TABLE I. Complement-Fixation Titers and Body Weight Change of Rats in a Vitamin B_{12} Deficient State.

Diet and immunization	No. of rats	Complement-fixation titers 0	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1280	1:2560	Avg body wt, g Init.	Final
B_{12} deficient													
1 inj.	38	38	—	—	—	—	—	—	—	—	—	45	112
3 "	36*	—	—	—	—	8	12	15	1	—	—		
B_{12} control (inanition)													
1 inj.	19	2	8	9	—	—	—	—	—	—	—	45	115
3 "	17*	—	—	—	—	—	—	2	8	7	—		
B_{12} control *(ad lib.)*													
1 inj.	21	2	10	8	1	—	—	—	—	—	—	45	171
3 "	21	—	—	—	—	—	—	—	5	14	2		

* Two rats died.

bodies when either a relatively small or large amount of antigenic material was injected. When a relatively small amount (0.0073 mg N) of antigenic material was employed, no detectable complement-fixing antibody was present in the sera of the deficient animals. However, the sera of 90% of the inanition and *ad libitum* controls demonstrated complement-fixing antibody when the same amount of antigenic material was employed. When a relatively large amount (0.0365 mg N) of antigen was introduced, the sera of the deficient animals did not demonstrate antibody titers as high as either the inanition or *ad libitum* control animals.

Summary. This study indicates that a vit. B_{12} deficiency impaired the production of circulating complement-fixing antibody. The sera of the inanition control and the *ad libitum* control animals possessed antibody concentrations of approximately the same titers. This was evident when either 0.0073 mg N or 0.0365 mg N was employed as the antigen. Therefore, the specific vitamin deficiency and not inanition appears to be the significant factor affecting the production of circulating complement-fixing antibody under these experimental conditions.

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Protective Effect of Adrenal Steroid Administration on Irradiated Mice. (19888)

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Altering the resistance or radiosensitivity of animals to ionizing radiation and ascertaining the physiological processes behind such resistance or radiosensitivity have been the subjects of many investigations(1-4). The idea that the condition of stress set up in animals by radiation can be altered by the administration of certain hormones has also been stud-

TABLE I. Effects of Administration of Adrenal Steroids on Mortality Rate of DBA Mice Following Radiation with 500 r Dose to the Head.

Group	Compound	Steroid dose, mg/day	Days of administration	No. of animals ♂	No. of animals ♀	Mortality at 45 days ♂	Mortality at 45 days ♀
I*	C†	1	3 prerad.	12	12	0	0
II*	C	1	3 postrad.‡	8	8	4	0
III (control)	—		Irrad. only	12	12	12	12§
IV "	C	1	3 (no irrad.)	11	11	0	0
I*	DCA	.5	3 prerad.	12	12	0	0
II*	DCA	.5	3 postrad.‡	6	6	0	0
III (control)	—		Irrad. only	13	13	13	13
IV "	DCA	.5	3 (no irrad.)	11	11	0	0

* Although 45 days is indicated, these treated animals were still surviving and apparently well after 4 months.

† C = cortisone.

‡ Mice received cortisone or DCA immediately after radiation.

§ Two lived 52 days rather than 45 days after radiation.

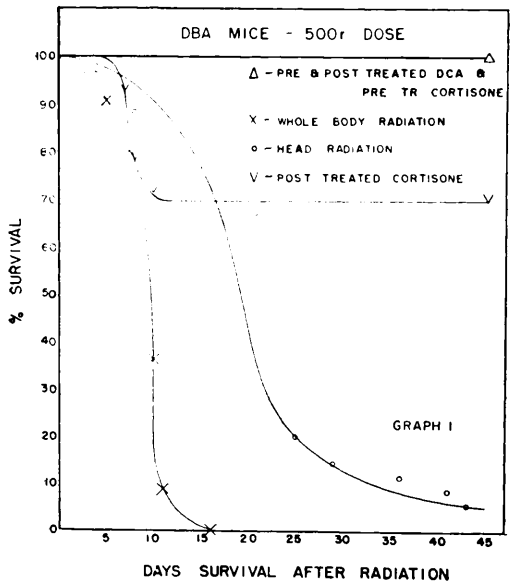
ied(5-7). Moreover, a direct relationship between the adrenal cortex and resistance to whole-body radiation has been postulated, but this postulate has been neither proved nor rejected. Therefore, it is the purpose of this study to endeavor to investigate the role of the pituitary-adrenal axis in radiosensitivity or resistance in mice or, more specifically, to determine the effect of cortisone and DCA as agents in minimizing the radiosensitivity in mice as a result of ionizing radiation.

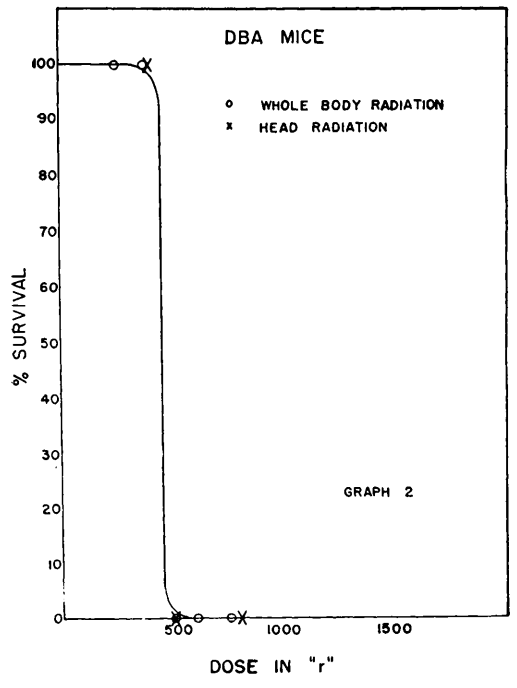
Materials. a. *Mice.* The mice used in these experiments were all from our own inbred strain of DBA mice. Both males and females, having an average age of 6 weeks and an average weight of 20 g, were used. Purina fox chow and water were available at all times. b. *Hormones.* The hormones used in these experiments were 11-dehydro-17 hydroxycorticosterone-21-acetate (Cortisone Acetate—Merck) and desoxycorticosterone acetate (Doca Acetate—Organon). c. *Radiation.* The x-rays used had a H.V.L. of 0.9 mm copper with a dose rate of 150 r/min. (air) at a distance of 30 cm. *Procedure.* The lethal dose curves for DBA mice with head and whole-body radiation were first established (Graph 2), and from these curves a dose of 500 r (air) was selected for radiation of the head. This dose produces death in 100% of the unprimed animals. Animals were primed to observe whether or not the aforementioned hormones would afford protection when a 500 r dose was administered to the head. In a subsequent paper lethal dosage curves for head radiation, whole-body radiation, and whole-body-except-head radiation for this (DBA) strain and other strains of mice will be presented. Preliminary data obtained to date show that there is a marked strain difference in the response to ionizing radiation. As shown in Table I, the mice were divided into 4 groups. The first group received injections of hormones prior to radiation, the second group was treated subsequent to the radiation, the third (control) group received radiation only, and the fourth (control) group received hormones only.

Results. It is evident from Table I that, whereas a dose of 500 r produced death in all of the control animals (group 3), those animals which had been fortified with hormones prior to irradiation were apparently unaffected, as judged by the mortality rate. The second group of mice, namely those which received the hormones subsequent to irradiation, also showed evidence of a protective effect of the hormones, but to a lesser degree than the first group which received the hormones prior to irradiation.

In order to further analyze the data with respect to time of survival, the results are plotted in Graph 1. The data for whole-body radiation with a dose of 500 r are included.

When a 500 r dose is delivered either to the whole body or to the head, a 100% mortality rate is obtained (Graph 2); however, mice receiving whole-body radiation succumb sooner than those receiving head radiation only. Over 200 mice were utilized to establish the





fact that a 500 r dose to the whole body is fatal.

Discussion. The foregoing data clearly indicate that administration of the gluco-corticoid, 11-dehydro-17-hydroxycorticosterone 21-acetate, or the minero-corticoid, desoxycorticosterone acetate, enhances the survival rate of DBA mice when radiated with a 500 r dose to the head. This investigation can be compared to investigations made by others despite the fact that other workers used whole-body radiation and different dose levels, hormones, strains of mice, and even different animals. Therefore, looking at the results of other investigators only on the basis of whether or not the hormones used afford protection against ionizing radiation, and yet not minimizing the importance of differences in strains, hormones, radiation dosages, etc., one can probably say that our findings agree with those of Ellinger (7), who has reported that 0.5 mg of desoxycorticosterone given after radiation reduces the mortality rate. However, these findings are in contradistinction of those of Straube *et al.*(8), and Graham *et al.*(9), who were unable to demonstrate a significant effect from DCA. Smith *et al.*(10) report the failure of cortisone or ACTH to reduce the mortality in irradiated mice. In our work with DBA irradiated mice, cortisone was shown to be effective. A strain difference in the metabolic handling of these compounds or variations in the effective dosage levels given may be significant factors in accounting for the apparent inconsistencies reported in the literature.

In this study a correlation is seen between whole-body and head radiation (Graph 2), for similar mortality levels are obtained in both cases with a 500 r dose. However, the mice receiving whole-body radiation succumb within 16 days, whereas the irradiated mice receiving 500 r to the head succumb around the 45th day (Graph 1). The more rapid death rate for whole-body irradiated mice may be due to a more rapid failure of functional reconstitution of one or more of the tissues or organs in the body, *e.g.*, the hematopoietic system and the endocrine system. From this difference in mortality time in our data, one can suppose that radiating just the head region involves a less direct impairment of radio-sensitive organs, *e.g.*, spleen, bone marrow(11), and adrenal glands(12). However, since the pituitary-adrenal axis is known to play an important role in metabolic activities, the irradiated mice receiving head radiation succumb eventually, possibly as a result of injury to pituitary cells which disturbs the elaboration of metabolic hormones required to

support normal metabolic activity. In other words, the pituitary gland, particularly the anterior lobe, is profoundly influenced by ionizing rays. As a result of this radiosensitivity along with other disfunctions, a state of adrenal insufficiency is established. From this one can assume that the extent of pituitary damage determines the degree of adrenal insufficiency. The fact that both cortisone and DCA are able to increase the survival time in DBA mice suggests that in this strain a state of adrenal insufficiency is avoided either by rendering the pituitary less sensitive to ionizing radiation or by preventing an early decrease in adrenal-cortical activity after irradiation, which, if prolonged, may possibly result terminally in a relative adrenal insufficiency and finally death.

Summary. 1. Young male and female DBA mice were exposed to 500 r head radiation or whole-body radiation. A correlation is observed between head and whole-body radiation, as judged by the mortality rate. In both instances a 500 r dose gives a 100% mortality rate, but mice receiving whole-body radiation succumb sooner. 2. Mice receiving 500 r head radiation and primed before or after radiation with cortisone or desoxycorticosterone showed evidence that both of these compounds afford protection from the lethal effect of ionizing radiation. 3. Interpretations of the role of the pituitary-adrenal axis under the conditions of these experiments are discussed.

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Stability of Mumps Antibody and Antigen at Various Temperatures.* (19889)

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During the course of an investigation on the antibody response of man to vaccination with the mumps antigen it became necessary to obtain information as to the stability of the mumps antibody and antigen. The stability of the complement-fixing (CF) antibody of immune sera was tested in relation to temperature variations during inactivation prior to the CF test, and following storage. The stability of the CF antigen and the CF antibody-producing antigen of a commercially prepared vaccine were also tested.

Materials and methods. The complement-fixation test. The test employed in these studies was developed by Habel(1). Commercial hemolysin was used in the amount of 2 units in 0.2 ml. Lyophilized guinea pig comple-

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