CCVI. SIMULTANEOUS ADMINISTRATION OF TESTICULAR HORMONE WITH ANTUITRIN AND PROLAN OR WITH DESICCATED THYROID.

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It is now well known that gonad-stimulating hormones, extracted from the anterior lobe of the hypophysis, or from pregnancy urine, do not influence the secondary sexual organs of castrated animals, since these hormones produce their effects by stimulation of the internal secretion of the testes, or possibly by activation of testicular hormone.

We were unable to find any data in the literature about the action of thyroid hormone on the sexual organs of castrated animals, and as our own investigations on this subject are not yet completed, they will be published later elsewhere. They already show, however, that if there is any influence on the secondary sexual organs of castrated rats it is only slight.

The aim of the present experiments is to investigate whether there is any relationship between the action of testicular hormone, injected into castrated male rats, and that of the thyroid or the anterior lobe of the hypophysis, when introduced simultaneously. By performing these experiments on castrated animals the activity of living testicular cells was excluded. Therefore, any changes obtained differing from the effect of testicular hormone alone should be ascribed to the direct alteration of activity of testicular hormone caused by hormones of the anterior lobe of the hypophysis or of the thyroids.

Since in castrated animals both the latter glands are present, the introduction of an additional amount of the hormones of the anterior lobe or of the thyroid should result in a condition similar to that caused by hypersecretion of these glands.

Technique.

It is unnecessary to discuss here whether the gonad-stimulating substances extracted from urine are completely identical with the hormones of the anterior lobe of the pituitary; in any case their influence on sexual glands is very similar. The preparation from urine was chosen in the present experiments, since such preparations of good quality are much more easily obtained than those extracted from the anterior lobe. We have used "antuitrin S," prepared by Messrs Parke, Davis and Company, for 2 experiments and a mixture of antuitrin S and "prolan," prepared by Messrs Bayer Products Ltd., for 3 experiments (see Table I). These preparations were introduced subcutaneously. Preliminary experiments on young and adult normal male rats have shown that both antuitrin and prolan were very active on the sexual organs in the doses used. As the source of thyroid hormone, desiccated thyroid gland, prepared by Messrs The British Drug Houses Ltd., was given. Each dose of thyroid powder was mixed with about

0.5 g. of wheat germ, moistened with water and given to the rats in small pellets before food; this mixture was greedily consumed in a few minutes. The amount of thyroid fed was calculated according to a special unit of body weight. The daily doses are given in Table I. A testicular hormone preparation, isolated from urine, and prepared and assayed on capons by Messrs Schering Ltd.¹ was used. Different batches of this preparation were used for the various experiments, as it was only supplied in comparatively small quantities at a time. We have not re-assayed the testicular preparations in rat units and in Table I the daily dose is stated in capon units as assayed by Messrs Schering Ltd. Different doses of testicular preparation were given to the rats of different litters (see Tables I and II). The daily doses of testicular and gonad-stimulating hormones were

Table I. *Daily dose of hormones; age and average weight of the castrated rats in each group of each litter.*

No. of litter	Daily dose of hormones				No. of rats in litter	Age in days		No. of days after castration at beginning of injections	Final weight of rats		
	Testicular c.u.	Antuitrin S R.U.	Antuitrin S + prolan R.U.	Thyroid in mg. per g. of body weight		At castration	When injections started		Receiving hormone		
									Control group	Testicular	Testicular + others
1	2.5	60	—	—	5	26	48	22	175	206	206
2	2.5	60	—	—	5	23	45	22	182	202	194
3	5.0	—	74	—	5	30	52	22	242	219	213
4	?	—	74	—	4	23	65	42	267	270	270
5	5.0	—	74	—	5	30	151	121	430	382	386
6	1.25	—	—	} 1 mg./10g.	8	27	47	20	207	218	207
7	1.25	—	—		4	23	43	20	—	154	152
8	2.5	—	—	} 1 mg./20 to 100g.	3	24	99	75	242	276	258
9	2.5	—	—		3	26	94	68	289	267	315
10	2.5	—	—		4	26	94	68	312	306	291

Table II. *Average percentage increase for each litter in weight of prostate with seminal vesicles in the group of rats injected with different batches of testicular hormone as compared with that of control uninjected rats.*

No. of batch	Daily dose of c.u. injected	No. of litter	% increase in weight of prostate + sem. vesicles
A. 12	1.25	6	123.0
	1.25	7	No control uninjected rats
	2.5	1	269.5
	2.5	2	204.6
76.4	2.5	8	232.7
	2.5	9	212.0
	2.5	10	211.5
10. 32. 1.	5.0	5	481.0
	5.0	3	173.3
Not marked	?	4	532.0

injected twice a day in half doses, each hormone being injected separately. 24 rats, belonging to 5 litters, were used for the experiments with antuitrin S or prolan and testicular hormone; and 22 rats, belonging to 5 other litters, were used for the experiment with thyroid and testicular hormone. Each litter except No. 7 was divided into 3 groups: Group I, control, untreated rats; Group II, rats injected with testicular hormone only; Group III, rats injected with the same dose of testicular hormone as group II and given in addition antuitrin S

¹ We wish to express our thanks to Messrs Schering Ltd., Messrs Parke Davis and Company and Messrs Bayer Products Ltd. for kindly supplying the preparations.

or antuitrin S and prolan, or thyroid (see Table I). Litter 7, consisting of 4 rats, was divided into two groups only, namely, II and III, without a group of control, untreated rats.

The injections of testicular hormone, antuitrin S and prolan, were all given for 10 consecutive days, but the thyroid-fed rats were given thyroid doses not only during these 10 days of injection but also for 7 days (litters Nos. 6 and 7) or 9 days (litters Nos. 8, 9 and 10) previously, making the total period of thyroid feeding 17 to 19 days. This was done to make the effect of thyroid administration more marked. To save space in Tables II and III only the percentage changes are summarised.

Table III. *Average percentage changes for each litter in weight of organs (calculated per 200 g. of body weight) and in final weight of rats in the group of rats receiving besides testicular hormone other hormones, as compared with that of the group of rats receiving testicular hormone alone.*

No. of litter	Retro-peritoneal fat	Prostate and seminal vesicles	Penis	Adrenals	Thyroid	Hypophysis	Thymus	Liver	Kidney	Spleen	Heart	Final weight of rats
Testicular hormone and antuitrin S or antuitrin S with prolan.												
1	- 2.9	+ 9.0	- 1.6	- 1.4	- 6.9	+ 6.0	+29.4	- 0.5	+ 0.9	+15.6	- 5.1	± 0
2	-19.6	+48.3	+13.1	+ 8.9	+ 6.7	- 3.8	- 3.2	- 3.9	+12.5	+22.5	+ 8.5	- 4.0
3	-13.5	+40.9	+ 6.4	+ 9.0	+10.7	- 2.1	- 9.2	-18.1	- 0.9	+ 8.0	+ 5.8	- 2.7
4	- 3.3	+10.7	+17.7	+ 3.9	-10.1	- 7.4	-16.3	- 0.7	- 2.0	+20.7	- 4.3	± 0
Average	- 9.8	+27.2	+ 8.9	+ 5.1	+ 0.1	- 1.8	- 0.2	- 5.8	- 2.6	+16.7	+ 1.2	- 1.7
5	+ 1.8	-24.6	+ 3.3	- 8.5	+ 6.8	-19.0	- 9.9	- 7.6	- 2.3	-12.1	-11.9	+ 1.0
Testicular hormone and thyroid powder.												
6	-17.5	- 5.6	- 0.8	+17.0	-23.5	+13.5	- 9.6	+ 6.8	+27.3	+47.2	+50.6	- 5.0
7	-57.0	- 7.1	+ 3.2	+31.8	-28.8	+10.3	+23.7	+17.1	+35.5	+54.5	+44.9	- 1.3
Average	-37.3	- 6.4	+ 1.2	+24.4	-26.2	+11.9	+ 7.1	+12.0	+31.4	+50.9	+47.8	- 3.2
8	-22.6	- 2.0	-12.0	+ 8.9	-11.7	+15.9	+34.0	+ 3.6	+11.2	+ 3.0	+ 7.6	- 6.5
9	- 6.6	+ 3.8	- 2.8	-23.9	-33.7	-26.6	-24.2	+ 2.5	+ 4.7	+12.4	+11.9	+18.0
10	+ 2.8	+ 5.1	- 3.7	- 2.1	+15.0	+14.5	+28.0	- 1.9	+ 2.8	- 1.4	+ 7.9	- 4.9
Average	- 8.8	+ 2.3	- 6.2	- 5.7	-10.1	+ 1.3	+12.6	+ 1.4	+ 6.2	+ 4.7	+ 9.1	+ 2.2

Simultaneous administration of testicular hormone with antuitrin S or with a mixture of antuitrin S and prolan.

This experiment was performed on litters 1 to 5 (Table I). The percentage increase in weight of the prostate with seminal vesicles in the group of rats injected with testicular hormone alone as compared with that of the control group of uninjected rats is shown in Table II (see litters 1 to 5). Different doses of different batches of this hormone produced an increase in weight of the prostate with seminal vesicles of from 123 to 532 %. As can be seen from Table III, in the rats receiving additional injections of antuitrin S or of antuitrin S and prolan, the effect of the testicular hormone was increased, taking an average of 4 litters of young rats, by 27.2 %, but in one litter of adult rats it was decreased by 24.6 %. The percentage increase reached 48.3 and 40.9 respectively, in litters 2 and 3, in two others it was very small.

Such slight and variable results indicate that in the absence of gonads the gonad-stimulating hormones used in our experiments did not influence the activity of the testicular hormone in a constant and pronounced way. From Table III it is also impossible to find a definite marked effect on the weight of the rats, on fat deposition or on the weight of the other organs investigated.

Simultaneous administration of testicular hormone with thyroid powder.

Litters 6 to 10 were used for this experiment (see Tables I, II and III). Litters 8 to 10 were given 1 mg. thyroid powder per 20 g. of body weight in the preliminary period of thyroid feeding, whilst during the period of simultaneous administration of hormones they were given a much smaller dose of 1 mg. per 100 g. of body weight. Litters 6 and 7 received a comparatively large dose, namely, 1 mg. per 10 g. of body weight during the whole period. We have, therefore, divided these 5 litters into two groups: litters 8-10 and litters 6-7. Only in the latter group receiving large doses were constant definite changes observed; as shown in Table III, these changes were a decrease in fat deposition and in the weight of the thyroids and an increase in the weight of the adrenals, liver, kidneys, spleen and heart. All these changes, however, are typical for rats fed with thyroid powder only; and from the results obtained it is possible only to conclude that testicular hormone injections did not counteract the effects of thyroid administration. The typical effect of testicular hormone on sexual organs was not in any way influenced by thyroid feeding (Table III). Smaller doses of thyroid only produced a much less noticeable thyroid effect and did not alter the effect on the sexual organs.

SUMMARY.

1. The effect of a testicular hormone preparation on the sexual, endocrine and other organs investigated of castrated male rats was not altered to a considerable extent by the additional administration of gonad-stimulating hormones extracted from urine or by feeding with desiccated thyroid powder in the doses given.
2. Testicular hormone preparation did not prevent the appearance of the typical changes produced by thyroid feeding, namely, a decrease in the fat deposition and in weight of thyroids and an increase in the weight of adrenals, liver, kidneys, spleen and heart.

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