# REGENERATION OF THE MAMMARY GLAND IN THE GUINEA PIG

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The study of mammary gland regeneration has received little attention. The first investigations in this field were concerned with relatively trivial lesions of the mammary glands [1, 2, 7]. Other investigations were in part concerned with transplantation of granulated mammary gland tissue at the site of excision of gland tissue [5, 6]. These investigations have shown that the process of regeneration of mammary gland tissue is closely connected with the physiological condition of the whole organism.

In recent years, techniques for determining mitotic activity in alveolar epithelial cells have been used in studying regeneration of the mammary gland [3, 4]. However, the results obtained from investigations involving different species of animal, appear somewhat contradictory.

Our aim has been to carry out a more detailed investigation of mammary gland regeneration following removel of 75% of the tissue of this organ.

## METHODS

The work was carried out on 70 female guinea pigs, the mean weight of which was 650-800 g at the beginning of the experiment. All the experimental animals had the whole of their right mammary gland and the posterior half of the left removed. The control animals underwent a pseudo-operation.

Some of the animals had their mammary glands excised in 2 stages. The first stages consisted of the removal of all the right mammary gland and then 15-20 days later when the wound had healed the second stage was carried out; this consisted of the removal of the posterior part of the left gland. The animals were killed 5-20 days after the second operation.

The rest of the experimental animals had both mammary glands (the whole of the right and about half of the left) removed at the same time. Fifteen to twenty days after the operation, these guinea pigs were mated with males and were killed and examined at various stages of gestation and lactation. Five animals from each group were killed and examined. At the same time we examined the same number of control animals.

The guinea pigs were killed at 11:00 a.m. Fragments of mammary gland tissue, all taken from one particular site, were fixed in Bouin's fluid, embedded in paraffin wax and sectioned at 8 $\mu$ thick; these sections were stained with hematoxylin-eosin. In addition to undertaking a general study of these histological preparations, we measured the diameter of the alveoli and the height of the alveolar epithelial cells with the aid of an eyepiece micrometer; we also counted the number of alveoli in the field of vision. Mitotic activity in the mammary gland epithelium was expressed in terms of the number of mitoses per thousand epithelial cells. Six thousand cells were examined in every case. The data obtained was assessed statistically using the Fisher-Student method.

## RESULTS

The weights of the guinea pig mammary glands are set out in Table 1, from which it may be seen that 5 days after the operation the residual portion of the left mammary gland had undergone a considerable increase in weight

TABLE 1. Weights of Mammary Glands in Experimental and Control Guinea Pigs

| Period of time after operation | Wt. of glands (in g) | | Relationship between wt. of gland in experimental animal to wt. of two glands in control |
|---|---|---|---|
| | experimental | control | |
| 5 Days | 3.050 | 5.178 | 58.3 |
| 10 Days | 2.386 | 5.006 | 47.4 |
| 20 Days | 2.160 | 5.294 | 40.4 |
| Middle of gestation | 2.660 | 6.834 | 38.9 |
| End of gestation | 3.836 | 8.875 | 43.2 |
| 5th Day of lactation | 8.104 | 17,334 | 46.5 |
| 20th Day of lactation | 5.359 | 10.190 | 52.9 |

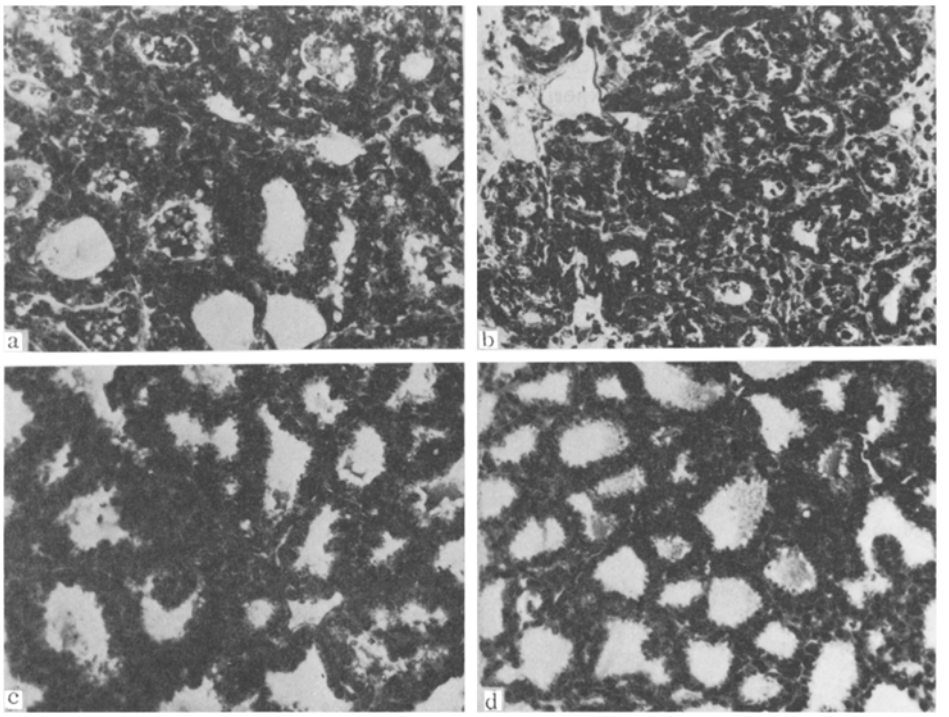
TABLE 2. Dimensions and Mitotic Coefficients (MK) of the Mammary Glands in Experimental and Control Guinea Pigs

| Group of animals | Period after operation | Diameter of alveoli (in microns) | Height of epithelial cells (in microns) | No. of alveoli per field of vision (mag. × 600) | MK (in %) |
|---|---|---|---|---|---|
| Experimental | 5 Days | 27.1 | 9.6 | 8 | 4.3 |
| | 10 Days | 29.7 | 10.5 | 9 | 3.7 |
| | 20 Days | 28.0 | 9.4 | 9 | 2.0 |
| | Middle of gestation | 29.6 | 10.1 | 11 | 3.1 |
| | End of gestation | 36.4 | 12.1 | 18 | 6.9 |
| | 5th Day of lactation | 63.3 | 12.0 | 9 | 2.3 |
| | 20th Day of lactation | 59.9 | 8.8 | 7 | 0.7 |
| Control | 5 Days | 28.1 | 8.8 | 7 | 1.7 |
| | 10 Days | 26.7 | 7.5 | 7 | 1.5 |
| | 20 Days | 27.2 | 7.5 | 8 | 1.9 |
| | Middle of gestation | 27.7 | 9.9 | 10 | 2.3 |
| | End of gestation | 32.5 | 10.3 | 15 | 4.5 |
| | 5th Day of lactation | 67.2 | 10.8 | 6 | 1.9 |
| | 20th Day of lactation | 47.8 | 8.6 | 6 | 0.4 |

and did, in fact, weigh more than the corresponding gland in the control animals. Subsequently the weights of the mammary glands underwent some diminution; by as much as 47.4% on the 10th day after operation and 40.4% on the 20th day.

The weights of the mammary glands began to increase again 80-84 days after the operation, i.e., during the second half of the gestation period, and they continued to increase during the lactation period. At the end of gestation the weight of the one mammary gland in the experimental animal was 43.2% that of the weights of the two glands in the control animal; by the end of the 5th end of lactation it was 46.5% and by the 20th day 52.9%.

An inflammatory reaction developed at the surface of the wound during the first few days after the operation and a necrotic mass was formed. This probably accounted for the weight of the mammary gland being greater on the 5th day following the operation than over the subsequent period. On examining histological preparations of the tissue at this time, it was possible to detect small groups of epithelial cells lying near the surface but not forming alveoli. Evidently these represent the remains of alveoli damaged as a result of the resection of the gland. The epithelial cells, occurring at some distance from the wound surface, were somewhat taller than those of the controls. No real difference in the diameter of the alveoli could be observed between the two groups, nor was the number of alveoli per field of vision any different (Table 2). However, the mitotic activity of the epithelial cells in the experimental animals was greater at this time than among the controls and this difference was statistically significant ($P < 0.05$).



Microstructure of the mammary gland of the guinea pig. At the end of gestation; a) gland, undergoing regeneration; b) control, on 5th day of lactation; c) experimental; d) control. Stained hematoxylin-eosin. Obj. × 20 oc. × 7.

By the tenth day after the operation a few, very small alveoli had formed near to the wound surface; these appeared to have been produced from the alveoli damaged at the time of the operation. No clearly defined zone of new growth from the wound surface could be observed. More significant changes were taking place at this time in the cells situated at some distance from the surface of the wound. These epithelial cells underwent some increase in height and the number of alveoli in this region also increased (c.f., Table 2). The difference in height of the epithelial cells and the difference in the number of alveoli per field of vision between the experimental series and the controls was statistically significant ($P < 0.05$). The mitotic activity of the epithelial cells on the tenth day after the operation was less than on the fifth day; however, compared with the controls, the difference was not statistically significant. New alveoli and mammary ducts were formed as a result of division of the epithelial cells.

On the 20th day after the operation, the changes to be observed in histological preparations were similar to those which were noticed on the 10th day. The only difference was a considerable increase in mitotic activity of the epithelium which had taken place by the 20th day, when, indeed, mitotic activity was back to normal.

During the second half of gestation, the structural elements of the mammary gland underwent some hypertrophy. This was particularly evident at the end of gestation (c.f., figure). The diameter of the alveoli, the height of the alveolar epithelial cells and the number of alveoli per field of vision were all greater in the experimental group compared with the control. Mitotic activity of the alveolar epithelium at the end of gestation was rather high in both groups, nevertheless, the difference between the two groups is statistically significant ($P < 0.05$).

During the period of lactation the secretory tissue of the regenerating glands was better developed than in the control animals. The alveoli were larger and consisted of epithelium having taller cells. The number of alveoli per field of vision also increased. Considerably less intra-alveolar tissue was found to occur in the regnerating mammary glands of the experimental animals than in the controls,and the former possessed no adipose tissue (c.f. figure). The mitotic activity of the alveolar epithelium during the period of lactation gradually diminished until the 20th day in both groups, by which time it was insignificant. The amount of milk produced by the regenerating gland over the period of the experiment amounted to 52% of that produced by the controls.

It may be said, therefore, that the greater part of the guinea pig mammary gland undergoes regeneration after excision and that the regenerative process is directed towards an increase in the mass of glandular tissue. The alveolar tissue at the wound surface which has been subjected to operational trauma exhibits only a slight amount of regeneration. In the main, the process of regeneration in the mammary gland is of the regenerative hypertrophic type, i.e., by an increase in the mass of the gland residuum. The increase is accompanied by an increase in the number of alveoli and ducts and also by alveolar hypertrophy. Regeneration of the mammary glands in guinea pigs occurred immediately after excision of 75% of the tissue of the gland but was still incomplete at the time of the first gestation and lactation after the operation. The weight of the regenerated gland attained on average only 50% of the weight of the entire organ in the control animals.

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