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Effect of Three Synthetic Steroid Compounds upon Weight and Work Performance of Adrenalectomized Rats.*

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The compound 11-desoxy-corticosterone acetate is the most active of the known steroid compounds in respect to its property of maintaining life of adrenalectomized animals. This compound (substance A) may be characterized as pregnene (4:5)–ol(21)–dione (3,20) acetate; its immediate precursor in the laboratory synthesis is (substance B) pregnene (5:6) diol (3,21) one (20) 21-mono-acetate; a third compound, (substance C) pregnene (4:5) triol (17,20, 21) one (3), was synthesized by Serini and Logemann.[1] In substance C the stereochemical arrangement at carbon 17 is opposite to that of those steroids occurring in the adrenal cortex which also have a hydroxy group at carbon 17. In these studies substance B was found to possess definite biologic activity altnough to a much less extent than substance A, and substance C appeared to be inactive in the doses tested.

Male rats of the Sprague Dawley strain which weighed approximately 180 g were used in these experiments. The diet was Purina Dog Chow. Bilateral adrenalectomies were performed in one stage under ether anesthesia. The test substances were dissolved in sesame oil and administered by subcutaneous injection twice daily. The amount of sesame oil injected was kept constant at 1 cc per day for each rat. Ten animals were maintained for 7 days without treatment. Eighty-one rats were treated for 7 days. On the 7th day each animal was weighed and then subjected to the work test. The animals were anesthetized with phenobarbital sodium. The left gastrocnemius muscle was weighted with 100 g and stimulated to contract 3 times per second. Each animal received 5 cc of water twice daily by subcutaneous injection for as long as the animal continued to work. In all of the experiments stimulation was continued

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1 Serini, A., and Logemann, W., *Berichte der Deutschen Chem. Gesellschaft*, 1938, **71**, 1362.

until the muscle ceased to respond. The details of the method have been described.[2, 3]

Seven days following adrenalectomy the average body-weight of

TABLE I.

Daily dose mg	Substances: pregnene (4:5) ol (21) dione (3,20) acetate		pregnene (5:6) diol (3,21) one (20) acetate		pregnene (4:5) triol (17,20,21) one (3)	
	Wt, g	Work	Wt, g	Work	Wt, g	Work
0.01	176	1543				
	180	2251				
	181	1525				
	174	1221				
0.03	186	3243	153	551		
	195	1810	172	1292		
	194	1971	152	1209		
	182	3532	167	613		
0.06	196	3745	140	dead		
	198	1929	176	1385		
	204	3283	166	882		
	198	1743	170	1410		
0.12	204	3050	178	2187		
	196	3984	162	1606		
	193	4152	178	2770		
	189	5956	177	2074		
0.25	210	5624	183	2263		
	214	4090	182	26		
	188	6695	183	2366		
	206	10024	196	2630		
0.50	216	3392	200	3910	139	16
	204	2405	187	2234	158	857
	186	5725	202	3085	170	830
	191	6890	209	3096	153	1145
1.00	198	8059	186	2586	137	463
	183	6024	205	3464	152	1082
	190	9622	220	3596	153	1467
	200	10355	207	3684	178	1673
2.00	222	18494	211	3496	145	924
	197	6645	204	2812	160	1781
	200	13289	209	4291	165	921
	212	11371	188	4490	157	625
5.00	200	12019	211	3496	154	756
	196	11149	204	2812		
	198	12806	209	4291		
	203	3935	188	4490		

[2] Heron, W. T., Hales, W. M., and Ingle, D. J., *Am. J. Physiol.*, 1934, **110**, 357.

[3] Ingle, D. J., *Am. J. Physiol.*, 1936, **116**, 622.

the 10 untreated rats was 150 g with a range of 134-163; the amounts of work performed averaged 1276 recorder revolutions with a range of 56-2399. Each recorder revolution is equivalent to approximately 400 g-cm of work. The values for body-weight and for work of the treated animals are presented in Table I.

As evidenced by the effect of these substances upon body-weight and upon work performance, the presence of a hydroxy group instead of a keto group on carbon 3 of the pregnene nucleus decreases but does not destroy these biologic effects of the compound. This compound was reported by Waterman and co-workers[4] to maintain the health of adrenalectomized dogs. The alteration of the molecule to the structure of substance C brought a still greater loss of activity so that substance C appeared to be biologically inactive in these tests. Earlier studies[5, 6] have demonstrated that although the work performance of adrenalectomized rats treated with substance A is improved over that of untreated animals, it remains very small as compared to sham operated animals. Similar values for work performance of animals treated with substance A were obtained in this study.

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Inhibition of Estrin-Deprivation Bleeding in Rhesus Monkey with Testosterone Derivatives Variously Administered.*

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Testosterone and its acetic and propionic acid esters have been shown to inhibit uterine bleeding in the castrate macaque primed with estrogens.[1] In the present experiments a similar effect was attained with methyl-testosterone and ethinyl-testosterone (pregneninolone) and with testosterone di-propionate administered in

[4] Waterman, L., Danby, M., Gaarenstroom, J. H., Spanhoff, R. W., and Uyldert, I. E., *Acta Brevia Neerlandica*, 1939, **9**, 75.

[5] Ingle, D. J., *Endocrinology*, 1940, **26**, 472.

[6] Ingle, D. J., *Endocrinology*, in press.

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[1] Hartman, C. G., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 87.