The animal was anesthetized with ether and the sample of blood then removed from the inferior vena cava.

The significance of this difference has not yet been worked out although the effect of adrenalectomy in both male and female, and of ovariectomy in the female has been studied. Neither of these two procedures alter the resting blood histamine as obtained by this method. It is, however, interesting to note that the histamine content of the ovary is 10 times that of the testis (Gaddum).[3] Also that recently Ungar and Dubois[4] have shown the presence of a histamine-like substance in human pregnancy urine.

Conclusions. The histamine content of the whole blood of the normal female rat is higher than that of the normal male rat.

10185 P

Effect of Local Application of Testosterone in an Ointment on Growth of Penis in the Rat.*

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The purpose of this experiment was to determine whether local application of testosterone to the penis in mammals would result in growth and development of this organ. This was suggested by the experimental evidence of absorption and systemic effects of androgens when applied to the skin[1] and the particularly intensified action of androgens on combs of chickens when applied locally.[2]

Twenty-four-day-old albino rats from our colony were used in these experiments. The treated and control animals in each group were arranged so that comparisons were made between litter mates. Each treated animal received 0.075 mg testosterone† daily by local application or subcutaneous injection for 22 days. The prepuce was drawn back and a measured amount of testosterone ointment or

3 Gaddum und Dale, *Gefässerweiternde Stoffe der Gewebe*, G. Thieme, 1936, p. 42.

4 Ungar, G., et Dubois, J., *C. R. de la Soc. de biol.*, 1937, **125**, 963.

* Supported in part by a grant from the Josiah Macy, Jr., Foundation.

1 Moore, C. R., Lamar, J. K., and Beck, N., *J. Am. Med. Assn.*, 1938, **111**, 11.

2 Fussgänger, R., *Med. Chem. Z.*, 1934, **2**, 194.

† We wish to thank Dr. Ernst Oppenheimer of Ciba Pharmaceutical Products for the testosterone used in this work.

plain lanolin was applied to the penis daily from a tuberculin syringe. The testosterone ointment was prepared by dissolving crystalline synthetic testosterone in heated anhydrous lanolin at a concentration of 3.5 mg per cc. The testosterone administered by subcutaneous injection was dissolved in peanut oil. The controls in this group received an equivalent amount of plain peanut oil.

The animals were killed and examined at the age of 47 days, 23 days after treatment had begun. At autopsy the penis was dissected free from the prepuce and surrounding tissue, measured from its distal end to the bulbo-cavernosus muscles, excised and weighed. The prostatic-seminal vesicle complex was dissected free and weighed. In group II the testes were also weighed.

Group I consisted of 5 litters. Each litter was divided into (A) castrated animals treated with testosterone (0.075 mg daily) ointment, (B) castrated animals treated with plain lanolin, and (C) untreated intact control animals. In the latter, the prepuce was drawn back daily but no treatment was administered. The number of animals and results are tabulated. The penes of the testosterone treated animals averaged 31% longer and weighed 71% more than those of the lanolin treated castrates and were approximately equal to those of the intact animals.

Group II consisted of 5 litters, each divided into (A) intact animals treated with testosterone (0.075 mg daily) ointment and (B) intact animals treated with plain lanolin. The number of animals used and the results are tabulated. In these animals no appreciable differences in penile length or weight were obtained. The testes weighed slightly less and the prostatic-seminal vesicle complex slightly more in the treated animals than in the untreated animals, but the differences are probably not significant.

Group III consisted of 5 litters, each divided into (A) castrated rats injected subcutaneously (0.075 mg daily) with testosterone in peanut oil and (B) castrate rats injected subcutaneously with plain peanut oil. The number of animals used and the results are given in Table I. The penes of the treated animals were 21% longer and weighed 114% more than those of the controls. The prostatic-seminal vesicle complex of the treated animals weighed 113% more than those of the control castrates.

Further investigations are being carried out to determine the effect of small doses on a large series of animals.

Summary. 1. Seventy-five gamma of testosterone in an ointment applied locally to the penes of castrate rats for 22 days results in growth of the penis of approximately the same order as that in un-

TABLE I.

Effect of Local Application of Testosterone in an Ointment on Growth of the Penis in the Rat.

Group	Animals	No.	Treatment	Avg wt, g	Avg length of penis, cm	Avg wt of penis, mg	Avg wt of prostatic Sem. Ves., mg	Avg wt of testes, g	Avg % increase length of penis	Avg % increase wt of penis	Avg % increase prostatic Sem. Ves.
I A	Castrated	8	Local application testosterone in lanolin	93.7	2.1	80	106	—	31	71	116
I B	”	9	Lanolin only	87.5	1.6	45	49	—			
I C	Intact	6	No treatment	90.0	2.1	89	124	—	31	98	153
II A	”	11	Local application testosterone in lanolin	85.0	2.0	79	161	0.952	5	5	18
II B	”	10	Lanolin only	84.0	1.9	75	136	0.989			
III A	Castrated	9	Subcutaneous injections testosterone in peanut oil	87.4	1.9	73	113	—	21	114	113
III B	”	9	Subcutaneous injections peanut oil only	88.7	1.6	34	53				

treated normal animals or in castrated animals treated by daily subcutaneous injections of the same amount of testosterone. 2. In the dosage used, growth of the prostatic-seminal vesicle complex in rats treated by local application of testosterone to the penis is similar to that obtained by subcutaneous injection. 3. As measured by gross testicular weights, the testes are not appreciably inhibited by local application of testosterone to the penis, in the dosage used.

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Intravenous Injection of Amino Acids on Glucose Utilization Rate of Hypophysectomized and Insulin-Treated Rabbits.

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The high utilization rate[1] of the hypophysectomized rabbit makes it an excellent preparation for the study of the factors influencing carbohydrate metabolism. We attempted to determine if, and to what extent this sugar requirement could be substituted by amino acids. For this we carried out the determination of the glucose utilization rate in fasted hypophysectomized rabbits by the method previously described,[1] *i. e.*, by determining the rate at which glucose must be injected intravenously to maintain the blood sugar at a constant normal level. Having established this rate, we measured the effect of injecting a solution of amino acids,* containing 1.0% nitrogen (Frederick Stearns and Co.). In the first animal studied it was found that the glucose injection rate necessary to maintain a normal blood sugar level was markedly decreased during the injection period of the amino acids. We found the lowered glucose utilization period persisted for some 24 hours after the stoppage of

[1] Greeley, P. O., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1070.

* We wish to express our appreciation to the Frederick Stearns and Company Laboratories for the supplies of amino acids used in this work. We are indebted to Doctor Melville Sahyun, Director of Biochemical Research of that Company, for the constitution of the preparation. He states, "The amino acids are prepared by hydrolysis of casein in sulphuric acid and the subsequent removal of sulphate, ammonia, calcium and phosphate; also the separation of the non-hydrolyzable fraction by adsorption so that the final preparation consists of the pure amino acids from casein hydrolysate." The distribution of amino acids in the mixture is probably similar to that of hydrolyzed casein from which it was prepared.