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## Effect of Androgen on Metabolism of Subcutaneous Corn-oil.\*

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We have reported that when corn-oil is administered subcutaneously to mice it is seen to disappear from the site of injection more rapidly in the male than in the female. The sex difference in rate of utilization of oil is abolished by castration.<sup>1</sup> In this communication there are described preliminary studies of the influence of crystalline testosterone and estradiol benzoate upon this phenomenon.

Twenty-seven stock white male mice 4 to 5 months of age were castrated, and a series of injections of corn-oil was started 17 days later. The oil was given into the subcutaneous tissues of the back in doses of 0.1 ml semiweekly until a total of 1.0 ml was received by each mouse. Details of the method employed for administration of oil and its recovery from the site of application after a given time may be found elsewhere.<sup>1</sup> One-third of the animals was given estradiol benzoate (*ca.* 0.3 mg/mouse), one-third testosterone propionate (*ca.* 15 mg/mouse), the remainder served as controls. The hormones<sup>†</sup> were crystalline powders, suspended in dilute gum acacia just before use. They were injected subcutaneously over the anterior thorax in 2 equal doses, the first being given at the time of the initial injection of oil and the second 2 weeks later.

One week after the last injection of oil the animals were sacrificed. Table I indicates that the androgen-treated castrates utilized injected oil at a more rapid rate than the controls. They likewise consumed more food and gained somewhat less weight. Of the mice receiving estrogen, 5 died, probably from overdosage of hormone. The remaining animals of this group appeared to behave like the controls, but it cannot be said with finality that female sex hormone is unrelated to this phenomenon until the experiment can be repeated.

There is an analogy between these observations and some aspects of the clinical findings in obesity: changes in endocrine physiology

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<sup>1</sup> Turner, Joseph C., and Mulliken, Barbara, *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **48**, 598.

<sup>†</sup> Supplied through the courtesy of Dr. E. Henderson of the Schering Corporation, Bloomfield, N.J.

TABLE I.

	Controls	Testosterone-treated*
Food g/mouse/day	4.1	4.7
Mean gain in wt, g	4.2	3.4
Ether-soluble material recovered from site of oil injection, mg.		
	366	113
	423	201
	452	281
	461	300
	463	325
	593	455
	598	464
	650	574
	690	
Mean	522 ± 25.3	339 ± 36
$\frac{\sum d^2}{n-1}$	112.7	150.9
Diff. of Mean x P E		183 ± 44 4.16

\*One animal died during the experiment.

such as castration or menopause are often followed by increase in body fat. Moreover, it has long been known that the metabolic rate of females is generally lower than that of males and the behavior of these mice affords another striking example of this peculiar dissimilarity of the sexes. The explanation of obesity based upon the law of conservation of energy forms, of course, a necessary part of any account of overall metabolism, but neglects biological relationships which operate at a different level. As examples, the recently discovered connection between androgens and nitrogen balance or the specific action of estrogens on the blood fat of birds may be mentioned. To account for the observed sex difference in rate at which injected oil is utilized any of several hypotheses might be adopted; we have been interested at this stage principally to determine whether the effect is mediated through the action of androgen or estrogen, or both. The data suggest that androgen may specifically increase the rate of utilization of depot fat. The method, through suitable modification, may prove useful in the study of this and similar problems as an index of the behavior of depot fat.

*Summary.* 1. The administration of testosterone propionate accelerates the rate of disappearance of corn-oil injected subcutaneously in castrate male mice. 2. It is suggested that this relationship is best explained by the hypothesis that androgen specifically increases the rate of utilization of depot fat.

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