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Androgens and Uterine Weight in the Immature Rat.*

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Astwood has demonstrated that 6 hours after the administration of estrogens to the 21-day-old rat, there is an increase in uterine weight.[1] This weight increase is largely due to increased hydration (edema) of the uterus. Pincus and Graubard have essentially confirmed these findings.[2] Zuckerman has stated that androgens also cause increased hydration of the uterus in the monkey.[3] Astwood in a brief report has stated that androgens will cause a uterine weight increase in rats similar to that caused by estrogens.[4]

The Astwood technic as originally proposed for estrogen assays is a very rapid and convenient one. Reports have appeared in which it has been applied to urinary estrogen assays.[5] Inasmuch as androgens are known to be present in the urines of normal, pregnant or castrate women, it seems of interest to report our findings as to the uterine weight-increasing effects of various androgens.

Findings. All animals were given the androgen subcutaneously in 0.1 cc of peanut oil and were killed 6 hours after the treatment. Peanut oil has previously been tested in this laboratory and found to contain neither estrogen nor androgen. The cervico-vaginal junctions were cut, the uteri carefully removed and immediately weighed on a Roller-Smith balance sensitive to 0.02 mg. The tissues were preserved in Bouin's fluid and representative uteri were examined microscopically. Detailed weight-findings are presented in tabular form (Table I).

The animals of Groups 1 and 2 were 21 days old. Group 1 served as controls (A). As can be noted in the table, 0.5 mg testosterone (Group 2) caused a statistically significant increase in uterine weight, 22.8% over that of the controls.

The 21-day-old animals used in these groups showed a great deal

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2 Pincus, G., and Graubard, M., *Endocrinology*, 1940, **26**, 684.

3 Zuckerman, S., *J. Endocrin.*, 1939, **1**, 147.

4 Astwood, E. B., *Proc. Am. Physiol. Soc.*, 1940, p. 6.

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TABLE I.
The Effect of Androgens on Uterine Weight.

Group	Treatment: Substance	Treatment: Mg	No. of animals	Body wt, g	Uterine wt, mg: Mean	Uterine wt, mg: Range	Uterine wt, mg: σ	Obtained difference	C.R.	% increase in uterine wt
1	Control A	—	20	28.4	21.74	15.66-29.8	0.273	—	—	—
2	Testosterone	0.5	20	28.6	26.81	19.4 -36.92	0.949	5.07	*3.94	22.8
3	Control B	—	20	28.3	21.05	15.74-27.04	0.182	—	—	—
4	Testosterone	0.1	20	28.02	21.78	16.52-27.56	0.249	0.73	2.94	3.4
5	Dehydroand.	1.5	20	28.2	26.29	17.90-37.92	1.14	5.24	*4.09	24.9
6	”	0.5	23	28.47	24.56	17.58-34.15	0.265	3.51	*3.44	16.6

σ (Standard Error of the Mean) $= \sqrt{\frac{\Sigma\delta^2}{n(n-1)}}$ C.R. = Critical Ratio $= \frac{\text{obtained difference}}{\sqrt{(\sigma_{m_1})^2 + (\sigma_{m_2})^2}}$

*Statistically significant increase in uterine weight over that of controls (C.R. > 3.0).

of variation in body weight (range 22 to 36 g). The uterine weights of the controls ranged from 15.66 to 29.8 mg with a standard error of the mean of 0.273 mg. The range and standard error were even larger in the testosterone-treated group (range: 19.4 to 36.92 mg and σ of 0.949).

An endeavor was made to keep the body weights less variable in the subsequent control and experimental groups (Groups 3 through 6) in the hope that the uterine weights would show less variability. Accordingly, the animals in these groups were limited to those of a body weight of 24 to 32 g, but varied in age from 19 to 23 days.

The uteri of the second control (B) group showed only a slightly smaller range but the intra-group variability was less (σ 0.182). In the remaining treated groups the range of the uterine weights was unaffected by more rigidly limiting the body weight, but with the exception of Group 5, the intra-group variability did seem to be decreased.

The animals of Group 4 were given 0.1 mg testosterone. The uteri of these animals were 3.4% larger than those of the controls (Group 3). This increase in uterine weight, however, fell slightly short of being statistically significant (C.R. was 2.94 instead of being 3.00 or over).

The animals of Group 5 were given 1.5 mg of the urinary androgen, dehydroandrosterone. The uteri of these animals were significantly increased in weight (24.9%). The animals of Group 6 were given 0.5 mg dehydroandrosterone. The uteri of these animals were also significantly larger (16.6%) than those of the controls.

Histological examination of the uteri from the treated animals revealed an appreciable edema of the endometrial stroma. This edema was either most noticeable in, or was limited to, the portion of the endometrial stroma closest to the muscular layer.

The unit as proposed by Astwood for use in estrogenic assay is the amount of estrogen that will cause a 34% increase in uterine weight. This weight increase is produced in 6 hours by 0.025 γ of estradiol or 0.3 γ of estrone. Our data are too limited to make any accurate comparison of the potency of androgens or estrogens in this regard. However, a 16.6% increase in uterine weight was obtained with the smallest dose of dehydroandrosterone used (0.5 mg). The *average* daily excretion of estrogen in the normal non-pregnant female has been calculated from the data of various authors[6, 7] as 190 to 464 international units, or equivalent in activity to 19.0 to 46.4 γ of estrone (63.3 to 154.66 "Astwood units"). The normal

[6] Smith, G. S., and Smith, O. W., *New England Med. J.*, 1936, **215**, 908.

[7] Palmer, A., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 273.

female excretes 30 to 100 international units of androgen daily.[8, 9] The known androgens in female urine and their relative amounts are in a proportion of 1.3 mg androsterone to 0.2 mg dehydroandrosterone.[10] An international unit of androsterone is 0.1 mg and of dehydroandrosterone is 0.3 mg. With the maximum excretion of 100 international units this would be equivalent to approximately 8.7 mg androsterone and 4.0 mg of dehydroandrosterone. These urinary androgens, unless carefully separated from the estrogenic fraction, could then be sufficient to interfere seriously with the accuracy of an assay by the Astwood method in the non-pregnant female.

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Effect of Crude Peanut Oil Extracts of Brown Fat on Metabolism of White Rat.

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This paper presents preliminary data on the effect of the intraperitoneal injection of crude peanut oil extracts of the brown fat of the woodchuck and the thirteen-lined ground squirrel on the heat production of the white rat.

The earlier literature on brown fat has been reviewed by Rasmussen.[1] Various theories as to function have been proposed, but there has been a paucity of chemical and biological studies. Brown fat has been noted in infants[2] and cretins.[3] More recent work has suggested a further relationship to metabolism.[4, 5, 6] Wendt[7] reported

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