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## Pituitary Hormone Antagonism.\*

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It is known that certain hypophyseal extracts will inhibit the increase in the size of the ovaries of immature rats, which occurs when gonad stimulating extracts are administered. In a previous note (Leonard<sup>1</sup>), it was stated that the growth hormone of the pituitary was not the inhibiting substance and it was suggested that a sex stimulating fraction or something associated with it, was the antagonistic agent. In further attempts to identify the inhibiting substance with known extracts of the pituitary, several gonad stimulating fractions and a thyroid stimulating fraction were used. The results obtained are reported here.

Antuitrin S† was injected subcutaneously into immature female rats of similar age and weight, in doses which produced ovaries weighing approximately 30 mg., in 5 days. Similar rats were treated for the same period with the same amount of Antuitrin S plus intraperitoneal injections of the several pituitary extracts to be tested for their inhibiting power. These were as follows: follicle-stimulating hormone (F.S.H.) and luteinizing hormone (L.H.) prepared from sheep pituitary (Fevold, *et al.*<sup>2</sup>), luteinizing hormone from horse pituitary, unfractionated pregnant mare serum, follicle stimulating urine (F.S.U.) prepared by alcoholic precipitation, and thyroid stimulator from the Schering Corporation.‡ These preparations were all tested and found to be active.

It is quite expedient that the fraction to be tested for inhibition be given intraperitoneally rather than subcutaneously or otherwise the presence of the inhibiting substance may not be detected (Leonard<sup>1</sup>).

The results of the experiments are summarized in Table I. It is readily seen that the luteinizing fraction prepared from sheep pitui-

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<sup>1</sup> Leonard, S. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **31**, 1157.

† The Antuitrin S was furnished through the kindness of Parke, Davis and Company.

<sup>2</sup> Fevold, H. L., Hisaw, F. L., Hellbaum, A., and Hertz, R., *Am. J. Physiol.*, 1933, **104**, 710.

‡ The thyroid stimulator was obtained from Dr. E. Schwenk, Bloomfield, N. J., through the courtesy of Dr. Philip E. Smith.

TABLE I.

Treatment	Av. Ovarian Wt. mg.	Av. Uterine Wt. mg.
Ant. S. (50 R.U.)	31.9	145.2
'' + 6.25 mg. L.H. (sheep)	15.7	52.2
Controls (same in all groups)	15.0	38.0
'' + 20 mg. preg. mare serum	30.6	114.2
Ant. S. (50 R.U.)	32.3	109.3
'' + .2 cc. F.S.H. (sheep)	22.1	81.9
Ant. S. (25 R.U.)	18.6	97.3
'' + 100 cc. equiv. of F.S.U.	46.0	83.4
Ant. S. (50 R.U.)	38.1	136.8
'' + 6 mg. Thyroid stimulator	43.6	124.3
Ant. S. (75 R.U.)	40.1	146.0
'' + 5 mg. L.H. (horse)	42.1	135.7
Ant. S. (75 R.U.)	33.1	109.5
'' + .2 cc. F.S.H. (sheep)	26.9	103.8

All extracts above were of known potency. .2 cc. of F.S.H. injected subcutaneously gave 25 mg. ovaries; 100 cc. equivalent of F.S.U. subcutaneously gave 26.2 mg. ovaries. The thyroid stimulator tested 1 Rowland-Parkes unit per 1.5 mg.

Each result is based on the average of 3 or more rats. All fractions tested for inhibition (excluding Ant. S) were injected intraperitoneally.

All rats were 22-25 days old at the beginning and were autopsied 5 days later.

tary was the only one to give a complete and definite inhibition of ovarian growth. The follicle stimulating substances from pituitary or urinary sources failed; the pregnant mare serum, the thyroid stimulator and the luteinizing hormone from horse pituitary also failed. It is noted that when F.S.U. was injected, there was a decided increase in ovarian weight over that produced by the Antuitrin S alone. This may have been due to some of the F.S.U. entering the subcutaneous tissue which would give an "Augmented" reaction with Antuitrin S.

It was again observed that whenever the inhibiting action is complete, the uterus of the immature rat fails to grow and the vagina does not open. In these experiments only the L.H. fraction from sheep pituitary inhibited uterine growth and vaginal canalization.

From the results in Table I, it is not possible to conclude that the luteinizing hormone *per se* is the inhibiting substance. The luteinizing fraction from horse pituitary did not inhibit the gonad stimulating action of Antuitrin S. Other experiments have also showed that L.H. from horse pituitary will not inhibit the pituitary follicle stimulator when injected in the same way.

It can only be concluded from these results that the inhibiting

principle is associated with the luteinizing hormone of certain pituitary glands. At present, the reaction itself can only be demonstrated in the immature and hypophysectomized rat. Attempts to inhibit the stimulation of adult rat ovaries by the injection of Antuitrin S and L.H. from sheep pituitaries were unsuccessful.

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## Negative Results of Iodides in Anaphylaxis in Guinea Pigs.

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Zifferblatt and Seelaus<sup>1</sup> have reported successful desensitization of guinea pigs by repeated intraperitoneal injection of an aqueous solution of iodine. This report would appear to lend support to the belief long held by many clinicians that in some asthmatics continued iodide administration rendered their attacks less frequent and severe. It, therefore, seemed worth while to see if iodide therapy in sensitized guinea pigs would also result in desensitization. The negative results obtained are stated in Table I.

All pigs received a subcutaneous injection of 1/20 ccm. of dog serum January 11.

TABLE I.

Treatment	½ ccm. dog serum I.V.	Result
None	Feb. 23	died
''	Mar. 2	lived
''	'' 6	died
100 mg. Iodalbumin (21.5% I) daily from Feb. 11	Feb. 23	lived
	'' 23	died
	Mar. 2	''
	'' 2	''
	'' 6	''
	'' 6	''
25 mg. K.I. I.P. daily from Feb. 11	Feb. 23	''
	Mar. 6	''

All pigs were autopsied and in those dying after the intravenous injections, the lungs showed typical distension.

Although the series is small the results are so negative that it may

<sup>1</sup> Zifferblatt and Seelaus, *Am. J. Med. Sci.*, 1934, **188**, 142.