The coccus, in culture, is a facultative aerobe, and decidedly positive to Gram's method of staining. It grows commonly in pairs and short chains whose individual cells are always spherical. Macroscopic colonization of the coccus under favorable growth conditions is comparable to that of the freshly isolated *B. influenzae.*

Cultures of the coccus injected into the rabbit induces after an incubation period of 4 to 5 days a pyrexia and leucopaenia. The coccus may be again recovered in culture from the filtered blood of the reacting animal.

The bouillon culture-filtrate of the coccus (after 5 to 7 days growth to 37° C.) produces in the skin of humans susceptible to measles a characteristic reaction, and no reaction in the convalescent or person immune to measles. This phase of the work has been done by Dr. J. Musser and is reported concurrently in this issue of the PROCEEDINGS.

[1] Hibbard, R. J., and Duval, C. W., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiii, 853-856.

[2] Tunnicliff, R., *J. Am. Med. Assn.*, 1917, lxviii, 1028.

[3] Caronia, *Pedicatia*, 1923, xxxi, 801.

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## Experimental Production of Carcinoma-like Epithelial Metaplasia in Mammary Gland of the Dog.*

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In a previous communication[1] the histological changes produced in the mammary gland of the rabbit by the inversion of nipple flaps were reported. Various proliferative changes in the inverted skin and glandular epithelium occasioned by the procedure were described. The defensive factors of the rabbit host to the continued growth of the stimulated and proliferating epithelium were noteworthy. Most of the nodules thus produced were eventually fibrosed or absorbed. Certain of the larger nodules, persisting now far more than a year, have been found to contain altered skin and its appendages which produce retention cystic masses.

As tumors of the mammary gland of the rabbit rarely occur it was concluded that even though the normal glandular epithelial cell

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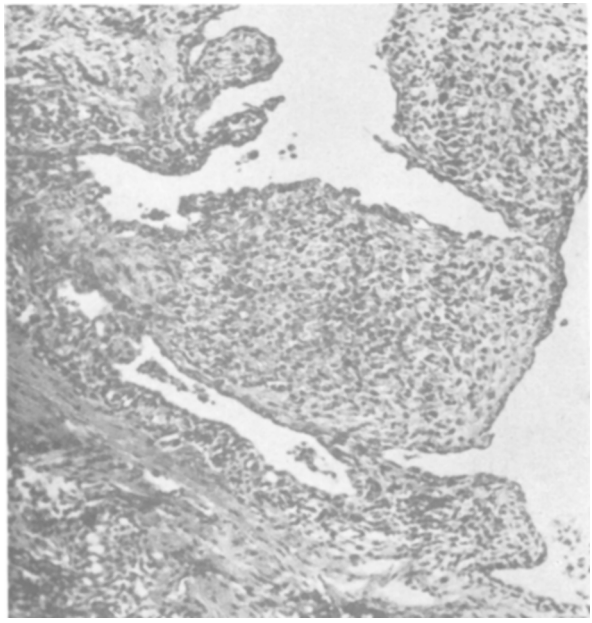

FIG. 1.
Papillary protrusions within the ducts shown after three months inversion.

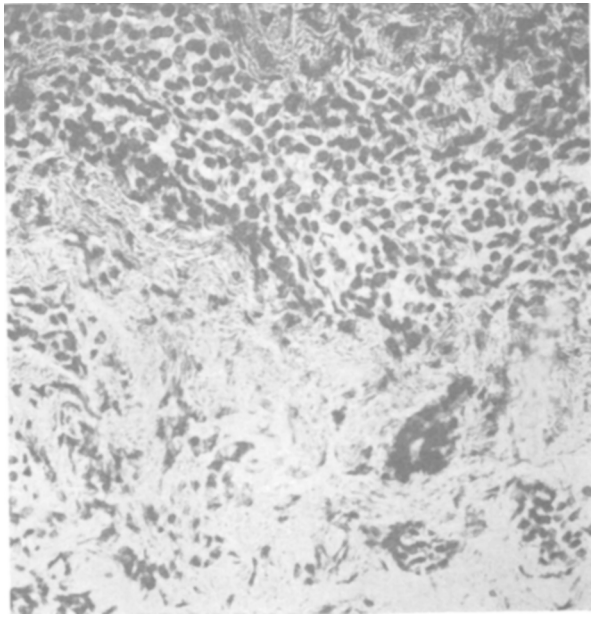

FIG. 2.
Epithelium growing at random is shown in upper portion and more or less normal ducts below.

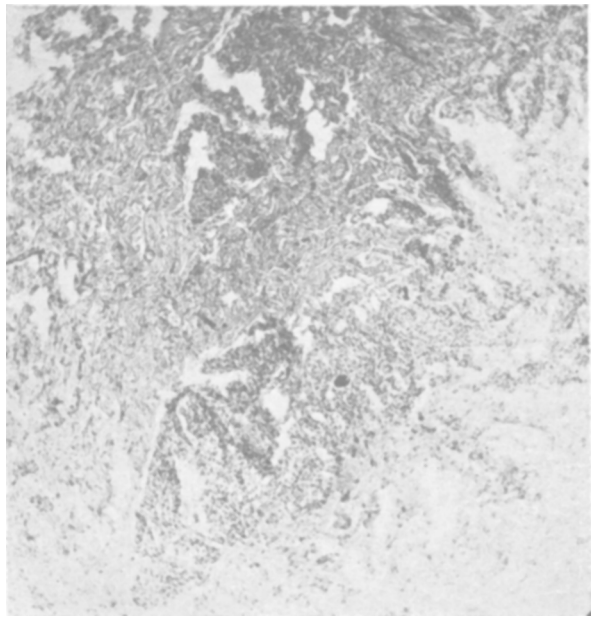

FIG. 3.
Low power to show epithelium growing throughout surrounding connective tissue.

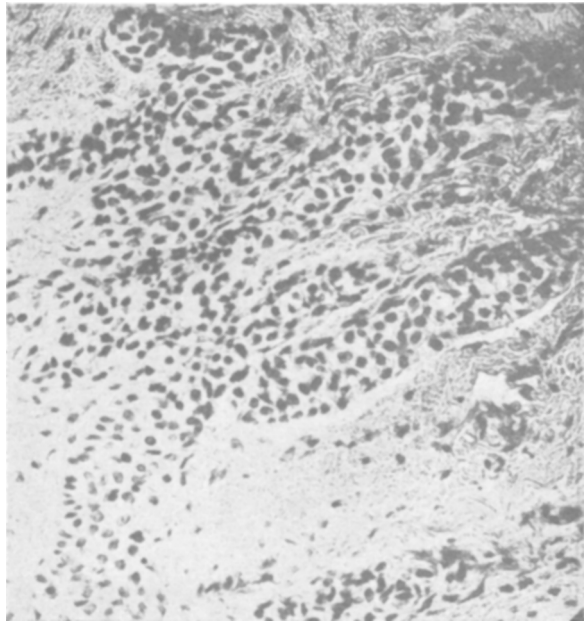

FIG. 4.
Cord-like masses of epithelium which have broken through the basement membrane after six months inversion.

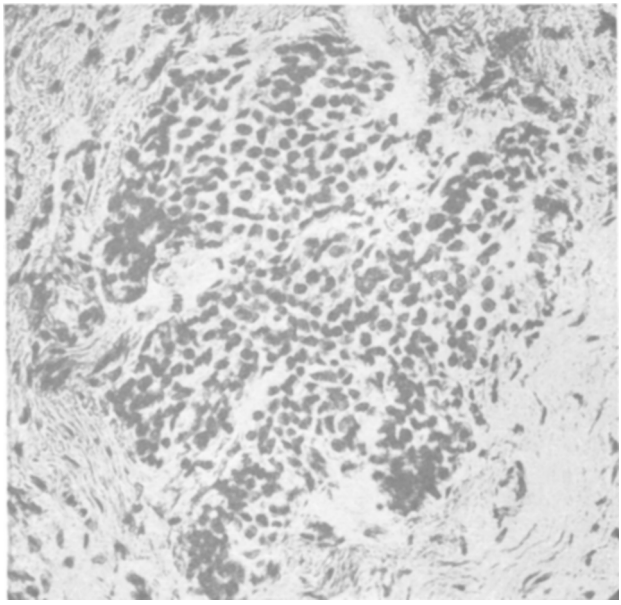

FIG. 5.
Epithelial cell masses are shown infiltrating into the adjacent connective tissue.

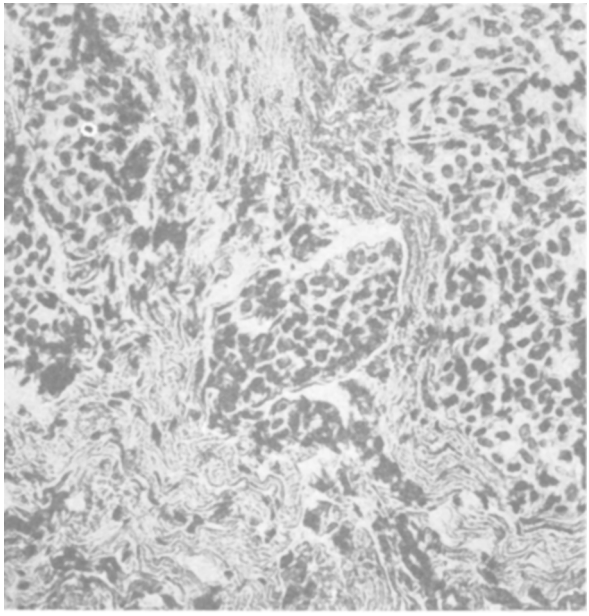

FIG. 6.
Alveolar arrangement of the epithelial cells shown in a nodule after seven months inversion.

relationships had been greatly disturbed and the epithelium provoked to considerable proliferation, the lack of susceptibility of the animal to such tumor growths or rather its capable defensive barriers prevented the continued growth.

For these reasons it was considered that some other animal of sufficient size and known to be susceptible to epithelial neoplasia of the mammary gland would be preferable. The literature shows that dogs are victims of mammary carcinoma. In 603 cases compiled by Stecker[2] 299 (49.5 per cent) were mammary carcinoma. In 50 of these, where the age was known, 23 occurred between the ages of 7 and 10 years. Feldman[3] studied 132 tumors from various animals among which 17 were from dogs. Of these 17 only 3 were carcinoma, the location of which are not mentioned. Although the incidence of occurrence of mammary carcinoma in the dog is difficult to ascertain, nevertheless such an animal is at times a victim to cancerous growth of the breast.

Seven female dogs of unknown age have thus far been employed. One of these showed slight lactation. They could only be judged as old where certain appearances such as worn teeth, advanced mammary gland development and the like were present. The age is an important feature, as the cancerous period in the dog like in the human, is noted especially during certain ages.

The procedure in general varied from the technique employed in the rabbit in that no inversion of the skin, as part of the flap, was made. An elliptical incision was carried around the nipple and the skin proximal to the nipple from this incision was removed. The portion of modified skin immediately over the nipple was clipped and scarified. The skin at the edge of the denuded surface was then dissected back for about 3 cms. thus leaving a protruding apex nearly devoid of epithelium. An incision penetrating the breast was made which extended to the underlying musculature. A suture was passed externally to the detached skin through to the underlying muscle at the base of the gland incision. The nipple was then threaded with this same suture, and returned along its path of entrance, and when drawn by both ends, detracted the nipple flap down to the musculature. The surface structures were then approximated with linen sutures, thus completely covering the operative area.

This procedure provoked a variable amount of inflammatory reaction with, at time, some suppuration, however no necrosis of the flap occurred. After from 3 to 7 months when all inflammatory signs had disappeared, portions of the persistent nodules were removed for examination. In all instances the mammary ducts showed

marked epithelial proliferations within the lumen, forming at times papillary protrusions. In the majority of nodules certain of the areas present the histological appearance of carcinoma, the epithelium proliferating beyond all normal confines of limiting basement membrane. These nodules thus far have become quiescent in their growth, and no evidence of metastasis to adjacent lymph nodes have as yet been observed. The histological picture of carcinoma is not general throughout the nodules, but only appears in certain areas. Thus while the histologic study reveals cell arrangements like those of carcinoma, the general growth activity and propensity of metastasis have thus far not been demonstrable. In other words the general character of the nodule is as yet analogous to the various "cell rests" that occur in the human body.

In the experiments herewith reported, histologic pictures like those of cancer have been produced by causing deranged epithelial cell relationship through nipple and gland inversion although its nodules have thus far not demonstrated the usual functional activities of cancer. It is to be noted, in this connection, that cancer of the breast of the dog, is as a whole, a less active process than that of the human and instances of fibrosis and metaplasia of these growths are reported.

[1] Harris, W. H., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiii, 840.

[2] Stecker, cited by Müller and Glass, Diseases of the Dog, 5th ed., 1926, 339.

[3] Feldman, W. H., *Am. J. Path.*, 1926, ii, 545.