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The functional activity of the breast in relation to mammary carcinoma in mice.

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The following experiments were designed to test the possible relation of functional disturbances of the breast to the incidence of mammary carcinoma in mice.

A carefully inbred strain of animals with a well-known low rate of tumor incidence was selected. Mammary tumors in females from this strain that are allowed to breed normally do not appear until the animals are between one and a half to two years of age. The females were large, vigorous, prolific individuals, and suckled their young successfully.

Females from the above strain were divided into two groups, one serving as a control was allowed to breed normally, *i. e.*, the females were remated only after nursing their litters for about six weeks. The test animals from the same family were then bred under the following procedures designed to subject the mammary tissues to abnormal conditions:

1. Females bred when very young (two to three months old), and their litters removed immediately after parturition, or not more than twelve hours later, and the mothers remated at the œstrus that promptly follow parturition.

2. Females bred when six to nine months old, and treated as in the above group.

3. Various combinations of alternating periods of suckling of one litter and non-suckling of the next litter, etc.

4. Ligating mammary ducts to the nipples on one side of the body when the females were about half way through the period of pregnancy, followed by suckling of litter and remating after weaning. The operative trauma was minimized as much as possible. No attempt was made to prevent suckling on the unoperated side of the body.

The results are based on the records of fifteen females with spontaneous tumors, all of which have been found to be mammary carcinoma on histological study.

Animals of Group 1 have bred very rapidly, having had as many as nine to eleven consecutive litters, with an average of only twenty-four days between the dates of parturition. In this group mammary tumors have appeared at an early age, *i. e.*, when the females were from eight to eleven months of age.

In Group 2 the age of the females at the time of tumor incidence is from eleven to twelve months. In this group a relatively low average of only four periods of pregnancy, followed by the prevention of suckling, precedes the onset of the tumors.

Animals of Group 3 show on the whole that, when periods of suckling alternate with periods of non-suckling, the tumors appear after fewer consecutive litters, as compared with the condition in Group 1.

Prevention of proper drainage of the breast has resulted in marked stasis of the mammary ducts. This is associated with the presence in the mammary gland of a considerable amount of decomposing, stagnated and probably chemically altered milk, which it is possible was sufficiently irritating to cause considerable disturbance within the breast.

Contributory evidence was given to this view by the histological study of serial sections of a considerable portion of the breast in mice with very early but definitely established mammary carcinoma. The cyclic relation between ovarian and mammary systems was obviously deranged by the experimental methods employed, and the breasts in rapidly breeding, non-suckling females were not able to properly reach a normal resting condition for any considerable period of time.

In mice breeding rapidly from an early age (Group 1) and not allowed to suckle their young, the breasts were apparently pre-

vented from reaching their normal degree of development; and it took a considerable number of consecutive litters, followed by periods of non-suckling, before the onset of tumor growth. Whereas, in animals older when first bred (Group 2) or in Group 3, where suckling at one period definitely established a large, well-developed breast to start with, it took fewer periods of pregnancy followed by non-suckling before the tumors became evident.

The tumors have appeared coincidentally with, or a day or two after, parturition. The animals have grown tumors and embryos at the same time.

Mammary ducts have been ligated with the consideration in mind of the possible significance of mammary duct stasis in relation to tumor growth. This group of animals contains only a few individuals, but nevertheless it is interesting to note that in the first animals tested within the last few weeks, two of the first females operated upon developed mammary tumors on the side of the body on which the ducts had been ligated.

Histological examination showed the presence of solid mammary carcinoma, associated with marked stasis of the duct system on the ligated side of the body.

The tumors that appeared in the four groups of experimental animals were definitely malignant in nature, with a rapid rate of growth and a marked tendency to local recurrence after operative removal. The breasts have usually shown evidence of multiple foci of tumor growth.

In the control group of animals containing females breeding regularly and suckling their young, the incidence of tumor growth is less than 5 per cent, and the tumors make their appearence only in animals between about eighteen to twenty-four months of age. Although this report is designed mainly as a preliminary report, and further data will be added in the near future, it has been thought sufficiently of interest to state now, that in the first group of fifteen animals, in which a dysfunction of the breast was brought about by non-traumatic means, thirteen females or eighty-seven per cent developed mammary carcinoma at comparatively early ages as described above.

The presence of the two females that developed mammary carcinoma when only six months of age following ligation of mammary ducts, means nothing when viewed alone, but is of interest in connection with the above mentioned groups.