16401

Volume of Oil and Route of Administration as Factors Influencing Testosterone Propionate Activity.

JAMES H. LEATHEM.

From the Department of Zoology and Bureau of Biological Research, Rutgers University, New Brunswick, N.J.

Seminal vesicle weight reaches a maximum in 72 hours following a single injection of testosterone propionate at a dosage of 0.25 mg. Under these circumstances, the androgen can be assayed in the rat since variation in dosage significantly influences the organ weight response.[1] This steroid is usually administered in oil and it seemed pertinent to investigate the volume of oil as a factor influencing the response since sesame oil has been shown not to be inert.[2] Furthermore, Crafts[3] found that sesame oil may prevent the expected effect from small dosages of androsterone in mice whereas Deanesly and Parkes[4] increased the effectiveness of androsterone in the rat by greatly increasing the volume of oil.

The route of administration, too, deserves consideration since subcutaneous and intramuscular injections are commonly used. The intraperitoneal route is reported as both an ineffective[5] and effective[6] mode of administration on repeated injections but the single injection response was not considered.

Immature male rats of the Long-Evans strain and 22-24 days of age were used in these experiments. A standard dose of 0.25 mg of testosterone propionate (Perandren, Ciba)* was used. Each group of animals was caged separately and 72 hours after the single injection the rats were autopsied and the fresh weight of the testes, seminal vesicles (including the coagulating gland) and ventral prostate was obtained.

The administration of a single subcutaneous injection of 0.25 mg of testosterone propionate in either 0.1, 0.4 or 0.8 cc of sesame oil induced similar organ weight changes in comparison with normal and oil injected controls (Table I). The androgen increased seminal vesicle weight more than 300% without regard to volume of oil and had a tendency, although not significantly, to be more effective in the larger volume. The ventral prostates were stimulated to the same degree in each group but the increase in weight was slight in comparison with the seminal vesicles. Testis weight was reduced by the androgen but body weight increased normally.

Fourteen rats received the 0.25 mg dosage of androgen dissolved in 1.6 cc of sesame oil. The steroid was administered subcutaneously in 2 sites on opposite sides of the body and in 0.8 cc amounts, the entire 1.6 cc being given at the same time. Seventy-two hours later seminal vesicle weight average 34.0 mg or "possibly significantly" greater than when smaller volumes and 1 injection were used. Ventral prostate weight averaged slightly greater than in the other groups, being 47.8 mg.

A study of the route of administration revealed that 0.25 mg of androgen in 0.1 cc sesame oil will increase seminal vesicle and ventral prostate weights to the same degree by either subcutaneous or intramuscular injections (Table II). The subcutaneous injections were made under the loose skin area of the dorsal neck aspect; the intramuscular injections were made into the medial thigh

1 Hays, H. W., and Mathieson, D. R., *Endocrinology*, 1945, **37**, 266.

2 Tobin, C. E., *J. Lab. and Clin. Med.*, 1944, **29**, 850.

3 Crafts, R. C., *Endocrinology*, 1942, **31**, 142.

4 Deanesly, R., and Parkes, A. S., *Lancet*, 1936, **1**, 837.

* Testosterone propionate (Perandren) was generously supplied by Ciba Pharmaceutical Products, Summit, N.J.

5 Deanesly, R., and Parkes, A. S., *Proc. Roy. Soc.*, 1937, **124**B, 279.

6 Rubinstein, H. S., *J. Urology*, 1944, **51**, 88.

TABLE I.
Volume of Sesame Oil and Response of Immature Male Rats to Single Subcutaneous Injection of Testosterone Propionate.

No. of rats	Treatment	Body wt		Avg organ wt, mg		
		Start, g	End, g	Testis	Seminal vesicles	Ventral prostate
16	None	47.3	54.1	384 ± 34*	8.2 ± 0.7	33.1 ± 2.1
10	.8 cc oil	42.8	49.8	319 ± 24	8.4 ± 3.5	28.0 ± 1.5
16	.25 mg in 0.1 cc	44.0	51.9	275 ± 14	27.5 ± 1.1	43.0 ± 2.2
14	.25 " " 0.4 "	43.8	51.6	270 ± 10	29.2 ± 1.5	41.8 ± 1.6
14	.25 " " 0.8 "	43.8	53.6	290 ± 13	30.2 ± 1.7	43.7 ± 1.6

$$^{*}\epsilon = \sqrt{\frac{\Sigma d^2}{N(N-1)}}$$

TABLE II.
Route of Administration and Immature Male Rat Response to a Single Injection of Testosterone Propionate.

No. of rats	Treatment	Body wt		Avg organ wt, mg		
		Start, g	End, g	Testis	Seminal vesicles	Ventral prostate
12	None	47.5	54.9	400 ± 42	9.7 ± 0.9	34.9 ± 1.9
13	.25 mg—intrap.	50.6	58.6	424 ± 50	12.2 ± 1.1	39.0 ± 3.0
12	.25 mg—subcu.	45.6	47.8	306 ± 30	29.2 ± 3.0	42.9 ± 3.0
16	.25 mg—intramusc.	46.3	60.7	305 ± 47	30.5 ± 2.2	43.6 ± 3.3

muscles. In contrast to these results, the intraperitoneal route exercised little effect on the seminal vesicles and ventral prostate and no effect on the testis.

Discussion. The response to testosterone propionate was not influenced by the volume of oil. Similar results were obtained with estrogens given in repeated dosages.[7] The volume of oil may, however, be a factor when steroids of low solubility are used or, in fact, may influence less active androgens.[3,4] The prostate responsiveness to androgen is considered as more acute than seminal vesicle responsiveness but certainly the degree of response favors the seminal vesicles following a single injection. The increase in prostate weight in a normal rat would permit little weight differential for assay purposes. Furthermore, Steadman and Krichesky[8] find that the varied prostatic lobes do not respond equally to testosterone propionate.

Summary. The increase in seminal vesicle and ventral prostate weights in immature male rats following a single subcutaneous injection of 0.25 mg of testosterone propionate is not influenced by the volume of oil (0.1-0.8 cc). Seminal vesicle weight increased to a greater degree than the ventral prostate weight whereas testes weight decreased. Subcutaneous and intramuscular routes of administration increased accessory sexual organ weight equally well in contrast to the intraperitoneal route which exercised little effect following one injection.

7 Pugsley, L. I., and Morrell, C. A., *Endocrinology*, 1943, **33**, 48.

8 Steadman, F. H., and Krichesky, B., *Endocrinology*, 1945, **37**, 89.