On the Relationship between Mammary, Sweat, and Sebaceous Glands

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SUMMARY

1. Stages are described in the development of the mammae of male rabbits responding to regular injections of oestrogen and progesterone.

2. It is suggested that the extra mammary lobes which develop under this treatment are derived from hair follicles and sebaceous glands by the loss of the hairs from the follicles and the proliferation of sebaceous glands and ducts.

3. This may throw light on the phylogenetic origin and homology of the mammary gland.

The sebaceous glands of the rabbit consist of clusters of about ten cells almost embedded in the wall of the hair follicles. The cells are large with an acidophobe cytoplasm and round nuclei. The outermost cells of larger glands are rather smaller, and possess somewhat flattened nuclei. This arrangement is different from that of the hair follicles where the outermost cells, corresponding to the deeper layers of the epidermis, have elongated nuclei and the inner cells have flattened nuclei; the cells in between have roundish nuclei.

In the nipple of the mammary gland of the male rabbit the sebaceous glands are about five to ten times the size of those elsewhere. The cells are about the usual size, and smaller cells with flattened nuclei are arranged around the outside. Glands of this size cannot be contained within the thickness of the wall of the hair follicle. Accordingly, they lie outside the follicle and are connected with it by a short duct composed chiefly of cells with rounded nuclei; or, at any rate, there is not a layer of cells having elongated nuclei on the outside of the duct. This duct, then, seems to be formed mainly of cells of the middle layers of the rete mucosum of the hair follicle which have burst through the investing columnar cells of the basal, or outer, layer of the follicular rete mucosum.

During the course of an endocrinological study, I have had occasion to take frequent biopsies of mammary glands of male rabbits which were undergoing a course of regular daily injections of oestrone and progesterone followed by a luteotropin (prolactin or lactotropin) injection. The progressive modifications of the hair follicles of the nipple and their sebaceous glands have proved of some interest.

The nipple of the male rabbit’s mamma is sparsely covered with hair all over. At its tip it is perforated by one, two, or three orifices which lead to the mammary ducts. These ducts are simple in section and branch very little at the base. There are no alveoli. The wall of the duct is about three cells thick and the cells have large round nuclei. The orifice of the duct is formed by a circular depression of the stratified epithelium of the skin of the nipple, which communicates at its bottom with the duct proper. The communication is somewhat eccentric—the duct does not open into the centre of the depression but slightly to one side; and the depression is filled with a corneal plug, composed of several layers of half-sloughed stratum corneum. This plug lies flush with the general surface of the nipple, and the epithelium of the depression has a basal layer of columnar cells with elongated nuclei. The nipple, like the greater part of the rabbit’s skin, is devoid of sweat glands.

A short period of regular daily injections of oestrone and progesterone results in a proliferation of the duct epithelium and a general enlargement of the nipple. The lumen of the ducts becomes more capacious and the walls fall into longitudinal folds. The sebaceous glands of the nipple enlarge and many follicles may be seen to have several sebaceous glands, or a multilobed one, each—a condition not seen in the normal male. There is, indeed, more sebaceous tissue present in the nipple of the male rabbit so treated than in that of the normal male. At the same time the openings of hair follicles near the apex of the nipple enlarge until each hair is lying at the side of a tube several times its diameter. This enlargement of the lumen occurs only in that part of the follicle distal to the opening of the sebaceous duct; that part below the opening of this duct remains at its original diameter and it is completely filled by the hair. The enlarged follicular opening is filled by a corneal plug similar to those on the orifice of the mammary ducts. At this stage the hair root may be seen to be degenerating, with pyknotic nuclei. A little later the hairs in these enlarged follicles are seen to be rootless; they are evidently being shed. Finally, the hair is shed and little remains of the deeper parts of the follicle, other than a small pouch at one side of the pit which is now an enlarged opening for several sebaceous glands. This pit, however, remains histologically distinct from the proper ducts of the sebaceous glands which open into it, for its epithelium possesses still a basal layer of columnar cells with elongated nuclei. The sebaceous duct is lined with material similar to that of the corneal plug, but much scantier in amount. The eccentricity of the opening of the sebaceous ducts into the bottom of the follicular pit is marked;
this is a remnant of the lateral position occupied by the glands in the normal follicle. It may be noted in passing that sebaceous glands without hairs are well known in the mammae of nulliparous human females (see, for example, Maximow and Bloom, 1944, p. 519).

All these stages may be seen in the first 10 days of a series of daily injections of oestrone and progesterone. After 25 days of such a series, the proliferation of mammary ducts is rather more pronounced and some secretory tissue has appeared at the lower end of the ducts—alveolar development has begun. But a more pronounced change than this is evident: where before there were only three mammary ducts at the most, there are now six or eight. Examination of serial sections shows that not all of these penetrate as yet to the base of the mamma, not all of them are branched, and not all of them bear alveoli. These less developed ducts are evidently new formations. At the distal end of the nipple the ducts cannot be differentiated from each other in microscopical sections. All have the orifice in the form of a depression of the epidermis, filled with a corneal plug, and communicating, at one side of its

![Diagram](image-url)
bottom, with the duct proper. In all, the base of the epidermal pit extends slightly deeper at the side opposite the opening of the duct. The duct proper is lined with a definite, though sparse, stratum corneum; it is clearly an epidermal invagination, though devoid of the usual basal layer of columnar cells present in the stratified epithelium of the skin and of the orificial depression.

The hairless follicular pits with their associated sebaceous glands are now absent from the apex of the nipple but are present a little distance from the apex. Even lower still are follicles as yet retaining their hairs.

![Figure 3](image)

**Figure 3.** Camera lucida drawings of almost horizontal serial sections through the region of junction of a mammary duct orifice with the duct proper, showing the asymmetry of the opening and the continuance of the orificial depression below the level of the opening. This may be a remnant of the proximal part of a hair follicle.

In the later stages of mammary development, induced by injection of sex hormones, only one fact is of interest in the present context. The amount of sebaceous tissue in the nipple, which at first rose under the influence of the sex hormones, begins to fall again after about the twentieth day, though there is perhaps still a heightened amount around its base. The subsequent development of the ducts and secretory tissue has been too well described by Lyons (1937, a and b) and by others to require repetition here.

It is generally assumed at present that the mammary tissue represents a specialized portion of sweat gland tissue (see Maximow and Bloom, 1944). The basis for this assumption is the resemblance between the myoepithelial or basket cell of the sweat gland and the muscular tissue of the nipple. But the 'basket cells' of the mammary gland are clearly marked off from the glandular cells by a basement membrane running between the two elements (fig. 4); they are unlike the basket cells of the sweat glands which lie inside the basement membrane. This has been illustrated many times without mention, in figures of sections of mammary glands published in textbooks of histology (e.g. Maximow and Bloom, 1944, p. 597, fig. 521, where the basket cells appear to lie in the thickness of the basement membrane). The resemblances between the musculature of the mammary gland and that of the sweat gland is not
sufficient for an homology to be drawn between the two types of gland on this evidence.

Is it valid, then, to derive the mammary gland from the other chief skin gland, the sebaceous gland? The histological evidence that I have before me inclines me to believe that it is. I would suggest that in the development which I have described, a number of new mammary lobes, that is, individual glands within the mamma, develop in addition to the extension of those already present. It appears that the orifice of each duct represents an enlarged hair follicle and the duct proper a sebaceous duct. There is no evidence to indicate whether or not the secreting tissue is developed from the sebaceous gland, but it seems reasonable to presume that this is so, if the other developmental sequences described above are correct. This development is fastest near the nipple and proceeds more slowly and incompletely farther down, so that intermediate stages may be found on the sides of the nipple. It is interesting to note that a small number of ducts in the nulliparous human female open at the side of the nipple, in the midst of a cluster of sebaceous gland lobes, into a pit which is devoid of hair (see Maximow and Bloom, 1944, p. 596, fig. 519). During gestation the sebaceous tissue disappears from these orifices and they become like those at the apex of the nipple.

If this interpretation of the origin of the extra mammary lobes and ducts in the male rabbit responding to oestrogen and progesterone is correct, then it is reasonable to suppose that the origin of all the mammary lobes is from sebaceous glands with their ducts and the associated hair follicle, though doubtless the ontogeny has been abbreviated and they normally develop directly.

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REFERENCES