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TOLERANCE TO WHOLE-BODY IRRADIATION OF PATIENTS WITH ADVANCED CANCER

by

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TOLERANCE TO WHOLE-BODY IRRADIATION OF PATIENTS WITH ADVANCED CANCER

By Lloyd F. Craver, M. D.

PROJECT

To determine the effects, clinical and hematological, on human beings subjected to prolonged daily repeated exposure of the entire body to filtered high voltage X rays in the Heublein Unit for total-body irradiation.

FACTORS

The Heublein Unit delivers X rays generated at 180 to 185 kv, filtered through 1.10 mm Cu + 1.05 mm Fe or 1.65 mm Cu + 2.07 mm Fe in one room, and 1.10 mm Cu + 0.75 mm Fe or 1.65 mm Cu + 1.78 mm Fe in the other room. In either room the thicker filter provides 0.85 r/hr, while the thinner filter provides 1.65 r/hr. The average target-body distance is about 300 cm.

It was requested that first some patients be treated with a dose of 10 r/day for 30 days, then some at 15 r/day for 20 days, then, if possible, some at 20 r/day for 15 days. This total dose of 300 r was arbitrarily selected on the basis of previous experience 1931 to 1933 and 1935 to 1942 with the Heublein unit. On the basis of that experience it was believed that 300 r could be tolerated in one course of treatment over a period of 10 to 30 days by individuals in good general condition, and should be a sufficient dose to yield some detectable effects on the blood count, and to serve as a guide to the clinical tolerance for whole-body irradiation.

SELECTION OF PATIENTS

This was the most difficult part of the project, calling for the selection of patients having meta-static cancer of such extent and distribution as to render their cases totally unsuitable for any accepted method of surgical or radiological treatment, yet in good enough general condition so that they might be expected not only to tolerate the exposure to 300 r of total-body irradiation in a period of 10 to 30 days, but to survive the combined effects of their disease and the irradiation for at least 6 months, in order that some conclusions might be drawn as to the later effects of the irradiation.

It was recognized that none of the lymphomas or leukemias would be suitable for this project, because of the sensitivity of the hematopoietic system in such cases both to irradiation and to various disorders incidental to the disease. Thus it was necessary to confine the selection to metastatic carcinomas, and metastatic sarcomas other than of the lymphoid system.

It was recognized, moreover, that in such advanced cases the further progress of the malignant neoplastic process, if indeed it did not cause the death of the patient sooner than 6 months after whole-body irradiation, would in any case be very likely to confuse the interpretation of the clinical and hematological effects of irradiation by reason either of changes in the patients' nutrition or other alterations attributable to the disease. However, it could be argued that if it could be shown that no definite or marked harm resulted in patients as sick as those to be chosen, it could certainly be concluded that healthy persons should be able to tolerate the projected dose of irradiation.

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The hope that, despite the negative results obtained in radioresistant metastatic cancer by use of doses up to 450 r in the Heublein Unit in 1931, there might, on further trial, nevertheless be found some beneficial clinical effect, offered justification for undertaking the project, aside from the primary purpose.

METHOD

Carefully selected patients were admitted to the Heublein Unit, where they received the prescribed daily dose of whole-body irradiation day after day without interruption. During the treatment a complete blood count, including a differential and platelet count, was made every 2 to 4 days. Upon completion of the treatment the patients were, as a rule, able to go home at once and were then seen at intervals of 1 to 4 weeks for clinical examination and blood counts, for as long as possible following the treatment.

MATERIAL

Patients treated between December 18, 1942, and August 29, 1944, are summarized in Table 1.

Table 1.

Case No.	Patient	Sex	Age	Diagnosis	Dose r/day	Total dose in r	End result
1	[REDACTED]	M	[REDACTED]	Melanoma	10	300	Died at home 31 days after treatment from progress of disease.
2	[REDACTED]	M	[REDACTED]	Teratoma testis, Metastasis to lungs	10	150	Died in hospital 71 days after treatment from progress of disease.
3	[REDACTED]	M	[REDACTED]	Melanoma	10	181	Died at home 49 days after treatment from progress of disease.
4	[REDACTED]	F	[REDACTED]	Carcinoma of breast	10	300	Last seen 4 months 4 days after treatment. Probably died soon afterward.
5	[REDACTED]	M	[REDACTED]	Carcinoma of male breast	10	300	Living 18 months after treatment, but had orchiectomy 1 year after treatment.
6	[REDACTED]	M	[REDACTED]	Pulmonary metastases of mucoepidermoid carcinoma of parotid	10	300	Living 19 months after treatment. Bedridden from 8 months after treatment until about 17 months after treatment. Then gained 25 pounds and became ambulant.
7	[REDACTED]	M	[REDACTED]	Metastatic adenocarcinoma, primary undetermined	15	300	Followed 4 1/2 months after treatment. Was then in a terminal institution.
8	[REDACTED]	M	[REDACTED]	Metastatic adenocarcinoma (primary in sigmoid?)	15	300	Last seen 7 1/4 months after treatment. Going to a terminal institution. Extensive liver metastases when last seen.

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DISCUSSION OF FOLLOW-UP

It was possible to see and obtain blood counts for a period longer than 6 months after treatment in only 3 of the 8 cases. Two patients (cases 2 and 3) were in such poor condition that it was necessary to discontinue the treatment when about half the projected dose had been administered, and they died 71 and 49 days, respectively, after treatment was stopped, apparently because of progress of the disease, and not as an effect of the irradiation. In case 1 the patient died at home one month after completing exposure to 300 r, but likewise apparently from progress of the disease. In these three known to have died, unfortunately, permission for necropsy was not obtained. In cases 4 and 7 the duration of survival is unknown, the patients having been last observed a little more than 4 months after completing 300 r (at 10 r/day in case 4, and at 15 r/day in case 7), but in each of these 2 cases the disease was rapidly becoming more advanced and there was no evidence that the downward course was due to any other factor than advance of cancer.

Of the 3 cases that were followed for more than 6 months (cases 5, 6, and 8), in case 8 the patient was failing rapidly, with extensive liver metastases when last observed, 7 1/4 months after treatment. In case 5 the widespread male breast carcinoma had been growing slowly but steadily for a year following total-body irradiation with 300 r at 10 r/day, and it was then decided for the sake of possible palliation to try orchiectomy, which has seemed on further observation for an additional 6 months to have had some slight palliative effect. In case 6, the patient has been followed for 19 months. From about 8 months to 17 months after treatment he was bedridden from progress of the disease and was considered terminally ill, escaping follow up for a period of 11 months, but in the last 2 months has become ambulant again, goes about alone and has gained 25 pounds. This improvement has occurred despite roentgen evidence of considerable increase in the bulk of numerous large pulmonary metastases of muco-epidermoid carcinoma of the parotid. It seems doubtful that the irradiation of the entire body, 300 r at 10 r/day given 19 months previously could in any way be responsible for this improvement, and per contram, it is a matter for speculation as to whether his bedridden state, occurring for 8 months following the irradiation and causing him to be unable to return for 11 months, was a late effect of the irradiation, an effect from which he has been recovering. The only other patient followed for a comparable time was the patient with male breast carcinoma followed for 18 months, who has continued at work and who may have benefitted somewhat from an orchiectomy done 1 year after total-body irradiation. He suffered no such bedridden period, although a man of 84 years of age, while the man who became temporarily bedridden was only 33 years old. On this slim basis it might be surmised that the 11-month period of disability in case 6 was not caused by the effects of radiation. Unfortunately no blood counts were obtained in case 6 while the patient was confined to his home.

HEMATOLOGICAL OBSERVATIONS

Case 1. [REDACTED]

Diagnosis: Melanoma of skin of neck, with widespread cutaneous and subcutaneous metastases. Only previous irradiation 11 X ray treatments to neck 8 months before Heublein therapy.

Between December 15, 1942 and January 14, 1943, received 300 r at rate of 10 r/day, of Heublein treatment.

During treatment no consistent changes were found in his blood count, although rather wide inconsistent variations were recorded. Following treatment there was recorded, after 8 days, a drop in total white cells to 8,000 from a previous range of from 8,000 to 14,800, and a drop in platelets to 138,000 from a previous range of from 142,000 to 344,000.

In the two subsequent counts, made 12 and 19 days following completion of treatment, the white cells dropped further, to 3,900 and 3,200; the red cell count dropped to 3.51 million on the 19th day, the hemoglobin to 68 per cent, and the platelets to 77,000.

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