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INDUSTRIAL MEDICINE ON THE PLUTONIUM PROJECT

Survey and Collected Papers

Edited by

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John E. Wirth, M.D. (Clinton), and James J. Nickson, M.D. (Chicago). Health Physics was developed under the supervision of Herbert M. Parker (Chicago, Clinton, Hanford), Ernest O. Wollan (Chicago), Karl Z. Morgan (Clinton), and John E. Rose (Chicago). Research in radiobiology was directed by Kenneth S. Cole (Chicago), Joseph G. Hamilton, M.D. (California), Howard J. Curtis (Clinton), and Egon Lorenz (National Cancer Institute). The investigations in uranium toxicolog were carried out at Michael Reese Hospital, Chicago, under the direction of Albert Tannenbaum, M.D., as part of the program of th Metallurgical Laboratory.

Practically all the work described in the Health Volumes was don between Sept. 1, 1942, and June 30, 1945. It was subject to the usua disadvantages of wartime research and development—chiefly hast and security regulations. On the other hand, it proceeded under ver advantageous financial support. Moreover, the security regulatio often had the advantageous effect of preventing publication of resear until experiments had been verified by collateral work.

Most of the writing was necessarily done rather hastily because, the early postwar period, many of the authors were returning to the regular positions in universities and elsewhere. Editing has be done in more leisurely fashion but with a severe shortage of comp tent manpower. With unlimited editorial personnel, much of the m terial could have been substantially shortened. Since this seem impracticable, most of the editorial effort has gone into the correcti of major errors and inconsistencies. We hope that not too many these have eluded us.

Raymond E. Zirkle
Editor, Health Volume

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GENERAL INTRODUCTION TO REPORTS ON MEDICINE, HEALTH PHYSICS, AND BIOLOGY*

By R. S. Stone
Formerly Associate Project Director for Health

From its inception, the Atomic Energy Project consisted of several individual projects; each had its own objectives, its own organization, and its own laboratories for research and development. A healthy rivalry existed among them; each hoped to be the first to reach its objectives. Their efforts were coordinated in the beginning by the Office of Scientific Research and Development and in the later stages by the Manhattan District of the U. S. Army Corps of Engineers. The group assigned to the problems of proving that a nuclear chain reaction could be achieved, of making a structure using this reaction to produce plutonium, and of developing a chemical process for isolating pure plutonium was established at the University of Chicago. For this purpose that university formed the Metallurgical Laboratory under the able leadership of Prof. Arthur H. Compton.

Early in 1942 the scientists of the Metallurgical Laboratory became convinced that a nuclear chain-reacting pile could be built. They realized the enormity of the health hazards that such a unit would create. Some of them had friends or acquaintances who had been injured in experimental work with x-rays or with radium, and many were aware of the harmful effects suffered by some of the workers in the radium-dial industry.

The exact nature and extent of the hazards to be encountered were not known. In general it was realized that the pile in which the chain reaction would take place would be a far greater source of fast and slow neutrons and gamma rays than could have been dreamed possible in earlier periods. It was estimated that the pieces of uranium that would have to be removed from the pile after fission had occurred

*Based on Univ. of Calif. Report NDP-48c.

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Paper 10

TOLERANCE TO WHOLE-BODY IRRADIATION OF PATIENTS WITH ADVANCED CANCER*

By L. F. Craver

1. PURPOSE

he purpose of this investigation was to determine the clinical and atological effects upon human beings of daily repeated exposure e entire body to filtered high-voltage x-rays in the Heublein unit otal-body irradiation.

2. FACTORS

e Heublein unit delivers x-rays generated at 180 to 185 kv, fil- through 1.10 mm Cu + 1.05 mm Fe or 1.65 mm Cu + 2.07 mm one room, and 1.10 mm Cu + 0.75 mm Fe or 1.65 mm Cu + 1.78 Fe in the other room. In either room the thicker filter provides per hour while the thinner filter provides 1.65 r per hour. The ge target-to-body distance is about 300 cm.

vas requested that first some patients be treated with a dose of per day for 30 days, then some at 15 r per day for 20 days, then, sible, some at 20 r per day for 15 days. This total dose of 300 r rbitrarily selected on the basis of previous experience, from to 1933 and from 1935 to 1942, with the Heublein unit. On the of that experience it was believed that 300 r could be tolerated course of treatment over a period of 10 to 30 days by individ- good general condition and that it should be a sufficient dose ld some detectable effects on the blood count and to serve as a to the clinical tolerance for whole-body irradiation.

d on Metallurgical Laboratory Report CH-3369.

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3. SELECTION OF PATIENTS

This was the most difficult part of the project, calling for the selection of patients having metastatic cancer of such extent and distribution as to render their cases totally unsuitable for any accepted method of surgical or radiological treatment, yet demanding that the patients be 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 also to survive the combined effects of their disease and the irradiation for at least six months in order that some conclusions might be drawn as to the later effects of the irradiation.

It was recognized that none of the patients with 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 subjects with 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 six 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 patient's nutrition or other alterations attributable to the disease. However, it could be argued that if it were possible to show 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.

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

4. 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

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om one to four weeks for clinical examination and blood counts for long as possible following the treatment.

5. MATERIAL

Histories of patients treated between Dec. 18, 1942, and Aug. 29, 14, are summarized in Tables 10.1 to 10.9.

6. DISCUSSION OF FOLLOW-UP

It was possible to see and obtain blood counts for a period longer n six months after treatment in only three of the eight cases. Two ients (cases 2 and 3) were in such poor condition that it was nec- ary to discontinue the treatment when about half the projected dose been administered, and they died 71 and 49 days, respectively, er treatment was stopped, apparently because of progress of the ease and not as an effect of the irradiation. In case 1 the patient d at home one month after receiving the total exposure of 300 r, likewise apparently from progress of the disease. In the case of se three patients known to have died, permission for necropsy was, ortunately, not obtained. In cases 4 and 7 the duration of survival nknown, the patients having been observed for the last time a little e than four months after having been exposed to 300 r (at 10 r day in case 4, and at 15 r per day in case 7); but in each of these cases the disease was rapidly becoming more advanced, and there no evidence that the downward course was due to any other factor advance of cancer.

case 8, one of the three cases (cases 5, 6, and 8) that were fol- d for more than six months, the patient was failing rapidly, with nsive liver metastases when last observed, seven and a quarter ths after treatment. In case 5 the widespread male-breast carci- a had been growing slowly but steadily for a year following total- irradiation with 300 r at 10 r per day, and it was then decided the sake of possible palliation to try orchiectomy, which seemed urther observation for an additional six months to have had some t palliative effect. In case 6 the patient was followed nineteen hs. From about eight to seventeen months after treatment he bedridden from progress of the disease and was considered ter- ally ill, escaping follow-up for a period of eleven months; but in the next two months he became ambulant again, went about e, and gained 25 lb. This improvement occurred despite roentgen nce of considerable increase in the bulk of numerous large onary metastases of mucoepidermoid carcinoma of the parotid. emed doubtful that the irradiation of the entire body, with 300 r

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at 10 r per day given nineteen months previously, could have been responsible in any way for this improvement; and, per contram, it is a matter for speculation as to whether the patient's bedridden state, occurring for eight months following the irradiation and causing him

Table 10.1 — Patients Treated between Dec. 18, 1942, and Aug. 29, 1944

Case no.	Sex	Age	Diagnosis	r/day	Dose total, r	End result
1	M	31	Melanoma	10	300	Died at home, from progress of disease, 31 days after treatment
2	M	25	Teratoma testis, metastasis to lungs	10	150	Died in hospital, from progress of disease, 71 days after treatment
3	M	44	Melanoma	10	161	Died at home, from progress of disease, 49 days after treatment
4	F	52	Carcinoma of breast	10	300	Last seen 4 months 4 days after treatment; probably died soon afterward
5	M	64	Carcinoma of male breast	10	300	Living 18 months after treatment, but had orchiectomy 1 year after treatment
6	M	33	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	M	46	Metastatic adenocarcinoma, primary undetermined	15	300	Followed 4½ months after treatment; was then in a terminal institution
8	M	51	Metastatic adenocarcinoma (primary in sigmoid?)	15	300	Last seen 7¼ months after treatment; going to a terminal institution; extensive liver metastases when last seen

to be unable to return for eleven months, was a late effect of the radiation, an effect from which he was recovering. The only other patient followed for a comparable time was the patient with [illegible] breast carcinoma followed for eighteen months, who continued at

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ıo may have benefited somewhat from an orchiectomy done one fter total-body irradiation. He suffered no such bedridden pe- ılthough a man sixty-four years of age; the man who became :arily bedridden was only thirty-three years old. On this slim 't might be surmised that the eleven-month period of disability : 6 was not caused by the effects of radiation. Unfortunately no ounts were obtained in case 6 while the patient was confined to ne.

Table 10.2—Case 1, Age 31, Melanoma

HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic	Hct
92	4.54	8.2	84			2	14		363	0.2	41
74	3.64	5.25	60				40		131		29
97	4.80	14.8	76	2		2	20				
100	4.85								252	1.0	50
75	3.71	7.8	74	1		3	22				
80	4.2	8.8	85			2	13		286		
78	3.81	11.6	75	2		5	18		258		
80	3.90	7.4	77	2		4	17		344		
79	3.94	8.0	76			1	23		189		27
80	3.94	9.8	85	1		2	12		142		
77	3.84	6.0	80			3	17		184		
80	4.04	7.1							178		
80	4.0	7.2	71			4	25		224		
94	4.93	5.0	80			1	19		138		
93	4.76	3.9	62			6	32		117		
68	3.51	3.2	58			5	37		77		
Died at home											

7. HEMATOLOGICAL OBSERVATIONS

Case 1, Male, Age Thirty-one Years. Diagnosis: Melanoma of neck, with widespread cutaneous and subcutaneous metas- Only previous irradiation was eleven x-ray treatments to neck ıonths before Heublein therapy.

een Dec. 15, 1942, and Jan. 4, 1943, patient received 300 r at 10 r per day of Heublein treatment.

ıg treatment no consistent changes were found in his blood although rather wide inconsistent variations were recorded. ing treatment there was recorded after 8 days a drop in total :ells to 5,000 from a previous range of from 6,000 to 14,800, drop in platelets to 138,000 from a previous range of from to 344,000.

two subsequent counts, made 12 and 19 days following com- of treatment, the white cells dropped further to 3,900 and

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3,200; the red cell count dropped to 3.51 million on the nineteenth day, the hemoglobin to 68 per cent, and the platelets to 77,000.

In view of the fact that the patient died of his disease only 26 days later it seems probable that these changes represented a terminal depression due to the disease, rather than a result of irradiation. In this case blood-chemistry determinations were made on serum bilirubin, serum total calcium, serum chlorides, serum cholesterol and

Table 10.3—Case 2, Age 25, Teratoma Testis, Metastasis to Lungs

Date	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic	Hct
12/21/42	79	4.14	7.05	85			7	8		199	0.4	37
12/22/42	79	4.02	6.3	81	1		2	16		193	1.2	35
12/24/42	78	3.81	9.2	83	2		2	13		168		
12/28/42	74	3.7	9.0	87			1	12		207		
12/31/42	75	3.7	15.0	89			1	10		223		
1/4/43	64	3.24	8.1	85				15		77.6		26
1/6/43	62	3.16	8.0	90	1		1	8		177		
1/9/43	60	3.14	7.2	91		1	1	7		188		
1/11/43	58	2.88	7.2	88	1		2	9		179		
1/26/43	52	2.60	6.2	97			2	1		156		
2/27/43	62	3.02	7.35	91			1	8		254		
3/11/43	57	2.97	6.1	95				5				
3/16/43	Died in hospital; no post-mortem											

cholesterol esters, alkaline phosphatase, serum inorganic phosphorus, serum protein, blood sugar, and blood urea nitrogen. No changes were found that seemed significant in relation to the radiation administered.

7.2 Case 2, Male, Age Twenty-five Years. Diagnosis: Teratoma testis, with metastasis to lungs. Only previous irradiation was an unknown amount administered five and six months previously, over the chest, at another hospital.

Between Dec. 21, 1942, and Jan. 14, 1943, patient received 10 r per day for 15 days of Heublein treatment. As he was beginning the sixteenth day of treatment it was obvious that his metastatic disease was progressing rapidly and he was becoming anemic. The red cell count had fallen from a pretreatment level of 4.14 million to 3.24 million, the hemoglobin had fallen from 79 to 64 per cent, and the platelets had dropped from 199,000 to 77,600. There was some doubt about the accuracy of the last platelet count, however, since it was so much out of line with one of 223,000 taken four days before and one of 177,000 taken two days later. Moreover, the platelet count during the following 23 days ranged from 156,000 to 254,000. In the

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.reatment period of 23 days after further anemia developed (red ; down to 2.6 million, hemoglobin to 52 per cent), and along with a ;ncy to a lower white cell count (to 6,200 from a previous range ›out 8,100 to 9,200) there developed a lymphopenia (lymphocytes 9 to 1 per cent, contrasted with a previous range of from 10 to :r cent).

.rther blood-count observations are believed valueless in this :, since the patient was turned back to the urology service because is unsuitability for continuation of Heublein treatment. He was

Table 10.4—Case 3, Age 44, Nonpigmented Melanoma

	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic	Hct
'43	75	3.85	18.6	70	7		3	20				
43	80	3.97	12.8	65	14		5	17				
43	65	3.23	12.4	78	7		1	14		229		
43	67	3.35	8.0	80	5		3	12		228		
/43	62	3.14	11.2	78	4		1	17		275		
/43	65	3.36	12.0	78	9	1	2	10		148		
/43	61	3.2	15.4	82	3		8	7		179		
/43	74	3.71	14.8	83	4		8	5		178		
/43	72	3.64	13.0	76	5		4	15		160		
43	67	3.57	16.1	80	2		2	16		144		
43	67	3.4	11.8	91	2			7		157		
43	63	3.18	10.2	79	1		5	15		153		
/43	61	3.14	15.4	75	3		1	21				
/43	63	3.14	19.0	75	7		4	14		163		
/43	61	3.07	14.0	88			1	11		135		
/43	61	3.14	21.2	70	8		6	16		173		
43	Died at home											

:n androgens for 20 days and soon afterward local x-ray therapy he chest. He died 71 days after Heublein treatment was discontin- . Necropsy was not permitted.

n this case, as in case 1, chemical determinations showed no sig- :cant variations.

.3 Case 3, Male, Age Forty-four Years. Diagnosis: Nonpig- nted melanoma (origin undetermined; bulky left axillary metasta- , subcutaneous and left mediastinal and pulmonary metastases). previous irradiation.

Between May 3 and May 20, 1943, patient received 10 r per day to a al of 161 r. Treatment was then discontinued because of progress 'he disease, indicated by fever, wheezing, and rapid growth of the ss in the left axilla. It was estimated then that the patient would survive more than one or two months longer. He was kept in the

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hospital until June 25, then was allowed to go home, and died at home July 8, 1943, 49 days after Heublein treatment was discontinued. Permission for necropsy was not obtained.

No consistent change in the blood count appeared to result from total-body irradiation in this case, except a moderate reduction in the platelet count. In the first week of treatment the platelets ranged from 228,000 to 275,000, whereas in the seven weeks of posttreatment

Table 10.5—Case 4, Age 52, Metastatic Breast Cancer

Date	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic
6/14/43	94	4.66	10.7	71			4	24		262	0.2
6/29/43	89	4.68	8.6	65	9			26			
7/3/43	81	4.29	6.2	74			4	23			
7/6/43	73	3.62	5.0	71	2		6	21			
7/8/43	74	3.66	6.2	84			2	14		319	0.8
7/13/43	80	4.13	8.6	68	2		3	27			
7/16/43	75	3.51	6.8								
7/20/43	91	4.47	8.7								
7/23/43	105	5.13	6.9	64	1			35		205.2	0.4
7/26/43	85	4.18	5.5	63		1		36			
7/28/43	87	4.29	5.4	81	2			17			
8/5/43	82	4.29	8.6	76	2		6	16		294	
8/26/43	71	3.4	4.0	63			4	30			
9/23/43	70	3.4	6.6	77			7	16			
10/25/43	87	4.43	11.8	76	1		2	19	2 myelocytes		
11/15/43	60	3.11	5.8								
12/1/43	58	2.94	3.2								
1/5/44	Believed to be in terminal home										

observation in the hospital the platelets ranged from 179,000 to 135,000.

Blood-chemistry determinations, as in case 1, made 2 days after treatment stopped, were compared with values for May 1, 2 days before treatment began, and showed no significant alterations.

7.4 Case 4, Female, Age Fifty-two Years. Diagnosis: Metastatic breast cancer (infiltrating duct carcinoma grade II+). Irradiation two years earlier, for recurrence of metastatic breast cancer, two months after left radical mastectomy, amounted to 1,750 r to each of three ports about the axilla, using 250 kv x-rays, and 1,500 r to each of two ports on the chest wall, using 100 kv x-rays. Patient's general condition was good, and her blood count was normal when she was selected for Heublein treatment.

Between June 28 and July 28, 1943, patient received 10 r per day for 30 days. No consistent change in the blood count was found during the treatment. In counts made one and two months after treatment

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there was a diminution in hemoglobin and red cells (values of 71 and 70 per cent hemoglobin, compared with a range of 73 to 105 per cent; and 3.4 million RBC, compared with a range of 3.5 to 5.13 million). One month after treatment the white cells numbered 4,000, compared

Table 10.6—Case 5, Age 64, Carcinoma of Male Breast, Bilateral

Date	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic
1/11/44	80	4.1	8.0	73	2		11	14		169	
1/14/44	85	4.2	6.8	72			2	25		136	
1/18/44	76	3.7	5.8	73	4		8	15		105	
1/22/44	81	4.1	8.8	76	1		8	15		134	
1/25/44	88	4.3	9.0	68	1	1	13	16		140	
1/28/44	90	4.4	5.8	75		1	7	17		125	
2/1/44	87	4.3	4.0	70	1		3	26		157	
2/5/44	88	4.4	7.2	72	5		13	10		123	
2/8/44	89	4.4	7.8	67	1	1	10	19		105	
2/18/44	88	4.4	5.1	68			8	23	Hematocrit 27.8	106	0.2
2/25/44	75	3.4	3.1	52	1		11	37		120	
3/3/44	89	4.5	2.7							145	
3/10/44	88	4.2	5.0	69			5	26		140	
3/17/44	84	4.2	6.3	62		2	6	30		134	
3/31/44	81	4.1	6.8	73	1		9	17		131	
4/14/44	83	4.3	9.1	74	2		8	16		208	
5/5/44	81	4.0	8.0	78	2		4	16		192	
5/26/44	78	3.7	6.9	62			6	32		Few	
6/22/44	80	3.9	8.4	68			4	28		114	
8/9/44	92	4.4	7.9	50			4	46		Normal	
9/22/44	63	3.1	14.8	66	2		2	30			
10/6/44	65	3.45	10.2								
10/20/44	65	3.3	8.0							217.6	
11/3/44	70	3.5	11.6	70			4	26			
11/17/44	76	3.7	7.9	67			3	31		Normal	
12/15/44	69	3.5	8.4	74				26		196	
1/12/45	58	2.5	10.2	58				42		156	
1/26/45	80	3.8	5.7	74			8	18		211.2	
2/8/45	Orchiectomy; case abandoned for further counts										
3/13/45	84	4.0	5.2	74	2		6	18		144	

with a previous range of from 5,000 to 10,700. However, in the second month the white cells had returned to 6,600. Three months after Heublein treatment the patient presented an increase of subcutaneous metastases and was still in good general condition, so that it seemed best to refer her back to the breast service for palliative local x-ray therapy. Therefore blood counts made subsequent to Oct. 25, 1943, should be disregarded in judging the effect of whole-body irradiation.

This patient was lost to follow-up after Nov. 30, 1943.

7.5 Case 5, Male, Age Sixty-four Years. Diagnosis: Carcinoma of male breast, bilateral. No previous irradiation.

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Between Jan. 10 and Feb. 10, 1944, patient received 10 r per day for 30 days. The only notable change in the patient's count that seemed attributable to radiation was found in the 22 days following treatment when his white cell count, which had ranged during treatment from 4,000 to 8,800 with no consistent trend, was found on

Table 10.7—Case 6, Age 33, Pulmonary Metastases of Mucoepidermoid Carcinoma of Parotid

Date	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic
12/11/43	98	5.9	9.6	71	3		1	25		203	
1/20/44	88	4.4	8.8	64	6		6	24		281	
1/22/44	86	4.2	8.4	61	7		7	25		171	
1/25/44	93	4.4	6.4	66	3		10	21		150	
1/28/44	92	4.5	5.0	74	2		8	16		198	
2/1/44	95	4.5	6.8	65	1		13	20		162	
2/5/44	95	4.4	7.1	82	4	1	6	7		110	
2/8/44	90	4.5	9.8	79	2		11	8		144	
2/11/44	93	4.5	8.8	73	2		14	11		145	
2/15/44	90	4.4	5.4	66	2		9	22		124	
2/18/44	88	4.4	6.8							123	
2/25/44	90	4.4	5.3	73	1		7	19		168	
3/3/44	84	4.3	3.7	62	4		4	30		150	
3/10/44	87	4.3	4.7	47	1		13	39		104	
3/17/44	80	4.0	4.6	61			6	33		147	
3/24/44	78	3.7	4.3	65			5	30		121	
4/14/44	88	4.4	6.9	65	1		10	24		211	
5/5/44	84	4.4	9.2	70			5	25		246	
5/26/44	80	3.9	5.8	69	3		5	23		157	
6/23/44	89	4.5	5.8	67				25		152	
8/4/44	87	4.4	6.9	79			2	18	1 myelocyte		
9/15/44	Patient reported almost bedridden										
3/15/45	Reported bedridden										
8/14/45	76	4.1	7.4	71	3		1	25			

Feb. 18 and 25 and Mar. 3 to fall progressively to 5,100, 3,100 and 2,700. On Feb. 25 (15 days after treatment) the differential count showed only 52 per cent polynuclear cells, whereas it had previously ranged from 67 to 75 per cent. Later changes are believed attributable to the spread of cancer en cuirasse and debility accompanying development of bone metastases.

This patient was still ambulant on Aug. 13, 1945, eighteen months after completing Heublein treatment. However, blood counts for this project were discontinued one year after Heublein treatment because at that time the case was turned back to the breast service for orchiectomy in hopes of palliation of the advancing cancer.

7.6 Case 6, Male, Age Thirty-three Years. Diagnosis: Mucoepidermoid carcinoma of parotid, widespread bilateral pulmonary

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etastases. No previous irradiation in eight years. Between Jan. 19 d Feb. 18, 1944, received 10 r per day for 30 days.

No consistent change was noted in this patient's blood counts either ring treatment or in the seven months following treatment that he ıs able to return for examination. In five weeks following treatment

Table 10.8—Case 7, Age 46, Metastatic Adenocarcinoma in Lungs, Supraclavicular Nodes, Ribs, and Cervical Spine. Primary Unknown. Tip of Spleen Palpable

Date	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic
/13/43	100	4.8	7.4	76			1	23			
13/44	106	5.3	7.3	52			6	42		84.6	0.2
:1/44	80	4.2	6.4	74	5		6	15		146	
:4/44	83	4.2	11.2	63	3		7	28		201	
:6/44	80	4.2	16.2	80	6		6	8		184	
:8/44	82	4.2	9.6	90			2	8		172	
/44	84	4.3	10.2	81	2		4	13		172	
3/44	80	4.1	8.7	78	2		2	18		Normal	
5/44	81	4.0	8.1	86	2		2	10		Normal	
3/44	62	3.1	8.2	86			4	10		Normal	
10/44	83	4.2	7.2	88	2		3	7		105	
12/44	80	4.1	8.2	84	4		2	10		124	
22/44	78	3.8	6.8	92			2	6		121	
29/44	78	3.8	8.4	79			7	14		112	
12/44	70	3.6	5.4	56			10	34		101	
26/44	75	3.8	5.4	68			4	28		187	
14/44	11.7 g	4.42	8.4	76	2			20			
3/44	12.4 g	4.11	7.25	78			2	20			
14/44	Transfusion 500 ml RBC in corn syrup										
16/44	12.5 g	4.63									
26/44	11.4 g	4.35	Moderate splenomegaly								
10/45	As yet no further reports										

gained 10 lb. Not until nearly six months after treatment did it :come obvious that the patient was losing ground in his general ›ndition, although his blood count remained essentially unchanged. would appear most likely that the deterioration in his health at that me and his subsequent bedridden state, which lasted from the eighth the seventeenth month after treatment, as previously discussed, ıs caused by the disease rather than by the treatment, although it ust be admitted that this is a matter of opinion.

7.7 Case 7, Male, Age Forty-six Years. Diagnosis: Metastatic lenocarcinoma in lungs, supraclavicular nodes, ribs, and cervical ›ine; primary site undetermined. Previous irradiation: nine treat- ents to right side of neck and one to left axilla about three months reviously. Factors unknown. Between Apr. 24 and May 14, 1944, ceived 15 r per day for 20 days.

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Toward the end of the period of treatment and for six weeks afterward there was a trend toward a decreased level of hemoglobin, red cells, and white cells. However, considering the wide extent of the patient's metastatic cancer, it is quite possible and perhaps more probable that these blood changes were caused by the disease rather than by the treatment.

Table 10.9—Case 8, Age 51, Carcinoma (of Sigmoid ?) Metastatic Adenocarcinoma in Supraclavicular Nodes

Date	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic
7/3/44	90	4.48	8.0	68				32		215	
8/7/44	75	3.7	13.4	69			2	29		Normal	
8/9/44	80	4.0	10.0	66			4	30		128	
8/12/44	75	3.7	9.0	64			3	33		118	
8/14/44	80	4.0	10.8	72			6	22		Decreased	
8/16/44	74	3.6	8.2	70			4	26			
8/19/44	77	3.8	10.3	70			10	20			
8/21/44	80	4.1	7.6	84			8	8			
8/24/44	77	3.7	6.8	70			10	20		179	
8/26/44	80	4.0	9.4	80			6	14			
8/28/44	83	4.2	8.2	80			6	14		Decreased	
9/6/44	78	3.9	8.4	78			12	10			
9/20/44	70	3.5	3.4	78			16	6		94.8	
11/12/44	78	3.9	9.8	62	2		8	28		218	
12/15/44	67	3.9	11.6	81				19		131.8	
1/12/45	80	3.7	10.2	69				31		286	
1/26/45	85	4.0	7.0	70				30		96	
2/23/45	84	4.3	5.2	69			6	25		263	
4/6/45	69	3.4	9.0	83			3	14		109	

After six weeks following treatment the patient was not seen again at Memorial Hospital. He was admitted to a terminal institution on July 12, 1944.

7.8 Case 8, Male, Age Fifty-one Years. Diagnosis: Metastatic adenocarcinoma of supraclavicular nodes (primary in sigmoid?) No previous irradiation.

Between Aug. 8 and 29, 1944, received 15 r per day for 20 days. No consistent change was noted in blood counts during or following the treatment which might not be attributed either to the disease or to technical errors. (Rather wide variations were reported.)

The case was followed until Apr. 6, 1945, a little over seven months after treatment. At that time the patient was admitted to a terminal institution.

8. SUMMARY

1. Eight patients having advanced metastatic cancer were exposed to heavily filtered 180 kv x-rays in the Heublein unit at hourly inten-

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ties of 0.85 or 1.65 r and for daily doses of 10 or 15 r up to the ojected total dose of 300 r delivered in either 20 or 30 days.

2. The projected total dose, 300 r, was attained in six cases. In o cases (cases 2 and 3) in which the total desired dose was not at-ined, the treatment was discontinued at 150 and 161 r, respec-ely, because of progress of the disease; and the disease caused ath in 71 and 49 days, respectively, afterward.

3. The projected minimum of six months of follow-up examination, inical and hematological, subsequent to exposure to total-body ir-ıdiation was attained in three of the eight cases (cases 5, 6, and 8). ı cases 1, 4, and 7, although the total projected dose, 300 r, was lministered, the progress of the cancer caused the cases to be lost routine follow-up in from one to four months.

4. In no case did there occur any deterioration in the blood count at might not reasonably be ascribed to the progress or complica-ɔns of the malignant neoplasm.

5. In the three cases followed for longer than six months (seven ıd one-quarter to nineteen months) there was no deterioration in ɜneral health not reasonably attributable entirely to the progress of e disease.

6. In one case (case 6) followed for nineteen months, a remarkable nprovement took place in the seventeenth month after treatment. he improvement is not credited to the treatment.

7. In no instance was there observed any suggestion of stimulation ĩ growth of neoplasm by the whole-body exposure to radiation.

Data gathered from previous experience (1931 to 1933 and 1935 to 942) with administration of whole-body roentgen therapy, involving oses of from 5 to 450 r, agree essentially with the findings reported ı this paper, although in cases of lymphoma and leukemia unfavor-ble clinical and hematological results were observed in some in-tances.

9. CONCLUSIONS

In eight cases of advanced metastatic malignant neoplasm in human ɔeings, exposure of the entire body to 180 kv heavily filtered x-rays ıt an intensity of 10 r per day (0.85 r per hour) or 15 r per day (1.65 · per hour), for total doses of 150 and 161 r in two cases and 300 r .n six cases, was not followed by clinical or hematological effects ascribable to the radiation, either during or within a month after ces-sation of exposure.

In five cases followed for from four to nineteen months after expo-ɜure there was, likewise, no deterioration in blood count or clinical ɜtate that could not reasonably be ascribed entirely to the progress ɔf the neoplastic disease.

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It seems proper to conclude, therefore, on the basis of these few cases, that since individuals so seriously ill of cancer could withstand up to 300 r of total-body 180 kv heavily filtered roentgen exposure, administered in a period of from 20 to 30 days, with no appearance of subsequent ill effects other than those apparently caused by the progress of the disease, such doses of radiation should be well tolerated by healthy persons.

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