

Dr. Saenger's memorandum of 12/6/71

An interview with Dr. Silberstein and Mr. Motter and Dr. Caper representing Senator Kennedy

The interview started about 1:15 and concluded about 3:00 p.m. After asking when Dr. Silberstein started, the next question regarded informed consent. Dr. Silberstein stated that the patient should know why we collect specimens, why there is so much inconvenience to the patient and he explained that the data was gotten in part so that people getting irradiated by a nuclear reactor or in time of warfare would be helped. There is the obvious cancer aspect.

Mr. Motter said that some people might claim that there is a difference in a project whether it is funded by D.O.D. instead of being funded by DHEW.

The question then shifted to the technique of whole body and partial body radiation therapy as to whether Dr. Silberstein regarded this as a research project or as accepted therapy and Dr. Silberstein then cited the extensive literature research which he had, pointing out that most of the studies were without comparisons being essentially Phase I or Phase II. Dr. Caper asked what Phase II studies are. Dr. Silberstein produced the article by Dr. Higgins. Mr. Motter asked how long Phase II studies last. Dr. Silberstein responded until patients were done. Dr. Caper asked why we had not embarked on a collaborative study with other institutions and Dr. Saenger responded that we had not yet gotten enough patients to consider. Dr. Caper then asked when and how do we go to a Phase III study. Dr. Saenger then responded by saying through a protocol developed by us which would be submitted to the Research Committee. He also

indicated that Dr. Silberstein had been at work since June, 1971 on a prospective study cancer of the colon metastatic to the liver. Both Mr. Motter and Dr. Caper indicated that such a project could be funded from the N.I.H.

The question then arose as to just how the informed consent interviews were conducted. Dr. Silberstein stated that he finds out about the patient from one of the house staff or from one of the radiation therapists or other physician in the institution. The chart is then reviewed. He then sees the patient. If the patient is disoriented or confused he is dropped from the study. It is then necessary to demonstrate that the tumor has in fact extended beyond the range of curative therapy and that metastases are present. Dr. Silberstein then sees the patient either in his office or at the patient's home, preferably with a relative. He spends the first interview determining whether the patient knows he has cancer and finding out what the patient's feelings are. Eventually in an appropriate way he indicates to the patient that the patient has a malignancy. The first session is regarded simply as a talk session. Depending on the patient's reaction at that time, Dr. Silberstein might discuss the possibility of this therapy. When the therapy is mentioned it is indicated that the information will be used for persons who would be over-irradiated in nuclear reactor accidents or for the benefit of soldiers on the battlefield. Mr. Motter "What do you say to the patient at that point?" Dr. Silberstein answered that this is a research program, that the treatment is given to a wider area with a lower dose to effect all of the possible cells involved. He emphasizes that the treatment is not a cure. There is evidence of relief of pain and a decrease in the size of the tumor. He tells the patient

what will hurt. At this time he is using ~~the~~ etiocholanolone which is painful. He emphasizes that there is no cost to the patient. The patient is not told about sham irradiation. He indicates to the patient that the patient will be admitted on Monday, will be treated on Tuesday and Wednesday and will go home either on Thursday or Friday unless there is a particular reason for the patient remaining in the hospital. Dr. Silberstein makes house calls if it is necessary. For example, on December 2, Dr. Silberstein did a bone marrow biopsy at the patient's house because the patient has arthritis and it is difficult for him to get back and forth. He feels that he makes a commitment to the patient to care for him during the remainder of his illness.

To get back to the content of the interview, the patient is then sent home to talk to his family to return on the following day. Then Dr. Silberstein reads the consent form and paraphrases it so that the patient can understand it and only after this time is the signature requested. Following this, there is a period of one to two weeks when the patient is undergoing preliminary evaluation and the patient is seen frequently during this time and asked whether he has further questions concerning the procedure. Mr. Motter asked at this point whether the patient signs on the 2nd day and Dr. Silberstein answered yes. The study is very complex. We arrange transportation back and forth to the Laboratory. The patients are seen here in the Laboratory for six weeks after treatment and then are returned to the Tumor Clinic after six weeks and Dr. Silberstein sees them there occasionally or Dr. Aron follows the patient. Dr. Silberstein indicated at this point that several patients called concerning

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the Washington Post article and were very much disturbed. Mr. Motter then asked how did the patients respond. Dr. Silberstein answered that two of the clinic were pretty hot concerning the Washington Post article. The father of one child was initially distressed at the thought that his child was being experimented on. He and his wife subsequently agreed that their child's radiation had been for therapeutic purposes, and who funded the lab tests wasn't of concern.

The parents of another child received several phone calls from neighbors telling them their child had been used as a "guinea pig". The parents then started reading newspaper accounts and stated to the radiotherapist that they thought the issue had been made a "political football." They were glad their son had been treated.

Mr. Motter raised the question as to whether the Department of Defense should fund this kind of research. He then went on to ask in how many instances had there been of patient refusal. Dr. Saenger recalled one instance. Dr. Silberstein recalled one instance and possibly a second. At this point, some of the political aspects of the problem emerged and Dr. Silberstein gave each of the men a copy of the Nature editorial. Dr. Silberstein then told the story of one woman whom he saw at home but who was terrified of coming into the hospital because of her fear of dying in the hospital and because her daughter was pregnant. Dr. Silberstein finally arranged for her to go to a psychiatric clinic where she got some relief. She subsequently died of her tumor. Dr. Silberstein

then pointed out that most physicians send patients of this type off to the nursing home to die. Our attitude here is to try and help the patients even though radiation therapy might not be the specific method which is most useful. He discussed one patient with melanoma who finally was taken to be baptized by Dr. Silberstein as an indication of the type of care which we try to give the patient. He then went on to explain his earlier training in the care of terminal cancer patients with Dr. William Crosby at New England Medical Center Hospital.

Mr. Motter then asked how he explained the theoretical basis of the response of cells at the very low doses which we give the patients when most therapists use much higher doses given locally. At this point Dr. Silberstein gave a long and somewhat involved explanation of cell survival curves indicating a D37 dose of 150 to 180 rad. Dr. Silberstein then went on to discuss the immune surveillance system pointing out that if some cells are destroyed then the immune system has a better chance of handling the remaining cells* At this point, Mr. Motter asked "Could we talk to the patients?" What would Dr. Silberstein's thoughts be to minimize any untoward psychological effect? Dr. Silberstein said that's hard. It depends on Dr. Galls' position. He then reiterated that it's hard. He is concerned about the anonymity of the patients and he is concerned that the patients would regard this as political footbaling. He thought it was grossly unfair to bring patients into this entire matter.

Mr. Motter - "We want to resolve whether there are issues involving the Senate Subcommittee which might bear on the way consent methods are used and the way they work. It is essential that something be heard from the actual participants." He stated that he thought the patients were already involved and interrogating them would be a rather minimal issue. Dr. Caper said that the real concern is that this is already a public issue. Dr. Saenger then asked as to whether there was some question as to the integrity of Dr. Silberstein and himself in regard to the statements which had been made. Mr. Motter replied that he considered himself an expert in the psychology of human behavior and that there was no question of the integrity of Dr. Saenger and Dr. Silberstein. He is concerned with what the patient conceives of the consent form, of what is in their minds. Are they aware what experiment is being done? What do they recall?

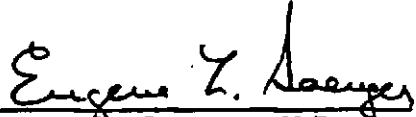
Dr. Saenger pointed out that although these questions were very interesting perhaps that a number of papers had been written on the subject and Dr. Silberstein mentioned the paper of Dr. Lasagna concerning consent forms and the use of aspirin. Mr. Motter then admitted that the questions which he was proposing to ask the patients were not very definitive and would only give sort of a general impression of how the patients felt. Dr. Saenger and Dr. Silberstein at that point asked just what they had in mind in the way of giving the patients informed consent. Mr. Motter said that he thought it might be possible to work out some way of asking the questions in an anonymous fashion so that the patients would not really become upset as to just why the questions were being asked or by whom.

Dr. Caper at that point admitted that there were some interesting and serious ethical questions being raised as to just how these interrogations might be carried out but stated that there was a very important question as to whether the patients really understand what is being done here. Dr. Silberstein stated at this point that there is no reason that a patient who is ill with cancer and has been treated some months before would necessarily remember the details of the consent form.

This is a personal impression of mine but there is no question in my mind that these men would dearly love to get directly at the patients and exploit them in any way possible to make a public issue out of the fact that one or more of these sick and infirm and poorly educated people could be maneuvered into a statement that they did not really remember as to just why they were being treated and that they might be experimented on without their knowledge. It seemed reasonably clear that the issues concerning our research were not nearly as important in their minds as in using this issue to get at the advisability of Department of Defense funding for this project. If they could block the D.O.D. in this research they could hobble the D.O.D. in all other biomedical research whenever they would choose to do so.

Mr. Motter at one point while Dr. Silberstein was out of the room pointed out to me that the data which we were collecting could be used by the Department of Defense as an offensive weapon and asked whether I had any knowledge that such a use was intended.

I replied that I had not even considered the problem and was really rather flabbergasted that anybody could consider information obtained on a project of such small magnitude as this one could be used as an offensive weapon. Also it is difficult to understand how an offensive weapon could be developed when the data obtained is not classified. The investigators will not do anything in this project of a classified nature.


Eugene E. Saenger, M.D.
12/6/71

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