December 6, 1971, 3:00 p.m.

MEETING WITH MR. MOTTER, STAFF OF SENATOR EDWARD KENNEDY
DR. CAPER, STAFF OF HEALTH, EDUCATION AND WELFARE

Dr. Eugene Saenger and I met with Mr. Motter and Dr. Caper for approximately two hours this afternoon, this being dictated ten minutes after taking leave of them.

There were several issues discussed among us.

I detailed the selection procedure whereby a patient is identified as having metastatic carcinoma before I speak to him. I deal first with the patient's psychological difficulties on learning that he has carcinoma. I quoted to Mr. Motter and Dr. Caper approximately what I tell each patient in terms of what we plan to do in our study, that it is not curative but it will reduce the number of tumor cells by approximately 70% (based upon dose response curves of mammalian cells), and that there was indeed reason for some hope. The patient is told that there is a significant chance that pain may be relieved and/or tumor size decreased, that we have had a large experience extending over 11 years with this form of therapy. The patient is further told that a psychologist would speak to him and help him with his feelings as well as testing radiation effects and that several blood and urine tests would be performed to measure the effects of radiation. It was emphasized that the patient is told several times that the tests to be obtained were to provide data on the effects of radiation and might be of value both in a general scientific way as well as to other human beings who might be irradiated by nuclear power reactors or in the course of warfare where large numbers of the civilian population as well as soldiers might be jeopardized. I further stated that until the last three patients with whom I have spoken I have not mentioned that the Defense Department was funding the research, but when I did so, two of the patients nodded and indicated that this distressed them in no way, while the third said "I'd do anything to help our boys!"

The process of informed consent was discussed where the individual is told in detail about the project and asked not to acquiesce at that time but to return a day later, with a relative if at all possible, where the entire project is again reviewed. At that time the consent form is signed. Mr. Motter and Dr. Caper indicated that they had seen our consent forms which have evolved over the past six years.

There was further discussion about the question of informed consent

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as to whether the patients did indeed understand what they had been told. I indicated that in a recent study (Lasagna, Archives of Internal Medicine 23: 682-688, June, 1969) ~~that~~ the more complete the research form detailing informed consent was, the lower the comprehension proved to be and that the greatest degree of comprehension in the study was less than 7 in 10. I noted that there are other studies indicating that the average patient retains something significantly less than 100% of what his doctor tells him concerning instructions on medications when he leaves the physician's office. On the basis of these data I suggested that no matter how many of our patients Mr. Motter and Dr. Caper might interview, they would find some who had not recalled everything on the informed consent form, since the individuals whom they would interview have not seen our consent form for periods of six months to three years. Hence, the value of their recall or lack thereof is highly questionable. For this reason I felt there were significant questions in my mind as to the value or purpose of Mr. Motter and Dr. Caper talking to our patients. These two individuals indicated that perhaps they could go anonymously or have another agent do the questioning of the patients so that the patients would not feel that they were being quizzed for testimony-gathering of a Senate subcommittee. We made it perfectly clear to Mr. Motter and Dr. Caper that this was acting wihtout informed consent of our patients and would be intolerable. I was impressed by the unwillingness of Mr. Motter to question patients if they knew exactly who he was and why he was asking these questions.

Dr. Caper raised the issue of controls and was given the statement of the International Union against Cancer which appears in the 1971 Archives of Surgery describing what phase I, II and III trials are. We made it clear that our study was in phase II and that we were attempting to compare our data to those of other studies to obtain significant values for our patient survival data (p values), but that data for this are lacking in the studies already in the literature. We emphasized that a phase II study strictly obviated the use of control subjects. In regard to a question as to whether a collaborative study might have been done in the past, I noted that our protocol was quite detailed, requiring the activities of a team of researchers: health physicists, cytologic technicians biochemists, psychiatrists and psychologists, plus internist and radiotherapist and that in order to provide similar care in other institutions all of our testing procedures would have to be followed if the results were to be truly comparable. Funding for this is clearly not available at this stage. However, a prospective study comparing whole or partial body radiation with chemotherapy involving multiple medical centers should be feasible if there is N.I.H. funding.

We indicated that over half of our patients had experienced either relief of pain or shrinkage of tumor, and that our survival data were as good as or better than chemotherapy and always better than

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untreated controls. However, our individual groups of patients are as yet too small to provide adequate confidence limits for publication. I emphasized that we had not published our data because it was not yet scientifically solid enough to do so. I noted that the Washington Post had tried to raise a false issue by reporting that we had not yet published on the therapeutic efficacy of the treatment. Dr. Caper raised the question as to whether the issue would have arisen had the Defense Department not been the primary source of funds and we agreed, I felt, that it would not. In subsequent conversation in Dr. Edward Gall's presence, as Dr. Caper and Mr. Motter were leaving, I noted that the role of the Defense Department in funding any sort of biological research to be the real issue. It seemed to be a political issue here rather than our study on therapy with its offshoots on the radiation effects on human beings. Dr. Caper agreed.

I was asked how I became interested in this sort of research and indicated that my background in hematology had included psychiatric training in dealing with dying patients, and that I felt that this project provided an outlet for what I had learned in supporting these individuals psychologically while attempting to treat them, and that what talents I had in this area would be best used here.

We were asked why a phase II study should last so long and indicated that when there are only 7 patients per year out of 500 cancer patients seen at the General Hospital (in any given year) who qualify, that it takes a number of years before one can accumulate enough patient data for an adequate phase II study. We have done statistical analysis to suggest that we need between 75 and 150 patients in order to obtain adequately narrow confidence limits.

I briefly detailed the history of whole body radiation, that it had been used since 1924, and cited numerous references up to the present decade on its use on both solid tumors and lymphoma-leukemia, and that in none of these studies have there been adequate controls for comparison.

It was emphasized in discussing informed consent again that any patient showing signs of disorientation is dropped from the study for fear that he would not understand what we were doing.

We also indicated that our reports on these patients have been submitted to the National Institutes of Health, through the Clinical Research Centers of both the Children's Hospital and Cincinnati General since 1968, so that this agency has also been aware of our work.

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I also discussed the response of our patients to the publicity recently given the study by the Washington Post, and that many of the living patients came forward immediately to offer support. In two families one of the parents was upset that the child might have been used as a "guinea pig" until the other parent made him realize that the issue had become a political football. Both of the families have indicated their verbal support of our therapeutic research.

I cited one example where a patient had refused to undergo the therapeutic irradiation because of her fear that she would never leave the hospital if she ever entered it. I detailed my working with her over her fears and referring her to our Central Psychiatric Clinic.

As the issue of the appropriateness of Defense Department funding rose again I gave both gentlemen a copy of an editorial in the October issue of Nature indicating that the issue of Defense Department funding was irrelevant.

We discussed the radiobiologic basis of our therapy, employing mammalian survival dose-response curves to illustrate my comments. I also noted that after one reduces the mass of a tumor to a certain level, the patient's immunologic system against cancer, which may have become paralyzed by a large amount of tumor antigen, may then be able to cope with the tumor again. I emphasized that these were theoretical considerations with adequate animal experimentation to back them up.

In summary, Mr. Motter and Dr. Caper indicated that they had no reason to doubt our integrity, the quality of our studies or their supervision by other University committees after talking to us. If this were so, Dr. Saenger then asked, why has this study been singled out to inquire about informed consent and medical ethics? Such experiments in therapeutics of humans are going on in Washington. We therefore indicated that we felt that medical ethics was not at all the issue here, that we had given them ample data to resolve this question. We did agree that there were many questions arising from the data that Mr. Motter and Dr. Caper had seen in the Washington Post which required an answer and that we felt we had done so. The real issue is apparently whether the Defense Department should be funding biomedical research, one which, as noted above, Dr. Caper agreed.

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