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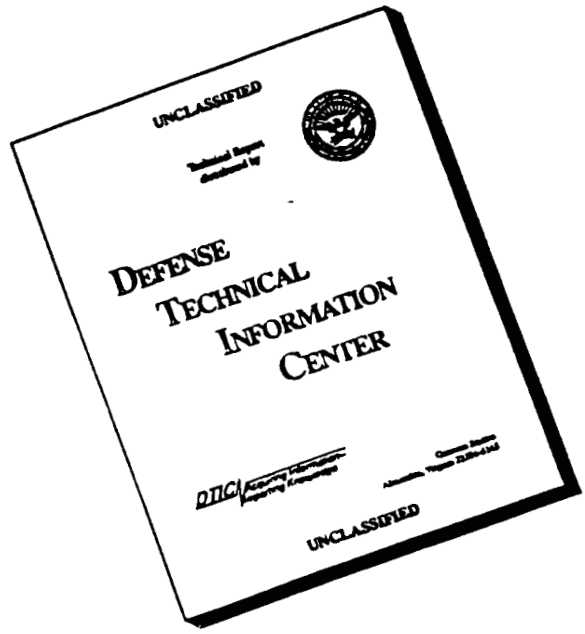

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QUARTERLY REPORT

TO THE

DEPARTMENT OF THE ARMY

ARMED FORCES SPECIAL WEAPONS PROJECT

Contract No. DA-49-007-MD-910

STUDY OF THE POST-IRRADIATION SYNDROME IN HUMANS

Period Covered by Report: November 1, 1957 - January 31, 1958

Date of Report : March 1, 1958

Investigator: James J. Nickson, M.D., Head, Section of Experimental Radiation, Division of Experimental Pathology, Member, Sloan-Kettering Institute;
Chief, Department of Radiation Therapy, Memorial Center

Address : Sloan-Kettering Institute for Cancer Research
410 East 68th Street, New York 21, New York

Supported by: Research and Development Division
Office of the Surgeon General
Department of the Army
Washington 25, D. C.

Abstract

1. Preparing Institution: Sloan-Kettering Institute for Cancer Research
410 East 68th Street, New York 21, New York

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4. Number of Pages, Illustrations : Five pages, two illustrations

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During the period of the report, two patients with disseminated cancer but considered to be in good medical condition received total body radiation. Both patients were followed and the post irradiation syndrome carefully scrutinised.

In the case of the first patient for whom this was the second course of radiation, there was no appreciable change in the platelet count during three months subsequent to her irradiation. The patient is currently being followed at monthly intervals.

The second patient showed hematologic depression following irradiation and developed bleeding diathesis on the third week post irradiation. Protamine sulphate was given to the patient on the 26th post irradiation day to alleviate this condition but in spite of this unfortunately the patient expired on the 32nd day post irradiation having developed acute pulmonary edema.

Work is continuing on the study of cell membrane actively following total body irradiation.

Urinary excretion patterns following total body irradiation is also being checked as an index of radiation exposure.

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Dr. Nickson

During the period of November 1, 1957 to January 31, 1958 two patients have received total body radiation and the postradiation syndrome closely scrutinized. Both patients had disseminated cancer but both were considered to be in good medical condition and did not appear to have any major deviations from normal in terms of hemopoietic, hepatic or renal functions.

Patient M. W. had received 18 mc of sodium 24 (for a calculated midplane dose of 50r), approximately 7 months prior to this admission, at the Brookhaven National Laboratory Medical Center. During this admission she was given 27 mc of sodium 24 for a calculated midplane dose of approximately 70 r with no immediate reaction. She has been followed for a period of three months. The patient appears to be in equilibrium with the neoplastic process, so that little advancement of her disease has been evident in the last year.

The interesting aspect of patient M. W. is the relative absence of hematologic depression following the second course of radiation (Fig. 1 and 2). In the patient's first radiation (this has been reported in detail in the annual report, dated October 1, 1957) there was a drop in the platelet count which reached a minimum at the 27th postirradiation day; with the second irradiation there was no appreciable change in the platelet counts during the three months subsequent to her irradiation. This patient is currently being followed at monthly intervals. She may be considered at a future date again as a candidate for total body irradiation, perhaps from an external source.

The second patient to be given total body irradiation, K. M., was a 42 year old white female with metastatic carcinoma of the breast

with lumbar spine and pulmonary metastases. 150r total body irradiation was delivered, utilizing the 1 Mev apparatus. This patient showed a prompt hematologic depression, such that by the 18th postirradiation day her platelet count fell from a base line 350,000 to below 100,000. The white blood count fell from a base line 8,500 to below 1,000 on the 20th postirradiation day. This patient developed bleeding diathesis in the third week postirradiation; bleeding time became prolonged to 8 minutes and clotting time to 14 minutes. During this time multiple petecchia and ecchymoses became apparent over the entire body and hemorrhage from the nasopharynx became a major problem requiring anterior and posterior packing.

On one previous occasion in a patient who had received total body irradiation, intravenous protamine sulphate had been administered with apparent amelioration of the bleeding diathesis. Because of this previous experience and because of the work of Jacobsen and Allen (1949) 50 mgm of protamine sulphate was given to this patient on the 26th postirradiation day. Table I summarizes the results.

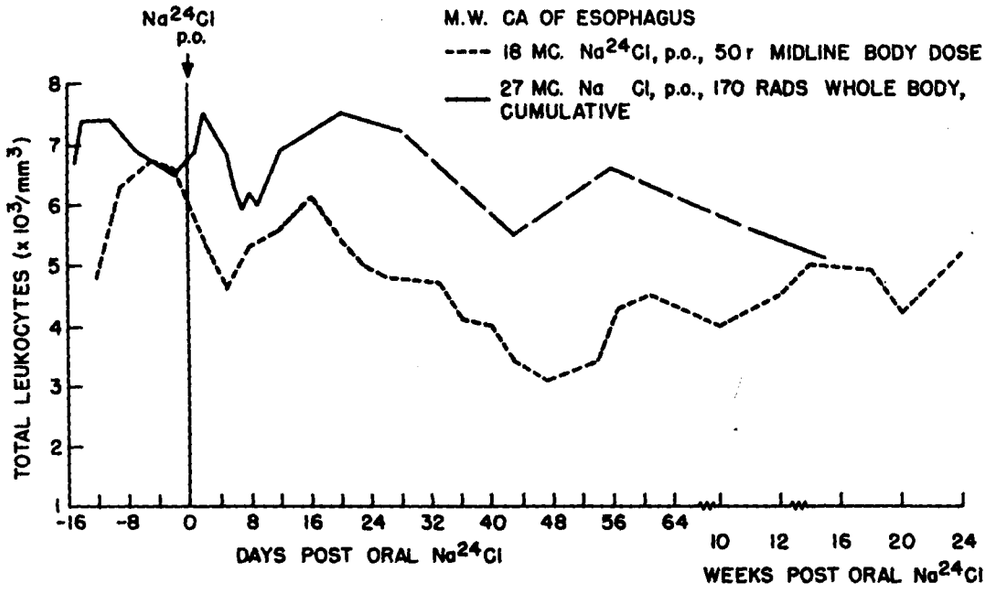
Twenty-four hours after the first injection of protamine and just prior to the second injection blood was taken for more detailed hematologic study. At this time it was found that the factor V content of the blood was increased, the proconvertin content was diminished, the prothrombin consumption time was 79% of normal, clot retraction non-existent, clotting time in glass 8 minutes, in silicon at 37° 1 hr. 45 min. (normal should be under 50 min.). The thromboplastin generation test was only slightly abnormal. The patient expired on the 32nd postirradiation day, having developed acute pulmonary edema.

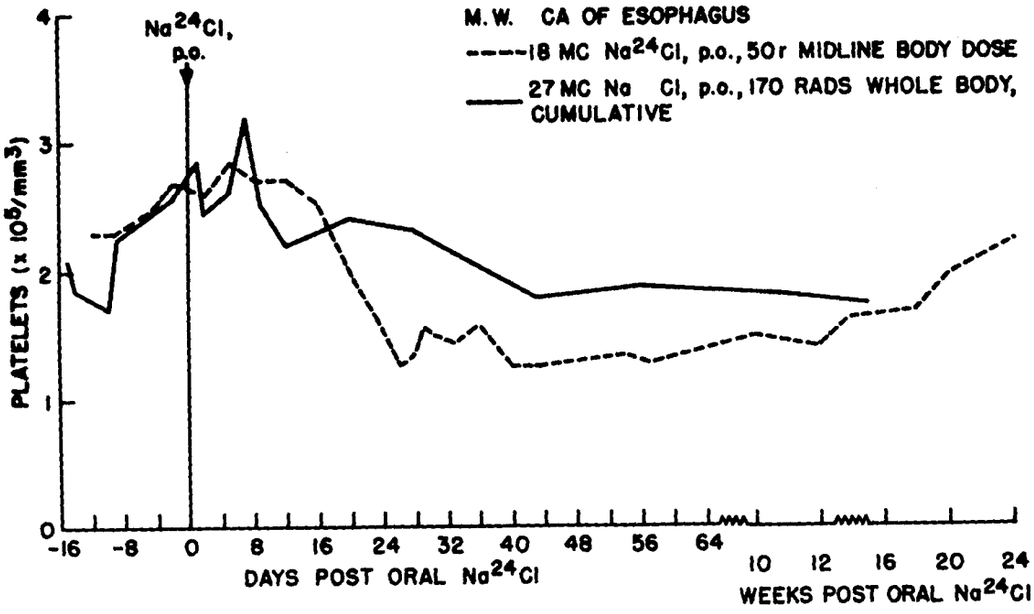
The post mortem revealed among other things acute subendocardial hemorrhages which may have contributed to the development of acute pulmonary edema and death.

Calculation of the glucose increment constant (K_b) and total glucose disappearance constant (K_a) revealed a marked shift in these factors following total body radiation. This appears to be statistically significant. The alteration in the glucose disappearance is in the direction of that found in the mild diabetic. These findings may indicate an effect of total body irradiation upon the enzyme mechanisms by which glucose is removed from the extracellular compartment and transported across cell membranes for oxidation.

Work continues on the study of the cellular membrane activity following total body irradiation utilizing K^{42} exchange data. This patient was studied pre and post-irradiation. These data are being analyzed further by means of an analogue computer to determine the extent of change in the rates of exchange of potassium and compartment size following total body irradiation.

Urinary excretion patterns following total body irradiation may prove to be a useful index of radiation exposure. In our most recent study, two metabolites appear to offer some promise. There was a 25% increase in urinary excretion of creatinine 4 to 8 days post total body irradiation. A three-fold increase in urinary pentose was observed within the first three days post-irradiation, with a second two-fold increase 10 to 12 days later. These are truly preliminary observations which warrant closer attention in the next patients to receive total body irradiation.





EFFECT OF PROTAMINE SULFATE ON HEMORRHAGIC DIATHESES OBSERVED FOLLOWING TOTAL BODY IRRADIATION
K.M. Ca of Breast.

50 mgm Protamine Sulfate, I.V.

Diathesis	Days Post Radiation	Pre-Injection	Time Post Injection (min) 10	30	60	18 hrs.
Bleeding Time (minutes)	26	7.0	5.0	2.75	3.0	11.25
	27	11.25	11.25	8.75	2.75	7.0
Clotting Time (minutes)	26	24.0	40.0	29.0	38.0	13.0
	27	13.0	37.25		20.0	10.5

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