

THE INFLUENCE OF THE NERVOUS SYSTEM ON THE MICROSTRUCTURE OF THE GLANDULAR TISSUE OF THE MAMMARY GLAND

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The experiments of M. M. Mironov [2] on the denervation of the udder in goats led I. P. Pavlov [3] to the view that the nervous system influences the activity of the mammary gland. He also postulated a trophic influence on the activity of the mammary gland, although up to the present no histological investigations have been carried out in support of this hypothesis.

Research is particularly lacking on the importance of the nervous system for the structure and formation of the parenchyma of the mammary gland. Elucidation of this aspect of neurogenic influence may be an important factor in understanding the complex process of the physiology of lactation.

EXPERIMENTAL METHOD

We studied the influence of the nervous system on the structure of the mammary gland by the method of denervation of the gland and subsequent histological investigation. The spermatic nerve and its branches were divided; the vessels were treated with 5% cabolic acid to inactivate the vascular nerves. In order to secure more complete isolation of the mammary gland from its main nerve connections, the skin incision around the gland was made in two stages and the whole gland freed from adjacent tissues. Great attention was paid to keeping the blood supply of the gland intact.

In the present paper we describe the results of experiments carried out on the mammary glands of guinea pigs undergoing operation in a state of sexual immaturity — aged from 1 to $1\frac{1}{2}$ months. For histological investigation the mammary gland of the guinea pig has a great advantage over those of large animals. Guinea pigs have a development cycle of short duration, they multiply rapidly and easily, and they possess well developed glandular tissue which corresponds in its structure to the mammary glands of higher animals. Of the 37 sexually immature guinea pigs undergoing operation we took the mammary glands from 18 for morphological investigation when the animals were in a typical sexually immature state; 9 guinea pigs were in various stages of pregnancy at the moment of fixation of the glands, and 10 were in the period of lactation. The mammary glands of the guinea pigs undergoing operation were taken for histological examination at various stages of development. For fixation we used Zenker's fluid and 12% formalin; in some cases celloidin, in others paraffin wax was used for embedding; sections were stained with Mayer's hemalum or Böhmer's hematoxylin with counterstaining with eosin, and iron hematosylin with counterstaining with Mallory's mixture. In addition, control investigations of the denervation were carried out by the Bielschowsky-Lavrent'ev silver method.

EXPERIMENTAL RESULTS

In a guinea pig $1\frac{1}{2}$ months old the mammary gland tissue is in its initial stage of development (Fig. 1, A). It has the appearance of a small number of large, slightly branched ducts, terminating in ill-defined end portions.

The epithelium of the ducts and the end portions consists of narrow, high cells with oval and elongated nuclei. The borders of the cells are ill-defined. The lumen of some of the ducts contains a secretion which on the fixed preparations has a friable appearance.

The epithelial tubes are surrounded by a small, discrete layer of fibrous connective tissue which gives way to septa subdividing the mass of fatty tissue which forms the main basis of the gland. The structure of the denervated gland in the same animal 15 days after operation does not differ from that of the control gland (Fig. 1, B). The slightly branched epithelial tubes terminate in ill-defined end portions. The epithelium is of the same type throughout. Connective tissue is present mainly around the epithelial tubes and in the form of fine septa subdividing the fatty tissue.

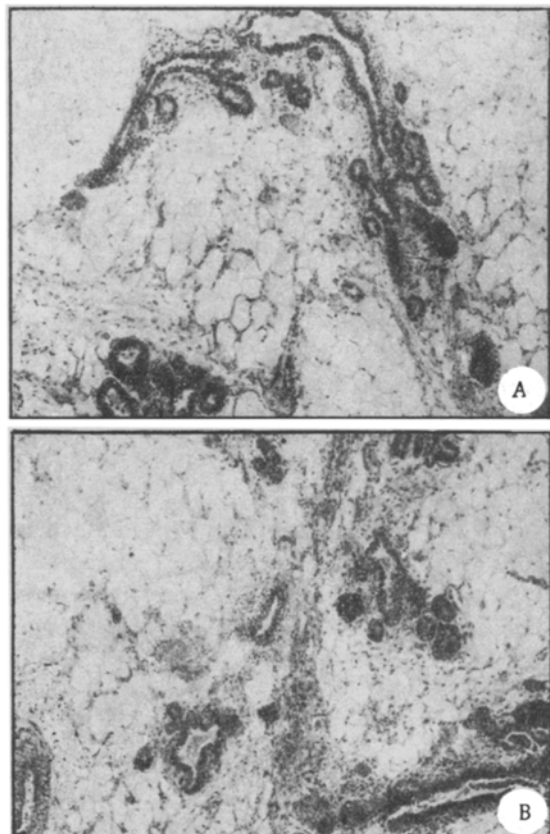


Fig. 1. Normal (A) and denervated (B) mammary gland of guinea pigs at the age of $1\frac{1}{2}$ months. Stained with hematoxylin-eosin. Objective 15, ocular 5 \times .

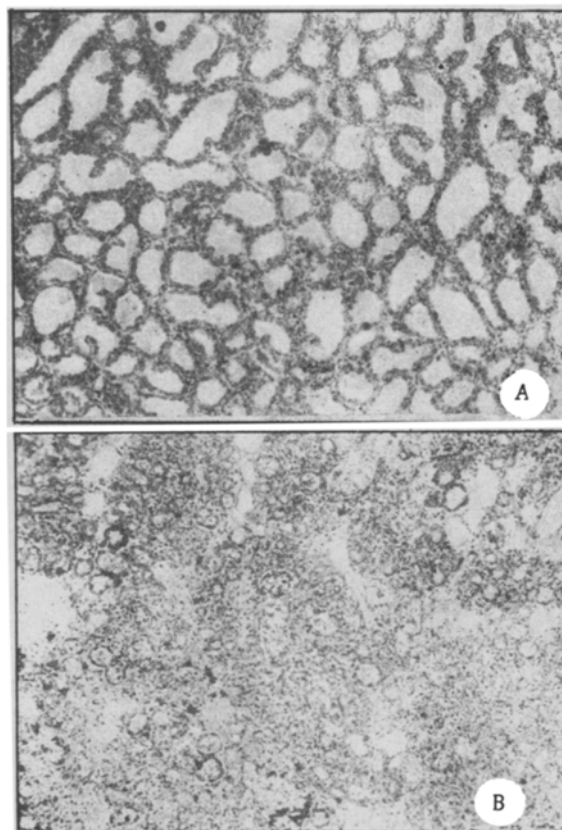


Fig. 2. Normal (A) and denervated (B) mammary gland of a guinea pig on the second day of lactation. Stained with iron-hematoxylin and Mallory's mixture. Objective 15, ocular 5 \times .

The structure of the glandular tissue showed quite a different picture after denervation carried out on sexually immature animals, if their mammary glands were taken for histological investigation at various periods of pregnancy or lactation. At the onset and in the middle of pregnancy the changes observed mainly took the form of retardation of development of the glandular tissue of the denervated mammary gland.

At the end of pregnancy more pronounced changes were observed in the structure of the parenchyma of the gland characterized by delay in formation of the mammary glands deprived of their main nerve connections. The tissue of control glands of these animals consists of clearly formed glandular lobules, separated by narrow connective tissue septa. Each lobule contains a large number of alveoli, a considerable proportion of which have cavities filled with secretion. Alveoli of various shapes — from spherical to elongated — are lined with cubical epithelium with round or slightly oval nuclei. Side by side with alveoli of this type are seen alveoli without cavities.

They are formed of low epithelial cells, in close contact with each other, and containing elongated nuclei. The efferent ducts are moderately distended by the secretion with which they are filled. In places the epithelium of the ducts is in a single layer and is very much thickened. The interlobular connective tissue is clearly shown and is formed here and there of more compact or looser fibrous tissue.

The glandular tissue of the denervated glands in this group of animals is less well developed than in the control group. This is shown in the first place by the predominance of connective over glandular tissue. Alongside the relatively formed alveoli there are branching epithelial tubes without clearly defined alveoli. The majority of the alveoli are without lumen, showing their inactive condition. The alveolar epithelial cells are most often cubical and contain oval or round nuclei, occupying the greater part of the cell. In only a few alveoli is the lumen filled with secretion. The epithelium of these alveoli is cylindrical or cubical, with round nuclei. The lumen of the efferent ducts are very dilated; in cross section they are irregular, sometimes stellate in shape. The double layer of epithelium of the ducts is condensed and the cell nuclei are situated parallel to the lumen. The latter is filled with secretion and cells.

Particularly severe changes in the structure of the glandular tissue following denervation of the mammary glands of the sexually immature guinea pigs are observed during lactation of the animals. These changes are associated with abnormal formation of glandular tissue and are expressed by disturbance of the normal development of the gland and of the course of the secretory process. An example of this group of experiments is the mammary gland of a guinea pig undergoing operation at the age of 1 month and killed $14\frac{1}{2}$ weeks later, on the 2nd day of lactation.

Normally the mammary gland of a lactating guinea pig shows well-developed glandular tissue (Fig. 2, A). The majority of the alveoli are very dilated and filled with milk. The epithelial cells are large and, depending on the state of secretion, vary in shape from cubical to flattened. The epithelial cells contain round nuclei; sometimes cells containing two nuclei are found. Alongside functioning lobules are seen lobules in a resting state. The lumen of the efferent ducts are filled with milk; their epithelium is flattened and their nuclei elongated. The interlobular and interalveolar connective tissue is in the form of fine, tense septa. All this is characteristic of the gland in a state of active secretion.

The denervated gland of this guinea pig differs appreciably from the control (Fig. 2, B). It contains a large number of nonfunctioning lobules. The alveoli in the lobules are greatly altered and have a very polymorphic appearance. In the majority of cases the epithelium of the vesicles shows some degree of degenerative change. Alveoli with epithelium showing relatively little change are rarely encountered. In some alveoli there is an appearance of desolation: the vesicles are in a resting state and the lumen is not distinguishable. In other cases the lumen of the vesicles are preserved but their epithelium is low, with flattened nuclei, situated directly by the lumen; this indicates the absence of a regenerative process after apocrine secretion. In some alveoli the epithelium shows a return to a more simplified pattern. Now and then it can be seen that fat droplets are formed in certain cells but are not excreted, so that these cells have a distended appearance and their nucleus is pressed towards the basal side. The alveoli with a lumen are often filled with contents, not ordinary milk but an altered secretion, with a coarse granular appearance in the films, sometimes with remains of desquamated epithelial cells. The ducts are stretched, and lined with flattened epithelium. Between the collagen fibers there is a considerable amount of amorphous material, giving the loose connective tissue of the interlobular septa a somewhat edematous appearance.

From the results obtained we are able to confirm that removal of the main nerve connections from the mammary glands of sexually immature animals is reflected mainly in the subsequent development of the glands at the most active periods of their formation and activity. Besides general failure to develop or delay in the formation of the parenchyma of the denervated gland in relation to the normal functional state of the animal, disorders are observed in the course of the secretory process. These disorders are manifested both in degenerative processes affecting the epithelium of the alveoli and ducts and in interference with the expulsion of droplets of fat from the secreting cells. As a result an accumulation of fat in the epithelial cells takes place; they take on a swollen appearance with rounded apical edges, which is a sign of absence of the normal outflow of secretion into the lumen of the alveoli.

Investigation of the denervated glandular tissue in the preactive period of its formation, i.e. in the sexually immature guinea pig, showed no abnormal tendencies. Thus, denervation of the mammary gland has no immediate

effect on the structure of the glandular tissue of the sexually immature animal. However, at periods when the activity of the mammary gland normally appears, the denervated gland is seen to develop imperfectly, on account of the unpreparedness of the glandular tissue for normal functioning. This unpreparedness is the consequence of disturbance of certain intimate processes taking place in the mammary gland in the postnatal period, requiring the participation of the nervous system for their effect. Here is clearly seen the trophic influence of the nervous system in the development of the glandular tissue, without which the normal formation of the mammary gland is impossible.

Our findings are in agreement with the results of the research of A. G. Ginetsinskii et al. on denervation of the kidney [1] and of L. A. Chudnovskii on denervation of the ovary [4]. These authors point out that denervation of the organ in the early postnatal period causes it to develop imperfectly, with disturbance of its subsequent activity.

SUMMARY

The author describes the results of experiments on the denervation of the mammary gland in guinea pigs with subsequent histological study. Thirty-seven sexually immature guinea pigs were operated. The mammary glands were taken for examination in 18 sexually immature guinea pigs, in 9 — at various periods of pregnancy and in 10 — during lactation. The denervation in sexually immature guinea pigs does not cause any direct changes in the structure of the mammary gland up to the period of preparation to lactation. Both, during the latter period and during lactation the operation of denervation of the mammary gland alters considerably its histological structure. The above experiments show the pronounced effect rendered by the nervous system on the normal function of the mammary gland.

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* In Russian.