

EFFECT OF SOME HORMONAL FACTORS ON GROWTH OF TRANSPLANTED HARDING-PASSY MELANOMA

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Castration of C57BL mice before transplantation of Harding-Passy melanoma stimulated growth of the tumor. Injection of progesterone and cortisone inhibited growth of the melanoma. Castration after transplantation of the tumor, like injection of diethylstilbestrol dipropionate and methyltestosterone had no visible effect on tumor development.

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The study of the various factors influencing tumor growth may be useful for the development of more effective methods of treatment. The effect of certain hormones on growth of experimental melanomas is interesting in this respect. It has been shown that the melanophore hormone and ACTH stimulated growth of melanomas of the human skin in tissue culture. Progesterone and estradiol gave only a slight stimulation effect, and testosterone either had no effect on the melanoma or inhibited its growth slightly. Hydrocortisone in small doses inhibited growth of the melanoma cells, while large doses caused death of the whole culture [2].

We have studied the effect of castration, and also of injection of progesterone, methyltestosterone, diethylstilbestrol dipropionate, and cortisone on growth of a transplanted Harding-Passy melanoma.

EXPERIMENTAL METHOD

Experiments were carried out on 300 male and female C57BL mice (mean weight 18-20 g).

The tumor was transplanted subcutaneously by the usual method [1], using 0.2 ml of a homogenized suspension diluted 1 : 3.

In the experiments of series I, the animals were castrated while a mock operation was carried out on the control mice. Two days after the operation the tumor was transplanted into the animals.

In the experiments of series II, the melanoma was transplanted first; when the diameter of the tumor had reached 6-15 mm, the experimental animals were castrated and the mock operation performed on the controls.

In the experiments of series III, the action of hormones was tested. On the 20th-21st day after transplantation of the tumor, when its diameter had reached 6-15 mm, the experimental animals began to receive hormones by daily subcutaneous injection in 0.2 ml physiological saline in the right or left side of the trunk for 10 days in the following doses per mouse: 1 mg progesterone, 1 mg methyltestosterone, 100 and 20 μ g diethyltestosterone dipropionate (the dose of 100 μ g was subsequently discontinued because of its high toxicity), and 100 and 200 μ g cortisone. The control animals received subcutaneous injections of 0.2 ml physiological saline.

In the course of the experiment periodic measurements were made of three mutually perpendicular diameters of the tumor nodules, and their product was calculated and assumed to be approximately proportional to the volume of the nodule. At the end of the experiment, the tumor nodules were weighed and their arithmetic mean weight was calculated for the experimental and control animals, the difference between these means being assessed with the aid of Student's criterion. On the assumption that tumor growth obeys

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TABLE 1. Effect of Castration on Growth of Harding-Passy Melanoma

Expt. No.	Sex	No. of animals	Groups of animals	Duration of observation after tumor transplantation (in days)	Mean wt. of nodule at end of experiment (in g)	Mean wt. of tumor nodule in experimental animals compared w/cont. (%)	Difference in wt. (in %)	P
Preliminary castration								
1	Females	9	Experiment	38	2,8	322,0	+222	<0,001
	"	9	Control	38	0,9	100,0		
2	Females	11	Experiment	37	12,7	254,0	+154	<0,001
	"	11	Control	37	5,0	100,0		
3	Males	14	Experiment	38	5,6	200,0	+100	<0,001
	"	14	Control	38	2,8	100,0		
Subsequent castration								
6	Males	9	Experiment	19	2,9	144,0	+44	>0,01
	"	9	Control	19	2,03	100,0		

TABLE 2. Effect of Hormones on Growth of Harding-Passy Melanoma

Experiment No.	Sex	No. of animals	Hormone injected	Dose per mouse	Duration of observation after transplantation of tumor (in days)	Time taken for tumor to double its volume after 10 days (in days)	Mean wt. of tumor nodule at end of experiment (in g)	Mean wt. of tumor nodule in experimental group compared with control (in %)	Difference in weight (in %)	P
7	Males	11	Progesterone	1 mg	33	3,6	1,9	50,4	-49,6	<0,001
	Males	11	Methyltestosterone	1 mg	33	3,3	2,21	59,5	-40,5	<0,001
	Males	11	Physiological saline	0,2 ml	33	2,4	3,77	100,0		
8	Males	13	Diethylstilbestrol dipropionate	20 µg	32	2,5	0,6	60,0	-40,0	>0,05
	Males	13	Physiological saline	0,2 ml	32	2,4	1,0	100,0		
9	Fe-males	24	Cortisone	200 µg	29	3,8	0,57	41,3	-58,7	<0,001
	Fe-males	24	Cortisone	100 µg	29	2,5	1,62	88,0	-12,0	>0,1
	Fe-males	24	Physiological saline	0,2 ml	29	2,7	1,38	100,0		
10	Fe-males	29	Cortisone	200 µg	29	3,9	0,27	72,9	-27,1	<0,01
			Physiological saline	0,2 ml	29	3,2	0,34	100,0		

an exponential law, the time taken for the tumor to double its volume was calculated from the results of these measurements for the animals receiving hormones and the controls.

EXPERIMENTAL RESULTS

Table 1, shows that castration of females performed before transplantation of the tumor stimulated its growth: the weight of tumor in the castrated females was 2.5 and 3.2 times greater than its weight in the control animals. The dynamics of tumor growth shows, however, that an increase in its rate of growth in the castrated females was observed only at the very beginning; 15-16 days after transplantation, the tumor nodules were much larger than in the control series. The ratio between the products of the three diameters of the tumor in the castrated females to its value in the control females was 5.8 : 1 in experiment No. 1 and 2.4 : 1 in experiment No.2. Later, throughout the rest of the experiment this ratio changed only negligibly, its values after 30-31 days being 5 : 1 and 2.1 : 1 respectively.

Preliminary castration of the males also stimulated tumor growth; the weight of the tumor nodules in the castrated males was twice that in the controls (Table 1). However, the dynamics of tumor growth in the males differed from that in the females. From the observations conducted on the living animals, the ratio between the products of three diameters of the tumor in the experimental and control animals 21 days after transplantation (1 measurement) was 0.8 : 1, rising after 30 days to 1 : 1, while after 37 days the tumors in the castrated males were larger than in the controls (2 : 1).

In contrast to preliminary castration, if this operation was performed after transplantation of the tumor, just as in the case of injection of diethylstilbestrol dipropionate and methyltestosterone, it had no significant effect on growth of the preformed tumor nodule (compare Tables 1 and 2). Of the other hormones tested, progesterone and cortisone in doses of 200 μ g per mouse inhibited growth of the melanoma (Table 2).

LITERATURE CITED

1. A. D. Timofeevski (Editor), Models and Methods of Experimental Oncology [in Russian], Moscow (1960).
2. O. Miodushevskaya, Abstracts of Proceedings of the Eighth International Cancer Congress [in Russian], Moscow (1962), p. 190.