

weight. Only in the case of denervation atrophy, the contractile power per weight unit shows a diminution, and this loss in power corresponds roughly to the simultaneously observed diminution in birefringence. This parallelism between contractile power per weight unit and birefringence can serve as a further indication that the sub-microscopic crystalline structure of the muscle is essential for the contractile mechanism.

Summary. Although in muscular atrophy, either due to final or upper neurone lesions, or due to tenotomy, there is a distinct weight loss after 9 to 10 days, the muscles have at that time still the same contractile power per weight unit and the same birefringence as normal muscles. But 3 to 5 weeks after onset of the atrophy, only muscles atrophying due to upper neurone lesions or to tenotomy have still the contractile power per weight unit and the birefringence of normal muscle. However, for denervated muscle, contractile power and birefringence are distinctly diminished at that time. Only in the latter type of atrophy does the submicroscopic crystalline structure, so essential for the contraction process, become seriously impaired.

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Excretion of Pregnanediol in Women with Virilism.

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Butler and Marrian¹ in reporting the isolation of a steroid compound pregnane-3-17-20-triol, from the urine of 2 women with virilism caused by "enlarged adrenals," also noted the presence of "appreciable amounts of pregnandiols." Venning, Weil and Browne² later reported the finding of considerable amounts of sodium pregnandiols glucuronide (12 mg to 30 mg per day) in 2 cases of virilism, one of which was subsequently found to have an adrenal cortex carcinoma and, the other, adrenal cortex hyperplasia.

During the past 2 years, we have been performing pregnandiols excretion studies in women with the arrhenomimetic (virilism) syndrome. In the present communication, we wish to report the results of these studies.

¹ Butler, G. C., and Marrian, G. F., *J. Biol. Chem.*, 1937, **119**, 565; *Nature*, 1938, **142**, 400.

² Venning, E. H., Weil, P. G., and Browne, J. S. L., *J. Biol. Chem.*, *Sci. Proc.*, 1939, **128**, CVII.

Methods and Materials. A total of 7 cases was studied. These consisted of 2 cases proven by operation to be adrenal cortex carcinomas and 5 cases of amenorrhea and hypertrichosis of undetermined etiology. Sodium pregnandiol glucuronidate determinations³ were performed on single 24-, 48-, or 72-hour specimens, for periods varying from 6 to 32 days.

Results. Pregnandiol Excretion in Patients with Adrenal Cortex Carcinoma. In the 2 patients in whom adrenal cortex carcinomas were found, the pregnandiol excretion varied in one from 9 to 20 mg per day and, in the other, from 12 to 18 mg per day. In one patient (I.E.), in whom it was possible to obtain post-operative urines, these were found to contain no detectable amount of pregnandiol after removal of the tumor.

Pregnandiol Excretion in Patients with Arrhenomimetic Syndrome (without adrenal cortex carcinoma). In the 5 cases in this group, X-rays of the adrenals after intravenous pyelogram and peri-renal insufflation failed to reveal any evidence of adrenal tumor or enlargement. Two of these (E.W. and T.S.) were explored surgically without revealing any evidence of adrenal neoplasm. In all of these, no pregnandiol was found in the urine.

Discussion. The 5 cases of virilism who did not excrete pregnandiol have been under observation for periods varying from 6 months to 3 years, without any clinical manifestations suggesting adrenal, ovarian or pituitary neoplasm. On the basis of the stationary clinical picture in these cases, it seems justifiable to assume that the syndrome is not due to a neoplasm but rather to a functional disturbance involving the adrenal cortex.

In contrast to these, the 2 cases with proven adrenal cortex carcinoma had consistently high pregnandiol excretion. Comparable amounts of pregnandiol are found only in pregnancy or during the corpus luteum phase of a normal menstrual cycle. Furthermore, in one patient in whom studies were performed after removal of the tumor, the pregnandiol disappeared from the urine.

It appears from these studies that the excretion of pregnandiol in appreciable amounts (9 to 20 mg daily) in women with the virilism syndrome, in the absence of pregnancy, indicates hyperactivity of the adrenal cortex which could be due to hyperplasia or carcinoma of the adrenal cortex. The excretion of pregnandiol may be of diagnostic value to differentiate virilism caused by adrenal cortex hyperplasia or neoplasia from other types.

³ Venning, E. H., *J. Biol. Chem.*, 1937, **119**, 473.