

identical with the control series. This may indicate that even though the mesenteric vascular bed did not participate in the generalized vasoconstrictive reaction the rest of the vascular system constricts rapidly, and the animals bleed out the available blood at a normal rate of speed. There appeared to be little protection against the bowel changes since in the 8 animals that died there was the usual hemorrhagic intestinal necrosis.

In evaluation of this regional sympathectomy several problems inherent in the procedure itself should be considered. The splanchnic bed is only one segment of the vascular tree participating in vasoconstrictor activity during shock. As such it would be unreasonable to expect from its denervation the same hemodynamic effect as is obtained from chemically induced total sympathetic blockade. The trauma of the denervation procedure and the subsequent diarrhea, which these animals almost invariably exhibit, may have weakened the animal's resistance to the stress of shock. Furthermore, an increased sensitivity of end organs to circulating epinephrine and norepinephrine may have obviated some of the protective effects of the operation. Lastly, while sympathectomy produces vasodilation, it also causes spasm of the intestinal musculature which may compress its blood supply and limit further its beneficial effect.

Nevertheless, this postganglionic mesenteric sympathectomy produced hemodynamic changes in hemorrhagic shock which ap-

proached those produced by dibenzyline pre-treatment and yet did not afford the same overall beneficial result. It would appear that dibenzyline protects from hemorrhagic shock by acting on organs other than the intestine.

Summary. A postganglionic mesenteric sympathectomy was performed in a series of dogs who subsequently were subjected to irreversible hemorrhagic shock. Hemodynamic changes resulted which mimicked those produced in a series of dibenzyline pretreated animals but offered no significant improvement in survival when compared to a control series.

1. Remington, J. W., Hamilton, W. F., Boyd, G. H., Jr., Hamilton, W. F., Jr., Caddell, H. M., *Am. J. Physiol.*, 1950, v161, 116.
2. Overton, R. C., DeBailey, M. E., *Ann. Surg.*, 1956, v143, 439.
3. Inglis, F. G., Hampson, L. G., Gurd, F. N., *ibid.*, 1959, v149, 43.
4. Hershey, S. G., Zweifach, B. W., Metz, B. S. L., *Anesthesiology*, 1954, v15, 589.
5. Lillehei, R. C., *Surgery*, 1957, v42, 1043.
6. Lillehei, R. C., McLean, L., *Ann. Surg.*, 1958, v148, 513.
7. Lium, R., *Surgery*, 1941, v9, 538.
8. Berger, R. L., Lium, R., *Ann. Surg.*, 1960, v152, 266.
9. Fine, J., *New England J. Med.*, 1954, v250, 889.
10. Wiggers, H. C., Ingraham, R. C., Roemhild, F., Goldberg, H., *Am. J. Physiol.*, 1948, v153, 511.

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Metabolic and Serum Lipid Effects of Δ^1 -Testolactone.* (27474)

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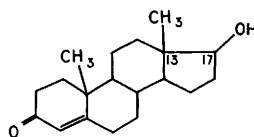
In atherosclerosis research and cancer chemotherapy the search continues for steroidal derivatives in which the characteristic endo-

crine effects of the parent compound are lacking or markedly attenuated. Testolactone is reported to be anabolic but not androgenic in the rat(1). Δ^1 -Testolactone is reported to be lacking in androgenic effect in women, although it appears to be as useful as testosterone propionate in the treatment of metastatic breast cancer(2). The present investi-

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TABLE I. Effect of Δ^1 -Testolactone (Aqueous) Administration of Serum Lipids and Lipoproteins and on Nitrogen Balance.

Sub- ject	Serum lipids (mg/100 ml) *				Lipoprotein lipid per 100 ml of serum						Mean change in nitrogen balance, g/d	Body wt, kg	Remarks	
	No. of sera	Total cho- lesterol	Phospho- lipid	Tri- glyceride	No. of samples	Cholesterol		Phospholipid						
						α	β	α	β	$d < 1.019$ —mg—				$d < 1.019$ —mg—
LM	10	149 $\pm$ 3	213 $\pm$ 3	210 $\pm$ 7	1	36	49	67	87	50	60	0	54.3	Control. Constant diet.
	3	131 $\pm$ 4 ^a	183 $\pm$ 7 ^a	238 $\pm$ 32 ^c	2	28	49	55	78	41	64	+0.07	54.1	Rx 50-200 mg/d for 32 days (total 3200 mg).
LW	4	235 $\pm$ 8	298 $\pm$ 9	75 $\pm$ 11	1	72	150	35	156	101	31	0	62.6	Control. Constant diet.
	4	201 $\pm$ 7 ^b	252 $\pm$ 9 ^a	64 $\pm$ 1 ^c	2	55	119	21	111	91	22	-0.53	62.6	Rx 200-400 mg/d for 18 days (total 4800 mg).
PG	8	237 $\pm$ 3	276 $\pm$ 8	102 $\pm$ 4	2	52	143	31	118	100	30	0	93.1	Control. Constant diet.
	2	217 $\pm$ 5 ^a	271 $\pm$ 9 ^c	84 $\pm$ 1 ^a	1	49	120	58	116	94	50	+0.07	93.5	Rx 400 mg/d for 8 days (total 3200 mg).
MW	9	354 $\pm$ 14	337 $\pm$ 10	65 $\pm$ 3	2	72	233	30	135	161	19	—	83.1	Control. Conventional diet at home.
	3	341 $\pm$ 16 ^c	319 $\pm$ 6 ^c	57 $\pm$ 7 ^c	2	66	255	36	122	176	27	—	84.7	Rx 100-200 mg 3 times weekly for 8 wk (total 3100 mg).

* Mean $\pm$ stand. error. Differences in mean values were analyzed by t test for serum lipids only.^a $p < .01$ ^b $p < .02$ ^c $p > .05$ 

TESTOSTERONE

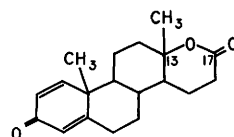
 Δ^1 - TESTOLACTONE

FIG. 1.

gation was initiated as part of a continuing study of the relationship of steroidal structure to the protein anabolic, androgenic and lipoprotein effects of testosterone derivatives (Fig. 1).

Four subjects were utilized: 1) L.M., a 48-year-old hypogonadal man with myotonic dystrophy; serum triglyceride concentrations and lower density β lipoprotein and chylomicron ($d < 1.019$ g/ml) lipids slightly increased. 2) L.W., a 48-year-old oophorectomized woman with normal serum lipids and lipoproteins. 3) P.G., a 55-year-old man with idiopathic osteoporosis; lipids and lipoproteins normal. 4) M.W., a 41-year-old premenopausal woman with primary (idiopathic) hypercholesterolemia (hyperbetalipoproteinemia) (3).

Δ^1 -Testolactone[†] was administered intramuscularly as an aqueous suspension, 100 mg/ml, in doses of from 50 to 400 mg daily.

Serum lipids and lipoproteins were determined according to methods described previously (3). Metabolic balance studies were carried out in the first 3 subjects according to the format of Reifstein, Albright and Wells (4). Nitrogen, creatinine and electrolytes were determined by standard methods, urinary gonadotropins by the non-dialysis method of Klinefelter, Albright and Griswold (5).

Results. No significant change in nitrogen, sodium, potassium or phosphorus balance or body weight occurred in the 3 subjects who were treated for periods of from 8 to 32 days under metabolic balance conditions.

In these 3 subjects there was a slight but statistically significant reduction of serum total cholesterol levels (Table I). Phospholipid levels also decreased, but significantly so only

[†] Supplied by Squibb Inst. for Med. Research, New Brunswick, N. J.

in subjects L.M. and L.W. Serum triglyceride levels fell significantly in subject P.G.

No significant change in serum lipids occurred in the hypercholesterolemic subject M.W., whose diet was not constant.

Alpha lipoprotein cholesterol and phospholipids diminished, absolutely as well as relatively, in all but subject P.G. in whom no change occurred. Beta and lower density lipoprotein lipids showed no consistent patterns of response. The β lipoprotein lipids in subject M.W. with hyperbetalipoproteinemia did not diminish nor did the $d < 1.019$ g/ml lipoprotein lipids in the mildly hyperlipemic subject L.M.

Δ^1 -Testololactone did not affect libido in the hypogonadal man nor lead to changes in breasts, vagina or hair growth in the women. No decrease in the elevated urinary gonadotropin excretion occurred in the oophorectomized subject.

Discussion. Androgens such as testosterone propionate and methyltestosterone characteristically enhance protein anabolism and diminish α lipoprotein concentrations. Beta lipoprotein concentrations usually increase (6,7), although this response is somewhat variable. Recent studies of 17-methylandrostan(2,3-c)pyrazole suggested an association of lipoprotein effects with protein anabolic properties, since both were apparent with doses too small to elicit an overt androgenic response(8).

Although large doses of Δ^1 -testololactone produced only slight decreases in α lipoprotein lipids, these changes are characteristic of testosterone. The lack of protein anabolic or

clinically manifest androgenic response suggests that dissociation of anabolic and androgenic effects from serum lipoprotein effects may have been achieved.

Summary. Δ^1 -Testololactone administration caused no protein anabolic or androgenic effects in 4 subjects. Serum cholesterol and phospholipid levels fell, however, as did α lipoprotein lipids in three. The α lipoprotein effect is typical of testosterone and suggests a separation of lipoprotein from androgenic-anabolic properties in a testosterone derivative

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1. Shemano, I., Gordan, G. S., Eisenberg, E., *PROC. SOC. EXP. BIOL. AND MED.*, 1951, v78, 612.
2. Segaloff, A., Weeth, J. B., Rongone, E. L., Murison, P. J., Bowers, C. Y., *Cancer*, 1960, v13, 1017.
3. Furman, R. H., Howard, R. P., Lakshmi, K., Norcia, L. N., *Am. J. Clin. Nutrition*, 1961, v9, 73.
4. Reifenstein, E. C., Jr., Albright, F., Wells, S. L., *J. Clin. Endocrinol.*, 1945, v5, 367. Correction, *idem, ibid.*, 1946, v6, 232.
5. Klinefelter, H. F., Jr., Albright, F., Griswold, G. C., *J. Clin. Endocrinol.*, 1943, v3, 529.
6. Russ, E. M., Eder, H. A., Barr, D. P., *Am. J. Med.*, 1955, v19, 4.
7. Furman, R. H., Howard, R. P., Norcia, L. N., Keaty, E. C., *ibid.*, 1958, v24, 80.
8. Howard, R. P., Furman, R. H., *J. Clin. Endocrinol.*, 1962, v22, 43.

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Effect of Hydrocortisone on Blood Pooling Due to Cobra Venom.* (27475)

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Clinical(1-4), and some experimental(5,6) evidence suggests that steroids are of value, in treatment of envenomation, but the mech-

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anism of this beneficial effect is not known. Experiments reported below were undertaken to determine if hydrocortisone changes the rate of pooling of blood in the perfused ani-