Effect of Progesterone on the Development of Mammary Cancer in C3H Mice

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In experiments by Lipschütz, Murillo, and Vargas (3) it was shown that progesterone given in a proportion of 150:1 of estradiol prevented the uterine fibromatosis otherwise provoked by estradiol in guinea pigs. Heiman (1) investigated the effect of progesterone on the incidence of mammary cancer in RIII mice and found that the occurrence of these tumors was considerably reduced thereby. Progesterone counteracted also the growth-accelerating action of the estrogen on the mammary glands.

Furthermore, progesterone and testosterone have an affinity in some of their biological activities, and Lipschütz, Vargas, and Ruz (4) found that, like progesterone, testosterone propionate supplied in a proportion of 22:1 prevented the induction of uterine fibromas by estradiol. Lacassagne (2), and Nathanson and Andervont (5) reported that spontaneous mammary cancer in mice could be prevented to a large extent by the repeated administration of testosterone propionate. Moreover, it has been repeatedly suggested that in addition to hereditary factors in pure strain mice with high incidence of mammary cancer an excessive secretion of estrogen may determine the incidence of these tumors, and that this excess may be held in check by testosterone and progesterone. In view of these varied considerations it seemed of interest to investigate the effect of progesterone on the incidence of spontaneous mammary tumors in a pure strain of mice.

Method of the Experiment and Results

Female mice of C3H strain were used. All the mice were kept in the same room, from 1 to 5 mice in one metal cage. The diet consisted of Millard-Marsh basal diet, oats, puppy biscuit, rat cake, brown bread, marmite, cod liver oil, and water *ad libitum*. The treatment started after one litter was born; and the mothers were permitted to suckle the young.

Thirty animals received subcutaneous injections each week of 1 mgm. crystallized progesterone dissolved in 0.2 cc. arachis oil; 20 controls received the oil only. The mice were inspected weekly for appearance of tumors.

Tables I and II show that no difference could be established in the incidence of tumors, nor in the age of the appearance of the tumors in the treated and untreated mice. The treated mice received 6 to 34 mgm., in the average 21 mgm., progesterone. Up to date, 3 animals of each group remained free of tumors. The tumor-free mice were not invariably daughters of tumor-free mothers.

Table I: Frequency and Age of Incidence of Tumors in Progesterone-Treated Animals

Tumor in mother of animal in experiment	Age of mice in days		Number of injections
	Treatment started	Tumor appeared	
+	73	335	29
+	92	253	19
+	35	302	34
+	35	302	34
—	220	469	34
+	212	419	23
+	223	473	32
+	66	302	28
+	69	275	23
+	66	245	20
—	190	233	6
+	84	nil(340)*	32
+	102	234	16
—	94	275	22
+	81	nil(326)*	30
+	87	220	16
+	76	258	24
+	115	262	16
+	75	229	19
—	133	252	12
+	82	180	14
+	147	245	13
+	126	231	13
+	167	258	11
+	140	214	10
+	110	215	15
+	131	265	18
+	95	nil(229)*	18
Mean	116	280	20.8

(3 animals without tumors)

* The figures in brackets represent the age of the animal at the end of the experiment.

Note: Two of the treated and 1 control animal died (without tumor) during the first 3 to 4 weeks of the experiment and are not included in the tables.

TABLE II. FREQUENCY AND AGE OF INCIDENCE OF TUMORS IN CONTROL ANIMALS

Tumor in mother of animal in experiment	Age of mice in days		Number of injections
	Treatment started	Tumor appeared	
+	73	344	32
—	129	349	26
+	143	210	8
+	157	245	10
+	178	335	19
+	178	224	5
—	224	453	27
+	145	338	25
+	97	255	18
+	185	259	10
+	97	227	17
+	88	290	23
+	88	340	32
+	78	315	21
+	196	237	5
—	91	nil(325)*	31
+	63	nil(274)*	28
—	119	196	10
—	69	nil(273)*	27
Mean	126	288	19.8

(3 animals without tumors)

* The figures in brackets represent the age of the animal at the end of the experiment.

DISCUSSION

While the present investigations were in progress the paper by Heiman (1) appeared dealing with the effect of progesterone and testosterone propionate on the mammary tumors in RIII mice. The complete failure in the present experiments to produce any beneficial effect by the administration of progesterone on the mammary cancer in mice may be attributable to the employment of a different strain of mice. The dosage of progesterone was higher than in the experiments of Heiman which makes a direct comparison difficult. On the supposition that progesterone acts by reducing the output of gonadotropic hormone of the pituitary it seems unlikely that an increased dose would counteract this effect. The different results observed show the need for care in attempting to generalize results even in different strains of the same species and emphasizes the difficulty of attempting to carry over results obtained in experimental animals to human pathology.

SUMMARY

Thirty mice of a high mammary cancer strain (C3H) received subcutaneous injections of 1 mgm. of progesterone weekly. No differences could be established in the frequency and the age of the appearance of tumors in these mice and in the 20 control animals receiving injections of the solvent only.

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