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Influence of Testis on Induction of Ovarian Tumors of Mice by X-rays. (22433)

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Absence of ovarian tumorigenesis when only a single ovary is irradiated suggests that the mechanism of induction of mouse ovarian tumors by x-rays is similar to that involved in tumor development within an ovary transplanted to a castrated animal's spleen(1). In either case a functional ovary *in situ* inhibits the development of ovarian tumors; this inhibition is said to result from suppression of output of excessive pituitary gonadotrophin (1,2).

Results. When Balb/c female mice received 200r of x-rays, ovarian tumors were present 16 months post-irradiation in 20 of 22. Ovarian tumor development was suppressed in all of 36 mice by isologous Balb/c subcutaneous ovarian grafts made within 24 hours following irradiation. If only a single ovary was irradiated, tumors developed in 3 of 37, indicating suppression of tumorigenesis by the functional ovary in 92%. When the functional ovary was removed immediately post-irradiation, tumors appeared in 58 of 66 irradiated ovaries. Only those ovaries exceeding 3 mm in diameter were considered tumorous.

Injection of estrogenic hormone has been shown to inhibit x-ray induced ovarian tu-

morigenesis, whereas injected androgen was relatively ineffective(3). To determine whether the functioning testis inhibits the development of ovarian tumors by x-rays, x-irradiated ovaries were grafted subcutaneously into both intact and castrated male Balb/c mice; the donor Balb/c females and the recipient males of this strain were 6-8 weeks of age at the time of grafting. Grafts were made within an hour after whole body x-irradiation of the intact female donor. The x-ray-treated mice were exposed to general body irradiation in cardboard boxes at 30 cm target-skin distance, 140 kv, 2-1 mm aluminum filters, dose rate 70r per minute.

Ovarian tumors developed in 10 of 12 intact males bearing irradiated ovarian transplants (13 of 24, or 54% of grafts). Similar tumors appeared in irradiated ovaries residing in all of 18 castrated male hosts (29 of 34, or 85% of grafts). The latent period of tumor induction was not significantly different in castrated and intact mice (12-16 months). Except for a tendency toward areas of undifferentiated carcinoma, histologically the neoplasms were the same as those occurring in the Balb/c strain following irradiation of the ovary *in situ*(1). Although seminal vesicle development was not maximum in all intact graft-bearing males, stimulation was sufficient to indicate testicular androgenic activity.

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In contrast to ovarian secretion, which remarkably inhibits x-ray induced ovarian tumorigenesis in mice, secretion of the testis is not similarly inhibitory. Presently Balb/c ovaries are being grafted into the spleens of intact and castrated Balb/c mice to determine the degree to which ovarian tumor development induced by transplanting an ovary into the spleen is inhibited by the testis. Adequate data on this point do not appear in the literature.

Testosterone inhibits the abnormal release of pituitary gonadotrophin after x-irradiation of female mice(4). Since neither injected (3) nor endogenously produced androgen effectively (in contrast to estrogen) inhibits ovarian tumorigenesis, in many cases exposure of the ovaries to elevated blood levels of gonadotrophins may not be essential for ovarian tumor formation induced by x-rays. It is possible that estrogenic hormone may

act directly on the ovary to suppress tumor development.

Summary. When irradiated ovaries were grafted into intact as well as castrated male Balb/c mice, ovarian tumorigenesis proceeded. Functional normal ovarian grafts into previously irradiated Balb/c females inhibited tumorigenesis in the irradiated ovary. It appears that irradiation-induced ovarian tumorigenesis in this inbred strain is inhibited almost completely by ovarian, but only to a minor degree by testicular secretion.

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Presence of Erythropoietic Factor in Plasma of Normal and Hypophysectomized Rats Following Bleeding.* (22434)

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Carnat and Deflandre(1) discovered a factor in the plasma of anemic rabbits which would stimulate erythropoiesis. This factor, "erythropoietine" or "hematopoietine," has been demonstrated by many other investigators in the plasma of rabbits made anemic by repeated bleeding or by injection of phenylhydrazine(2-8). It has also been demonstrated in the plasma of rats(9,10) and in the human(11).

The influence of the endocrine glands on hemopoiesis is being actively investigated, and the anemia which follows removal of the hypophysis is well established; the present investigation was undertaken in an attempt to determine whether the anemia in the hy-

pophysectomized animal can be related to the absence of such a plasma factor.

Methods. Adult female rats of 3 to 4 months of age and of the Sprague-Dawley strain were used in this experiment. All rats were fed Purina chow *ad libitum* supplemented once a week by lettuce. Completeness of hypophysectomies was verified by examination of the organ site at autopsy with a binocular dissecting microscope. *Donor rats*, from which plasma was obtained, were divided into 6 groups: (1) normal unbled rats; (2) and (3) bled normal rats; (4) hypophysectomized rats not yet anemic; and (5) and (6) bled hypophysectomized animals. One group of normal rats was made anemic by removing 4 cc of blood on day 1, and 2 cc on day 3, the rats being exsanguinated on day 5. At that time the hematocrit averaged 22% as compared to 43% for the normal unbled

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