mechanism of shock is completely known the voluntary neuromuscular factor may be found closely related to the production of toxins[22-25] and to local fluid loss from capillaries.[26-28]

Summary. The limited evidence in this paper supports the claim that hemorrhagic shock profoundly alters the morphology of the motor end plates and finally produces loss of structural innervation of many muscle fibers in a single voluntary muscle. This histologic change is highly irregular in the different muscles of the rat, therefore large numbers of specimens from different muscles were teased. Gold staining masses of axonic materials drain out into and between the muscle fibers coincident in time with the loss of motor innervation due to the increased permeability of the end plates. The epilemmal axons, exhausted of their substances, are in many places likewise denuded of their hypolemmal end plates. There is therefore a real anatomic breakdown of many motor end plates and histologic alteration of certain skeletal muscles in hemorrhagic shock.

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Cutaneous Application of Ethinyl Estradiol in Alcohol.

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It has been shown by Zondek[1] and Moore[2] that the estrogens, estrone and estradiol benzoate, respectively, were absorbed through the skin when administered by inunction in any oily vehicle. Later Zondek[3] showed that percutaneous absorption was even more effective when estrone was placed in an alcoholic solvent.

With the introduction of ethinyl estradiol, the new synthetic ester of the natural steroid estrogen estradiol in which the hydroxyl of carbon 17 is replaced with an ethine group,[4] it was considered advisable to test for percutaneous absorption of this hormone, in an alcoholic solution, on the pituitary, gonads, reproductive tract and body growth of the albino rat.

Experimental procedure and methods. Ethinyl estradiol‡ was dissolved in absolute alcohol to facilitate evaporation after application. One calibrated drop, or 2 in a few

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‡ Grateful acknowledgment is made to Dr. Gregory Stragnell and the Schering Corporation for the ethinyl estradiol.

TABLE I.
Sample Data of Effects of Ethinyl Estradiol on Adult White Rats (20 daily treatments).

No. of animals	Avg body wt gain (g)	Daily dosage (γ)	Avg wt compared to normal†		
			(2) Ovaries and fallopian tubes	Uterus	Pituitary
		Series I—Spayed Adult Females—age, 3½-4 months.			
		(Spayed 21 days prior to treatment; 20 daily treatments; autopsy day 21.)			
4	71	Con.	—	1.00	1.00
2	45	0.10*	—	5.34	2.40
2	54	0.25	—	3.63	2.20
3	23	1.00	—	4.20	1.40
3	36	10.00	—	6.22	4.00
2	24	20.00	—	4.04	2.60
		Series II—Adult Intact Females—age 3½-4 months.			
		(20 daily treatments; autopsy day 21.)			
4	53	Con.	1.00	1.00	1.00
4	38	0.10	0.84	0.92	1.67
3	41	0.25	0.88	1.08	1.50
3	31	1.00	0.79	1.02	1.50
3	26	10.00	1.00	1.43	3.00
3	37	20.00	1.05	1.50	2.17
1	18	40.00	1.28	1.44	2.67

			(2) Testes	(2) Seminal vesicles	Pituitary	Ventral Prostate
		Series III—Castrated Adult Males.				
		(Castrated day 98; treatments days 122-142; autopsy day 143.)				
2	14	Con.	—	1.00	1.00	1.00
2	-4	0.25	—	1.30	1.33	1.60
2	2	1.00	—	1.78	1.67	2.00
1	-4	20.00	—	1.74	2.67	2.00
1	30	40.00	—	1.83	1.83	1.60
		Series IV—Adult Intact Males.				
		(Treatments, days 84-104; autopsy, day 105.)				
2	23	Con.	1.00	1.00	1.00	1.00
2	7	0.25	0.73	0.22	1.25	0.31
1	12	1.00	0.23	0.22	1.00	0.18
1	24	20.00	0.23	0.20	3.00	0.16

* 1 γ = 10 rat units.
† Normal = 1.00, calculated on average weight in mg/100 g of body weight.

cases, of this solution containing a known amount of the crystalline hormone (0.1 γ to 40.0 γ/day, Table I) was applied daily for 20 days without massage, to a clean-shaven area on the suprascapular region of albino rats. Littermates and rats of comparable ages were used and separately caged so as to avoid contamination of the treated area.

Sixty-nine rats were divided into 4 series with suitable controls as follows: Series I (20 animals), spayed females—both immature and adult; Series II (26 animals), intact females—immature and adult; Series III (10 animals), castrated males—immature and adult; and Series IV (13 animals), intact males—immature and adult. Vaginal smears from all females were made daily starting 5 days before the first application. Autopsy was made on the day following the last treatment and fresh weights of tissues obtained. The tissues were then fixed and prepared for histological examination.

To determine whether the effect of ethinyl estradiol on the body weight increase was significant, it was necessary to compute the "P" value of the body weight gains of each treated group of each dosage level and of all the treated animals taken as one group regardless of dosage (Table II). These statistics were calculated by determining the significance of difference between means of small samples and the "P" value obtained by use of "Student's" t-test for unique samples.[5]

Results and Summary. 1. The estrogenic

[5] Fisher, R. A., *Statistical Methods for Research Workers.*

TABLE II.
"P" Values and Body Weight Gains of Treated Groups Compared to Untreated Groups.

$$S.D. = \sqrt{V\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}$$

Series	Group	Avg body wt gain (g) Control	Treated	"P" value*
I.	Adult spayed females	71	34	<0.01
II.	" intact "	53	34	0.03
III.	Castrated adult males	14	4	0.60
IV.	Immature intact "	65	36	0.04
"	Adult " "	23	12	0.40

* <0.05 is significant.

hormone, ethinyl estradiol, in an alcoholic solution was absorbed through the skin of albino rats very effectively by cutaneous application without massage and in this vehicle appeared to give a complete substitution for the natural estrogenic internal secretion from the ovary. This would seem to indicate a very simple and reliable means of cutaneous application. Effective absorption of this estrogen through the skin was evidenced by the pronounced influence similar to that generally known of other estrogens on the pituitaries, ovaries, uteri, vagina, testes, seminal vesicles and ventral prostates as determined by gross weights (Table I) and histological studies. 2. The potency of an alcoholic solution of ethinyl estradiol applied to the skin was further substantiated by the fact that estrus was induced in both spayed and intact females in 24 hours and that the daily dosage of 0.1 γ was sufficient to substitute for the loss of the ovaries in castrates as evidenced by uterine weights (Table I). 3. Some retardation of body growth gain (Table II) was caused by the estrogenic treatment in the adult females (spayed and intact) and in immature males. Whether the retardation of body growth was due to some specific toxicity or to some other factor was not determined, however, no visible toxic effects were witnessed in daily observations on the eating habits, general skin and hair condition.

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Effect of Sulfhydryl Reagents on Adenosinetriphosphatase Activity of Myosin.

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Myosin, the main constituent of contractile muscle fibers, has been identified by Engelhardt and Ljubimova[1,2] with adenosinetriphosphatase, the enzyme which catalyzes the breakdown of adenosinetriphosphate (ATP) to adenosinediphosphate and inorganic phosphate. Needham[3] and Bailey[4] have confirmed this discovery.

Needham[3] reported that iodoacetate had no effect on the adenosinetriphosphatase activity of myosin, while glycine and ammonium chloride (reagents known to abolish the nitroprusside test of myosin) actually increased enzyme activity. Needham came to the con-

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