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Production of Uterine Tumors in the Guinea Pig by Local Implantation of Estrogen Pellets.

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Observers have long noted a relationship between ovarian activity and uterine fibromyomatous tumors in the human, and recently several workers have been able to produce similar growths in the uteri of guinea pigs.[1] The latter has been accomplished by the regular subcutaneous injection of large amounts of estrogenic substances over long periods of time. (18% of their injected animals showed uterine fibroids.) We were interested in determining whether the implantation of crystalline estrogen locally in the uterus would give rise to fibromyomatous growths in a higher percentage of instances than has been found with subcutaneous administered estrogen. Pellets of *estradiol benzoate,* each weighing approximately 3 mg were implanted in the uterine horn of each of 12 adult virgin female guinea pigs. This was done by carefully raising the peritoneum from the uterine muscle and placing the pellet into the pocket thus formed. A black silk suture served both to close the pocket and act as a marker. In 6 of these guinea pigs small pellets of cork or paraffin were introduced in a similar manner into the opposite horn. These animals were left undisturbed for 32 to 150 days and were then sacrificed.

In 3 other pigs a black silk suture was employed to close empty pockets and an injection of estradiol benzoate of 10,000 R.U. was administered subcutaneously every 20 days for a total of 60,000 R.U. In 2 additional animals we implanted 3 mg pellets of *estrone* into the uterus, and in 5 pigs 3 mg pellets of testosterone proprionate. Finally, in 2 animals a pellet of *estradiol benzoate* was placed in one horn of the uterus and a testosterone propionate pellet in the other. All of these animals were kept under observation for 150 days and then sacrificed.

Results. Seven unoperated controls were normal. In the 12 guinea pigs in which estradiol benzoate pellets were implanted into one horn of the uterus, either alone or with a paraffin or cork control

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1 Nelson, Warren O., *Endocrinology*, 1939, **24**, 50.

in the second horn, fibromyomatous tumors were found surrounding the estrogenic pellet in 9 cases. No tumors were found around the cork or paraffin implants. Hydrometria were observed in 6 of the animals and were associated with hydrosalpinx in 2 cases. Pyometria alone were noted in 2 pigs and were associated with hydrometria in 2 others. Fibromyomatous tumors were therefore observed in 75% of the animals.

The 3 pigs injected with estradiol benzoate subcutaneously in which silk sutures were introduced into the uterine peritoneum showed no masses. The 2 animals in which estrone pellets were implanted showed no tumors and the 2 animals in which estrogenic and androgenic pellets were implanted showed tumors only at the sites of the implantation of the estrogenic pellets.

Microscopically, the firm gray tumors were composed of varying amounts of muscular, fibrous, and collagenous tissues. The smaller ones contained a large proportion of muscle fibers but the larger ones consisted predominantly of fibrous tissue. In many scattered areas throughout the entire uterus, fibrous tissue replacement of uterine muscle was noted, particularly near the implanted estrogenic pellet. Many of these areas had associated with them collagenous deposition. The collagen was found particularly at the periphery of the fibrous tissue and appeared to be the first step in the replacement of muscle by fibrous tissue. Other microscopic changes resembled those previously described by many workers. The endometrial glands were cystic, showing widespread degeneration and necrosis leading in several cases to pyometria. The cervical epithelium was hyperplastic showing increased keratinization and down-

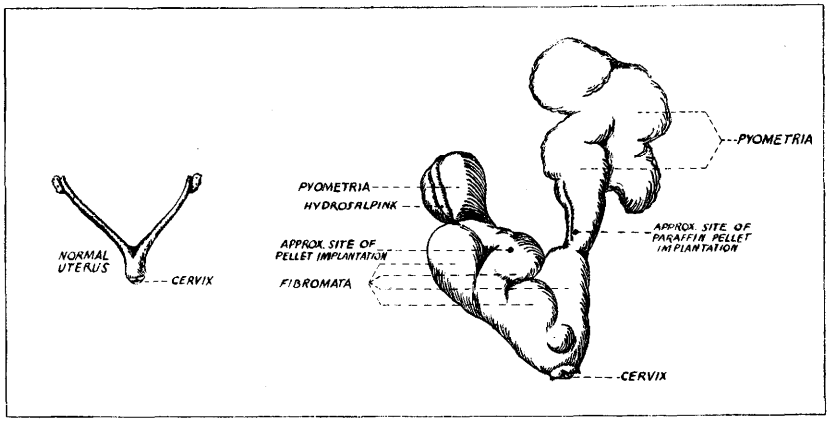

FIG. 1.

Life size drawing of the uterus before implantation and the same uterus 150 days after the implantation of 3 mg of estradiol benzoate.

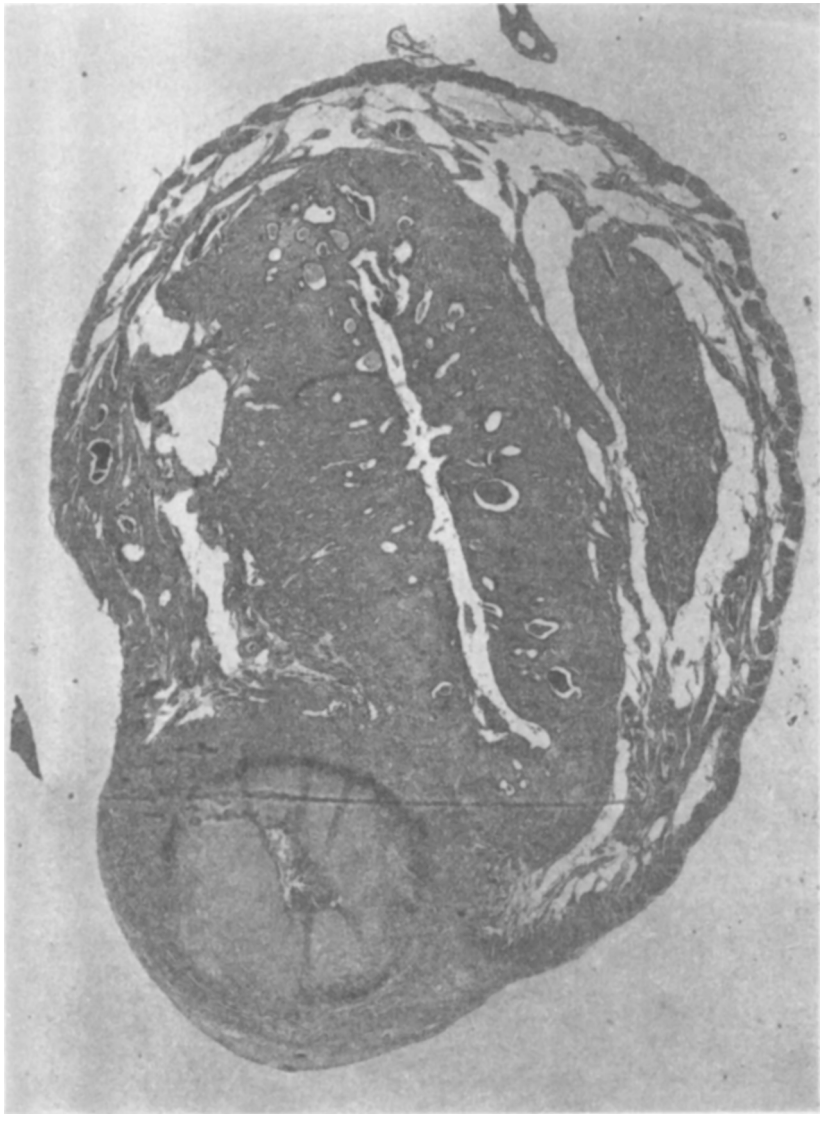

FIG. 2.
This section (low power) was taken so as to include a small tumor and the adjacent uterus.

growths into the submucosa with pearl formation. The vagina was also markedly cornified with thickening of the prickle cell layer and penetration of epithelial cords into the submucosa and pearl formation.

Summary. Small pellets of estradiol benzoate implanted locally

into the uterus produced fibromyomatous tumors in 9 out of 12 guinea pigs (75%) after intervals varying from 32 to 150 days. Estrone in the same concentration did not produce tumors in 2 animals. From the findings made in 2 additional animals, it appears that androgen may have a tendency to limit the extent to which the estrogen is able to produce these tumors.

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Androsterone Effect on Pituitary and Mammary Gland.*

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Two estrogens, estrone and estradiol benzoate,[1] and one androgen, testosterone propionate,[2] have been shown to augment the lactogen content of the rat pituitary gland. These substances are likewise capable of inducing mammary gland growth. The administration of androsterone,[3, 4] however, has produced no detectable growth of the rat mammary gland. It was, therefore, of much interest to determine the influence of androsterone on the lactogen content of the pituitary gland.

Thirty sexually mature rats were ovariectomized and paired on the basis of body weight. One of each pair was injected subcu-

* Journal Series Paper of the New Jersey Agricultural Experiment Station, Department of Dairy Husbandry.

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