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A STUDY OF THE EFFECTS OF TOTAL AND PARTIAL BODY RADIATION ON IRON METABOLISM AND HEMATOPOIESIS

PROGRESS REPORT FOR PERIOD
1 September 1956 to 1 March 1957

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ABSTRACT

The hematopoietic response of patients treated by total body radiation during the management of inoperable cancer has been re-examined. The problem still is to recognize a predictable and quantitative relation between radiation exposure and biologic response. In previous reports attention has been given to:

1. Response of patients receiving total body radiation in single doses of 100r - 200r with conventional (250 Kv) therapy equipment.
2. Patients receiving total body radiation in doses well within tolerance (25r, 50r - 100r in divided doses) with the 2 m e v Van de Graaff unit using rotating or stationary fields.

The majority of patients in both groups received partial body radiation some time during the course of their disease. In all cases the hematopoietic response has been observed and, except for an occasional patient who failed to return, follow-up continued as long as the patients' condition permitted. In this report, the cases were selected from all those receiving total body and partial body radiation because their histories contained information pertinent to this analysis.

PROGRESS

In evaluating the hematopoietic response to total body radiation, the factors of general condition of the patient, diagnosis of cancer or other chronic disease, and the influence of other forms of therapy must be considered. While a "usual hematologic pattern" is anticipated following total body radiation, this has been difficult to define with any precision because of

inconstant description of data on dose, time, and biologic response. Hypothetically, a patient receiving a given exposure of total body radiation in a given time would show a predictable pattern of hematopoietic depression. Any variation from this pattern might be studied with a view to identifying other responsible factors.

It is not generally appreciated that dose and amount (of any agent, radiation or drugs) are not synonyms. Dose takes into account effect, and to keep this constant it may be necessary to alter amount. A constant amount may produce varied effect and therefore represents a different dose when differences between patients, and in the same patient from time to time, are taken into account. Dose cannot exist without measurement but neither can it exist without relating measurement to biological effect. An orally administered amount of a drug is diluted by intestinal content, absorbed across intestinal mucosa, further diluted in the blood stream, transferred across capillary walls and mixed with interstitial fluid throughout the body to act upon cell membrane or cytoplasm at some particular site. To this process of dilution is added the effect of utilization, destruction, storage and excretion; the actual amount of the drug producing the desired effect is almost beyond conjecture. Still, it is evident that some level of consistent relation exists between such gross measurement of an agent and biologic response because of the many examples of effective specific therapy.

Radiation, like drugs, produces its effect through chemical or biochemical reactions at the cellular level but prescription of amount of radiation is possible with an accuracy that is seldom attained with other forms of therapy. By direct measurements or standard practices of calculation, the intensity of radiation at any site, on the surface or within the living organism can be

determined. This precision is advantageously applied in partial body radiation where a desired clinical effect can be produced in the treated site with a useful degree of certainty.

In total body rediation, despite the advantage of precision in measured amount of radiation, we lack an early end point short of lethality. Malaise, drowsiness, nausea and vomiting are subject to the element of suggestion. Hematologic responses, cell counts, platelet counts, iron metabolism are sensitive but unstable indices. Biochemical leads stray beyond the limits of practical application.

The hematologic picture remains the most useful indicator since it is sensitive to radiation and is the biologic response most susceptible to measurement. The deficiency lies in the uncertainty of the quantitative relation between measured amount of radiation and degree of hematopoietic depression. There is a consistent and quantitative relation between partial body radiation and regression of tumor and normal tissue tolerance which accounts for the clinical usefulness of radiotherapy.

Our data on patients receivng partial body radiation is compared with that of patients receiving whole body radiation, seeking to identify a pattern that may prove useful in this over-all study.

Figure 1 shows the depression of white blood count when total body radiation is given to patients previously treated with partial body radiation.

Figure 2 shows the depression of white blood count when total body radiation is followed by partial body radiation in 30 days or less.

Figure 3 shows the depression of white blood count in patients receiving total body radiation only (doses 100r to 200r x 2).

No definite pattern is found to distinguish these three groups of patients except that there does seem to be accumulative effect for total body radiation and partial body radiation. The most prolonged depression of white blood count occurred in the group of patients receiving total body radiation followed by partial body radiation in 30 days or less. The range of depression within the three groups is similar. It is to be expected that for the small number of patients involved, the variety of diagnoses, the varying general condition, and the different ages, any consistent relation between radiation absorbed and hematologic response would be masked.

Figure 4. Depression of white blood count: comparison of six patients under 50 years of age and six patients over 50 years of age. In general, the depression of white blood count in the younger age group is slower and, although no less severe, all show recovery. Depression in the older age group is, in general, more rapid and recovery occurred in only three of six patients. Although this does not establish the importance of age, it does indicate that a quantitative effect of total body radiation upon the hematologic response will be influenced by other factors.

Figure 5. Depression of platelet count: patients receiving 200r total body radiation only and 200r total body radiation plus partial body radiation. The more abrupt the depression of platelet count, the more serious is its significance. The patients who recovered in both groups were those with slower rates of depression.

The validity of the observation is not certain but of the five patients showing recovery, four were under 50 years of age. All patients who failed to show recovery were over 50 except one, aged 48.

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FUTURE

1. Data on whole body radiation effects will be accumulated to increase the dependability of observations or conclusions. This includes single and repeated exposure under stationary and rotation conditions.

2. Separately or in combination, the effects of partial body radiation will be accumulated to establish that a constant relation may exist between radiation and hematologic response when similar conditions of exposure and similar patients are considered.

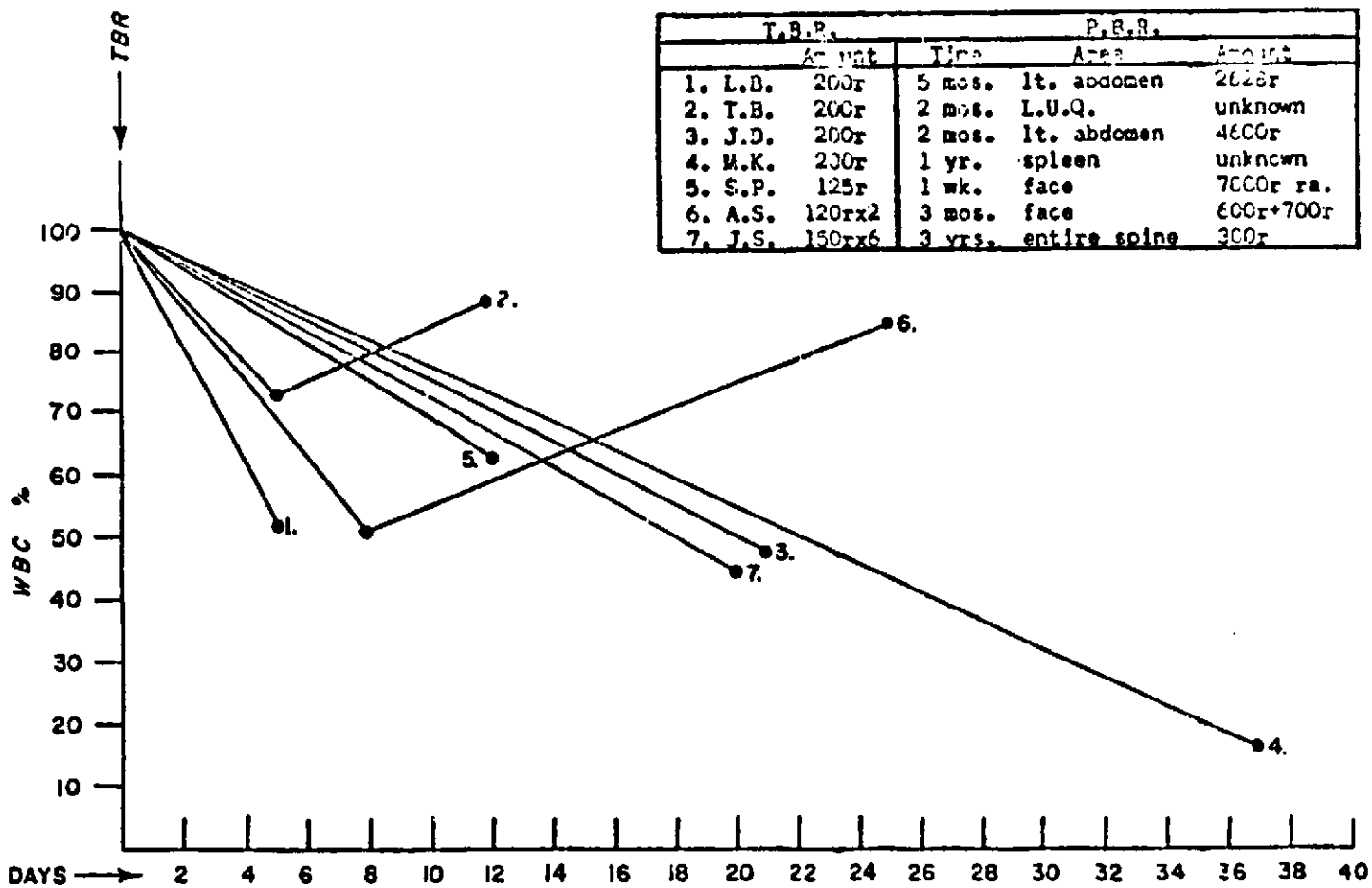
Further observations will be made on groups where age, general condition, diagnosis, and site and volume irradiated can be evaluated separately.

3. If a consistent relation can be established for controlled conditions of partial body radiation, and if differences can be identified between partial body radiation of different sites, for example between thorax, upper abdomen, and lower abdomen, two possibilities should be investigated.

a. For anatomical or geometric reasons, unequal amounts of radiation may be delivered to or absorbed in a critical area in individuals receiving similar total body exposure.

b. Selective shielding of a critical area may modify the response to total body radiation in a consistent and favorable direction.

Fig. 1. Depression of W.B.C. when Total Body Radiation is given to patients previously treated by partial body radiation.



	T.B.R.		P.R.R.	
	Amount	Time	Area	Amount
1. L.B.	200r	5 mos.	lt. abdomen	2028r
2. T.B.	200r	2 mos.	L.U.Q.	unknown
3. J.D.	200r	2 mos.	lt. abdomen	4600r
4. M.K.	200r	1 yr.	spleen	unknown
5. S.P.	125r	1 wk.	face	7000r ra.
6. A.S.	120rx2	3 mos.	face	600r+700r
7. J.S.	150rx6	3 yrs.	entire spine	300r

Table I. In this table a group of patients with a variety of lesions requiring partial body radiation to different parts of the body are compared. The white blood counts are compared in percentage depression and time to maximum depression. Correlation is attempted with total body volume and volume of tissue irradiated, with total body surface and surface area irradiated.

Although for clinical purposes a predictable effect upon tumor and tolerance obtains in these cases, a pattern of white blood count response is not clearly revealed in any of the attempted relationships.

Table II, Figure 6. This is a group of patients of similar age receiving comparable treatment by comparable technic to the thoracic region. When age, diagnosis, general condition, and area treated are similar, there is surprising uniformity in the relation between radiation exposure in terms of tumor dose and hematopoietic depression in terms of white blood count.

Recognition of a predictable and quantitative relation between whole body radiation exposure and biologic response would require uniform conditions of whole body radiation exposure in a group of individuals of uniform physical condition. The direction of future investigation should be to identify the factors which influence radiation effect and to evaluate their importance when conditions are not similar. Hypothetically, there is a predictable minimal lethal dose and the amount of radiation required would vary with physical conditions governing radiation exposure and biologic conditions modifying individual response. The direction of investigations should be to identify and describe these variables.

Re: A STUDY OF THE EFFECTS OF TOTAL AND PARTIAL BODY RADIATION ON IRON METABOLISM AND HEMATOPOIESIS

Progress report for period 1 September 1956 to 1 March 1957

In a copy of the above progress report mailed to you on March 8, 1957, page 5 was a duplicate of page 4. Please replace it with the correct page 5 which is here enclosed.

Fig. 2. Depression of White Blood Count when Total Body Radiation is Followed by Partial Body Radiation in 30 Days or Less

	T.B.R.	P.B.R.		
	Dose	Days	Area	Amount
1. C.B.	200r	9	Face	1410r
2. B.J.	200r	10	Spine	3[illegible]0r
3. J.C.	200r	13	Spine	675r
4. A.H.	200r	13	Shoulder	1200r
5. W.N.	200r	9	Spine	400r
6. J.R.	200r	30	Rt. abdomen	1800r
7. S.W.	200r	1[illegible]	Lt. ribs	1540r

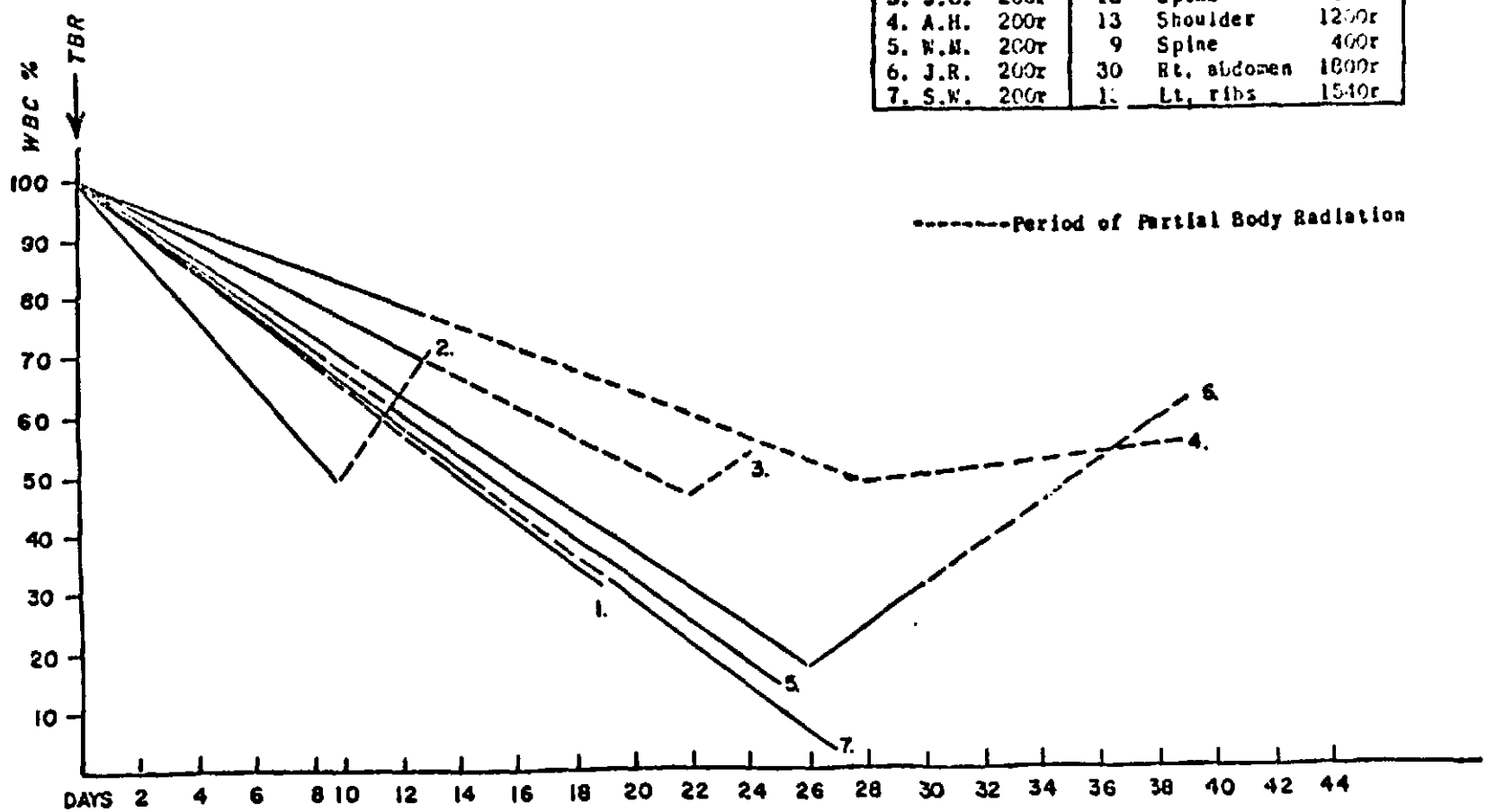


Fig. 3. Depression of White Blood Count in Patients Receiving Total Body Radiation Only

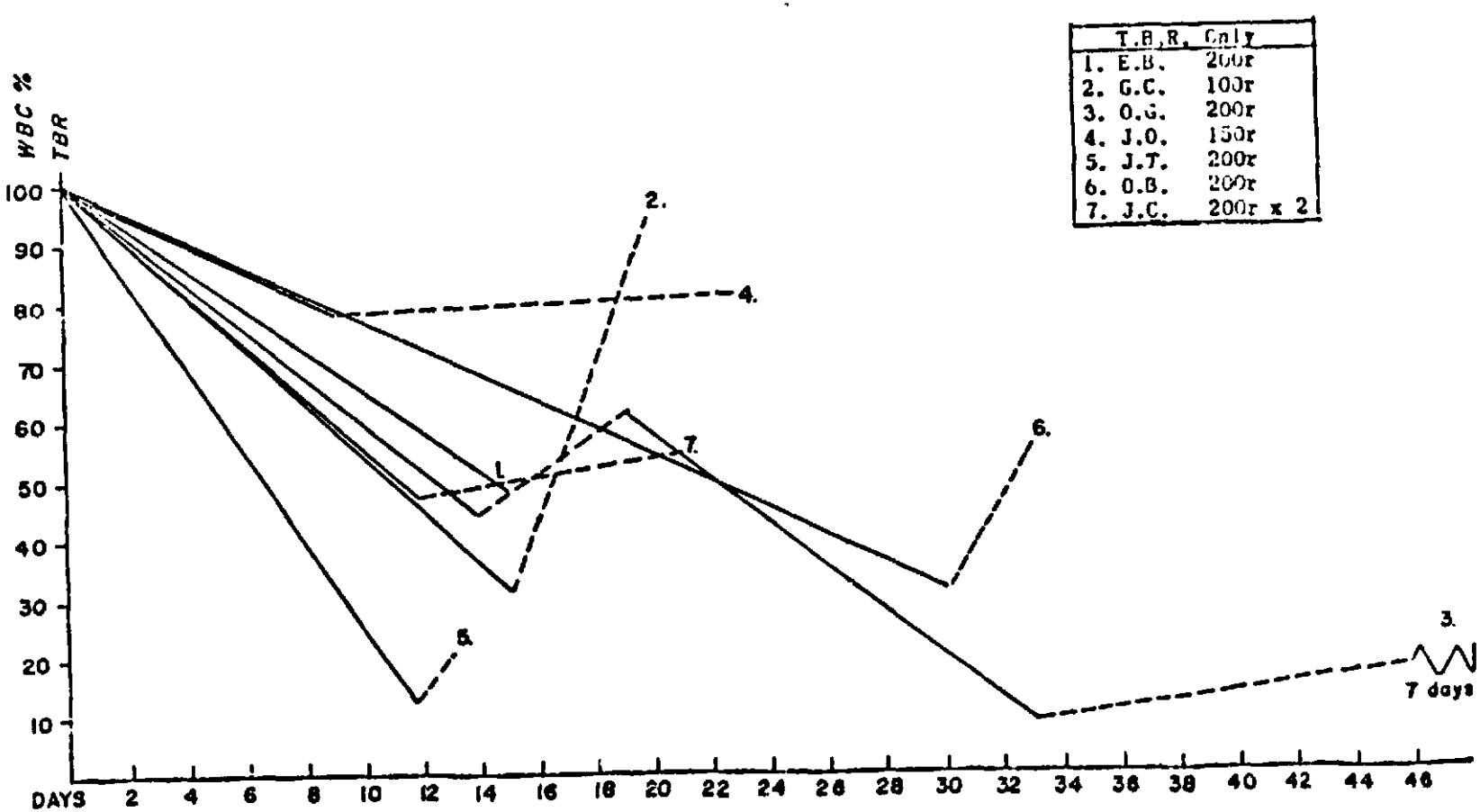


Fig. 4. Depression of White Blood Count Following Total Body Radiation: Comparison of 6 patients under 50 and 6 patients over 50 years of age

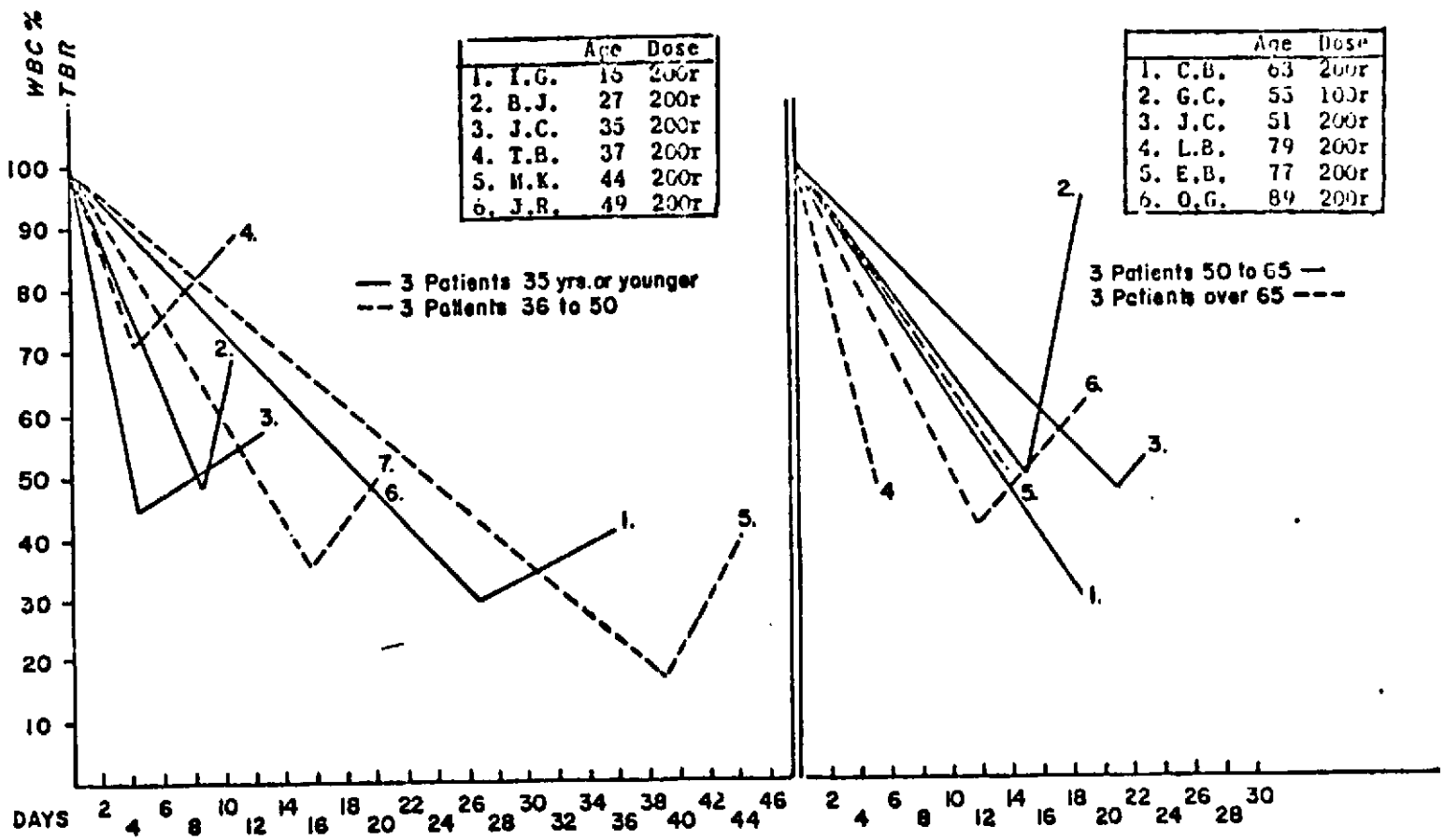


Fig. 5. Depression of Platelet Count in Patients Receiving T[illegible]al Body Radiation

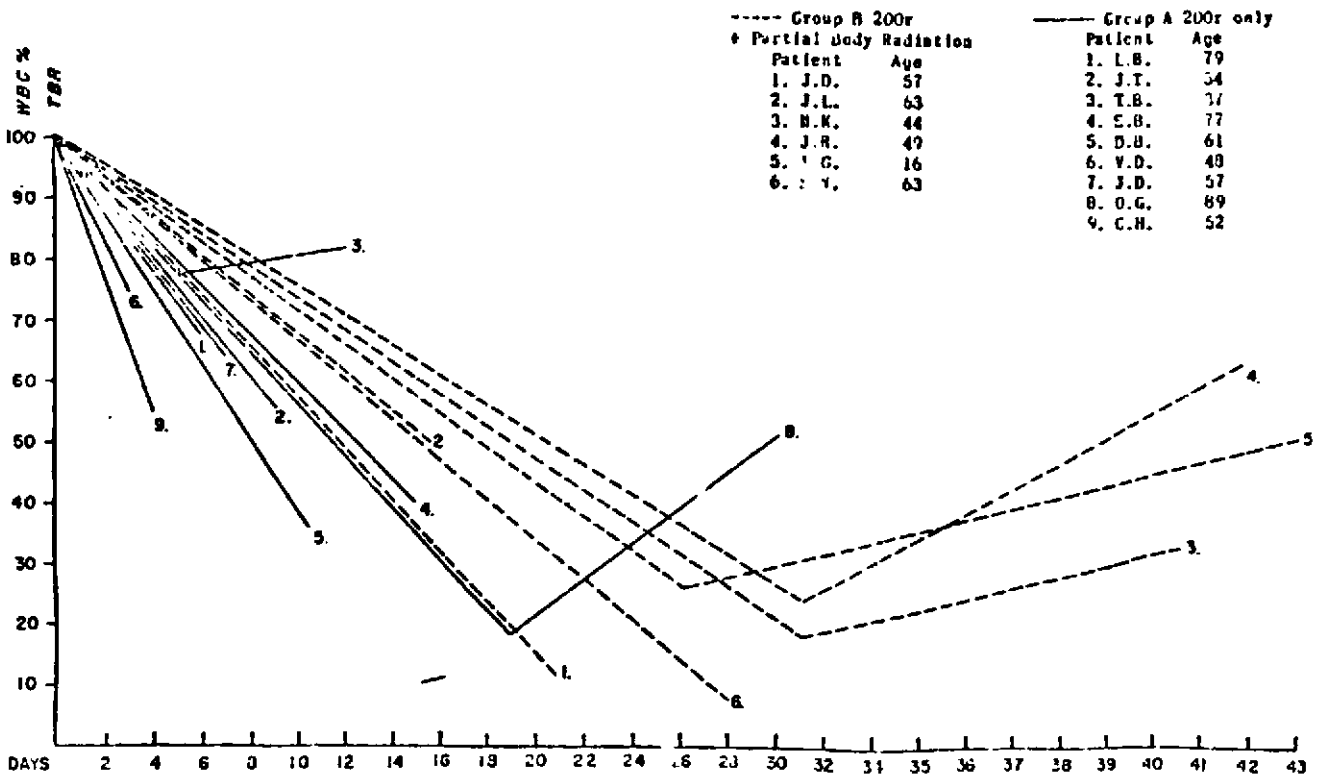


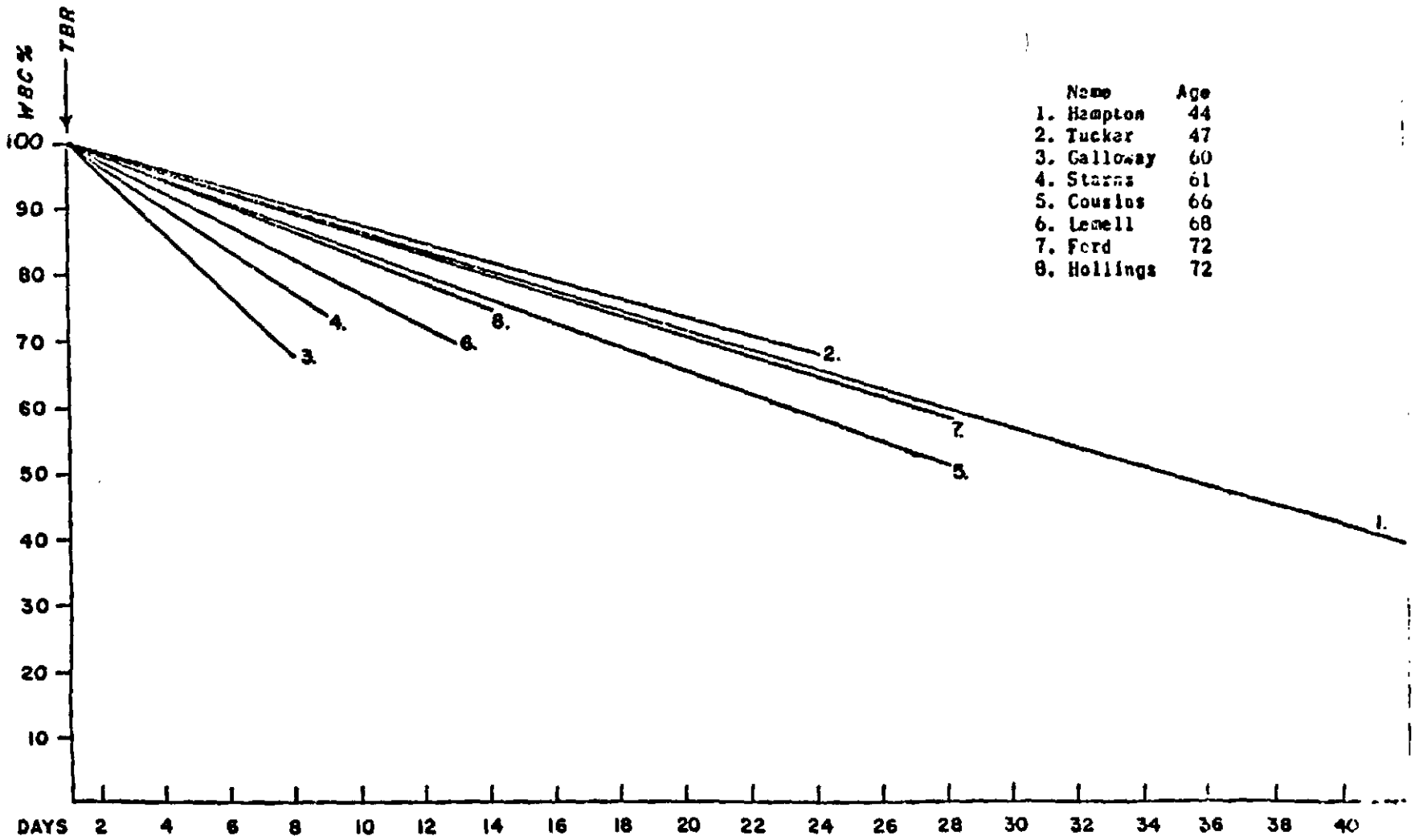
TABLE I

Diagnosis & No. of fields	Size of fields cm	Total Body Surface cm^2	Surface Area irradiated cm^2	Surface Area irradiated %	Total Body volume cc	Volume of Tissue irradiated cc.	Volume of Tissue irradiated %	Tumor Dose r/days	W.B.C. %	Depression time (days)
Ca. of cervix 2 opposing	10 x 15 5 cm split	15,500	300	1.9	61,234	2,000	3.2	3000/26	0	0
Thymoma 1 anterior 2 Post. oblique	10 x 15 8 x 15	15,400	600	3.8	60,700	3,550	5.9	2500/14	43	28
Hypernephroma 2 opposing	15 x 15	21,200	450	2.1	86,700	4,500	5.1	4000/25	32	17
Ca. of breast 2 tangential 1 supraclavicular	10 x 15 10 x 15	15,700	550	3.5	61,200	2,550	4.1	3990/23	38	15
Ca. of lung 2 opposing 1 lateral	12 x 12 12 x 12	21,000	468	2.2	93,000	3,740	4.0	4250/23	88	19
Metastatic seminoma 2 opposing	15 x 25	18,500	750	4.0	73,481	8,625	11.7	3000/12	55	36
Ca. of liver 2 opposing	20 x 20	18,500	800	4.3	76,200	8,000	10.5	2000/13	10	21
Ca. of cervix 4 oblique	10 x 10	16,200	515	3.1	61,200	5,260	8.5	3000/16	45	18

TABLE II

Name	Volume Irradiated %	W.B.C. Depression %	Time in Days	Tumor Dose r
Lemell	2.6	31	13	3250
Starns	3.0	26	8	3250
Galloway	5.0	32	8	4750
Tucker	5.3	32	24	5000
Cousins	5.9	43	28	2500
Hampton	6.2	63	44	5500
Ford	6.5	37	28	5000
Hollingsworth	12.0	25	14	4130

Fig. 6. Depression of White Blood Count in Patients Receiving Partial Body Radiation for Thoracic Lesions



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