CXIV. THE CO-OPERATIVE ACTIVITY OF TESTOSTERONE PROPIONATE WITH Δ^5 -ANDROSTENEDIOL AND WITH OESTRADIOL IN MALE RATS

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IN our previous papers we studied the effect on the organs of castrated rats of testosterone propionate injected alone [Korenchevsky *et al.* 1937, 2] and of Δ^5 -androstenediol injected alone and in combination with oestrone [Korenchevsky *et al.* 1937, 1]. Since the different male and female sexual compounds may be present simultaneously in the organism, in this paper we investigated the effects produced by the addition of androstenediol or oestradiol to testosterone propionate on the weights of the organs of castrated rats. The histological results will be published elsewhere.

Technique

The general technique was the same as that used in the two papers mentioned above. 36 male rats, castrated before sexual maturity, were used for the experiment. The average final age was 127 days and the period of injection was 19 consecutive days. 50 γ of testosterone propionate were injected 3 times a week, 30 γ of oestradiol were injected 4 times a week and 600 γ of androstenediol were injected daily. In selecting the doses the different strengths of action of the compounds on the sexual organs were taken into consideration in order that the results obtained might be clear and conclusive. The data obtained are summarized in Table I in which only the averages of the actual weights are given. All the organs examined in this experiment are included in the table.

The effect of testosterone propionate injected simultaneously with Δ^5 -androstenediol

Comparison of the figures in col. I with those in cols. II and III shows the effects of the injection of testosterone propionate and androstenediol alone.

In our previous experiment [Korenchevsky *et al.* 1937, 2, Table I, p. 477] the smallest dose (167 γ daily) of testosterone propionate was not so small as that used in the present experiment, but the changes in the sexual organs, adrenals, thymus and gain in body weight were of the same kind though greater in degree.

Since the dose of androstenediol used in the present experiment was the same as the larger dose (600 γ daily) used in the previous experiment [Korenchevsky *et al.* 1937, 1, Table III, p. 471] these two results are comparable. The effects on the sexual organs were about the same in the two experiments, but there were some differences in the changes in the adrenals (effect less in the present experiment), the thymus (effect greater), the fat deposition (no decrease) and the gain in body weight (no decrease), which differences are probably explained by the considerable difference between the ages of the rats used in the

Table I. *Effect on castrated male rats of testosterone propionate injected alone or in combination with androstenediol or oestradiol*

Organ	I Control rats	II Testo- sterone propionate 150 γ	III Andro- stenediol 4200 γ	Rats injected per week with			VI Oestra- diol 120 γ + testo- sterone propionate 150 γ
				Testo- sterone propionate 150 γ + andro- stenediol 4200 γ	IV Oestra- diol 120 γ	V Oestra- diol 120 γ	
Seminal vesicles (mg.)	12	113	40	196	40	141	
Prostate (mg.)	61	245	124	339	79	260	
Penis (mg.)	76	197	145	232	81	200	
Preputial glands (mg.)	57	111	128	172	71	93	
Adrenals (mg.)	80	67	71	69	94	88	
Thymus (mg.)	333	283	211	208	235	249	
Retroperitoneal fat (g.)	15.2	18.3	17.2	19.2	14.2	12.3	
Final body weight (g.)	324	355	337	370	305	296	
Gain (+) or loss (-) in body weight (g.)	+8	+28	+8	+20	-14	+1	
No. of rats in group	7	7	5	6	5	6	

previous (69 days) and present experiments (127 days) and between the respective periods after castration when injections were started.

The effect of simultaneous injections of testosterone propionate and androstenediol is shown in col. IV of Table I (present paper). These two hormones were found to have a co-operative action on the sexual organs, especially on the seminal vesicles, on which the effect was greater than would be given by summation of the effects of the two hormones.

An exactly similar kind of co-operation was previously noted in the case of testosterone and androstenedione [Korenchevsky *et al.* 1937, 1, p. 469, Table I, cols. VI, VIII and IX].

Effect of testosterone propionate injected simultaneously with oestradiol

Sexual organs. With a dose of 120 γ of oestradiol per week the appetite of both male and female rats decreases, the gain in body weight is checked (e.g. col. V, Table I, present paper) and in some rats a fall in body weight may even be observed. Thus taking into consideration that approximately the maximum physiological effect on the sexual organs is obtained with such a dose of oestradiol, this dose must be considered to be both large and on the limit of toxicity.

The effects of oestradiol and oestrone on the sexual and other organs have already been described in our previous papers [Korenchevsky & Dennison, 1934, 1, 2; 1935; Korenchevsky *et al.* 1936]. The chief change consists in an increase in the weight of the seminal vesicles (and of the coagulating gland which is weighed together with the seminal vesicles). This increase is chiefly due to the growth of the fibrous and muscular tissue in these organs. The increase in weight of the prostate is small and, whilst the weights of the penis and preputial glands may increase slightly, in most cases these two organs show no constant change in weight [e.g. Korenchevsky *et al.* 1936, Table IV, p. 565].

The effects of oestradiol shown in col. V of Table I in the present paper are in agreement with these observations. Whilst a definite increase in the weight of the seminal vesicles was obtained, the changes in the other sexual organs were small, especially when the variability in the weight of the preputial glands is

taken into consideration. This result is a striking contrast to effects of testosterone propionate (col. II) and androstenediol (col. III) both of which stimulated the development of all the sexual organs. The addition of oestradiol to testosterone propionate injections (col. VI) brought about a slight increase in the effect on the seminal vesicles, but no definite changes were seen in the effects on the other sexual organs (cf. cols. II and VI).

The co-operative effect on the male sexual organs of oestrone or oestradiol with some of the other male hormones has also been shown in our earlier papers (androsterone [Korenchevsky *et al.* 1935]; *transdehydroandrosterone* [Korenchevsky & Dennison, 1936]; testosterone [Korenchevsky *et al.* 1936]; urinary hormone concentrates [Korenchevsky & Dennison, 1934, 2]). This co-operative effect of oestrone on the male sexual organs was not seen, however, with androstenedione and androstenediol in the doses used [Korenchevsky *et al.* 1937, 1].

Other organs. After the injection of oestradiol alone or in combination with testosterone propionate the adrenals were found to be larger (cols. V and VI) than those of the rats injected with testosterone propionate alone (col. II). We have already described a similar "oestrone" effect on adrenals in the case of the simultaneous injection of oestrone with androsterone, with androstenedione and with androstenediol (see the papers mentioned above).

There was also a slight increase in the rate of involution of the thymus and a decrease in the gain in body weight when oestradiol and testosterone propionate were injected simultaneously. We had previously observed these results after the simultaneous injection of oestrone with androsterone and with testosterone.

SUMMARY

1. Experiments were performed on 36 castrated rats belonging to 7 litters in order to examine the effects of simultaneous injection of testosterone propionate with Δ^5 -androstenediol or oestradiol.
2. Co-operative activity between testosterone propionate and androstenediol was seen in the effects on all the sexual organs and on the thymus.
3. The addition of oestradiol to testosterone propionate, in the doses used, caused an increase in the weight of the seminal vesicles (slight) and of the adrenals (considerable), a decrease in the rate of involution of the thymus (slight) and in the gain in body weight (considerable).
4. The results obtained were compared with those of our previous experiments in which the other sexual hormones were examined.

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