



**BROWN UNIVERSITY** Division of Biology and Medicine  
DEPARTMENT OF COMMUNITY HEALTH

Statement to Congress, Subcommittee on Administrative 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, shored 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.*

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 political 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." Schloendorff 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 its 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

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## **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 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.

<b>Issue</b>	<b>Real Medicine</b>	<b>Military Research</b>
<b>TREATMENT FOR NAUSEA AND VOMITING</b>	<b>PROVIDED</b>	<b>DENIED</b>
<b>PSYCHOLOGICAL AND PEER COUNSELING</b>	<b>PROVIDED</b>	<b>PATIENTS PSYCHOLOGICALLY ISOLATED</b>
<b>DOSE RATE</b>	<b>SLOW</b>	<b>FAST</b>
<b>DOSE DIRECTION</b>	<b>MULTI-DIRECTIONAL</b>	<b>UNI-DIRECTIONAL</b>

**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..."**