HYPOPHYSEAL INHIBITORS. THE EFFECT OF SYGETIN ON UTERINE DEVELOPMENT IN THE SEXUALLY IMMATURE MOUSE

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In our previous research [1] it was shown that in the course of physiological aging in women a period is observed which is characterized by increased activity of several divisions of the diencephalohypophyseal system.

This condition leads to an increase with advancing age of hypercholesteremia, of adiposis and of the incidence of hypertension, diabetes mellitus and certain other pathological disorders. The increased activity of the diencephalohypophyseal system is also of definite importance in the course of carcinoma of the breast, which is shown in particular by the possible therapeutic effects of estrogens, in spite of the increase which they cause in the proliferative processes in the breast. An increase in the activity of the diencephalon also lies at the basis of the development of the menopause and of the period which precedes it, of persistence of follicles developing as the result of excessive secretion of the follicle-stimulating hormone of the hypophysis [1].

These findings made it imperative to investigate the possibility of depression of the increased diencephalo-hypophyseal activity. Sex hormones – mainly the estrogens – are at the present time among the most active measures in this direction. The presence of marked peripheral effects, however, makes their clinical use much more difficult. The separation of the central effect of the estrogens and their specific estrogenic action is of great importance in this respect. Dodds [4] considers that such a separation is impossible. With the development of p-oxypropiophenone [3], however, in which the central action is retained but the estrogenic action is considerably weakened, this view must be altered.

EXPERIMENTAL METHOD AND RESULTS

In view of the above, we studied the action of sygetin, an analog of synestrol prepared by S. F. Torf and N. V. Khromov-Borisov.

This substance was put forward as a water-soluble estrogen and was tested in accordance with the usual methods of administration of the estrogens [2].

In order to determine the relationship between the central and estrogenic effects, we administered sygetin to sexually immature female white mice (weighing 7.0-9.0 g) for 3 weeks, i.e., for the period during which sexual maturation was observed to be completed in the control group. We regarded the preservation of the infantilism of the sexual organs, as judged by the weight of the uterus, as an index of the depression of the gonadotropic function of the hypophysis,

The following results were obtained. Sygetin in a dose of 100-200 γ/day, given in the form of two subcutaneous injections, totally inhibited sexual maturation (Table 1, see figure).

TABLE 1

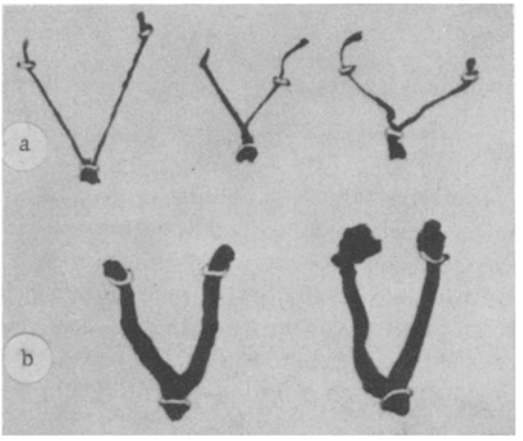
The Effect of Administration of Sygetin on Uterine Development in Mice

Serial No.	Duration of observations	Daily dose (in γ)	Weight of uterus (in mg)	
			Experiment	Control
1	From 11/23/57 to 12/13/57	20	13,6	36,0
2		20	10,1	23,0
3		20	42,2	—
4	From 2/27/58 to 3/21/58	100	9,0	85,0
5		100	10,5	24,0
6		100	5,5	88,0
7	From 6/23/58 to 7/16/58	200	8,5	60,0
8		200	9,0	78,0
9		200	8,0	—
Mean results, not counting those relating to No. 3			9,3	56,2

TABLE 2

The Effect of Implantation of Tablets Containing 5 mg of Sygetin on Uterine Development in Mice

Duration of observations (in days)	Weight of uterus (in mg)	
	Experiment	Control
19	7,0	55,0
19	10,0	60,0
20	5,0	45,0
20	9,0	58,0
20	7,0	—
30	12,0	—
30	10,0	—
35	14,0	—
39	45,0	100,0
44	47,0	



Delay in the development of the uterus in mice by sygetin. a) In six-week-old mice, receiving the preparation; b) in control animals of the same age.

The action of the preparation was also shown when given by implantation of cholesterol-lanolin tablets containing 15% sygetin (5 mg), and in these conditions, moreover, restoration of the gonadotropic function was observed after complete absorption of the tablet (on the 5th-7th week)(Table 2).

Sygetin, synthesized as a water-soluble estrogen, is thus a drug in which the central action (depression of gonadotropins) takes place in doses which have no estrogenic effect.

SUMMARY

In connection with the study of the role played by the increase of diencephalohypophyseal activity with age in the development of a series of pathological processes, the author investigated the effect of sygetin on the sexual maturation of mice. It was demonstrated that sygetin is a diencephalohypophyseal inhibitor.

LITERATURE CITED

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