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A Comparison of Interstitial Cell-Stimulating, Ovarian-Stimulating, and Inhibiting Actions of Pituitary Glands of Different Species.

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There is very little data concerning the luteinizing hormone content of various kinds of pituitaries which are used in experimental work. It has not been accurately established in what amounts the gonad-stimulating hormones exist in the pituitaries of different species of animals. Recently a method of assay has been described which permits the accurate determination of the LH present in pituitary tissue in the presence of the other gonadotropic factor FSH.[1] In most assay methods the FSH acts synergistically with LH, and thus confuses the results.

Likewise, there are no data available regarding the capacity of pituitary glands from different species to inhibit the action of FSH in producing follicular development in the ovaries of immature rats. It has been variously reported (a) that this factor is separate and distinct from the follicle-stimulating and the luteinizing hormone[2, 3] and (b) that it is the luteinizing hormone which produces this effect under the proper conditions.[4, 5]

This paper reports the quantitative assay of the LH content and also the inhibiting action of the pituitary glands of sheep, hog, and beef. The potencies of these pituitary tissues in stimulating ovarian development in the immature female rat are also recorded to give a comparative idea of the FSH potency.

Methods of Assay. The increase in the weight of the seminal vesicles of immature male rats has been used as a measure of the luteinizing hormone, since it has been shown that the LH stimulates the production of male hormone in the male rat.[6] It was also shown that FSH augments the action of LH in the production of male hormone,[6] so that in its presence the results were not a true measure

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2 Evans, H. M., Korpi, K., Pencharz, R. I., and Simpson, M. E., *Univ. Calif., Pub. Anat.*, 1936, **1**, 237.

3 Bunde, C. A., and Hellbaum, A. A., *Am. J. Physiol.*, 1939, **125**, 290.

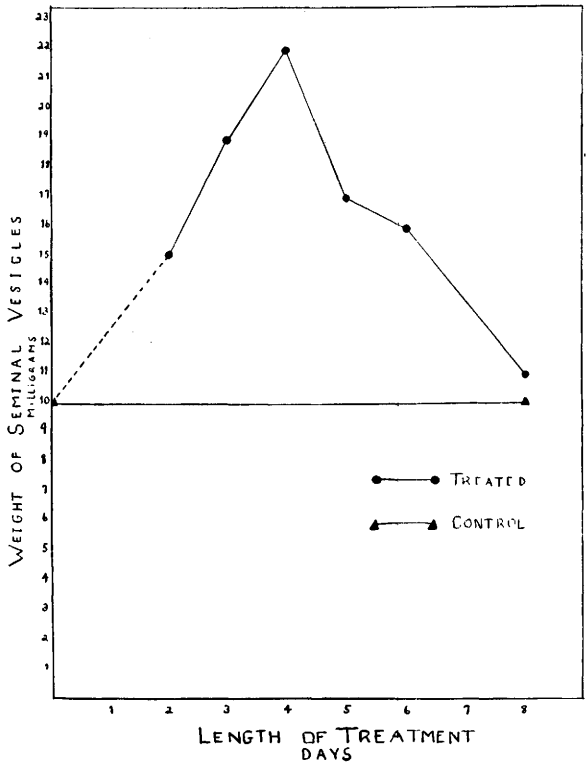
4 Jensen, H., Simpson, M. E., Tolksdorf, S., and Evans, H. M., *Endocrinology*, 1939, **25**, 57.

5 Fevold, H. L., and Fiske, V. M., *Endocrinology*, 1939, **24**, 823.

6 Greep, R. O., Fevold, H. L., and Hisaw, F. L., *Anat. Rec.*, 1936, **65**, 261.

FIGURE I

RESPONSE OF THE SEMINAL VESICLES OF IMMATURE MALE RATS TO A CONSTANT AMOUNT OF LH INJECTED FOR VARIOUS LENGTHS OF TIME



of the LH. However, if the pituitary material is injected intraperitoneally, FSH is no longer effective, while LH is as active as when injected subcutaneously. It is thus possible to negate the augmenting action of FSH, and the LH activity can be accurately determined.

The pituitary extract was injected intraperitoneally twice daily, morning and evening, in 0.25 cc doses into immature male rats (21 days old) for 4 days, since it was found that injections of a constant amount of LH given for this length of time resulted in the maximum response of the seminal vesicles. (Fig. I.)

A unit of LH is taken as the smallest amount of pituitary tissue necessary to produce a 100% increase in the weight of the seminal vesicles of the injected animals over those of the uninjected controls.

The inhibiting potency of the pituitary glands was determined in the following manner. Enough FSH was given subcutaneously over a period of 4 days to immature female rats (21 days old) to

produce an increase of 300% in the weights of the ovaries. The pituitary preparations to be tested were injected simultaneously intraperitoneally and an inhibiting unit was taken as that amount of pituitary material which would reduce the response to 150%.

The ovarian-stimulating potency was determined by injecting the preparations twice daily for 4 days into immature female rats (21 days old) and weighing the ovaries the morning of the fifth day. At the time of autopsy the ovaries were also observed to determine if they were primarily follicular or luteinized.

Preparation of Materials to be Tested. Acetone-desiccated pituitary powders or fresh pituitary tissue were extracted with an alkaline solvent at pH 8.0, and the extractives precipitated with acetone. The precipitate was thoroughly extracted with distilled water to remove the gonadotropic hormones, leaving as a residue the material rendered insoluble by the acetone precipitation, apparently because of denaturization. The aqueous extracts were then dried and stored as powders. This water-soluble material was always precipitated with tannic acid before injections, and injected as fine aqueous emulsions. In this manner the absorption rate should be as nearly equal from preparation to preparation, irrespective of the impurities, thereby avoiding one source of error.

Results. Table I presents the results of the assay of pituitaries of different species for the luteinizing hormone. It is at once apparent that sheep pituitary glands are the best source of LH and that beef pituitary glands contain the least. With the hog pituitary materials the results vary considerably, but in all cases the LH content is lower than in those of sheep. In 2 of the hog preparations very small amounts of LH were present, as indicated not only by the inability of these 2 preparations to stimulate male hormone secretion but also by the fact that the ovarian development, produced by these

TABLE I.
Interstitial Cell-Stimulating, Ovarian-Stimulating, and Inhibiting-Actions of Pituitary Tissue of Sheep, Hog and Beef.

Preparation	LH content, Ru/Kg	Ovarian development, Ru/Kg	Inhibiting action, Ru/Kg	Ratios	
				LH/ov.	Lh/inhib.
Sheep pit. powder	143,000	16,000		9.0	
Fresh sheep pit.	20,000	20,000		1.0	
" " "	30,000	10,000	120,000	3.0	0.25
Hog pit. powder	2,000	12,500		0.16	
Fresh hog pit.	1,666	20,000		0.08	
" " "	5,000	15,000	20,000	0.33	0.25
" beef "	1,666	625		2.6	
" " "	2,000	666	10,000	1.6	0.2

preparations, was mainly follicular, with very little luteinization. The third hog preparation contained considerable amounts of LH. It is possible that this variation may be due to a difference in the physiological state of the animals being slaughtered at the time the various batches of pituitary glands were being collected, for it is well known that the pituitary glands of castrated animals contain less LH than do those of normal individuals.

The inhibiting action of sheep, hog and beef parallel their LH content, and the ratio of LH units to inhibiting units was a constant. This would lend support to the belief that the inhibiting property of pituitary extracts may be due to the luteinizing hormone.[4, 5]

Hog and sheep pituitary glands are approximately equally active in producing ovarian enlargement. This does not mean, however, that hog and sheep glands are equal in FSH potency, but rather that those of the hog have more FSH than those of sheep. This is indicated because there is more LH present in sheep pituitary preparations than in those of hogs. Ovarian development produced by unfractionated extracts is due to the interaction of FSH and LH. Consequently more FSH must be present in hog pituitary glands with the relative small amount of LH in order to produce the same ovarian enlargement as is produced with sheep preparations, which are rich in LH. The ovaries produced with sheep preparations were always heavily luteinized while those elicited by the injection of hog substance were mainly follicular.

Beef pituitary glands produce very little ovarian development and are therefore a poor source of FSH as well as LH.

Summary. (1) It was found that sheep pituitary glands contain the greatest amount of LH, while those from cattle had very little. Hog pituitary glands showed great variation with respect to LH content but in all cases contained much less than sheep glands. (2) The inhibiting action of the pituitary preparations paralleled their LH content. (3) Hog and sheep pituitary glands are approximately equal in producing ovarian hypertrophy. Hog preparations produced mainly follicular development while those of sheep caused the development of heavily luteinized ovaries. Hog glands, therefore, contain more FSH than those of sheep. Beef pituitary glands are a very poor source of FSH. (4) The FSH and LH content of different lots of pituitary glands of the same species varies within wide limits. Nevertheless, those of each species show definite characteristics, with respect to their FSH and LH content.