

Changes in Body Weight of Normal and Castrated Rats by Different Doses of Testosterone Propionate.*† (24682)

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Ability of testosterone propionate to increase body weight of castrated rats fed constant amounts(1) or *ad lib.*(2) is well established. The normal adult rat when fed constant food intake also responds to testosterone propionate by increase in body weight(3) but when fed *ad lib.* shows an entirely different response. It loses body weight(4). In view of this difference in response between normal and castrated rats fed *ad lib.*, a study of the effect of various doses of testosterone propionate was undertaken.

Procedure. Male rats (Holtzman) were castrated at 110 g body weight (40 days old) and another similar age group kept as normals. Rats were kept in individual cages in air-conditioned room at 25.5-26.5°C. Their diet was: casein 900, sucrose (granulated sugar) 300, cellulour 100, yeast (Fleischmann's No. 2019) 500, hydrogenated vegetable oil (primex) 400, Wesson's salt mixture 200, cod liver oil (Patch's) 12, and 30% tocopherol mixture.‡ Amount of food eaten and body weights of rats were determined 3 times/week. Daily subcutaneous injections of testosterone propionate‡ were begun 35 days after castration. Androgen was diluted with sesame oil so that each daily dose was contained in 0.05 ml of oil. Normal and castrated control animals received injections of sesame oil.

Results. Two sets of experiments were performed. In the first (Fig. 1A, 2A), 0.025 to 0.1 mg/day of testosterone propionate were used and in the second (Fig. 1B, 2B), 0.1 to 2.5 mg/day. Number of rats in each experiment is indicated in footnotes of Fig. 1, 2.

Normal rats. Testosterone propionate ini-

tially produced a slightly greater gain in body weight (Fig. 1A, B) maintained at only lowest dose (0.025 mg/day). Other doses produced a decrease in rate of body weight gain. Onset and degree of decrease was related to dose. At end of experiment every group of androgen treated rats except those at lowest dose had body weights less than those of control rats. Maximum decrease was attained at dose of 0.5 mg/day (Fig. 3). Further increase in dose did not produce any greater loss in body weight. On cessation of injections, loss in body weight continued for about another week, then an increase occurred, most marked in animals that received the higher doses of androgen (Fig. 1B). Food intake was increased above that of controls, in rats at low dose levels (Fig. 1A) while that in high dose levels (Fig. 1B), was decreased for about 3 weeks, then gradually returned towards that of controls. On cessation of injections a noticeable increase in food intake occurred in rats which received more than 0.1 mg/day. Thus, food consumption of rats in the respective groups varied with changes in body weights.

Castrated rats. Testosterone propionate produced an increase in rate of body weight gain of castrated rats at every dose level (Fig. 2A, B). Maximum increase in body weight, however, became less at doses above 0.1 mg/day (Fig. 3). Continuation of androgen treatment, moreover, resulted in a decrease in rate of body weight gain in those animals receiving more than 0.1 mg/day. Onset and degree of decrease was related to dose of androgen (Fig. 2A, B, 3). The extent of change was such that rats receiving 0.5 and 1 mg/day lost the equivalent of practically all the stimulated increase in weight and rats at 2.5 mg/day had lost more than androgen-induced increase in body weight.

All groups except those at the 2 highest dose levels showed initially an increase in food intake which later changed in parallel with

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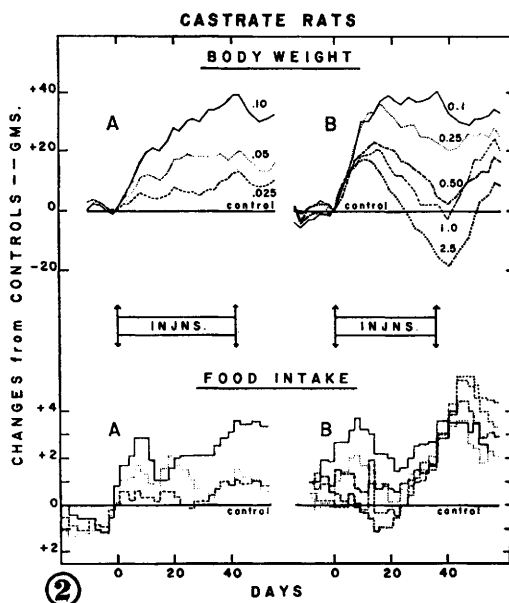
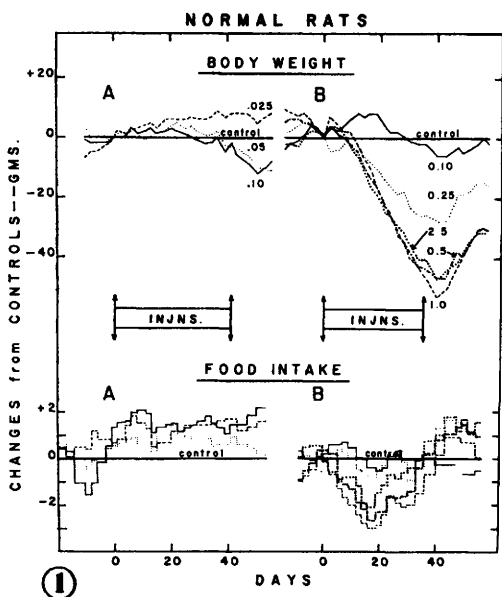


FIG. 1. Changes in body wt and food intake in normal rats inj. with various doses of testosterone propionate. Changes are from control rats which during inj. period gained 107 g in series A and 90 g in series B. Avg body wt at beginning of inj. were: Series A 301-315 g and series B 276-283 g per group. Series A contained 10 rats/group and series B, 5 to 8 rats/group. Dose of testosterone propionate (mg/day) is indicated beside body wt curves of respective groups.

FIG. 2. Changes in body wt and food intake in castrated rats inj. with various doses of testosterone propionate. Changes are from control rats which during inj. period gained 107 g in series A

maximum increases in body weight. After about 10 days food intakes returned toward control level, then increased again (Fig. 2A, B). Cessation of injections was followed within a few days by increase in food intake. This effect was most evident at higher dose levels.

Discussion. Testosterone propionate can inhibit body weight gain of both normal and castrated young adult rats. Inhibition, however, is preceded by an initial stimulation, slight and brief in normal rats, very marked in castrated rats. In both instances degree of stimulation is most evident at very low doses of androgen and becomes less at high dose levels.

The difference between normal and castrated rats seems to be due to metabolic status of the animals. When the castrated rat has been restored to normal state by exogenous androgen, it then shows the same or similar type of response in body weight and food intake as the normal rat. Thus, administration of excess androgen results in loss of body weight probably due to greater utilization of body fat in compensation for a decrease in food intake(*cf.* 4) and only a very slight inhibition of body growth(2,4). Thus, the changes represent not only protein-anabolic(1,2) but also fat-catabolic(2,4) action of the androgen.

The course of changes in body weight of castrated rats is very similar, indeed practically identical, to that of androgen-treated rats on a constant food intake(1). In both instances androgen produces an initial increase in body weight and with continued injection, a loss in body weight. Furthermore, this loss is accompanied by loss in body fat(2,4). The greater gain in body weight by rats fed *ad lib.* very likely is due to simultaneous increase in food intake. Thus, new tissue is formed not only through protein-anabolic action of the androgen but also to ingestion of extra food-stuffs. The initial gain in body weight of an-

and 77 in series B. Avg body wt at beginning of inj. were: Series A 254-260 g/group and series B 274-294 g/group. Series A contained 10 rats/group and series B 5 to 7 rats/group. Dose of testosterone propionate (mg/day) is indicated beside body wt curves of respective groups.

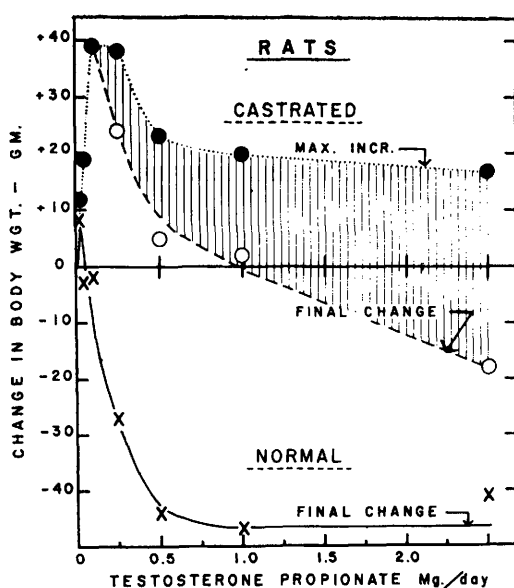


FIG. 3. Comparison of effect of dose of testosterone propionate on body wt of normal and castrated rats. See Fig. 1 and 2 for details.

drogen-treated normal rat fed *ad lib.* is much less than that of the normal rat on a constant food intake(3), and loss in body weight on continued injection is much greater.

Depression of normal body weight gain by testosterone propionate at doses above 0.1 mg/day in the growing castrated rat indicates that the physiological need of the rat is well below this level. Considerable stimulation was observed at the very low dose of 25 μ g/day. Body weight gain of immature normal rats also has been reported to be stimulated by

small doses(5,6,7) and depressed by large doses(6,8,9) of androgen. Other reports, however, indicated no effect(9,10,11) especially when low doses of androgen were administered.

Summary. Administration of testosterone propionate above physiological levels inhibits body weight gain of normal and castrated young adult rats. Inhibition in the normal rat appears in doses above 25 μ g/day and in castrated rats at above 100 μ g/day. In the castrated rat inhibition is preceded by increase in rate of body weight gain. Food consumption of both normal and castrated rats varied with changes in body weight.

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|| Large doses of testosterone propionate produce remarkable inhibition of growth in chicks (12) but have no effect on male guinea pig(13). Other species show responses similar to those in the rat.