

EFFECT OF EARLY THYMECTOMY ON GROWTH OF TRANSPLANTED MAMMARY
GLAND TUMORS ARISING IN C3Hf MICE

I. Yu. Videlets and E. V. Gruntenko

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Mammary gland tumors arising in factorless C3Hf mice, if transplanted into MTV-S⁺ and MTV-S⁻ recipients, were found to grow at the same rate and early thymectomy likewise had no effect on their growth. The more rapid growth of transplanted tumors in MTV-S⁺ than in MTV-S⁻ recipients after transplantation of mammary gland tumors from C3H/He mice and the inhibition of tumor growth after early thymectomy are evidently connected with special features of the immunological reaction to virus-induced antigens.

KEY WORDS: thymus; Bittner virus; mammary gland tumors.

Mammary gland tumors induced by Bittner virus grow faster after transplantation into MTV-S⁺ than into MTV-S⁻ (factorless) recipients [3, 9, 10]. It has been suggested that early infection of animals with Bittner virus determines the development of tolerance to specific tumor antigens [9] or immunostimulation of cells containing such antigens [3, 10, 11].

After thymectomy in the first week of life the development of mammary gland tumors induced in mice by Bittner virus is inhibited [1, 8, 5]. Early thymectomy on C3H/He mice inhibits growth of transplanted mammary gland tumors in them [2].

The cells of such tumors are known to contain specific tumor antigens induced by Bittner virus [4, 6, 7].

If the more rapid growth of tumors in MTV-S⁺ recipients and its inhibition after early thymectomy are attributable to the special features of the immunological reaction of such animals to virus-induced antigens, these phenomena should not be observed during transplantation of tumors arising in MTV-S⁻ mice.

EXPERIMENTAL METHOD

Experiments of Series I. Mice of the C3H/He strain or (C3H/He × C57BL)F₁ hybrids were used as the MTV-S⁺ animals and C3Hf or (C57BL × C3H/He)F₁ hybrids as the MTV-S⁻ group. Three tumors arising spontaneously in a colony of C3Hf mice were used: OMZh_f-2, OMZh_f-3, and OMZh_f-4. The MTV-S⁺ and MTV-S⁻ mice were inoculated simultaneously with 0.2 ml of a 10% suspension of tumor cells subcutaneously in the dorsal region. The sex and age of the animals of the different groups were identical. The age of the mice at the time of inoculation was 2.5-3 months.

Experiments of Series II. These experiments were carried out on C3H/He and C3Hf mice. The experimental animals were thymectomized on the sixth day after birth. Control groups consisted of intact mice. At the age of 3 months the mice were inoculated with 0.2 ml of a 10% suspension of OMZh_f-2 or OMZh_f-4 tumor cells subcutaneously in the dorsal region.

In the experiments of series I and II the appearance of tumors was recorded by inspection and palpation of the mice every 3-4 days starting from the tenth day after transplantation of the tumors. If not all the animals developed tumors, the percentage of animals in the

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TABLE 1. Rate of Growth of Transplanted Mammary Gland Tumors of C3Hf Mice in MTV-S⁺ and MTV-S⁻ Recipients

Tumor	Recipient	n	Sex	% of successful takes	Mean latent period (in days)	Mean weight of tumor in group at end of experiment
OMZhf- =2	C3H/He	20	♂	85	—	2,25 ± 0,37
	C3Hf	21	♂	100*		2,02 ± 0,37
OMZhf- =2	C3H/He	25	♀	84	—	0,7 ± 0,14
	C3Hf	27	♀	100*		0,7 ± 0,14
OMZhf- =3	C3H/He	20	♂	72	—	2,0 ± 0,21
	C3Hf	20	♂	79		2,6 ± 0,25
OMZhf- =4	C3H/He	21	♂	100	12,1 ± 0,8	1,2 ± 0,1
	C3Hf	25	♂	100	14,5 ± 1,2	1,2 ± 0,17
OMZhf- =4	(C3H/He × C57BL)	20	♀	100	12,3 ± 0,64	2,3 ± 0,22
	(C57BL × C3H/He)	20	♀	100	12,1 ± 0,64	2,2 ± 0,22

*Differences statistically significant.

TABLE 2. Rate of Growth of Transplanted Mammary Gland Tumors of C3Hf Mice in Thymectomized and Intact Recipients (MTV-S⁺ and MTV-S⁻) (M ± m)

Tumor	Recipient	n	Sex	% of successful takes	Mean latent period (in days)	Mean weight of tumor in group at end of experiment
OMZhf = 2	C3H/He, thymectomized	23	♀	83	—	0,6 ± 0,14
	C3H/He, intact	25	♀	84		0,7 ± 0,14
OMZhf = 4	C3H/He, thymectomized	21	♂	100	13,9 ± 0,8	1,2 ± 0,14
	C3H/He, intact	24	♂	100	12,1 ± 0,8	1,2 ± 0,10
OMZhf = 2	C3Hf, thymectomized	22	♀	71	—	0,4 ± 0,1
	C3Hf, intact	26	♀	70		0,4 ± 0,1

group in which tumors appeared was calculated. If tumors appeared in 100% of cases the mean time of appearance of the tumors in the group was calculated. At the end of the experiment the animals were killed and the weight of the tumor and the body weight without the tumor were determined for each mouse. In the thymectomized mice the completeness of the operation was verified at the end of the experiment and no remnants of the thymus were found in any of the mice. The experimental results were subjected to statistical analysis. The significance of differences in the weight of the tumor was determined by Student's criterion and the significance of differences in the percentage transplantation by Fisher's criterion.

EXPERIMENTAL RESULTS

The results of the experiments of series I are given in Table 1. No significant differences were found between the mean weight of the tumor in the MTV-S⁺ and MTV-S⁻ recipients, but after transplantation of the OMZhf-2 tumor a significantly higher percentage of transplanted tumors was found in the C3Hf mice than in the C3H/He mice. In the case of the other two tumors no significant differences were found in the percentage of successfully transplanted tumors or in the duration of the mean latent period between the MTV-S⁺ or S⁻ recipients. Infection of the recipients at an early age with Bittner virus thus did not lead to more rapid growth of the transplanted tumors arising in the MTV-S⁻ mice.

The results of the experiments of series II are given in Table 2. Early thymectomy on C3H/He (MTV-S⁺) mice had no inhibitory action on the rate of growth of the transplanted mammary gland tumors arising in MTV-S⁻ mice of the C3Hf strain. In C3Hf (S⁻) mice early thymectomy likewise did not affect the rate of growth of the transplanted S⁻ tumor of the C3Hf mice. Both the percentage of successfully transplanted tumors (or the mean latent period) and the mean weight of the tumor at the end of the experiment were in fact the same in the thymectomized and intact recipients.

The results thus indicate that the more rapid growth of the tumor in the MTV-S⁺ mice and its delay after early thymectomy were connected with the immunological response to virus-

induced tumor antigens. Infection of the mice immediately after birth with Bittner virus specifically altered the immunological response to virus-induced antigens. These changes evidently consisted essentially of the development of immunostimulation of virus-transformed cells or of distortion of the immune response as in the enhancement phenomenon. Early thymectomy, with its immunodepressive action, reduced this immune response to virus-induced antigens of the tumor cells. When the tumor appeared in factorless mice and evidently contained no virus-induced antigens, thymectomy had no effect on its growth in either the MTV-S⁺ or the MTV-S⁻ recipients.

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CARCINOGENIC ACTION OF DIETHYLSTILBESTROL ON FROGS

V. V. Khudolei and V. S. Ermoshchenkov

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Diethylstilbestrol in a dose of 480-4400 µg, injected subcutaneously into frogs (*Rana temporaria*), gave rise to hemocytoblastosis and hepatocellular carcinoma in eight of the 38 animals (21%) after 15.6 weeks.

KEY WORDS: diethylstilbestrol; frogs; hemocytoblastosis; hepatocellular carcinoma.

It is now firmly established that dyshormonal disturbances play an important role in the genesis of some tumors of man and animals. Large doses of estrogens, given *in vivo*, give rise to various neoplastic changes [6]. In the context of comparative oncological investigations in the laboratory, the study of the sensitivity of lower vertebrates to the carcinogenic action of hormones is of particular interest. Diethylstilbestrol, if given to trout with the food, is known to induce hepatomas in these fish [5]. No such investigations have been carried out on amphibians.

The object of this investigation was to study the action of diethylstilbestrol propionate on *Tana temporaria*.

EXPERIMENTAL METHOD

Experiments were carried out on tailless amphibians (*Rana temporaria*) of both sexes aged 1-1.5 years. For the duration of the tests 98 (46 female and 52 male) experimental animals

Laboratory of Chemical Carcinogenic Agents, N. N. Petrov Research Institute of Oncology, Ministry of Health of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR L. M. Shabad.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 81, No. 6, pp. 723-724, June, 1976. Original article submitted December 1, 1975.

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