

one or the other of the 2 sorts of sera and such as gave negative or weak reactions with both.

6429

Study of Endocrine Factors Influencing Mammary Development and Secretion in the Mouse.

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At sexual maturity the mammary gland of the female mouse consists of the primary duct (galactophore) system. Theelin injections or ovarian implants induce a similar galactophore development in both castrate males and females. No response of the mature female gland is noted after theelin treatment. This is in agreement with the findings of Turner *et al.*,¹ that theelin, theelol or crude estrogenic extracts will not influence the mammae beyond the development of the galactophores. Thus the follicular hormone seems responsible for the establishment of the primary duct system.

It is more or less generally believed that the corpus luteum governs the advanced development of the mammary gland. A satisfactory luteal extract was not obtained. However, luteinization of the ovaries by extracts of the anterior lobe pituitary* or of pregnancy urine† induces development of the secondary ducts (interlobular canals) and later of the alveolar anlagen. In the intact animal this development is much more rapid after pituitary administration than after Antuitrin S. After ovariectomy, neither of these substances will bring about growth of the interlobular canals. Total hysterectomy also inhibits their development even though functional corpora lutea are present in the ovaries. If hysterectomy is done before the appearance of any interlobular canals, they do not appear even after extended periods of luteinizing treatment. Interlobular canals only partially developed at the time of hysterectomy are inhibited from any further growth. Thus it appears that the formation of these secondary ducts is dependent upon the uterus, the activity of which is in turn governed by the corpus luteum.

¹ Turner, C. W., Frank, A. H., Gardiner, W. U., Schultze, A. B., and Gomez, E. T., *Anat. Rec.*, 1932, **53**, 227.

* Pituitary extract whole gland (sheep).

† Antuitrin S.

In the normally developing mammae the alveolar anlagen appear after the interlobular canal system is well established, forming as dense nodular masses which balloon out into grape-cluster lobules when they pass into the secretory phase. Experimentally, pituitary extract induces formation of alveolar tissue in an hysterectomized or ovariectomized animal providing there is some interlobular tissue present at the time of the operation. Antuitrin S is ineffective in the absence of either the ovaries or the uterus.

Hysterectomy, ovariectomy, or both combined, allow the alveoli to go directly into the secretory state as soon as they are formed under the influence of pituitary extract. Interruption of the ovary-uterus complex seems to favor the appearance of milk. In the normal animal it is quite likely that the alveoli form under a pituitary influence but are kept in an inactive state by the presence of some uterine substance which is lost at parturition. Hysterectomy as early as the eleventh day of gestation in the mouse is followed by active milk formation within 48 hours. Frankl² inhibited milk secretion at term by placental grafts. It is evident that after the mammae are built up, the lactation stimulus is more effective in the absence of a uterine factor.

In the mouse the mammae regress very markedly after the lactation period. The interlobular canals and the alveoli become greatly atrophied but not completely resorbed. In case of a subsequent pregnancy they regenerate during the same periods that they form *de novo* in the primiparous animal. This progressive regeneration may be interpreted as additional evidence that the components of the mammary duct system are formed under different influences.

The more rapid response to pituitary treatment than to Antuitrin S indicates that it might have a direct effect on the mammae. This is confirmed by the recent report of Riddle, Bates and Dykshorn,³ claiming to have isolated a substance (prolactin) from the anterior pituitary which acts directly on the mammae.

The extracts used in this study were generously supplied by Dr. E. P. Bugbee and Dr. O. Kamm through the courtesy of Parke, Davis & Co.

² Frankl, O., *Am. J. Ob. and Gyn.*, 1923, **6**, 399.

³ Riddle, O., Bates, R. W., and Dykshorn, S. W., *Proc. Soc. Exp. Biol. and Med.*, 1932, **29**, 1211.