

Although we do not know how much of the benefit of steroid retention enemas in treatment of ulcerative colitis is from local effect and how much from systemic absorption of the steroid, there is no doubt that a substantial amount of 6-methyl-prednisolone is absorbed. Evidence suggests that this drug is absorbed very rapidly, metabolized rapidly, and that half of the quantity absorbed and excreted in the urine is excreted in less than 6 hours.

Conclusion. 6-methyl-prednisolone is absorbed rapidly and in substantial amounts from the rectum in normal individuals and in patients with ulcerative colitis. Half of the 6-methyl-prednisolone absorbed from the rectum and excreted in the urine is eliminated within 6 hours. The beneficial action of 6-methyl-prednisolone retention enemas may be systemic as well as local.

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Action of Prolactin on Seminal Vesicles of Guinea Pig.* (25418)

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The function of prolactin (lactogenic hormone, luteotrophic hormone or LTH) in the male mammal is not well established. Pasqualini(1) reported a marked increase in secretions of seminal vesicles of castrate rats after administration of LTH for 3 consecutive days following priming dose of testosterone propionate. Influence of LTH on the prostate was not significant. Pasqualini considered that the action of LTH was directly on the seminal vesicles but manifested itself only when the wall of seminal vesicles was rendered reactive by action of testosterone. Chase *et al.*(2) observed minimal growth of seminal

vesicles of castrate Sprague-Dawley rats with administration of LTH or LTH in combination with TP. Testosterone and STH together caused a significant increase in weight and proportion of glandular tissue of the ventral prostate and seminal vesicles. Their data suggest that LTH may act in a synergistic manner to stimulate accessories of the male rat. Everett(3,4) showed that pituitary autografts to the kidney capsule of female rats favored continuous secretion of LTH and maintained corpora lutea in a functional state at least 4 to 5 times the duration of pregnancy. Rennels (Univ. of Texas, personal communication) pointed out that the pituitary of male rat transplanted to kidney capsule of female rat was equally capable of producing LTH and maintained corpora lutea in a functional state. In view of these observations it became of interest to see if the autografted pitui-

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TABLE I. Effect of Prolactin (LTH) and Testosterone Propionate (TP) on Seminal Vesicles of Intact, Castrate, Hypophysectomized and Pituitary Autografted Male Guinea Pigs.

Group	Treatment		No. of animals	Body wt (g)		Sem. ves. wt (g)	Epithelial ht (m μ)
	TP (μ g)	LTH (I.U.)		Initial	Final		
Long term series							
Intact control			6	507	777	1873	17.8
		15	6	503	770	2036	18.0
Castrate control			3	510	715	352	8.1
		"	3	520	714	314	8.0
	12.5	"	3	530	670	490	8.0
		30	3	557	777	739	11.5
	"	"	3	517	705	364	8.8
Hypophysectomized			3	460	710	218	8.0
	"	15	3	510	805	326	9.0
	"	30	3	525	655	510	12.9
Pituitary autograft			3	490	564	222	7.8
	"		3	540	779	591	13.2
	"		3	530	640	478	8.5
Short term series							
Castrate control			3	510	690	356	8.4
		30	3	531	583	363	8.7
*	25	"	3	573	580	879	17.8
*	"	30	3	575	616	870	17.7
*	"	60	3	530	760	1331	18.2
Intact control			3	515	744	2048	18.0

* Inj. with priming dose of 100 γ of TP for 6 days, followed by treatment indicated in Table for 7 days.

tary in the male guinea pig would function likewise. Experiments here reported are a pilot study, because dose levels of LTH in the guinea pig had to be established and combinations of LTH and TP relative to physiological conditions had to be checked. The consequence of this is evident in the design of the experiment in that many groups are involved, each containing only a few animals.

Materials and methods. Sixty-three male guinea pigs of a heterogeneous strain were used in 2 series of experiments, a long and short term series. Forty-five animals in the long term series were subjected to different operative procedures and placed in Groups 1 to 13 (Table I). All operations were performed when animals were 65 days old. Hypophysectomy was accomplished by parapharyngeal approach under ether anesthesia and when the gland was to be transplanted it was sucked into sterile cannula and placed in sterile physiological saline at room temperature. Autografts were made immediately by placing the gland under the left kidney capsule following the method of Everett(4). In Group 13, castration was done the same day

immediately following autograft of pituitary gland. Daily intramuscular injections of testosterone propionate or prolactin were begun the day following surgery and continued for 8 weeks.§|| Prolactin (NIH-SP-1) used is a highly purified sheep preparation, estimated to contain 20 I.U./mg, and distributed by the Nat. Insts. of Health. Pyrogen-free water at pH 7.0 was the solvent for the prolactin powder. On day following last injection, the animals were sacrificed by decapitation and sex accessories, pituitary, adrenals and testes were removed and weighed. Seminal vesicles were not freed of their contents before weighing. Bits of tissue from all these structures were fixed in Zenker's fluid, sectioned at 7 μ and stained with Groat's tetrachrome stain. The sella turcica of hypophysectomized animals was examined under magnification for presence of pituitary fragments. In the short term series, 18 male guinea pigs were castrated at 65 days of age. Six weeks

§ Prolactin was a gift from Endocrinology Study Section, Nat. Insts. of Health.

|| Testosterone propionate was a gift from Ciba Pharmaceutical Products, Summit, N. J.

later, when sex accessories had attained maximum regression, they were divided into 5 groups and treated as indicated in Table I. Group 14 received no treatment. Groups 16, 17 and 18 were injected for 6 days with 100 μ g of testosterone propionate/day after which they were injected for 7 days with 25 μ g of testosterone propionate. In addition to above treatment, Groups 17 and 18 received 30 and 60 I.U. of LTH daily, respectively during last 7 days. Group 15 received only 30 I.U. of LTH daily during last 7 days without prior priming with TP. Animals were sacrificed the day following last injection and processed as in the long term series.

Results. In the long term series (Table I), castrates (Group 3) showed atrophy of seminal vesicles. The same condition was also seen in castrates treated with 15 I.U. LTH (Group 4), subminimal TP (12.5 μ g) and 15 I.U. LTH (Group 5) or subminimal TP only (Group 7). Appearance of epithelium and average cell height in these groups was nearly the same (8.1 to 8.8 $m\mu$). The nuclei were located basally and supranuclear zone was small. However, castrates treated with subminimal TP and 30 I.U. LTH (Group 6), exhibited seminal vesicles nearly double the size and weight of other treated groups (Groups 4, 5 and 7). Average cell height of epithelium was 11.5 $m\mu$. Epithelium was slightly columnar, nuclei basal and supranuclear zone was tall and had a number of secretory granules in the cytoplasm. There was no visible accumulation of secretion in the seminal vesicles. Hypophysectomized animals receiving no treatment (Group 8) or those receiving subminimal TP and 30 I.U. LTH (Group 10) exhibited marked heightening of epithelium but with no visible secretion in the seminal vesicles. Since amount of secretion in seminal vesicles of different groups was too small for quantitative estimation, only a subjective evaluation was possible. In Groups 6 and 10 all of the seminal vesicles exhibited the responses indicated, with much uniformity present at the cellular level.

Pituitary autografted animals without further treatment (Group 11) showed marked atrophy of seminal vesicles corresponding to those of castrates, while those receiving sub-

minimal TP (Group 12) evidenced an increase in weight of seminal vesicles and a cell height average of 13.2 $m\mu$. Autografted castrates receiving same level of TP (Group 13) did not show any increase in epithelial height and resembled those of castrates.

The object of the short term series (Table I) was to verify and to test results of Pasqualini and Chase and check on a higher dose of LTH. In those treated with 30 I.U. LTH daily (Group 15) weight of seminal vesicles and appearance of epithelium were similar to castrates. Those treated with TP only (Group 16) had seminal vesicles weighing nearly double that of castrates and the epithelium was considerably higher (average cell height of epithelium 17.8 $m\mu$). In animals treated with TP and 30 I.U. LTH daily (Group 17), weight of seminal vesicles was nearly the same as in those treated with TP only (Group 16). Appearance of epithelium was more like that of intact animals than androgen treated castrates. Nuclei were located basally in a row and the supranuclear zone of cytoplasm was tall and granular. A significant difference was noticed in Group 18 treated with TP and 60 I.U. LTH daily where weight of seminal vesicles was approximately twice that of groups treated with TP (Group 16) or those treated with TP and 30 I.U. LTH (Group 17). Average cell height of epithelium was the same as that of intact controls or those treated with TP only (17.8 $m\mu$). All of the seminal vesicles of Groups 16, 17, 18 responded uniformly.

In neither series did the prostates, adrenals, pituitaries, testes and mammary glands show any significant differences in structure or size in the different groups treated with various levels of LTH.

Discussion. In long and short term series it appeared that seminal vesicles only, among sex accessories, were sensitive to LTH administration. While LTH alone had no effect on seminal vesicles of the castrate guinea pig, it did however cause a significant increase in weight and stimulated the epithelium of seminal vesicles primed with TP. Comparison of histological appearance of seminal vesicles in Group 6 with Group 17 of the short term series indicated that the epithelium was stimu-

lated. Presence of secretion in seminal vesicles of Group 17 only, indicated that higher priming dose of TP was required before LTH could cause it to become secretory. Doubling the dose of LTH to 60 I.U. daily (Group 18) caused corresponding increase in weight of seminal vesicles. Since there is no increase in height of epithelium the increase in weight could be accounted for primarily by increase in amount of secretion or by hyperplasia caused by LTH.

The difference in appearance of seminal vesicle epithelium between autografted intact (Group 12) and autografted castrates (Group 13) may indicate that there was a small amount of secretion of gonadotrophic hormones by transplanted pituitary which stimulated the Leydig cells to produce testosterone. This augmented the subminimal TP injected exogenously. It is also possible that the epithelial response by autografted intact animals may indicate that small amounts of LTH were being produced by the graft. This acted synergistically with subminimal TP to bring about responses similar to those seen in animals receiving subminimal TP and a high dose of LTH.

When comparing groups 16 and 17, there seemed to be no significant change in seminal vesicle morphology resulting from daily administration of 30 I.U. LTH over that resulting from TP itself. Contrasting these 2 groups with Group 18 which received 60 I.U. LTH, it appeared as if some stimulation was

obtained other than by TP. Thirty I.U. LTH acting with subminimal dose of TP in the long term study groups did show stimulation. It is clear that many levels of LTH must be tested, however, some quantitative relationships of effectiveness have been suggested.

Summary and conclusions. The role of LTH (lutetotrophic hormone, prolactin or lactogenic hormone) in stimulating epithelium of seminal vesicles of castrated guinea pigs has been tested in 2 series of experiments. LTH alone had no effect on seminal vesicles of castrates. LTH together with subminimal testosterone propionate caused significant increase in weight of seminal vesicles as well as height of epithelium. A high priming dose of TP was required before LTH stimulated visible secretion. Doubling the dose of LTH after priming with TP caused a corresponding increase in seminal vesicle weight. Prostates, testes, mammary glands, adrenals and pituitaries did not show any significant differences in structure or size when various levels of LTH were present. The results are in agreement with the findings of Pasqualini(1) and Chase *et al.*(2).

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Distribution of Red Blood Cells Between Tissues of Mouse.* (25419)

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Red blood cells labeled with radioactive isotopes are presently being employed in a variety of experimental conditions for determination of circulating red blood cell volume.

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In general, the technic consists of intravenous injection of labeled erythrocytes followed by sampling of blood after a period of time considered adequate for complete vascular mixing. Usually, this time interval is derived from the blood radioactivity curve and represents the point at which blood radioactivity achieves a constant level. While this interval may be suitable for determination of the cir-