THREE CASES

OF

TUMOUR ARISING FROM SKIN-GLANDS IN THE DOG,

SHOWING THE CONNECTION BETWEEN

DISORDER OF THE GLANDULAR STRUCTURE AND FUNCTION AND CANCEROUS INVASION OF THE CONNECTIVE TISSUE.

BY

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I. *Anatomical characters of the skin-glands of the dog; their identity with a special layer of glandular substance in the human axilla, and with a conglobate form of gland hitherto undescribed.*

The glands in the dog's skin, in which the three tumours about to be described take origin, are generally spoken of as sweat-glands, but a brief consideration of the facts will show that that designation is applied loosely if not erroneously. According to the popular belief, dogs do not perspire through the skin; and that is one sufficient reason why the glands in question should not be called sweat-glands. It is only in the sole of the foot, according

to Leydig,[1] that the skin of the dog is provided with those glomerular coils discharging by a long duct, to which the name of sweat-gland is ordinarily applied. According to the same author, the so-called sweat-glands of the dog's skin open by a comparatively short duct into the hair-follicles at a point somewhat below the opening of the sebaceous glands, and that statement is confirmed by Stirling.[2] It will appear in the sequel that the same kind of skin-glands occur also in the comparatively hairless parts of the dog and open directly on the surface of the body. Although the skin-glands of the dog differ from the ordinary sweat-glands of man both in their great size and in the character of their epithelium and the nature of their secretion, as well as in another point to be mentioned, yet they have essentially the same glomerular or convoluted plan of tubular structure as the ordinary sweat-glands, and that seems to be the chief reason why they have been generally spoken of as a large form of sweat-gland. The tube is much wider than that of the sweat-gland, and it is coiled or convoluted not in the form of a spherical glomerulus with a long duct, but in an elongated form stretching through the corium towards the surface, the duct being proportionately shortened. They may be compared to the vesiculæ seminales in miniature. The gland in section, as shown in fig. 4 (Plate III), looks like a lobule made up of a number of wide acini lined by columnar or cubical epithelium, and these acinus-like crypts or recesses of the coiled tube have a close resemblance to the alveoli of the thyroid body. They are, however, all in free communication, and the secretion formed in the deeper recesses must pass through the more superficial on its way to the outlet.

The most conspicuous and distinguishing feature of the glands, by means of which they can always be identified with great ease, is an investment of plain muscular fibres round each crypt or acinus, presenting a ribbed appearance

[1] Leydig, 'Histologie des Menschen und der Thiere,' 1857, p. 87.

[2] W. Stirling, 'Journ. of Anat. and Physiol.' vol. x, 1876, p. 471.

as regular as that of a willow basket. These unstriped muscular fibres are arranged in parallel order, with narrow intervals between them, as in a close palisade, and they constitute a substantial basement membrane upon which the epithelial cells are directly seated. In fig. 4, the basket-work of muscular fibres is represented by thin dark lines, according to the appearance of the preparation under a low power; the dark lines are not so much the muscular fibres themselves, as the highly refracting intervals between them. The fibres are about three times as broad as the intervals which separate them and their substance is for the most part transparent. One of the most characteristic appearances is that of a regular row of projecting ends of the fibres where they have been cut across. The same palisade-like arrangement is sometimes indistinctly seen in the glomerular sweat-glands of man, and it has been asserted that the latter are likewise uniformly provided with a muscular coat. That would be a morphological point of resemblance between the two kinds of glands, in addition to the convoluted tubular plan of structure common to both; but there are none the less differences between them wide enough to justify the striking out of the larger form of skin-glands altogether from the category of sweat-glands.

It is well known that skin-glands, the same as those of the dog, are found not only in other mammalians and in some batrachians, but also in the human axilla, the areola of the breast, the groin, &c. The references made to the axillary skin-glands in recent histological works are apt to convey the impression that the glands are embedded in, or in close connection with, the corium like the ordinary glomerular sweat-glands. But their most characteristic and distinctive occurrence in the axilla is not in the substance of the skin, but as a separate and circumscribed layer, of brownish colour and lobulated surface, adhering to the under surface of the skin. This glandular layer will most probably be met with at the deepest part of the cutaneous recess, over the area where the skin adheres

most closely to the axillary fascia. In a large number of observations made in the dissecting-room, I have found the glandular structure sometimes as large as a florin and as thick, but more often reduced to a few scattered small lobules, apt to be mistaken for fat lobules, and not unfrequently wanting altogether. In a microscopic section, the tubular coils are found to be separated from one another and enclosed in a large quantity of connective tissue. Good specimens of plain muscular fibres may be obtained with great ease by teasing a minute portion of the glandular structure. These observations for the most part agree with the statement of Sappey,[1] who speaks of the skin-glands of the axilla as being collected into a circular layer under the skin, three to four centimètres in diameter and two millimètres in thickness. They are described also by Kölliker[2] as forming a continuous layer under the skin, and by Frey[3] as being crowded together in a distinct stratum.

The axillary glandular stratum in man is so variously developed and so often wanting altogether, that it may be regarded as a rudimentary organ of cutaneous secretion.

The axillary odour which characterises certain individuals of both sexes is probably associated with the presence of a well-developed stratum of the glandular substance.

This view of the axillary skin-glands in man, as a separate organ in a rudimentary or obsolescent form, is borne out by an observation which I have made for another animal. In one of the Monotremes (*Ornithorhynchus*) there is a body, of the shape and size of a bean, situated beneath the skin at the lower end of the humerus. It was described by Meckel, in his monograph on that animal,[4] as the *glandula humeralis lymphatica*, and that

[1] Sappey, 'Traité d'Anatomie descriptive,' vol. 3, p. 505.

[2] Kölliker, 'Handbuch der Gewebelehre,' 1852, p. 147.

[3] Frey, 'Handbuch der Histologie,' 1870, p. 596.

[4] J. F. Meckel, 'Ornithorhynchi paradoxi Descriptio anatomica,' Leipzig, 1826.

designation does not appear to have been changed by subsequent writers.[1] Its texture, however, is more spongy than that of a lymphatic gland, and with the help of a microscopic section, it is not difficult to make out its remarkable structure. It is made up exclusively of innumerable small crypts or acini freely communicating, their walls having the perfectly distinctive rib-like structure of close-set plain muscular fibres, and their interior being lined by polyhedric epithelial cells. The structure is shown in the accompanying drawing (fig. 1, Pl. III) made by me several years ago from a section of the gland; the palisade-like arrangement of plain muscular fibres, with epithelial cells resting directly on them, is without question the same structure which occurs in the glands of the dog's skin and in the glandular stratum of the human axilla. I did not succeed in tracing the duct of the organ, and it was probably the inability to find a duct that led Meckel to describe the body as a lymphatic gland. It has the conglobate form of a lymphatic gland, and both its size and its compactness indicate a very complex degree of coiling or convolution of the continuous tube, of which it may be said to consist. I take this opportunity of putting on record an observation (with drawing) which belongs as much to comparative anatomy as to the general subject of this communication.

According to an observation of Sappey's,[2] the large axillary skin-glands in man sometimes extend to the lateral and anterior regions of the thorax; and I have in one instance found perfect examples of them in intimate association with the breast structure. The case was that of a woman, aged thirty-eight, who had a large soft cancerous tumour removed from the outer part of the mammary region by Mr. Le Gros Clark, at St. Thomas's Hospital, in 1873. I made microscopic sections of the tumour as well as of the structure adjoining it; and in the latter I found several minute cysts, about the size of

[1] Owen, Art. "Monotremata," in Todd's 'Cyclop. of Anat. and Physiol.'

[2] Quoted by Henle, 'Handbuch der Anatomie des Menschen,' vol. 2, p. 35.

a pin's head, which proved to be dilatations of the peculiar axillary skin-glands, and were so labelled by me at the time. The walls of each cyst showed, in the most exquisite form, a considerable expanse of plain muscular fibres in close parallel order; a portion of that muscular-fibre membrane is drawn in fig. 2 (Pl. III), and the characteristic large-sized epithelium seated directly on the muscular coat is shown in fig. 3. These glands were in close proximity to ordinary lobules of the breast, but there was little difficulty in distinguishing the one kind of structure from the other. As regards the tumour from whose margin they were taken, I am still unable to decide whether it should be referred to the breast, according to the original view of it, or whether it was a tumour growing from a somewhat aberrant deposit of the axillary skin-glands, and belonging, therefore, to the same class of tumours as the three from the dog's skin which I am about to describe. In favour of the latter hypothesis is the unusually large size of the epithelial cells of the tumour, and the fact that the mammary structure, as found in the piece of tissue taken from near the tumour, was everywhere quiescent and upfolded, while there were several groups of the axillary skin-glands, besides those dilated to form the small cysts, which showed a certain amount of disordered structure.[1]

[1] An appearance very similar to that of the muscular-fibre membrane drawn in fig. 2 has lately been described and figured (C. W. Mansell Moullin, "The Membrana propria of the Mammary Gland," 'Journ. of Anat. and Physiol.,' vol. 15, p. 346, April, 1881) as the membrana propria of the acini of the breast itself. The appearance was found in a tumour of the mammary region which "consisted of nothing but fibrous tissue studded with minute cysts;" it is described as a tumour of the breast. Each cyst was "surrounded by parallel rows of long tapering cell-like bodies ranged side by side with the greatest regularity, and fitting in between each other, but not nearly touching." I do not wish to pronounce a confident opinion on preparations which I have not seen, but I am sure that such a membrana propria in the mammary acini is not to be seen in any of the numerous preparations of the breast made by myself, while an entirely different kind of supporting tissue of the mammary epithelium is described by all systematic writers on the breast.

II. *Disorder of the structure and function of the skin-glands in the dog, leading to tumour formation.*

The tumours about to be described were removed during life from three dogs at the Brown Institution in 1874-5, and were carefully prepared (in bichromate of potash and afterwards in alcohol) for microscopic examination. Tumour No. 1 is a thin oblong strip removed from the back, about 3 inches long, and half as broad, and about $\frac{3}{8}$ths of an inch thick. It had a granulation-like surface, which proved to arise from a diseased condition of the hair follicles. Tumour No. 2 is a nodular enlargement, the size of a walnut, removed from a comparatively hairless region of the skin, which was unbroken over the tumour. No. 3 is a circular fungus-like growth of scirrhous hardness, with a sloughing surface, about 3 inches in circumference, and $\frac{1}{2}$ an inch to 1 inch in thickness, removed from the back. The three tumours are grouped together on the common ground of an implication of the skin-glands, but there are important differences between them. No. 1 has the disorder of the skin-glands in its deeper parts, but it has a thin layer of independent disease on the surface, starting from the hair-follicles. No. 2 is purely and simply a tumour of the skin-glands. In No. 3 there is the important addition of cancerous infection of the connective tissue. The first two taken together will serve to illustrate the initial disorder of the secreting structure and function, and the third case will be made the occasion of showing how the additional element of cancerous infection comes in.

The preparations from tumours No. 1 and No. 2 show clearly the nature of the contents of the secreting structure, or the character of the secretion. The cross section of the glandular tube is often filled with a homogeneous mucous fluid, sometimes of a brown colour; at other times the space is occupied by a heap of uniform spherical cells of granular substance and yellowish-brown pigmentation,

and without visible nucleus; and in a few instances the cells, lying free in the centre, are more or less perfect nucleated epithelium. It may be made a question whether the mucus-like secretion is produced at the expense of successive renewals of the individual cells lining the tubule, or whether the same cells may continue to give out drops of secretion from their interior for an indefinite time. But as regards the spherical granular masses, wherever such occur within the tubules, there is no doubt that they at least are the actual epithelial cells transformed and detached. They correspond to one of the "three orders of secretion" spoken of by Goodsir,[1] and, in fact, to an order of secretion less elaborated than the mucous fluid which may be taken as the ordinary functional product of the skin-glands. That the secretory product of a gland is not always fluid, but sometimes solid or cellular, is proved not only by the facts observed by Goodsir in certain glands of the invertebrata, but also by my own observations on the periodical processes of the breast.[2] Again, the thick or semi-solid secretions such as those of the sebaceous and ceruminous glands are generally admitted to be formed out of epithelial cells which have been shed bodily into the cavities of the gland.

In tumours No. 1 and No. 2, the cast-off cells of the secreting structure, or the solid products of the secretion, are found not only in the lumen of the tubules, but also, and indeed more frequently, in the spaces of the surrounding connective tissue. Fig. 4 represents the usual appearance, in section, of the skin-glands in tumour No. 1. Not only are the intervals between the coils of the tubule packed with large epithelial cells, granular and not granular, but the same cast-off cells of the secretion are found impacted in rows in the connective tissue of the corium, and these rows or processions of cells sometimes extend to comparatively distant parts of the connective

[1] Goodsir, "Secreting Structures," 'Anatomical Memoirs,' vol. ii, p. 422.

[2] 'Contributions to the Physiology and Pathology of the Breast, &c. London, 1878.

tissue. This remarkable and not generally recognised accompaniment of secretion is one that I have already described for the breast under a variety of circumstances, both of health and disease. The occurrence of precisely the same phenomenon in connection with the secretion of the skin-glands in the dog, leads me to think that the doctrine of cellular waste products of secretion, escaping not by the ordinary outlet but into the surrounding connective-tissue spaces, is a well-founded doctrine, and one that is applicable, in disease at least, to other glands besides the breast- and the skin-glands. The peculiar circumstances of the breast, in particular the remarkable periodicity of its function, give occasion to accumulations of waste products of the secretion when there is no suggestion of anything abnormal. In the skin-glands of the dog it is obvious that there is a liability, at least, to such extra-glandular accumulations of epithelial cells or cell-products, whatever be the occasion which calls forth the liability. The most singular fact as regards the skin-glands of the dog is, that the cells collected in the spaces of the connective tissue surrounding the glands are not only of the large spherical granular and pigmented kind, which are clearly enough identical with the cast-off products of the secretion, but also cells that have the cubical or polyhedric shape and the finely granular or homogeneous protoplasm of the perfect epithelium as observed *in sitû*. The occurrence of both kinds of cells in the connective-tissue spaces is shown in fig. 5, drawn from a preparation of tumour No. 1 under a higher power. The one side of the figure shows the profile view of the epithelium *in sitû*, and the other side shows the face view of the same, while the connective-tissue spaces round about may be seen to contain both the perfect cubical epithelial cells with a well-defined nucleus, and also granular pigmented spherical cells of somewhat larger size and with the nucleus obscured. In the preparations from this tumour, there are absolutely no instances of lymphoid cells or leucocytes in the spaces of the connec-

tive tissue, but all the cells are of large size and epithelial character. They are identical with the secreting epithelium, either in its perfect or in its transformed condition; they are found in greatest numbers in the immediate neighbourhood of the gland-lobules, and, when they are found at some distance from the lobule, it is at the same time evident from their processional grouping and somewhat compressed shape that they have been carried thither from the glandular structures within which they were produced. None of the cells have been observed in the act of passing through the wall of the glandular tube, and, in the circumstances of the case, it is hardly to be expected that that observation ever will be made. We are, in this matter, the less dependent on direct and continuous observation of the movements of cells, inasmuch as the cells are easily identified in many cases by their pigmentation, and in general by their size and epithelial character. The same kind of cells are found both within and without the gland, and those that are outside the gland must have escaped from it.

The tumour No. 1 was a thin strip of new formation which consisted partly of a hypertrophic stratum on the surface, having its seat in the hair follicles, and partly of the entirely distinct products of glandular disturbance infiltrated into the deeper parts. It is not improbable that the disease of the hair follicles may have occurred first; and, as the skin-glands open into the hair-follicles, any hypertrophic condition of the latter would probably cause obstruction to the escape of the glandular secretion and ultimately lead to that glandular disorder and epithelial infiltration which has been specially dwelt upon in connection with tumour No. 1. In the case of tumour No. 2 the almost hairless cutaneous surface is unbroken, and the tumour is owing simply and solely to the disorder of the glandular structure and function. The appearances in this tumour may be grouped under three heads:—(1) The dilatation of the glands and the multiplication of epithelial cells on their walls; (2) the enormous accumu-

lation of cellular products of the secretion in the connective-tissue spaces of the corium; (3) the cancerous infection of the fixed connective-tissue cells of the corium. The dilatation of the glands is in some parts considerable, but never amounts to cystic formation. The epithelial lining is occasionally more than one row of cells deep, and may even be raised into papillary eminences. The deeper cells are sometimes merely nuclear bodies like leucocytes or catarrhal cells; in other cases, as in fig. 6 (Plate IV), they are the large spherical pigmented elements already described. The figure No. 6 shows a portion of the wall of a glandular tube with the large cells lying both *in sitû* and also in the spaces of the connective tissue. The appearance in that figure is more complex than in fig. 5 from the former tumour. It is more like a catarrhal condition, not only from the occasional admixture of nuclear or true catarrhal cells, but also from the reticular condition of the surrounding connective tissue, a condition resembling that of chronic inflammation. It is, perhaps, not going beyond the legitimate use of terms to describe as catarrhal that state of the secreting structure in which the cellular products are not discharged from the surface, but are diverted through the basement membrane to accumulate in the spaces of the subjacent connective tissue.

The second factor in the formation of the tumour No. 2 is the enormous accumulation of epithelial products in the spaces of the corium. A great part of the bulk of the tumour consists of infiltrated cells, which are usually of the large spherical granular and pigmented kind. In some places every interfibrillar space of the corium over a wide area is packed full of such cells in linear procession. It is important to observe that the cells do not appear to multiply by division after they have been carried into the connective-tissue spaces; the increase in their number is rather to be referred to successive additions from the original seat of production, viz. the glandular tubules. If the large granular pigmented cells produce by fission any of the smaller cells that are

often to be seen in large numbers beside them, they must lose their granular substance and become reduced to a nuclear state before they begin to divide.

The third factor in the formation of tumour No. 2 is the cancerous infection of the fixed connective-tissue cells of the corium; and inasmuch as that important subject is better illustrated by the appearances in tumour No. 3, I shall include what remains to be said of tumour No. 2 in the next section.

III. *Cancerous infection of the corium and subcutaneous connective tissue, following on disorder of the structure and function of skin-glands.*

Tumour No. 3 was a circular fungus-like growth in the skin of the back, with a thin upper stratum in a state of slough. It was of scirrhous hardness, and in minute structure it consisted of a dense stroma everywhere split up into numerous narrow bands, the meshes or alveolar spaces enclosing exquisitely-formed epithelial cells of a cubical or polyhedric shape with a nucleus and finely granular or homogeneous protoplasm. The tumour was evidently a cancer, but it was at the same time not an epithelioma; and it was not clear at first sight how such a tumour could be connected with any cutaneous structure. However, a more careful search within the area of the tumour brought to light two or three clusters of skin-glands; and, by way of furnishing evidence on that important point, I have drawn in fig. 8 a group of three or four such glandular crypts exactly as they lay in the midst of a tract of the stroma of the tumour. The basket-work of plain muscular fibres can nowhere be seen more clearly than in some of these tubules, and the size and form of the epithelial cells are equally distinctive. The skin-glands have been the point of departure of tumour No. 3, as of tumours Nos. 1 and 2, but in the third tumour it is more difficult to trace its structure back to the

glandular structure from which it started. Only a few crypts or alveoli of the normal gland tubules remain, these being found wherever there are any relatively broad areas of the corium left. Everywhere there is going on a formation of epithelial cells in the interstices of the connective tissue, so that the latter is split into narrower and narrower bands, and is in the end represented by single threads or fibres separating the linear rows or alveolar groups of epithelium.

That production of epithelial cells from the fixed connective-tissue cells of the corium is the prominent feature of tumour No. 3, overshadowing everything else in it. Fig. 9 (Pl. IV) gives a panoramic view of the transformation of connective-tissue cells into epithelium. The almost hidden connective-tissue cells of the corium become, throughout the whole region, plump and granular; they then appear in the form of cubical nuclei; and ultimately they acquire a protoplasmic investment, which brings them to the semblance and size of epithelial cells. But there are still traces of the original plan of glandular structure underlying that radically new cancerous process. The formation of rows of epithelial cells in the interstices of the connective tissue in many places follows concentric lines round the original gland tubules. The epithelial new formation breaks out in ever-widening circles in the tissue surrounding the tubule, so that there results an appearance as if the tubule had been greatly dilated, and as if the dilated cavity had come to be occupied with linear columns of epithelium. That extension of the area of the original tubule is not a mechanical encroachment upon the surrounding connective tissue, but it is a transforming encroachment, whereby the cells of the connective tissue become epithelial cells, and are left lying in successive concentric rows within a wide space continuous with the original lumen of the gland. The first step in that remarkable process of cancerous invasion appears to be illustrated in some of the tubules of tumour No. 2, fig. 7 (Pl. IV) being a drawing of one of them. The drawing is

taken from one side of a tubule, which shows in the other parts of its circuit the same condition that is drawn in fig. 6, viz. an accumulation of large spherical and other cells, both in the deeper layers of the epithelium lining the tubule and also in the spaces of the connective tissue nearest to the basement membrane. That part of the circuit of the tubule drawn in fig. 7 appears to me to exemplify, when compared with fig. 6, the step or the leap from a process of merely functional disturbance to a cancerous process. The connective tissue on the other side of the basement membrane is not occupied by cast-off cellular products of the secreting structure, but by a row of its own cells which have emerged from their hidden and quiescent state, have become plump and granular, and have to some extent assumed the cubical form and the regular order of epithelial cells. These characters are to be seen in the uniform row of cells next to, or perhaps within, the basement membrane, and the deeper rows of the connective tissue are following in the same direction. That abnormal formation of epithelium from the underlying connective tissue advances around the crypt or tubule in ever widening circles until the whole stroma or supporting tissue of the gland is incorporated, as it were, into the glandular structure. The cancerous infection in tumour No. 3 is for the most part the same in plan as I have described and figured, in a former paper, for a case of scirrhus of the breast; and the language which I have applied to the latter is literally applicable to the present case: "Under ordinary circumstances the row of epithelial cells on the wall of the acinus would be separated from the subjacent tissue by a more or less obvious basement membrane; whether an actual and substantial basement membrane be present or not, nothing can be clearer than the total separation of the epithelium from the tissue next to it. But here the line of demarcation of epithelium from connective tissue is broken through. . . The breaking down of the wall of partition between epithelial and sub-epithelial tissues,

as shown in fig. 6, illustrates the real nature of the cancerous invasion in the breast. The disease has spread from the glandular tissue to the connective tissue, and no limits can now be set to its progress. . . The disease has entered on a tissue which goes all through the body. The primary disturbance of the glandular epithelium has practically ceased to be the disease; it is the infection of the other tissue that now determines the extent and the rate of progress of the malady."[1]

As I have, in the paper from which the foregoing quotation is taken, and in earlier papers on tumour-infection of the liver and of lymphatic glands,[2] discussed at length the question of cancerous infection, both of the tissues in the immediate neighbourhood of the primary disease and the metastatic infection in more distant parts and organs, I shall not occupy more space here than to state briefly my view of the relation between the primary disturbance of glandular structure and function and the cancerous infection of the neighbourhood which follows it, and in the end overshadows it. There is nothing cancerous in the glandular disorder itself, and in some cases it does not differ essentially from a catarrhal disorder. The morbid cellular products of the secretion, which are for the most part large spherical granular masses, easily identified are sometimes found, as in fig. 6 (Pl. IV), occupying the spaces underneath the epithelial lining of the tubule; but they are found in greatest abundance in the spaces of the connective tissue in the immediate neighbourhood of the tubule as well as at some distance from it. Those cast-off cells of the secretion, whether they remain on the wall of the tubule or get carried away into the connective tissue round about, are not permanent and growing elements of cancerous formation, but they are the agents of awakening the cancerous formation in the quiescent cells of the

[1] "The Infection of the Connective Tissue in Scirrhous Cancers of the Breast," 'Journ. of Anat. and Physiol.,' vol. xiv, 1879, pp. 47, 48.

[2] Report of the Medical Officer of the Privy Council, &c.,' for 1874 and 1876.

connective tissue with which they come in contact. They are often found in enormous numbers in the spaces of the connective tissue, but those heaps appear to have been formed by successive additions from the original seat of production within the gland rather than by fission among themselves. Their granular and pigmented substance sometimes disappears, and it is conceivable that the nucleus left behind may become an active and multiplying cell. The large granular cast-off epithelial cells are concerned in cancer as infecting cells; and with their infecting property their activity appears for the most part to cease. They are like a fertilising influence scattered in the connective-tissue soil; they carry in them a seminal virtue which impregnates the quiescent connective-tissue corpuscles, causing them first to return to their embryonic characters, and then to develop towards an epithelial form and grouping, according to the particular pattern of the epithelial structure in which the fertilising or spermatic cells had been produced.

One of the forms of infection consists in the breaking down of the barrier formed by the basement membrane and the inclusion within the circuit of the tubule of successive rows of connective-tissue cells, infected to become epithelial; that form predominates in tumour No. 3, and an explanation of it has been already attempted with reference to figs. 6 and 7. It is more usual, however, in cancer of the breast and of other organs to find the cancerous infection breaking out at numerous points in the connective tissue, and producing linear processions or alveolar groups of epithelial cells in the midst of that tissue. There are parts of tumour No. 2 where that form of infection appears to be going on, and those are the parts to which the large granular infecting cells have been carried. In the paper already quoted, on scirrhus of the breast, I have endeavoured to show that the linear and alveolar grouping of the cast off cells of the secretion, amounting to an infiltration in the literal sense of the word, determines the often observed linear and alveolar

pattern of cancerous "infiltration" as the term is ordinarily understood in clinical practice.

Whether or not all the cast-off glandular cells have a spermatic or infecting property, it is obvious from tumour No. 1, and from parts of tumour No. 2, that epithelial infection of the connective-tissue cells does not always follow the accumulation of epithelial products in the spaces of that tissue. It requires certain favouring or predisposing conditions of the connective tissue before infection can be kindled. There are no very obvious structural or physical differences in the cutis of the three dogs, to account for the differences in the nature of their respective tumours. According to Thiersch,[1] the predisposing cause of epithelioma of the skin is a certain senile and relaxed condition of the corium. Inasmuch as cancer in general is a disease occurring after middle life, it is conceivable that there may be a condition of the connective tissue in that period which predisposes it to epithelial infection. But it is at the same time clear that there must be other reasons for that predisposition, such as heredity or chronic irritation, which are special to the individual.

[1] Thiersch, 'Der Epithelial-Krebs, namentlich der Haut,' 1865, pp. 79, 80.

DESCRIPTION OF PLATES III, IV.

Tumours from Skin-glands in the Dog (Dr. Charles Creighton).

PLATE III.

FIG. 1.—Section of the glandula humeralis of the ornithorhynchus, showing the basket-work of plain muscular fibres in the walls of the convoluted tubules. × 150.

FIG. 2.—Stratum of plain muscular fibres forming the wall of a minute cyst in the tissue near a tumour of the pectoral region in a woman. × 300.

FIG. 3.—Another portion of the same, showing the polyhedric epithelial cells seated directly on the muscular-fibre membrane. × 300.

FIG. 4.—Section of a glandular coil of the dog's skin, from Case 1, showing the infiltration of cast-off cells of the secreting structure into the surrounding connective-tissue spaces. × 120.

FIG. 5.—From a preparation of the same case, under a higher power, showing the face view of the epithelium *in situ* in the one part, and the profile view in another, with epithelial infiltration of the surrounding tissue. × 350.

PLATE IV.

FIG. 6.—Portion of the wall of a tubule in Case 2, showing large spherical granular cells in spaces of the epithelial layer, and the same kind of cells in the spaces of the subjacent connective tissue. × 350.

FIG. 7.—Another portion of the wall of a tubule in Case 2, showing the epithelial infection of the connective-tissue cells. × 350.

FIG. 8.—Remnants of normal glandular structure in the stroma of Case 3; the plain muscular fibres mostly represented (as also in fig. 4) by the dark lines corresponding to the highly-refracting intervals between the fibres. × 120.

FIG. 9.—From tumour No. 3, showing various stages of the formation of epithelial cells from the connective-tissue cells of the corium. × 350.

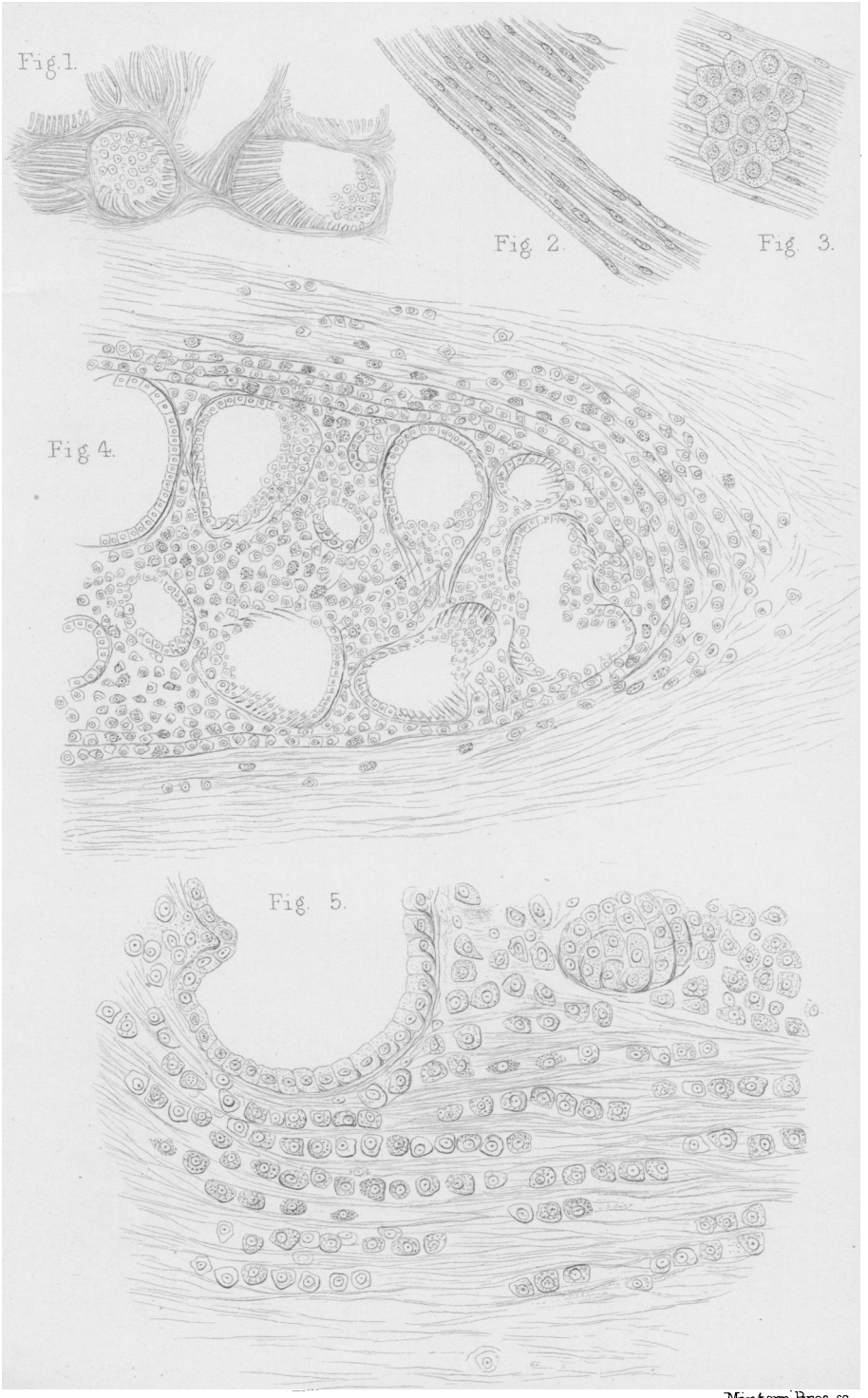
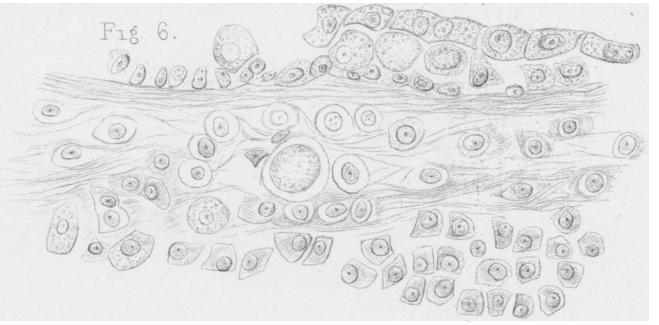
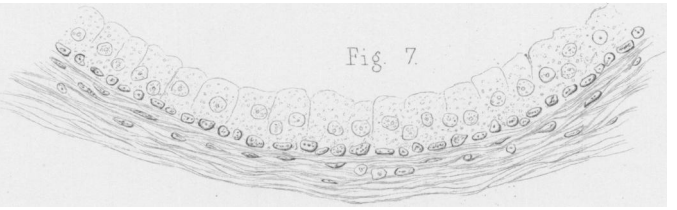
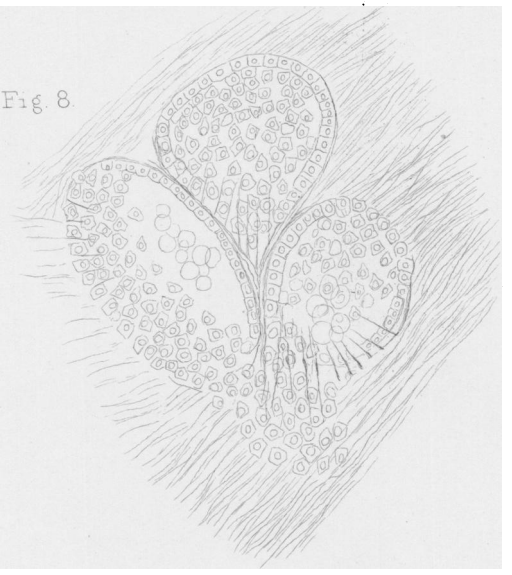
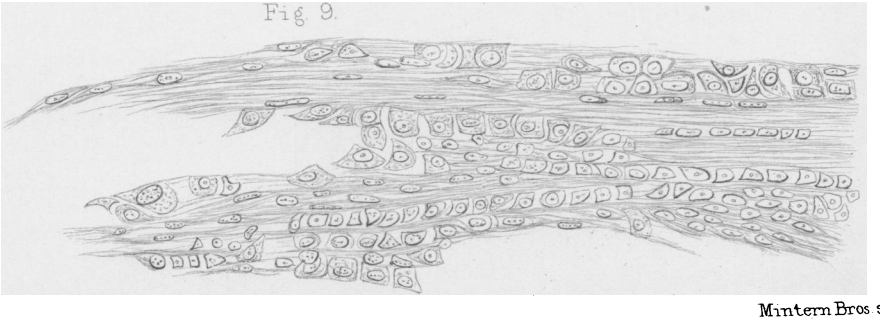


Fig 1.
Fig 2.
Fig 3.
Fig 4.
Fig 5.









C. Creighton del. Mintern Bros. sc.