

EFFECT OF THYROID HORMONES ON HYDROCORTISONE - TRANSCORTIN COMPLEX FORMATION IN GONADECTOMIZED GUINEA PIGS

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Gonadectomy in male guinea pigs is followed by a marked increase in the binding power of transcortin 3 weeks after the operation, whereas in females this index at the same period is indistinguishable from normal. Administration of thyroid from the 11th to the 22nd days inclusive after the operation to castrated animals of both sexes does not produce a significant increase in the binding level.

Studies of binding of hydrocortisone (H) by transcortin in guinea pigs have shown [2] that administration of thyroid is followed by a persistent increase in the binding power of the plasma in males but a decrease in females. According to the literature, estrogens in man and other biological species stimulate the formation of corticosteroid-binding globulin (CBG), while testosterone inhibits this process [1, 11].

Since an increase in the concentration of thyroid hormones in the body modifies activity of the gonads [6, 8, 9], in the present investigation the effect of thyroid on H-binding with transcortin was studied in castrated guinea pigs of both sexes.

EXPERIMENTAL METHOD

Experiments were carried out on 93 male and 52 female guinea pigs weighing 280-350 g. Gonadectomy was performed under ether anesthesia. Completeness of removal of the gonads was verified post mortem. Ten days after castration, administration of thyroid as a suspension in carrot juice to the animals was commenced [2]. Control guinea pigs received carrot juice only by mouth. The animals were sacrificed 3 days (total dose of thyroid 0.6 g), 7 days (total dose 2.4 g), and 12 days (total dose 4.3 g) after the beginning of thyroid administration. In addition, in a special series of experiments on females receiving thyroid for 12 days, on the last 4 days the animals received estradiol by subcutaneous injection in a daily dose of 500 μ g. The control for this group consisted of castrated males receiving injections of the same dose of estradiol. The adrenals of all control and experimental guinea pigs were weighed. The concentration of 17-hydroxycorticosteroids (17-HCS) was determined in the blood plasma of the decapitated animals by the Porter-Silber method in the modification of Yudaev and Pankov [3], and the binding power of transcortin was determined by a modification of De Moor's gel-filtration method [4].

EXPERIMENTAL RESULTS

The binding power of transcortin in male guinea pigs was considerably increased on the 14th day after castration ($P < 0.001$), and it remained at the same level until the 23rd day after castration. In females, on the 14th day after gonadectomy, the binding power of transcortin was reduced ($P < 0.01$), but later it returned to normal (18th and 23rd days after the operation; $P > 0.5$; Fig. 1).

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TABLE 1. Plasma 17-HCS Concentration and Weight of Adrenals in Castrated Guinea Pigs Receiving Thyroid ($M \pm m$)

Sex of animals	Duration of experiment					
	3 days					
	control			experiment		
	17-HCS (in $\mu\text{g } \%$)	wt. of adrenals		17-HCS (in $\mu\text{g } \%$)	wt. of adrenals	
		absolute (in mg)	relative, in mg/100 g body wt.		absolute (in mg)	relative, in mg/100 g body wt.
Females <i>n</i>	79.4 \pm 10.3 8	151.8 \pm 4.9 8	48.1 \pm 2.2 8	124.7 \pm 8.3 10	164.9 \pm 10.4 10	65.2 \pm 5.1 10
Males <i>n</i>	117.5 \pm 11.4 9	117.1 \pm 5.2 10	44.0 \pm 2.2 10	134.1 \pm 18.5 11	123.5 \pm 7.4 11	48.4 \pm 3.6 11

Sex of animals	Duration of experiment					
	7 days					
	control			experiment		
	17-HCS (in $\mu\text{g } \%$)	wt. of adrenals		17-HCS (in $\mu\text{g } \%$)	wt. of adrenals	
		absolute (in mg)	relative, in mg/100 g body wt.		absolute (in mg)	relative, in mg/100 g body wt.
Females <i>n</i>	46.7 \pm 5.6 7	152.5 \pm 4.4 8	44.6 \pm 1.5 8	56.4 \pm 4.6 9	162.9 \pm 4.2 9	58.5 \pm 1.8 9
Males <i>n</i>	104.5 \pm 12.8 8	157.7 \pm 10.4 9	47.7 \pm 3.6 9	145.1 \pm 13.1 9	171.0 \pm 6.3 9	64.7 \pm 2.9 9

Sex of animals	Duration of experiment					
	12 days					
	control			experiment		
	17-HCS (in $\mu\text{g } \%$)	wt. of adrenals		17-HCS (in $\mu\text{g } \%$)	wt. of adrenals	
		absolute (in mg)	relative in mg/100 g body wt.		absolute (in mg)	relative, in mg/100 g body wt.
Females <i>n</i>	77.2 \pm 4.3 7	153.9 \pm 7.5 8	46.3 \pm 4.4 8	129.8 \pm 18.3 11	198.1 \pm 5.6 11	84.7 \pm 3.5 11
Males <i>n</i>	50.6 \pm 8.2 15	168.9 \pm 6.6 7	52.7 \pm 3.8 7	146.8 \pm 18.6 18	174.1 \pm 9.7 7	70.3 \pm 4.8 7

Administration of thyroid (Fig. 2) to males led to a gradual decrease in the binding activity of the protein ($P < 0.05$, 7 days after, and $P < 0.001$, 12 days after the beginning of thyroid administration). In females a very small increase ($P > 0.1$) in CBG activity was observed after administration of thyroid for 3 days, while after 7 and 12 days the level of H-binding with transcortin was reduced ($P < 0.001$ and $P < 0.01$ respectively). Meanwhile, in castrated animals (especially males), the plasma 17-HCS concentration was increased. Administration of thyroid to the castrated animals (Table 1) led to further increase in the 17-HCS concentration and to an increase in the relative weight of the adrenals ($P < 0.02$).

Administration of estradiol to the castrated females, whether receiving thyroid or not, sharply reduced the CBG activity ($P < 0.001$).

The conflicting nature of the data relating to adrenocortical function after gonadectomy in the animals of the two sexes was evidently due to the time elapsing after the operation [12] and to species-specific differences [5].

It will be noted that in female guinea pigs the binding power of transcortin, which was reduced 2 weeks after the operation, subsequently returned to normal, whereas in males it remained high. The reasons for

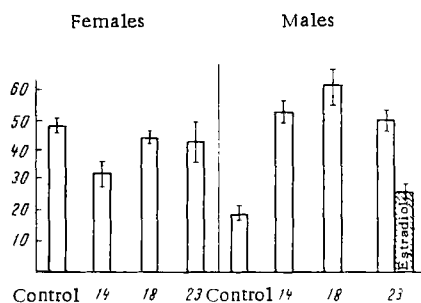


Fig. 1. Effect of gonadectomy on binding power of transcortin. Abscissa, days after gonadectomy; ordinate, binding power of transcortin (in $\mu\text{g}\%$).

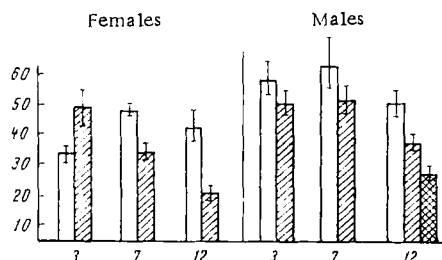


Fig. 2. Binding power of transcortin in gonadectomized guinea pigs during thyroid administration. Unshaded columns denote castrated animals; obliquely shaded columns, animals receiving thyroid; cross-hatched columns, animals receiving thyroid + estradiol. Abscissa, days of thyroid administration; ordinate, binding power of transcortin (in $\mu\text{g}\%$).

the change in CBG activity in castrated animals have received little study. Diamond et al. [7] found a marked increase in the level of H-binding with the plasma proteins of the blood 3 months after gonadectomy in both female and male guinea pigs. The comparison of these data with the present findings suggests that the view that sex hormones have an inhibitory or stimulant action on transcortin formation is purely arbitrary. This is shown, in the writers' opinion, by the decrease in CBG activity in castrated males after administration of estradiol. It may be that the effect of sex hormones depends, not on their absolute concentrations, but on their relative concentrations.

In addition, other endocrine factors, whose activity may be modified after castration, may also participate in the action of sex hormones on transcortin formation.

As mentioned above, in intact male guinea pigs receiving thyroid the level of H-binding with transcortin rose considerably with effect from the fourth day of administration. In intact females, the binding activity of transcortin was not increased at any time during the first 12 days. In the present investigation on gonadectomized animals of both sexes receiving thyroid, no significant increase in CBG activity likewise could be obtained. It can thus be concluded that thyroid hormones do not exert a direct stimulant action in guinea pigs on transcortin formation, a result which is not in agreement with the findings of Labrie et al. [10], who worked with rats. The changes in binding observed in guinea pigs receiving thyroid hormones evidently depend on the combined effect of hormones of various endocrine glands, in physiological equilibrium and interlinked with each other, and acting in a definite order. Changes in gonad function during administration of thyroid hormones to guinea pigs are among the mechanisms by which thyroid hormones may influence transcortin formation in the animals of this species.

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