

CHANGES IN PRODUCTION OF GONADOTROPIC  
HORMONES AND ANDROGENS  
DURING EXPERIMENTAL REPRODUCTION  
OF TUMORS OF THE TESTIS

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An increase in the content of follicle-stimulating and luteinizing hormones in the pituitary and of 17-ketosteroids in the urine was found in experiments on rats and guinea pigs during the experimental reproduction of tumors of the testis by intratesticular injections of dimethylbenzanthracene, methylcholanthrene, and emulsions of zinc sulfate and copper sulfate. Against the background of an excess of gonadotropins and androgens in the animal (in cases of cryptorchidism, administration of testosterone propionate) exposure to the carcinogens led to the more frequent development of tumors of the testis.

A definite role of hormones in the genesis of tumors of the testis has been stipulated [1, 2, 5, 6, 8], but the dynamics of the gonadotropin and androgen levels during the development of testicular tumors have not been investigated.

The present investigation was carried out for this purpose.

## EXPERIMENTAL METHOD

Experiments were carried out on 97 sexually mature noninbred rats and 94 guinea pigs. The experimental animals received a single intratesticular injection of dimethylbenzanthracene (DMBA), methylcholanthrene (MC), astringent emulsions of zinc and copper sulfates, and also these emulsions after the operative production of cryptorchidism or in conjunction with injections of testosterone propionate. The number of animals and the experimental conditions are shown in Table 1. The carcinogens and astringent emulsions were injected into the right testis after surgical exteriorization. A 1% solution of testosterone propionate (0.02 ml) was injected subcutaneously once every two weeks. Cryptorchidism was produced by the usual method [3]. The tumors were investigated morphologically. The content of gonadotropic hormones in the pituitary and of total 17-ketosteroids in the urine was determined at intervals [10]. A homogenate of the pituitary gland of the experimental animal in physiological saline was injected subcutaneously into infantile male mice in a dose of 0.2 ml daily for three days. The mice were sacrificed 72 h after the beginning of the injections, and the testes with the prostate and seminal vesicles were weighed. The content of follicle-stimulating hormone (FSH) was estimated from the increase in weight of the testes [4], while the content of luteinizing hormone (LH) was estimated from the increase in weight of the seminal vesicles and prostate of the mice [3, 7, 9].

## EXPERIMENTAL RESULTS

A single injection of the carcinogens and astringent emulsions into the testis usually led to atrophy and deformation of the gland, while in some animals proliferative changes and tumors developed. When DMBA was given, proliferation of the spermatogenic epithelium was observed in five of the 25 (20%) rats,

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TABLE 1. Content of Gonadotropins in Pituitary and of Total Neutral 17-Ketosteroids in Urine of Animals with Tumors in the Testis ( $M \pm m$ )

Experimental conditions	Number of animals		Content of LH in pituitary (increase in weight of prostate and seminal vesicles, in mg)	FSH (increase in weight of testis, in mg)	Content of total 17-ketosteroids in urine (in mg/day)
	in experiment	with tumors			
2.5 mg DMBA in 0.5 ml apricot oil	25 rats	3 (12%)	$18.7 \pm 1.18$	$96.67 \pm 20.8$	$0.044 \pm 0.004$
2.5 mg MC in 0.05 ml apricot oil	40 »	2 (5%)	$13.3 \pm 0.19$	$99 \pm 1.0$	$0.065 \pm 0.012$
10% sol. of $ZnSO_4$ in 1.5% sol. formalin and apricot oil (0.05 ml)	21 guinea pigs	8 (38%)*	$13.73 \pm 0.013$	$83.5 \pm 5.67$	$0.113 \pm 0.009$
5% sol. of $CuSO_4$ in 1.5% sol. formalin and apricot oil (0.05 ml)	20 guinea pigs	5 (25%)*	$13.63 \pm 0.042$	$84.17 \pm 4.5$	$0.177 \pm 0.01$
Cryptorchidism	22 rats	1	16	74	0.049
10% sol. $ZnSO_4$ in 1.5% formalin sol. and oil (0.05 ml)	14 guinea pigs	3 (21.4%)	$17 \pm 0.81$	$101 \pm 8.24$	$0.231 \pm 0.06$
5% sol. $CuSO_4$ in 1.5% sol. formalin and oil (0.05 ml) and testosterone propionate	18 »	1	14.2	95	$0.19 \pm 0.028$
5% sol. of $CuSO_4$ in 1.5% sol. of formalin and oil (0.05 ml) and cryptorchidism	11 »	3 (27.2%)	$15.5 \pm 0.4$	$130 \pm 9.21$	$0.245 \pm 0.05$
Intact	10 rats	—	$5.82 \pm 0.62$	$35.28 \pm 5.24$	$0.024 \pm 0.005$
	10 guinea pigs	—	$9.77 \pm 0.64$	$43.07 \pm 15.93$	$0.13 \pm 0.035$

\* Only proliferation changes observed in the testis.

while tumors (teratoma and sarcoma) were found in three (12%) animals. Injection of MC caused proliferation in seven of the 40 (17.5%) experimental rats, while tumors (teratoma and sarcoma) developed in two animals. After injection of the astringent emulsion of zinc sulfate, proliferation of the spermatogenic and interstitial cells took place in eight of 21 (38%) guinea pigs, while after injection of copper sulfate emulsion these changes developed in five of the 20 (25%) guinea pigs. No tumors were found after injection of the astringent emulsions.

In the animals with precancerous and cancerous changes in the testis there was some increase in the content of gonadotropic hormones (FSH and LH) in the pituitary and of total 17-ketosteroids in the urine (Table 1). It is important to emphasize that these changes occurred long (in the 3rd-5th week of the experiment) before the appearance of the first tumor (in the 7th-27th week of the experiment). This suggests that the change in the content of gonadotropins and androgens plays an important role in the development of neoplasms.

To assess the effect of increased production of gonadotropins and androgens on the development of testicular tumors, experiments were carried out in which cryptorchidism was produced and injections of testosterone propionate were given in association with the action of the astringent emulsion. The starting point of these investigations was the fact that atrophy of the testis due to cryptorchidism leads to increased production of gonadotropins by the pituitary and of androgens by the opposite testis and adrenals. The combined use of the astringent emulsions and testosterone propionate or injection of these emulsions into animals with cryptorchidism should also have increased the hormonal changes and led to the more frequent development of tumors than when these factors were used separately.

As was to be expected, cryptorchidism was accompanied by an increase in the FSH and LH levels in the pituitary and by some increase in the concentration of 17-ketosteroids in the urine. One rat developed a tumor of the interstitial tissue of the testis; atrophy of the testis was observed in most animals. Hormonal stimulation in conjunction with the action of the astringent emulsions also increased the production of gonadotropins and androgens, and by a greater degree than administration of the astringent emulsions only. In the animals of the corresponding groups proliferative changes and neoplastic growth of the spermatogenic and interstitial cells of the testis were observed. Injection of zinc sulfate emulsion in conjunction with testosterone propionate led to the development of a tumor of the testis (two teratomas and one tumor from the interstitial cells) in three of the 14 guinea pigs. When copper sulfate emulsion was injected with testosterone propionate, one of the 18 animals developed a teratoma. Injection of copper sulfate into animals

with cryptorchidism of the same testis caused the development of a tumor (two teratomas and a tumor from the interstitial cells) in three of the 11 (27.2%) guinea pigs.

It can accordingly be concluded that the development of malignant diseases of the testis is accompanied by increased production of gonadotropins and androgens, and that this promotes the proliferative and neoplastic changes in the testis.

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