CARCINOMA MAMMAE OCCURRING IN A MALE MOUSE
UNDER CONTINUED TREATMENT WITH OESTRIN

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Many years ago Lathrop and Leo Loeb showed by experimental work that some connection exists in mice between ovarian activity and carcinoma of the mamma. This general conclusion was confirmed and amplified by further experiments carried out by Cori and by W. S. Murray. The discovery by Doisy, Veler, and Thayer, and by Butenandt, in 1929, of methods for preparing the ovarian hormone, oestrin, in a pure form opened the way to further and more exact inquiry into the problem of this association between ovarian activity and cancer of the breast.

Lacassagne (1932, 1933) gave weekly injections of oestrin (folliculin) to 5 male mice belonging to a strain in which 72 per cent of the females are subject to spontaneous mammary cancer, the males not being subject to this development. Mammary cancer appeared in every one of the 5 males and in 5 of 7 females treated in this manner. Using mice belonging to strains in which mammary cancer occurred spontaneously in only 2 per cent of the females, and treating them in the same way as those of the preceding experiment, he found that mammary tumours developed in 2 of 8 males and in 1 of 7 females. These tumours appeared at a more advanced age than those produced in the strain which had a high natural incidence of cancer. In yet another strain of mice no neoplasia took place among 7 males treated by weekly injections of oestrin in the same manner as in the preceding experiments.

The writer has treated upwards of 130 male mice, of which 20 had been castrated, for prolonged periods with a chemically pure preparation of ketohydroxyoestrin, supplied most generously by Dr. Girard. One drop of solution of this oestrin in benzene (0.01 per cent) was applied twice a week to the skin of the interscapular region by means of a paint brush. The mice used were not of any pure strain; they were stock mice purchased from a dealer. Among the mice so treated only one case of carcinoma mammae has occurred. In view, however, of the rarity of cancer of the breast in male mice, it may be worth while to put this single case on record. An additional reason for doing so is the fact that, among the mice in which cancer did not develop in the course of these experiments, there were several instances in which microscopic sections showed local areas of hypertrophy of the mammary epithelium which seemed to differ in degree only from intraductal carcinoma. Examples of this condition were shown by the writer in the course of a Hunterian Lecture given at the Royal College of Surgeons.
of England in January 1935, an abstract of which is awaiting publication.

The history of the mouse which developed cancer is as follows:

Mouse 873 was castrated Sept. 30, 1933, and applications of oestrin were commenced Oct. 4, 1933. On March 28, 1934, that is to say 175 days after the commencement of treatment with oestrin, the mouse was found to have a tumour measuring 19 × 14 mm. in the right axillary region. This tumor was removed on the same day under an anesthetic and an autograft was made in the right groin. Ten young mice were given grafts; none of these gave rise to tumors.

On May 25, 1934, fifty-eight days after excision of the tumour and autografting, there was a well grown mass at the site of the autograft; the mouse was sick and was therefore killed. At the post-mortem examination no recurrence of growth was found at the site of the operation, but the autograft in the groin had penetrated the abdominal wall and was fungating into the peritoneum, of which the parietal and visceral layers showed numerous metastases. The bladder and other pelvic organs were imbedded in masses of tumour, and both lungs showed numerous nodules. Microscopic sections (Figs. 1, 2 and 3) show that the primary tumour, autograft, and pulmonary metastases all resemble in character the original tumour removed from the axilla.

Note: Since the notes of the above case were accepted for publication two mammary tumors have developed in another castrated mouse of the same general series. These tumors, which were first noticed on the 291st day of the experiment, appear macroscopically and microscopically to be carcinomata. The mouse was one of twenty which had been treated not only with oestrin, but in addition had received ten applications of luteosterone (progestin) at intervals of about five days during the first fifty-five days of the experiment, after which period treatment was continued with oestrin alone. The
Fig. 2. Section of the autograft fifty-eight days after implantation. × 120

Fig. 3. Section of lung showing metastatic deposits resembling the primary tumour. × 120
luteosterone used was a pure sample which had been prepared at this Institute from pregnandiol by Mr. G. A. D. Haslewood, by the method of Butenandt and Schmidt (Ber. deutsch. chem. Gesellsch. 67: 1901, 1934, and had been kindly supplied by him for the purpose of this experiment.

References


