animals after hypophysectomy. This finding of Gilman and Goodman[2] is confirmed by our results.

It has been previously shown that large doses or prolonged injections of theelin[6] or of testosterone propionate[3, 7] depress the gonad-stimulating power of the anterior hypophysis. While we have noted this, our results also show that these preparations do not affect the posterior lobe in its ability to secrete an antidiuretic substance following dehydration. Furthermore, progesterone and antuitrin S similarly have no effect. In one respect, therefore, the sex hormones are not directly related to posterior pituitary activity. Indirect relationships, of course, may be possible.

Conclusions. Prolonged injections of large doses of theelin, progesterone, testosterone propionate and antuitrin S do not alter the ability of dehydrated rats to excrete an antidiuretic substance. Since this substance appears to be of hypophyseal origin, these sex hormones have no direct relationship to this phase of posterior pituitary activity.

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Effects of a Digested Pituitary Extract on Reproductive Tract of Hypophysectomized Adult Male Rats.

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The work of McShan and Meyer[1] and Chen and van Dyke[2] has shown that the luteinizing ability of pituitary gonadotropic extracts can be largely destroyed by tryptic digestion. These treated preparations produced remarkably specific gametogenic effects in normal and hypophysectomized immature female and male rats.

Greep and Fevold[3] have shown that the hypophyseal fraction LH acts on the interstitial cells of hypophysectomized adult male rats causing the secretion of male hormone, whereas the FSH preparation will sustain or repair the gametogenic processes without stimulating the testes to endocrine function. However, with dosages of FSH in

[3] Hamilton, J. B., and Wolfe, J. M., *Endo.*, 1938, **22**, 360.

[7] Moore, C. R., and Price, D., *Endo.*, 1937, **21**, 313.

[1] McShan, W. H., and Meyer, R. K., *J. Biol. Chem.*, 1938, **126**, 361.

[2] Chen, G., and van Dyke, H. B., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 172.

[3] Greep, R. O., and Fevold, H. L., *Endocrinology*, 1937, **21**, 611.

excess of the minimal requirements for normal tubular function slight but definite growth of the accessories occurred. Since the hypophysectomized adult male rat offers quite a satisfactory test animal for determining the "purity" of the FSH fraction, it, therefore, seemed of interest to investigate its response to a digested pituitary extract in which the luteinizing action had been largely abolished.

Digestion* of the original (horse) pituitary extract was carried out in a manner identical with that employed by Chen and van Dyke.[2] The injections were made once daily from the 10th to the 20th postoperative day with necropsy on the day following the last injection. The effects of the digested and of the control non-digested extracts on the weight of the testes and seminal vesicles are shown in Table I. The non-digested extract produced marked growth of the testes and the seminal vesicles attained a larger size even than those of normal animals of comparable weight. Histologically the testes resembled those of normal adult rats except for an increased amount of interstitial tissue (Fig. 1, 2).

The digested material though less active in stimulating testicular growth did nevertheless, with adequate dosage, produce considerable enlargement. The spermatogenic processes, interrupted by 10 days total hypophyseal deficiency (Fig. 3), were restored to normal by the trypsin digests given in daily doses of 1 and 4 mg (Fig. 5, 6) but not in daily doses of 0.2 mg (Fig. 4). Spermatozoa were abundant in the epididymides and motility was normal when the two higher doses were administered. The atrophic interstitial cells remained unchanged (Fig. 3, 6), although in some animals the dose of digested extract was 4 times as great as that which clearly maintained

TABLE I.

Material	Daily dosage, mg powder	No. animals	Testes, mg	Empty seminal vesicles, mg
Non-digested pituitary powder	0.2	2	2349	656
Digested pituitary powder	0.2	2	864	84.4
	1.0	2	1210	100.8
	4.0	3	2035	111.9
Hypophysectomized	10 days	2	1795	104
"	20 "	2	855	102
Unoperated controls		3	2603	343.3

* The enzyme used (Merck's trypsin) was of the same preparation as that employed by Chen and van Dyke.[2]

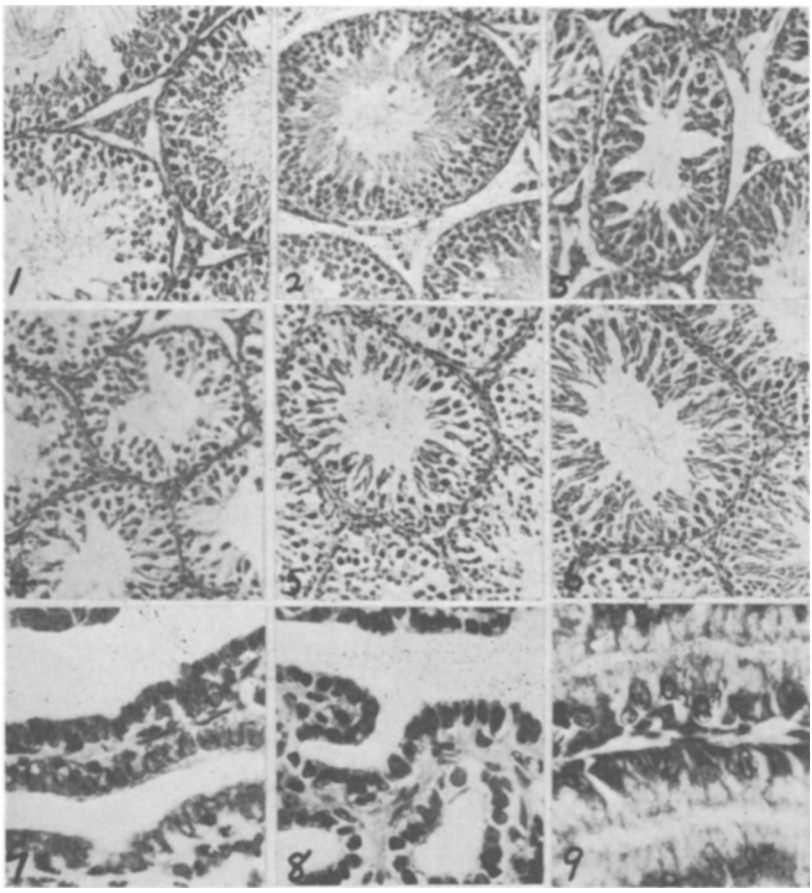

Fig. 1-6 (all ×120) are photomicrographs of adult rat testes; all injections were made on days 10-20 after hypophysectomy. 1. Operated rat receiving 0.2 mg non-digested pituitary powder daily. 2. Normal rat. 3. Untreated rat 10 days after hypophysectomy. 4, 5, and 6, hypophysectomized rats receiving 0.2, 1, and 4 mg digested pituitary powder daily respectively.

Fig. 7-9 (all ×540) show the epithelium of the seminal vesicles 10 days after operation (7), after 10 days treatment with 4 mg digested pituitary extract daily (8), and after similar treatment with 0.2 mg non-digested extract daily (9).

spermatogenesis. The weights of the seminal vesicles showed a total absence of any growth effect; microscopic examination also failed to reveal any stimulation of the glandular epithelium (compare Fig. 7, 8, 9). The scrotal area of these animals also remained in such an atrophic state that the gonads were restrained in the upper portion of the inguinal canal. Whatever effect this position may have on the testicular response to FSH presumably would be unfavorable.

Another experiment in which an extract of sheep pituitary glands

was digested by this same enzyme preparation has yielded results which are similar to those just described.

Conclusions. Digestion of an anterior pituitary extract by trypsin under suitable conditions may destroy interstitial-cell stimulating activity, leaving a pure gametogenic effect in adult hypophysectomized male rats. It appears that interstitial-cell stimulation or luteinization is caused by the same substance which is largely destroyed by the digestion.

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Effect of Induced Hypercholesterolemia on Antibody-Response in Rabbits.

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Although it is generally assumed that cholesterol in blood and tissue is related in some manner to processes of immunity,[1, 2] the mechanism of this action is not clearly understood. It seemed important to determine whether the production of antibodies by the organism was influenced by the level of cholesterol in the blood.

Seventeen rabbits (9 controls and 8 experimental) varying in age from 3 to 5 months were fed Ralston-Purina rabbit-chow once daily. Hypercholesterolemia was produced in the experimental group by feeding 1 g of cholesterol mixed with the food 3 times a week for a period of 5 to 8 weeks. After this time, the blood-cholesterol usually exceeded 350 mg per 100 cc and immunization was then begun. The feeding of cholesterol to the experimental group was continued throughout the experiment.

All animals received intravenous injections of increasing amounts of a typhoid vaccine containing 10^9 organisms in 1 cc. Injections of 0.2, 0.3, 0.4, 0.6, 0.8, 0.9, and 1.0 cc were made on the 1st and 5th, 8th, 11th, 14th, 16th, 19th, and 21st day respectively.

Agglutinative tests were done before injections of vaccine and at weekly intervals for 5 weeks thereafter. The titer was that dilution which, after refrigeration overnight and after careful agitation, still showed macroscopic clumping. The results are given in Table I.

1 Muller, G. L., *Medicine*, 1930, **9**, 119.

2 Stoesser, A. V., and McQuarrie, I., *Am. J. Dis. Child.*, 1935, **49**, 658.