EFFECT OF AN EXTRACT TAKEN FROM A MAMMARY GLAND TUMOR ON FOLLICLE-STIMULATING FUNCTION OF THE RAT PITUITARY

(UDC 612.433.62-06 : 618.19-006-018]-08)

I. O. Smirnova and V. I. Samoilov

Laboratory of Experimental Hormone Therapy (Head—Candidate of Biological Sciences N. I. Lazarev), Institute of Experimental and Clinical Oncology (Director—Member of the Academy of Medical Sciences USSR, Professor N. N. Blokhin), Academy of Medical Sciences USSR, Moscow

(Presented by Member of the Academy of Medical Sciences USSR A. D. Timofeevskii)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 59, No. 4, pp. 92-94, April, 1965
Original article submitted September 11, 1963

It has been established in a number of investigations that as a result of the injection of aqueous salt extract from cancerous tissue of mammary glands into mice of low-cancer lines, they develop malignant tumors of the mammary glands [3, 4, 6].

According to the data of the Laboratory of Experimental Hormone Therapy, the appearance of cancer of the mammary glands necessitates prolonged and continuous influence of simultaneously introduced estrogens and follicle-stimulating hormone (FSH) [2]; the latter is the deciding factor in the appearance of proliferative processes in the mammary gland [5].

In the light of these data, it was natural to assume that the carcinogenic effect of an extract from cancerous tissue reduces to the fact that this extract produces hyperfunction of FSH (this leads to an increase in the estrogen level). At the same time, a prolonged increase in the estrogen and FSH levels gives rise first to hyperplasia, and then to mastopathy and cancer of the mammary gland.

The purpose of this work was to elucidate the question of whether an extract from cancerous tissue of the mammary gland can stimulate the manufacture of follicle-stimulating hormone.

EXPERIMENTAL PROCEDURE

The scheme of the experiment was the following. Newborn rats received injections of extracts prepared from transplanted tissue of cancer of the mammary glands of RMK-1 rats, obtained according to the methods used in such investigations. As the standard of the amount of substance injected into one animal, we took the protein content in the first extract that we obtained, which in all experiments was equal to 1.28 mg.

A total of 22 litters of noninbred rats were used in the experiments. The control and experimental groups were made up in such a way that to each female or male (experimental) that received the extract, no less than one female or male in the same litter, which received injections of physiologic solution (control), corresponded. The experimental animals of the first group received injections of an extract from transplanted tissue of cancer of the mammary gland of a rat of the 28th generation twice—on the sixth and eighth days of life. According to N. N. Medvedev's recommendation [4], half the single dose of the extract was injected under the skin of the side surface of the rat, and then, without removing the needle, it was moved into the abdominal cavity, into which the remainder of the inoculum was injected. Under conditions of increased FSH production, the appearance of pretumoral changes in the mammary glands might have been expected at the period of the onset of sexual maturation (after two to three months), although the appearance of tumors should have occurred far later. Hence, two months after the last injection the animals were killed, and the follicle-stimulating activity of the anterior lobe of the pituitary was determined (according to the increase in weight of the uteri of sexually immature mice). We consider the justification of the use of this method to determine the FSH content in the pituitary to be demonstrated by studies conducted in the Laboratory of Experimental Hormone Therapy [1].

Results of the Influence of Water-Salt Extract from RMK-1 Tissue of the 28th Generation on the FSH Content in the Rat Pituitary

Sex	Influence	Body weight (in g)	Weight of organs (in mg)			FSH content in the pituitary
			adrenals	uterus *	ventral prostate	
♀	Physiologic solution	105±5	37,5±7,9	96±28	—	0,97
	Extract	111±9	44,7±8,3	202±30	—	1,62
♂	Physiologic solution	118±10	36,6±6,3	—	92	3,52
	Extract	124±13	37,0±9,5	—	134	2,20

*The difference between the experimental and control groups is reliable at P = 0.025.

EXPERIMENTAL RESULTS

The FSH content in the pituitaries of the experimental females proved increased in comparison with its level in the control animals (see table). The injection of the extract produced a distinct increase in the weight of the uterus in the experimental females in comparison with the control, from 96 ± 28 to 202 ± 30 mg; this difference was also noted in a comparison of the control and experimental animals within each litter and proved reliable when the data were summed for all 7 litters used in this experiment (P = 0.025). The body weight, as well as the weight of the adrenals in the females varied negligibly under the influence of the extract (see table).

In the males, under the influence of injection of the extract, there was a decrease in the FSH content in the pituitary during the experiment. The weight of the ventral prostate in the experimental males rose in comparison with the controls. The body weight of the experimental males was somewhat higher than in the control, while the weight of the adrenals did not differ.

The absence of any distinct differences in the body weight and adrenals in the animals of the control and experimental groups indicates that the detected changes in the endocrine organs evidently are not related to exhaustion of the animals or to stress reactions and may be considered as specific.

In the experiment described, we attempted to introduce still another control group of animals, which was injected with an extract from tissue of a hyperplastic mammary gland of a rat at the last week of pregnancy. We should mention that in the extracted tissues of the hyperplastic mammary gland, a pronounced secretion was observed; this may also have been the cause of the toxicity of the preparation: 48 out of 60 animals (80%) died as a result of this injection during the first week. The injection of tissue of an extract from RMK-1 of the 24th generation proved just as toxic. This tissue at the twelfth generation was subjected to deep freezing and was kept in this state for half a year, after which the transplants were renewed. It is interesting that secretory phenomena were pronounced in the tissue of this tumor also, an extract from which also proved toxic (47 out of 63 baby rats died, i.e., 75%). Our investigations established that the FHS content in the pituitaries of 7 females that received an extract of tissue of hyperplastic nontumoral mammary gland was not increased.

From the data obtained it follows that an aqueous salt extract from tissue of a malignantly degenerated mammary gland leads to an increase in the FSH content in the pituitary under the condition of two influences of it on female newborn rats. This confirms the hypothesis advanced above, on the possibility of influence of an extract from the mammary glands of humans suffering from cancer on the process of development of malignant tumors of the mammary glands in mice. In this case, the extract evidently stimulates the production of estrogens, while prolonged increased manufacture of FSH and estrogens causes the development of cancer of the mammary glands.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.