ovaries weighed 29.6 mg., those of the animal receiving 200 cc. equivalent of urine weighed 39.6 mg., and those of the animal receiving 400 cc. equivalent weighed 80.3 mg.

The uteri in all cases were markedly enlarged and the vaginas were open. In the ovaries of the largest animal, corpora lutea were found, none being present in the controls. Thyroids and adrenals were not significantly increased in size.

These results, while not based on a large number of animals, were all consistent in producing the follicular stimulating effect which is characteristic of such urines and is in marked contrast to the effects of pregnancy urine. The guinea pig, like the hypophysectomized rat, can be used qualitatively to differentiate the urinary gonadotropic hormones.

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Studies on Ovarian Inhibiting Action of Certain Pituitary Extracts.

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It has been amply demonstrated that hypophyseal extracts containing the growth principle will prevent the gonad-stimulating action of hypophyseal or pregnancy urine extracts in immature or hypophysectomized rats (Smith, Evans, Reiss and Leonard). This inhibitory action was first ascribed by Evans and his coworkers to the growth hormone but later work led them to abandon their original thesis. Investigations along similar lines also indicated that the growth hormone is not the antagonistic principle. Results obtained on the study of this reaction constitute this report.

Sexually immature female rats were given 10 R.U. of pregnancy urine extract (Antuitrin S)† subcutaneously, which approximately doubled the weights of the ovaries in 5 days. Littermates which were concurrently injected with pregnancy urine and extracts of beef and sheep pituitaries containing growth hormone (doses 1 cc. to 5 cc.) prepared after the method of Van Dyke,[1] failed to show

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1 Van Dyke, *J. Pharm. Exp. Therap.*, 1930, **40**, 413.

the increase in weight of the ovaries. The repressing effect of the pituitary extracts upon the stimulated ovaries was also revealed by the infantile uteri and the closed vaginas of the young animals. For example, the average ovarian weight of 4 rats in one litter treated with Antuitrin S was 24.3 mg., the average of 4 littermates treated in the same manner plus the hypophyseal extract was 13.6 mg., a decrease of 44%. The uteri weighed 66.7% less and the vaginas of this latter group failed to open.‡ In testing the various pituitary fractions for inhibition and in each of the subsequent tests, no less than 12 animals were used, 6 receiving the pregnancy urine and 6 receiving the combined injections. An ovarian weight of 15 mg. was taken for the uninjected controls which is the average size for immature rats of similar age in the colony.

The inhibiting pituitary fraction was administered intraperitoneally because subcutaneous injections with pregnancy urine usually resulted in "augmentation" in the size of the ovaries due to the presence of the hypophyseal gonadotropic hormone. The gonadotropic hormones are not as effective when given intraperitoneally (unpublished data) and failed to produce the increased gonadotropic effect, presumably because of the hasty elimination resulting from this method of administration.

Of 2 samples of growth hormones from proprietary sources, both of tested potency, one failed to inhibit the action of Antuitrin S in doses up to 5 cc., and the other repressed the ovaries in doses of 1 cc. to 3 cc. The extract which was more potent for growth failed to inhibit. The ability of a pituitary fraction to repress the development of a stimulated rat ovary is apparently independent of its growth hormone content.

Further studies on the nature of the inhibiting substance revealed that it was destroyed by boiling but not by precipitation with alcohol. When adult female rats were injected intraperitoneally with the several preparations containing growth hormone, it was observed that the ovaries increased in size instead of becoming smaller. Interestingly, the preparation which gave the best inhibition produced the heaviest ovaries in the adult rats. This seems to indicate that the properties of the inhibiting substance are more like those of the gonadotropic hormones. Experiments are being pursued at present to test this assumption.

‡ Over 150 animals were used in these experiments, using only littermates for controls.