in their reports to the Defense Department, and I agree with them.

Mr. BRYANT. Maybe you better elaborate on that. You say that is what they say.

Dr. EGILMAN. In the reports to the Defense Department they say the purpose of the research was to determine the effects of radiation on soldiers who might be in a nuclear war. That is what the researchers said. There is no cancer treatment mentioned in the first five or six years of this study at all, anywhere. Nowhere. It is their words, not mine.

Mr. BRYANT. Mr. Mann.

Mr. MANN. Thank you, Mr. Chairman.

Dr. Egilman, just to clarify, could you lay out exactly where it is that you and Dr. Cox disagree?

Dr. EGILMAN. Sure. I took a few notes. Thank you for that question.

He said the doses were not meant to be lethal. Well—or not known to be lethal. That is not true. Neither was true. The doses were given up to 300 rads. It was known after Hiroshima—from Hiroshima that the lethal dose that would kill 50 percent of the population was 300 rads.

Not only that, the researchers themselves used this information, combined with the research information at Oak Ridge where they were irradiating radiosensitive tumors, to publish a little abstract to help people understand how much it took to kill people. So they used their information to revise the estimate of how much it took to kill someone. So for sure they knew that the dose was sufficient to kill some of the people.

They themselves found that eight of the people died as a result of the radiation. It is written as a cause of death at least in one of the medical charts that I have reviewed. I haven't reviewed them all.

So certainly the researchers at the time knew that the doses could be lethal to some of the individuals.

Mr. MANN. I am trying to focus—excuse me—on exactly where it is that you and Dr. Cox, who had no part in the project, disagree.

Dr. EGILMAN. He said that the doses were not known to be lethal.

Mr. MANN. So, No. 1, he said the doses are not, and you say they are.

Dr. EGILMAN. I say they are, and they were known to the researchers to be so. And I explained why he said it was reasonable to test the hypothesis that with whole body radiation what would not work.

I disagree. It had previously been shown in the 1940s and 1950s not to work. Shields Warren wrote an article in Scientific American, in case you weren't reading the general medical literature in 1959, that specifically said whole body radiation should not be used for gastrointestinal tumors and other radioresistant tumors. He didn't even have to read the medical literature. You could get Scientific American at good magazine stores. Clearly, it was known to be ineffective by the time this research started and not to be indicated.

And there are reasons for that. This radioresistant tumor takes a high dose to kill it. And if it is spread throughout the body, the high dose that will kill the tumor will kill the patient for sure. The dose that is are given here, 300 rads is a low number. If you have a cervical cancer or a breast cancer, you are going to get 5,000 rads. That is what it takes to kill a radioresistant tumor.

You couldn't give 5,000 rads to a person. You couldn't even give 600 rads. Six hundred rads would kill everybody.

So the thing is the radiosensitive tissue, the bone marrow, is affected by a much lower dose. You kill the radiosensitive tumor; you kill the patient. You can't get to a dose high enough to kill the

radioresistant tumor that is spread throughout the body. That was known and commented on and said in 1942.

Mr. MANN. That is the second difference. What else?

Dr. EGILMAN. Well, the informed consent, I think I explained that one.

And then the issue about the fact that it is used now. Now, that is a use of 1990s standards looking at the 1960. It is used now because we have perfected bone marrow transplants. It is a misrepresentation to say because whole body radiation is used now it was OK to use it then. We use it now because we know how to deal with the bone marrow suppression. We didn't then.

Mr. MANN. How did we learn?

Dr. EGILMAN. We didn't learn from this study. We learned from other studies.

Mr. MANN. How do you go about moving from where you are to where you are today? You said something had been perfected. What is that? Not the result of experiments?

Dr. EGILMAN. It was, but it was well-controlled studies that were looking at that for a particular reason. And when you do those studies you inform people, OK?

I am not critical of doing research. I am critical of doing research that doesn't inform people of potential risks of the facts at the time that were known.

It is true. What you said is true. Science must do research. Some of the research may be lethal to some of the people. And that was true then and that is true now. But when you do it you let them know.

Mr. MANN. Anything else, in terms of differences between you and Dr. Cox?

Dr. EGILMAN. Well, I guess the only one would have been something he didn't say but something that came out. I think it would have been important to announce that the institution from whence he came did similar work funded by the same agency. That I think to me is a relevant piece of information in evaluating the comments.

Mr. MANN. University of Texas?

Dr. EGILMAN. M.D. Anderson is one of the institutions that got funding from the same agency to do the same work. I think that is important.

Mr. MANN. Anything else?

Dr. EGILMAN. That is all I can think of right now.

Mr. MANN. Let me ask you to help me. I am, obviously, not a physician. I practiced law for 25 years. We have got a radiotherapist who, obviously, is trained in the field. As I understood your earlier testimony, you are an internist. You are a part-time faculty member at Brown, teaching medical ethics. Why should I believe you and not him or vice versa?

Dr. EGILMAN. I think you need to read the documents. I think they speak for themselves. I read you from some of the patient records. The physicians at the time thought that in the case of Mr. Larkins that he should receive chemotherapy. They wrote that down. Those are their words, not mine. According to them radiotherapy was definitely out of the picture.

I don't think you need to be a physician to evaluate that. I don't think you need to be a physician to evaluate someone vomiting 3 days and not getting treatment. I think you can read the records in most of these cases.

Read the Suskind report. Ignore his conclusions. Read him for the facts. Suskind's analysis of the facts are quite similar to mine.

Mr. MANN. His conclusion is quite different.

Dr. EGILMAN. His conclusions are quite different, but the facts are the same.

So if you believe that there is no disagreement about the facts, I trust the public to make up their own mind about the conclusions.

Mr. MANN. I have and will, I am sure, continue to spend a lot of time trying to understand the facts. Your testimony is helpful. But it certainly is—I am unable at this point to reach a conclusion with quite the certainty that you can. This is part of the purpose of today and whatever happens after today.

You talked about palliation, if that is the right pronunciation. The Suskind ad hoc committee report criticizes the protocol but doesn't disagree with the conclusions.

Do you disagree with the conclusions of the final report that in some percentage of the patients the result of whole body radiation was the tumor size was reduced? That in some percentage of patients pain was lessened in some percentage the patients? The length of life after their whole body radiation was longer than what would have been projected for the alternative chemotherapy that might have been used? Or even what could have been projected had no whole body radiation or chemotherapy been applied?

Dr. EGILMAN. Well, here I am an expert, being an epidemiologist in addition to an internist.

In terms of the evaluation of the outcomes, Dr. Suskind says the data was insufficient to compare the outcomes of these patients to any other similar patients.

But, of course, the historian part would refer you to the comments of, I think, Dr. Gaffney, who said that you couldn't evaluate the data and you couldn't hope to evaluate the data because there were no controls given and the cancers were all different types of cancers. And there weren't enough cancers to come up with any conclusions about what went on in terms of impacting on treatment.

In order to answer the beginning part about whether you could retrospectively analyze this data for palliation, I don't know until I go through all the records. As you know, I only got the records on Friday, and I haven't had time to—I have gotten time to get a few things out of them, but I haven't had time to do a statistical analysis of those questions.

But I don't think there is going to be any ability to really answer the question because you need to compare. How can you know if these people benefitted when there was no comparison group and there was no systematic way of recording the data? You just have to go throughout charts and see what you can get.

I would need maybe—if the university wants to provide me with redacted records on 300 similar patients and we can see what was reported on those patients, we could compare how much pain those patients who had normal treatment versus the ones who had mili-

tary research performed on them did in terms of palliation. I think that is the only way to look at that question.

Mr. MANN. As you know, the Suskind report says no plan for systematic study of palliative effects was made in a retrospective review of the charts, following the data where elicited. So it looks like the Suskind group at least did that. Thirty percent had a decrease in tumor size of 50 percent or greater. That is objective, I guess.

Dr. EGILMAN. I haven't seen—in the records I have seen, I don't see that information. So I don't know where it comes from.

Mr. MANN. You have been working on this, Dr. Egilman. How long have you had an interest in this project and how did you first learn about the issues that we are discussing today?

Dr. EGILMAN. I first learned about it when I was here in 1984 from Dr. Stevens.

Mr. MANN. I have other questions, but I will yield until the second round.

Mr. BRYANT. Mr. Portman.

Mr. PORTMAN. Thank you, Mr. Chairman.

Thank you for being here, Dr. Egilman.

You state very clearly in your testimony that cancer therapy was not the purpose of the research project. In fact, you went so far in your response to Mr. Bryant as to say there is no cancer research mentioned anywhere.

I am looking at the 1958 response back from the Department of Defense regarding the proposal, which was really the approval of the project, and I quote, "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."

And it goes on to say, "In addition, if by such means the dose could be determined it would be of inestimable value in the case of atomic or nuclear warfare."

Have you seen this?

Dr. EGILMAN. I haven't, but that doesn't contradict what I have said. That is a reviewer's comment, isn't it?

Mr. PORTMAN. It is a comment from the DOD reviewing the research contract.

Dr. EGILMAN. Right. It is not from the contract. It is not part of the proposal.

I could read the proposal and say, gee, if I didn't know anything about the previous research that had been done that showed this wasn't true, that it didn't work, and I looked at this, just relying on what the researchers said, I might think that, too. There is no evidence that that reviewer knew about the other articles that I talked about from 20 years before.

Just because—I mean, could you look at the research now and say, gee, maybe it was helpful, maybe it could have been helpful, as Dr. Cox did? Of course. I have reviewed the previous research, and I know that if you had done that at the time you would have seen that this was not an effort in cancer treatment because it had already been tried and failed.

Mr. PORTMAN. This was in 1958. This wasn't looking retrospectively. I think it is inaccurate to say there is no mention anywhere in the record. This is something I just found looking in the record here.

The issue of informed consent is, of course, one of the ones that we are very interested in, and it is something that you addressed very articulately in your testimony, your written testimony. You have not had the opportunity to address what you view as the actual standards in place at great length, but you mentioned various indicia of what that might have been, including a letter, as I understand, from 1967 from a physician at the General Hospital.

What in your view were the standards that were in place, taking into account the Hippocratic Oath, taking into account all the various standards that were out there, for that critical time period, particularly in the early 1960s?

Dr. EGILMAN. The standards would have been to verbally inform them of the risks, at least, and to record for medical/legal reasons, if no other, that the person had been informed of those risks. And certainly by 1965 there was a university committee established that required formal signed informed consent forms. So that by then we know that the patient would have signed a consent form, and I think that I would agree with the people at the time who said that the risks should be explicit.

All I can—I mean, I am not trying to put a 1990's face on this. I am telling you that Dr. Gaffney and others at the time said that the informed consent was inadequate and made specific recommendations about how it would be changed. I think the recommendations that they made at the time were the standard of the time and were adequate for the time and, in fact, would be adequate for now.

Mr. PORTMAN. Written consent, as you note, I think, in your testimony, was used then. In fact, some have said that it antedated or predated that requirement or that recommendation to the university by 2 years. But in your response, again, to Chairman Bryant you had said that none were informed of possible risks.

And we just talked about informed consent. We talked about how verbal consent in that period, particularly in the early 1960s, might have been appropriate. Dr. Cox, in fact, testified that there was, in his view, a requirement I think for verbal consent, not written, in 1960, at least.

I just wonder, do you know whether there was verbal consent or not during that period? You have said that people were not informed of the risks. Have you interviewed the doctors? Have you interviewed people to know whether there was, in fact, verbal consent during that period?

Dr. EGILMAN. Well, the researchers in the Suskind report—Suskind comments on that. And let me just see what he says about that. "Patients and families were not informed about the possibility of transient nausea and vomiting since such symptoms may be induced by suggestion. Typically, such side effects can occur a few days after treatment."

That is a quote from the paper that I just said. So the researchers themselves said the patients weren't told of that. That was part of their study. It would have messed up the military aspects of the study.

Mr. PORTMAN. Part of your concern is about the demographics of the patient group, which is a concern of mine as well. We have heard from others that the study reflected the general patient pop-

ulation at the General Hospital. Would that change your view as to the study group?

Dr. EGILMAN. No. This was a national problem. The DOD sought people here and at Charity and Tulane. NASA sought people at Oak Ridge.

As far as I can tell, Afro-Americans were their first choice. When they couldn't find them, they accepted poor whites. I believe that that was a national policy, not a local policy, and that the site selections were not random by any means.

I think they picked people who they thought were powerless, and that is why they picked people who had low educational level and who had low IQs. And I think that was also the reason for selecting African-Americans. They didn't want to be questioned by the patients.

If it was cancer therapy, if people really thought that this was a way to cure cancer, there are lots of hospitals in this town that take care of affluent white people. Those hospitals could have been selected.

Mr. PORTMAN. Just to be specific here, you said in a couple of instances that DOD selected the patients. That is not my understanding and that certainly isn't what we are hearing from DOD in 1994.

Dr. EGILMAN. They selected institutions. Institutions. I mean, look, you can say, oh, that is what happened to be at the institution, which is apparently what you are saying. What I am telling you is it was no secret who was at the institution. It wasn't some random selection of institutions around the country that happened to serve predominantly poor people and African-Americans. Those are the places they picked to do the work, for the most part.

Mr. PORTMAN. Having been associated with U.C. Hospital in 1984, as you said, are there other research institutions, to your knowledge, at that time, in 1960, that would have been appropriate for this kind of research?

Dr. EGILMAN. I don't think the research was appropriate. You mean in 1984? What is the time——

Mr. PORTMAN. I am saying you have some knowledge of the University Hospital and General Hospital. You indicate that DOD selected the hospital.

It is my understanding that it was an unsolicited proposal, one; and, two, that at that time, in 1960—and I would certainly think that continues today—that the then General Hospital, University Hospital, was the preeminent research facility in Cincinnati. Is that your understanding or not?

Dr. EGILMAN. That is my understanding.

But in the paper yesterday I saw some advertisements for people. If you had sinus infections, there is a research protocol. And you can go to two or three different places and get in a research protocol for sinus infections.

So if you have a real research project and you want to do a lot of patients—after all, this was 88 patients over 12 years, not real fast. You need a lot more patients than that to do a research project. You could always advertise. And if you can't advertise, if the DOD won't fund your small ad in the Inquirer, you could always call your colleagues up at the other institutions.

Certainly Children's was able to appropriately send patients from Children's to the University of Cincinnati.

These patients, as I saw from the records, took a bus. Presumably, the bus went from affluent areas of town to the university. It didn't just go from the university to the poor areas of town. So if it was good cancer research, unfortunately, the white, affluent people in town were deprived of the ability to participate in it.

Mr. PORTMAN. Thank you. I have no further questions.

Mr. BRYANT. Dr. Egilman, I am curious to know your view of the Federal Government's role in this. As I understand it, the University of Cincinnati solicited the support of the Defense Department in funding this study.

Dr. EGILMAN. Right.

Mr. BRYANT. Is that correct?

Dr. EGILMAN. That is what I understand.

Mr. BRYANT. And the Defense Department contributed to it, assuming I am sure—and correct me if this assumption is wrong—that they would not be the only source of funding.

Dr. EGILMAN. That part I don't know. I think they were not the only source. I think that the University used this other general research fund—

By the way, that is another area of disagreement. I don't think NIH ever approved this consent form. There was general research, as I understand, at the University, and some of those funded the treatment.

Now, some of those funds—and also it is here from some of the charts—medicare funding was used. Now, it is my understanding—I don't know if this was true at the time. Medicare doesn't fund clinical research, only treatment.

So that one of the Federal questions I think that is involved here is were medicare and medicare funds diverted to clinical research. That is a Federal question.

Mr. BRYANT. In view of all of that, doesn't that auger a little bit against the assertion that this is explicitly military research being done on people? I mean, it was—after all, the University of Cincinnati solicited help in funding this from the Department of Defense but, as you just stated, had other sources involved in funding the research as well.

Dr. EGILMAN. The research would not have gone on like this had the military not wanted it to go on. The fact that civilian money were used doesn't mitigate the fact that it appears completely to have been done for military purposes and not medical purposes. The fact that they diverted money from general research monies or from medicare or medicaid funding doesn't seem to mitigate the purpose of the research or change the purpose of the research.

It might have been funded by some private foundation and still had a military purpose. The purpose doesn't depend on the funding. I don't criticize it because the Defense Department funded it.

Mr. BRYANT. Do you think that this totally lacked therapeutic purpose?

Dr. EGILMAN. Oh, yes.

Mr. BRYANT. You don't think there was ever any intent to develop a way to solve cancer problems through whole body irradiation?

Dr. EGILMAN. Not at this time, not with this therapeutic modality, not when there were only 13 of the 75 who received bone marrow transplants.

What about the other 75? It was known not to work on them.

Mr. BRYANT. That is a pretty strong position you take. You are basically saying Dr. Saenger and those others that attempted in subsequent years to characterize this as a way to try to find a way to cure or make more comfortable cancer patients were not telling the truth and what they were really trying to do was get information for the armed services.

Dr. EGILMAN. Well, look, no cancer therapy study was published until it was criticized. No cancer therapy protocol was written until 1966, and that was limited to the bone marrow radiation combination.

So, I mean, as they say, the facts speak for themselves. No research started until the Defense Department agreed to fund it, and it was stopped when the Defense Department withdrew funding.

I don't think those are all coincidences. Perhaps I am a cynic, but I think there is a relationship there.

Mr. BRYANT. Very well.

Mr. Mann.

Mr. MANN. Dr. Stevens, you indicated you had a couple of recommendations that you were interested in making. I would be pleased to hear that.

Dr. STEPHENS. All right. If I might just make a few other comments first.

Mr. MANN. Sure.

Dr. STEPHENS. I would just like to clear this up.

The doctors did not give 300 rads of total body radiation, as I am sure they will remind us. Three hundred referred to partial body radiation. And there was only one person who received 250 rads of total body radiation. The high dosages were 150 and 200 rads.

With regard to the cancer study, if I might just read part of the statement I gave you:

> Was a cancer study being carried out?
>
> There was no publication or report on cancer study during the 11 years of the study. No design for cancer study was ever produced during the actual course of the experiments, although a study on cancer was issued after the fact and as a result of public revelations. There is no reference to an ongoing cancer project in the DOD reports. There is no evidence of close follow-up by the team of the patients who survived more than 60 days—and often less than that.
>
> When the team had completed its radiation injury test it seemed to have no more interest in the patients or their cancers. If there was a cancer project, who were the doctors? Where is the design? By whom was it funded? What were its results and how were they being reported?

I know it has been said that we were in the cold war and maybe we needed to do this kind of research to protect ourselves against enemies abroad. But I say even if that was true—and sometimes I think the cold war was an invention of people who wanted to benefit from the arms race anyway—but if that was true, then maybe these doctors should have experimented on other doctors or on themselves, which is not unprecedented, actually, in the history of human experimentation.

But—I am sorry. You asked me——

Mr. MANN. You indicated, Dr. Stevens, you had a couple of recommendations for us.

Dr. STEPHENS. Yes, I did. I think if we regard these experiments just as an anomaly of the cold war we may be missing the point. I think there was abuse of patients in those days, and there is abuse today.

Let's consider it this way. If people had had in those days national health insurance, and especially of the medicare or single-payer kind where you can choose your doctors, they would not have been trapped in a charity hospital, or even, let's say, in a cheap HMO, which may also today not be giving good care.

That is—I want to look at what we are doing today and see what this project of the sixties helps us to understand about today.

I would appeal to you, the three of you, to consider, this matter closely, to search your hearts and minds to see if you can support a people's national health insurance as many of your colleagues are doing. I am not quite sure whether any of you are already supporting a single-payer system. It would have solved the problem back then. This would not have happened.

Mr. BRYANT. Will the gentleman yield?

I guess I don't understand—and I definitely do not want to get into a discussion about national health insurance here. I have had two weeks of that at home, and I would like to talk today about this matter.

But I don't understand what the point you are making is. We are talking here about experimentation which was defended by the University as having been for therapeutic purposes. Many of the facts seem to indicate otherwise, as has been laid out by Dr. Egilman.

Dr. STEPHENS. With health insurance, people would not have had to go to that public hospital. These people had no choice. They had no national health insurance such as nearly all developed countries did have at that time and do have today.

Mr. BRYANT. You are saying that—I guess you are ignoring or finding less than—I guess you are assuming that the statements that these people had a hopeless circumstance and were willing to undergo very risky treatment was not credible.

Dr. STEPHENS. No, I don't see any contradiction there. I am just saying that they would have been able to go to their own private doctors. They wouldn't have been the victims of this kind of medical violence by researchers. That is a recommendation I have.

Mr. MANN. Did you have a second one, Dr. Stephens?

Dr. STEPHENS. Yes, I do. I think neither one of these may be terribly popular, but I hope some people at least will think about them. I think that we need to have common citizens, users of institutions, on all our bodies on hospital boards, on review boards, on university boards, where now we have almost entirely wealthy businessmen and attorneys.

After all, the university board could have played a part in stopping these tests much sooner than they did, and in recent months they could have responded to the desperate pleas of families to know what happened to them several months before they did respond. They only responded because of enormous public pressure on them and when they had no choice. They allowed over 600 peo-

ple to wonder for many weeks whether their families had been irradiated or not.

So I think if we had had users, common citizens, nonspecialists, on these boards, on the board of the hospital, for instance, things might have been different. And I just appeal to you that whatever legislation regarding medical matters comes before you, surely this is something to consider. I think we must learn these kinds of things, from what happened in that public hospital.

Mr. MANN. Thank you.

I have one more question of Dr. Egilman. You refer to this 1950 letter from Dr. Hamilton. Could you share a copy of that with us? And who was he?

Dr. EGILMAN. He was a physician in California. He wrote the letter to Shields Warren, who was the head of the Atomic Energy Commission. And he was discussing the research needs similar to the ones that were conducted here.

Mr. MANN. Was he a researcher?

Dr. EGILMAN. He was a physician researcher. He is the gentleman who started injecting healthy patients with plutonium.

Mr. MANN. Hamilton did?

Dr. EGILMAN. Hamilton, before he wrote that letter. He wasn't concerned about the ethics. He was concerned that it might become public and that the public would be concerned about the ethics.

Mr. MANN. Thank you, Mr. Chairman.

Mr. BRYANT. Mr. Portman.

Mr. PORTMAN. Thank you, Mr. Chairman.

Dr. Stephens, thank you for being here today. Just a couple of quick questions.

No. 1, you had said in response to Mr. Bryant, my view is that many of the patients were not terminally ill.

Dr. STEPHENS. Right.

Mr. PORTMAN. If you could just tell us a little further what you base that on, number one, and then tell us whether you have any medical training, whether you have had any experience in that field. I am not sure what your field is. I believe you are a professor at the University in English.

Dr. STEPHENS. Right.

Mr. PORTMAN. If you could just expand on that in terms of the question as to whether the patients were terminally ill or not.

Dr. STEPHENS. Well, I didn't bring the file of patient histories that I have with me. I can't skim through them and see just how many might be considered to be in that category. But I do remember very clearly that two people stand out that would not have seemed, I think, to most people to be terminal.

The woman I mentioned, was irradiated in the first group of patients and lived 5 years after receiving the high dose of radiation, at least 5 years. We don't have her date of death. It is hard to consider that she was terminal.

And then I remember another woman shortly after that irradiation who lived over 3 years. And there were a good many who lived a couple of years. Again, these are people who might have died. Some of those people received the high doses that were killing people. You either begin to get better or die, generally, within about 40 days.

I am sorry I don't have figures on how many people this might be. Of course, in some cases it is hard to tell.

We have discovered already, by the way, that there are problems and errors in the patient histories that I originally examined 22 years ago when I wrote the JFA report. When I examine the original summaries and we compare them to what we now have in the medical records, there are discrepancies.

Mr. PORTMAN. Getting back to my favorite issue of informed consent, just to further flesh out, again, your comments to Mr. Bryant in that regard, you had said that there is absolutely no evidence of informed consent. Some patients——

Dr. STEPHENS. Of the first 5 years.

Mr. PORTMAN. Of the first 5 years. Some patients, of course, in those 5 years said no. Why did they say no?

Dr. STEPHENS. I am sorry. I am not aware of that.

Mr. PORTMAN. The records that we have indicate that some patients were asked to participate, and they said that they didn't want to.

Dr. STEPHENS. Well, I am sorry. I didn't remember that.

Mr. PORTMAN. I just wonder if there was no information given as to the risks and benefits, how that decision would have been——

Dr. STEPHENS. Where do you find that? Is that in one of the so-called DOD reports?

Mr. PORTMAN. It is in several documents that I have seen, Dr. Saenger's report.

Dr. STEPHENS. Oh, Dr. Saenger's. OK. Well——

Mr. PORTMAN. We will find that out and let you know. I think I saw it in the ad hoc report, but I am not sure.

Dr. STEPHENS. I would like to see it.

Mr. PORTMAN. It is an interesting issue in terms of the consent. There was no written consent, as you say, during that time period.

Dr. STEPHENS. Yes, no evidence of any kind of consent. Let's don't forget that in their own reports the doctors say the patients were told "they were being treated for their disease." That is a direct quote. I have included this in my original analysis. There are several such direct quotes, more than several, in those first five years of reports to the DOD. A number of times we read the patient is being told he is being treated for his disease.

Mr. PORTMAN. Thank you, Professor Stephens.

No further questions, Mr. Chairman.

Mr. BRYANT. I have no further questions.

Would you like to add anything? We would be happy to hear it.

Dr. EGILMAN. Just with respect to the last question.

Dr. Suskind noted that the researchers excluded terminal patients from the study. "Some of the reasons for patient rejection included advanced stage of malignancies leading to disorientation, stupor and/or coma and terminal advanced malignant disease in which the life expectancy was only a few weeks."

Mr. BRYANT. Leading to a conclusion that——

Dr. EGILMAN. Well, we know the therapy didn't help them, so there is only two conclusions. Some of the people lived a considerable amount of time. We know the therapy didn't help them. There is only one conclusion left then, that they weren't terminal when they were irradiated. That is the only conclusion.

Otherwise, there are two possibilities. One is they were terminal, and the therapy helped them. If that is true, then we have spent 20 years—we were wrong. They were right. But we have denied people this great therapy for 22 years. I don't think that is what we have been doing.

Clearly, the patients were not terminal. The therapy didn't help them. And that is from the life expectancy on the charts.

Mr. MANN. Dr. Egilman, you started that comment quoting something from Dr. Suskind's report. Where is that?

Dr. EGILMAN. Page 27.

Mr. MANN. Yes, sir.

Dr. EGILMAN. Wait a minute.

Mr. MANN. You were making the point that patients who were so advanced that their life expectancy was only a few weeks were excluded from the study.

Dr. EGILMAN. That is what Suskind said.

Mr. MANN. But you are not disagreeing—at least the information that we have—or are you disagreeing—all the information we have indicates you weren't even qualified to be a part of the study unless your cancer was advanced and you were terminal and alternative therapies were not thought to be beneficial.

Dr. EGILMAN. Well, you have to be a little careful here. We are all terminal, Congressman Mann. We will all die.

Terminal from a medical sense means, as they defined it, within several weeks or certainly within six months. And many of the patients, perhaps most of the patients, would not have been considered to be terminal within weeks or months, and so, therefore, would not be defined as medically terminal. They were terminal the way we are all terminal. We all die. It is a question of how soon.

Mr. MANN. Are you suggesting that having cancer was not a prerequisite for being in the study?

Dr. EGILMAN. No. They all had cancer. And they all had cancer that was likely to result in their death. It is a question of how long. People can live with cancer for months, years.

Mr. MANN. It was more subtle than that. It was cancer that had spread in the body, as I understand it. And it was cancer that, at least if you accept the premise of the research, was not going to be—chemotherapy was not going to do anything except perhaps arrest the speed of the cancer, the speed of death.

And they argue—and this is part of what we are trying to find out. They argue that the whole body irradiation in some instances was more effective and resulted in a longer length of life than the alternatives that were available.

Dr. EGILMAN. Okay. Let me deal with those one at a time.

First, there was therapy, as—25 or 26 of these patients had colon cancers. As you heard from my reading, the researchers themselves were aware of the fact that there was palliative treatment for the colon cancers. And they themselves wrote that that is the preferred treatment in 1971. That is their opinion. That has got to be the current standard at the time.

The second question is how reasonable is it to think that whole body radiation might have helped the others. For that I refer you

to what I already read about the previous studies that had looked at this and those patients that had shown it wasn't effective.

In addition, you have heard that radiosensitive tissues, bone marrow, get destroyed with 100 to 300 rads, certainly 400 or 500 rads. You have also heard that radioresistant tumors like GI cancer and breast, the ones that were treated here, take thousands of rads to kill the tissue, to kill the cancer.

So it was not medically reasonable, it was not scientifically reasonable to think that giving someone 300 rads half body or 150 rads whole body would in any way touch the radioresistant malignant spread of cancer without wiping out their bone marrow first.

The dose differences between radioresistant and radiosensitive are quite high, thousands versus hundreds. So there wasn't a medical rationale and scientific rationale, and that fact was noted in 1942.

I am not telling you something that I figured out last week. I am telling you something that was published. This scientific rationale, this medical thinking, was published by Craver in 1943.

Dr. STEPHENS. May I reply again to your question about my own specialty not being medicine?

Mr. PORTMAN. Sure.

Dr. STEPHENS. May I do so?

Mr. PORTMAN. Yes, ma'am.

Dr. STEPHENS. It relates to my recommendation that we have common citizens on all boards that decide how hospitals and universities and medical services shall be organized. If we can't do that, we are not a democracy, in my opinion.

I am an English professor, all right. Medicine is not a magic science. It is not a body of knowledge different from all other bodies of knowledge that only certified people can understand.

Mr. PORTMAN. I appreciate that response. I asked that question, in the context of your statement as to the patients being terminally ill or not, which is in my mind a medical issue and a diagnostic issue.

We asked about—where it said the patients had not agreed, on page 26 of the ad hoc report, you see something about two patients did not agree to be treated. That is what I was referring to.

Dr. STEPHENS. May I say that I am extremely happy that I have been able to work lately with Dr. Egilman, because, of course, I am not a physician. There is a great deal I don't know about cancer.

Mr. PORTMAN. Thank you very much.

Mr. BRYANT. Thank you very much for your testimony.

Thank you, Dr. Egilman, for traveling here today.

At this time we will ask our fourth panelist to come forward, which consists of Dr. Eugene Saenger, Professor Emeritus of Radiology, University of Cincinnati.

Dr. Saenger, thank you very much for being here today. At this time, we would ask you to proceed.

STATEMENT OF EUGENE SAENGER, M.D., PROFESSOR EMERITUS OF RADIOLOGY, UNIVERSITY OF CINCINNATI

Dr. SAENGER. Thank you, Mr. Chairman.

There is a great deal to respond to in this hearing, and I will begin by stressing the important points that we wish to bring out concerning our work.

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

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

The third and most important, treatment was given only if benefit to the patient was anticipated.

Patients were chiefly from the General Hospital. Selection was based only on the presence of advanced cancer and where no other therapy was considered to be as or more effective than the available chemotherapy.

Race, IQ or socioeconomic standing were not selection factors. Treatment was paid for by the 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. Patients were told that the treatment might help them and were cautioned that it might not. Some patients chose not to be treated.

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

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.

In addition, observations in laboratory tests were carried out to seek effects of radiation on cancer patients and on the changes that could be ascribed to radiation.

The background for this project originated in my observations over the previous 20 years that cancer patients treated with radiation might be benefited by more careful evaluation of the effects of this kind of treatment. 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.

Animal studies indicated better tumor regression by localized radiation followed by total body irradiation for lymphoma and carcinoma in mice. Human studies for treatment of advanced cancer, for far advanced solid tumors prior to 1960 suggested the value of total body radiation.

It was employed in several American medical centers and internationally. Treatment was given with success in relieving pain, shrinking tumors and, in some cases, prolonging survival.

A major reason that we could begin this work resulted from several developments. First, the cobalt 60 teletherapy unit was installed in General Hospital in 1958, the first in the State of Ohio.

Harold Perry, M.D., our first full-time radiation therapist, came from Memorial Sloan-Kettering Cancer Institute in New York and was familiar with total and partial body radiation techniques. James G. Kereiakes, Ph.D., a physicist, joined the department in 1959. He performed the calculations regarding the administration of the doses prescribed by the treating physician.

I believe that there could be implications of this treatment for 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. The Army recognized the importance of cancer therapy in this regard.

This proposal was reviewed by J. A. Isherwood, M.D., for the Army Medical Research and Development Command. And, to quote,

> 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.

Patients were not recruited. Patients were referred for this form of therapy mostly from the tumor clinic, outpatient or inpatient. I was not involved in patient selection or in determination of the extent of dose or the regions involved. These decisions were made solely by the attending physicians, internists and surgeons and by radiotherapists.

There were 24 patients entered into the study who were not given total or partial body irradiation. Some were rejected because it was thought the patient would not benefit. Several patients and their families declined treatment. Some were treated by other means.

In 1962, we developed for the DOD a document concerning the eligibility of patients for therapy—in 1962. And it stated,

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

Race was not a factor in selection, only the type of cancer and 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 the Cincinnati General Hospital.

Again, IQ was not a factor in patient selection.

The subject of informed consent—I believe we sort of fell in a period when there was a change in the general understanding of informed consent. In our study, informed consent for therapy was obtained by the attending physicians. In the 1940s and 1950s, informed consent was verbal, except for the general brief signed informed consent required by the hospital from all patients who were hospitalized for whatever services they required.

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, this project began the use of written informed consent 2 years before it was required in our medical center. It clearly indicated that the risks of treatment were discussed.

One criticism of our work stems from the instructions of the attend personnel not to inquire concerning nausea, vomiting and diarrhea in the first few days after treatment. Since both nausea and vomiting could be induced by suggestive questions, we requested

that no questions be asked as to how the patient felt within these first few days.

This restriction did not in any way restrict the administration of drugs such as Compazine to relieve symptoms. Of interest is that, after treatment, 44 percent of the patients who were treated had no nausea and vomiting, 27 percent noted it for three hours or less, and 14 percent had symptoms for 6 hours or less. These responses are comparable to chemotherapy at the time.

Funding. As noted earlier, most costs of treatment were paid by the Cincinnati General Hospital. This amounts to about $483,000. There were no professional costs or physicians fees for patient care. Some funding was obtained from the NIH through the General Clinical Research Center of our hospital, which was a unit funded by the NIH.

The records of each patient in the hospital on that service were submitted to the NIH and approved. In addition, several of the postgraduate fellows in another NIH training grant of our department participated in this study.

DOD funding was utilized solely for observation of patient symptoms and for the extensive laboratory tests carried out. 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 treatment.

The total DOD contract was about $671,000.

Mortalities. In the group of patients who received radiation there were three categories in which there were enough patients to compare with other patients in our hospital treated differently or with comparable groups described 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. This can be seen clearly in our 1973 paper and the graphs that are there.

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 disease, the patients received chemotherapy and/or local radiation therapy both before and immediately after total or partial body irradiation. 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 cancer itself.

There were 20 cases in which patients survived longer than 1 year. Except for the one patient with Ewing's sarcoma who remains alive after 25 years, the longest survivor lived 9 years. Two other relatively long survivors lived 5 years each.

Palliation was successful with relief of pain in 31 percent of patients. There was decrease in tumor size in 31 percent and an increase in well-being found in 30 percent. No change was observed in 31 percent.

Because of the radiation induced hematological depression, bone marrow storage and reinfusion began in 1964. With the improvement in techniques to include harvest of the marrow under general anesthesia and replacement immediately after total body irradiation, it became possible to avoid the characteristic depression of the white cells in five patients.

This promising development was stopped at the time of the termination of the contract. This pioneering use of bone marrow has been and is being used today.

Review by others. The UC Faculty Research Committee. Our protocol was submitted to this newly formed committee in March 1966. Provisional approval was given in 1967, with recommendations for review of therapeutic efficacy, bone marrow infusion as a supportive measure and some revisions in the study design. At no time was the project disapproved by the faculty research committee as it received exhaustive and critical reviews, and it was approved again in 1971.

The ad hoc committee of the University of Cincinnati began a complete review of this project in 1971. Among the findings were that phase III studies should be initiated with better criteria for the determination of palliative effects and that bone marrow transplantation should 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 a psychiatrist and psychologist, coupled with home visits.

The American College of Radiology. You have already heard of the three gentlemen who visited us. This distinguished group made two visits to our hospital. Their major findings were as follows:

One, the project is validly conceived, stated, executed, controlled and followed up.

Two, the patient's selection based on clinical consideration conforms with good medical practice.

Three, the records, publications, the patient-follow-up are voluminous and commendable.

Four, 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.

And, five, should this project come before the Senate or one of its committees in some fashion, we would urge your support for its continuation.

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 have 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 have not been borne by their agency. They stated also that funds of the Defense Nuclear Agency have 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 relevant to national defense.

From the National Institutes of Health, D.T. Chalkley, Ph.D., Chief, Office of Protection from Risks, 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 that they had."

Secrecy. This study received widespread publicity in the 1970's. We responded to all questions about it at the time, including an open press conference. The study resulted in 13 published papers, nine DASA reports and 24 scientific presentations.

What about the status of total body irradiation and partial body irradiation since 1971? It is apparently a common misunderstanding that the use of these methods of treatment for therapy has been discontinued. This statement is incorrect.

Doses. Our doses were at a low level of 100 to 200 rads total volume. I might state there—that in the documents that you have there is a typo. It says, 300. It should be 200. And up to 300 rads partial body radiation between 1960 and 1970.

In other centers, doses now range from 600 to 1,200 rads in single or divided doses of total body and with sequential hemibody radiation in these same dose ranges.

Fractionation, that is the splitting of these doses over a period of several days, has replaced single large doses of, say, 1,200 rads, because of the complication of radiation pneumonitis.

Among the solid tumors treated during these two decades have been cancers of the breast, prostate, lung, colon, and some sarcomas.

At the University of Cincinnati Department of Radiation Oncology, from 1979 on, total and partial body radiation were administered to adults and children for leukemias, lymphomas, cancers of the breast, prostate, and neuroblastoma.

Nationally, uses of total body and partial body irradiation have grown steadily since 1970 and are used more widely today than ever before.

To conclude this presentation of several decades, I speak to you as a survivor of cancer, having been treated with radiation and surgery.

Our work has contributed significantly to the better treatment of patients with far advanced cancer and to our better understanding of the effect of radiation on humans in a time when nuclear warfare once again seems possible.

Thank you.

Mr. BRYANT. Thank you, Dr. Saenger.

[The prepared statement of Dr. Saenger follows:]

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

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.

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.

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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

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)

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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.

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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-fluorouacil 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

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

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

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.

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CURRICULUM VITAE

EUGENE L. SAENGER, M.D.
PROFESSOR EMERITUS OF RADIOLOGY
UNIVERSITY OF CINCINNATI COLLEGE OF MEDICINE

Personal

Date of Birth: March 5, 1917

Place of Birth: Cincinnati, Ohio (Hamilton County)

Home Address: 9160 Given Road
Cincinnati, Ohio 45243
(513) 793-1373

Office Address: University of Cincinnati Hospital
234 Goodman Street - M.L. #569
Cincinnati, Ohio 45267-0569
Telephone: (513) 558-9042
Facsimile: (513) 558-4715

Married: Sue R. Saenger

Education:

A.B. - Cum Laude, Biochemical Sciences, Harvard University, 1938

M.D. - University of Cincinnati College of Medicine, 1942

Internship, Cincinnati General Hospital, 1942-43

Assistant Resident and Resident in Radiology, Cincinnati General Hospital, 1943-46

Diplomate, American Board of Radiology, 1946

Diplomate, American Board of Nuclear Medicine, 1972

Appointments

Professor Emeritus of Radiology, University of Cincinnati College of Medicine, September 1987

Professor of Radiology, University of Cincinnati College of Medicine, 1962-1987

Director, Eugene L. Saenger Radioisotope Laboratory, University of Cincinnati College of Medicine, 1950-1987

Vice-Chairman, Department of Radiology, University of Cincinnati College of Medicine, 1975-1987

Assistant and Associate Professor of Radiology, University of Cincinnati College of Medicine, 1949-1962

Radiation Therapist, Children's Hospital Medical Center, Cincinnati, Ohio, 1947-Present

Major, U.S. Army Medical Corps; Chief, Radioisotope Laboratory, Brooke Army Hospital, Ft. Sam Houston, Texas, 1953-1955

Consultant in Radiology, Brooke Army Hospital, Ft. Sam Houston, Texas, 1956-1977

Consultant, Oak Ridge Operations Office, Division of Biology, U.S. Atomic Energy Commission, Oak Ridge, Tennessee, 1958-Present

Consultant, Division of Compliance, U.S. Atomic Energy Commission (now U.S. Nuclear Regulatory Commission), Washington, D.C., 1962-1987

Consultant in Radiology, Lackland AFB Hospital, Lackland AFB, Texas, 1959-1975

Consultant, Radiological Health Research Activities, USPHS, Taft Engineering Center, 1964-1969

Consultant, Medical Advisory Committee, Defense Atomic Support Agency, Washington, D.C., 1965-1971

Representative for State of Ohio to the Medical Liaison Officer Network, Environmental Protection Agency, 1968-1984

Consultant on Radiology Training, DHEW/PHS, National Institute of General Medical Sciences, NIH, Bethesda, Maryland, 1967-1970

Consultant to the Office of the Director, DHHS/PHS/FDA, Center for Devices and Radiological Health, Rockville, Maryland, 1969-Present

Consultant, Radiation Bio-Effects and Epidemiology Advisory Committee, DHEW/PHS, Washington, D.C., 1970-1971

Consultant, Radiation Science & Protection Fellowship Board, Oak Ridge Associated Universities, Oak Ridge, Tennessee, 1970-Present

Consultant to Surgeon General, U.S. Air Force, in Nuclear Medicine, 1970-1975

Consultant, Wright-Patterson Air Force Base, Ohio, 1977-Present

Board of Directors, Center of Science and Industry, Cincinnati, Ohio, 1964-1969

Chairman, Radiation Safety Committee, University of Cincinnati, 1964-1985; Member, 1985-1989

Board of Trustees, Community Chest & Council, Cincinnati, Ohio, 1964-1970; Executive Committee, 1970

President, Public Health Federation, Cincinnati, Ohio, 1965-1969

Executive Committee, Health Planning Association of the Central Ohio River Valley (CORVA), 1970-1972

Environmental Health Planning Committee of the Central Ohio River Valley (CORVA) 1970-1972

Advisory Committee to the Federal Radiation Council, National Academy of Sciences, Washington, D.C., 1964-1972

Associate Editor, Journal of Nuclear Medicine, 1960-1970

Program Director in Radiological Sciences (National Cancer Institute and National Institute of General Medical Sciences, NIH) Training Program, University of Cincinnati, 1959-1970

Program Director for studies in metabolism of radiation following whole-body irradiation (Department of Defense) 1960-1971

Co-investigator, Biomedical Computing Center, University of Cincinnati College of Medicine, 1962-1966

Chairman, Cancer Control Council, Public Health Federation, Cincinnati, Ohio, 1961-1968

Board of Directors, Cancer Control Council, Cincinnati, Ohio, 1964-1970

Board of Governors, Ohio Valley Chapter of the Arthritis and Rheumatism Foundation, 1961-1968

Board, Hamilton County Chapter of the American Cancer Society, 1963-1967

Governor's Advisory Board on Atomic Energy, State of Ohio, 1963-1972

Member, Medical Advisory Committee to Department of Health, State of Ohio, 1962-1969

Member, Honorary Editorial Advisory Board of the Journal of Applied Radiology, 1972

Radiation Research Society, Member - Finance Committee, 1977-1981

Health Physics Society, Chairman - Legislation Committee, 1968-1969

Health Physics Society, Member - Board of Directors, 1966-1969

National Committee on Radiation Protection, National Bureau of Standards, Member Subcommittee on Radium, Cobalt-60 and Cesium-137, 1952-1965

National Council on Radiation Protection and Measurements (NCRP), Board of Directors, 1967-1983; Honorary Member status 1983

NCRP, Member - Subcommittee for Revision of Handbook 73, 1966

NCRP, Chairman - Budget and Finance Committee, 1968-1973

NCRP, Chairman - Scientific Committee #29 on Brachytherapy Devices, 1968-1972

NCRP, Chairman - Ad Hoc Thyroid Blocking Committee, 1972-1978

NCRP, Member - Scientific Committee #44 on Radiation Associated with Medical Examinations, 1973-Present

NCRP, Chairman - Resources Development Program, 1986-1990

American Roentgen Ray Society, Representative to the National Council on Radiation Protection and Measurements, 1960-Present

Society of Nuclear Medicine, Member - Board of Directors, 1966-1969

Society of Nuclear Medicine, Member - Radiation Protection Committee, 1966-1969

Society of Nuclear Medicine, Chairman - Subcommittee on Post Graduate Training in Nuclear Medicine, 1969-1971

Society of Nuclear Medicine, Member - By-Laws Committee, 1969-1972

Society of Nuclear Medicine, Member - Committee on Education and Training, 1969-1971

Society of Nuclear Medicine, Chairman - Committee on Public Health and Efficacy, 1972-1984; Member, 1984-1987

Society of Nuclear Medicine, Member - Subcommittee on Risks of Low Level Ionizing Radiation, 1980-Present

Society of Nuclear Medicine, Principal Investigator - U.S. Department of Energy Contract, "The Efficacy of Clinical Diagnostic Procedures Utilized in Nuclear Medicine", 1977-1983

5

American College of Radiology, Member - Subcommittee on Radiological Aspects of Disaster Planning, 1964-1969

American College of Radiology, Member - Commission on Radiologic Units, Standards, and Protection, 1969-1988; Chairman, 1989-Present

American College of Radiology, Chairman - Committee on Research and Development in Nuclear Medicine, 1969-1972

American College of Radiology, Member - Commission on Public Health, 1969-1971

American College of Radiology, Member - Subcommittee on Nuclear Medicine Technology, 1969-1975

American College of Radiology, Member - Committee on Quality Assurance and Efficacy, 1972-Present

American College of Radiology, Member - Committee on Radiation Physics, 1977-1982

American College of Radiology, Member - Commission on Nuclear Medicine, 1977-1986

American College of Radiology, Member - Medical Legal Committee, 1986-Present

National Consultant, Office of the Radiation Safety Officer of the Veterans Administration, 1974

Member, Ad Hoc Committee to Evaluate the Health and Safety Aspects of ^{238}Pu in the Environment Adjacent to the Mound Laboratory, 1975

Argonne National Laboratory, Member - Review Committee for the Radiological and Environmental Research Division, 1976-1977

International Commission on Radiological Protection, Member - Committee #3 on Protection in Medicine, 1977-1984

Federated Council of Nuclear Medicine Organizations, Representative - American College of Nuclear Physicians, 1977-1980

Federated Council of Nuclear Medicine Organizations, Secretary-Treasurer, 1978-1980

BEIR Report (The Effects on Populations of Exposure to Low Levels of Ionizing Radiation), National Academy of Sciences, National Research Council, Member of Committee, 1972

Reactor Safety Study (WASH-1400), An Assessment of Accident Risks in U.S. Commercial Nuclear Power Plants, Appendix IV, United States Nuclear Regulatory Commission, October 1975, Member-Advisory Group on Health Effects

Consultant, Pan American Health Organization, World Health Organization, Mexico City, Mexico, December 1980

Co-founder and President, Society for Medical Decision Making, September 1979; Historian 1979-1985

Member, Oversight Committee on the Radioepidemiologic Tables (OCRET), National Research Council, Commission on Life Sciences, August 1983-January 1985

Member, U.S. Department of Energy Ad Hoc Committee on Neutron Quality Factor, January-December 1985

Chairman, Advisory Committee of the Charles M. Barrett Cancer Center, University of Cincinnati, 1984-1986

Health Effects Model for Nuclear Power Plant Accident Consequence Analysis, (NUREG/CR-4214) Prepared by Sandia National Laboratories, Albuquerque, NM for the Division of Risk Analysis and Operations, U.S. Nuclear Regulatory Commission, July 1985, Member, Advisory Committee

Consultant, 7th Medical Command, U.S. Army, Heidelberg, West Germany, May 1986

Member, AMA Committee on Non-Military Radiation Emergencies, August 1986; conference November 19-21, 1986

Director, Region I, Cancer Control Consortium of Ohio (CCCO), 1985-1989

Honorary member, Medical Academy of SR Croatia, February 1988

Ad Hoc Consultant to:
- U.S. Department of Justice
- U.S. Department of Energy
- U.S. Environmental Protection Agency
- U.S. Department of Defense
- U.S. Department of Health and Human Services, Food and Drug Administration

International Atomic Energy Agency
Member, Expert Committee of IAEA to the USSR to evaluate the late effects of Chernobyl, July 1990

Marquis' Who's Who

American Men and Women of Science

Lectureships:

Annual Oration, "Radiologists, Medical Radiation and the Public Health", presented at the Radiological Society of North America, Chicago, Illinois, December 4, 1968

Aubrey O. Hampton Lecture, "Radiation 1971 - Just How Safe?", Harvard Medical School, Massachusetts General Hospital, Boston, April 4, 1971

Wright H. Langham Memorial Lecture, "Radiation Accidents - 3 Decades of Facts and Fancies", University of Kentucky Medical Center, Lexington, Kentucky, November 15, 1977

Annual Failla Lecture, "Benefits vs Risks of Medical Radiation: New Concepts and Problems", presented to the Greater New York Chapter of the Health Physics Society, Columbia University, New York, December 7, 1977

Brookhaven National Laboratory, "'Safe' Tracer Dose in Human Experimentation", Islip, New York, April 7, 1978

Tenth Annual Conference on Radiation Control, "Efficacy of Nuclear Medicine Procedures", Harrisburg, Pennsylvania, April 30-May 4, 1978

Harvard University School of Public Health, Planning for Nuclear Emergencies, (seminar), "Medical-Legal Aspects of Radiation Exposure", Boston, Massachusetts, May 8-12, 1978 (through 1986)

Society of Nuclear Medicine Refresher Course, "Radiation Effects and Radiation Protection", Anaheim, California, June 1978

Radiological Society of North American Refresher Course, "Recent Advances in Radiation Epidemiology", Chicago, Illinois, November 1978 (repeated 1979, 1980)

Food and Drug Administration, Bureau of Radiological Health, "Efficacy Studies in Lung Scanning: Design and Implementation", Rockville, Maryland, March 20, 1979

Armed Forces Radiobiological Research Institute (AFRRI), "The Experienced Effects of Ionizing Radiation on the Body", Bethesda, Maryland, May 23, 1979

Guest Lecturer, "Efficacy and Efficiency of the Diagnostic Application of Radiation and Radionuclides", organized by the Government of the Federal Republic of Germany and the World Health Organization, Neuherberg, West Germany, December 5-7, 1979

Literary Club, "Perceptions of Risk", Cincinnati, Ohio, February 18, 1980

Society of Nuclear Medicine Continuing Education Course, "Nuclear Power, Nuclear Medicine and the Public", Detroit, Michigan, June 25, 1980

Guest Lecturer, "Low Level Radiation Risks", University of Texas Health Science Center, Houston, Texas, July 25, 1980

Guest Lecturer, Nuclear Radiation Risks - A Utility-Medical Dialogue, "Case Histories of Lawsuits for Overexposure", sponsored by the International Institute of Safety and Health, Washington, D.C., September 22-23, 1980

"Hospital Preparation for the Management of Radiation Accidents", course presented by the E.L. Saenger Radioisotope Laboratory, September 29-30, 1980 (repeated September, 1981)

Guest Lecturer and Banquet Address, Los Alamos Scientific Laboratory, Life Sciences Symposium, "Medical Aspects of Radiation: Radiation Burns", Los Alamos, New Mexico, October 8-10, 1980

"Aspects of Nuclear Medicine", Medical Society of the District of Columbia Annual Scientific Assembly, White Sulphur Springs, West Virginia, October 24-26, 1980

Society of Nuclear Medicine Refresher Course, "What Nuclear Medicine Professionals Should Know About Nuclear Warfare", Las Vegas, Nevada, June 17, 1981

Guest Lecturer and Member of Faculty, "Regional Seminar on General Procedures to Manage Persons Receiving Whole or Partial Body Irradiation", co-sponsored by the Pan American Health Organization and the Government of Brazil, Itaipava, Brazil, December 11-22, 1982

Guest Lecturer, "The Role of the Physician in Medico-legal Claims Associated with Radiation Injury", sponsored by the Pacific-Sierra Corporation, in Albuquerque, New Mexico, March 4-6, 1982

Sixth Annual Lauriston S. Taylor Lecture, "Ethics, Trade-Offs and Medical Radiation", presented to the National Council on Radiation Protection and Measurements, Washington, D.C., April 6, 1982

"High Level Radiation", invited Grand Rounds presentation, Hamot Medical Center, Erie, Pennsylvania, April 29, 1982

Guest Lecturer, "Medical Management of Radiation Injuries", sponsored by the Radiation Management Corporation of Philadelphia, in Atlantic City, New Jersey, May 6, 1982

Guest Lecturer, "Medical Management of Radiation Casualties", sponsored by the REMS Corporation of Albuquerque, in South Haven, Michigan, May 24-26, 1982

Society of Nuclear Medicine Continuing Education Course, "ALARA - What is Reasonable", Miami Beach, Florida, June 17, 1982

"Diagnostic Efficacy - Lung Imaging as a Model. The Society of Nuclear Medicine Efficacy Study", 29th Annual Meeting of the Society of Nuclear Medicine, Miami Beach, Florida, June 15-18, 1982

Guest Lecturer, A Symposium: Health Aspects of Nuclear Power Plant Incidents, "Regional Organization of Medical Care", sponsored by the New York Academy of Medicine and the New York State Department of Health, New York, New York, April 7-8, 1983

Guest Lecturer, 23rd Annual Symposium on Trauma, "Irradiation Trauma", sponsored by the Michigan Committee on Trauma, The American College of Surgeons, Lakeshore Continuing Medical Education, Inc. and Muskegon County Medical Foundation, Muskegon, Michigan, September 21, 1983

Guest Lecturer, International Conference on Nuclear Medicine, "Efficacy Analysis in Nuclear Medicine - Lung Scanning as a Model" and "Potentials for TC-99m Myocardial Imaging Agents", Rhodes, Greece, April 24-29, 1984

Guest Lecturer, Medical/Legal Aspects of Radiation Induced Cancer, "Impact of Compensation Legislation on Medical Sciences", sponsored by the Radiation Management Corporation, Philadelphia, Pennsylvania, September 5-7, 1984

Guest Lecturer, "Probability of Causation", sponsored by Electric Boat Company, Groton, Connecticut, May 14, 1985

Guest Lecturer, "Determination of Clinical Efficacy: Nuclear Medicine as Applied to Lung Scanning", sponsored by University of Connecticut, Farmington, Connecticut, May 15, 1985

Guest Lecturer, Medical Aspects of Radiation Emergencies, "New Trends in Triage and Treatment of the Accident Victim", sponsored by Yale University School of Medicine, Lawrence & Memorial Hospitals, New London, Connecticut, May 16, 1985

Guest Lecturer, Emergency Planning and Response, "Case Studies of Radiation Accidents" and "Legal Implications: Long Term Risk and Compensation", Health Physics Summer School, Evanston, Illinois, June 3-7, 1985

Guest Lecturer, 1985 International Congress of Radiology, "Efficacy and Cost Effectiveness of Diagnostic Tests: Lung Scans for Pulmonary Embolism", "Medical-Legal Problems for the Radiologist as a Consultant"; also served as co-moderator of session entitled "Decision Making and Image Selection", Honolulu, Hawaii, July 8-12, 1985

Guest Lecturer, Advanced Management of Radiation Accidents, "Early Medical Decisions", and "Legal Aspects-A Physician's View" sponsored by the University of New Mexico School of Medicine, Albuquerque, New Mexico, October 3-5, 1985

Guest Lecturer, Toxicology: Basic Science and Clinical Research, "New Thoughts About Radiation Accidents", sponsored by the University Association for Emergency Medicine and the International Research Institute for Emergency Medicine, San Francisco, California, February 13-14, 1986

Guest Lecturer, "Should There Be a Limit of Patient Exposure Based on Risk?", sponsored by Brookhaven National Laboratory, Upton, L.I., New York, April 7, 1986

Guest Lecturer, "Nuclear Accident Management", Society of Nuclear Medicine Annual Meeting refresher course, presented in June of 1986, 1987 and 1988

Guest Lecturer, "Acute Effects of Radiation", International Conference on Non-Military Radiation Emergencies, sponsored by the American Medical Association, Washington, D.C., November 19-21, 1986

Recipient of the 28th George Charles de Hevesy Nuclear Pioneer Award, presented at the 34th Annual Meeting of the Society of Nuclear Medicine, Toronto, Ontario, Canada, June 2, 1987

Co-chair, Special Session: Chernobyl, "Diagnosis and Treatment of Acute Radiation Injury", presented at the Health Physics Society Annual Meeting, Salt Lake City, UT, July 5-10, 1987

Keynote address, Physician's Role in Nuclear Mass Casualties: Applications of the Chernobyl Experience, "The Physician's Role in Nuclear Energy", sponsored by the Department of Radiation Therapy, Hospital of the University of Pennsylvania and Radiation Management Consultants, Cincinnati, OH, September 11-13, 1987

Guest Lecturer, "Benefit, Risk and Cost-Effectiveness in Medical Radiation", sponsored by the U.S. Food and Drug Administration, Center for Drug Evaluation and Research, Rockville, MD, October 28, 1987

Recipient of the Daniel Drake Award, the most prestigious award given by the University of Cincinnati College of Medicine for outstanding contributions to medicine and science, June 1988

Amy Bowles Lawrence Distinguished Scientist in Research Medicine, at the Donner Laboratory and the Lawrence Berkeley Laboratory of the University of California, Berkeley, CA, June 13-15, 1988 (Dr. Saenger was the inaugural Lawrence Lecturer)

Clarence C. Lushbaugh Lecture on Controversial Radiation Concepts, "The NIMBY Syndrome", at the Oak Ridge Associated Universities, Oak Ridge, TN, October 21, 1988 (Dr. Saenger was the inaugural Lushbaugh Lecturer)

Guest Lecturer, Topics in Radiological Health for Physicians, "Medical Management of Irradiated Patients", sponsored by the Medical College of Ohio, Toledo, OH, January 19-20, 1990

Guest Lecturer, "Is the Environment Around DOE Plants as Hazardous as Represented?", sponsored by the Eastern Chapter, Health Physics Society, Oak Ridge, TN, March 20, 1990

Guest Lecturer, Occupational Health in Nuclear Facilities, "Counseling the Radiation Worker and Family", sponsored by REAC/TS, Oak Ridge Associated Universities, Oak Ridge, TN, August 17, 1990

Guest Lecturer, Clinical Approaches to Medicine in the Nuclear Industry, "Medical Management of the Irradiated Patient", sponsored by Radiation Management Consultants, held in Orlando, FL, October 11, 1990

Guest Lecturer, 26th Radiology Congress of the German Democratic Republic, "Acute Local Radiation Injury", "Diagnosis and Treatment of the Acute Radiation Syndrome" and "Late Effects from Radiation", Heringsdorf, East Germany, October 23-24, 1990

Guest Lecturer, Soviet Refugee Health and Mental Health: Twenty Years of Soviet Resettlement, "Chernobyl: Fallout Revisited", sponsored by the Office of Refugee Health, Office of the Assistant Secretary of Health, DHHS, Chicago, IL, December 10-12, 1991

Guest Lecturer, Radiation Protection in Medicine, "Implications of the New Risk Estimates". Annual meeting of the National Council on Radiation Protection and Measurements, Arlington, VA, April 1-2, 1992

"Medico Legal Issues Associated with Ionizing Radiation", presented at the annual meeting of the American Roentgen Ray Society, San Francisco, California, April 25-30, 1993

Recipient of the 1993 Gold Medal of the Radiological Society of North American (RSNA), the highest honor of the Society, presented at the RSNA Annual Meeting, Chicago, Illinois, November 30, 1993

Professional Societies:

Academy of Medicine of Hamilton County
Alpha Omega Alpha
American Association for the Advancement of Science
American College of Nuclear Physicians
American College of Radiology
American Medical Association
American Radium Society
American Roentgen Ray Society
Cincinnati Radiation Society
Greater Cincinnati Radiological Society
Health Physics Society
Ohio State Medical Association
Ohio State Radiological Society
Radiation Research Society
Radiological Society of North America
Sigma Xi
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Society of Nuclear Medicine
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Office Memorandum • UNITED STATES GOVERNMENT

MEDDH-SP

TO : Chief, Radiological Service
Walter Reed Army Medical Center

DATE: 20 October 1958

FROM : Asst Chief, Biophysics and Astronautics Research Branch, U. S. Army Medical Research and Development Command

SUBJECT: Application for Research Contract

1. The inclosed copy of research proposal entitled, "Metabolic Changes in Humans Following Total Body Radiation," has been submitted for our consideration by Dr. Eugene L. Saenger of the University of Cincinnati, College of Medicine, Cincinnati, Ohio.

2. Request review of the attached proposal and please give your recommendation as to whether or not this study should be supported by the Army Medical Service.

1 Incl
OTSG Form 108

ARTHUR D. SULLIVAN
Lt Colonel, MSC

MEDDR

TO: Asst Ch, Biophysics & Astronautics Research Branch, US Army Medical Research & Development Command

FROM: Chief, Radiological Svc, WRAH

DATE: 22 Oct 195[illegible]
Collsherwood/rk/6[illegible]

1. Recommend approval.

2. Much work has been done on the effects of total body irradiation in animals. There has been no real effort to date for similar studies on humans. The validity of the assumption that animal reaction is identical with that in humans is purely assumption. There is definite need for basic work in this field. 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. The applicant, Dr. Saenger, is well qualified to conduct such research. He is not only an enthusiastic and tireless worker but has the ability to stimulate his co-workers and assistants. He has an unusual analytical mind and is an excellent organizer and administrator. I believe the facilities which he has available are well adapted to the project. It is believed that any funds spent on such a project are well worthwhile.

1 Incl
n/c

JOHN A. ISHERWOOD
Colonel, MC
Chief, Radiological Service

CONSENT FOR SPECIAL STUDY AND TREATMENT

I,_____, do hereby give my consent to the members of the professional staff of the Cincinnati General Hospital, University of Cincinnati College of Medicine, to administer to me whole or partial body irradiation on or about_____, 196__.

The nature and purpose of this therapy, possible alternative methods of treatment, the risks involved, the possibility of complications, and prognosis have been fully explained to me. The special study and research nature of this treatment has been discussed with me and is understood by me.

Consent is given for photographs and publication for the advancement of medical education.

_____
Signature

Witnesses to signature:

_____

_____

Relationship_____
(patient or guardian)

Date_____ AM / PM_____
(Mo. Day Yr.)

Place_____
(Ward - Clinic - Unit)

Chart No._____

Original: to patient's chart
Copies: to Co-60 file
to TBR file

5/1/65

CONSENT FOR SPECIAL STUDY AND TREATMENT

I,_____, do hereby give my consent to the members of the professional staff of the Cincinnati General Hospital, University of Cincinnati College of Medicine, to perform a bone marrow aspiration and to store my bone marrow on or about _____, 196___.

The nature and purpose of this therapy, the risks involved, the possibility of complications, and prognosis have been fully explained to me. The special study and research nature of this treatment has been discussed with me and is understood by me.

Consent is also given for reinfusion (giving the marrow back to me) when the members of the professional staff recommend it.

Consent is given for photographs and publication for the advancement of medical education.

_____
Signature

Witnesses to signature:

_____

_____

Relationship_____
(patient or guardian)

Date_____ AM PM_____
(No. Day Yr.)

Place_____
(Ward - Clinic - Unit)

Chart No._____

Original: to patient's chart
Copies: to Co-60 file
to TBR file

5/1/65

UNIVERSITY OF CINCINNATI MEDICAL CENTER
FACULTY COMMITTEE ON RESEARCH
VOLUNTARY CONSENT STATEMENT

*I_____ of _____
(Patient) · (normal subject) (place - city)

being of the age of majority and of sound mind and body, voluntarily and without force or duress, consent to participate in a scientific investigation which is not directed specically to my own benefit, but in consideration for the expected advancement of medical knowledge, which may result for the benefit of mankind.

I have been informed of and understand the nature, duration, and purpose of the study, the method and means by which it is to be conducted, the inconvenience and hazards to be expected, and the effects upon my health and person which may possibly come from participation in the experiment, as follows:

Purpose: To kill tumor cells and at the same time study the effects of radiation on blood and urine:

Procedure: Radiation of the whole body.

Risks: The chance of infection or mild bleeding to be treated with marrow transplant, drugs, or transfusion as needed.

I understand that I may, at any time during the course of the experiment, revoke my consent, in writing, and withdraw from the experiment.

I acknowledge that no guarantee or assurance has been made to me as to the results that may be obtained, and I hereby waive any and all claims for liability, except for negligence, on the part of the medical personnel involved, the University of Cincinnati, its Hospital and its Medical School, which otherwise might have inured to me or my heirs, as a result of this medical procedure.

I certify that I have read and am competent to fully understand this consent and that the explanations listed above were, in fact, made.

Volunteer_____ Date_____

Investigator_____ Date_____

Witness (1)_____ Date_____

*In case of subject under age, the parent or guardian should be the responsible party and should sign on his behalf.

NOTE: Copy to Patient/normal subject, Research File and Patient's Chart.

I certify that I have read and am competent to understand this consent and that the explanation listed above was, in fact, made.

Volunteer_____ Date_____

Investigator_____ Date_____

Witness (1)_____ Date_____

* Incase of subject under age, the parent or guardian should be the responsible party and should sign on his behalf.

NOTE: Copy to Patient/Normal subject, Research File and Patient's Chart.

FACULTY COMMITTEE ON RESEARCH
VOLUNTARY CONSENT STATEMENT

*I_____of_____
(Patient) (Normal subject)

being of the age of majority and of sound mind and body, voluntarily and without force or duress, consent to participate in a scientific investigation which is not only directed specifically to my own benefit, but also in consideration for the expected advancement of medical knowledge, which may result for the benefit of mankind.

I have been informed of and understand the nature, duration, and purpose of the study, the method and means by which it is to be conducted, the inconvenience and hazards to be expected, and the effects upon my health and person which may possibly come from participation in the experiment, as follows:

Purpose: To kill tumor cells and at the same time study the effects of radiation on blood and urine.

Procedure: Radiation of the whole body.

Risks: Radiation treatment employed is used to kill tumor cells but at the same other, normal, cells of your body will be affected. The only cells affected which would cause any risk to you are those cells in your bone marrow. The bone marrow is a "blood factory" where white cells that fight infection, the platelets which help blood clot, and the red cells which carry oxygen to your tissues are made. The bone marrow's ability to make these cells will be decreased for four or five weeks after you receive your radiation. If you receive a dose of radiation of 200 rads or more, which your doctor will tell you, your blood counts will fall to levels where infection or bleeding could be a problem. The bleeding can be treated by transfusion of red cells and platelets and the infection by antibiotics. In addition, we prevent such low blood counts with the use of a bone marrow transplant which will be discussed with you in a separate voluntary consent statement. If your radiation dose is only given to part of the body there is no risk of danger or unusually low blood counts.

I understand that I may, at any time during the course of the experiment, revoke my consent, in writing, and withdraw from the experiment.

I acknowledge that no guarantee or assurance has been made to me as to the results that may be obtained, and I hereby waive any and all claims for liability, except for negligence, on the part of the medical personnel involved, the University of Cincinnati its Hospital and its Medical School, which otherwise might have inured to me or my heirs, as a result of this medical procedure.

I certify that I have read and am competent to understand this consent and that the explanation listed above was, in fact, made.

Volunteer_____ Date_____

Investigator_____ Date_____

Witness (1)_____ Date_____

* Incase of subject under age, the parent or guardian should be the responsible party and should sign on his behalf.

NOTE: Copy to Patient/Normal subject, Research File and Patient's Chart.

BIOCHEMICAL AND BIOLOGICAL TESTS FOR PATIENTS UNDERGOING TOTAL BODY IRRADIATION AND PARTIAL BODY IRRADIATION

Pre and Post Radiation Observations*

1. Complete history and physical examination
2. Hematocrit, hemoglobin, leukocyte count and differential
3. Electrocardiogram, chest X-ray, urinalysis
4. Sequential multiple analyses (SMA-12) for blood chemistry determination, prothrombin time, creatinine phosphokinase levels, partial thromboplastin time
5. Blood and urine amylase
6. Ultraviolet absorbing compounds in urine
7. Bone marrow aspiration
8. Blood typing and cross matching if bone marrow transfusion is to be done
9. Tritiated thymidine uptake for lymphocyte viability
10. Histochemistry and electron microscopy of bone marrow pre and post etiocholanolone
11. Chromosome analysis
12. Nitroblue tetrazolium study of granulocyte function
13. Serum glycoprotein assay
14. Serum amino acid assay
15. Bacteriophage titers

16. Urinalysis for hydroxyproline levels
17. Psychological testing
18. Urinary taurine for correlation with leukocyte count
19. BAIBA in urine
20. Kynurenic and xanthurenic acids
21. Deoxycytidine
22. Xanthine and hypoxanthine in urine.
23. Urinary phosphate
24. Glutathione
25. Routine electrophoresis and immunoelectrophoresis
26. Quantitative precipitin studies

- These observations and tests have varied as some tests do not seem useful and new ones suggest that they may be valuable.

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WHOLE BODY AND PARTIAL BODY RADIOTHERAPY OF ADVANCED CANCER*

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THE purpose of these investigations has been to improve the treatment and general clinical management and if possible the length of survival of patients with advanced cancer. Systemic effects of radiation therapy have been given particular attention in our work.

In the period February 19, 1960, through August 31, 1971, 85 adults were given whole or partial body radiation as therapy for far advanced cancer.

This paper will report on the survival of patients in 3 categories: colon; lung; and breast.

Prophylactic whole body radiation therapy was given to 3 children with localized Ewing's sarcoma and this experience will be discussed briefly.

Investigations of biochemical, cytologic and psychologic tests have been reported elsewhere.[8,11,50]

Our experience with the adjuvant use of autologous bone marrow will also be described.

ANIMAL STUDIES

The animal investigations basic to our work stem from the studies of Hollcroft *et al.*[13–16] These authors demonstrated better tumor regression when whole body irradiation was preceded by localized radiation therapy than when localized radiation therapy was given alone both for lymphoma and carcinoma in mice. The studies of Jacobson *et al.*[18,19] showed the importance of shielding of the spleen and other organs and parts of the body in preventing high dose radiation lethality in the mouse.

BRIEF REVIEW OF TOTAL BODY IRRADIATION IN MAN

Total body irradiation was first employed in 1923 by Chaoul and Lange.[7] Its use in 270 cases over the next 20 years was reviewed by Medinger and Craver.[32] These authors found the greatest palliation in the lymphomas and myeloproliferative diseases, but also noted improvement in multiple myeloma. Thirty-five patients with advanced carcinoma or sarcoma were included in this series, most of them receiving their total body radiation between 1931 and 1933.

Loeffler *et al.*[30] compared total body irradiation in single doses up to 150 r with nitrogen mustard and triethylene melamine and found that neither chemotherapy nor radiotherapy differed in hematologic effects, but that the patients receiving radiation did not experience the malaise of varying severity noted by all patients receiving the chemotherapeutic agents. Subjective improvement was noted only in the radiotherapy group.

Collins and Loeffler[9] gave total body irradiation in single exposure up to 200 roentgens and found this form of systemic therapy "a useful addition to the management of advanced cancer." The malignancies treated included lymphoma, chronic

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myelogenous leukemia and multiple myeloma.

Interest in total body irradiation in the treatment of Ewing's sarcoma, a tumor of children which carries a high mortality, has been aroused by reports from Milburn *et al.*,[22] Jenkins *et al.*,[21] and Rider and Hasselback.[19] In a small series so treated, survival appeared to be moderately improved compared to larger series treated by conventional local radiotherapy and/or ablative surgery. These groups felt further evaluation of this form of therapy to be most important.

Additional data have been published by the Medical Division of Oak Ridge Associated Universities,[1] concerning total body radiation therapy of lymphoproliferative and myeloproliferative disease.

Summaries of the frequent use of total body irradiation for the therapy of leukemia appear in an article by Buckner *et al.*[4] and in a comprehensive review of bone marrow transplantation by Bortin.[3]

Whole body radiation in routine clinical therapy has been and is currently used for leukemia,[22,23] lymphoma,[23–26,33] Hodgkin's disease,[2] polycythemia vera,[6] cancer of breast,[31] cancer of thyroid,[8] cancer of prostate,[10,21] and multiple myeloma.[8,22] Such therapy may be given by external radiation therapy (as in this particular study) or in the form of various radionuclides.

STUDY DESIGN

The studies reported here were initially considered as being in Phase I (to determine whether the treatment was toxic or not) and subsequently as Phase II (whether treatment appears effective or not but without controls). In reviewing these data it has been possible to find some comparable material in the literature. In one category, cancer of bronchus, comparable data were available in our institution.

INFORMED CONSENT AND INSTITUTIONAL REVIEW

All patients gave informed consent in accordance with directives of the Faculty Research Committee of the University of Cincinnati College of Medicine and those of the National Institutes of Health. The use of formal informed consent forms in this study antedated the above requirements by 2 years. The project is reviewed and approved regularly by the above Committee.

ELIGIBILITY OF PATIENTS

Patients become eligible for this form of treatment if they have advanced cancer for which cure could not be anticipated. Three children with localized Ewing's tumor at Children's Hospital were given whole body radiation as part of the curative attempt after the primary tumor had been ablated with local radiotherapy.

Biopsy proof of the malignancy has been established in all instances. Clinical data in each case have been reviewed by several physicians to be certain that the tumor had indeed extended from its primary site and that curative therapy was not applicable. This preliminary evaluation is followed by an observation period of 7–14 days to observe the general condition of the patient and to carry out baseline laboratory tests to be as certain as possible that the condition of the patient is relatively stable. Frequently this determination is difficult since the patients have serious illnesses of long standing and often have had considerable previous therapy.

Patients remain in the hospital as long as is necessary. Prior to the use of autologous bone marrow transfusion, hospitalization was occasionally as long as 8–10 weeks. Length of stay was also dependent upon the severity of the clinical manifestations stemming from the cancer. With the use of partial body irradiation and bone marrow infusion, hospitalization has been greatly shortened. The follow-up procedure is continuous during the lifetime of the patient.

A total of 112 subjects were initially entered in the study through August 31, 1971. During the screening period of 7–14 days, 24 of them (21 per cent) were not continued in the study and did not receive whole or partial body irradiation. Chief

among the reasons for elimination was an indication in the pretreatment phase that some risk from wide-field radiation might ensue or that another method of treatment was considered preferable. In some, a very rapid progress of the disease made inclusion undesirable. The treatment was completed in 85 adults and 3 children between April 1960 and August 31, 1971. Three patients have received 2 separate courses of treatment in this program. Follow-up time for survivors is reported through August 31, 1972.

PATIENT DOSIMETRY

The radiation is delivered by a cobalt 60 teletherapy unit under the following exposure conditions: The beam is directed horizontally at a wall 342 cm. away with the midline of the patient at 286 cm. from the source. For whole body exposures, the radiation beam size for the 60 per cent isodose curve at the patient midline distance is a square approximately 120 cm.×120 cm. The patient is placed in the sitting position with legs raised and head tilted slightly forward. Radiation is given by delivering half the specified exposure laterally through one side of the patient, the patient is then turned and the other half exposure delivered laterally through the other side. The combined dose of the 2 radiation fields provides a good homogeneous dose distribution through the patient. The maximum variation in lateral dose distribution was ±13 per cent for 1 patient who had a lateral trunk dimension of 36 cm.

The exposure to the patient is determined using a percentage depth dose table corrected for the source-to-skin distance used for the patient. Using the corrected depth dose at patient midline (1/2 lateral dimension at the trunk in the plane of the xiphoid) and a conversion factor of 0.957 rads/roentgen for cobalt 60 gamma radiation, the midline air exposure required to give a desired midline absorbed dose in rads is calculated. The validity of this procedure was established with measurements in an Alderson Rando Phantom using thermoluminescence dosimeters. Over the course of the study, the air exposure rates at the distance indicated above varied from 3 to 6 per minute.

For individuals receiving partial body radiation, the teletherapy collimator is used to restrict the beam. The xiphoid is used as the boundary of the field for upper and lower body exposures. The lateral dimensions of the patient in the plane of the xiphoid is again used for calculating the desired midline dose. As for the whole body exposure, the dose is delivered bilaterally. Additional information on the dosimetry aspects of this study has been published by Kereiakes *et al.*[27]

ANALYSIS OF SURVIVAL DATA

In considering the survival data there was a lack of consistent selection bias both in recommendation that a patient be eligible for treatment and in regard to the dose. The principal investigator had no part in determination of therapy in any given case except for outlining the general principles of the therapeutic regime. The choice in the case of each patient was made by several radiation therapists, 3 having been associated with the project during the 10 year period. In addition, 2 internists have had active roles in the selection and medical care of each patient. The dose of radiation to be given was decided upon by the radiation therapist in consultation with the internist.

There are 3 categories of patients (those with carcinoma of the colon, lung and breast) which are large enough to permit some analyses of survival. Each group will be discussed separately.

Survival data are given in days from the diagnosis of far advanced disease, since this convention has been used frequently in the literature and permits comparison of our survival data with published reports.

CANCER OF THE COLON AND RECTUM

Twenty-nine patients with this tumor comprised the largest single category (Table 1). In all cases the patients were classed

TABLE I

CANCER OF COLON—ALL CASES BY LENGTH OF SURVIVAL OF ADVANCED DISEASE

(29 Patients)

Study No.*	Age	Sex/Race	Survival After D_x (days)	Survival After R_x (days)	Dose† (rads)
106	58	F /W	40	25	300 LB
109	56	M/W	116	80	300 LB
052	60	M/W	120	91	200 LB
033	64	M/N	126	86	100
082	49	F /N	136	33	300 LB
015	61	M/N	143	32	100
007	62	M/N	181	121	100
067	52	F /N	192	163	100 LB
049	75	M/N	213	169	200 LB
050	80	M/N	220	197	200 UB
036	64	M/N	261	238	100
064	54	F /N	262	188	300 LB
091	62	F /W	295	52	200
063	38	M/W	299	244	300 LB
066	63	M/N	327	203	200 LB
107	58	F/W	347	89	200
047	57	M/W	411	147	150 LB
111	52	F /N	434	307	200
062	60	M/N	451	270	150
096	42	M/N	583	439	100
113	72	F /N	632	381	100
098/103	45	F /N	912	474	200+300 LB
020	69	F /N	946	885	200
006	67	M/W	982	740	54
101	76	M/N	983	864	257 LB
100	76	M/N	1,258	900	300 LB
023	44	M/N	1,261	651	200
095/104	66	F /N	1,437	704	200+300 LB
108	66	F /W	1,691	584	300 UB

* Study No. refers to the roster of patients described serially in Technical Reports: No. 6–15[10], 18–29[6], 31–36[6], 6–64[8], 66–70[11], 77–82[6], 83–91[6], 92–103[6], 104–111[10], 112–113 personal communication.[ZLS]

† Dose in rads at the midline. Where no letter follows the dose, whole body radiation was given. LB = lower body irradiation; UB = upper body irradiation. The dividing point is the xiphoid.

Median survival—327 days.

as far advanced and in a few instances as terminal. Four patients were not included in the study for medical reasons, or because the patients themselves declined participation in the study.

In order to make an appropriate comparison, several published series were reviewed. Series of cases of colon cancer metastatic to liver were utilized, since they were the best found by us with appropriate time periods of metastasis available for comparison. Stearns and Binkley,[21] in 32 patients with colon cancer with liver metastases, found a median survival time of 11 months after palliative resection of the primary tumor; in 28 of their patients in whom only biopsy or diversion was performed, the median survival was 8 months. In 353 patients with untreated colon cancer metastatic to liver, Pestana *et al.*[27] reported a median survival of 9 months. Figure 1 presents an analysis of 177 patients with liver metastases and no subsequent therapy reported by Jaffe *et al.*[29] There is also a group of 61 patients reported by Rapoport and Burleson[28] treated with 5-fluorouracil.

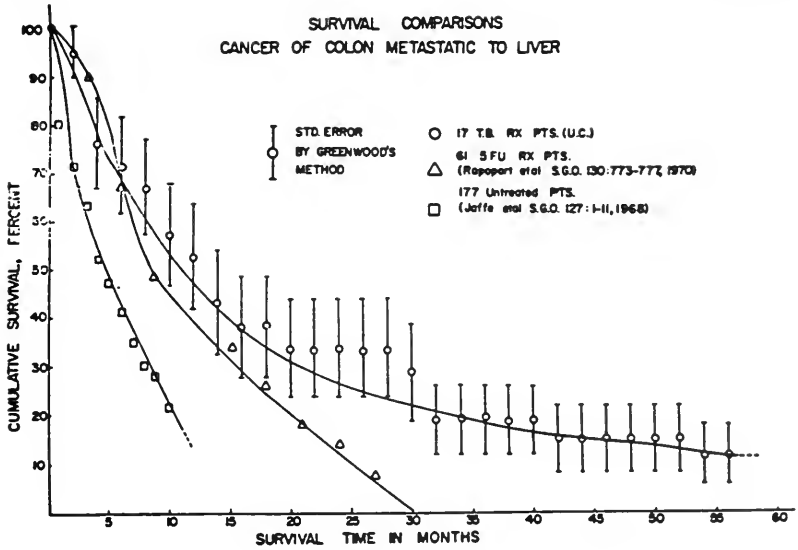

Fig. 1.

The 22 patients in our series with proven metastatic carcinoma of the colon to the liver treated by irradiation are also shown in Figure 1.

The median survival time for untreated patients was 146 days; for patients treated only with 5-fluorouracil, 255 days; and, among our patients with liver metastases, 391 days (Table II). A life table analysis was performed and indicates that the treatment given to our patients was approximately equivalent to the group given 5-fluorouracil. There was no evidence that the median survival time was shortened by total or partial body irradiation (Fig. 1). It should be appreciated that 5 of our patients had received or are receiving 5-fluorouracil in addition to the radiation therapy (3 of these with liver metastases).

The median survival for the entire group of 29 patients (22 with liver metastases) was 327 days.

CANCER OF THE BRONCHUS

This group of 15 patients (Table III) had far advanced disease with distant metastases at the time of treatment. The best comparison group was from our own institution reported by Horwitz *et al.*[16] The median survival of the 15 patients receiving whole body irradiation was 193 days from the time of diagnosis. The median survival of 61 patients seen at Cincinnati General Hospital from December, 1961, to June, 1964, was 135 days. In 15 of the 17 cases with distant metastases excluded by Horwitz *et al.* from their study (see caption to Fig. 2), the median survival was 32 days.

This last group of patients with distant metastases constitutes the most appropriate comparison group. When the median survival* of 15 patients mentioned by Horwitz *et al.*[16] is compared with the 15

* Two of the 17 patients excluded in the Horwitz *et al.*[16] study were treated by whole body radiation.

patients treated by whole body irradiation, the survival times are significantly different (Chi square 11.63, $p < 0.005$) (Fig. 3).

EWING'S TUMOR

This subgroup of 3 patients constituted the only one in which an attempt at curative therapy was made; all 3 patients are surviving. The times of survival are 854, 1,243 and 1,553 days from the time of diagnosis to August 31, 1972. The patient with the longest survival has recently developed a solitary pulmonary metastasis. The use of whole body irradiation to eliminate small clumps of cells in the disease has been reported by others.[21,22]

A fourth patient with Ewing's tumor had pulmonary metastases when first seen. Therapy in that case was only palliative.

TABLE II

CANCER OF COLON—CASES WITH METASTASES TO LIVER

(22 Patients)

Study No.*	Survival After D_x (days)	Survival After R_x (days)
106	40	25
109	116	80
052	120	91
033	126	86
082	136	33
015	143	121
067	192	163
036	261	238
091	295	52
066	327	203
107	347	89
111	434	307
062	451	270
096	583	439
113	632	381
098	912	474
006	982	740
101	983	864
100	1,258	900
023	1,261	651
095	1,437	704
108	1,691	584

* See footnote to Table 1.
Median survival—391 days.

TABLE III

LUNG CANCER—SURVIVAL IN DAYS AFTER D_x

(15 Patients)

Study No.*	Survival After D_x (days)	Survival After R_x (days)	Dose (rads)
053	57	28	200
056	103	38	100 UB
086	116	20	100
078	126	61	200
088	135	7	150
081	144	24	100
051	163	74	150
070	193	68	150
102	266	22	200 Trunk
018	333	298	200
044	349	196	100
011	419	323	100
112	683	403	100
025	797	33	150
084/097	855	643	300 UB+100

* See footnote to Table 1.
Median survival—193 days.

CANCER OF THE BREAST

In 15 cases treated by us the median survival from diagnosis to death was 479 days and after treatment to death was 446 days (Table IV). Two comparable reports in the literature include the one by the Committee on Estrogens and Androgens[18] and the other by Samp and Ansfield using 5-fluorouracil.[19] Again a life table analysis was done for our 15 patients and indicates that the survival of our patients appears somewhat better than that of the patients treated solely by estrogens and androgens, but not quite as good as the group treated with 5-fluorouracil (Fig. 4). The patients survive longer than those receiving the "standard therapy" as described by Samp and Ansfield;[18] this includes appropriate administration of estrogen and androgen, oophorectomy, local irradiation, adrenalectomy and hypophysectomy.

OTHER CANCERS

A remaining group of 25 cases reflected several different kinds of cancer. It is not

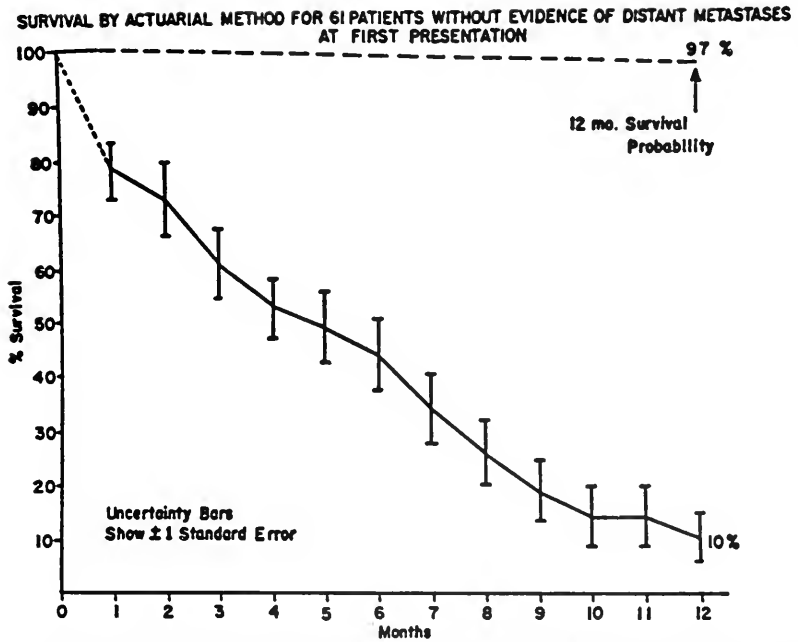

FIG. 2. The survival by actuarial analysis is shown for a total of 61 patients with carcinoma of the bronchus and distant metastases, who presented between December, 1961 and June, 1964 at Cincinnati General Hospital. The only patients excluded from this group are those in whom distant metastases were present at the time of diagnosis (17 patients). If they were to be included, the 1 year survival figure would drop to about 7 per cent. It is emphasized that these figures take account of all cases seen (including those apparently "early" and amenable to complete surgical resection). Although other reported figures may be somewhat higher, differences are more realistically attributable to biologic factors rather than to therapy.[16]

possible to make an analysis of these at this point since the individual case groups are too small to warrant this

DISCUSSION

RELATION OF RADIATION THERAPY TO PATIENT DEATH

Some analyses can be made which give information on this point.

The doses of whole body radiation given could initiate only the hematologic form of the acute radiation syndrome. In the healthy individual, after prodromal symptoms of malaise and vomiting lasting about 6–48 hours, there is a latent period lasting until 18–21 days after exposure. At this time there is a marked rapid fall in white blood cells and platelets and a less rapid fall of red blood cells reaching a nadir at 30–40 days and then recovering. These changes are associated frequently with episodes of infection and bleeding. Epilation will occur at doses over 300 rads.

Many of these patients had received much radiation and chemotherapy prior to total or partial body treatment and in

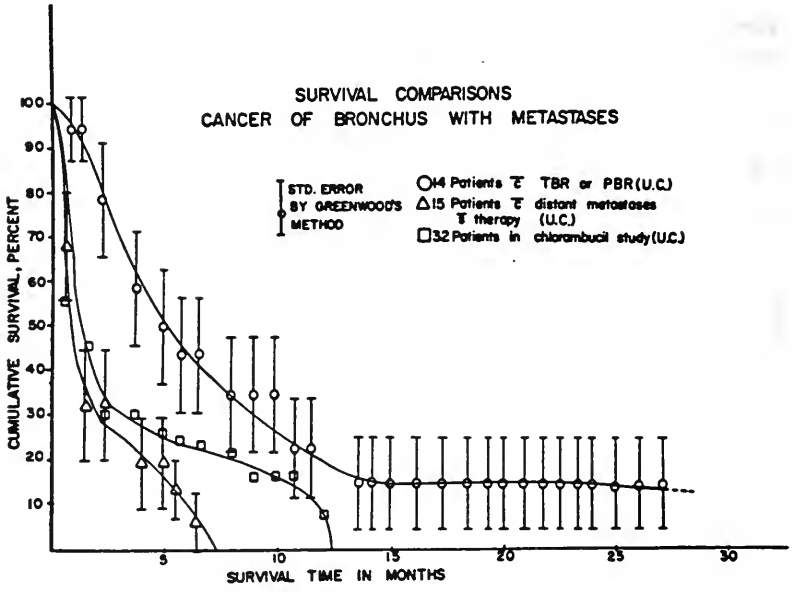

FIG. 3.

many cases this treatment was followed immediately by planned local therapy to various portions of the body.

If one assumes that all severe drops in blood cell count and all instances of hypocellular or acellular marrow at death were due only to radiation and not influenced by the type or extent of cancer and effects of previous therapy, then one can identify 8 cases in which there is a possibility of the therapy contributing to mortality. Of this subgroup, 2 patients received localized radiation between total body irradiation and death at 31 and 32 days, respectively. Two had extensive previous chemotherapy and 1 also had local radiotherapy. In 2 other cases, autologous marrow transfusion was unsuccessful because the preradiation marrow was hypocellular. Both of these latter patients had had intensive localized irradiation and 1 had received intensive chemotherapy.

TABLE IV

CANCER OF BREAST—SURVIVAL POST D_x

(15 Patients)

Study No.*	Survival After D_x (days)	Survival After R_x (days)	Dose (rads)
089	101	16	200 Trunk
055	175	156	200 UB
029	285	152	150
060	316	30	150
045	138	25	150
022	473	10	150
094	473	354	150 Trunk
031	479	446	100
079	554	209	100
010	783	48	100
008	1,056	91	100
035	1,068	859	150
040	1,095	1,063	100
083	1,098	264	100
092	1,308	1,143	150 Trunk

* See footnote to Table 1.
Median survival—479 days.

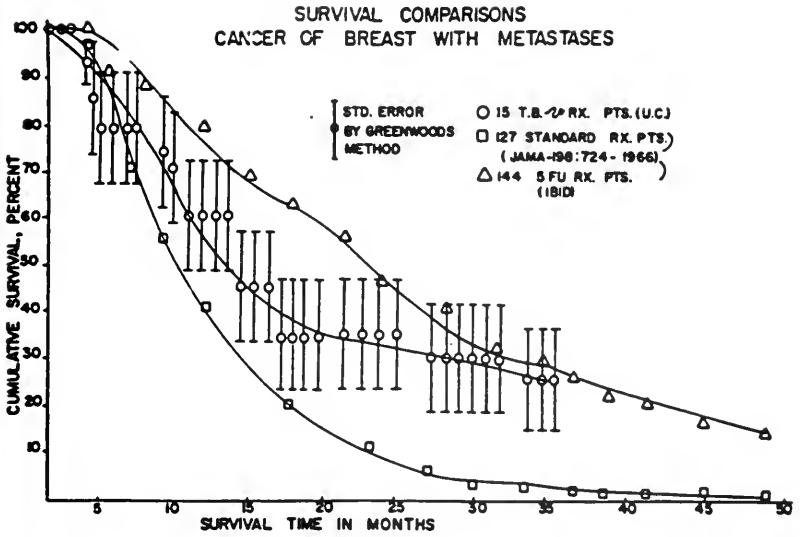

FIG. 4.

Of the 19 patients who died within 20–60 days, 11 showed clear evidence of well functioning marrow with steady or rising white blood cell counts and absence of bleeding and infection at the time of death.

The time from diagnosis to death of the 24 patients entered in the study who were not treated has been analyzed. There were 4 who died in a 20–60 day interval:

	No. of deaths in 20–60 days	*Patients surviving or dying at other times*	*Total*
Patients not given radiation	4	20	24
Patients given radiation	19	63	82

Fisher's exact probability test yields a p value of 0.16, indicating that there is no difference between the 2 groups. Therefore one may conclude that in other patients described, the effect of whole and partial body radiation therapy was less important in contributing to death than was the extent of disease in these patients. Another interpretation would be that a physician selecting far advanced cancer patients for a given treatment would have about the same degree of difficulty in selecting any form of treatment for these very ill patients. The same probabilities, p=0.19, 0.2 and 0.21 are found for patients dying between 0 and 20 days post treatment, from 0–60 days, and from 20–40 days, when compared to the untreated group. Current status of survival for these 88 treated patients is as follows:

Prophylactic therapy (Ewing's tumor)	3
Others surviving as of August 31, 1972	7
Deaths possibly attributable to irradiation	8
Deaths attributable to tumor	70
	88

REACTIONS FROM TREATMENT AND EFFECTS OF PALLIATION

The acute radiation syndrome develops in stages. In the prodromal stage, nausea and vomiting of a transient nature occur.

These complaints are often highly subjective; therefore, they are not discussed with the patient before treatment.

The analysis of our 88 treated patients shows that 44 per cent experienced no symptoms at all, that 27 per cent had transient nausea and vomiting within 3 hours, 14 per cent within 6 hours and 3 per cent within 12 hours. In only 4 patients (4 per cent) were the nausea and vomiting of a severe nature (Table v).

These symptoms are no greater than found after surgery or after treatment with cancer chemotherapy drugs, the reactions of which are often far more severe than those from these kinds of radiation therapy. Lahiri *et al.*[29] observed that when 5-fluorouracil is given orally at a dose of 15 mg./kg. daily for 6 days, and then weekly at the same dose, nausea, vomiting, diarrhea or stomatitis are found in 55 per cent of the patients treated, and marrow depression is observed in 50 per cent. A recent study by the Western Cooperative Cancer Chemotherapy Group, employing 5-fluorouracil without a loading dose at 15 mg./kg./wk. for a month, reported mild to major gastrointestinal or hematologic toxicity in 85.5 per cent of 430 patients.[17] Higgins *et al.*[12] in treating cancer of the colon using 12 mg./kg. of 5-fluorouracil intravenously for 5 successive days, observed that 27.9 per cent of 359 patients experienced a toxic reaction. The same group reported one or more surgical complications following resection of colon carcinoma in 29.6 per cent of 433 patients. Parsons *et al.*[35] note that 61–72 per cent of patients suffering from so-called radiation sickness responded favorably to placebo medication, indicating that suggestibility may have a big part to play in the appearance and control of these symptoms. Mukherji *et al.*[34] in evaluating the effectiveness of a combination of 4 drugs in the treatment of 23 patients with lymphosarcoma and reticulum cell sarcoma found severe myelosuppression in 4 patients (17 per cent) and possibly attributed this depression to their deaths from infection.

During the latent period of 18–21 days the patient is asymptomatic. The period of manifest illness then begins with evidence of malaise, infection and bleeding. These findings occur only with whole body irradiation and not with partial body treatment. Also when marrow is successfully replaced these findings do not occur.

Table V

INCIDENCE OF NAUSEA AND VOMITING IN 88 CANCER PATIENTS RECEIVING WHOLE AND/OR PARTIAL BODY RADIATION THERAPY

	Patients	Per Cent
No nausea or vomiting	39	44
Nausea and/or vomiting up to 3 hours after R_x	23	27
Nausea and/or vomiting up to 6 hours after R_x	12	14
Nausea and/or vomiting up to 12 hours after R_x	3	3
Nausea and/or vomiting up to 24 hours after R_x	7	8
Nausea and/or vomiting up to 48 hours after R_x	0	—
Nausea and/or vomiting 48 hours +	4	4
	88	100

In regard to palliation, a review of patient records shows that some palliation was achieved in 56 per cent and that 31 per cent were made neither better nor worse (Table vi). In another 3 cases we were unable to obtain follow-up history concerning palliative effects. The 3 cases of Ewing's tumor are not included in this table as therapy was prophylactic.

POSSIBLE UNIQUE MECHANISMS OF WHOLE AND PARTIAL BODY IRRADIATION

Whole body irradiation in the doses reported herein could be effective against cancer in several ways: (1) alteration of the immune mechanism of the body altering the balance in favor of the host; (2) by a direct effect on the metabolism of the cancer cells. In this case wide-field radiotherapy would have one advantage over drug therapy, since it would reach all cancer cells without depending upon blood

TABLE VI

PALLIATIVE EFFECTS* OF TREATMENT

(85 Patients†)

	Per Cent
Relief of pain	31
Decrease in tumor size	31
Increase in activity	13
Increase in well being (weight gain, appetite improvement, subjective statement by patient)	30
One or more of the above	56
No change	31
Lost to follow-up for evaluation of palliation	4
Death between 20 and 60 days possibly attributable to radiation	9

* In some of the patients there was more than one indication of improvement; thus, the percentages exceed 100 per cent.

† 3 children with Ewing's tumor received prophylactic treatment and are not included in this analysis.

supply, or chemical and pharmacologic distribution.

Partial body irradiation could be compared to regional isolation perfusion with antineoplastic drugs, again being certain to reach all tumor cells within the irradiated volume and lacking the more hazardous systemic effects of total body irradiation.

The effectiveness of both methods may be explained by the fact that small tumor foci are more sensitive to treatment than large foci and that single cancer cells are more susceptible than clumps of cells.

PSYCHOLOGIC AND PSYCHIATRIC EVALUATION OF PATIENTS

A unique and important aspect of the research work in this project has been the attempt to evaluate and distinguish between the manifestations of cancer and the effects of radiation therapy in regard to psychologic and psychiatric changes. For example, others have reported on personality types in certain cancers,[2] but no studies were presented investigating the effects of treatment.

In 1969, we reported on the effect of total and partial body irradiation on the cognitive and emotional processes of 16 patients.[11] This number has been increased to 43. These studies consisted of administration of a battery of tests to each patient in the pretreatment phase, during sham and actual treatment and during a 6 week post-treatment period. Tests which have been utilized included the Halstead Battery, Wechsler-Bellevue Adult Intelligence Scale, some tests of intellectual impairment modified from Reitan, and the 5 minute verbal content test of Gottschalk and Gleser. There has been some change in the several tests which we have been using during this phase of the total project; *i.e.*, not all tests have been used continually.

In the baseline data of 39 patients tested, the median intelligence quotient was 87 and the mean also 87. There were 41 per cent of subjects with I.Q. values of 95–116, 47 per cent between 71–95, and 12 per cent between 63–70. The distribution of intelligence factors as measured by several tests is representative of the population served by the General Hospital.

It is clear that the intensive study and the above testing have had a helpful effect in increasing the level of motivation to cooperate, as exhibited by all patients so studied.

The need for careful handling of the cancer patient by all members of the medical team is emphasized by the consistent evidence of depression over the 7 week study period. The depression is lessened with clinical improvement and attention to patient needs. It is also less in patients with long survival (over 100 days) as would be expected. Similarly, hope is directly related to survival. Anxiety dips sharply during sham treatment; it increases just prior to actual treatment, then decreases and levels off. Outward hostility tends to increase at the time of post sham treatment, then dips and remains quite stable. Hope as measured by the content analysis of verbal behavior is related to satisfactory human relations in the patient's life situation.

USE OF AUTOLOGOUS BONE MARROW TRANSPLANTATION

Because of radiation-induced hematologic depression, autologous bone marrow storage and reinfusion were instituted in 1964. Employing the method of Kurnick,[28] marrow was removed from the posterior iliac crest under local anesthesia, to an average value approximating 300 cc. It was mixed with Osgood-glycerol medium and stored at −83° C. following a programmed temperature reduction of 1° C. per minute. Prior to reinfusion dextrose was added, and then the marrow was given intravenously, initially without filtration, at a rate of 50 to 60 cc. per minute. The first 2 patients who received a marrow transfusion in our study, Patients 051 and 053, were infused with frozen marrow 24 and 19 days post irradiation, respectively, at a time when the marrow sinusoids were relatively empty of precursor cells, with the expectation that there would be more room for the transplant to take. Marrow viability in these 2 procedures was 55 and 57 per cent.[45]

Patient 051 experienced moderate hemoglobinuria not seen in Patient 053 after infusion. Marrow was given in both cases 2 to 3 weeks post irradiation; hence, it was impossible to distinguish spontaneous marrow recovery from successful marrow autotransfusion.

Because hemoglobinuria had been noted, a triple filter system was developed and marrow autotransplantations on Patients 070, 077, 078, 087, 090, 091, 095, 098, 099, 107 and 111 have all been performed employing this filter system.[48]

In marrow transplants of Patients 070, 077, and 078, the delay between the removal of marrow and transfusion was 11, 2 and 0 days, respectively. The platelet count of Patient 078 never fell below 125,000 per mm.^{3}, but the white blood cell count dropped as low as 900, suggesting possible effectiveness of the technique for the first time.

For the next 8 patients the technique was therefore modified, so that a larger volume of marrow (500 cc.) was removed from the patient under general anesthesia. The patient was then irradiated and the marrow replaced intravenously on the same day as it was removed. The results in Table VII indicate the success attendant on the modification of this procedure. Five patients receiving 200 rads of whole body radiation showed mean white blood counts to be 2,820 ± 804 cells per mm.^{3} at the nadir. In 7 patients given the same dose but no autograft, the level at the nadir was 850 ± 380 cells per mm.^{3}, the 2 means being significantly different (Table VIII). The first patient transplanted with our new technique (Patient 087) was followed in the Clinical Research Center, Cincinnati Children's Hospital, for over 6 weeks without any evidence of illness. Subsequently patients receiving these whole body doses have only been hospitalized for a total of 5 days or less. The degree of marrow depression in the successfully transplanted patient is such that hemorrhage and infection are not observed.

The 3 failures in the revised transplantation technique have been Patient 090, 099 and 107. Patient 090 suffered a cerebrovascular accident unrelated to her tumor or her radiotherapy. The latter 2 patients (099, 107) had had widespread radiotherapy which had affected the reticuloendothelial framework necessary for stem cell development, and preliminary cell aspirates in allegedly unirradiated areas did appear hypocellular. Patient 107 appeared to possess normal granulocyte reserves, one of our marrow screening parameters, only because we were given an incorrectly high body weight on which to base our etiocholanolone dosage, thus falsely elevating the marrow granulocyte reserves. From this unfortunate experience we now insist that a candidate for marrow autotransplantation have a normal iliac marrow aspirate histologically, a normal bone marrow scan employing technetium 99m sulfur colloid, and normal granulocyte reserves measured with etiocholanolone (after we weigh the patient) as indicators of normal marrow function. At autopsy, Pa-

TABLE VII

WHOLE BODY IRRADIATION WITH MARROW TRANSPLANTATION

Study No.*	Type of Transplant	Whole Body Dose (rads)	Date of Marrow Removed	Date of R_x	Date of Marrow Reinfused	No. of Cells Reinfused	Viability	Marrow Frozen	Complications of Infusion	Outcome of Autograft
051	Auto	150	4/26/65	5/1/65	5/25/65	1.6×10^8	55%	Yes	†Hemoglobinuria for 1 day	Did not take
053	Auto	200	5/ 4/65	5/ 8/65	5/27/65	1.4×10^8	57%	Yes	†None	Did not take
070	Auto	150	5/ 4/65	3/ 2/67	3/13/67	0.33×10^8	68%	Yes	None	Did not take
077	Auto	200	10/31/67	11/ 7/67	11/ 9/67	0.79×10^8	48%	Yes	Hemoglobinuria for 12 hours	Did not take
078	Auto	200	11/ 4/67	12/ 5/67	12/ 5/67	4.16×10^8	96%	No	None	Possible partial take with platelets never below 125,000/mm.³ but leukocytes 900/mm.³
087	Iso	200	3/ 3/69	2/27/69	3/ 3/69	4.38×10^8	99%	No	None	Take
090	Auto	150	2/ 2/69	2/ 2/69	2/ 2/69	15.6×10^8	96%	No	None	Cerebrovascular accident killed patient 6th day after R_x
091	Auto	200	7/ 2/69	7/ 2/69	7/ 2/69	4.6×10^8	98%	No	None	Take
095	Auto	200	11/ 5/69	11/ 5/69	11/ 5/69	3.07×10^8	97%	No	None	Take
098	Auto	200	1/27/70	1/27/70	1/27/70	7.42×10^8	98%	No	Transient hypotension before infusion	Take
099	Auto	230	3/ 3/70	3/ 3/70	3/ 3/70	5.32×10^8	95%	No	None	No take
107	Auto	200	12/15/70	12/15/70	12/15/70	3.2×10^8	95%	No	None	Take doubtful-leukopenia but on sepsis
111	Auto	200	5/19/71	5/19/71	5/19/71	7.4×10^8	96%	No	None	Take

* See footnote to Table 1.
† Unfiltered marrow infused.

TABLE VIII

RESULTS OF SUCCESSFUL ISO- AND AUTOTRANSPLANTS OF MARROW AFTER 200 RADS MIDLINE WHOLE BODY IRRADIATION

Study No.	Day of Leukocyte Nadir	Leukocyte Count at Nadir (cells/mm.³)	Nucleated Cell Count Infused Per Kilogram Body Weight‡
087	26	2,100	1.6×10^8
091	25	4,100	2.3×10^8
095	33	2,700	0.6×10^8
098	28	2,200	1.7×10^8
111	31	3,000	1.4×10^8
Mean	28.6	2,820±804†	1.5×10^8
Mean of Controls*	24	850±380†	—

* 7 patients receiving 200 rads whole body radiation without transplantation of marrow.
† The means differ significantly by the t test at $p<0.001$ and by the Wilcoxon two sample test at $p<0.02$.
‡ It has been estimated that 1.1×10^7 cells/kg. are required for a successful marrow iso- or autotransplant.[48]

tient 099, who died on Day 31 post irradiation, had widespread carcinoma of the pancreas. Patient 107 survived her pancytopenia without any evidence of sepsis. Patient 111 had no significant cytopenia and her hospitalization (including autotransplant) lasted only 4 days.

This technique has been of advantage in simplifying the patient's course and eliminating the long period of hospitalization needed prior to transfusion. The possibility of reinfusing tumor cells in the untreated marrow exists, but the elimination of this problem awaits the development of successful methods of marrow allotransplantation.

SUMMARY

1. Whole and/or partial body radiation therapy given in single doses has shown beneficial effects in the control of certain advanced cancers. The palliative effects compare favorably with results using anticancer drugs as commonly reported in the medical literature.

Irradiation certainly seems to improve survival in the untreated patient with cancers of colon, lung and breast.

2. The use of autologous marrow reinfusion immediately after radiation therapy minimizes the characteristic marrow depression otherwise observed. The degree of illness following infusion is greatly lessened and hospitalization greatly shortened.

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January 3, 1972

The Honorable Mike Gravel
1251 New Senate Office Building
Washington, D. C.

Dear Senator Gravel:

This letter represents our response to your request of us to inquire into the whole-body radiation therapy project being conducted by Dr. Eugene L. Saenger and his colleagues at the University of Cincinnati. We have made our inquiry and our broad conclusions are as follows:

1. In the normal context of a clinical investigation, the project is validly conceived, stated, executed, controlled and followed up. The appropriate scientific and professional committees of the University of Cincinnati have performed their functions during the course of the project.

2. The process of patient selection based upon 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.

Though physicians do not invariably share with the public the ways in which they reach professional conclusions, we think it appropriate to your inquiry to detail below the way in which we reached these conclusions. Our acceptance of your request was based upon the realization that senators have need of expert, impartial medical and scientific advice in evaluating complex biomedical problems. Should you desire further information, we will again endeavor to be responsive.

The committee

As I noted in my earlier letter to you, the College is seldom called upon to investigate the scientific efforts of any of its members and thus has no standing committee with such a charge. Instead, I asked two leading radiation therapists and a third distinguished physician to undertake the inquiry. They are:

Dr. Henry Kaplan, chairman and professor of radiology at Stanford University Medical School in Palo Alto, California. Dr. Kaplan is internationally known for his pioneering work in several areas of cancer therapy. He has been a member of various cancer study and advisory groups including the Committee of Consultants to Conquer Cancer which recently advised the Senate. His extensive bibliography includes descriptions of his work on Hodgkin's disease involving extensive radiation of patients. Dr. Kaplan is currently chairman of our Commission on Cancer.

Dr. Frank R. Hendrickson, chairman of the department of radiation therapy at Chicago's Presbyterian-St. Luke's Hospital. Dr. Hendrickson is also a faculty member of the University of Illinois College of Medicine and the Rush Medical College as well as a consultant to the Veterans Administration and a member of various national cancer bodies. His bibliography includes reports of his treatment of children afflicted with Ewing's sarcoma with radiation. He is the present chairman of our Commission on Radiation Therapy.

Dr. Samuel Taylor, III, a distinguished internist and oncologist at Presbyterian-St. Luke's Hospital in Chicago. He is the founder of the American College of Physicians cancer program. He is a professor of medicine at Rush. Dr. Taylor's wide experience as a senior investigator in the field of cancer provided us with a view from another discipline. He is a long time expert in chemotherapy of disseminated cancer.

Mr. Otha Linton, director of our Washington Office, provided staff support to the group and coordinated their inquiry with Dr. Saenger and his colleagues.

Nature of the inquiry

Drs. Kaplan and Hendrickson and Mr. Linton met with Dr. Saenger and Dr. Charles M. Barrett, director of radiation therapy at the University of Cincinnati, November 29 in Chicago. The discussion covered the background of the project and the purposes, objectives and achievements of the effort to date. Dr. Saenger then provided the committee with published papers and summary materials about the project.

On December 16, Drs. Kaplan, Hendrickson and Taylor met in Cincinnati with Dr. Saenger, other members of his team, two members of the University of Cincinnati human investigation committee, and the chairman of the special university committee which was created by the president to review the project.

Those interviewed were, from the UC Human Research Committee, Dr. Evelyn V. Hess, professor of medicine and Dr. Harvey C. Knowles, Jr., professor of medicine, from the special university committee to review the Saenger project, Dr. Raymond R. Suskind, professor of environmental health and medicine, from the department of radiology and the study team, Drs. Charles M. Barrett, Harry Horwitz, Bernard S. Aron and Edward B. Silberstein, physicists, Drs. I-Wen Chen and James G. Keriakes, and the psychologist, Mrs. Carolyn N. Winget.

Dr. Saenger and everyone at the university were willing to recognize our competence and to cooperate fully with our inquiry. The committee members were extended full cooperation and can conclude that they apprised themselves of the situation to the same extent that they would have needed to do as members of an NIH study section or site review team. Each member of the committee has served in such a capacity.

The committee viewed the project as it was designed---as a clinical investigation of a modality for the care of cancer patients with extensive and incurable disease. Phase one investigations follow basic animal work and always precede randomized clinical trials which may or may not be justified on the basis of the first human applications.

In the opinion of the committee, the team at Cincinnati had abundant bases in the literature for undertaking its study. The participants are fully qualified to undertake the investigation, both from the viewpoint of good patient care and importantly the possibility that new and valuable clinical information could be obtained.

Our committee did not concern itself with the implications which have been raised concerning partial funding of the effort by the Department of Defense. We did note that DOD funds were used only to support the laboratory and psychological studies but not the treatment or the care of the patient. The basic costs were borne by the university and its teaching hospitals.

Because of the prevalence of cancer which has been noted so recently by the Senate, the House of Representatives and the President, those charged with the care of cancer patients have need for every possible bit of information concerning the methods and modalities which we use to treat these patients. In our opinion, this project has the possibility of contributing useful clinical information.

It is worth noting that if others have had access only to the reports made to DOD on its part of the project or if they somehow failed to understand that the fact of extensive followup in no way departed or detracted from fundamental precepts of good patient care, then it follows that they might reach conclusions different from those of our committee.

The nature of cancer investigations and treatment

In clinical investigations of cancer, we are concerned both with the basic cancer process and with its manifestations in humans and specifically in the patients who present themselves for care. The treatment of an individual represents a series of choices for his physicians which are based upon diagnostic findings and their best judgement. Since humans respond to the assault of cancer and to attempt to treat it as uniquely as they do to most other things, generalizations here have statistical value but limited application to individuals.

There are many forms of cancer. Each type has in common the loss of intracellular control upon which normal cells depend to regulate their growth. The cancers differ in cellular types and in the site of origin of a primary lesion within the body as well as the bodily pathways through which they may spread. Thus, for example, the problem of defining and treating a solid tumor may differ radically from the approach to a form of leukemia.

Physicians have three fundamental modalities which may be used singly or combined to attempt to cure or control cancers. These are extirpative surgery, high energy radiation and chemicals. Hormones also are used to attempt to alter the course of certain cancers involving the endocrine system.

The choice of treatment must be decided for each patient. The decision is based upon the type of cancer, its location, its size, its degree of spread and upon the age and general health of the patient. Ideally, the therapeutic decision is made in a cancer conference involving physicians from the different disciplines appropriate to the problem at hand. By the nature of the disease, any cancer therapy must be regarded as heroic. The cancer patient must accept lesser probabilities of success and more stringent side effects of treatment than usually befall sufferers from other diseases.

Timing is all important in the treatment of most cancers. A small, early cancer may be removed surgically or destroyed with radiation. But if the cancer has begun to spread beyond its original site and beyond the surgical or radiation field, the destruction of the primary lesion will not suffice to save the patient.

Unfortunately, many patients still are diagnosed as having far advanced cancer which must be judged unlikely to respond to any standard curative effort. These patients may have undergone various treatments without success. Or they may have had a "silent" primary cancer which was diagnosed only after it began to spread through the body.

The physician having the care of a patient with advanced cancer has three practical choices. One is to do nothing, allowing the disease to take its course. Another is to attempt palliation, an effort to retard the tumor growth and/or to ease the pain of the patient. The third is to attempt drastic or radical treatments not commonly accepted as reliable or efficacious for patients having a greater chance of success. The third approach carries the long-shot possibility of direct patient gain. The doctor and patient must agree that something of benefit to others may be learned from the effort.

Thus, the effort to improve cancer treatments has been based upon the first application of new or questionable techniques to those patients having nothing to lose by their failure because there is no known treatment available. Often, the effectiveness of the technique must be measured in time of survival, relief of pain, or from certain body measurements, rather than in terms of overt tumor destruction. Efforts must be made to isolate and measure the specific timing, dosages, procedures and restraints which can be observed to alter the course of the disease. When a form of treatment has been shown to have some measurable beneficial effect on far advanced patients it can be considered for general use.

The nature of cancer investigation requires that more than one therapist must undertake a new modality at each stage of its development before it can be accepte for general usage. If an improvement in some tool or resource becomes available, such as the advent of supervoltage radiation sources then previous studies may be repeated with profit.

Both the high energy radiation and the several chemicals now used in cancer therap have harmful effects upon patients. So does radical surgery. The choice must be made to refrain from curative efforts when the destruction of the tumor would involve unacceptable side effects of a localized or systemic nature. Thus, efforts to control or relieve side effects are equally significant with those to destroy the tumor.

When radiation is used as the tumoricidal agent, the effort is made to limit its effects by tailoring the dose to the suspect area and by using a series of tolerabl exposures to destroy the cancer cells without damaging vital organs and adjacent normal tissues. If a cancer is widespread, then a tumoricidal dose of radiation presents problems which, for the most part, remain unsolved. Lesser amounts of radiation have been used in various ways as part of efforts to retard tumor growth, to relieve pain or to alter the pattern of cancer development.

The literature of radiation therapy offers substantial numbers of citations of efforts to use whole or partial body radiation for the palliation of advanced cancers. The conclusion, broadly, must be that the concept has not been sufficient productive to recommend generally nor so lacking in effect to be abandoned as an approach.

The Cincinnati project

The actual treatment of patients was begun in 1960 by Dr. Saenger and his colleague as a clinical assessment of the use of sublethal whole body radiation for the palliation of patients with a variety of disseminated cancers. The premise was that the level of radiation selected would have a retardant effect upon the growth of the tumor cells throughout the body and that the patient, for the most part, could tolerate the side effects of systemic radiation.

The second part of the premise was that patients who were closely followed after their cancer treatments could indicate both the physical and psychological reaction to the therapeutic effort over a period of several weeks. This clinical assessment provided a new dimension to previous studies of the use of whole body radiation.

Beginning in 1964, the group began to use the technique of autologous bone marrow transplants as a means of overcoming the marrow depression otherwise inescapable after whole body radiation. The technique after some modification involves the extraction of 300 to 600 cubic centimeters (about a pint or so) of marrow from the posterior iliac crest just before the radiation exposure. The same day, the marrow is filtered and reinjected into the patient. As a clinical procedure, this has succeeded in averting most of the extended radiation syndrome effects previous observed in patients in this series and in other whole body studies.

Efforts to minimize late effects, such as the drop in white cells and platelets and the decrease in red blood cells which are classic to radiation syndromes, began in 1965. This method using autologous bone marrow immediately after radiation therapy, became practical early in 1969.

The concept of whole body radiation as a method of treating cancer is not new with the Cincinnati project. There is voluminous literature reporting controlled animal experiments which are highly useful but not indicative of human responses to human tumors. The literature reporting on human exposures dates back to efforts in 1923. A review of reports to 1942 showed more than 270 patients thus treated with fairly little encouragement. Since these patients in all cases had disseminated tumors and the radiation sources available were in the orthovoltage range, the results were not surprising.

The advent of supervoltage generators and particularly cobalt 60 sources prompted additional studies to assess the effect of higher energy radiation and led to a new round of studies. In 1953, V. P. Collins and R. K. Loeffler called the use of 200 roentgens whole body "a useful addition to the management of advanced cancer."

A current bibliography contains some 86 scientific articles on the subject, excluding Dr. Saenger's contributions. Whole body projects have been undertaken in more than 42 U. S. medical centers. At present, efforts are underway using whole or partial body radiation for the control of leukemia, Hodgkin's disease, polycythemia vera, multiple myeloma, and disseminated cancers of the breast, thyroid and prostate. In very small groups, whole body radiation has been used successfully in curative efforts against Ewing's sarcoma, a bone tumor primarily of children.

The Cincinnati study through the end of 1970 involved a total of 106 patients referred from the Tumor Clinic of the Cincinnati General Hospital. These were patients found by biopsy and clinical examination to have disseminated tumors. They "were chosen because they suffered from advanced and widespread neoplastic disease such that cure could not be anticipated," in Dr. Saenger's words.

All of the patients underwent a 7 to 14 day assessment period to reaffirm the diagnosis and to determine whether their disease and their general health would make the radiation attempt feasible. Some 24 patients were rejected and received no radiation on the basis of their clinical assessment. Some of the 82 patients later treated received sham radiation sessions during the assessment period but none actually were exposed until after a decision by the team which determined the treatment could be beneficial.

The patients had a variety of tumors. The largest group was 25 with cancers originating in the colon and rectum. A second group of 14 had tumors of the bronchus. Fifteen women had disseminated breast cancer. There were 25 patients with miscellaneous tumors. Three children had Ewing's sarcoma and were treated for curative effect. One of the 25 patients with miscellaneous tumors had Ewing's sarcoma with metastases too widespread for a curative effort.

Discussions with the patients and members of their families are standard in any cancer therapy situation and were a part of this project from its beginning. Specific patient consent forms have been used since 1965, when this step was recommended by the National Institutes of Health.

Since 1963, patients selected for the study were interviewed on succeeding days by the internist in the project before being asked to sign a consent form for the therapy. When possible and in all cases of children, the interview included one or more members of the family who also consented to the treatment. Except for the three children with Ewing's sarcoma, all were told that their cancers had been defined as incurable and that the treatment would be attempted in an effort to prolong their lives and possibly to retard or shrink the tumors. They were told that the information gained from the study was hoped to be helpful to other patients. In the last few years they were told that the information might have military as well as clinical significance.

The patients were told that there could be some side effects from the radiation exposure and that the team would wish to keep in close touch with them for a period of weeks to study their reactions both to the advances in their disease and to the impact of the radiation. The possible side effects were not described in detail nor emphasized to avoid subjective inducement of the symptoms.

So far as the side effects were concerned, the team reported that 45 percent had no vomiting or nausea after the radiation. Some 24 percent experienced transient vomiting and nausea within three hours and another 17 percent had the same symptoms within 12 hours of exposure. Another 9 percent continued vomiting up to 24 hours. Only five percent had prolonged and severe vomiting and nausea.

It is worth noting that these symptoms are certainly no greater than those experienced by patients treated either by surgery or by any of the systemic drugs now being used clinically on disseminated cancers.

The patients were selected by clinicians at the Cincinnati General Hospital from the population served by that institution solely on the basis of their tumor diagnosis. Since CGH is a institution, none of the patients were private patients. The three children with Ewing's sarcoma were referred by physicians at the affiliat Cinainnati Children's Hospital.

Extensive psychological studies were done on 39 patients. It was possible to establish their IQs. The median on the studied group was 87. The range was from 116 to a low of 63. Some 31 of the treated patients were caucasian and 51 were negro. In both race and IQ the group was representative of the patients served by CGH.

The three children who were treated definitively for Ewing's sarcoma remained alive from one to four years after treatment. From the other 79, for whom only palliatic was expected, five others survived as of October of 1971, the longest by more than six years.

The clinical assessment of the effort indicated that (with overlapping percentages) 29 percent felt relief of pain, 30 percent showed a measureble decrease in primary tumor size, 11 percent reported an increase in activity on their own part following treatment and 29 percent reported an increase in "well-being." About 29 percent showed no evidence of improvement or change. Four percent were lost to followup. A group of 10 percent or eight patients died from 20 to 60 days after the whole body exposure.

It is not possible to determine positively that those patients who died within 60 days of the treatment would not have succumbed to their disease within that period, even though the clinical assessment had been that their disease was stable enough to justify their inclusion in the study. However, it was noted from the followup studies that their bone marrow function was subnormal and thus relatable to radiation syndrome.

In terms of survival, the Cincinnati group reported results showing an extension of days over untreated patients in each of the tumor categories. However, results were not markedly superior to the survival results reported by other investigators using various chemicals or other combinations.

The survival figures are clouded by the fact that many of the patients included in the sample had already undergone one or more types of treatment unsuccessfully, often only a short time before their inclusion in the study. Some of the patients in the study also received extensive followup treatment, sometimes involving further radiation of the primary tumor area.

Thus, the patients received a therapeutic regimen which was clinically judged most efficacious for their survival and palliation, however much the added efforts blurred the observation of the effects of the single whole body exposure.

In specific terms of survival, Dr. Saenger was able to draw rough comparisons which indicated the benefit of some treatment over none. He found that his results compared to those gained by other investigators using surgical resections, drugs such as 5-fluorouracil and, for the breast cancer patients, estrogens and androgens.

In Dr. Saenger's words, "The relatively small numbers of patients in these groups (his and the ones compared from the literature) preclude any claim to therapeutic superiority. On the other hand, it seems reasonable to continue therapy for these gravely ill individuals since this method of treatment is less elaborate and with no greater risk than many present forms of chemotherapy."

In this conclusion, the ACR committee would concur. The committee would also observe that the protocols, reviews by appropriate institutional authorities, attention to patient interests and responsibilities and reporting are all consistent with accepted good clinical and scientific practice.

Responses to Senator Gravel's questions

Some of the points raised in the questions in your letter of November 10 are covered at least in general above. Some are not. Hence, the questions and specific responses are detailed below.

1. ANIMAL DATA: Don't experimental animal trials as a rule precede human trials in the testing of new medical therapies and drugs? What animal trials using partial or whole-body irradiation to treat cancer were completed before Dr. Saenger began his human experimentation? Did Dr. Saenger begin his special "therapy" before or after Defense Department support?

ANSWER: The literature on radiation biology is substantial with regard to animal trials of whole body radiation for a variety of purposes. One bibliography is appended. Almost always, clinical researchers have had the benefit of animal work to test the toxicity of their materials and to develop general patterns of biological response. However, since inter-species differences never allow the total transfer of animal data to human usage, it is necessary to undertake clinical trials under proper conditions to test any new therapy or agent. It is not necessary for a clinical researcher himself to undertake animal work if he has access to and a good understanding of the literature on the subject. This was the case of Dr. Saenger and his colleagues.

As an example of the application of animal studies to human uses, the use of autologous bone marrow transplants and the basic understanding of the influence of marrow stem cells on mammalian survival after whole body radiation exposure were worked out in animal experiments. The marrow transplants are a most important part of the Cincinnati investigation. The detailed biochemistry not only permits a more complete analysis of the response of these patients but also could point the way to other researchers who are attempting systemic therapy with radiation and with investigative chemicals.

It was a necessary part of the clinical investigation for Dr. Saenger to determine the optimal amount of marrow to extract, the most effective way to handle it and the best timing for its reinjection into the patient. At the beginning of this work, Dr. Saenger and his group extracted the marrow and froze it to retain it for the 18 to 21 days during which blood white and red cell levels are expected to decline. With subsequent patients, they determined that the prompt reinjection of the marrow the same day the radiation was administered averted much of the blood depleting effect of the radiation.

Since Dr. Saenger in this instance applied to the Department of Defense, rather than another funding agency, for the support for the extensive biochemical work-up which would provide the "new" element of information from the survey, his preparations preceded the 1960 data at which the actual project was funded by DOD and patient treatment began. As noted, the support for the patient treatment and management was provided by the University of Cincinnati and its hospitals. The DOD funds were applied only to the biochemistry and subsequently the psychological testing which allowed a more complete assessment of the effort.

2. FOLLOWUP STUDIES: How does Dr. Saenger follow up his own patients to find out if his "treatment" has been helpful or harmful to them? Does he measure the tumors he hoped to reduce, for instance?

ANSWER: As noted, the followup on these patients is considerably more complete than is possible for most tumor clinics. The followup consisted of clinical observations and diagnostic studies and frequent doctor-patient contacts between both the internists and the radiation therapists on the team with the patients who had been treated. In addition, the team psychologist maintained contact, not only for her tests but also as a further supportive measure.

The data on biochemical responses and upon psychological reactions is valuable but simply too extensive in terms of manpower and laboratory facilities to be possible for every cancer patient, even in the best of cancer centers.

The assessment of results was made by clinical observations of the patient which indicate the elements of well-being and systemic function plus laboratory analyses of blood condition and voiding functions plus x-ray diagnosis to check the size and penetration of solid tumors. In many of the patients, the primary tumor had been excised surgically or treated previously with a prophylactic dose of radiation, leaving management of the metastases as the major clinical concern. It is worth noting that only 4 percent of the 82 patients in the 10-year series were lost to complete followup. A detailed report on these results is cited in the preceding section.

3. CONTROL GROUPS: What control groups does Dr. Saenger have, or has he arranged for at our great cancer research institutes, so that he can determine how his special "treatment" is working?

ANSWER: The question of specific control groups and randomized samples does not usually arise until after the completion and evaluation of the type of study currently underway by Dr. Saenger. He advises that planning for a more elaborate phase three study began last June on the basis of assessment of the 10-year results of the present effort.

The literature contains sufficient studies of similar patients and comparable sized samples treated by other methods to allow basic comparisons of tumor regression, post-treatment symptoms and survival times after palliation.

Again, it is worth noting that the extent of preparations and followup on each patient and the number of cancer patients at CGH who are suitable for an aggressive palliation study have combined to limit the size of the group under investigation. A phase three study appears feasible at Cincinnati but will require a substantial commitment of staffing and financing from some source other than patient care funds.

4. PRIVATE PATIENTS: Does Dr. Saenger treat any private cancer patients, or offer consultation on private cases? Does he recommend or use his partial or whole-body radiation "therapy" on paying patients? Does he know any doctor who does?

ANSWER: Dr. Saenger and his colleagues are full-time faculty members of the University of Cincinnati College of Medicine and have no private practice in the ordinary sense. Their patient care responsibilities are restricted to patients at the city-operated Cincinnati General Hospital and its affilieted institutions. A very few patients were referred to the group from doctors at the Holmes Hospital, a private practice institution affiliated with the university. However, those patients were not charged for the treatment and medical care involved in their participation in the study.

At this point, Dr. Saenger does not use his treatment on "paying patients" because he has none. He does not recommend his technique to other physicians because the investigation is not yet complete and the results are not indicative of immediate application to clinical situations apart from a research effort. Dr. Saenger would encourage other qualified researchers to duplicate his project or to modify his techniques on the basis that results to date are sufficiently promising to warrant further investigation both by his group and by others.

As noted above, some type of partial or whole body radiation is used in more than 42 different U. S. medical centers. A total list of these is not available, but they do include both public institutions like the University of Cincinnati and private ones where most patients are charged for their care and treatment. Thus, it is likely that instances could be found in which patients did pay for this treatment approach. However, the scientific literature does not ordinarily cite the question of patient payment in reporting on clinical research. The ACR committee was not in a position to make any extended inquiry on this point.

5. TRICKERY: Is there any trickery of the patients involved?

a.) Do the patients really understand the experiment is largely to help the Defense Department prepare for nuclear warfare?

b.) Do you consider the release the patients sign to be sufficient evidence that they understand?

c.) Do the patients understand that the experiment may cause them severe discomfort, such as hours of vomiting?

d.) Do the patients understand that partial or whole-body irradiation may shorten their lives, and if so, by how much?

e.) Do the patients understand whether or not there exists any basis for suggesting that the "treatment" may reduce the size of their tumors or reduce their pain (as Dr. Saenger suggests in the Washington Post, Oct. 8, 1971)?

The question of informed consent was investigated extensively by the ACR committee. The University of Cincinnati Committee for Human Investigation was formed in 1965, as it was in most other institutions, and has had a parallel development under the guidelines of the National Institutes of Health. Their consent forms have been gradually modified over the years and the sophistication of their review has increased in a parallel fashion.

It is the opinion of the ACR committee that at the present time and through the years the UC committee has functioned effectively and comparably to similar committees at any of the other leading institutions which conduct cancer research. It is likely that the UC committee has performed its function better than the average group because of the volume of projects generated by the medical faculty and the professional competence of the people involved.

The current consent seeking procedure was reviewed by the ACR committee. The team internist (Dr. Silberstein) interviews patients two times at least 24 hours apart and discusses in extensive detail the procedures that will be undertaken. This is done not only for the patient but also for members of his family, when available. The specific and detailed consent forms are not presented to the patient until the completion of the second interview. The form in use is modified for specificity from the basic ones prepared by the National Institutes of Health.

Except in the case of the three children with Ewing's sarcoma who were treated curatively, the patients knew before being referred to the study team that they had malignant disease for which no curative treatment is possible. They knew that the efforts of the study team were not offered as curative.

Many patients expressed a desire to participate in the study and possibly to help the plight of other cancer patients in the future. The documented psychologica studies which were incorporated in the project beginning in 1965 give the study group more than the usual assurance that their explanations and the required forms were understood by the patients and by their families.

The ACR committee felt that the patients were adequately informed about the nature of the proposed therapy and about the consequences. As noted above, the patients were not informed in detail about the side effects of radiation because of the psychological influence of expectation involved in both nausea and vomiting. As mentioned in the project narrative, about half of the patients did not experience unpleasant side effects and most of the others had only transient symptoms. It should also be noted that since most of the patients had undergone previous cancer treatments, often involving radiation or systemic chemicals, they were aware from previous experience of the types of sequellae which might be encountered.

The patients were advised that the project was designed in the hope that the radiation would relieve the pain of their cancer, that it might shrink the size of the primary tumor or retard the development of metastases. No guarantees of any of those results were offered.

In the ACR committee's view, the assertion in question 5 a. that the experiment "is largely to help the Defense Department prepare for nuclear warfare" is not correct. This is not the primary purpose of the effort and to have advised the patients to that effect would have been misleading.

The patients were not specifically informed that the partial support came from DOD any more than other patients in other studies at Cincinnati or elsewhere are advised of the specific agency support of projects in which they are involved. The Cincinnati patients were told that support came in part from a national agency.

At the time the patients were counseled prior to the request for execution of the informed consent form, they were advised that the possible findings may have more than clinical implications and could be helpful to persons receiving whole body radiation in industrial accidents, military activities or as fallout from a nuclear detonation.

The question of the source of support for a project is not construed by the ACR committee or by most medical investigators as being relevant to the issue of informed consent. In this case, the DOD exercised no control over patient selection or clinical treatment and indeed did not require descriptions of that part of the project been directed primarily toward the assessment of whole body effects of radiation rather than the management of disseminated cancer by radiation, the study group could not have incorporated the autologous marrow transplants which so drastically altered the classic radiation response.

Though this letter has extended to substantial length, it obviously represents a summary of the facts of the Cincinnati study and a precis of the opinions of the College's committee members on that study and on the basic issues of cancer investigation in humans. As we indicated at the beginning of the letter, we would be happy to attempt further discussion of any point on which you may still have concern.

Sincerely,

Robert W. McConnell, M. D.
President
American College of Radiology

COMPTROLLER GENERAL OF THE UNITED STATES
WASHINGTON, D.C. 20548

MAY 26 1972

B-164031(2)

Dear Mr. Chairman:

Pursuant to your request of December 23, 1971, and discussions with your office, we obtained documents relating to (1) the whole-body irradiation program at the University of Cincinnati Medical Center and (2) the policy of the Department of Defense on the subject of the protection of humans used in medical research projects under contract. The enclosure to this letter identifies the documents obtained by us and made available to your office during our work.

Concerning the policy on the subject of the protection of humans used in medical research projects, an official of the Department advised us that the policy of the Department was set forth in Department of Defense Instruction 5030.29, dated May 12, 1964. The instruction, which is applicable to all components of the Department and to its contractors or grantees, states that:

"The Department of Defense assumes full responsibility for the protection of humans involved in research under its sponsorship whether this involves investigational drugs or other hazards.

"Each Military Department will establish within the office of its Surgeon General a formal Review Board of professional personnel to consider each research proposal from within that Military Department or from its contractors or grantees which may involve the use of human subjects in the clinical investigation of new drugs. Before a clinical test with an investigational drug may be performed under the sponsorship of a Military Department--

"1. the plan of the test and other pertinent details must be submitted to the appropriate Review Board,

"2. the Board must indicate its approval, and

"3. the approval must be confirmed by the respective Surgeon General."

With the exception of certain reports that were required to be filed with the Food and Drug Administration of the Department of Health, Education, and Welfare in the case of investigational new drugs, no procedures were specified in the instruction with regard to the use of human subjects for other research purposes. The reports to be filed with the Food and Drug Administration were set forth in a Memorandum of Understanding between the Department of Health, Education, and Welfare and the Department of Defense, dated February 1964, which contained the procedures to be followed to ensure that the requirements of the Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 355), and the regulations issued under the act are fully met.

Although the instruction appeared to be directed primarily toward the investigational use of drugs, an official of the Department of Defense advised us that the instruction applied to all medical research projects. He stated also that each service directed its own research projects without control from the Department.

We contacted officials of the Departments of the Army, Navy, and Air Force and of the Defense Nuclear Agency, formerly known as the Defense Atomic Support Agency (the organizational entity within the Department of Defense that had contracts with the University of Cincinnati relating to the whole-body irradiation program), to determine whether they had any instructions or regulations that were applicable to the use of humans in medical research work under contract. The officials were not aware of any instructions or regulations, other than the instructions and regulations implementing Instruction 5030.29, involving the use of human subjects that would apply to contractors conducting medical research for their organizations.

An official of the Department of the Air Force advised us that the Air Force did not conduct medical research under contract. Officials of the Departments of the Army and Navy stated that, although most medical research had been conducted in-house, some had been performed under contract. They stated also that, when work is to be performed under contract, they must be satisfied that patient consent forms will be used and that human subjects will be adequately protected before a contract is executed.

B-164031(2)

An official of the Defense Nuclear Agency advised us that, although the Defense Nuclear Agency did not have any contracts for the use of human subjects for medical research, the following language had been included in all medical contracts after August 1971.

> "The COR [Contracting Officer's Representative] shall be informed in writing of any project plans on the part of the Contractor to employ new, experimental, and investigational drugs or other hazards in research involving human subjects, and such experimentation shall be specifically authorized by the Contracting Officer in writing prior to the prosecution of such research. Without the concurrence and authorization by the Contracting Officer for the specified drug or other hazard involved, such research shall not be performed. (The purpose of this clause is to insure compliance with the Department of Defense Instruction, 5030.29, 1964 May 12, entitled 'Investigational Use of Drugs or Other Hazards by the Department of Defense', a copy of which is furnished to the Contractor with this Contract)."

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.

We plan to make no further distribution of this report unless copies are specifically requested, and then we shall make distribution only after your agreement has been obtained or public announcement has been made by you concerning the

B-164031(2)

contents of the report. We trust these comments will serve the purpose of your inquiry.

Sincerely yours,

Comptroller General
of the United States

Enclosure

The Honorable Edward M. Kennedy
Chairman, Subcommittee on Health
Committee on Labor and Public Welfare
United States Senate

December 9, 1974

Honorable Sam Nunn
United States Senate
Washington, D.C. 20510

Dear Senator Nunn:

Thank you for your notes of November 20, 1974, addressed to the Department of Health, Education, and Welfare and to the Department of Defense, enclosing Mrs. Lloyd B. Milford's letters of November 7 and, particularly, for Dr. H. Peter Metzger's highly inaccurate column from the Atlanta Journal.

The regulatory issuance described by Doctor Metzger as something ". . . the U.S. Department of Health, Education, and Welfare (HEW), has finally come up with . . . ." are proposed 1974 amendments to existing 1973 regulations which in turn codified a 1971 departmental policy which grew out of a Public Health Service policy dating back to 1966 and earlier years. These pre-existing policies reflected the same concerns raised in Doctor Metzger's article. We are enclosing the relevant issuances and the "Institutional Guide . . ." to this policy which touch on many of these issues. Your attention is specifically called to the requirement that all of our grantees adopt their own moral and ethical codes to guide their research, and to the long list of such codes on the last pages of the Guide. Our grants and contracts support research in a wide spectrum of religious and secularly controlled scientific institutions.

The column by Doctor Metzger dwells at some length on an alleged abuse of research procedures at the University of Cincinnati between 1960 and 1971. Doctor Metzger does not mention that an investigation by the General Accounting Office failed to disclose any substantive association between Department of Health, Education, and Welfare and Department of Defense research activities at this institution and the case-by-case treatment of the Cincinnati patients. The University never accepted Defense funds to "zap" patients. The patients were treated individually for the diseases they had.

Whole-body radiation at levels of a few hundred rads is lethal only when it destroys the blood building cells of the bone marrow. In the treatment of these patients who had widespread metastatic cancer, a large part of the marrow was first removed, the patient was then treated and the marrow returned. None of the patients involved died from radiation sickness.

Page 2 - Honorable Sam Nunn

though two of them did die with unusually low white blood cell counts. In all instances, death was clearly attributable to the advance of cancer, or to intercurrent disease associated with advanced cancer.

The last paragraph of Doctor Metzger's article contains the basic error--that the patients were being given whole-body radiation for localized cancer. Nothing could be farther from the truth. All of the patients had had prior--and unsuccessful--surgery for localized cancer, most of them had had additional surgery or localized radiation, all by now had widespread metastases making further surgery or localized radiation ineffective.

Doctor Metzger fails to note the finding by the American College of Radiology that this treatment was at least as effective as drug therapy for certain types of cancer and, in the case of Ewing's sarcoma, a childhood bone cancer, appeared to be far superior to any other treatment then available.

Sincerely yours,

D. T. Chalkley, Ph.D.
Chief, Office for Protection
from Research Risks
Office of the Director

3 Enclosures
May 30, 1974, Federal Register
August 23, 1974, Federal Register
"Institutional Guide . . ."

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

December 13, 1974

Mrs. Lloyd B. Wilford
165 Woodlawn Avenue
Decatur, Georgia 30030

Dear Mrs. Wilford:

In typical bureaucratic fashion it is highly probable that most of the copies of your November 7, 1974, letter to the Department of Health, Education, and Welfare will end up on my desk. You will, as a consequence, probably receive several essentially identical responses.

We are enclosing a copy of our reply to Senator Nunn and copies of the enclosures. As an old protozoologist, I can assure you that the Department does not propose, permit, or countenance research that confuses patients with paramecium. I trust that the letter indicates our long concern with these issues. I will be glad to send you copies of our policy issuances dating back as far as 1953, if you are interested. They do not reflect the interests of immoral and depraved persons.

Doctor Metzger appears to have relied on newspaper "morgue" material that was years old and grossly inaccurate. If medical research was carried out in such a sloppy fashion we would still be giving mothers thalidomide. The accusations are a libel on both the Department of Defense and the University of Cincinnati.

Senator Kennedy's concerns were widely circulated in the Cincinnati papers, yet none of the patients of their survivors made any issue of the matter. The University refused to release the patients' names not only because of legal restrictions, but because of severe survivors' reactions to a previous attempt by a T.V. network to document the study with the University's cooperation.

Several of the Ewing's sarcoma cases treated at the hospital are still alive and well several years after treatment, though the average survival of such patients is less than 6 months. It is to be regretted that this incident has halted what promised to be a very significant addition to our armamentarium against metastatic cancer. Similar work is going ahead in Canada, and in future years this country may well move even further ahead of us in the field of radiotherapy.

Sincerely yours,

D. T. Chalkley, Ph.D.
Chief, Office for Protection
from Research Risks
Office of the Director

Enclosure

MRS. LLOYD B. WILFORD
165 WOODLAWN AVENUE
DECATUR, GEORGIA 30030

November 7, 1974

Department of Health, Education and Welfare
Washington, D.C. 20214

Gentlemen:

I find the attached almost beyond belief. STOP THIS!

Where is the health, education, or welfare in a program that treats a human as it would a protozoan? Why should federal money be used in such programs at all? We should not allow such programs, much less finance them.

Thousands of cancer victimswho read this will suffer the uncertainty of the nature of the treatments they receive, many apparently with reason. Research on human fetuses, aborted or otherwise, should never be allowed. You cannot possibly dare to continue or allow to continue such immoral and depraved crimes against citizens whether aborted, mentally ill victims of our society, or other innocents; certainly not in the name of the people of the United States.

Stop it. In the name of God.

Sincerely,

Dorothy Wilford

cc: Senators Nunn and Talmadge
Representative Blackburn
Secretary of the Army Callaway

20-D The Atlanta Journal

HEW Takes Aim at Human Testing

By H. PETER METZGER, Phd.
Enterprise Science News Service

It usually takes some great improvement in a situation to realize just how bad things have been all along. Consider regulations governing medical experiments performed on human beings.

In the face of some flagrantly immoral abuses in the past, the U.S. Department of Health, Education and Welfare (HEW), has finally come up with some proposed rules on how federal money can be spent when people are used as the subjects of laboratory experiments. The proposal will be open for public comment (write HEW) until Nov. 21.

Included in some of the newly suggested rules are:

—Institutionalized mental patients can no longer be used as a cheap and convenient source of subjects for medical research which is unrelated to their particular disability.

—Drugs can no longer be administered to women about to undergo abortion, just to see what effect the drugs will have on the fetus.

—Research on aborted human fetuses should be done only after the appropriate animal studies have been exhausted.

—Most importantly, consent committees must be established to make sure that the patient's consent to take part in an experiment is given only after his having been fully informed of the nature of the experiments and particularly, of any risks involved.

Most readers would quite naturally assume that such rules have been in effect in civilized nations for decades, if not centuries, but that is not the case.

What's worse, HEW had to be forced into action by Congress (Sen. Edward M. Kennedy in particular), and by the occasional horror stories given exposure by the press before it would finally act. And at that, HEW's proposals were published more than a month after the date promised originally, and do not apply to research on children at all. . . . . .

If you think that other professionals, particularly in medical science, have been effective in the past in policing their own ranks, consider the University of Cincinnati study done for the Pentagon between 1960 and 1971.

The Cincinnati patients were not told that the true purpose of the experiments was to determine the combat effectiveness of troops after radiation sustained on the battlefield during an atomic war. Instead, they were told that the radiation they were to receive might diminish their own cancers. All but three were charity patients and of lower than average IQ.

They were also not told that the 200 rad doses to their whole bodies, not just the cancer itself, were death-dealing in themselves.

Although all of the subjects had incurable cancers, they were not in the final stages of the disease nor even close to death. In a Defense Department document, according to a University of Cincinnati faculty report on the subject, the doctors described the patients as "in relatively good health" and "clinically stable, many of them working daily."

But "seven of the 18 receiving the higher doses (150 to 200 rads) died within 33 days," close to 40 per cent, said the faculty report. In all, at least 87 patients were used as subjects.

The study was dropped in 1972 when the president of the University refused to accept additional Pentagon money to pay for zapping cancer patients.

Sen. Mike Gravel asked some outside physicians to investigate. Although the study was discredited, the American College of Radiology (ACR) came to the rescue of the radiologists who ran the project. A three-doctor committee appointed by the head of the ACR actually commended the project.

The ACR report does not identify other centers in the country where whole-body radiation is used for localized cancers, nor will hospital authorities in Cincinnati allow Sen. Kennedy's staff to interview the surviving patients. All of which illustrates how naive it is to expect medical experimenters to police themselves.

Published in Scientific Literature

PUBLISHED PAPERS - Under DASA Contract - Radiation Effects in Cancer Patients

Comparison of Serum Phenylalanine Levels with Growth in Guthries's Inhibition Assay in Newborn Infants. Carolyn Scheel and Helen K. Berry. The Jour. of Pediatrics, Vol. 61, No. 4, pp. 610-616, October 1962.

Deoxycytidine in Urine of Humans after Whole-Body Irradiation. Helen K. Berry, Eugene L. Saenger, Harold Perry, Ben I. Friedman, James G. Kereiakes and Carolyn Scheel. Science, October 18, 1963, Vol. 142, No. 3590, pp. 396-398.

Deoxycytidine Levels in the Urine of X-irradiated Rats. James G. Kereiakes, Eugene L. Saenger, and Helen Berry. Abstracted in Radiation Research, Vol. 22, No. 1, May 1964.

Urinary Excretion of Amino Acids and Nucleosides by Cancer Patients Following Whole-Body Irradiation. E.L. Saenger, J.G. Kereiakes and Helen Berry. Abstracted in Radiation Research, Vol. 22, No. 1, May 1964.

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Hematologic Effects of Total-Body Radiation in the Human Being. Gould A. Andrew, C.C. Lushbaugh, Ralph J. Kniseley, David A. White and Ben I. Friedman. This paper was presented at the International Atomic Energy Agency Panel on the Effects of Various Types of Ionizing Radiation from Different Sources on the Haematopoietic Tissues, meeting in Vienna, Austria, May 17-20, 1966. Published in Proceedings by IAEA, Vienna, 1967, STI/PUB/134, pages 75-83.

Effects of Whole and Half Body Irradiation in Human Beings with Cancer. E.L. Saenger, B.I. Friedman, J.G. Kereiakes and H. Perry. Published in the Proceeding of the Third International Congress of Radiation, Cortina d'Ampezzo, Italy, June 26-July 2, 1966, p. 191, abstract #759.

Effects of Total Partial Body Therapeutic Irradiation in Man. Eugene L. Saenger. Published in Proceedings of the 1st International Symposium on the Biological Interpretation of Dose from Accelerator-Produced Radiation - Held at the Lawrence Radiation Laboratory, Berkeley, California, March 13-16, 1967. Published U.S. Atomic Energy Commission/Division of Technical Information, CONF-670305, p. 114-227.

Colorimetric Analysis of Deoxycytidine in Urine After Separation by Ion-Exchange Column Chromatography. I-Wen Chen, James G. Kereiakes, Ben I. Friedman and Eugene L. Saenger. Analytical Biochemistry, Vol. 23, No. 2, May 1968, pp. 230-240.

Radiation-Induced Urinary Excretion of Deoxycytidine by Rats and Humans. I-Wen Chen, James G. Kereiakes, Ben I. Friedman and Eugene L. Saenger. Radiology, Vol. 9 No. 2, pp. 343-348, August 1968.

Total and Half Body Irradiation: Effect on Cognitive and Emotional Processes. Louis A. Gottschalk, Robert Kunkel, Theodore H. Wohl, Eugene L. Saenger and Carolyn N. Winget. Arch. Gen. Psychiat. Vol. 21, pp. 574-580, Nov. 1969.

Cytologic-Biochemical Radiation Dosimeters in Man. E.G. Silberstein, I-Wen Chen, E.L. Saenger and J.G. Kereiakes. Published in Proceedings "Biochemical Indicators of Radiation Injury in Man "International Atomic Energy Agency, PL-409/13, pp. 181-214, Vienna, 1971.

PRESENTATIONS

Bone Marrow Dosimetry in a Cobalt 60 Irradiated Tissue Equivalent Human Phantom. presented by James G. Kereiakes at the Second International Conference on Medical Physics, Boston, Massachusetts August 11-15, 1969.

Effect of Total and Partial Body Radiation on Cognitive-Intellectual Functioning and Emotional Reactions, C.C. Gleser, C.N. Winget, R.L. Kunkel and E.L. Saenger. Presented at the DASA Medical Coordination Conference "Radiation-Induced Incapacitation/Performance Decrement", Armed Forces Radiobiology Research Institute, Bethesda, Md. 18-19 November 1969.

Cytologic-Biochemical Indicators of Radiation Injury in Man. Presented by E.B. Silberstein at the WHO/IAEA Conference, Paris, June 22-26, 1970.

The Changing Picture of Bone Marrow Granulocyte Reserves in Irradiated Patients. Presented at the Experimental Hematology Society by E.B. Silberstein, November 12-13, 1970, Pittsburgh.

Presentations listed below were made by staff of the Radioisotope Lab. at the Joint Oak Ridge Associated Universities-Defense Atomic Support Agency Information Exchange Program "Radiation Effects on Biological Systems," Oak Ridge, Tenn. March 29-30, 1971.

A Closed System for Marrow Transplantation - E.B. Silberstein

Chromosome Aberrations as a Dosimeter of Whole Body Irradiation - E.B. Silberstein

Active Bone Marrow Doses in Whole-Body and Partial Body Exposures - J.G. Kereiakes

Serum and Urinary Amylase Activities in Irradiated Cancer Patients - E.L. Saenger

The Relationship of Nausea and Vomiting to Radiation Dose - E.L. Saenger

In vitro studies of Chromosome aberrations caused by Irradiation - E.B. Silberstein

Ultraviolet-Absorbing Compounds in Urine of Two Irradiated Cancer Patients as Determined by High-Resolution Column Chromatography - E.L. Saenger

Active Bone Marrow Dose Related to Hematological Changes in Whole Body and Partial Body Exposures - J.G. Kereiakes, E.B. Silberstein, E.L. Saenger, W.G. Van De Riet and C. Born - submitted for presentation at the Annual Meeting of the Radiological Society of North American in December 1971.

Bone Marrow Dose in Whole and Partial Body Cobalt 60 tissue-equivalent human phantom. C. Born, J.G. Kereiakes, G.K. Gahr and G.H. Simmons, presented at the annual meeting of the AAPM, Houston, Texas, July 1971.

PRESENTATION - Made under DASA contract - Radiation effects on cancer patients

Radiation Casualties-Newer Aspects of Mass Casualty Care. Presented by Eugene L. Saenger and Max L.M. Boone, at the Thirteenth County Medical Societies Conference on Disaster Medical Care, American Medical Association, Chicago, Illinois, November 4, 1962.

Deoxycytidine Levels in the Urine of X-irradiated Rats. Presented by James G. Kereiakes at the Annual Meeting of the Radiation Research Society, May 1964, Miami Beach, Florida.

Urinary Excretion of Amino Acids and Nucleosides by Cancer Patients Following Whole-Body Irradiation, presented by E.L. Saenger at the Annual Meeting of the Radiation Research Society, May 1964 at Miami Beach, Florida.

Autologous Bone Marrow Storage and Infusion in Patients Receiving Whole Body Radiation. Presented by Ben I. Friedman at the American College of Physicians Regional Meeting in Pittsburgh on November 20, 1965.

Effect of Whole and Half-Body Irradiation in Human Beings with Cancer. Presented by Eugene L. Saenger at the Third International Congress of Radiation Research, Cortina d"Ampezzo, Italy, June 26, July 2, 1966.

Hope and Denial in Metastatic Carcinoma - A Preliminary Report. Presented by Dr. Robert L. Kunkel at a Psychosomatic Meeting in New Orleans, 1966.

Effects of Total and Partial Body Therapeutic Irradiation in Man. Presented by Eugene L. Saenger at the Proceedings of the 1st International Symposium on the Biological Interpretation of Dose from Accelerator-Produced Radiation. Held at the Lawrence Radiation Laboratory, Berkeley, California, March 13-16, 1967.

Quantitive Analysis of Deoxycytidine in the Urine of Irradiated Cancer Patients and Rats. Presented by James G. Kereiakes at the DASA Symposium, U.S. Naval Radiological Defense Laboratory, San Francisco, California, April 9-11, 1968.

The Management of the Acute Radiation Syndrome in Man. Presented by Eugene L. Saenger at the DASA Symposium, U.S. Naval Radiological Defense Laboratory, San Francisco, California, April 9-11, 1968.

Bone Marrow Dosimetry in a Cobalt 60 Irradiated Tissue-Equivalent Human Phantom. Presented by James G. Kereiakes at the DASA Medical Coordination Conference, Air Force Weapons Laboratory, Kirkland Air Force Base, New Mexico, May 27-29, 1969.

Radiation-Induced Urinary Excretion of Deoxycytidine by Rats and Humans. Presented by I-Wen Chen at the Annual Meeting of the Radiological Society of North America, Chicago, Illinois, December, 1967.

TECHNICAL REPORTS

Submitted by University of Cincinnati to
Defense Nuclear Agency (DNA) formerly DASA

Report Period	Title	Contract No.	DASA Report No.
Feb. 1960 thru Oct. 1961	Metabolic Changes in Humans Following Total Body Radiation	DA-49-146-XZ-029	None Assigned
Nov. 1961 thru Apr. 1963	Metabolic Changes in Humans Following Total Body Radiation	DA-49-146-XZ-029	DASA 1422
May 1963 thru Feb. 1964	Metabolic Changes in Humans Following Total Body Radiation	DA-49-146-XZ-029	DASA 1633
Feb. 1960 thru Apr. 1966	Metabolic Changes in Humans Following Total Body Radiation	DA-49-146-XZ-315	DASA 1844
May 1966 thru Apr. 1967	Metabolic Changes in Humans Following Total Body Radiation	DA-49-146-XZ-315	DASA 2179
May 1967 thru Apr. 1968	Radiation Effects in Man; Manifestations and Therapeutic Efforts	DA-49-146-XZ-315	DASA 2163
May 1968 thru Apr. 1969	Radiation Effects in Man; Manifestations and Therapeutic Efforts	DA-49-146-XZ-315	DASA 2428
May 1969 thru Apr. 1970	Radiation Effects in Man; Manifestations and Therapeutic Efforts	DASA01-69-C-0131	DASA 2599
May 1970 thru Apr. 1971	Radiation Effects in Man; Manifestations and Therapeutic Efforts	DASA01-69-C-0131	DNA 2751T

Mr. BRYANT. You testified that funding was obtained from the National Institutes of Health and that most costs were paid by Cincinnati General Hospital.

We have found one indication, as I mentioned earlier today, that the National Institutes of Health refused to participate on the grounds of its concern about the moral implications of going forward.

Dr. SAENGER. Yes. I mentioned in my presentation the National Institutes of Health maintained a General Clinical Research Center for the purpose of metabolic study which was available to any program within the medical center which would satisfy their requirements. One had to submit a protocol and so on. And we were allotted one bed there for a period of time. And we had several patients on this service.

And in order for us to maintain that service—maintain that availability, it was required that we submit the protocol and the course of these patients. And we used this in great part for our development of autologous marrow harvesting and reinfusion.

And this—this was—these were the reports that Dr. Chalkley of the Office of Risk Protection at the NIH responded to in his comments to a letter that he had received. Did I make that clear?

Mr. BRYANT. Not exactly. You might elaborate a little bit.

Dr. SAENGER. The NIH maintained a service, a ward, in our hospital, which they paid for totally. When a patient was put in that ward the funds were supplied totally by the NIH. This ward was there for conducting nutritional balance studies, looking at metabolic studies for a variety of purposes.

And we put several of our patients in this particular service so that we could study particularly the autologous bone marrow transplantation technique that we were working out. It took us some time to do that before we were successful in the five patients to whom I referred.

In order that the NIH could maintain this funding we had to give them reports of the protocol and the progress of the patients, and we did that. And these were approved.

Now the other research projects that we submitted to the NIH were turned down for purposes which I don't recall exactly at this moment. They accepted this work that we did with the General Clinical Research Center.

Mr. BRYANT. Are you saying that this—I am looking for some clarification. We have had implication from some of the documents we saw that the NIH refused to go along with the whole body radiation treatment experiments because of moral questions. Does your answer indicate they did go along with it?

Dr. SAENGER. They did go along in the studies of these several patients that we reported. And we then made a subsequent request for additional funding after our contract with the DOD was terminated. And it was those—that was that proposal I think that they declined.

Mr. BRYANT. On the grounds that they had some moral——

Dr. SAENGER. I do not know the grounds.

Mr. BRYANT. Well, our indications are that they were concerned about the moral implications of it. Is that a surprise to you?

Dr. SAENGER. As to what?

Mr. BRYANT. About the moral indications.

Dr. SAENGER. I think there was some difference of opinion about informed consent. I might say, in that regard, from the time we developed the first informed consent in 1965 we submitted several additional informed consents which I believe you have in your documents. These were done at the request of the Human Research Committee and were approved.

Our final informed consent technique that we used was a 2-day informed consent where the patient would be—where the study would be explained to the patient and/or his family or other—minister, lawyer, whoever—on one day. And on a second day we would again repeat this process. And if the patient agreed to it then it would be a signed, informed concept.

So we went through a rather elaborate series of improvements on informed consent.

Mr. BRYANT. The first question would be, did these people have the capacity to understand what was being told to them and to give consent? That was one of the criticisms raised, that they were not capable of understanding what you were asking them about and, therefore, not able to give informed consent. Could you respond to that?

Dr. SAENGER. My response to that—our physicians who carried out the informed consent procedure were very careful to explain this work to the patients in most if not in all cases prior to the written informed consent period. We had one of our nurses or other research associates accompany the physician with the patient so that this explanation would be carried out so that they would understand it.

And we do have several recordings where we had taped the informed consent procedure with the patients.

Mr. BRYANT. Dr. Egilman further pointed out there was a 25 percent chance of very rapid death from the whole body radiation treatment. I ask the question, why weren't these people told they might die rather than in several months or years but instead in a few weeks?

Dr. SAENGER. I have looked at a great many written informed consent procedures that have been developed over the years. I have yet to see one in which the risk of death is explicitly stated in the written informed consents that I have reviewed.

Mr. BRYANT. Well, I don't wish to impose a standard, a 1994 standard on actions back in the 1960's and early 1970's, but it does seem to me to be a fairly simple concept that if a person is ill and is probably going to live many more months or probably even a couple of years, if they run a significant risk of dying immediately or within a few weeks, that that is something that you would just normally tell them.

Dr. SAENGER. I think we explained to the patients that they might benefit and they very well may not benefit from the treatment. I don't think that we could be guarantors of results because, as you can see from our studies, we had some 20 patients who lived longer than a year.

And I think that it is really impossible to determine in any single case how long a patient will survive. We had some patients who we

thought would not survive, and they seemed to improve tremendously and live for several months.

Mr. BRYANT. I think you are confirming Dr. Egilman's statement that these patients were not told that they would, as a result of the whole body radiation, die much more rapidly due to the treatment.

Dr. SAENGER. I don't think that in anyone's experience it is possible to foretell the exact time of death after any treatment which is given. We gave this treatment with the understanding that it would improve the patient's welfare either by prolonging survival—we did the best we could in that regard—and we gave them the very best we were capable of in terms of shrinking tumors, improving well-being.

We got many statements from these patients which support what I am saying to you.

Mr. BRYANT. Mr. Mann.

Mr. MANN. Mr. Chairman, thank you.

Just to follow up on that point, Dr. Saenger, do you agree with Dr. Shields' statement that Dr. Egilman quoted that there was 25 percent mortality?

Dr. SAENGER. I do not agree with that at all.

Mr. MANN. So how—what was the risk then of death within a few weeks of treatment? Dr. Shields said one in four. How would you——

Dr. SAENGER. I think there was a risk of death within a short period of time after treatment. But the question is what was the risk due to. In our opinion, in reviewing these charts over and over again, it seemed to us that the primary reason for death within a few weeks after the treatment or in a few cases within a few days was the growth and the—the rapid growth of a tumor rather than the treatment.

If you look at the amount of radiation which we gave to these people in light of the further development of whole and partial body radiation, we find the patients today are living with doses of 600 to 1,200 rads, and our doses of up to 200 rads were really at a very low dose compared to what we see in survival today.

And it is not reasonable to assign radiation as the sole or major contributing cause of death in this series of patients.

Mr. MANN. Your paper that you published in 1973 does suggest that eight of the patients may have had their death accelerated as a result of the whole body radiation. Isn't that true?

Dr. SAENGER. What we said in that paper was if one assumes that all severe drops in blood cell count and all instances of hypocellular or acellular death were due only to radiation and not influenced by the type or extent of cancer and the effects of previous therapy, then one can identify eight cases in which there is a possibility of therapy contributing to mortality.

The fact that—that was the statement in the paper.

The fact is that these patients did have far advanced cancer and had other forms of therapy before and after. And, therefore, the assumption is just that. It is not what actually occurred. We have looked at these charts recently and find the course of these patients—the downhill course of these patients to have been due to cancer.

Mr. MANN. It is no longer possible that those eight died because of treatment?

Dr. SAENGER. I am sorry?

Mr. MANN. Are you saying that the statement in the paper of 20 years ago that it was possible that those eight had mortality advanced because of treatment is no longer, in your opinion, the case?

Dr. SAENGER. That is my opinion. May I continue?

Mr. MANN. Yes, I am sorry.

Dr. SAENGER. Also, statistically, we would have found the mortality of these patients would have differed from the mortality of patients treated by other means.

In our patients, it does not differ. That we can see in the survival curves in our 1973 paper.

Mr. MANN. Now, I want to go to your own documents, which I think are the most difficult part of all this, at least for me.

I have looked at your 1958 proposal to DOD, the contract with DOD, as I indicated in my opening comments, the reports that were made periodically from the beginning of the study in February 1960 until April 1967. And in none of those documents can I find any indication that there is any purpose to the study whatever other than to identify a biological marker or biological link that would allow the Department of Defense to administer simple tests and determine how much radiation a soldier in battle had received.

And the question I think we all have is, if this was about treatment and this was about therapy, why would there be no mention in all these documents for all those years?

Dr. SAENGER. I would like to refer you to our 1962 document prepared for the Defense Atomic Agency.

Mr. MANN. I have it. Yes, sir.

Dr. SAENGER. The eligibility for patients entering this treatment was spelled out. "There is a reasonable chance of therapeutic benefit to the patient. The likelihood of damage to the patient is no greater than that encountered in comparable therapy of another type."

Furthermore, I would refer you to the statement of J.A. Isherwood——

Mr. MANN. That we discussed earlier?

Dr. SAENGER. Yes, that was discussed earlier. That clearly identifies the attempt to improve the condition of cancer patients with that therapy.

Mr. MANN. Focusing on that, your 1958 proposal says nothing about patient therapy. And Dr. Isherwood sort of gratuitously starts talking about the project will be of great value in the field of cancer. How would he know that? What did he have beyond the proposal that would allow him to reach such a conclusion?

Dr. SAENGER. Well, I really can't answer that except to say to you that we had discussed this proposal with the Department of Defense people involved, so that I think we had indicated that this was the primary intent of our work. The reason that we phrased our reports to the Department of Defense in the way we did is that that was what they were interested in and that is what we tried to tell them about.

But that did not have anything to do—that did not interfere in any way with the therapeutic intent of the program.

Mr. MANN. Doctor, you referred to a 1962 document that you submitted to DOD. For what reason—what were the circumstances that led to the drafting and submittal of that document?

Dr. SAENGER. My recollection was that the DOD had requested us to give them an overview of where we thought this whole program was going, and at the time we made that report.

Mr. MANN. Just tracking through what we have here so that—the reports, we are saying, other than the 1962 document, were titling the project, metabolic changes in humans following total body irradiation and the aims and scope of the project had continued——

Let me just read from one of the reports. This is November 1961, to April 1963. This information is necessary to provide knowledge of combat effectiveness of troops and to develop additional methods of diagnosis, prognosis, prophylaxis, and treatment of injuries that would be suffered, as I understand, from radiation.

That continues to be pretty much the way it is all characterized until suddenly the report that was released after April 1968, the title is changed. The title now is, "Radiation Effects in Man: Manifestations and Therapeutic Efforts." That was the title that was used for the reports that were submitted for the period of the project, May 1967 until March 1972.

What was the reason for the change in title?

Dr. SAENGER. I think part of that developed from our work with autologous bone marrow transplantation and our effort to be able to control the depression of bone marrow.

We also found at that time, in that work, that with the use of autologous bone marrow infusion, reinfusion, that the patients did not seem, at least clinically to me, to get as sick as they did before in the period immediately after radiation. And certainly their course was ameliorated by the fact that their blood count came back to normal much more quickly than they did before we used that technique.

Mr. MANN. So the therapeutic efforts would be describing the use of bone marrow transplant?

Dr. SAENGER. If you look at our initial proposal in 1958 to the development of this entire project, I like to think we became more and more sophisticated in what we were doing and became more knowledgeable about the effects of radiation, and we understood a great deal more about the therapeutic benefits that we were achieving.

Mr. MANN. There is one last report that covers the time period April 1971 to March 1972. This continues to have this new title. But it also—and I think it is the first time that the purpose of the study is described in this way.

March 1972, the purpose is as follows:

> The purpose of these investigations has been to improve the treatment and general clinical management and, if possible, the length of survival of patients with advanced cancer since systemic effects of radiation therapy have been given particular attention in our work.

In fact, there is virtually no mention of Pentagon interest or Pentagon purpose. Now why was the purpose of the work characterized so dramatically differently in March 1972?

Dr. SAENGER. May I get a copy of that?

Mr. MANN. Yes, sir.

Dr. SAENGER. That was the April 1971 to 1972——

Mr. MANN. April 1971, to March 1972, yes, sir.

Dr. SAENGER. I think, Congressman, you will find that to be almost the exact duplicate of the published paper in 1971.

Mr. MANN. I think that is true. But, as I understand, this is the final report of which I am aware to the Department of Defense. And the question is why the purposes of the work are so dramatically transformed or at least stated in such a dramatically different fashion.

Dr. SAENGER. I thought it was a pretty good report. I summarized what we had learned over the 10-year period.

Mr. MANN. I am not questioning that.

The question is—I read to you what the purpose was stated to be of the work in your earlier reports. And it was all focused on the battlefield and so forth. And, suddenly, the battlefield and the Pentagon is not mentioned. I was curious.

The question is, what is the reason for the different characterization?

Dr. SAENGER. I think part of the reason for the characterization is that we—this whole research came under a great deal of criticism, and we were pointing out what the value and the benefits of our therapeutic part of the study was, in addition to the information which we gave to the Department of Defense.

Mr. MANN. Thank you.

Now, I want to ask a few questions out of Dr. Suskind's study. Dr. Suskind is present, I notice. We appreciate his presence.

But on page 12 of the report—I am quoting—although whole body radiation is widely used for many forms of radiosensitive tumors, no information is available to the committee which indicates that this form of treatment is used elsewhere in radioresistant or localized cancers as used at the University of Cincinnati. The first one is, do you agree with that statement?

Dr. SAENGER. Well, there are three references that are cited there. We have cited in the documents that we have prepared for this a great many papers on this subject. And this was written by the committee. It was not written by me.

Mr. MANN. Do you disagree with his statement, sir?

Dr. SAENGER. All I can say is it is the committee's opinion. I did not write this report.

Mr. MANN. Yes, sir. Do you agree or disagree——

Dr. SAENGER. I don't have to agree or disagree with it. Their survey of the literature is their survey.

Mr. MANN. I am asking you, sir, whether, in your professional judgment or professional opinion, do you—you—I am asking you to develop an opinion. Do you agree or not agree?

Dr. SAENGER. This says that the committee didn't find—it says, the committee—no information is available to the committee. I was not a member of the committee, and I did not review this report. If they didn't find information in this regard, which we have supplied in our bibliography, submitted to this—to your committee, I don't know what to say about it.

Mr. MANN. So you believe, in your opinion, the treatment was being used elsewhere in radioresistant or localized cancers?

Dr. SAENGER. In the diseases that we treated, I would say yes.

Mr. MANN. Quoting again from the study, this is page 14:

> The committee, however, was unable to find any written protocol in which the purpose of the study, which is determined palliative effects of whole body irradiation, until the protocol entitled, The Therapeutic Effect of Total Body Irradiation Followed by Infusion of Stored Analogous Marrow in Humans was resubmitted to the Chairman of the research committee by Dr. Ben Friedman, then principal investigator, on April 13, 1967.

Dr. SAENGER. Again, I would have to refer you to our statement made to DASA in 1962. I cannot say whether Dr. Suskind's committee was familiar with that statement or not.

Mr. MANN. So your 1962 document to DOD is a written protocol?

Dr. SAENGER. I think it is fairly explicit.

Mr. MANN. All right, sir. I am going to yield for the moment. I will pick up on the second round.

Mr. BRYANT. Mr. Portman.

Mr. PORTMAN. Thank you, Mr. Chairman.

Dr. Saenger, thank you for agreeing to be before us today.

Just to back up, again. My view is that the role of this subcommittee is to help determine the appropriateness of compensation for the families, and it is in that context that I ask these questions.

And first, of course, informed consent. You have mentioned in your response to Mr. Bryant and I believe in your testimony that the attending physicians were responsible for providing information as to risks, benefits and so on. I just wondered—perhaps this is in the record. I haven't seen it. And there are many documents I have reviewed. But who were these people that were informing the patients—who were these the internists or radiologists? Who were the attending physicians?

Dr. SAENGER. The principal ones I have identified: Dr. Harold Perry, who was responsible for the radiotherapy in our institution from about 1957 until about 1965; Dr. Horowitz, a radiation therapist, who was from about 1965 to 1968; Dr. Ben Friedman, an internist and hematologist who was with us from about 1963 to 1965 or 1966—I can't give you these exact dates; I don't have them—Dr. Silberstein, who began in 1967, I believe; and Dr. Bernard Aron, who began in about 1966.

Now these are all board certified specialists in their fields either of radiation oncology or internal medicine, nuclear medicine. And I think they are very responsible physicians and have been very highly regarded in this community and nationally.

Mr. PORTMAN. Further, on the issue of informed consent, having heard a lot about that today and having looked at it quite a bit over the last few months, there is a lot of conflict, I believe, out there between, as an example, the Hippocratic Oath on the one hand, and codes that were adopted later, the various practices of hospitals and so on. We have heard today that standards of disclosure were evolving during this time period, the 1950s and 1960s.

My question to you is, do you believe that the experiments deviated in any way from the standards that govern informed consent at that time?

Dr. SAENGER. Absolutely not. I think we complied fully with informed consent. I think we were in the advance of techniques of informed consent throughout this study.

Mr. PORTMAN. There has been discussion today about radiation doses being lethal or close to lethal. You stated earlier in response to Mr. Bryant's question that today there continue to be whole body radiation treatments. You indicated that the rads were higher, although I am a little confused as to the intervals. If you could perhaps flesh that out a little further and then just give us your opinion as a radiologist as to the question of lethal or nonlethal dose in the period of 1971.

Dr. SAENGER. When we began our works we were feeling our way very gingerly, and we believed that somewhere around 150 to 200 rads of whole body radiation was about as high as we could go without getting into trouble.

After our project was terminated, at the point when we were able to maintain better control of the patients with our autologous bone marrow infusion, we then find from looking at the literature that other centers continuing in this work, many treating the same and different cancers, were using doses of two, three and four times the size, the amount that we were using, with success.

If you go back and look at what we were doing, it would seem to indicate very strongly that the doses that we were considering as getting pretty close to a danger point were really not. And this is one of the reasons that we were able to conclude that the deaths in many of these patients, as they died, were due to the progress of their cancer, which was growing exponentially, rather than as a result of the comparatively small doses of radiation that we were giving both whole body and partial body.

Mr. PORTMAN. Again, could you just flesh out a little further as to today's practices in terms of levels of—I believe you talked about levels in the 600 to 1,200 range but indicated that treatment would perhaps be given at intervals. This is today's practice.

Dr. SAENGER. Today's practice in some institutions, they still will give 1,000 to 1,200 rads as a single dose. Now what is found in those patients is that they don't die of the acute radiation syndrome. They die of a subsequent radiation pneumonitis.

And in order to get around the problem of dying of radiation pneumonitis and still accomplish the intended therapy, which is to either treat the cancers or ablate the bone marrow, it has been found that one can fractionate the dose. And by that you would perhaps give four doses of 300 rads, say, a day or every other day, for a period of time. You would give 200 rads a day times five to get—for five days to get to 1,000 rads.

Furthermore, in today's treatment of cancer, these patients now are getting several series over a period of weeks of intensive chemotherapy, then getting this total body therapy and then going back to intensive chemotherapy. So that the amount of chemicals and radiation which are damaging to the bone marrow are really in terms of what we were doing back in the 1960's. It is sort of, I guess, fantastic. And patients are surviving this.

Mr. PORTMAN. The final question in the area of informed consent. This has to do with the selection of the patients. Many patients had a lower level of education. Many are indigent.

I know in response to an earlier question you indicated you weren't involved in the selection. If you have anything further on that, I would be happy to hear about it.

But my concern is, really, do you think that that is relevant? Does that bear on the informed consent question specifically? Would that same patient group be selected today, even with the evolving higher standards of informed consent?

Dr. SAENGER. I would like to respond to that because I think it is a very important question. It has been of great interest to me to first listen to several of the taped consent interviews which we have with several of our patients. And irrespective of their IQs or level of illness and so on, I can tell you that from my experience of some 50 years in handling cancer patients, that these patients were thoroughly aware of their situation. They understood that we were going to try and do something for them which might be helpful and might not.

In addition to that, we did something that is unique in the field of studying radiation effects in cancer patients. We had a very elaborate program of investigating the psychological and psychiatric reactions of these patients to their treatment. And part of this consisted of 5-minute interviews where the psychologist would simply take a tape-recorder and put this in front of the patient and say, talk for 5 minutes about anything you want to.

Now, what happens in these situations was that these patients are first interviewed in that fashion immediately when they began on our study program. That took us usually 2 or 3 weeks to get them all prepared, worked up, as we say, tested with our various laboratory tests and undergoing sham radiation, which we did carry out. And each time we had this interview.

Then the patients were interviewed just before they were treated, just after they were treated, and for a 3-day interval, I believe, a 7-day interval, as long sometimes as 6 weeks.

I have only listened to a few of these tapes, and I can tell you that these patients are understanding, sensitive and alert to their conditions, to their treatment, to their progress, to the fact that their tumors are growing, that sometimes they feel better, sometimes they feel worse, and they are as sensitive as any individual in this room today.

And I do not believe that all of this talk about the poor and uneducated and low IQs and so on had anything to do with their ability to perceive their situation in life and how it is progressing.

Mr. PORTMAN. The next major issue is the DOD role, the Government role in all of this.

I, too, have questions about your reports back to DOD. Congressman Mann quoted from a couple of those reports.

I wish DOD were still at the panel because I would like to hear—and perhaps we can now, Dr. Soper, hear from you later about other examples where DOD responded with an institution in terms of the effects versus the treatment, because it seems to me that Dr. Saenger's statement that this is what DOD was interested in and concerned about and, therefore, that was what was in the report might be something that we should look into in terms of other reporting that was done in other experiments around the country.

But my general question, I suppose, is, would you have gone ahead without DOD?

Dr. SAENGER. Yes. We had Dr. Perry. We had Dr. Kereiakes. We had the physical equipment and so on. And we would have proceeded whether or not we had DOD's support. DOD's support was not used for the treatment of the patients.

As we have emphasized, the GAO investigated this question, and I think the conclusion is inescapable that the DOD function was entirely separate from the therapy of the patients.

Mr. PORTMAN. My final question really is how DOD used the information. There is very little in the file that I find, at least as to DOD reporting back on how it used the information that the experiments in Cincinnati provided to them. Are you aware of any DOD reports generated during the study period or after the study period as to how they used the information that was provided?

Dr. SAENGER. I cannot give you the exact times that I met with DOD people, the DNA personnel and other Army and other commands. But there were several meetings which I attended. There was data that I worked on with them to develop the manuals which they use in the field for the commanders and for the personnel in the field in the event of nuclear warfare.

I don't have the information that Dr. Soper had about the exact manuals today. But I have participated in these, and I know—at least I am led to believe that our information was useful to the DOD in this regard.

I know that some of the studies, the psychological studies were of some help in interpreting what they find is a very important consideration of performance.

Mr. PORTMAN. And you are led to believe that some of the information provided was useful in compiling manuals——

Dr. SAENGER. I attended some conferences from time to time with DOD personnel. The only thing I can't tell you today is the exact date, location of those meetings. I think I could find some of this information.

Mr. PORTMAN. I think some of that is relevant—at least in my mind it is relevant to the issue of the DOD role.

Thank you very much, Dr. Saenger.

Mr. BRYANT. Dr. Saenger, you mentioned a moment ago—I am sorry. Dr. Egilman referred earlier and you made some reference to this business of treatment for nausea. And his comment was to the effect that ill patients who were nauseated were not given nausea treatment for up to three days, which was not the normal practice, as he stated it. Would you repeat what you said earlier about that?

Dr. SAENGER. What I said earlier about that was that we asked the ward personnel and the attending people not to ask specifically are you nauseated, do you feel like vomiting, because we found, as I think many of us observe in raising children and so on, if you ask leading questions you very often elicit responses, particularly for things which are somewhat suggestible such as nausea and vomiting.

On the other hand, we have taken a great deal of pride in the quality of our nursing care on the tumor wards of the General Hospital over a period of some 50 years that I have been associated

with that institution. And I can tell you at that these patients were not left all alone and completely neglected and so on. That is simply not so.

I think, on the other hand, you have to realize the situation of people who are desperately ill. They have very unpleasant things happen to them. They get sick. They throw up. They lose control of their bodily functions. They don't immediately always have someone to come and clean them up. And when family members come in and see them in these rather sad states, everybody gets pretty upset. And I have had this personal experience with members of my family, and I am sure all of you have.

But these patients under no consideration were abandoned or left out in a field and so on. It is just not so. That is not the quality of medical care that has been given in our institution during my entire career, earlier or later.

Mr. BRYANT. If a patient was nauseated, were they given antinausea medication?

Dr. SAENGER. If they complained. All they had to do was say, I don't feel good, and the patients were given whatever therapy—I mean, whether it was Compazine or some other antiemetic or cracked ice.

Mr. BRYANT. So your only policy in this regard was don't go and ask them?

Dr. SAENGER. Just don't ask the leading question. That was the only thing that we requested. And we only requested that for a period of 3 or 4 days. This was not something that would go on for a period of weeks.

Mr. BRYANT. So for a period of 3 or 4 days, during their course of these whole body——

Dr. SAENGER. Immediately after the irradiation. Immediately after the total body irradiation.

Mr. BRYANT. You made reference also to psychological isolation of the patient. Do you recall any instructions that the patients be put in rooms all by themselves and left alone?

Dr. SAENGER. I do not recall that specific incident. The wards in which the patient were hospitalized were at that time generally open wards. There would be maybe anywhere from 2 to 5 to 10 beds on these wards, more or less.

It was the custom from the time I was an intern when a patient became critically and terminally ill, having a lot of things going on, if there was a single room in the wards of the hospital the patient sometimes was moved in it for two reasons: one, that the family could be there, that they could get some care from the family and from the nurses; and also so they would not disturb the other patients who were less sick on the ward.

That was the general, I guess, nursing practice at the hospital.

Mr. BRYANT. But that would be, I assume, the policy for all patients at all times, would it not?

Dr. SAENGER. That is my impression. I don't think there was anything particular—I think the patients that we treated were treated as well, hopefully better, than any other patient in the hospital but certainly not less well. They were certainly not isolated or disregarded.

Mr. BRYANT. Finally, the reference to what the Defense Department paid for. I don't understand how you segregate the different parts of this treatment. A patient is ill, has what you diagnose as terminal cancer, and they are given whole body radiation treatment, which they are informed in advance is experimental. What did the Defense Department pay for?

Dr. SAENGER. What was the DOD getting?

Mr. BRYANT. Not what were they getting. What were they paying for?

Dr. SAENGER. What they were paying for was a detailed observation of the progression of the manifestations of radiation, the manifestations that could be related to radiation such as nausea, vomiting, diarrhea, weakness and so on, and for a long string of laboratory tests which are included in the material which you have in one of the appendices.

Mr. BRYANT. The cost of hospitalization and cost of treatment——

Dr. SAENGER [continuing]. Was not paid for by DOD. In other words, in those days, as I recall, at General Hospital, you would come in and you would be charged, say, $100 a day that would cover everything that happened to you. You did not have these rather elaborate accounting systems that we have in hospitals today.

That money was paid by the General Hospital. That was part of—the General Hospital was supported at that time by the general revenues of the city of Cincinnati. And they allotted so much money and then you could apportion that by what was——

Mr. BRYANT. What portion of the treatment was funded by the Department of Defense?

Dr. SAENGER. No portion of the treatment was funded by the Department of Defense. If a patient got penicillin because of an infection, if they got intravenous fluids, if the patient had to have an infected area operated upon, et cetera, if the patient was irradiated, that was not paid for by DOD.

Mr. BRYANT. You had a grant from DOD——

Dr. SAENGER. The grant paid for statisticians—I am sorry—for clerical people, technologists, doing laboratory tests, some supervisory care by various Ph.D.s. I think occasionally M.D.s would get some small funds in that regard, but the treating physicians were not paid by DOD.

Mr. BRYANT. Therefore, the U.S. Government, through the Department of Defense, played a role in this only insofar as they funded research on the results of the treatment which otherwise were paid for by the hospital; is that correct?

Dr. SAENGER. I think you stated probably better than I did.

Mr. BRYANT. Was my statement correct?

Dr. SAENGER. I think it is correct. Yes, sir.

Mr. BRYANT. Mr. Mann.

Mr. MANN. Dr. Saenger, just continuing in that same line, you stated a few moments ago that the Pentagon funding in no way influenced the study. The study would have taken place either way. My understanding——

Dr. SAENGER. The therapy.

Mr. MANN. Yes, sir. My understanding is that the course of therapy, the application of radiation, whole body radiation of these tumors, did not, in fact, start before the Pentagon funding and, in fact, stopped when the Pentagon funding stopped; isn't that true?

Dr. SAENGER. The therapy did not start before the DOD funding.

By the time we got all of our activities in place, the tests and so on, we wanted to train our technologists, train our physicians and so on, in what we wanted to do, it took about a year to get ourselves together.

Now, since 1970, or 1971 when the project was terminated, we somehow in our records cannot find what was done in total body radiation and partial body radiation in our hospital until 1979. From 1979 on, this form of therapy was used in a variety of conditions, which I described in my presentation. So that—we do have a gap in that period which is mostly one of recovery of records, so I can't answer your question from 1970 to 1979.

From 1979 on, these patients weren't treated.

Mr. MANN. So the use of whole body radiation in treating patients at U.C. did not begin until the Pentagon funding began. And we have no evidence that between 1971, when the Pentagon began funding the program, and when your participation in that program ended in 1979, that whole body radiation was continued.

Dr. SAENGER. I can't answer that. From 1979 on, this method of therapy was continued.

Mr. MANN. We have no evidence, so we don't know.

Dr. SAENGER. That is right.

Mr. MANN. Now, earlier with Dr. Soper we were talking about the difference between solicited and unsolicited proposals. Had there been discussions with DOD before you submitted a formal proposal?

Dr. SAENGER. I believe we had had discussions, but I don't have any documents for that. Our proposal was considered in the category which was in common parlance then as an unsolicited proposal. In other words, they did not come to me and say, Dr. Saenger, will you consider to do the things that we did? I said to them, I think we can find information which will be of help to you in this particular thing, as we described in the proposals.

Mr. MANN. I want to refer to the report that was done by the American College of Radiologists which talked about the fact that the number of cancer patients at Cincinnati General Hospital who are suitable for an aggressive palliation study have limited the size of the group under investigation. Do you agree with that statement?

Dr. SAENGER. Yes, I do.

Mr. MANN. Now, given that the purpose of this research, as you have indicated to us, in your opinion was to advance medical knowledge and so forth and it also held out some benefit, you told us, for patients that had the opportunity to participate, did you ever make an attempt to find suitable patients who met the criteria of the work with other hospitals in Cincinnati?

Dr. SAENGER. We did not—no, we did not go to other hospitals.

Mr. MANN. Is there a reason for that?

Dr. SAENGER. In getting our patients, you may recall that we said—the patients were referred to us. Now, by the time the pa-

tient got to us, the patient was considered for chemotherapy, perhaps for surgery, perhaps for no therapy whatsoever. And so we got a limited group of patients finally into the study.

And even after that about, roughly, a quarter of the patients who were admitted into the study, we never did treat for various reasons, as I mentioned. Either we didn't think after we analyzed them and worked them up that they would benefit from the treatment or we should treat them otherwise or they declined. There was always the option that the patient could withdraw from the study.

Mr. MANN. I guess my point is if this was a therapy that held out hope or advance for a patient who participated and then, from the standpoint of your research goals, it would have been helpful to have more patients. I am not sure I understand why you weren't making the program in which you were known to the other hospitals in Cincinnati so that patients who meet the criteria could be asked to participate. This would deal with the concerns expressed about the demographics of this population.

Dr. SAENGER. In looking over our records it appears there were five private patients who were referred and then became part of the General Hospital study. They did come from private physicians.

Mr. MANN. Holmes Hospital or——

Dr. SAENGER. I think one or two were from Holmes. Another two or three were from outside and were admitted to the service of the General Hospital.

Mr. MANN. Five out of the 88——

Dr. SAENGER. Then the three children, too.

Mr. MANN. They are included in the five or in addition to the five?

Dr. SAENGER. In addition to the five.

Mr. MANN. So five adults and three children.

Dr. SAENGER. We did not have a vigorous solicitation campaign. You know, if you take the 88 patients whom we treated over a period of 10 years, at eight patients a year we are not—I mean, this isn't a tremendous—I mean, this is not what we would consider a very high volume of people being studied.

Mr. MANN. Let me go back to some of the things that others have said and just ask you to comment.

In the ad hoc committee report chaired by Dr. Suskind, the statement is made on page 59 that, prior to 1966, the design of the study to measure the palliative effects of whole body radiation or partial body radiation was unstructured and not uniformly applied, particularly as regards uniform definition and methods of reporting.

Do you disagree with that statement?

Dr. SAENGER. I would say there is nothing that we did in the study that couldn't have been improved. We were trying to improve it as we went along. Statements like that—I think our Human Research Committee had made some comments along that line. We tried to improve the recording of palliative effects.

Mr. MANN. Similar statements are made on page 61 and page 64.

Of course, this speaks to the point that Dr. Egilman was making, that these design problems make it difficult now to—or at the time it made it difficult to measure what you were accomplishing from

a palliative perspective. He would argue—I guess that supports his conclusion that that was never much of a purpose at all.

Do you care to comment on that point?

Dr. SAENGER. Well, I have participated over my career in designing quite a few studies, some of them interinstitutional, some of them involving tens of thousands of patients, and the problem of designing studies is always a very difficult one.

There have been a number of critics of our studies who point out the deficiencies in the design, and I myself always have had problems in saying that the design is adequate or inadequate to some degree, and it is something to which all of us have to suffer. We have to improve our design and so on. And I can't disagree with what Dr. Suskind's committee said.

All I can say is that our design was the best we could do at the time, and, you know, in retrospective it may or may not have been inadequate. I thought the information we got out of it in the final analysis was pretty good. Whether it was as good as other people might have done, that is an individual matter.

Mr. MANN. Dr. Gaffney's letter was read at length by Dr. Egilman. Do you know who T. Gaffney is?

Dr. SAENGER. Yes, I do.

Mr. MANN. I take it he was involved in the review that UC conducted of the bone marrow transplant aspect of the project. Is that your understanding?

Dr. SAENGER. I am sorry?

Mr. MANN. My understanding is—I was asking if it is true that Dr. Gaffney was involved in the UC review of the bone marrow transplant part of the project. Is that true?

Dr. SAENGER. I don't know what you are quoting from. If you say it is true, I don't know—I wouldn't dispute he was involved.

I would only say this. If you look at all the comments that were made by—the fact that the research committee at that time, they at no time disapproved our project. In 1971, at the time that the president of the university terminated the DOD contract, we received a letter of approval from the faculty research committee and from the dean of the medical school, so that we must have done something that was right.

None of these things—this problem of determining this autologous bone marrow reinfusion. We worked on that from 1964 until 1968 until we got some good results. This was at the very early stages of these techniques, at least at our institution.

Mr. MANN. Thank you, Dr. Saenger.

Mr. BRYANT. Mr. Portman.

Mr. PORTMAN. I just have a few additional questions really related primarily to DOD's role.

We have heard different analyses of the DOD funding. It seems to me that Chairman Bryant has gone into that in enough detail. But my question is, what percent, if you could tell us—and perhaps you don't know this off the top of your head—but what percent of the total funding for the project, the $651,400, came from the Department of Defense?

Dr. SAENGER. Are you talking about the combination of therapy and the DOD?

Mr. PORTMAN. Yes.

Dr. SAENGER. We estimated—this is a very crude estimate—I think it would be some $416,000. I gave a figure—I don't want to contradict myself, but——

Mr. PORTMAN. $43,422——

Dr. SAENGER. $483,000. I don't want to tell you this is the best estimate I could possibly make.

In terms of the General Hospital at that period of time, our accounting system was, to say the least, rudimentary, and we made an estimate based on the average cost of a hospital day and then we added on some figures because of the additional cost for the radiation therapy and extra—some additional medication and so on, multiplied it by the number of patients, and that is how you got the number.

But I must tell you it was a very crude figure. If you take that, the $483,000 and the $650,000, it comes to about a million one and whatever fraction——

Mr. PORTMAN. Almost 40 percent.

Dr. SAENGER. Forty percent one, 60 percent the other.

Mr. PORTMAN. But the figure of $483,000 does not include physicians costs or professional fees——

Dr. SAENGER. I want to clarify that all of us who worked at the General Hospital were on salary. Whether I treated one of the patients you heard about this morning or I treated you, I was neither richer nor poorer for this service. We were on straight salary. Whatever we did was part of the job.

Mr. PORTMAN. The second question on the DOD side is, to the extent patients were told about the military uses of the data that was being compiled, how much were people told and when were they told of the military use of the data?

Dr. SAENGER. This was really sort of a mixed bag. We had asked, along with not asking about nausea and vomiting, the patients were not told, to my knowledge, were not told that they were being—that this information was being used by the Department of Defense.

Unbeknownst to me, several of the physicians who were attending the patients and obtaining the informed consent had mentioned to these that there may be some use of the information for problems in a radiation accident. So that there was some knowledge.

Now, this is by word of mouth, as the informed consents were, and we cannot document this in writing. They were told of the risks. It was only, I think, in about 1967 or so that mention was made that this information would be used for people in the battlefield. So that this is somewhat——

Now, you must understand that in terms of what other patients were told in other studies, there were no people, no patients to my knowledge, certainly in that era and even today who are told the funding source or necessarily what the purpose of the study was. That varies with different investigators. Perhaps today that is more explicit than it was.

But, certainly, talking to many investigators in internal medicine, surgery and other fields, they never disclosed the funding source for some purpose of the study other than whatever it was they told the patient about the benefits and risks.

Mr. PORTMAN. Thank you, Dr. Saenger.

That is all I have, Mr. Chairman.

Mr. BRYANT. I just have a couple of final questions.

You indicated that the proposal to have the Department of Defense participate with you was unsolicited. How did you all know that the Department of Defense funds were available?

Dr. SAENGER. I am sure—again, I can't give you a firm answer, but I am sure that this developed from some conversations which I had with members of the Department of Defense saying this—these were my interests. And they said, well, you know, we are sort of interested in the same things you are interested in. And then I made my unsolicited proposal.

Mr. BRYANT. Were you searching for funding, calling a whole lot of agencies at once? How did you——

Dr. SAENGER. In those days I think we were all searching for funding. This was a general problem, and I think it is true today. People are looking for funding.

Mr. BRYANT. Also, if the Department of Defense was really only buying results from you—and correct me if I am wrong but that is kind of what I read what you are saying as being—they weren't paying for any of this activity. They were paying for the lab work and for the studies and for the results of it. Is that correct?

Dr. SAENGER. Well, that is what—I don't understand your question, Congressman.

Mr. BRYANT. The actual administering of the treatment to these patients that has been the subject of controversy here today was paid for by the hospital.

Dr. SAENGER. By the hospital, right.

Mr. BRYANT. And as I understood what you said—I understood what you said to be that the Department of Defense was paying for results, in effect.

Dr. SAENGER. Well, we weren't guaranteeing them results. We were trying to elicit changes, either biochemical or chromosomes, blood counts, et cetera, et cetera, that we thought we could predict knowing what the effects of radiation might be. And, as you can see, we tried a number of different things.

We did not guarantee them—or, for instance, let's say we had a contract to build an airplane. We would guarantee at some period the plane would be available. But this was a research in which the outcome was not a guaranteed——

Mr. BRYANT. I didn't mean to imply results—pay you to accomplish a stated goal. I mean to pay for the results of the information, the findings from this work. That is what they were paying for, is that correct?

Dr. SAENGER. Yes, that is what we put in our reports.

Mr. BRYANT. I am curious why they made their payments over a 10-year period—on an annual basis over a 10-year period. I just wondered if that is consistent with that explanation.

Dr. SAENGER. There were contracts. We submitted new proposals as our work developed. We submitted new proposals. We got—we stopped doing certain tests. We instituted new tests. We instituted this whole program of psychological and psychiatric testing and so on.

And the project gradually changed. We finally got into some aspects of the bone marrow preservation and so on.

I mean, this was a changing project. It wasn't a static proposal. I don't know if I am answering your question.

Mr. BRYANT. Dr. Saenger, thank you very much for appearing today and testifying on this matter.

We would like to express our thanks once again to Judge Weber and his staff for making the courtroom available to us and all of those who have been helpful in making this hearing a success.

With that, the subcommittee hearing is adjourned.

[Whereupon, at 2:55 p.m., the subcommittee adjourned.]

APPENDIX

MATERIAL SUBMITTED FOR THE HEARING

The Testimony of Gloria Nelson

AMELIA JACKSON
PATIENT NO - 67

On October 21, 1966, after being discharged for General Hospital, Ms Jackson was a very weak ill woman. She was unable to take care of herself properly, and depended on the family for all her basic needs. She experienced bleeding from her rectum, loss of appetite, nausea, vomiting, weight loss, and was in constant pain. Her condition never improved.

Within a few weeks she was readmitted to General Hospital. The family was informed she should be transferred to Drake Hospital. Ms Jackson indicated she was afraid and wanted to return home. She was transported home, where she was loved and cared for by us until she died on March 25, 1967.

The family of Amelia Jackson would like for this committee to know, that for the entire 163 days after receiving the irradiation, her condition continued to deteriorate. We feel that the 100 rads of partial-body irradiation administered to her was cruel and didn't help her condition in any way. It's our belief that she may have lived longer if this experiment had not taken place.

A doctor is someone you trust. His job is to do everything in his power to alleviate your pain and suffering. However, this was not the case. She was always crying, moaning, groaning, and in excruciating pain. Ms Jackson was used to further Dr. Saeger's professional goals. It was purely an ambitious and callous act. Neither Ms Jackson nor the family were informed or consented to her being used in an experiment conducted by Dr. Saeger, and funded by the Department of Defense. There has clearly been a cover up by means of the Government, General Hospital, Dr. Saeger and City of Cincinnati. We cannot believe that they consented to such atrocities to be financed by the government; utilizing Ms Jackson's and the family's tax paying dollars.

The Testimony of Joe Larkins

April 11, 1994

My name is Joe P. Larkins. I am now 52 years old. My Father, Willard L. Larkins, passed away in 1971. I was 30 years old at the time. My family consisted of myself, an older sister and my parents. When my Father passed away, he and my Mother were in the process of raising a grandchild (my sister's son). Neither of my patents were well-educated, but my Father was hard-working and honest. We always had clean and decent clothes to go to school in and we always had ample food on the table. It doesn't take a well-educated person to be hard-working or honest. If Cincinnati General Hospital and the Doctor's therein had been honest, there is of course, the possibility that my Father could have lived for several more years. Instead, he went from a fairly able-bodied middle-aged Father and Husband to a premature death caused by an "experiment". My Father did not know that he was being used as a guinea pig; my Mother did not know; as his children, we were not informed of the procedures to be used nor of the risks involved.

I feel as though Dr. Saenger and the other "Doctors"involved, if you will, knew that the high levels of radiation which they administered to these patients had the very real probability of being fatal. Oh, how right that is! My Father was very much a family man, yet these people killed him as surely as if they had put a gun to his head and pulled the proverbial trigger. These "Doctors" left my Mother, with no job skills, to raise a grandchild as best as she could. My Mother lived until 1983, but she was a broken woman after my Father's premature and unexpected death.

I know that my Father knew that something was very wrong with the treatments being given to him at Cincinnati General. He even asked me "Son, what are they doing to me? They're trying to kill me!" That's how bad the pain he endured after the treatment was. He suffered so needlessly. What really gets me about this situation is the fact that the Pentagon contracted with these Doctors and this hospital to test the effects of radiation on the human body. Everyone realizes that Cincinnati General Hospital, now the University of Cincinnati Hospital, treated many low-education, low-income patients. I guess they felt that in some way, the fact that these patients were not rich, upper-class citizens, gave them the right to experiment with

their bodies without informed consent. NOT SO! I feel sure these physician/researchers were well-paid for their part and it would be very interesting to know the types and dollar amounts of the grants given to Cincinnati General by the Federal government. I feel sure that all parties, with the exception of the poor, unsuspecting patients and their families, were well-compensated. But since when, in our society, does one man or even a group of them, have the right to play God? A very good example of this is our 20th century "assisted suicide Doctor". This man is contacted by terminally-ill patients who wish to end their own lives with dignity and choose, by their own voilition, not to suffer needlessly for years. These people make the decision to die in peace, yet our great judicial system, along with the medical community, brought this compassionate physician up on charges. The differences in these deaths and the death of my Father are that my Father did not choose to die - someone else made that decision for him, without consulting or informing him and they were amply compensated for it. I feel that the price they should be required to pay to the families of the people they killed, should be exceedingly high. I also feel that the Federal government should be named as a co-conspirator in this case, because that's exactly what it was - a conspiracy. No person, and I emphsize 'NO', person would willingly consent to a treatment with any degree of fatality involved. People, both you and I, simply value life too much. I think that is the big thing here - the patients were not informed. I know that behavior of this sort would not be tolerated by the medical community today. But then again, this entire mess was surrounded by a thick veil of secrecy on both the doctors' part and on the part of Cincinnati General Hospital. It is still being closely guarded and kept under yet another veil of secrecy to this very day by the University of Cincinnati, in that they have yet to provide the medical records of the patients involved in this experiment/ I beseige you to order the University of Cincinnati to release the patient records, in their entirety, to the next of kin immediately. They are hedging to save their own skin. I was promised my Father's complete medical file over a month ago; as of this writing, I have nothing.

I only hope that you, the Congressional Committee, see fit, as members of the human race, to break this matter wide open here and now and award just compensation to the families of the victims. I feel that the Physicians involved and also the federal government (the Pentagon) should pay and also I beg you to strip any and all of the Doctors involved of all their medical credentials that they hold. If justice prevails in this matter, and I have faith that it will, a strong message will be sent to our government officials and the private physicians (to whom people entrust their lives and the lives of their loved ones) that behavior of this

sort will simpley not be tolerated, that justice will in fact be both swift and severe. I pray that a situation such as this will never again be faced by a group of people. If this statement to you, the Congressional Committee, does anything to help in the name of justice, then my Father's death and the sorrow and hardships that his familty faced, will not have been completely in vain.

Thank you.

Ms. Catherine O. Hager
590 Delta Avenue
Cincinnati, OH 45226
513-871-8773

April 7, 1994

#051

To: Total Body Radiation Subcommittee and Whom it may concern;

In January, 1994 I began noticing articles in The Cincinnati Enquirer regarding Total Body Radiation experimentation done on cancer patients in the 1960's at Cincinnati General Hospital. Since I knew my father, Joseph Mitchell, was treated at that hospital for cancer during that period of time, I contacted Linda Reeves at The Cincinnati Enquirer. After a brief discussion with Linda, it was determined that my father had indeed been involved in the Total Body Radiation experimentation as patient #051, the first patient to be identified. From this point, my husband and I, along with the assistance of the news media attempted to piece together any records available regarding my father's treatments at the hospital.

In October, 1963, my father was diagnosed with lung cancer in the right lung, and was admitted to Cincinnati General Hospital. Surgery was scheduled for November, 1963. Although there is no notation of this scheduled surgery in his medical records, we have a letter which was written by my father to my sister detailing the planned operation. For some unknown reason the surgery was canceled on the day it was scheduled to take place, with no explanation. The surgery was never rescheduled. Instead, my father was given a schedule of dates to return to the hospital for Cobalt Treatments. At this point, I asked the doctor why the surgery was canceled. He told me he was too weak for surgery and decided to opt for the Cobalt Treatments instead.

In reality, my father was not in a weakened state at that time but was in relatively good health, still working and living a normal life. It wasn't until the Cobalt Treatments started that my father began to go down hill. After 35 days of treatments my father was so weak that he had to retire from work and move closer to my family so we could help care for him.

In early 1965, my father was again admitted to Cincinnati General Hospital with severe chest pains. It was at this time he was subjected to the Total Body Radiation. He immediately started on a drastic downhill spiral. After much suffering, my father died on July 14, 1965 - 74 days after the Total Body Radiation. (150 DAYS)

Since Total Body Radiation had not been performed on cancer patients at Cincinnati General Hospital prior to the Government funding of 1960, I feel that my father, along with other cancer patients, were hand picked and used in Total Body Radiation; not as a treatment for cancer, as they had been told, but as a cover-up for a study performed for the Department of Defense to determine possible effects on soldiers in nuclear warfare.

It might be noted that at the time my father died, two of my brothers were in the U.S. Air Force. One in Vietnam in the war zone. The Red Cross had to locate him and bring him home for the funeral. Both brothers have since retired from the Air Force.

Isn't it ironic that two of my brothers were serving this country in the military, while at the same time The United States Government was sponsoring experiments which shortened or ended their father's life.

Respectfully,

Catherine O. Hager

Catherine O. Hager (Mitchell)

COH;cmh

Enclosure

Sat 2. 1963.

Dear Isabell,

I am sorry honey I need your help.

First I am going to have an operation 1st part of the week.

The doctor is not giving out the right news to the family.

It is going to be a long serious of operating, I will be about 2 months here, it's very serious only a 50-50 chance to come through as all I have left is ~~to~~ a lung, so therefore I ask you to do all you can to help mum as much as possible while I am in here I can tell you more when I see you again but please do not take it too hard I am trusting everything will turn out right which is doughtfull see you soon

Love Dad. x

1st Note

Isabell
read this when
you get home O.K.
Dad.

died
1965

JFA Report in typescript, as originally issued. Identical to "A Report to the Campus Community" included in C. Record attachment (Jan. 26 1972) (Use either copy.)

A REPORT TO THE CAMPUS COMMUNITY

Since last October a committee of the Junior Faculty Association of the University of Cincinnati has been investigating the radiation experiments at the University Medical Center. We have interviewed doctors involved, and we have studied with care the reports of the research team to the Defense Department, as well as the team's publications on radiation in medical journals, and many other pertinent documents. Our committee has had extensive help from members of the medical community.

For reasons that we will present below, we have come to the conclusion that many patients in this project paid severely for their participation and often without even knowing that they were part of an experiment. We feel that the evidence clearly calls into question the manner in which these human experiments were designed and carried out. We therefore urge the president of the University to terminate this project and to instruct the Medical Center to cooperate fully with the congressional hearings to be held next month.

We are addressing ourselves in this report to what we believe to be the three most crucial questions to be asked about this project:

(1) Was cancer study the main object of the experiments?

(2) What were the real risks to the patients?

(3) Did the patients give their informed consent to being used as experimental subjects?

To begin with, we have been unable to find any evidence of a planned, systematic cancer study. It seems unlikely that the team would not have mentioned, somewhere in the 900 pages of the Department of Defense (DOD) reports, the fact that they were conducting the DOD project in conjunction with a specific cancer research study, had this indeed been the case. Nor has the team made public, even during the recent months, a design for cancer study in any way comparable to the detailed proposals for DOD radiation studies, proposals which have been repeatedly and painstakingly modified and amplified over the eleven years of the project.

We also point out that there is no evidence in the DOD reports that any patients were irradiated before the beginning of the DOD project in February 1960; the two projects, research on cancer and research on radiation injury (if indeed there were "two"), seem to have been coterminous.

Consistently throughout the reports to the DOD the doctors make statements that indicate that the selection of patients and the radiation dose given them was at least partly tailored to the needs of the DOD project. For instance, we find that in the first description of their project the team states that they will generally not irradiate women with active menstrual cycles. The menstrual cycle, they say, affects the appearance of amino acids in the urine and at this time the team is studying amino acids in the urine of irradiated subjects in hopes of finding an indicator for radiation injury. Such a statement as the following, which appears in the 1970 report, points clearly to the fact that the main reason for increasing the dose over the years was to improve the data--not on cancer treatment--but on radiation injury:

> Clearly much more in vivo data are required [for indicator studies] with good dosimetry [where the radiation exposure can be controlled]. We are pursuing this goal at whole-body radiation doses up to 250 rads with even higher doses planned with the support of marrow auto-transfusion and laminar-flow "sterile" rooms. Large-volume partial-body irradiation is also being performed to learn more about the efficacy of chromosome aberrations as a radiation dosimeter. . . . [1970, page 22]

Also, consider the wording in this initial sentence of a 1964 publication on dosimeters by the Saenger team in Radiation Research: "In an effort to evaluate the metabolic effects of single doses of whole body radiation in the human being, patients able to maintain their nutrition with disseminated neoplasms were given therapeutic doses of whole body radiation with Cobalt-60 teletherapy." And in the 1971 DOD report we find these particularly chilling lines:

> This [report] brings to 43 the total number of patients who have undergone assessment for the effects of total or partial body irradiation on their cognitive-intellectual functioning and emotional reactions. In terms of the characteristics of the overall sample, the addition of the new patients will serve to improve the ratio of whites to Negroes, to increase slightly the average educational attainment, and to decrease the average age. The trend noted in the 1969-70 report toward recruiting patients in comparatively better physical condition has continued. [1971, page 72]

Finally, we repeat the now rather well-known fact that there has been no publication by this team specifically on total

or partial body radiation as cancer treatment. One of the doctors, Dr. Edward Silberstein, wrote to the chairman of the JFA committee last November 14 as follows:

> I hope I made clear to you on Monday that we have not yet published the results of therapy because of the variable duration of patients' clinical course with cancer following treatment and the need to have an adequate sample of patients before one makes any statements about the efficacy of one's therapy. Since I am limited to treating 7 or 8 patients a year, I cannot, as a responsible scientist, issue claims about what we can do therapeutically for patients over a short period of time.

Is it conceivable that in an authentic cancer research study, no results would be reported after eleven years and the radiation of 87 patients? If no pattern had emerged after the irradiation of 87 patients--indeed after 10 or 20--would this in itself not have been worth communicating to other cancer specialists? We also question why, if this were a serious study of the effects of radiation on cancer, so few autopsies were performed.

We can only conclude that the purpose of irradiating cancer patients at General Hospital was primarily to study radiation injury for the DOD and that incurable cancer patients were used because (a) they were going to die anyway and (b) they "might" benefit from the radiation in terms of reducing pain or slowing the spread of cancer.

We move now to the question of the real risks to the patients and the effects on them of the radiation. We begin with this crucial statistic: of the 87 irradiated subjects whose histories are given in the DOD reports, 21 died within 38 days--or 24%.

What is even more serious is that of the first 40 patients given total-body radiation before the advent of bone marrow transplants, 7 of the 18 receiving the higher doses (150 or 200 rads) died within 38 days--or 39%. That the higher doses were much more lethal than the lower doses is clearly borne out by the fact that of the 22 patients receiving 100 rads or under, only 10% succumbed within the 38-day period. The full statistics on this early period of the project, as we have abstracted them from the reports, are as follows:

First 40 total-body subjects (1960-66):

Of those receiving			200 rads,	2 of 6	died	within	38 days
"	"	"	150 rads,	5 of 12	"	"	" "
"	"	"	100 rads,	1 of 14	"	"	" "
"	"	"under	100 rads,	1 of 8	"	"	" "

150 rads or over: 7 of 18
under 150 rads: 2 of 22

Of the total 87 patients, it may be added that 4 died within 10 days, 7 within 20 days.

These statistics are all the more alarming when one juxtaposes them with the doctors' descriptions of the patients at the time of radiation. Throughout the DOD documents the doctors report that though all their subjects are patients with incurable cancer they are not in the final stages of disease or close to death. Patients as a group are described over and over again as having "relatively good nutritional status," "normal renal function," and "stable hemograms." We offer this sentence from the DOD report of 1969: "The patients who are irradiated, all of whom have inoperable, metastatic carcinoma but are in relatively good health, provide us with an opportunity to study multiple facets of the effects of radiation in man rather than in experimental animals," (page 1). In the 1970 report the doctors write:

> Several of the subjects were tumour-free and essentially normal (following radiation-induced tumour regression) receiving prophylactic whole-body radiation. The rest had metastatic carcinomas which were inoperable and not amenable to conventional chemotherapy. Nevertheless, these patients were all clinically stable, many of them working daily. [1970, page 2]

Even of the group described above, 2 died within a month--one on day 31 and one on day 22.

In regard to possible benefits, we assume that any benefits that would balance out these enormous risks would have to be very plain and dramatic. Yet this is not at all the case. The American College of Radiology (ACR) team stated that about a third of the patients reported a decrease of pain (the medical histories show, by the way, that some patients had an increase of pain following radiation) and a greater "sense of well-being" and that a third had decrease in primary tumor size. Dr. Saenger has said that he feels the statistics for long-term survivors--a small number of patients lived several years after radiation--will show

that total and partial body radiation is "promising" as cancer treatment. But even that much is clouded by (a) the fact that many subjects received other kinds of therapy before or after radiation and (b) the fact that the Saenger team used no control group. The doctors state in the later DOD reports that they are carrying out their experiments in conformity with the Helsinki Code (which dates from 1964); yet the code clearly states that the health of the patient must always be the first consideration in trying out new kinds of therapy:

> I.4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

But let us assume for the moment that those we address are not convinced, even by the number of short survivors plus the patients' conditions at time of radiation, that many died of radiation injury rather than simply from their disease. There is yet another kind of evidence that radiation injury was a major cause of death. It has been known for some time that a major injurious effect of radiation is bone marrow failure. The bone marrow's ability to make white and red blood cells can begin to fail as early as 6 days post radiation; the critical period for marrow failure then comes from 25 to 40 days post radiation. In summarizing in 1966 the marrow problems for their first fifty patients, the doctors themselves make the following statement: "The total white count falls to a low point 25 to 40 days after irradiation. There was a persistent lymphopenia which persisted for 40 to 60 days" (page 31). Can it be merely a coincidence that the short survivors are bunched in exactly that critical 25-40-day period?--that, for instance, no less than 9 subjects died from 31-38 days? In this same 1966 report, in fact, the doctors state outright that "severe hematologic depression was found in most patients who expired," and they note that because of this, they are beginning work on bone marrow transplants--far too late, in our opinion. In the 1963 report, they write that "Delineation of disease score [a rating for blood problems], radiation score [the rating adjusted after radiation] and total continued to be of value in ascribing the importance of radiation in precipitating demise" (page 9).

A distressing aspect of the doctors' public disclosures about this project has been their misleading statements concerning the protection given the patients by bone marrow transplants. It has not been made clear that of the first 50 patients only 2 received transplants and that neither of these transplants was a clear success (the first subject died, in spite of the infusion, 28 days post radiation).

The team from the American College of Radiology reported that it felt the research team could not be censured for not giving bone marrow transplants during the early years for the simple reason that the technique had not then been perfected. But since the doctors could not protect the patients from bone marrow failure, were they justified in giving the higher doses of radiation? Among those first 50 patients, we point out again, 7 of the 18 high-dose subjects did not live beyond 38 days.

Why did the doctors not discontinue high dose radiation as soon as they began to lose patients from bone marrow failure? It is perfectly clear that in the first six years of the project, the less radiation given the better the patient was likely to do. It has, in fact, only been within the last year or so that the doctors have had much success with the transplants; it is still not completely clear that bone marrow transplants offer a certain way of protecting all patients.

We move now to the third question: Did the patients give their informed consent to being used as experimental subjects? We note to begin with that during the first five years of the project no consent form seems to have been used at all; none is mentioned in the DOD reports for these years, and the absence of written consent is corroborated by the ACR. In fact, it is clear from the DOD reports that during these years the doctors were not attempting to justify the radiation as experimental cancer treatment but simply as "therapy" or "palliation treatment," as it is in these words that the radiation is constantly described. Patients seem to have been told nothing except that the radiation was part of their treatment. Over and over again in the reports we find such lines as these:

> The patient is told that he is to receive treatment to help his sickness. [1961, page 3]
>
> The patient is told that he is to receive treatment to help his disease. [1963, page 4]

In 1965 a short consent form was initiated, but it made no mention of specific risks from radiation injury, merely asking the patient to state that "the risks involved" and "the possibility of complications" had been explained and that "the special study and research nature of this treatment has been discussed with me and is understood by me." For what the patients were told we have only the doctors' word. Another form, used as late as December 1970, states the risks as follows: "The chance of infection or mild bleeding to be treated with marrow transplant, drugs, or transfusion as needed," and the first line of that form

reads as follows:

> I (the subject) being of the age of majority and of sound mind and body, voluntarily and without force or duress, consent to participate in a scientific investigation which is not directed specifically to my own benefit, but in consideration for the expected advancement of medical knowledge, which may result for the benefit of mankind.

The latest consent form, a revision of the above made last spring and signed by only a handful of patients, includes under "Risks" a long paragraph regarding bone marrow problems and alters the lead sentence to read "not only directed specifically to my own benefit, but also in consideration for the expected advancement of medical knowledge. . . ." It is a very unhappy fact that it was this last form, only in use for a few months, that Dr. Edward Gall, director of the Medical Center, chose to release to the newspapers. This form was printed entire in the Cincinnati Post, with a statement saying it was signed by "every adult patient" of the project.

In our view none of the consent forms properly states the real risk to the patients--that is, the risk of death from bone marrow failure within 40 days. We feel, in fact, that no conceivable consent form, particularly in view of the subjects' low level of education, would have justified the doctors in subjecting the patients to the higher doses of radiation.

In conclusion, we want to comment on the recent report by the American College of Radiology, which finds nothing whatever to criticize in these experiments and urges that they be continued. We are confident that this report will not be taken seriously by anyone properly informed about this project. The ACR omits from their report the more damaging statistics on patient survival. The only statistic they give is as follows: "A group of 10 per cent or eight patients died from 20 to 60 days after the whole body exposure." We find 14 total-body subjects who died within this period (not to mention 5 partial-body)--or 23%, and of course this figure takes no account of the 7 subjects who died within the first 20 days. The ACR doctors contribute, in other words, to the deceptive impression that the main side effects from radiation were nausea and vomiting within the first few days.

As for the special committee appointed by the president, we regret very much that the existence of such a committee was kept secret for so long and that even today the names of the committee members have not been revealed. It has been

impossible for us, or any other party interested in the project or having special information about it, to communicate with the committee. We hope that even in this unpromising context, however, the committee will seriously address itself to the real questions surrounding this project and will make a recommendation that we all can support.

The Junior Faculty Association committee has not been secret, and we have asked in the campus newspaper for the assistance of all interested parties. We also succeeded finally in having a full set of the DOD reports made available in the reference room of the UC library for all to inspect, and all are invited to check our facts and figures in these public documents.

We are confident that those who examine the evidence for themselves will join with us in urging the president to terminate this project and to assure the public that the Medical Center will make a full disclosure of all the facts at the congressional hearings.

Printed at JFA expense.

Date: April 4, 1994

To: Robert B. Newman, Attorney at Law

From: Members of the Maude Jacobs Family

Subject: Radiation Testing at UC (Cincinnati General Hospital)

This correspondence is regarding Maude Jacobs, a female caucasian, who was an unsuspecting victim of the radiation tests conducted by the University of Cincinnati. Maude was born in Whitesburg, Kentucky on June 7, 1916. The third grade was her final year of formal education. By the time she was thirteen years old, she was married and had given birth to her first child. She bore seven children in all, six girls and one son. She was a beautiful woman with a lovely radiant smile. She was impeccable about her children's appearance, as well as her own. Her devotion to her family was obvious to anyone who knew her. Maude lived her life below the poverty level, but was a proud and dignified woman. She was genuinely happy with the simple things in life. Her delight was cooking and caring for her children. When she died she was a widow and left three minor children at home.

According to information from CGH (Cincinnati General Hospital), Maude was diagnosed with breast cancer on July 17, 1964. A treatment of hexamethylmelamine began on July 27,1964 and was completed on August 18, 1964. With this medication her primary tumor receded markedly. On November 7, 1964 total body irradiation was administered. The midline absorbed tissue dose was 150 rad (250 r midline air dose). At the termination of the treatment she had severe vomiting for twenty-four hours, in spite of intramuscular compazine. Before treatment she had a normal hemogram. Seven days after treatment the white blood count began to fall. The platelet count fell around fourteen days after treatment. The WBC was 1,000 and platelet count was 80,000 twenty-three days after treatment. On the twenty-fourth day, the WBC was 850 and platelet count was 38,000. Maude died December 2, 1964. Twenty-five days after total body irradiation. She was study number 045. (Documentation from CGH attached.)

Two letters written by Maude to her sister Arlie less than two months before her death describes how she felt, and also indicates she thought the doctors did not know what was wrong with her. She talks of living near her oldest daughter, Lillian, who is very helpful to Maude. She also is pleased to be home with her children, but feels sorry because she is too tired in the evenings after preparing dinner to watch television with them. She refers to the expense of her medication and said prayer helps her more than the doctors. These letters demonstrate her education level, but also reveal her devotion to her children. Maude had no knowledge of the seriousness of her cancer much less knowledge of the radiation

treatment. She did not expect to die. If she had, she would have discussed the future care of her minor daughters with the rest of the family. Her death was so sudden and unexpected the family was totally unprepared. The three young daughters eventually were put in St. Aloysius Orphanage. (The two letters from Maude to her sister are attached.)

The family was **NEVER** informed of the radiation test or it's purpose. Nor was anyone ever asked to sign a consent form or give verbal permission for testing. Some of the memories which were dismissed without attaching importance now make sense or at least raise suspicion. Her daughter Irene was seven months pregnant at the time and was having a difficult pregnancy. She remembers Maude's bright smile and cheerfulness, then remembers a private room and no more smiles or happy faces. Irene remembers being afraid of going into that room. Maude asked her to feel her head and when she did it felt full of soft tumors. Her body felt like sand. Even in the hallway she could hear Maude's delirious talk.

Maude's daughter Sherry was twelve years old and remembers the private room, but at the time didn't know it was uncommon for a person without insurance. Sherry remembers the orphanage and being split up from her two younger sisters. The youngest girl, Kim, eventually went to a foster family.

Robert Murphy, one of Maude's grandson's, remembers thinking how nice it was to have a private room without insurance. Bill Murphy, another grandson recalls visiting her in the private room, but not wondering why she was there. He remembers her conversation as "out of her head".

Her oldest daughter, Lillian Murphy Pagano, lived downstairs from Maude and was her primary care provider. Lillian was never contacted or consulted about her mother's treatment. She remembers a drastic mood change associated with rapid physical deterioration. She too recalls the private room at the end. She remembers thinking her body felt like sand. She was concerned too for Irene, because of her pregnancy and the worsening of their mother's health so rapidly. Lillian's concern grew as Maude quickly became disoriented and no longer recognized anyone. She was violently ill and talking utter nonsense. Maude died before her time everyone felt. Her family lived for the next twenty-nine plus years with the sadness of her death, but also had warm memories to console them.

Since the details of the experiments became public, the entire family has been drastically affected. Now guilt has replaced the sadness and comments like "I should have known" or "I should have asked" are commonplace. Reliving Maude's last days over and over, remembering differently now why she was so violently ill, how she suffered, and now a reason for the private room. Her death is now a nightmare. She died without comfort and dignity. She was discriminated against and selected because of her background. No benefit was ever planned for Maude. She was a number, a statistic.

Her children want an apology. They want to know nothing they could have done would have altered the results. They want Maude to know they are sorry if they disappointed her because she suffered needlessly without intervention from them. They also need a quick resolution so this too can be a memory. Already too much damage has been realized.

Lillian Murphy Pagano (Maude's oldest daughter) feels personally responsible for her death. She became obsessed with Maude's death, often calling other family members several times a day to go over some part of her last days again and again. She was found several times at three or four o'clock in the morning with a fixed stare and silent sobs. Eventually she was rushed to the hospital with a suspected heart attack. After a short stay of a few days, some testing, several prescriptions, and instructions to avoid stressful situations, she was permitted to go home. Anxiety struck again within a few weeks. This time she was gone. Lillian's daughter found her, called 911, and received over the phone guidance for delivering CPR. When paramedics arrived, she was given multiple shock treatments to revive her. It is estimated she was dead for four minutes. She was on a respirator and in a coma; she also had several seizures. The doctor's gave her a 50% chance of pulling through, but warned all about the possibility of permanent brain damage. She has regained consciousness, but is still in critical condition at this writing. She recognizes family members, but is mentally unstable. The extent of damage is still unknown. Her family has been told she will need twenty- four care and cannot be exposed to **ANY** stressful situations. She doesn't talk about Maude now. She doesn't even remember who visited her an hour ago.

The ordeal with the UC experiments must come to a swift conclusion. This is the saga of only one family, there is supposed to be eighty-seven more victims with families. It's amazing how something that was a remote, barely thought of memory, now is resurrected and grown into an unwelcome demanding problem. A problem that can consume your days and affect people from twenty-nine years of family growth --- people Maude never could have known.

This letter was compiled from the hearts and thoughts of Maude Jacob's children:
Lillian Murphy Pagano (nee Phillips)
Irene Froman (nee Phillips)
Bob Phillips
Betty Wolfe (nee Phillips)
Sherry Brabant (nee Jacobs)
Janet Baker (nee Jacobs)
Kim Swedo (nee Jacobs)

Attachments

My Aunt Louise Richmond passed away from Colon Cancer in March, 1968. She was only 49 years of age. My Mother Viola Macklin (one of Louise's older sister) brought her from Cleveland, Ohio to Cincinnati, Ohio for medical care of her cancer at the General Hospital.

Instead of medical treatment, my Aunt Louise, unknowingly was used as an experimental subject at General Hospital in their radiation experiment. Within weeks of her admission, her health rapidly and painfully deteriorated and ultimately leading to her death.

Regrettably, the news of the General Hospital Radiation experiment has recalled many agonizing memories for myself and my family. The death of a loved one, under normal circumstances is difficult, but now with the added knowledge of my Aunt sacrificial involvement in the radiation experiment, my family members must relive the misery, now with twice the anguish.

Various family members can vividly recall the evening visits to the hospital as we accompanied our mother to visit Aunt Louise. The torturing cries of pain that greeted us as we entered into the hospital ward had become all to familiar to us. She would be lying in her hospital bed trembling and shaking from her agonizing pain so forcefully that the bed itself would be visibly vibrating.

Throughout the visit, my Aunt Louise would cling on to my mother's arm crying and begging her to take her home. She would repeatedly say, "please Viola take me home with you, I['m in so much pain, they are hurting me, they are trying to kill me".

The visits would always end with my mother tearing herself away from my Aunt Louise only to hear her cry in pleading desperation as we walked away. For seemly, hours after we left the hospital and even after reaching home my mother would cry from the guilt she felt for my Aunt's severe pain and suffering. My mother would routinely rock herself to sleep while crying and humming spiritual songs to relieve the burdensome feeling of her most recent experience/visit to my Aunt Louise.

After my Aunt Louise' death in March, 1968, my mother would often ask us if they (the Doctors at General Hospital) were really giving her the correct treatments for cancer.

We had no idea Aunt Louise was a part of a Defense Department experiment. We're sure if she had known she was a guinea pig, she would not have participated.

My mother would often recall the visit and continued to blame herself for the pain and anguish my Aunt Louise had experienced. My mother carried this unwarranted guilt to her death, and now we have been forced to carry this guilt as well in memory of my mother and aunt.

CRUUS

TO : Congressional Committee
FROM: Herbert F. Varin
DATE: April 4,1994

Study # 075 N.C.
Chart # CGH 409-278

My mothers name was Nina L. Cline, a loving and caring mother, whose only hope was to see her grandchild before she died. She did 10 months before her death. She was also very close to her sister, and her sisters children, who were all very helpful with my mother during her cancer.

My mother was diagnosed with cancer in 1962, she put a lot of hope and faith in her doctors and General Hospital who were treating her. She often talked to me and other family members about her treatment, but at no time did she mention being apart of any experiments for the government. She would have talked to me and other family members before ever consenting to any experiments.

I am appalled to think that Dr. Eugene Saenger, his associates and our Federal Government would join is such an inhumane act. I also believe Dr. Eugene Saenger violated his moral and ethical obligation toward his patients.

We were taught as children and young adult, to believe in our Federal Government, that they would make all the right decisions concerning our welfare as people. For the government to sponsor a radiation experiment of this nature, on my mother and other patients was totally immoral.

Herbert F. Varin (Son)

Herbert F Varin

TO: **Chairperson of the Congressional Committee**

RE: **The Partial and Whole Body Radiation Experiment Conducted from 1960-1971**

FROM: **Mr. Woody Plair and Family of Mrs. Beatrice Plair**

This letter was very difficult to write for us, the family of our departed wife, mother and grandmother. We conversed of many traumatic thoughts and feelings regarding our loss.

Herein is the summation of our collective thoughts and feelings. Dr. Saenger states that the patients and families gave their consent to receive partial or whole body radiation. For the record, our mother loved life and she would have never given her consent to any treatment that would have shortened her life or cause her the pain, we observed. She never knew she was part of the Cold War Radiation Experiment. As a family, we were never told of her participation in partial or whole radiation. We would have not given our consent for her participation in an experiment. At no point in the supposed treatments of our mother did anyone tell our father nor her children that she was part of a dangerous and life threatening experiment.

What we can say to the Sub-committee is that we remember our mother complaining of increased pain, especially following the radiation exposures. We can told you how our mother told us she felt as though she was on "fire" or "burning all over". We can tell this committee, we resent our mother being used as a human Guinea Pig and the implication by Dr. Saenger that our mother agreed to have her body exposed to radiation injury that would lead to serious pain and shortening of her life.

The Plair family asked this Sub-committee to help us to bring the people who we feel shortened our mother's life to justice.

In a society where life, especially human life appears to be worth less and less, we and other families are depending on this Sub-committee to send a clear message to Dr. Saenger and associates, the University of Cincinnati Medical Center and the Defense Department that human life is still important.

We must let the world know that here in America, what makes us different and greater than other countries is that we truly value each and every human being regardless of their I.Q., education, race, creed, color or position in our society. If we allow this travesty of justice to go unchallenged others may be unknowingly experimented upon in the future.

Respectfully submitted,

Mr. Woody Plair and Family

To Someone Who Will Listen:

I was 30 years old when my mother was stricken with cancer. She had six other children, three very young at home, the oldest was 12. She was born (my mother) in Whitesburg, KY, 1916, only went to the Second Grade of Grade School, was married at 13 years of age. When cancer struck she had no money. Her husband had only been dead a short time and she was struggling to care for her three girls at home. She wanted to spend as much time as she had left enjoying her three daughters. She was being treated as an out-patient at General Hospital. One day near the end nurse called told her to come to hospital clinic. She took a taxi because no one was available to drive her. She came home weak and vomiting. She was admitted to hospital and only lasted less than a month. When we (the family) found out recently about the 150 Rad she had received my older sister felt she was to blame because she did not go with her in taxi to clinic. She had to be hospitalized herself and may need constant care. A younger sister has M.S. and has not been told for fear she won't be able to cope with it. I'm sure all the other families that are still alive are having similar problems. My prayers are with them too. As you can tell from my letter, I don't have a good education. Should I be afraid to be treated in a hospital? Afraid of being used for testing some other chemical to benefit our government. Or carry a Donor's Card so if they wanted an organ they could take it at will? Something needs to be done it is up to you. I'm helpless.

Thank you.

Bob Phillips
Son of Maud Jacobs #45

#055 Lillie Wright

Chart No. 44174

My mother Lillie Wright was admitted to Cincinnati General Hospital Aug 23, 1965. She was sent there for a biospy. She was confined to the hospital for one 1 week.

The summary I recieved of her illness revealed that her biospy was performed. Aug 30, 1965 diagnosis was Carcinoma of the breast. On September she was given partial body irrodation 200 rad midline. On October 8, 1965 local x-ray therapy began. In 53 days she(Lillie Wright) had recieved 2000 rads to her left and right chest.

On December 1, 1965 x-ray was begun on the imtermammary chain and to the anterior and posterior above the collarbone region (supraclavicular). She received 4000 in 40 days. Her white blood cell count fell to a low of 2200 on December 3, 1965. These doses of radiation in my opinion was enough to destroy bone marrow and white blood cells and even the patient.

We the family of Lillie Wright was not notified about these radiation treatments or any other procedures which may have taken place. We did not sign any papers to permit this experiment to be done on her(Lillie Wright).

Zettie M. Smith
513-751-5269
3468 Hallwood Pl
Cincinnati OH 45229

The doctor at the hospital gave her sample tubes of oniment to use on her breasts, her back and abdomen. Her skin was burned on both breast. Her back and abdomen. There was raw flesh exposed where once there were skin.

I had to apply this oniment to those exposed areas.When I applied this oniment to those raw areas she was in such excruciating pain I cried. She was given enough oniment for 1 week. She was given Morphine which last 1or 2 weeks. I do not recall the name on the oniment tubes (3) but both of these product was given to her around December of 1965.

Neither of these medication helped her. When a person is real ill I was under the impression someone have to sign for medication such as morphine for a patient which is terminally ill. She was kept in the dark about the treatments she was receiving. She never talked about it.

It's not fair to treat another human being as a guinea pig because they are poor and uneducated. Some of our parents didn't have the privileges we are blessed with today.

I took my mother back to the hospital Feb 12, 1965 around 10:30 or 11:00. My nephew and I stayed at the hospital until 3:00 am I asked the receptionist if they were re-admitting her and she said yes we should go home and get some rest. When I return home my husband called me from his job and told me my mother had died. The people at the hospital never did call me to inform me of her death.

I'm her daughter, I should have been informed about her death before I left the hospital. I was at the hospital at 3:00 am the death certificate states she died at this time. Feb 13, 1966. I thought the nearest relative was to be informed first.

How I feel about my mother participating in the experiment.

I'm very angry about this doctor taking it upon himself to use poor live, uneducated human beings for his personal fame and gain. These human beings had the right to live the rest of their lives until God was ready for them to die. Not to die because man want to find out what effect it would have on soldiers in the war zone.

My family have been deprived of what days my mother could have lived. I know she wasn't educated but she knew something was wrong but she didn't know what it was.

I don't like it because she Lillie Wright was kept in the dark about this experiment. It's a disgrace to use high doses of radiation on anyone why didn't you experiment on your love one? No because they are special to you. Remember someday you will reap your just reward.

KIRCHER, ROBINSON, COOK, NEWMAN & WELCH

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IN DAYTON: (513) 235-1974

TO: Nicole Jenkins

LOCATION: _____

FAX NUMBER: 202 - 225 3673

TELEPHONE NUMBER: _____

FROM: Bob Newman

DATE: _____

NUMBER OF PAGES (INCLUDING COVER SHEET): _____

COMMENTS: _____

Date: April 4, 1994

To: Robert B. Newman, Attorney at Law

From: Members of the Maude Jacobs Family

Subject: Radiation Testing at UC (Cincinnati General Hospital)

This correspondence is regarding Maude Jacobs, a female caucasian, who was an unsuspecting victim of the radiation tests conducted by the University of Cincinnati. Maude was born in Whitesburg, Kentucky on June 7, 1916. The third grade was her final year of formal education. By the time she was thirteen years old, she was married and had given birth to her first child. She bore seven children in all, six girls and one son. She was a beautiful woman with a lovely radiant smile. She was impeccable about her children's appearance, as well as her own. Her devotion to her family was obvious to anyone who knew her. Maude lived her life below the poverty level, but was a proud and dignified woman. She was genuinely happy with the simple things in life. Her delight was cooking and caring for her children. When she died she was a widow and left three minor children at home.

According to information from CGH (Cincinnati General Hospital), Maude was diagnosed with breast cancer on July 17, 1964. A treatment of hexamethylmelamine began on July 27,1964 and was completed on August 18, 1964. With this medication her primary tumor receded markedly. On November 7, 1964 total body irradiation was administered. The midline absorbed tissue dose was 150 rad (250 r midline air dose). At the termination of the treatment she had severe vomiting for twenty-four hours, in spite of intramuscular compazine. Before treatment she had a normal hemogram. Seven days after treatment the white blood count began to fall. The platelet count fell around fourteen days after treatment. The WBC was 1,000 and platelet count was 80,000 twenty-three days after treatment. On the twenty-fourth day, the WBC was 850 and platelet count was 38,000. Maude died December 2, 1964. Twenty-five days after total body irradiation. She was study number 045. (Documentation from CGH attached.)

Two letters written by Maude to her sister Arlie less than two months before her death describes how she felt, and also indicates she thought the doctors did not know what was wrong with her. She talks of living near her oldest daughter, Lillian, who is very helpful to Maude. She also is pleased to be home with her children, but feels sorry because she is too tired in the evenings after preparing dinner to watch television with them. She refers to the expense of her medication and said prayer helps her more than the doctors. These letters demonstrate her education level, but also

doctors. These letters demonstrate her education level, but also reveal her devotion to her children. Maude had no knowledge of the seriousness of her cancer much less knowledge of the radiation

treatment. She did not expect to die. If she had, she would have discussed the future care of her minor daughters with the rest of the family. Her death was so sudden and unexpected the family was totally unprepared. The three young daughters eventually were put in St. Aloysius Orphanage. (The two letters from Maude to her sister are attached.)

The family was **NEVER** informed of the radiation test or it's purpose. Nor was anyone ever asked to sign a consent form or give verbal permission for testing. Some of the memories which were dismissed without attaching importance now make sense or at least raise suspicion. Her daughter Irene was seven months pregnant at the time and was having a difficult pregnancy. She remembers Maude's bright smile and cheerfulness, then remembers a private room and no more smiles or happy faces. Irene remembers being afraid of going into that room. Maude asked her to feel her head and when she did it felt full of soft tumors. Her body felt like sand. Even in the hallway she could hear Maude's delirious talk.

Maude's daughter Sherry was twelve years old and remembers the private room, but at the time didn't know it was uncommon for a person without insurance. Sherry remembers the orphanage and being split up from her two younger sisters. The youngest girl, Kim, eventually went to a foster family.

Robert Murphy, one of Maude's grandson's, remembers thinking how nice it was to have a private room without insurance. Bill Murphy, another grandson recalls visiting her in the private room, but not wondering why she was there. He remembers her conversation as "out of her head".

Her oldest daughter, Lillian Murphy Pagano, lived downstairs from Maude and was her primary care provider. Lillian was never contacted or consulted about her mother's treatment. She remembers a drastic mood change associated with rapid physical deterioration. She too recalls the private room at the end. She remembers thinking her body felt like sand. She was concerned too for Irene, because of her pregnancy and the worsening of their mother's health so rapidly. Lillian's concern grew as Maude quickly became disoriented and no longer recognized anyone. She was violently ill and talking utter nonsense. Maude died before her time everyone felt. Her family lived for the next twenty-nine plus years with the sadness of her death, but also had warm memories to console them.

Since the details of the experiments became public, the entire family has been drastically affected. Now guilt has replaced the sadness and comments like "I should have known" or "I should have asked" are commonplace. Reliving Maude's last days over and over, remembering differently now why she was so violently ill, how she suffered, and now a reason for the private room. Her death is now a nightmare. She died without comfort and dignity. She was

Her children want an apology. They want to know nothing they could have done would have altered the results. They want Maude to know they are sorry if they disappointed her because she suffered needlessly without intervention from them. They also need a quick resolution so this too can be a memory. Already too much damage has been realized.

Lillian Murphy Pagano (Maude's oldest daughter) feels personally responsible for her death. She became obsessed with Maude's death, often calling other family members several times a day to go over some part of her last days again and again. She was found several times at three or four o'clock in the morning with a fixed stare and silent sobs. Eventually she was rushed to the hospital with a suspected heart attack. After a short stay of a few days, some testing, several prescriptions, and instructions to avoid stressful situations, she was permitted to go home. Anxiety struck again within a few weeks. This time she was gone. Lillian's daughter found her, called 911, and received over the phone guidance for delivering CPR. When paramedics arrived, she was given multiple shock treatments to revive her. It is estimated she was dead for four minutes. She was on a respirator and in a coma; she also had several seizures. The doctor's gave her a 50% chance of pulling through, but warned all about the possibility of permanent brain damage. She has regained consciousness, but is still in critical condition at this writing. She recognizes family members, but is mentally unstable. The extent of damage is still unknown. Her family has been told she will need twenty- four care and cannot be exposed to **ANY** stressful situations. She doesn't talk about Maude now. She doesn't even remember who visited her an hour ago.

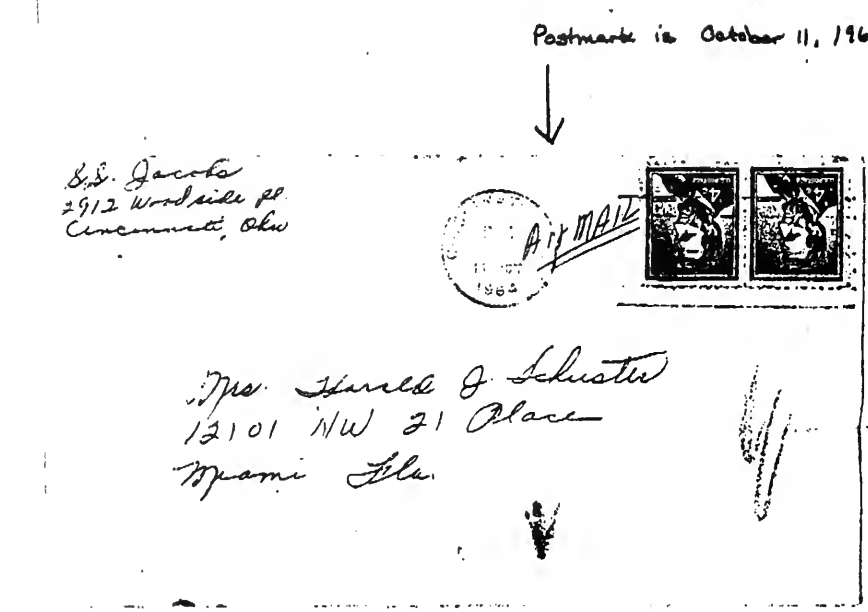
The ordeal with the UC experiments must come to a swift conclusion. This is the saga of only one family, there is supposed to be eighty-seven more victims with families. It's amazing how something that was a remote, barely thought of memory, now is resurrected and grown into an unwelcome demanding problem. A problem that can consume your days and affect people from twenty-nine years of family growth --- people Maude never could have known.

This letter was compiled from the hearts and thoughts of Maude Jacob's children:
Lillian Murphy Pagano (nee Phillips)
Irene Froman (nee Phillips)
Bob Phillips
Betty Wolfe (nee Phillips)
Sherry Brabant (nee Jacobs)
Janet Baker (nee Jacobs)
Kim Swedo (nee Jacobs)

Attachments

attachment

Postmark is October 11, 1964



attachment

Cinti 19 ohio

Dear aide Just few lines
To answer your letter Sherry she
ancered hers Yesterday While I was
Cooking Supper Well Every thing
almost The Same Except My Legs
are Little Better now Dont Worri
Dress Shes it take me few Minutes
to get on My feet But I Can walk
Little Better Except When night
Comes I Go tired and Sore I have
To go to Bed early The Children
wonts me to Sit up Watch TV with
Them the I feel So Sorry for them Some
times But By the time The Day Done
I am Done by my Back hurts me So
Bad it Just Grin away I Dont Think
The Doctors Nos What is wrong With
me They didnt help me Prayer help
me God Brought Me Through Well aide
it geting Dark I got fix Them Some
Supper I Hope You Can Read This
give Care The address it Shes wonts
it Shayne I Cannot Wrote her But I
Hate Bill Cobb See her I See Write Soon
as I Can Keep me Busy rite now Be Long
So Long for Now from Mrs Childress
2912 Woodlawn Pl

Dear aile
Just few Lines To Let
You no I got Moved and Kids
is in school I Con Crept a
round the house do Little Work
to's Care of Children but is
about I dont think I Ever will
Walk good again it Ben So
Long now I Cant Walk any Better
I Hold To the Furnitur half time
To do My Work ah well at Least
I am home With my Children I thought
I Better try Writing You in Place
of Phonin Rite Now My Medison
for Pain Cost So much they Will
give me all the Medison I need Except
Them Pain Pills Which Cost 5 or 6
about 20 Pills Each time Well aile
I Moved To 2912 Woodlick Place in
Carrollt Got Nice Apartment only 6 0
Month Close to Till She help me
all time My Phone is 751-1629
I will Close for now aile I got Get
Supper for the Kids I'll try Write You
More next time Love & Ever from
My aile and Children till Con Tell Hows

KIRCHER, ROBINSON, COOK, NEWMAN & WELCH

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DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
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WASHINGTON 25, D. C.

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Budget Bureau No. 49-R333

APPLICATION FOR RESEARCH CONTRACT - PART 1

DO NOT WRITE IN THIS SPACE
☐ NEW ☐ RENEWAL
CONTRACT NUMBER

1. TITLE OF PROJECT
Metabolic changes in Humans following Total Body Radiation

2. DATE RESEARCH CONTRACT TO BEGIN
1 February 1951

3. NAME AND OFFICIAL POSITION OF RESPONSIBLE INVESTIGATOR
Eugene L. Saenger, M.D., Associate Clinical Professor of Radiology

4. DATE OF APPLICATION
25 September 1953

5. PRINCIPAL PROFESSIONAL ASSISTANT (S)
George M. Guest, M.D., Professor of Research Pediatrics
Helen R. Berry, M.A., Research Associate, Children's Hospital Research Foundation
Harold Perry, M.D., Assistant Professor of Radiology

6. OTHER PROJECTS IN WHICH YOU ARE PARTICIPATING AND SOURCE OF SUPPORT (*Other government contracts or funds from civilian foundations, etc.*)
a) Incidence of Neoplasia in Irradiated Children; supported by National Institutes of Health, P.H.S., C-2073
b) Preparation of Handbook on Medical Aspects of Radiation Accidents, supported by U.S. Atomic Energy Commission, contract no. AT(30-1)-2166

7. NAME AND LOCATION OF INSTITUTION WHERE WORK WILL BE PERFORMED
Departments of Radiology, University of Cincinnati, College of Medicine, Cincinnati, Ohio

SIGNATURE OF RESPONSIBLE INVESTIGATOR

8. APPLICATION APPROVED BY OFFICIAL AUTHORIZED TO SIGN FOR INSTITUTION	9. APPLICATION APPROVED BY HEAD OF DEPARTMENT WHERE WORK IS TO BE PERFORMED
NAME PRINTED OR TYPED: Stanley E. Dorst, M.D.	NAME PRINTED OR TYPED: Benjamin Felson, M.D.
SIGNATURE	SIGNATURE
OFFICIAL TITLE: Dean, College of Medicine	OFFICIAL TITLE: Professor of Radiology and Head of Department of Radiology
INSTITUTION: University of Cincinnati	

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Budget Bureau No. 49-R344

APPLICATION FOR RESEARCH CONTRACT - PART II

TITLE OF PROJECT: Metabolic changes in Humans following Total Body Radiation

FUNDS REQUESTED (*One year only*)

REQUIREMENTS	BUDGET: REQUESTED (From Office of The Surgeon General)	BUDGET: OTHER SOURCES *
1. PERSONNEL (*List positions, salaries, and names of professional personnel, if known*)		
Technician (fulltime)	$ 4400.00	-
Technician (fulltime)	4000.00	-
Physicist (part time)	1000.00	Univ. Cinti.
Clinician (part time)	2000.00	" "
Statistician (part time)	1000.00	" "
Secretary (part time)	1500.00	" "
total	$ 13,900.00	
2. EQUIPMENT (*Itemize*) Remodeling of laboratory room $900.00		
Densitometer & filters $400.00	Ultraviolet lamp 100.00	
Centrifugal chromatograph 250.00	Vanslyke apparatus 350.00	
Freeze drying apparatus & Vacuum pump 200.00	chromatographic columns 200.00	
Refrigerator 250.00	Colorimeter 450.00	
Spray equipment 150.00	total $3350.00	
3. CONSUMABLE SUPPLIES (*Itemize*)		
Miscellaneous glassware & micropipettes	570.00	
Chemicals, chromatography paper & supplies	1740.00	
Phantoms, etc.	200.00	
	$2510.00	
4. TRAVEL (*State Purpose*)		
Conferences and scientific meetings	500.00	
5. *SUB-TOTAL*	$20,220.00	
6. OVERHEAD (*Established by official auditors with concurrence of institution or research agency and contracting officer, and may be based upon percentage of total salaries and wages, or percentage of total cost of the project. Indicate below.*) Provisional 30% of salaries	4685.00	
——PERCENT OF SALARIES AND WAGES ——PERCENT TOTAL COST		
7. TOTAL BUDGET 25 085	$24,905.00	
8. ESTIMATE OF FUTURE REQUIREMENTS (*To be filled out only if type of project indicates that it will continue for more than a year*)		
FIRST ADDITIONAL YEAR	*21,775.00	
SECOND ADDITIONAL YEAR	*21,775.00	

* *Other Sources - from the school, other contracts, other government agencies, foundations, etc.*

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN

(Include background, specific aims, methods of procedure in detail, significance of the research. Use additional pages, if necessary.)

3. Scientific background.

Several reports have described changes in nitrogen metabolism following irradiation (1,2,3). All have shown increase in nitrogen excretion following total body irradiation to various laboratory animals. Mefford and Martens (4) have studied amino-aciduria by paper chromatography in rats. Katz and Hasterlik (5), and Hempelmann, Lisco and Hoffman (6) have studied amino-aciduria following radiation in humans by means of paper chromatography. Hempelmann, et al, found amino-aciduria in 3 of their 9 cases.

Katz and Hasterlik reported increases of as high as ten times normal values of total daily amino acid excretion in 4 patients. Quantities of individual amino acids excreted varied from 2 - 20 times normal values. Abnormal values were found as early as 12 hours following exposure, and increased levels persisted for as long as 5 months. No direct quantitative relation to radiation dose could be established.

These findings suggest that amino-aciduria may serve as an indicator of the biological response of humans to irradiation. The reports of amino-aciduria in humans have described the findings in individuals exposed in reactor accidents (3,6) and no control measurements were possible. The proposed investigation will include studies of amino-acid excretion before and after irradiation both to the whole body and to portions of the body. The urinary excretion of amino acids will be measured both by paper chromatography and total amino acid nitrogen in order to find a relatively simple technique for biological effects of irradiation. Significant increases in total amino acids and individual amino acids will be sought. The amino acid levels will be compared to levels of creatine (10) and urea (11).

These studies will be valuable in the understanding of the mechanisms of amino-aciduria. Preliminary studies by our group have demonstrated that transient amino-aciduria will also occur with extensive surgical procedures and with infection. Studies of 5 patients exposed at the Y-12 accident at Oak Ridge in June 1958 showed elevated excretion of beta aminoisobutyric acid with levels related to the total dose received by the individual.

4. Scientific Scope of the Proposed Research.

Amino-aciduria following irradiation has been reported in humans and animals. The purposes of this investigation is to study this phenomenon to

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN

(Include background, specific aims, methods of procedure in detail, significance of this research. Use additional pages, if necessary.)

elucidate some of the mechanisms responsible for amino-aciduria and to determine whether it is a practical biological test of radiation exposure.

The Design of the Proposed Research is as follows:

1. Comparison of techniques for determination of urinary amino acids by the Van Slyke and chromatographic techniques.
2. Determination of excretion of urinary amino acids at various dosages of total body irradiation.
3. A study of the effects of partial versus total body irradiation on urinary amino acid excretion.
4. Studies of the immune mechanisms of humans receiving total body irradiation.

Selection of Patients

Patients for total body irradiation will be limited to adult males who have proven metastatic malignancy but are in good nutritional state. The studies will be limited to males because of the variations in amino-aciduria found with the menstrual cycle in women. These patients will be used for parts 1 and 2. In part 3 male patients who are receiving radiation therapy for neoplasms will also be included. Except in special cases noted below, patients with lymphomas will not be used in these studies. All patients will be hospitalized at the Cincinnati General Hospital. They will have histories, physical examinations, routine hematological and urine studies and other laboratory studies as needed.

Factors for irradiation are as follows:

Westinghouse Quadrocondex constant potential therapy unit 250 KV, 15 Ma, filtration 2.0 mm Cu + 1 mm Al., H.V.L. 2.0 mm Cu. TCD 200 cm. Also total body irradiation will be carried out with Cobalt 60 teletherapy. Measurements will be checked by the Victoreen condenser r-meter and calibrated Sondir dosimeters using masonite and water phantoms. The technique of irradiation will be similar to that of Sinclair & Cole (12).

Urine Studies

Part 1. Comparison of paper Chromatography and Total Amino Acid Nitrogen Excretion.

Two groups of 6 adult males will receive 50 r of total body irradiation in a single dose. Group A will consist of patients with relatively radio-resistant tumors (e.g.

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN

(Include background, specific aims, methods of procedure in detail, significance of the research. Use additional pages, if necessary.)

stomach, bowel, brain) and Group B of patients with highly radio-sensitive tumors (lymphomas).

Prior to irradiation urines will be collected for several days to serve as controls. All urines will be collected for 24 hour periods. An aliquot from the early morning fasting samnie will be refrigerated and the remainder pooled with the 24 hour urine below. The voidings will then be collected, refrigerated, pooled and frozen for the 24-hour periods. All samples will be analyzed in triplicate by both techniques for fasting and pooled values. If the initial fasting specimen provides enough data, the test can be simplified.

Total urinary amino acids will be determined by the method of Van Slyke, MacFayden and Hamilton (7). Two dimensional paper partition chromatography will be carried out according to the methods of Block, Durrum and Zweig (1).

The 24 hour urines will be analyzed for uric acid, urea creatine, creatinine and total nitrogen. An attempt will be made to maintain the patients in approximately the same nitrogen equilibrium.

The values obtained by the two methods will be compared by analysis of variance and by determination of regression coefficients of the values of the Van Slyke method versus those of chromatography. In addition comparison of amino acid excretion in patients with known destruction of large masses of tumor (Group A) can be compared to those in whom such a phenomenon is unlikely (Group B).

Part 2. Determination of Excretion of Urinary Amino Acids at Various Doses of Total Body Irradiation

Patients to be studied will include those individuals with metastatic neoplasms and also patients who are receiving radiation therapy in an attempt to cure or palliate various neoplasms. Patients in this study will not have had previous irradiation so as to avoid carry-over effects. In the initial selection of patients the group of patients with metastatic neoplasms cannot be selected at random from a normal population for inclusion in the study since normal individuals cannot be given total body radiation.

Selection criteria are as follows:

1. Patient to have proven dissemination of neoplasm.
2. Patient to have proven evidence of metastasis.
3. Patient to be in satisfactory nutritional state.

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT ...letabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN
(Include background, specific aims, methods of procedure in detail, significance of this research. Use additional pages, if necessary.)

The patients will be selected for these subgroups of total body irradiation by randomization. Subgroup A will serve as controls and will have all procedures carried out except that they will receive sham irradiation only. Subgroup B will receive 25 r and Subgroup C will receive 50 r. Each group will consist of 4 patients. The mean values of total amino acids in the urine of the three groups will be tested for significant differences by analysis of variance. Subgroup A will be tested against Subgroups B and C. Also Subgroup B will be tested against Subgroup C. Further groups will be studied at 100 r and 200 r.

If there is no significant difference between B and C, then additional subgroups will be studied at exposures of 3, 5, 10 and 20 r of total body irradiation. One of the possible reasons that a relation between radiation exposure and amino acid excretion may reach a plateau value below 25 r of total body irradiation. It is for this reason that these additional groups may require study. Patients will be placed in these several groups by the same technique of randomization as described above. Another group of sham irradiated controls will be provided in order not to lose independence of comparisons.

At the conclusion of these studies further analysis of the data will be carried out with calculations based on the integral dose received by each patient. The dosage response relationship will then be determined.

Part 3. Study of the Effects of Partial versus Total Body Irradiation on Urinary ...ino Acid Excretion

After suitable base line values are established as described Part 2, further studies will be carried out in order to compare total body irradiation with doses of localized irradiation to give equal integral dosage. For example, if a patient receives total body irradiation with an integral dose of 50,000 gram roentgens, his amino-aciduria will be compared with that of an individual who has received an equal integral dose with all irradiation given to a localized region of the body. One group of patients will receive the dose to the upper abdomen, another group to the chest, another group to the head and neck. These patients will have determinations of urinary amino acids before receiving radiation and will be followed afterwards for a period of one to three years.

The first group to be studied will be those patients who receive localized irradiation to the kidneys and liver. Since irradiation to different organs

(2)

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RESEARCH PLAN

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may provide a mechanism for amino-aciduria (see Part I) it will be valuable to determine the levels of amino-aciduria following this type of irradiation. It must be recognized that in applying radiation to the human it is not possible to irradiate the liver without irradiating the kidneys and conversely one cannot irradiate the kidneys without irradiating the liver. If the amino-aciduria is of the same order of magnitude as that found with total body irradiation, it will suggest that irradiation of either or both of the organs is responsible for these findings. The second group to be studied are those individuals receiving localized radiation to the chest. If the amino-aciduria approaches levels equal to those found with total body irradiation in comparable integral doses, increased tissue breakdown should be suspected.

From a practical viewpoint these two groups will be studied simultaneously depending upon clinical material available on the Tumor Service of the Cincinnati General Hospital.

Part d.

In cooperation with Dr. A.J. Lucchesi of the Radiobiology Department, U.S. Army Medical Research Laboratory, Ft. Knox, Ky, we shall supply blood serum samples from all patients irradiated as described previously. Samples will be obtained just prior to irradiation, just after irradiation and ten days after irradiation. They will be sent to Dr. Lucchesi for his studies.

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5. Matz, ...J. and Easterlin, R.E., J. National Cancer Inst., 15:1035 (1955).
6. Hornbrook, L.H., Hisco, R. and Hellman, J.D., ... Int. Ed. 56:277 (1916).
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8. Moore, S., and Stein, ...H., J. Biol. Chem. 211: 907 (1954).
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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT: Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN
(Include background, specific aims, methods of procedure in detail, significance of this research. Use additional pages, if necessary.)

10. Anderson, D.R. Effects of Radiation on Creatine Metabolism. Radiation Research 7:500 (1957)
11. Kay, [illegible], Early, J.C. and Entenman, C. Radiation Research 6:93-109 (1957)
12. Sinclair, [illegible] and Cole, A. , Technique and dosimetry for whole body x-irradiation of patients. UCLA Report No. 57-79 Mar. 1957.

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APPLICATION FOR RESEARCH CONTRACT - PART IV

BIOGRAPHY

(Biographical sketches required on responsible investigator and principal professional assistants only. If this is a request for renewal utilizing essentially the same personnel as previously, biographical sketches will not be necessary.)

1. NAME	2. ADDRESS	3. AGE
Eugene L. Saenger, M.D.	Radioisotope Laboratory, Cincinnati General Hospital, Cincinnati 29, Ohio	41

4. EDUCATIONAL BACKGROUND *(College and/or University)*

Harvard College A.B., cum laude Biochemical Sciences 1933
University Cincinnati, College of Medicine, M.D. 1942

5. RESEARCH TRAINING *(List of institutions, research director, subject and dates)*

Interne General Hospital, Cincinnati 1942-1943
Resident in Radiology, General Hospital 1943-46
Chief Radioisotope Unit, Brooke Army Hospital, FCMT 1954-55
Consultant Surgical Research Unit 1951-55
Director, Radioisotope Laboratory, Univ. of Cinti, Coll. of Medicine 1950-
Assistant Professor of Radiology 1951-57
Assoc. Clinical Professor of Radiology 1957-
Consultant Brooke Army Hospital 1950-

6. OTHER INFORMATION BEARING ON QUALIFICATIONS *(Hospital appointments, professional societies, specialty board, etc.)*

Attending Radiologist, Cincinnati General Hospital;
Radiation Therapist Children's Hospital, Cincinnati, Ohio;
Diplomate, American Board of Radiology, Member
American Roentgen Ray Society, Radiological Society of North America, Health Physics Society; Phi Beta Kappa, Phi

7. BIBLIOGRAPHY *(Do not list more than ten publications)*

1. Saenger, E.L., et al, Emergency Measures and precautions in Radium accidents. Jour. Med. Assn. 149:815-819 June 28, 1952.
2. Results of Therapy with Radioactive Iodine-131 in Hyperthyroidism. Ohio State Med. Jour. 50:25-27, Jan 1954. E.L. Saenger, et al.
3. Saenger, E.L., et al, Letterer-Siwe's Disease. Problems in Diagnosis and Treatment. Amer. Jour. Roent., and Therapy & Nucl. Med. Vol. I, No. 3, March 1964.
4. Protection against radiations from radium, cobalt-60, and cesium-137; National Bureau of Standards Handbook 64, section 7, accidents entailing radiation hazards, Sept. 1954. Saenger, E.L., et al.
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APPLICATION FOR RESEARCH CONTRACT - PART IV

BIOGRAPHY

(Biographical sketches required on responsible investigator and principal professional assistants only. If this is a request for renewal utilizing essentially the same personnel as previously, biographical sketches will not be necessary.)

1. NAME	2. ADDRESS	3. AGE
Guest, George Martin, M.D.	Children's Hospital Research Foundation, Cincinnati 29, Ohio	6[illegible]

4. EDUCATIONAL BACKGROUND *(College and/or University)*

Ohio Wesleyan University, Delaware, Ohio 1916-18
University of Cincinnati, A.B. 1920
" " " College of Medicine M.D. 1922
" " " " " " M.S. 1923

5. RESEARCH TRAINING *(List of institutions, research director, subject and dates)*

Cincinnati General Hospital, Resident in Pathology and Instructor Pathology 1923-1[illegible]
Institut Pasteur, Brussels, Bel[illegible], Fellow of the Commission for Relief in Belgium Educational Foundation 1[illegible]-1,25
Boston Children's Hospital, Intern in Pediatrics, Resident Bacteriologist and Asst[illegible] in Bacteriology, Harvard Medical School 1926-1927
University of Cincinnati, College of Medicine, Dept. of Pediatrics: Asst Prof. 1[illegible]
" " " " " Assoc. Prof. 1[illegible]
" " " " " Prof. of Research Pediatrics 1[illegible]

6. OTHER INFORMATION BEARING ON QUALIFICATIONS *(Hospital appointments, professional societies, specialty board, etc.)*

[illegible] (President 1,32) Alpha Omega Alpha
Sigma Xi
[illegible] Soc. of Clinical Chemists
Certificate of the Am. Board of Pediatrics 1936
[illegible] Societies

7. BIBLIOGRAPHY *(Do not list more than ten publications)*

1. Guest, G[illegible] et al, Centrifuge method for the determination of the volume of cells in blood, J. Lab. & Clin. Med. 1:757-767, April 1,31.
2. Guest, G[illegible] et al, Hematologic methods in detecting nutritional anemia, i. Nutrition: The newer diagnostic methods, 17th ann. conf., Mead Johnson Memorial Fund, [illegible] pp. 153-175, 1,33.
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APPLICATION FOR RESEARCH CONTRACT - PART IV

BIOGRAPHY

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1. NAME	2. ADDRESS	3. AGE
Helen K. Berry	Children's Hospital Research Foundation, Cincinnati 27, Ohio	33

4. EDUCATIONAL BACKGROUND *(College and/or University)*

University of Texas, M.A. 1949

5. RESEARCH TRAINING *(List of institutions, research director, subject and dates)*

Research Scientist, Biochemical Institute, University of Texas 1947-53

6. OTHER INFORMATION BEARING ON QUALIFICATIONS *(Hospital appointments, professional societies, specialty board, etc.)*

Research Associate - Children's Hospital Research Foundation

American Association for the Advancement of Science

Sigma Xi

7. BIBLIOGRAPHY *(Do not list more than ten publications)*

Individual Metabolic Patterns and Human Disease with Dr. R.J. Williams, also other articles on technique of paper chromatography.

7435 Fair Oaks Drive
Cincinnati, OH 45237
April 6, 1994

Dear Congressman Mann,

I am writing this letter as requested by your office, to be considered by your committee as an addition to the oral testimony that you will be hearing in committee.

I am a retired oncology nurse. I worked for twenty-five years at University Hospital. Ten years were as a staff nurse and fifteen years in Radiation Oncology.

My employment covered the time frame of some of the Radiation experiments that were under the supervision of Dr. Eugene Sanger.

I did have personal contact with one of the study patients, and it was obvious to me that she knew that she was on an experimental treatment. She spoke openly and appropriately about her illness and her treatment. This indicated to me that she was a willing and knowledgeable participant. Her family was also present. The day that I took care of her she was also being interviewed by a psychologist associated with the project. This would also indicate that this was a treatment and an experiment that she had consented to.

While it is not always possible to draw general conclusions from a particular event, it seems unlikely that they would only get informed consent from this particular patient. It is more likely that this was the procedure for all patients on the study.

In addition there were three children treated, one of whom is still living. At the time that these children were treated, a diagnosis of Ewing sarcoma was usually a death sentence. Frequently these children suffered mutilating surgery to no avail. When Childrens Hospital sends a child for radiation it is only after much deliberation by the physician and appropriate discussions with parents. They would never send a child without the parents consent.

I feel that the physicians involved conducted their work in a very high ethical, professional and caring manner. They do not deserve the criticism that has been thrust upon them.

Yours truly,

Sonya G. Margalia, R.N., O.C.N.

Congress of the United States
House of Representatives
Washington, DC 20515–3501

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APPLICATION FOR RESEARCH CONTRACT - PART 1

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CONTRACT NUMBER

1. TITLE OF PROJECT
Metabolic changes in Humans following Total Body Irradiation

2. DATE RESEARCH CONTRACT TO BEGIN
1 February 1953

3. NAME AND OFFICIAL POSITION OF RESPONSIBLE INVESTIGATOR
Eugene L. Saenger, M.D., Associate Clinical Professor of Radiology

4. DATE OF APPLICATION
25 September 1953

5. PRINCIPAL PROFESSIONAL ASSISTANT (S)
George M. Guest, M.D., Professor of Research Pediatrics
Helen M. Berry, M.A., Research Associate, Children's Hospital Research Foundation
Harold Perry, M.D., Assistant Professor of Radiology

6. OTHER PROJECTS IN WHICH YOU ARE PARTICIPATING AND SOURCE OF SUPPORT (Other government contracts or funds from civilian foundations, etc.)
a) Incidence of Neoplasia in Irradiated Children: supported by National Institutes of Health, P.H.S., C-2973

b) Preparation of Handbook on Medical Aspects of Radiation Accidents, supported by U.S. Atomic Energy Commission, contract no. AT(30-1)-2166

7. NAME AND LOCATION OF INSTITUTION WHERE WORK WILL BE PERFORMED
Departments of Radiology, University of Cincinnati, College of Medicine, Cincinnati, Ohio

SIGNATURE OF RESPONSIBLE INVESTIGATOR

8. APPLICATION APPROVED BY OFFICIAL AUTHORIZED TO SIGN FOR INSTITUTION

NAME PRINTED OR TYPED
Stanley E. Dorst, M.D.

SIGNATURE

OFFICIAL TITLE
Dean, College of Medicine

INSTITUTION
University of Cincinnati

9. APPLICATION APPROVED BY HEAD OF DEPARTMENT WHERE WORK IS TO BE PERFORMED

NAME PRINTED OR TYPED
Benjamin Felson, M.D.

SIGNATURE

OFFICIAL TITLE
Professor of Radiology and Head of Department of Radiology

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APPLICATION FOR RESEARCH CONTRACT - PART II

TITLE OF PROJECT: Metabolic changes in Humans following Total Body Radiation

FUNDS REQUESTED (*One year only*)

REQUIREMENTS	BUDGET: REQUESTED (From Office of The Surgeon General)	BUDGET: OTHER SOURCES *
1. PERSONNEL (*List positions, salaries, and names of professional personnel, if known*)		
Technician (fulltime)	$ 4400.00	-
Technician (fulltime)	4000.00	-
Physicist (part time)	1000.00	Univ. Cinti.
Clinician (part time)	2000.00	" "
Statistician (part time)	1000.00	" "
Secretary (part time)	1500.00	" "
total	$ 13,900.00	
2. EQUIPMENT (*Itemize*) Remodeling of laboratory room $900.00		
Densitometer & filters $600.00	Ultraviolet lamp 100.00	
Centrifugal chromatograph 250.00	Van Slyke apparatus 350.00	
Freeze drying apparatus & Vacuum pump 200.00	chromatographic columns 200.00	
Refrigerator 250.00	Colorimeter 450.00	
Spray equipment 150.00	total $3250.00	
3. CONSUMABLE SUPPLIES (*Itemize*)		
Miscellaneous glassware & micropipettes	570.00	
Chemicals, chromatography paper & supplies	1740.00	
Phantoms, etc.	200.00	
	$2510.00	
4. TRAVEL (*State Purpose*)		
Conferences and scientific meetings	500.00	
5. *SUB-TOTAL*	$20,220.00	
6. OVERHEAD (*Established by official auditors with concurrence of institution or research agency and contracting officer, and may be based upon percentage of total salaries and wages, or percentage of total cost of the project. Indicate below.*) Provisional 35% of Salaries	7% 4685.00	
—PERCENT OF SALARIES AND WAGES — —PERCENT TOTAL COST		
7. TOTAL BUDGET 25085	$24,905.00	

8. ESTIMATE OF FUTURE REQUIREMENTS
(*To be filled out only if type of project indicates that it will continue for more than a year*)

FIRST ADDITIONAL YEAR	$21,775.00
SECOND ADDITIONAL YEAR	$21,775.00

* *Other Sources - from the school, other contracts, other government agencies, foundations, etc.*

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN

(Include background, specific aims, methods of procedure in detail, significance of this research. Use additional pages, if necessary.)

3. Scientific background.

Several reports have described changes in nitrogen metabolism following irradiation (1, 2, 3). All have shown increase in nitrogen excretion following total body irradiation to various laboratory animals. Mefford and Martens (4) have studied amino-aciduria by paper chromatography in rats. Katz and Masterlik (5), and Hempelmann, Lisco and Hoffman (6) have studied amino-aciduria following radiation in humans by means of paper chromatography. Hempelmann, et al, found amino-aciduria in 3 of their 9 cases.

Katz and Masterlik reported increases of as high as ten times normal values of total daily amino acid excretion in 4 patients. Quantities of individual amino acids excreted varied from 2 - 20 times normal values. Abnormal values were found as early as 12 hours following exposure, and increased levels persisted for as long as 5 months. No direct quantitative relation to radiation dose could be established.

These findings suggest that amino-aciduria may serve as an indicator of the biological response of humans to irradiation. The reports of amino-aciduria in humans have described the findings in individuals exposed in reactor accidents (3, 6) and no control measurements were possible. The proposed investigation will include studies of amino-acid excretion before and after irradiation both to the whole body and to portions of the body. The urinary excretion of amino acids will be measured both by paper chromatography and total amino acid nitrogen in order to find a relatively simple technique for biological effects of irradiation. Significant increases in total amino acids and individual amino acids will be sought. The amino acid levels will be compared to levels of creatine (10) and urea (11).

These studies will be valuable in the understanding of the mechanisms of amino-aciduria. Preliminary studies by our group have demonstrated that transient amino-aciduria will also occur with extensive surgical procedures and with infection. Studies of 5 patients exposed at the Y-12 accident at Oak Ridge in June 1958 showed elevated excretion of beta aminoisobutyric acid with levels related to the total dose received by the individual.

4. Scientific Scope of the Proposed Research.

Amino-aciduria following irradiation has been reported in humans and animals. The purposes of this investigation is to study this phenomenon to

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT: Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN

(Include background, specific aims, methods of procedure in detail, significance of this research. Use additional pages, if necessary.)

elucidate some of the mechanisms responsible for amino-aciduria and to determine whether it is a practical biological test of radiation exposure.

The Design of the Proposed Research is as follows:

1. Comparison of techniques for determination of urinary amino acids by the Van Slyke and chromatographic techniques.
2. Determination of excretion of urinary amino acids at various dosages of total body irradiation.
3. A study of the effects of partial versus total body irradiation on urinary amino acid excretion.
4. Studies of the immune mechanisms of humans receiving total body irradiation.

Selection of Patients

Patients for total body irradiation will be limited to adult males who have proven metastatic malignancy but are in good nutritional state. The studies will be limited to males because of the variations in amino-aciduria found with the menstrual cycle in women. These patients will be used for parts 1 and 2. In part 3 male patients who are receiving radiation therapy for neoplasms will also be included. Except in special cases as noted below, patients with lymphomas will not be used in these studies. All patients will be hospitalized at the Cincinnati General Hospital. They will have histories, physical examinations, routine hematological and urine studies and other laboratory studies as needed.

Factors for irradiation are as follows:

Westinghouse Quadrocondex constant potential therapy unit 250 KV, 15 Ma, filtration 2.0 mm Cu + 1 mm Al., H.V.L. 2.0 mm Cu. TSD 200 cm. Also total body irradiation will be carried out with Cobalt 60 teletherapy. Measurements will be checked by the Victoreen condenser r-meter and calibrated Sondir dosimeters using mannonite and water phantoms. The technique of irradiation will be similar to that of Sinclair & Cole (12).

Urine Studies

Part 1. Comparison of paper Chromatography and Total Amino Acid Nitrogen Determination.

Two groups of 6 adult males will receive 50 r of total body irradiation in a single dose. Group A will consist of patients with relatively radio-resistant tumors.

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT ...etabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN

(Include background, specific aims, methods of procedure in detail, significance of this research. Use additional pages, if necessary.)

stomach, bowel, brain) and Group B of patients with highly radio-sensitive tumors (lymphomas).

Prior to irradiation urines will be collected for several days to serve as controls. All urines will be collected for 24 hour periods. An aliquot from the early morning fasting samnie will be refrigerated and the remainder pooled with the 24 hour urine below. The voidings will then be collected, refrigerated, pooled and frozen for the 24-hour periods. All samples will be analyzed in triplicate by both techniques for fasting and pooled values. If the initial fasting specimen provides enough data, the test can be simplified.

Total urinary amino acids will be determined by the method of Van Slyke, MacFayden and Hamilton (7). Two dimensional paper partition chromatography will be carried out according to the methods of Block, Durrum and Zweig (1).

The 24 hour urines will be analyzed for uric acid, urea creatine, creatinine and total nitrogen. An attempt will be made to maintain the patients in approximately the same nitrogen equilibrium.

The values obtained by the two methods will be compared by analysis of variance and by determination of regression coefficients of the values of the Van Slyke method versus those of chromatography. In addition comparison of amino acid excretion in patients with known destruction of large masses of tumor (Group A) can be compared to those in whom such a phenomenon is unlikely (Group B).

Part 2. Determination of Excretion of Urinary Amino Acids at Various Doses of Total Body Irradiation

Patients to be studied will include those individuals with metastatic neoplasms and also patients who are receiving radiation therapy in an attempt to cure or palliate various neoplasms. Patients in this study will not have had previous irradiation so as to avoid carry-over effects. In the initial selection of patients the group of patients with metastatic neoplasms cannot be selected at random from a normal population for inclusion in the study since normal individuals cannot be given total body radiation.

Selection criteria are as follows:

1. Patient to have proven diagnosis of neoplasm.
2. Patient to have proven evidence of metastasis.
3. Patient to be in equilibratory nutritional state.

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TITLE OF PROJECT Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN
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The patients will be selected for three subgroups of total body irradiation by randomization. Subgroup A will serve as controls and will have all procedures carried out except that they will receive sham irradiation only. Subgroup B will receive 25 r and Subgroup C will receive 50 r. Each group will consist of 4 patients. The mean values of total amino acids in the urine of the three groups will be tested for significant differences by analysis of variance. Subgroup A will be tested against subgroups B and C. Also Subgroup B will be tested against Subgroup C. Further groups will be studied at 100 r and 200 r.

If there is no significant difference between B and C, then additional subgroups will be studied at exposures of 5, 8, 12 and 20 r of total body irradiation. One of the possible reasons that a relation between radiation exposure and amino acid excretion may reach a plateau value below 25 r of total body irradiation. It is for this reason that these additional groups may require study. Patients will be placed in these several groups by the same technique of randomization as described above. Another group of sham irradiated controls will be provided in order not to lose independence of comparisons.

At the conclusion of these studies further analysis of the data will be carried out with calculations based on the integral dose received by each patient. The dosage response relationship will then be determined.

Part 3. Study of the Effects of Partial versus Total Body Irradiation on Urinary Amino Acid Excretion

After suitable base line values are established as described Part 2, further studies will be carried out in order to compare total body irradiation with cases of localized irradiation to give equal integral dosage. For example, if a patient receives total body irradiation with an integral dose of 50,000 gram roentgens, his amino-aciduria will be compared with that of an individual who has received an equal integral dose with all irradiation given to a localized region of the body. One group of patients will receive the dose to the upper abdomen, another group to the chest, another group to the head and neck. These patients will have determinations of urinary amino acids before receiving radiation and will be followed afterwards for a period of one to three years.

The first group to be studied will be those patients who receive localized irradiation to the kidneys and liver. Since irradiation to different regions

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TITLE OF PROJECT: Metabolic Changes in Humans Following Total Body Radiation

RESEARCH PLAN
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may provide a mechanism for amino-aciduria (see Part I) it will be valuable to determine the levels of amino-aciduria following this type of irradiation. It must be recognized that in applying radiation to the human it is not possible to irradiate the liver without irradiating the kidneys and conversely one cannot irradiate the kidneys without irradiating the liver. If the amino-aciduria is of the same order of magnitude as that found with total body irradiation, it will suggest that irradiation of either or both of the organs is responsible for these findings. The second group to be studied are those individuals receiving localized radiation to the chest. If the amino-aciduria approaches levels equal to those found with total body irradiation in comparable fractional doses, increased tissue breakdown should be suspected.

From a practical viewpoint these two groups will be studied simultaneously depending upon clinical material available on the Tumor Service of the Cincinnati General Hospital.

Part 4.

In cooperation with Dr. A.J. Lucchesi of the Radiobiology Department, U.S. Army Medical Research Laboratory, Ft. Knox, Ky, we shall supply blood serum samples from all patients irradiated as described previously. Samples will be obtained just prior to irradiation, just after irradiation and ten days after irradiation. They will be sent to Dr. Lucchesi for his studies.

BIBLIOGRAPHY

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2. Cusmilson, G.L., and Moloteky, ..., ... J. Physiol. 171: 319 (1952).
3. White, J., Burr, I.M., and Mander. Argonne National Laboratory Quarterly Report, Feb. thr. April 1952, 4774.
4. Mefford, ...D., Martens, H.H., Science, 122:329, (1955).
5. Katz, ...J. and Kasterlik, H.S., J. National Cancer Inst., 15:1035 (1955).
6. Hornbrook, L.H., Lisco, H. and Hoffman, J.D., Arm. Int. Med. 36:272 (1952).
7. Van Slyke, D.D., MacFayden, D.A. and Hamilton, P.B. J. Biol. Chem. 150: 231, (1943).
8. Moore, S., and Stein, ...H., J. Biol. Chem. 211: 907 (1954).
9. Block, ...J., ... Durrum, E.L. and ...ivij, J., A Manual of Paper Chromatography and Paper ...lectrophoresis, Academic Press, Inc., New York 1955.

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APPLICATION FOR RESEARCH CONTRACT - PART III

TITLE OF PROJECT Metabolic Changes in Humans Following Total Body Radiation

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10. Anderson, D.R. Effects of Radiation on Creatine Metabolism. Radiation Research 7:500 (1957)
11. Kay, [illegible], Darby, J.C. and Entenman, C. Radiation Research 6:93-109 (1957)
12. Sinclair, W.K. and Cole, A. , Technique and dosimetry for whole body x-irradiation of patients. USAF Report No. 57-79 Mar. 1957.

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APPLICATION FOR RESEARCH CONTRACT - PART IV

BIOGRAPHY

(Biographical sketches required on responsible investigator and principal professional assistants only. If this is a request for renewal utilizing essentially the same personnel as previously, biographical sketches will not be necessary.)

1. NAME	2. ADDRESS	3. AGE
Eugene L. Saenger, M.D.	Radioisotope Laboratory, Cincinnati General Hospital, Cincinnati 29, Ohio	41

4. EDUCATIONAL BACKGROUND *(College and/or University)*

Harvard College A.B., cum laude Biochemical Sciences 1938
University Cincinnati, College of Medicine, M.D. 1942

5. RESEARCH TRAINING *(List of institutions, research director, subject and dates)*

Interne General Hospital, Cincinnati 1942-1943
Resident in Radiology, General Hospital 1943-46
Chief Radioisotope Unit, Brooke Army Hospital, FCHT 1954-55
Consultant Surgical Research Unit 1951-55
Director, Radioisotope Laboratory, Univ. of Cinti. Coll. of Medicine 1950-
Assistant Professor of Radiology 1951-57
Assoc. Clinical Professor of Radiology 1957-
Consultant Brooke Army Hospital 1956-

6. OTHER INFORMATION BEARING ON QUALIFICATIONS *(Hospital appointments, professional societies, specialty board, etc.)*

Attending Radiologist, Cincinnati General Hospital;
Radiation Therapist Children's Hospital, Cincinnati, Ohio;
Diplomate, American Board of Radiology, Member
American Roentgen Ray Society, Radiological Society of North America, Health Physics Society; Alpha Omega Alpha

7. BIBLIOGRAPHY *(Do not list more than ten publications)*

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SS FORM

DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
RESEARCH AND DEVELOPMENT DIVISION
WASHINGTON 25, D. C.

Form Approved
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APPLICATION FOR RESEARCH CONTRACT - PART IV

BIOGRAPHY

(Biographical sketches required on responsible investigator and principal professional assistants only. If this is a request for renewal utilizing essentially the same personnel as previously, biographical sketches will not be necessary.)

1. NAME: Guest, George Martin, M.D.

2. ADDRESS: Children's Hospital Research Foundation, Cincinnati 29, Ohio

3. AGE: (illegible)

4. EDUCATIONAL BACKGROUND *(College and/or University)*

Ohio Wesleyan University, Delaware, Ohio 1916-19
University of Cincinnati, B.S. 1920
" " " College of Medicine M.D. 1923
" " " " " " M.S. 1923

5. RESEARCH TRAINING *(List of institutions, research director, subject and dates)*

Cincinnati General Hospital, Resident in Pathology and Instructor Pathology 1923-1925
Institut Pasteur, Brussels, Belgium, Fellow of the Commission for Relief in Belgium Educational Foundation 1925-1926
Boston Children's Hospital, Intern in Pediatrics, Resident Bacteriologist and Asst. [illegible] in Bacteriology, Harvard Medical School 1926-1927
University of Cincinnati, College of Medicine, Dept. of Pediatrics: Asst. Prof. 1927-[illegible]
" " " " Assoc. Prof. [illegible]
" " " " Prof. of Research Pediatrics 1947-

6. OTHER INFORMATION BEARING ON QUALIFICATIONS *(Hospital appointments, professional societies, specialty board, etc.)*

[illegible] (Member of Scientific Committee 1938) Alpha Omega Alpha
Soc. for Clinical Research (President 1942) Sigma Xi
Am. Soc. of Biological Chemists
Certified Diplomate of the Am. Board of Pediatrics 1936
Clinical Professor, Pediatrics

7. BIBLIOGRAPHY *(Do not list more than ten publications)*

1. Guest, G. [illegible], et al, Colorimetric method for the determination of the volatile acids in blood, J. Lab. & Clin. Med. 17:757-767, April 1932.
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DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
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WASHINGTON 25, D. C.

Form Approved
Budget Bureau No. 49-R344

APPLICATION FOR RESEARCH CONTRACT - PART IV

BIOGRAPHY

(Biographical sketches required on responsible investigator and principal professional assistants only. If this is a request for renewal utilizing essentially the same personnel as previously, biographical sketches will not be necessary.)

1. NAME	2. ADDRESS	3. AGE
Helen K. Berry	Children's Hospital Research Foundation, Cincinnati 21, Ohio	33

4. EDUCATIONAL BACKGROUND *(College and/or University)*

University of Texas, M.A. 1949

5. RESEARCH TRAINING *(List of institutions, research director, subject and dates)*

Research Scientist, Biochemical Institute, University of Texas 1947-53

6. OTHER INFORMATION BEARING ON QUALIFICATIONS *(Hospital appointments, professional societies, specialty board, etc.)*

Research Associate - Children's Hospital Research Foundation

American Association for the Advancement of Science

Sigma Xi

7. BIBLIOGRAPHY *(Do not list more than ten publications)*

Individual Metabolic Patterns and Human Disease with Dr. R.J. Williams, also other articles on technique of paper chromatography.

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April 22, 1994

Nichole Jenkins, Esq.
Staff Counsel to the House
Judiciary Committee
Subcommittee on Administrative Law and
Governmental Relations
2138 Rayburn House Office Bldg., Room B351A
Washington, DC 20515

Re: House Judiciary Committee Subcommittee on
Administrative Law and Governmental Relations
Hearing on Radiation Experiments Conducted By the
University of Cincinnati Medical School

Dear Ms. Jenkins:

It appeared to me from some comments I read in the press that not all of the subcommittee members were aware that the Department of Defense had been told very clearly in 1962 that patient selection was made only if there was a "reasonable chance of therapeutic benefit to the patient."

The fact that patients chosen for the post-treatment observation of radiation effects were being chosen from a group receiving therapy is reinforced by the reference on p. 5 that the use of patients receiving therapeutic radiation may be introducing unrecognized biases into the investigation. Those statements were made at a time when there was no controversy surrounding this investigation or the source of funds for the post-treatment observations. This report was authored long before the existence of a faculty research committee. The statements, therefore, are entitled to a great deal of weight, and there is no legitimate reason to challenge their credibility.

I would like this letter and the 1962 Report included as part of the record.

Thank you for your help.

Sincerely yours,

R. Joseph Parker

RJP:vra
Encl.: "An Appraisal of Human Studies In Radiobiological Aspects of Weapons Effects" November 14, 1962

cc: Eugene L. Saenger, M.D.
Congressman John Bryant (w/encl.)
Congressman David Mann (w/encl.)
Congressman Rob Portman (w/encl.)

AN APPRAISAL OF HUMAN STUDIES IN RADIOBIOLOGICAL ASPECTS OF WEAPONS EFFECTS

Eugene L. Saenger, M. D.
Ben J. Friedman, M. D.

Radioisotope Laboratory University of Cincinnati
College of Medicine

Prepared for DASA under Contract DA-49-146-XZ-029

November 14, 1962

AN APPRAISAL OF HUMAN STUDIES IN RADIOBIOLOGICAL ASPECTS OF WEAPONS EFFECTS

A. Introduction

This memorandum considers the significance of utilizing human data to determine radiation effects and to develop appropriate countermeasures in relation to weapons effects. There are two broad categories of study which require elucidation. One concerns itself with effects on humans, the second with effects on the environment in which human beings exist.

In the initial consideration of these two categories one can reasonably assign effects on the eko-systems to groups other than the Defense Atomic Support Agency. These studies of effects on all types of flora and fauna are of great importance and little consideration has been given to the long term effects of high doses of radiation.

The primary problem of human effects of high doses - both acute and chronic - requires considerable further analysis in regard to proper allotment of research time and effort. The obvious concern is the division of support between animal and human investigation.

B. Philosophy of Approach

In any problem in radiobiology one is interested in two aspects. The first is the discovery of general laws or principles which are essentially the same for all animals, all mammals, all large animals, etc. The second aspect is the documentation of specific information concerning man. If a general principle can be demonstrated in several types of animals, one may then assume that it is probably true for humans. For example, repeated studies have shown that if an animal is placed under severe stress, e.g., exercise to exhaustion or thermal burns, its tolerance to a given dose of radiation is less than an animal lacking the same stress. It is reasonable to assume that human beings under stress tolerate radiation less well than a healthy individual. Qualitatively such a concept is of great value; quantitatively it is of less help since one is not able to extrapolate the specific stress effects to different species of animals or to people. Nor is one able to predict the effect of a given stress in a human being after observing it in an animal. Anderson (1) states that the use of laboratory animals in radiation research programmes is necessary in order to obtain a better understanding of a number of the basic changes resulting from radiation injury. Extrapolation from animal to man is different if not impossible.

It is, however, quite apparent that many high dose effects simply cannot be studied in humans because of obvious humanitarian considerations. One cannot subject people to whole body doses of 800 rad although such a study would be

entirely feasible in an animal. Thus many experiments of radiobiological interest will continue to be done in animals.

Nevertheless, it is essential to consider further well planned studies in patients so long as the following criteria are fulfilled:

1. There is a reasonable change of therapeutic benefit to the patient.
2. The likelihood of damage to the patient is no greater than that encountered from comparable therapy of another type.
3. 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.

The type of patient usually selected for whole body radiation exposure is an individual with cancer which is far enough advanced either by direct extension of tumor or by metastatic spread so as to eliminate consideration of attempts at curative therapy. Usually these patients receive nonspecific supportive treatment or palliative treatment by surgery, radiation or chemicals. The consequence of these forms of therapy are usually helpful but sometimes the sequelae or complications of the various treatments are in themselves life threatening and constitute a hazard to the patient. Hence, whole body radiation therapy is no more likely to produce untoward sequelae than many other currently accepted treatments of other types.

Animal studies (2) have suggested that small doses of whole body radiation actually potentiate the effect of subsequent radiation given locally to tumor areas. In acute radiation injury of humans interesting contributions have been made by a number of workers. Hempelmann et al (3) have described the salient features of acute radiation injury and these observations have been amplified by Andrewe et al (4) Shipman (5), Howland et al (6) and others. An excellent review adding certain new diagnostic criteria was presented by Thoma and Wald. (7)

Observations following therapeutic whole body radiation have been made by Collins (8), King (9) and Muller et al (10).

Although too few patients have been treated by whole body radiation at the University of Cincinnati College to be valid statistically, we have made several interesting observations. In general, these studies have demonstrated the relative innocuous nature of doses at or below 100 rad and have continued to confirm the well known hematological changes. At 150 and at 200 rad we have had responses to radiation of the type seen in group II of the acute radiation syndrome. We have had two cases, one at 150 and one at 200 rad, expire while

manifesting the hematologic abnormalities of group III of the acute radiation syndrome. These responses are in cancer patients suggesting that the more serious response may not be due solely to radiation. These findings also suggest that patients with various illnesses may be unusually susceptible to radiation doses whereas "healthy" patients may be less affected. One wonders whether the effect of prolonged stress as found in fatigue would produce similar effects. Searches for biological indicators other than blood changes have to date been unrewarding primarily because very few biochemical systems have been carefully studied in humans. Certain indicators such as urinary beta amino isobutyric acid which have appeared to be useful in accident victims, seem in cancer patients to be much less predictive than one would have anticipated.

C. Role of Future Human Research in Relation to Remainder of Radiobiology Program

When one considers the nature of the total problem of weapons effects it is surprising to see the paucity of human studies. This problem is probably the single most important area of biological weapons investigation to be pursued in the next decade. Much valuable diagnostic, prognostic, behavioral and therapeutic information can be gleaned from well planned and executed studies in this area.

Continuing and future studies of acute external whole body radiation fall logically into the following categories:

1. Clinical evaluation - effect of various doses on signs, symptoms routine laboratory tests or new tests (newer biological indicators).
2. Metabolic effects - Effects of various doses on nutrition, fluids and electrolytes and biochemical systems of interest (including changes in the immune system). Use of labeled precursors.
3. Behavioral effects - Effects of radiation at various dose levels on human performance.
4. Dose rate response - Changes in effects with very high, very low and mixed dose rates, together with evaluation of single and multiple doses should be made. The concept of equivalent residual dose (ERD) (Rept. #29) should be investigated.
5. Partial body irradiation - Comparison of effects of shielding of various parts of the body.
6. Prognosis - Development of criteria for patient care based on the observations from these studies.
7. Therapeutic methods - Adequate supportive care of patient receiving radiation. Development of new methods of prevention and treatment of radiation injury.
8. Use of healthy volunteers - Limited use of normal volunteers based on preceding careful investigation of therapy and accident patients.

D. Specific Areas of Endeavor:

1. Clinical Evaluation - All patients who receive whole body radiation for any purposes should be evaluated carefully utilizing all clinical and laboratory observations which can be reasonably obtained. Clinical patterns related to dose, coexisting disease, nutrition and other parameters may thus be identified.

It would seem important to carry these observations further at various dose levels as most planning for capabilities of humans after exposure depend on a knowledge of their expected performance.

2. Metabolic Effects - Continuing metabolic studies are needed. Little is known of nutritional requirements and fluid and electrolyte changes in humans. Some investigators state that these aspects are not important in radiation injury on the basis of animal studies. There has not been enough human research in this area to provide convincing data at any dose level. Such information is essential in planning patient care.

Changes in DNA-RNA systems in so complex a mammal as man may be difficult to find. Some preliminary observations in our laboratory indicate that further studies in this general area may be fruitful. Many other systems might be suggested as shown by the observations of Gerber et al (11) regarding creatinuria, beta aminoisobutyric acid and hydroxy proline. The use of labeled precursors is suggested since at some time it will be necessary to determine whether certain changes following irradiation are due to specific biochemical alterations or are due to nonspecific stress.

Changes in the immune system have to date eluded most observers who have sought them. With the renewed interest in immunology centering both about the lymphocyte and thymus, new techniques of study should be sought.

3. Behavioral Effects - One of the questions most frequently asked by individuals responsible for planning for nuclear warfare concerns the effect of a given dose of radiation on subsequent capability and performance of an individual or group. It is apparently not easy to find a suitable test or battery of tests which measure the important human functions of performance or decision making such that one or more tests could be used before and after exposure to radiation.

Appropriate performance tests should be developed or adapted. These tests should be given to subjects before and after exposure to ascertain changes in the capability of the individual.

4. Dose Response Studies - Most studies have been carried out with rates such that the dose is delivered within 30-300 minutes. If a dose of 200 rad is delivered in approximately 90 minutes and produces a given effect it becomes

important to determine the change in effects if this dose is given in 0.5 - 5 minutes. There is much speculation about this problem at a human level based on animal studies but no precise data has been obtained in humans. Similarly the effect of low dose rates should be studied particularly in relation to performance testing. The effects of high doses (100 - 200 rad) followed by daily doses to test the concepts of equivalent residual dose (12) would be of importance. Fractionation studies should be continued.

5. Partial Body Studies - Patients in whom various parts of the body have been shielded would be compared to patients who have received whole body radiation using a variety of indices.

6. Prognosis - The vast amount of data which could be generated by the studies described herein should be collected, tabulated and prepared for computer analysis so as to make these data easily available for physicians, commanders et al. This function might well be assigned to the office of the Surgeon of DASA or other representatives of the respective Surgeons General to insure presentation of the data in its most useful form.

7. Therapeutic Methods - In view of the hazards involved in this form of therapy, before increasing the dose beyond 200 rad all measures to protect the patient must be available and ready for immediate use. The patient should be in a clean area with an aseptic treatment room available. Autologous marrow should be stored and ready for reinfusion before therapy. Optimum time for reinfusion will have to be determined.

In general one might consider studying antiradiation drugs in humans. In spite of the great volume of animal work in this area, most drugs have various drawbacks for human use. One such drawback is that it is not possible to do drug testing at an LD_{50} level in humans. With the development of additional biological indicators, however, such drugs might be studied at lower dose levels.

8. Use of Healthy Volunteers - Once patients from the therapy group are being managed so that their hematologic consequences of radiation have been controlled then it will be advisable to utilize a less ill, more normal group of individuals for study.

Consideration should be given to the use of volunteers because of the possible biases introduced, and perhaps unrecognized, in patients receiving therapeutic radiation. Similarly in accident victims complete pre exposure data is usually not available.

E. FUTURE PLANS REGARDING FUNDING: The studies described above will require the participation of a number of research centers and the development of at least a limited number of special facilities such as radiation units capable of very high and very low dose rates and appropriate clean and aseptic rooms as

well as other laboratory facilities.

If one assumes that the ratio of funds for all human radiation research is about 5% of the total finding of biomedical research one might also assume that present "high dose" or acute studies represent no more than 0.5 - 1% of this total budget.

Therefore, a three to fourfold increase in research funds in the above areas is recommended for the next three to five years. After that time the total funds should again be doubled.

At such a time as there is no threat of thermonuclear war, these programs could be greatly reduced or even eliminated.

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12. Exposure to Radiation. Report No. 29. National Committee on Radiation Protection and Measurements. Univ. Chicago 1962.

April 2, 1994

To Whom It May Concern:

My name is Josef Jerome Kahr. I am one of five great nephews of the late Margaret Bacon. She was partially responsible for my upbringing. She was also an intricle part of my life for 13 wonderful years. She shared a residence with myself and her sister, Lillian Joan Kahr, who was my grandmother and my legal guardian.

The death of my great aunt was a very hard matter for me to accept. The heartfelt joys that we shared turned into faded memories. All the happy times we spent together turned into heartaches and sorrow. Her death felt like a lethal weapon that wounded my soul and left an emptiness that will never go away.

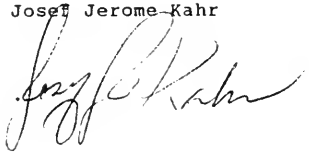
The thought of my great aunt suffering through needless and unauthorized radiation treatments is totally repugnant. Nothing will ever bring my great aunt back, but I feel something should be done to those parties that are responsible for doing radiation experiments on her without her consent.

It is unthinkable that a hospital misused and prematurely ended the life of my great aunt, Margaret Bacon.

The hospital had no right to play God!

Sincerely,

Josef Jerome Kahr



April 8,1994

TO Whom IT May Concern:

My Name is Margaret J. Willis. I am the great niece of the late Margaret Bacon. She was a very inportant part of my life and upbringing. She also had a hand in the upbringing of my late mother Ella Margaret Willis. In her latter years she she shared a residence with her sister, Lillian Joan Kahr, my grandmother.

When my Aunt Margaret became ill my mother,grandmother,and other members of the family had to talk her into going into the hospital. That is when I found out she had cancer. MY mother, grandmother and myself went to the hospital to visit Aunt Bacon ,and I wondered why she was laying with blood over her sheet.

I think this may of had something to do with why my mother refused treatment of cancer.due to the death of her aunt. Just the thought of my great aunt suffering through needless and unauthorized radiation treatments is totally repugnant. Nothing will ever bring back my Aunt Margaret, I do feel something should be done to those parties responsible for the radiation experiments with out consent.

This in it self makes you very leary of going to a hospital that would let this go on.

Sincerely,

Ms. Margaret J. Willis

April 4, 1994

AMELIA JACKSON
PATIENT NO - 67

On October 21, 1966, after being discharged for General Hospital, Ms Jackson was a very weak ill woman. She was unable to take care of herself properly, and depended on the family for all her basic needs. She experienced bleeding from her rectum, loss of appetite, nausea, vomiting, weight loss, and was in constant pain. Her condition never improved.

Within a few weeks she was readmitted to General Hospital. The family was informed she should be transferred to Drake Hospital. Ms Jackson indicated she was afraid and wanted to return home. She was transported home, where she was loved and cared for by us until she died on March 25, 1967.

The family of Amelia Jackson would like for this committee to know, that for the entire 163 days after receiving the irradiation, her condition continued to deteriorate. We feel that the 100 rads of partial-body irradiation administered to her was cruel and didn't help her condition in any way. It's our belief that she may have lived longer if this experiment had not taken place.

A doctor is someone you trust. His job is to do everything in his power to alleviate your pain and suffering. However, this was not the case. She was always crying, moaning, groaning, and in excruciating pain. Ms Jackson was used to further Dr. Saeger's professional goals. It was purely an ambitious and callous act. Neither Ms Jackson nor the family were informed or consented to her being used in an experiment conducted by Dr. Saeger, and funded by the Department of Defense. There has clearly been a cover up by means of the Government, General Hospital, Dr. Saeger and City of Cincinnati. We cannot believe that they consented to such atrocities to be financed by the government; utilizing Ms Jackson's and the family's tax paying dollars.

Vickie Longmire
Gloria Welch

My Aunt Louise Richmond passed away from Colon Cancer in March, 1968. She was only 49 years of age. My Mother Viola Macklin (one of Louise's older sister) brought her from Cleveland, Ohio to Cincinnati, Ohio for medical care of her cancer at the General Hospital.

Instead of medical treatment, my Aunt Louise, unknowingly was used as an experimental subject at General Hospital in their radiation experiment. Within weeks of her admission, her health rapidly and painfully deteriorated and ultimately leading to her death.

Regrettably, the news of the General Hospital Radiation experiment has recalled many agonizing memories for myself and my family. The death of a loved one, under normal circumstances is difficult, but now with the added knowledge of my Aunt sacrificial involvement in the radiation experiment, my family members must relive the misery, now with twice the anguish.

Various family members can vividly recall the evening visits to the hospital as we accompanied our mother to visit Aunt Louise. The torturing cries of pain that greeted us as we entered into the hospital ward had become all to familiar to us. She would be lying in her hospital bed trembling and shaking from her agonizing pain so forcefully that the bed itself would be visibly vibrating.

Throughout the visit, my Aunt Louise would cling on to my mother's arm crying and begging her to take her home. She would repeatedly say, "please Viola take me home with you, I['m in so much pain, they are hurting me, they are trying to kill me".

The visits would always end with my mother tearing herself away from my Aunt Louise only to hear her cry in pleading desperation as we walked away. For seemly, hours after we left the hospital and even after reaching home my mother would cry from the guilt she felt for my Aunt's severe pain and suffering. My mother would routinely rock herself to sleep while crying and humming spiritual songs to relieve the burdensome feeling of her most recent experience/visit to my Aunt Louise.

After my Aunt Louise' death in March, 1968, my mother would often ask us if they (the Doctors at General Hospital) were really giving her the correct treatments for cancer.

We had no idea Aunt Louise was a part of a Defense Department experiment. We're sure if she had known she was a guinea pig, she would not have participated.

My mother would often recall the visit and continued to blame herself for the pain and anguish my Aunt Louise had experienced. My mother carried this unwarranted guilt to her death, and now we have been forced to carry this guilt as well in memory of my mother and aunt.

Statement of Katie
Cavus

Date: April 4, 1994

To: Robert B. Newman, Attorney at Law

From: Members of the Maude Jacobs Family

Subject: Radiation Testing at UC (Cincinnati General Hospital)

This correspondence is regarding Maude Jacobs, a female caucasian, who was an unsuspecting victim of the radiation tests conducted by the University of Cincinnati. Maude was born in Whitesburg, Kentucky on June 7, 1916. The third grade was her final year of formal education. By the time she was thirteen years old, she was married and had given birth to her first child. She bore seven children in all, six girls and one son. She was a beautiful woman with a lovely radiant smile. She was impeccable about her children's appearance, as well as her own. Her devotion to her family was obvious to anyone who knew her. Maude lived her life below the poverty level, but was a proud and dignified woman. She was genuinely happy with the simple things in life. Her delight was cooking and caring for her children. When she died she was a widow and left three minor children at home.

According to information from CGH (Cincinnati General Hospital), Maude was diagnosed with breast cancer on July 17, 1964. A treatment of hexamethylmelamine began on July 27,1964 and was completed on August 18, 1964. With this medication her primary tumor receded markedly. On November 7, 1964 total body irradiation was administered. The midline absorbed tissue dose was 150 rad (250 r midline air dose). At the termination of the treatment she had severe vomiting for twenty-four hours, in spite of intramuscular compazine. Before treatment she had a normal hemogram. Seven days after treatment the white blood count began to fall. The platelet count fell around fourteen days after treatment. The WBC was 1,000 and platelet count was 80,000 twenty-three days after treatment. On the twenty-fourth day, the WBC was 850 and platelet count was 38,000. Maude died December 2, 1964. Twenty-five days after total body irradiation. She was study number 045. (Documentation from CGH attached.)

Two letters written by Maude to her sister Arlie less than two months before her death describes how she felt, and also indicates she thought the doctors did not know what was wrong with her. She talks of living near her oldest daughter, Lillian, who is very helpful to Maude. She also is pleased to be home with her children, but feels sorry because she is too tired in the evenings after preparing dinner to watch television with them. She refers to the expense of her medication and said prayer helps her more than the doctors. These letters demonstrate her education level, but also reveal her devotion to her children. Maude had no knowledge of the seriousness of her cancer much less knowledge of the radiation

treatment. She did not expect to die. If she had, she would have discussed the future care of her minor daughters with the rest of the family. Her death was so sudden and unexpected the family was totally unprepared. The three young daughters eventually were put in St. Aloysius Orphanage. (The two letters from Maude to her sister are attached.)

The family was **NEVER** informed of the radiation test or it's purpose. Nor was anyone ever asked to sign a consent form or give verbal permission for testing. Some of the memories which were dismissed without attaching importance now make sense or at least raise suspicion. Her daughter Irene was seven months pregnant at the time and was having a difficult pregnancy. She remembers Maude's bright smile and cheerfulness, then remembers a private room and no more smiles or happy faces. Irene remembers being afraid of going into that room. Maude asked her to feel her head and when she did it felt full of soft tumors. Her body felt like sand. Even in the hallway she could hear Maude's delirious talk.

Maude's daughter Sherry was twelve years old and remembers the private room, but at the time didn't know it was uncommon for a person without insurance. Sherry remembers the orphanage and being split up from her two younger sisters. The youngest girl, Kim, eventually went to a foster family.

Robert Murphy, one of Maude's grandson's, remembers thinking how nice it was to have a private room without insurance. Bill Murphy, another grandson recalls visiting her in the private room, but not wondering why she was there. He remembers her conversation as "out of her head".

Her oldest daughter, Lillian Murphy Pagano, lived downstairs from Maude and was her primary care provider. Lillian was never contacted or consulted about her mother's treatment. She remembers a drastic mood change associated with rapid physical deterioration. She too recalls the private room at the end. She remembers thinking her body felt like sand. She was concerned too for Irene, because of her pregnancy and the worsening of their mother's health so rapidly. Lillian's concern grew as Maude quickly became disoriented and no longer recognized anyone. She was violently ill and talking utter nonsense. Maude died before her time everyone felt. Her family lived for the next twenty-nine plus years with the sadness of her death, but also had warm memories to console them.

Since the details of the experiments became public, the entire family has been drastically affected. Now guilt has replaced the sadness and comments like "I should have known" or "I should have asked" are commonplace. Reliving Maude's last days over and over, remembering differently now why she was so violently ill, how she suffered, and now a reason for the private room. Her death is now a nightmare. She died without comfort and dignity. She was discriminated against and selected because of her background. No benefit was ever planned for Maude. She was a number, a statistic.

Her children want an apology. They want to know nothing they could have done would have altered the results. They want Maude to know they are sorry if they disappointed her because she suffered needlessly without intervention from them. They also need a quick resolution so this too can be a memory. Already too much damage has been realized.

Lillian Murphy Pagano (Maude's oldest daughter) feels personally responsible for her death. She became obsessed with Maude's death, often calling other family members several times a day to go over some part of her last days again and again. She was found several times at three or four o'clock in the morning with a fixed stare and silent sobs. Eventually she was rushed to the hospital with a suspected heart attack. After a short stay of a few days, some testing, several prescriptions, and instructions to avoid stressful situations, she was permitted to go home. Anxiety struck again within a few weeks. This time she was gone. Lillian's daughter found her, called 911, and received over the phone guidance for delivering CPR. When paramedics arrived, she was given multiple shock treatments to revive her. It is estimated she was dead for four minutes. She was on a respirator and in a coma; she also had several seizures. The doctor's gave her a 50% chance of pulling through, but warned all about the possibility of permanent brain damage. She has regained consciousness, but is still in critical condition at this writing. She recognizes family members, but is mentally unstable. The extent of damage is still unknown. Her family has been told she will need twenty- four care and cannot be exposed to ANY stressful situations. She doesn't talk about Maude now. She doesn't even remember who visited her an hour ago.

The ordeal with the UC experiments must come to a swift conclusion. This is the saga of only one family, there is supposed to be eighty-seven more victims with families. It's amazing how something that was a remote, barely thought of memory, now is resurrected and grown into an unwelcome demanding problem. A problem that can consume your days and affect people from twenty-nine years of family growth --- people Maude never could have known.

This letter was compiled from the hearts and thoughts of Maude Jacob's children:
Lillian Murphy Pagano (nee Phillips)
Irene Froman (nee Phillips)
Bob Phillips
Betty Wolfe (nee Phillips)
Sherry Brabant (nee Jacobs)
Janet Baker (nee Jacobs)
Kim Swedo (nee Jacobs)

Attachments

Joe Larkins
974 Whisper Cove
Winter Haven FLA
33880
813 299-5133

March 31, 1994

To Whom It May Concern:

My name is Joe P. Larkins. I am now 52 years old. My Father, Willard L. Larkins, passed away in 1971. I was 30 years old at the time. My family consisted of myself, an older sister and my parents. When my Father passed away, he and my Mother were in the process of raising a grandchild (my sister's son). Neither of my patents were well-educated, but my Father was hard-working and honest. We always had clean and decent clothes to go to school in and we always had ample food on the table. It doesn't take a well-educated person to be hard-working or honest. If Cincinnati General Hospital and the Doctor's therein had been honest, there is of course, the possibility that my Father could have lived for several more years. Instead, he went from a fairly able-bodied middle-aged Father and Husband to a premature death caused by an "experiment". My Father did not know that he was being used as a guinea pig; my Mother did not know; as his children, we were not informed of the procedures to be used nor of the risks involved.

I feel as though Dr. Saenger and the other "Doctors"involved, if you will, knew that the high levels of radiation which they administered to these patients had the very real probability of being fatal. Oh, how right that is! My Father was very much a family man, yet these people killed him as surely as if they had put a gun to his head and pulled the proverbial trigger. These "Doctors" left my Mother, with no job skills, to raise a grandchild as best as she could. My Mother lived until 1983, but she was a broken woman after my Father's premature and unexpected death.

I know that my Father knew that something was very wrong with the treatments being given to him at Cincinnati General. He even asked me "Son, what are they doing to me? They're trying to kill me!" That's how bad the pain he endured after the treatment was. He suffered so needlessly. What really gets me about this situation is the fact that the Pentagon contracted with these Doctors and this hospital to test the effects of radiation on the human body. Everyone realizes that Cincinnati General Hospital, now the University of Cincinnati Hospital, treated many low-education, low-income patients. I guess they felt that in some way, the fact that these patients were not rich, upper-class citizens, gave them the right to experiment with

their bodies without informed consent. NOT SO! I feel sure these physician/researchers were well-paid for their part and it would be very interesting to know the types and dollar amounts of the grants given to Cincinnati General by the Federal government. I feel sure that all parties, with the exception of the poor, unsuspecting patients and their families, were well-compensated. But since when, in our society, does one man or even a group of them, have the right to play God? A very good example of this is our 20th century "assisted suicide Doctor". This man is contacted by terminally-ill patients who wish to end their own lives with dignity and choose, by their own voilition, not to suffer needlessly for years. These people make the decision to die in peace, yet our great judicial system, along with the medical community, brought this compassionate physician up on charges. The differences in these deaths and the death of my Father are that my Father did not choose to die - someone else made that decision for him, without consulting or informing him and they were amply compensated for it. I feel that the price they should be required to pay to the families of the people they killed, should be exceedingly high. I also feel that the Federal government should be named as a co-conspirator in this case, because that's exactly what it was - a conspiracy. No person, and I emphsize 'NO', person would willingly consent to a treatment with any degree of fatality involved. People, both you and I, simply value life too much. I think that is the big thing here - the patients were not informed. I know that behavior of this sort would not be tolerated by the medical community today. But then again, this entire mess was surrounded by a thick veil of secrecy on both the doctors' part and on the part of Cincinnati General Hospital. It is still being closely guarded and kept under yet another veil of secrecy to this very day by the University of Cincinnati, in that they have yet to provide the medical records of the patients involved in this experiment/ I beseige you to order the University of Cincinnati to release the patient records, in their entirety, to the next of kin immediately. They are hedging to save their own skin. I was promised my Father's complete medical file over a month ago; as of this writing, I have nothing.

I only hope that you, the Congressional Committee, see fit, as members of the human race, to break this matter wide open here and now and award just compensation to the families of the victims. I feel that the Physicians involved and also the federal government (the Pentagon) should pay and also I beg you to strip any and all of the Doctors involved of all their medical credentials that they hold. If justice prevails in this matter, and I have faith that it will, a strong message will be sent to our government officials and the private physicians (to whom people entrust their lives and the lives of their loved ones) that behavior of this

sort will simpley not be tolerated, that justice will in fact be both swift and severe. I pray that a situation such as this will never again be faced by a group of people. If this statement to you, the Congressional Committee, does anything to help in the name of justice, then my Father's death and the sorrow and hardships that his familty faced, will not have been completely in vain.

Thank you.

TO: **Chairperson of the Congressional Committee**

RE: **The Partial and Whole Body Radiation Experiment Conducted from 1960-1971**

FROM: **Mr. Woody Plair and Family of Mrs. Beatrice Plair**

This letter was very difficult to write for us, the family of our departed wife, mother and grandmother. We conversed of many traumatic thoughts and feelings regarding our loss.

Herein is the summation of our collective thoughts and feelings. Dr. Saenger states that the patients and families gave their consent to receive partial or whole body radiation. For the record, our mother loved life and she would have never given her consent to any treatment that would have shortened her life or cause her the pain, we observed. She never knew she was part of the Cold War Radiation Experiment. As a family, we were never told of her participation in partial or whole radiation. We would have not given our consent for her participation in an experiment. At no point in the supposed treatments of our mother did anyone tell our father nor her children that she was part of a dangerous and life threatening experiment.

What we can say to the Sub-committee is that we remember our mother complaining of increased pain, especially following the radiation exposures. We can told you how our mother told us she felt as though she was on "fire" or "burning all over". We can tell this committee, we resent our mother being used as a human Guinea Pig and the implication by Dr. Saenger that our mother agreed to have her body exposed to radiation injury that would lead to serious pain and shortening of her life.

The Plair family asked this Sub-committee to help us to bring the people who we feel shortened our mother's life to justice.

In a society where life, especially human life appears to be worth less and less, we and other families are depending on this Sub-committee to send a clear message to Dr. Saenger and associates, the University of Cincinnati Medical Center and the Defense Department that human life is still important.

We must let the world know that here in America, what makes us different and greater than other countries is that we truly value each and every human being regardless of their I.Q., education, race, creed, color or position in our society. If we allow this travesty of justice to go unchallenged others may be unknowingly experimented upon in the future.

Respectfully submitted,

Mr. Woody Plair and Family

To Someone Who Will Listen:

I was 30 years old when my mother was stricken with cancer. She had six other children, three very young at home, the oldest was 12. She was born (my mother) in Whitesburg, KY, 1916, only went to the Second Grade of Grade School, was married at 13 years of age. When cancer struck she had no money. Her husband had only been dead a short time and she was struggling to care for her three girls at home. She wanted to spend as much time as she had left enjoying her three daughters. She was being treated as an out-patient at General Hospital. One day near the end nurse called told her to come to hospital clinic. She took a taxi because no one was available to drive her. She came home weak and vomiting. She was admitted to hospital and only lasted less than a month. When we (the family) found out recently about the 150 Rad she had received my older sister felt she was to blame because she did not go with her in taxi to clinic. She had to be hospitalized herself and may need constant care. A younger sister has M.S. and has not been told for fear she won't be able to cope with it. I'm sure all the other families that are still alive are having similar problems. My prayers are with them too. As you can tell from my letter, I don't have a good education. Should I be afraid to be treated in a hospital? Afraid of being used for testing some other chemical to benefit our government. Or carry a Donor's Card so if they wanted an organ they could take it at will? Something needs to be done it is up to you. I'm helpless.

Thank you.

Bob Phillips
Son of Maud Jacobs #45

TO : Congressional Committee
FROM: Herbert F. Varin
DATE: April 4,1994

Study # 075 N.C.
Chart # CGH 409-278

My mothers name was Nina L. Cline, a loving and caring mother, whose only hope was to see her grandchild before she died. She did 10 months before her death. She was also very close to her sister, and her sisters children, who were all very helpful with my mother during her cancer.

My mother was diagnosed with cancer in 1962, she put a lot of hope and faith in her doctors and General Hospital who were treating her. She often talked to me and other family members about her treatment, but at no time did she mention being apart of any experiments for the government. She would have talked to me and other family members before ever consenting to any experiments.

I am appalled to think that Dr. Eugene Saenger, his associates and our Federal Government would join is such an inhumane act. I also believe Dr. Eugene Saenger violated his moral and ethical obligation toward his patients.

We were taught as children and young adult, to believe in our Federal Government, that they would make all the right decisions concerning our welfare as people. For the government to sponsor a radiation experiment of this nature, on my mother and other patients was totally immoral.

Herbert F. Varin (Son)

Herbert F Varin

RADIATION EXPERIMENTS

TO WHOM IT MAY CONCERN!
MY NAME IS JOE KAHR SR.,MRS MARGARET BACON WAS MY MOTHERS SISTER,WHICH IS MY AUNT.
I ALSO,LIKE MANY OF OUR RELATIVES WAS PARTLY RAISED BY MY AUNT MARGARET BACON OF WHOM I HAVE VERY FOND MEMORIES OF.

IWAS ENCOURAGED BY HER HOSPITAL DOCTOR TO CONVINCE HER (SINCE SHE DID NOT WANT TO ENTER A HOSPITAL ANYWAY)THAT GENERAL HOSPITAL(THE HOSPITAL SHE WAS IN AT THAT TIME),HAD THE BEST RADIATION FACILITIES IN THE CITY WHICH COULD HELP HER SITUATION IMMENSELY.
AFTER A WHILE,SHE AS WELL AS I BOTH BELIEVED THE DOCTOR .

IF YOU KNEW THIS FAMILY,THEN YOU WOULD KNOW THAT WE ARE THE LAST OF ANY INDIVIDUALS TO COMPLAIN.
HOWEVER WHEN IT REACHES THIS POINT,THEN WE CAN NO LONGER REMAIN THE SILENT INDIVIDUALS THAT WE ARE.
SHE NEVER ASKED FOR MUCH,NOR DID IT TAKE MUCH TO SATISFY HER.
HOWEVER,BEING A HUMAN RADIATION GUINEA PIG IN THIS TYPE OF DEATHLY SITUATION IS DESPICABLE,WHEN ONE SUCH AS HER LOVED LIFE AS SHE DID.

THE FIRST THING MY AUNT AND I NOTICED AS WE ENTERED THE CINCINNATI GENERAL HOSPITAL,WAS THE AMAZING UNIVERSALISM WHICH WAS EXPRESSED IN SUCH PROFOUND ELOQUENT AND EQUIVALENT LANGUAGE,THE DIGNITY AND WORTH OF ALL PATIENTS,WHICH THEN WAS MENTIONED THAT ALL PATIENTS WERE TREATED EQUALLY.
ON ONE HAND,IT WAS PROFESSED TO US,THE NOBLE PRINCIPALS AND EXPECTATIONS OF THE HOSPITAL. BUT IT SEEMS THAT ON THE OTHER HAND THAT SOMEONE WAS SADLY PRACTICING THE VERY OPPOSITE OF THOES EXPECTATIONS THAT WE WERE ORIENTATED WITH.

IAM SURE THAT SHE AS WELL AS OTHERS WANTED TO BE CONTENT BUT IT SEEMS THAT SHE WAS USED AS AN EXPERIMENTAL OBJECT AND BECAME THE VETERAN OF CREATED SUFFERING.
I NEVER DREAMED THAT THIS FAMILY WOULD EVER BE EXPOSED OR WRONGED BY SUCH AN IMMORAL AND UNJUST SITUATION.
I FEEL THAT I MUST SPEAK NOW BEFORE IT IS TAKEN FOR GRANTED THAT WE ARE STILL ONE BIG HAPPY FAMILY,NOW OPPOSED TO WHAT WE USE TO BE.

IT SEEMS THAT THIS NOW IS THE KIND OF ENVIROMENT IN WHICH WE LIVE. HOW CAN WE AVOID BEING DEPRESSED WHEN WE DISCOVER THAT ALL PRIOR GENUINE CODE OF ETHICS ARE SLOWLY CHANGING FOR THE WORST.
WE ALL AS LOVED ONES ARE INVOLVED IN A NETWORK OF MUTUALITY,TIED IN A SINGLE PROMINENCE OF DESTINEY. WHAT EVER EFFECTS ONE FAMILY DIRECTLY, EFFECTS ALL FAMILIES INDIRECTLY.
WE CAN ONLY AND WILL ONLY SURVIVE THIS EMOTIONAL

CATASTROPHE,BECAUSE IT SEEMS THAT WE HAVE NO ALTERNATIVE IF WE WISH TO KEEP OUR SANITY.

IT IS A TORTUROUS LOGIC TO USE THE TRAGIC RESULTS OF THE HOSPITAL OR GOVERNMENTS REASONING AS AN ARGUMENT FOR THE CONTINUATION OF RADIATION EXPERIMENTS DURING THAT TIME.

WE SHOULD HOPE THAT NEVER AGAIN SHOULD WE OR ANYONE ELSE HAVE TO RESIGN OURSELVES TO SUCH AN OUTRAGE.

THE TORMENTED AND UNHAPPY FAMILY OF MRS MARGARET BACON.

April 8, 1994

To Whom It May Concern:

It is our feeling that our mother was not informed of the true nature of the radiation she received at Cincinnati General Hospital. It was her belief and ours that the radiation "therapy" was being performed to (1) reduce the pain due to her cancer and (2) to kill tumor cells in order to possibly extend her life expectancy. This is what we were led to believe by the physicians and other health professionals in charge of our mother's care. We all were led to believe that the radiation therapy would also benefit mankind in determining the efficacy of these treatments, to help cancer patients in the future.

As a family, one small consolation in watching our mother die a slow and painful death from cancer was the fact that her participation in the treatments would represent a positive outcome from her death in the form of her helping others who shared her fate.

Having found out the truth about what really happened to our mother has not only brought back painful memories of seeing her suffering, we must now live with the knowledge that this suffering (excruciating physical pain, intense fear, despair, and many other terrible effects of the treatments) was intensified and not alleviated by these radiation experiments. This has caused even greater pain and suffering knowing that our mother was treated no better than a laboratory animal thereby robbing her of her human dignity and the right to live out her final days as comfortably as possible. We believe her life was shortened immeasurably by these physicians making god-like choices which they had no right to make.

Sincerely,

Elyse A. Feltrup
Daughter of Rose E. Strohm

April 8, 1994
Date

Stephen G. Strohm
Son of Rose E. Strohm

April 8, 1994
Date

FRANKLIN BUNCH FAMILY

To: CONGRESSIONAL COMMITTEE OF David MANN.

FROM: FAMILY OF FRANKLIN BUNCH

DATE: 4-8-94

I have CONTACTED ALL MY LIVING RELATIVES & They WAS NOT INFORMED OF OF ANY EXPERIMENT THAT WAS MADE FOR the DEFENSE DEPARTMENT OR any ONE ELSE.

NO ONE IN MY FAMILY WOULD have AGREED TO SUCH an EXPERIMENT any more THEN THE JEWS WOULD have OR DID, IN GERMAN DEATH CAMPS

We ASK THIS COMMITTEE NOT TO white wash THIS TORTURE & DEATH MATTER AFTER THIRTY (30) YEARS REMEMBER JUSTICE DELAYED IS JUSTICE DENIED

CONGRESSMAN I ASK YOU WHAT ARE YOUR LOVED ONES WORTH TO YOU.

Clarence Bunch (BROTHER)
772 STRAIGHT, CINN, OH 45214

March 29, 1994

TO THE CONGRESSIONAL COMMITTEE OF MR. DAVID MANN:

I, Doris Baker, only have a few things to say. One is why were we kept in the dark about my great grandmother and the other is why didn't they tell her about it? Her life, was her's and God's, not their's.

I had to take care of her as a young pregnant 17 year old mother day and night. They said she didn't return, she couldn't even walk by herself. I had to lift her to the bathroom. I watched her slowly die. She tried to fight it; even when they told her she was dying. At times, she was in so much pain. I would ask her what was wrong and she would say nothing, but I saw the tears in her eyes and the pain.

You know, I almost lost my baby, because I was tired and run down from taking care of my grandmother. My child was born on 10/20/64 and only weighed 2 pounds. Please someone tell me why?

That lady was my life, for personal reasons. After 30 years is still hurts, because she was my protector. So you see she never would have agreed to be a guinea pig for no one, because she loved life. When you shortened her life, you caused my brother and I alot of pain until this day. So please someone be honest with my family and I. Because no one was honest with Mrs. Gertrude Newell. She was just a case number and a piece of meat to them to experiment on for their use.

Sincerely,

Doris J. Baker

#055 Lillie Wright

Chart No. 44174

My mother Lillie Wright was admitted to Cincinnati General Hospital Aug 23, 1965. She was sent there for a biospy. She was confined to the hospital for one 1 week.

The summary I recieved of her illness revealed that her biospy was performed. Aug 30, 1965 diagnosis was Carcinoma of the breast. On September she was given partial body irrodation 200 rad midline. On October 8, 1965 local x-ray therapy began. In 53 days she(Lillie Wright) had recieved 2000 rads to her left and right chest.

On December 1, 1965 x-ray was begun on the imtermammary chain and to the anterior and posterior above the collarbone region (supraclavicular). She received 4000 in 40 days. Her white blood cell count fell to a low of 2200 on December 3, 1965. These doses of radiation in my opinion was enough to destroy bone marrow and white blood cells and even the patient.

We the family of Lillie Wright was not notified about these radiation treatments or any other procedures which may have taken place. We did not sign any papers to permit this experiment to be done on her(Lillie Wright).

Lettie M. Smith
513-751-5269
3468 Hallwood Pl
Cincinnati OH 45229

The doctor at the hospital gave her sample tubes of oniment to use on her breasts, her back and abdomen. Her skin was burned on both breast. Her back and abdomen. There was raw flesh exposed where once there were skin.

I had to apply this oniment to those exposed areas.When I applied this oniment to those raw areas she was in such excruciating pain I cried. She was given enough oniment for 1 week. She was given Morphine which last 1or 2 weeks. I do not recall the name on the oniment tubes (3) but both of these product was given to her around December of 1965.

Neither of these medication helped her. When a person is real ill I was under the impression someone have to sign for medication such as morphine for a patient which is terminally ill. She was kept in the dark about the treatments she was receiving. She never talked about it.

It's not fair to treat another human being as a guinea pig because they are poor and uneducated. Some of our parents didn't have the privileges we are blessed with today.

I took my mother back to the hospital Feb 12, 1965 around 10:30 or 11:00. My nephew and I stayed at the hospital until 3:00 am I asked the receptionist if they were re-admitting her and she said yes we should go home and get some rest. When I return home my husband called me from his job and told me my mother had died. The people at the hospital never did call me to inform me of her death.

I'm her daughter, I should have been informed about her death before I left the hospital. I was at the hospital at 3:00 am the death certificate states she died at this time. Feb 13, 1966. I thought the nearest relative was to be informed first.

How I feel about my mother participating in the experiment.

I'm very angry about this doctor taking it upon himself to use poor live, uneducated human beings for his personal fame and gain. These human beings had the right to live the rest of their lives until God was ready for them to die. Not to die because man want to find out what effect it would have on soldiers in the war zone.

My family have been deprived of what days my mother could have lived. I know she wasn't educated but she knew something was wrong but she didn't know what it was.

I don't like it because she Lillie Wright was kept in the dark about this experiment. It's a disgrace to use high doses of radiation on anyone why didn't you experiment on your love one? No because they are special to you. Remember someday you will reap your just reward.

Jan. 4-1994

On behalf of the Goodwin Family in the Death of our mother Estella Goodwin. on Jan. 4, 1966 at General Hospital now University Hospital.

The radiation she received was a total surprise to us. We were told her treatment would be Cobalt treatment

Reading my mothers name in the news paper concering radiation testing was a total surprise to me and my siblings. How could a Hospital and Doctors she trusted do this to her or any person.

Otisteen Goodwin
+ Family

Date: 4-6-1994

My brother was diagnosed as having Hodgkins disease at General Hospital in 1963. Since we were not familiar with the disease or any treatment, we did not question the Doctors, nor were we told what they were using on him, all only know he kept getting worse. I, as well as others in our family were taking him back to the Hospital for scheduled treatments for a long period of time. We thought they were trying to help him but whatever it was made him suffer horribly. We did not know they were using the Radiation Experiment. My brother did not know either.

Franklin D. Bunch died in 1964 without any of our family knowing what happened.

Massie Lee Oliver
11048 Gaines St
North Bend, Ohio 45052

84-514 1025

April 1, 1994

STATEMENT FOR CONGRESSIONAL HEARING REGARDING EXCESS RADIATION USAGE AT CINCINNATI GENERAL HOSPITAL

By: Peggy Carboina (Brooksbank) Granddaughter of John Edgar Webster
1049 Belvoir Lane
Cincinnati, Ohio 45238
(513) 451-8427

Regarding Mr. John Edgar Webster

John Edgar Webster, father of Lucille H. Webster Brooksbank was admitted to General Hosptial around January or February of 1962. He was told he had cancer at that time. Also during this time my grandfather was living with us, meaning my mother, father and brothers and sisters. I recall my mother telling us that the hospital had a new treatment for cancer patients like my grandfather. That this treatment will cure his cancer. My mother was extremely excited after hearing the news of this newly discovered treatment. She, as well as all of us was led to believe that this treatment was the miracle of the century. Never was any family member advised that this treatment was an experimental venture with the United States Government. I recall my grandfather stating to me that after his cancer was cured with this new procedure he was going to take a trip to California to visit his eldest son whom he had not seen in four years. Before that treatments began, my grandfather was completely mobile, and functioned normally. Then the treatment began.

After my grandfather's cancer treatment, he was very weak, confined to his hospital bed and could not keep any food down including water. He was in constant severe pain. We visted my grandfather on a daily basis. Prior to his treatment we would give him back rubs, hugs, whatever. After the treatment we were advised by hosptial officials not to touch his body. He began to lose weight rapidly. We watched him physically deteriorate totally. However, his mind stayed alert. He would cry due to such pain. We heard him pray that God would take him so the pain would stop.

On the day my grandfather died, we were getting ready to go the the hosptial when the hospital called and advised my mother that grandpa was dying and that we should hurry. As we arrived to the floor we were met by nurses in front of his room telling us that my grandfather was dead. My mother wanted to see my grandfather's body. The nurse refused. My mother advised the nurse that she wasn't afraid of him while he was alive, why would she be afraid of him dead. The nurse still refused. My mother pushed the nurse aside and we entered his room. As we looked at him we noticed he had a yellowish-green color. Not a grey dead look. My mother asked the nurse why he was so discolored. She stated some people look that way at the time of their death. My mother advised that there was to be no autopsy. It wasn't until this investigation began did I discover that an autopsy was performed against the wishes of my mother. Never were we advised that this radiation treatment was an experiment in any fashion. Nor were any papers granting such an experiment signed. I strongly believe that the victims of these treatments were used as laboratory animals to see just how much radiation the human body could take.

Respectively Submitted,

Peggy A. Carboina

Peggy A. Carboina

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