needed glycine. It is of interest that Weinstock *et al.*(8) have recently shown proteolytic activity of muscle from vit. E-deficient rabbits to be increased. This could account for the observed increase in other free amino acids of dystrophic muscle.

On the basis of these observations, it is concluded that vit. E-deficiency in rabbits is characterized by a distinct pattern change in the free amino acid levels of various tissues. The decrease in glycine suggests that it is in some unknown way implicated in the dystrophic state.

Summary. 1. Concentration of free amino acids from 6 tissues of normal and vit. E-deficient rabbits has been determined by Dowex-50 chromatography. 2. There was a general increase in free amino acids of muscle, heart, spleen, and liver of dystrophic animals. Only glycine and serine were markedly reduced. 3. Kidney and especially brain showed a general decrease in free amino acids. 4. Concentration of glycine was more consistently reduced in various tissues than other amino acids.

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Received December 13, 1956. P.S.E.B.M., 1957, v94.

Comparative Androgenic and Anabolic Effects of Several Steroids. (23039)

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The common androgens, testosterone propionate and methyl testosterone, produce anabolic as well as androgenic effects(1,2). In man, the androgenic activity frequently limits the use of these compounds as anabolic agents. Attempts to increase relative anabolic potency have led to development of methyl androstenediol(3) (Methostan, Methandriol), androstanolone(4) (Neodrol, Stanlone) and 17 - ethyl - 19 - nortestosterone(5) (Nilevar). The present study was underaken to compare the anabolic and androgenic potencies of these newer agents with testosterone propionate, methyl testosterone and unesterified testosterone.

Materials and methods. The method used was that of Eisenberg and Gordan(6). The rats were castrated at 23-25 days of age. Starting 3 weeks later, the compounds dissolved in corn oil, were administered intramuscularly daily for 7 days. Testosterone, testosterone propionate and methyl testosterone were compared with methyl androstenediol, androstanolone and 17-ethyl-19-nortestosterone. Eight rats were used at each dose level and total doses of 0.02 to 5 mg per rat were administered. A total of 432 rats was used; of these, 88 served as oil-treated controls. Gains in body weight, as well as terminal weights of the seminal vesicle and ventral prostate glands and levator ani muscles, were examined and compared with these parameters in controls autopsied at the same time. The regression lines shown in Fig. 1 were calculated by the method of least squares using only those values at and above the minimal effective range.

Results. Anabolic effects. Increase in weight of the levator ani muscle was used as a measure of anabolic activity. In Fig. 1, the differences between weight of this muscle in the treated animals and in controls run at the same time are plotted against the log of the dose. Marked anabolic responses were

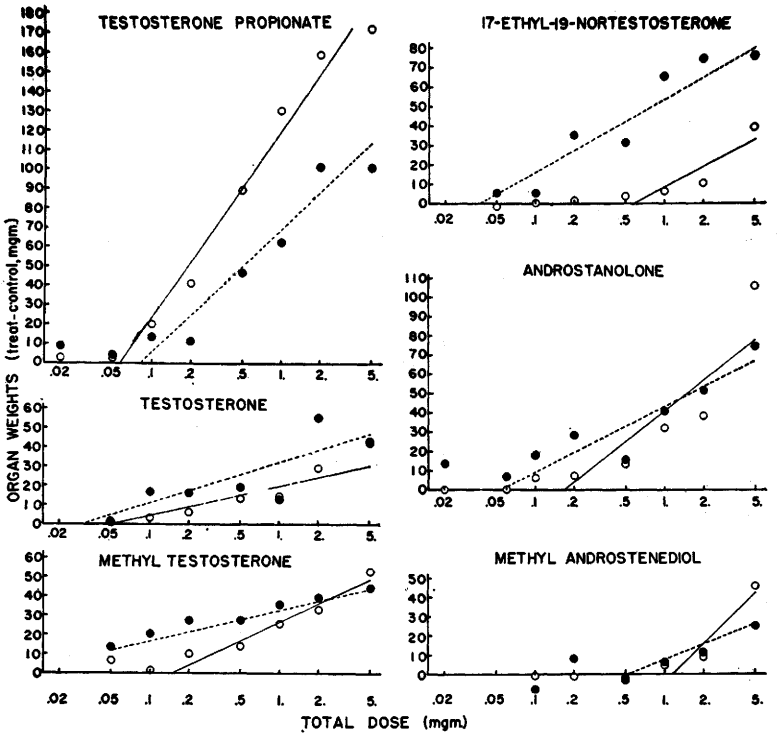

FIG. 1. Responses of seminal vesicles (open circles) and levator ani muscles (solid circles) of castrated male rats to graded doses (log scale) of various steroids. Each point is the difference between avg organ weights of a group of 8 treated animals and controls run simultaneously. Regression lines were calculated by the method of least squares from those values which showed a significant increase over the controls. Solid lines indicate androgenic potency while broken lines represent anabolic effects.

obtained with testosterone propionate, 17-ethyl-19-nortestosterone, and androstanolone while curves for testosterone and methyl testosterone exhibited a more gentle slope. Methyl androstenediol was much less active than the other compounds.

Body weight. Overall gain for the 88 control animals was 36 g during the week of treatment. Groups of 8 animals each showed average gains ranging from 31 to 41 g. In general, doses of these steroids which caused significant increases in levator ani muscle weight also caused gains in body weight in excess of the gains seen in the controls. With 8 animals per group these increased gains were not always statistically greater than the controls. The pooled results at anabolic dose levels are presented in Table I. Significantly increased gains in body weight were obtained with testosterone, testosterone propionate, androstanolone and 17-ethyl-19-nortestosterone. Although the table does not show a significant increase with methyl testosterone, at the 5 mg dose level the increase obtained with this compound was significant. The data on methyl androstenediol are from a single group of rats and no increased gain was obtained with this compound at the doses used.

Androgenic activity. Relative androgenic potencies of these steroids are also depicted in Fig. 1. Testosterone propionate was by far the most potent androgen studied and its androgenic effect, as measured by increase in seminal vesicle weight, far exceeded anabolic response, as indicated by increase in the weight of the levator ani muscle. With testosterone, methyl testosterone, and androstanolone androgenic and anabolic responses to a given dose, as shown by these parameters, were reasonably close together. However, it will be noted that methyl androstenediol showed little androgenic or anabolic activity

TABLE I. Effects of Various Steroids on Gains in Body Weight in Castrated Rats.

	Dose range, mg	No. of rats	Mean body wt, g	Mean diff. from control, g	t
Control		88	35.58		
Testosterone propionate	.2-5.	40	41.90	6.32 ± 1.06*	5.96
Testosterone	1. -5.	23	42.43	6.85 ± 1.31	5.23
Methyl testosterone	1. -5.	24	37.54	1.96 ± 1.28	1.53
Methyl androstenediol	5.	8	34.25	−1.33 ± 2.06	− .65
Androstanolone	.5-5.	31	42.51	6.93 ± 1.17	5.92
17-Ethyl-19-nortestosterone	.2-5.	40	39.42	3.84 ± 1.06	3.62

* ± stand. error.

TABLE II. Androgenic and Anabolic Responses to Various Steroids in Castrated Rats.

Compound	Total dose (mg) required to produce 100% increase in sem. ves. wt	Total dose (mg) required to produce 50% increase in lev. ani wt	Potency relative to testosterone propionate (%) Androgenic	Anabolic	Potency ratio, anabolic/androgenic
Testosterone propionate	.073	.26	100	100	1.00
Testosterone	.21	1.00	35	26	.74
Methyl testosterone	.30	1.00	24	26	1.08
Methyl androstenediol	1.6	3.65	5	7	1.58
Androstanolone	.24	.45	30	58	1.93
17-Ethyl-19-nortestosterone	1.10	.25	7	104	14.85

while 17-ethyl-19-nortestosterone had marked anabolic activity combined with a low androgenic potency. Increases in the weights of the ventral prostate glands were similar in degree to the changes in seminal vesicle weights so the data are not presented here. These effects on the ventral prostate confirm the conclusions regarding relative androgenic potency of these steroids.

Discussion. Hershberger *et al.*(7) proposed the anabolic ratio as a measure of degree of separation of anabolic and androgenic effects. They used smaller rats and calculated androgenic effect from the weight of the ventral prostate gland. With our older rats it was observed that this ratio was fairly constant only when the organ responses were marked, that is, when increase over the controls was at least 20 mg.

From Fig. 1 the doses required to produce a 100% increase in seminal vesicle weight (to 20.2 mg) and a 50% increase in levator ani weight (to 97.0 mg) were calculated. The potency relative to testosterone propionate at these points was determined (Table II). From these data, the anabolic/androgenic ratio was calculated. Since the slopes of the various lines differed, the calculated ratios in Table II hold only for this set of conditions. Slight separation of anabolic and androgenic effects was obtained with androstanolone, which gave a ratio of 1.9:1 and methyl-androstenediol with a ratio of 1.6:1, while 17-ethyl-19-nortestosterone showed a much greater separation with a ratio of 15:1.

Gordan *et al.*(8) reported that methyl androstenediol had an anabolic potency equivalent to that of methyl testosterone but that it produced androgenic effects only at excessively high doses. Hershberger *et al.*(7) found this compound to have only 5% the anabolic potency of testosterone propionate with no separation of activities. Barnes *et al.*(9), using younger rats than were studied in the current report, and treating for a longer period, found that methyl androstenediol had an androgenic potency of 2.1% and a myotrophic potency of 2.2% compared to testosterone propionate giving a ratio of 1. From our results corresponding values of 7.1 and 4.5% were obtained, with a ratio of 1.6. These results agree with those of Barnes *et al.* rather than with those of Gordan *et al.* Henderson and Weinberg(10) found that when administered subcutaneously in rats, using the seminal vesicles as the end point this compound was about ⅓ as androgenic as testosterone, but its effect on the capon comb, after

parenteral administration, was only 2% that of testosterone.

Kochakian(2) reported that androstanolone was about as androgenic as testosterone propionate in castrated mice. He used a very limited number of doses. The renotropic effects of the two compounds were also similar. Barnes *et al.*(9), using rats, calculated a myotrophic potency of 21.8% and an androgenic potency of 13.2%, thus giving a ratio of 1.6. Again our corresponding figures are slightly higher or 58% and 30% respectively, but the ratio is similar, 1.9. Barnes *et al.* also reported that the cyclopentyl-propionate of 19-nortestosterone was about 1.5 times as potent as testosterone propionate as an anabolic agent and ascribed to it an anabolic/androgenic ratio of 9.3. Our results show 17-ethyl-19-nortestosterone to have a myotrophic potency of 104% and an androgenic potency of only 7% giving an anabolic/androgenic ratio of 15, thus showing the widest separation of effect hitherto reported.

Summary. The androgenic and anabolic effects of testosterone, testosterone propionate, methyl testosterone, methyl androstenediol, androstanolone and 17-ethyl-19-nortestosterone (Nilevar) were compared. The greatest androgenic responses were obtained with testosterone propionate while the most marked anabolic effects were observed with either testosterone propionate or 17-ethyl-19-nortestosterone. Compared to testosterone propionate, methyl androstenediol and androstanolone showed a small increase in the anabolic: androgenic potency ratio but a much more marked increase was observed with 17-ethyl-19-nortestosterone.

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Received December 18, 1956. P.S.E.B.M., 1957, v94.

Effects of Age, Castration and/or Steroids upon Hematocrit in Male Rats.* (23040)

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The effects of age, castration and steroids on the blood of male rats have been studied previously. It has been reported(1) that hemoglobin content rose from 50th to 150th day of life. Several investigators(2-4) have shown that gonadectomy causes mild, transient anemia; these workers and others(2-7) reported that this anemia could be repaired by subcutaneous injections of androgen. Estrogen has been reported to have a moderate (4) or no(7) effect on male rat blood. A recent review article discusses erythropoietic stimuli in additional species(8).

The micro-method of Strumia, Sample and Hart(9) permits hematocrit determinations with very small amounts of blood, thus allowing multiple determinations on a single ani-

* This investigation was supported in part by research grant from Duke University Council on Research.

† This work was done during tenure of Research Fellowship of Am. Heart Assn.