lation to effect the ovary weight. (4) The follicle-stimulation dose, as determined by ovary weight and development of follicles to macroscopic proportions, approximates the unit for follicle stimulation as determined by vaginal opening with estrus. Hence, the latter end-point may be used alone for testing dilutions known to be below the level of the minimum luteinizing dose. Such a combination of these 2 end-points may be used for the estimation of the relative concentration of the luteinizing and follicle-stimulating potentialities of test urines. (5) The uterine reactions to given doses of pregnancy urine are extremely variable so cannot be incorporated into the criteria of the unit dose. However, uterine hypertrophy in animals giving neither vaginal nor macroscopic ovarian responses should be considered as indication for microscopic investigation of the ovaries.

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Theelin and Progestin Injections on Uterus and Mammary Glands of Ovariectomized and Hypophysectomized Rabbits.

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The work of Gardner and Turner[1] suggests that the immediate stimulus for mammary growth is due to the ovarian hormones, theelin and progestin. But Corner[2] and others have obtained growth with anterior pituitary preparations in rabbits which have not been exposed to the influence of corpora lutea. The possibility arises that the ovarian hormones act through the pituitary. To test this point we ovariectomized 40 rabbits and kept them for 2 months to exhaust their supply of ovarian hormones. Then by the use of Firor's[3] technique we attempted to remove their pituitaries, We were completely successful in 10 cases; of these successes, 2 occurred while we were perfecting our techniques, 4 died during the 2 months after the operation before we commenced injections. This left us with 4 successful operations which were used for injection work. We sectioned the contents of the sella turcica in each case after the

1 Gardner, W. U., and Turner, C. W., *Mo. Ag. Exp. Sta. Res. Bull.* 196, 1933.
2 Corner, G. W., *Am. J. Physiol.*, 1930, **95**, 43.
3 Firor, W. M., *Am. J. Physiol.*, 1933, **104**, 204.

experiments. Doctor B. F. Kingsbury kindly examined the sections and confirmed the fact that the pituitaries had been completely removed.

Two months after the second operation all the rabbits were injected daily with 25 R.U. of Progynon B (kindly supplied by Doctor E. Schwenk of the Schering Corporation) and of 0.5 cc. of Progestin (equal to about 4 rabbit units) made in this laboratory. These injections were made over a period of 15 days and the rabbits were then killed. The dosage used was found by Turner and Frank[4] to be effective in producing mammary development in the ovariectomized rabbit, but it cannot be considered ideal for causing progestational proliferation of the uterus. When the rabbits were killed, the mammary glands were dissected out on their muscular plates, trimmed of fat and weighed. Later, they were stained with hematoxylin, stripped from the muscle and mounted. A single ovariectomized rabbit was kept as an uninjected control and killed 4 months after the ovariectomy.

The results showed clearly in all cases that mammary development can occur in the absence of the hypophysis as the result of injections of theelin plus progestin. The degree of development was almost the same in these animals as in those in which the hypophysis was not disturbed or was incompletely removed. The weights of the mammary areas in the ovariectomized injected rabbits averaged 34.7 gm. (4 cases) and in the ovariectomized hypophysectomized injected rabbits, 32.2 gm. (4 cases). The difference is possibly due to variations in the area of muscular tissue removed and cannot be regarded as significant, inspection of the glands did not suggest a difference in the degree of development. The weight of a similar area in the ovariectomized rabbit was 28.4 gm.

The uteri of the ovariectomized hypophysectomized injected rabbits showed some progestational proliferation, averaging 2 on Allen's[5] scale. The corresponding figure for the ovariectomized injected rabbits was 3¼. There seemed to be a lessened response in the absence of the hypophysis. But the number of cases is small. It is sufficient at present to state that progestational proliferation can take place to an extent in the absence of the hypophysis. Uterus weights were, for the double operation 5.5 gm., for the single operation 7.3 gm. and for the ovariectomized uninjected control 3.0 gm.

Our conclusions are that the ovarian hormones are capable of

[4] Turner, C. W., and Frank, A. H., *Mo. Ag. Exp. Sta. Res. Bull.* 174, 1932.

[5] Allen, W., *Am. J. Physiol.*, 1930, **92**, 186.

producing some uterine and mammary development in the absence of the hypophysis. This leads us to believe, in the absence of any other likely route, that their influence is direct. This part of the work is clear cut. There may be a greater uterine response with the hypophysis intact, but the numbers are too small to stress this. The results were consistent, however, and one of the hypophysectomized animals which received 3 times the dose of progestin given to the others showed no further development. Yet another ovariectomized rabbit similarly treated (not included in the averages) showed far more uterine development, and possibly a little more mammary development.