November 2, 1971

ANSWERS TO SENATOR GRAVEL'S QUESTIONS

1) Subject: Trickery

Is there any trickery of the patient involved?

a) Do the patients really understand that the experiment is largely to help the DOD prepare for nuclear warfare?

The purpose of this investigation has been to improve the radiation treatment of the patient with advanced cancer and to improve as well his general clinical management. All other considerations were secondary to this goal.

1) b) Do you consider the release the patients signed to be sufficient evidence that they understand?

From the beginning of the study all patients gave informed consent in conformity with national practices. Our method has been to discuss the program with the patients and one or more members of his family unless there are no relatives or they are not available. We then repeat this explanation a day later before asking for the written consent of the patient. The patients have not been specifically advised that financial support originated by the Department of Defense since in no other projects with which we are familiar is it considered necessary to inform the patient that research is funded by any agency of Federal or local government, by foundations, by the institution itself or by particular individuals. The nature and specific details of informed consent are reviewed by the Research Committee of the College of Medicine. The internist in charge of these patients has informed each patient verbally that data obtained from their individual studies may be of help to soldiers as well as to the civilian population in the event of a nuclear catastrophe.

The current forms have been in use since the Summer of 1971 when revised at the suggestion of the Human Research Committee to improve patient understanding of the problem.

The entire program is under continual review by the Research Committee of the College of Medicine University of Cincinnati. No patient has been treated without this approval. The treatment plan for the three children has also been approved by the Research Committee of Children's Hospital. Since some of the patients have been cared for in the General Clinical Research Centers of both the Cincinnati General Hospital and Children's Hospital Medical Center, the National Institues of Health receive reports of such indiciduals and thus have knowledge of the project.

1) c) Do the patients understand that the experiment may cause severe discomfort, such as hours of vomiting?

Very few medical treatments are without some discomfort, e.g., dental extraction. The analysis of our 82 treated patients shows that 45% experienced no symptoms at all, that 24% had transient nausea and vomiting within 3 hours, 13% within 6 hours and 4% within 12 hours. Thus in 86% (71 patients) these symptoms had stopped within 12 hours. In only 3 patients (4%) were the nausea and vomiting of a severe nature. (See attached Table)

INCIDENCE OF NAUSEA AND VOMITING IN 82 CANCER PATIENTS RECEIVING WHOLE AND/OR PARTIAL BODY COBALT-60 RADIATION THERAPY
April, 1960 thru December, 1970

	Patients	Percent
No Nausea nor Vomiting	37	45
Nausea and/or Vomiting up to 3 hours after R_x	20	24
Nausea and/or Vomiting up to 6 hours after R_x	11	13
Nausea and/or Vomiting up to 12 hours after R_x	3	4
Nausea and/or Vomiting up to 24 hours after R_x	7	9
Nausea and/or Vomiting up to 48 hours after R_x	0	-
Nausea and/or Vomiting 48 hours +	4	5
	82	100

1) d) Do the patients understand that partial or whole body irradiation may shorten their lives, and if so, by how much?

We have no evidence that this type of radiation at these single doses causes life shortening.

The possible hazards are set forth in the consent forms (attached) and these are discussed on at least two occasions with the patient and also with the patient's family whenever they are available.

1) e) Do the patients understand whether or not there exists any basis for suggesting the treatment may reduce the size of their tumor or reduce their pain as suggested in the Washington Post on October 8?

The basis for suggesting that these forms of treatment shrink tumors or reduce pain or delay growth of metastases have been drawn from careful clinical observations on these patients since therapy has been helpful in some but not all cases. In this regard our experience is quite comparable to that found in chemotherapy and localized radiation therapy. Descriptions of some of these responses are documented in the case histories of the 82 irradiated patients listed in the DASA technical reports (see list in appendix).

2. Subject: Animal data

Don't experimental animal trials, as a rule, precede human experimental trils in the testing of a new medical therapy mode? What animal trials using partial or whole body irradiation to treat cancer were completed before Dr. Saenger bagan his human experimentation. What were the results of the animal trials, and did Dr. Saenger begin his special therapy before or after DOD support?

The experimental animal data on which these studies were based stem from a series of reports of Hollcroft, Lorenz and Matthews of the National Cancer Institute, National Institutes of Health (1,2). In these studies the authors demonstrated better tumor regression with whole body radiation followed by localized radiation both for lymphoma and carcinoma in mice. ~~Subsequent studies by Michaelson and his co-workers ( ) demonstrated the marked increase in tolerance to partial body radiation as compared to total body radiation. This work was an extension of~~ the studies of Jacobson et al. (3) showing the importance of spleen shielding in preventing high dose radiation lethality in the mouse. Subsequently, Jacobson, et al. (4) showed a similar protective effect by shielding of the other parts of the body,hind leg, head, liver and intestine.

Meanwhile Collins and Loeffler (?) demonstrated an equivalence in the response of tumors of various types when the effect of total body radiation was compared to systemic cancer therapy given with nitrogen mustard and similar compounds. Since many of the anticancer chemotherapeutic agents seemed to have no better end results in far advanced cancer, it seemed reasonable to evaluate this method of therapy.

A number of earlier studies have been reported. Miller, Fletcher and Gerstner (5) reported on certain systemic and clinical effects in 263 cancer patients given whole body irradiation in doses of 15 to 200 r. They state "Critical evaluation of the procedures as a therapeutic tool was excluded from the report...." Other brief reports were those of Jacobs and Marasso (6) in 40 patients and of King (7) in 11 patients suggested that useful palliation had been achieved. From these reports and considering the clinical extent of disease in our patients the investigation of the further use of whole and partial body radiation was thought to be desirable.

REFERENCES

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~~3. Michaelson~~

4. Jacobson, L.O., Marlas, E. K., Robson, M.J., Gaston, E., and Zerkle, R.E. Effect of Spleen Protection on Mortality following X-irradiation. J. Lab. Clin. Med. 34: 1538-1543, 1949.

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8. King, R. E. Use of Total Body Radiation in the Treatment of Far Advanced Malignancies. JAMA 177: 610-613, 1961.

9. Loeffler, R.K., Collins, V.P. Hyman, G.A. Comparative Effects of Total Body Radiation, Nitrogen Mustard, and Triethylene Melamine on the Hematopoietic System of Terminal Cancer Patients. Science 118: 161-163, 1953.

3. Subject: Follow-up

How does Dr. Saenger follow-up his own patients to find out if his treatemtn has been helpful or harmful? Does he measure the tumors he hopes to reduce, for instance?

Followup on all our patients is assured in several ways. All patients are given the home telephone number of the internist caring for them, so that he is available for emergencies day or night and has either made house calls on many of the patients or personally transported them to the hospital.

Each patient is seen at least monthly in the Tumor Clinic of the Cincinnati General Hospital and frequently will come to the office of the program internist as well if he was unable to attend Tumor Clinic. Copies of all Tumor Clinic reports are sent to the program internist.

Patients are also seen at home at their convenience by the psychologist of the program who provides considerable emotional support. She is also on call for the patients at her office.

The followup procedure is continuous during the lifetime of the patient.

4. Subject: 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?

5) Subject: 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 for paying patients. Does he know any doctor who does?

I would appreciate an intermim reply to these inquiries.

Dr. Saenger is an academic full time physician at the College of Medicine. As such he engages in limited consultation and treatment but not retaining private fees for patient services.

The whole and partial body radiation procedures as used here remain investigative. Some private patients have been treated.

Whole body radiation for lymphoma, Hodgkin's disease, leukemia, polycythemia vera, cancer of breast, cancer of thyroid, cancer of prostate and multiple myeloma are used by physicians. Such therapy may be given by external radiation therapy (as in this particular study) or in the form of radioactive isotopes.