

MUCOSAL CYSTS AND THE SIGNIFICANCE OF THE STRATUM GRANULOSUM.¹

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IN September 1896, a child, æt. 18 months, was admitted into St. Thomas's Hospital, under the care of Mr. Makins.

A swelling in the neck had been noticed three months previously, and this commenced discharging seven weeks later. Upon examination a sinus was found on each side in the position of the lowest branchial cleft, about the level of the sterno-clavicular articulation. That on the right side appeared to be in connection with a cystic swelling $1\frac{1}{2}$ in. higher up, on pressing which a little fluid exuded. A horse-hair was passed into the right sinus and an incision made over the swelling, which was dissected away from the adjacent structures; the incision was afterwards prolonged down to the opening of the sinus, and the whole dissected away in one piece. At a subsequent date the left sinus was similarly dealt with. The cyst is thinly walled, 1.5 cm. in chief diameter, and after being hardened in alcohol was found quite filled with a white, friable coagulum, resulting from the action of the medium.

Microscopic examination of the contents showed in moderate numbers clear flattened epithelial cells, in all cases presenting a distinct nucleus, and considerable numbers of leucocytes in a state of fatty degeneration, together with a little free fat. Sections of the wall stained with hæmatoxylin and eosin show it to be composed of vascular fibrous tissue.

On the inner aspect of this is a well-preserved epithelial lining of the stratified squamous-celled kind. The lining consists, more particularly, of polyhedral cells, three or four deep, passing into flatter cells, until the free surface is reached. The whole of the flatter cells have well-stained granular nuclei and a clear, transparent cell body, but faintly stained with the eosin. In no way, either by affinity for eosin or nuclear obscuration, is any horny metaplasia indicated.

There is everywhere a complete absence of stratum granulosum or eleidin-holding cells.

In some of the sections the interesting fact appears that areas lined with typical columnar ciliated epithelium, of which many of the cells are distended with mucin, occur by the side of the other variety. Many "polynuclear" leucocytes are migrating between the epithelial cells; this accounts for the large numbers already noticed in the contents of the cyst.

Of similar histological structure is the wall of the following cyst, which was removed from the upper part of the side of the neck.

H. H., æt. 13 years, admitted under the care of Mr W. Anderson, January 13, 1897. A swelling had been noticed about eighteen months, and was unattended with pain or inconvenience. On examination it was found

¹ Read before the Pathological Society of London, 5th May 1897.

located beneath the right ramus of the lower jaw, extending from the angle behind to nearly the middle line in front. It lay partly above and partly below the level of the hyoid bone. When the cyst was dissected out the internal jugular and facial veins were found adherent to its under surface. The epithelial lining is of the stratified squamous-celled kind, in every detail like that of the pharyngeal or buccal mucosa. The deepest set of cells is vertically disposed; and these are succeeded by polyhedral, passing into flat cells. The superficial cells, however, nowhere form a homogeneous horny layer, and there is no trace of stratum granulosum.

Before discussing the question raised by these specimens, I may add the following:¹—An oval cyst about $1\frac{1}{4}$ in. in length, removed from the lower part of a child's neck. From its upper end there proceeds a tubular process about $\frac{3}{4}$ in. in length, which rose up in the direction of the sterno-mastoid muscle, and was closely related to the carotid sheath. A canal traverses the cord almost to its end, and freely communicates with the cyst. The entire length of the parts from the aperture in the skin is 3 cm.; the sinus itself beyond the cystic dilatation is 2 cm. long.

There had been a small, hard lump in the neck, as long as the patient could recollect; it was free of the skin, and moveable on the deep tissues, except just at its centre, where it discharged about an inch above the upper margin of the sternum and at the anterior border of the sterno-mastoid. I examined microscopically the wall of the cyst, selecting a piece from the back opposite to the aperture in the anterior wall; it consisted of common fibrous tissue, with a well-formed epithelial lining of long, slender, columnar cells, each of them furnished with a brush of cilia, and was devoid of glandular structures or crypts.

REMARKS.

It is hardly necessary to observe at the outset that the source of these cysts lies in branchial clefts, that the branchial clefts on either side of the neck arise from the conjunction of a series of diverticula from the primitive pharynx, with a corresponding lateral series of external invaginations, in kind analogous to the stomodæum; but that in the human subject, under normal circumstances, except in the case of the first or tympano-Eustachian passage, no communication is established between the external and internal recesses.

It is to the epithelial lining of these cysts that I wish to draw particular attention, with the object of justifying the nomenclature proposed in this communication, namely, that of *mucosal* as differentiated from dermoid cysts.

In the third example, the epithelium is of the ciliated columnar variety. The cyst, therefore, it is clear, represents the pharyngeal diverticulum, and not that arising from the exterior, its epithelial lining retaining the primitive columnar character of that proper to the part from which it has arisen. The preparation shows, in passing, how little invagination can be assigned to the exterior or epiblastic side; for though the posterior wall of the cyst opposite the opening of the fistula was selected for examination, it is nevertheless lined with ciliated columnar epithelium. It is not, then, a dermoid cyst, but one of which the wall consists of mucosa, and to which the term *mucosal*

¹ No. 2545, St. Thomas's Hospital Museum.

may, perhaps, be appropriately applied. The expression "mucous cyst" is generally agreed to mean a retention cyst arising in a mucous gland, and its extension to a cyst lined with mucous membrane would be a source of confusion. "Mucoid" means, like the substance, mucus. To the term "mucosal" no ambiguity can attach.

In the case of cysts lined with a columnar epithelium there can be no difficulty in drawing such a distinction. But what I submit is, that a certain number of the cysts hitherto classified as dermoid belong to the same category; they are mucosal, and to this class I should relegate the first two specimens recorded in this communication, namely, the cervical cysts lined with epithelium of the stratified squamous-celled variety.

The diagnostic criterion, then, between dermoid and mucosal cysts with squamous epithelium, is the presence or absence of a stratum granulosum, *i.e.* the layer of cells containing granules and flakes of eleidin, and intervening in the epidermis between the rete Malpighii and stratum lucidum.

In this diagnostic mark there is nothing new, for the absence of stratum granulosum in mucosal epithelium is a well-known histological fact; but the significance of this stratum in pathological formations, whether cystic or solid, appears to have been curiously overlooked.

Mr. Bland Sutton¹ has endeavoured to classify all cysts, whether lined with mucous membrane or skin, as dermoid, on the ground that the structures of skin and mucosa pass by gradations into one another. It may, however, be as truly said, that no better distinctions can be drawn between other tissues. Cartilage merges by imperceptible gradations into connective tissue, and connective tissue into bone. Nevertheless, no one for that reason calls bone cartilage, or cartilage connective tissue. The philosophical truth, that all divisions in biology are only artifices to aid the mind in its apprehension of facts is generally allowed; and, this being granted, no advantage can accrue from ignoring the subdivisions arising out of histological structure. If mucous membrane and skin, again, are to be considered identical, it is not easy to see why the former should be wiped out from histological nomenclature rather than the latter, and why the common integument should not be designated an external mucosa. It is, in short, impossible for all practical purposes to reject either of the terms, seeing that they indicate different structures. If the attempt is made it ends in the dilemma of having to describe mixed cysts (of mucosa and skin) as dermoids containing patches of skin (!), and it is exactly to this that Mr. Sutton is driven. If a cyst has a wall, in part of skin and in part of mucosa, it can be readily named, after the manner of all composite morbid growths, by the simple method of combining the terms; it is a dermo-mucosal cyst. The same terminology would, of course, be extended to internal membranes which bear hair, as that, *e.g.*,

¹ "Dermoids," London, 1889.

on the inner aspect of the rabbit's cheek. The hairy tract in the mouth of this animal is continuous with the proper external skin round the angle of the mouth, and is not hair-bearing mucosa, but skin in all its histological details, with an epithelium of eleidin-holding cells, and hairs set in groups as on the exterior of the body.

As to the variations of epithelium in these three cysts, no more explanation can be given than of those which occur during the course of development in the œsophagus and pharynx themselves, from which the cysts arose. The œsophagus is lined, in its primitive condition, with columnar epithelium, like that of the trachea and bronchi which are derived from it, but this is subsequently replaced by the stratified squamous-celled kind; the mutation, however, in the higher parts of the respiratory and alimentary passages is, as well known, very irregular in distribution. In one of the cysts from the neighbourhood of the sterno-clavicular articulation, the areas of squamous-celled epithelium lying between those of columnar might be attributed to the presence of the discharging sinus. I do not think that this is the true explanation; and I may particularly point out that in the cyst described from the upper part of the neck no such sinus had ever existed, yet it presents a typical stratified mucosal epithelium. This cyst, moreover, was lateral in position, and hence removed from the thyro-lingual category; it must be regarded, therefore, as having arisen in a residue of the pharyngeal diverticulum of the "cleft," and not in the remains of the epiblastic or external invagination, in which latter case its lining would have been true epidermis with eleidin-holding cells.

In true dermoid cysts I have never yet failed to discover a stratum granulosum. Fortunately there is a stain which selects the granular stratum with remarkable and unerring accuracy. If sections be treated by Gram's method, the granules and flakes of eleidin retain a brilliant violet colour in the midst of the decolorised tissue; and this in all doubtful cases is the surest means of conducting the observation. For especially in flattened cells, viewed edgewise, the chromatin "granules" of the nuclei may at times be taken as free in the cell body; but by the method named, as the colour of the whole of the chromatic substance is discharged, the danger of mistaking the chromatin of normal or of fragmented nuclei for the granules in question is obviated. None of the normal mucosæ lined with stratified epithelium, whether examined by this method or others, exhibit the stratum. On the contrary, not only in dermoid cysts provided with epidermal appendages, is a stratum granulosum invariably present, but I have found it without exception in cysts unprovided with hairs or glands, yet undoubtedly dermoid from their relations. Some such are encountered in positions where no epiblastic inclusion, attending the closure of clefts can take place, as, for example, on the limbs. I have examined three cysts of this class from the lower limb. One of these, about $2\frac{1}{2}$ in. in diameter, was removed from over

the great trochanter, and had been observed seven or eight years;¹ the question of an antecedent injury had not been inquired into. The second,² a cyst of the same dimensions, was removed from the outer aspect of the right thigh, in a housemaid, æt. 31, and had been observed as a slowly increasing painless swelling for thirteen years; there was no recollection of injury. The third example was excised from the inner side of the left thigh, and occurred in a man, æt. 46, a police constable. About twenty years previously, when he was working as a *farrier* he noticed a small swelling, which slowly increased till three years ago, since when its enlargement has been more rapid; the cyst was the size of a small orange.

J. H. Targett³ has recorded a large multilocular dermoid cyst, which was removed from the outer side of the right thigh, just above the knee-joint; here, too, no epidermal appendages were found on microscopical examination. The following may be added as a cyst of similar macroscopic and microscopic characters, and interesting in its relation to a definite traumatic cause. It was dissected out from the abdominal wall in the right lumbar region, and formed at the site of a bullet wound received twenty years previously; the bullet was searched for, but does not appear to have been discovered; there had been pain and discharge for many years. There is much leucocytic infiltration of the cyst wall; and the epidermal lining, devoid of appendages, but with well-marked stratum granulosum, presents the ingrowths met with in chronic inflammatory conditions of skin or mucous membrane.

Such dermoids are usually filled with glistening closely-packed flakes of epidermis, and have a smooth, white, silvery lining. In histological section their walls present the following structure. They have a corium of common connective or fibrous tissue invested with an epidermis, of which the deepest cells are set vertically; to these succeed a polyhedral series, and to these a flatter or squamous, shed into the interior of the cavity; between the polyhedral cells and the innermost or superficial scaly layers there is a well-marked stratum granulosum. In a certain few of such a history of antecedent injury has been forthcoming; and some (perhaps all) may, as Sutton supposes,⁴ be implantation cysts, or cysts due to the traumatic displacement of epidermis into or beneath the substance of the corium. No appendages are met with in such cysts, whether of the larger size, like those just noticed, or of the more insignificant seen on the palmar aspect of the fingers, or on the palm itself. And this, I believe, is the rule,—any hairs or glands that do occur in implantation cysts being there by direct implantation only.

It is well established that the epidermis which extends over

¹ No. 2554, St. Thomas's Hospital Museum.

² No. 2554, a, St. Thomas's Hospital Museum.

³ *Trans. Path. Soc. London*, 1889, vol. xl.

⁴ *Loc. cit.*

granulating surfaces never produces hairs or glandular appendages, and that which is implanted is, it may be presumed, in like case.

After embryonic life the epidermis apparently loses the capacity for development which such structures entail, and retains only that for growth, or hyperplasia.

In passing, I may notice that in vegetable tissues less even than this obtains, for here the epidermis is incapable of extending over open wounds at all; and where hairs, or glands, or stomata are concerned, these are never renewed. In the healing of open wounds in vegetable parenchyma (as I have discussed in the *Journ. Linnean Soc.*, London, vol. xix.), the repair proceeds beneath a crust or scab of dead cells, and is effected by subdivision of the cells of the parenchyma in planes parallel with the surface of the injury, which cells furnish in this way a cork cambium, from which, on the superficial aspect, a many-layered covering of cork is differentiated and heals the wound.

Thus, in the amputated surfaces of leaves, whether such succulent examples as Cotyledon, Crassula, Aloe, or the more ordinary kind (as Rhododendron, Ivy, Dahlia, Pear, Privet), no re-formation of stomata ensues, the surface being healed simply by an impervious zone of cork; and the same is true of the stems of Cactaceæ, which play the physiological parts of leaf and stem combined, and are as abundantly provided with stomata as ordinary foliage leaves.

Equally is there an absence of hair production upon the scarred surfaces of vegetable parenchyma; and this not only in the case of aerial organs, but in the growing tissues of the root. I have many times bisected the apex of the radicle in *Faba vulgaris*, placing a piece of mica in the fissure, to prevent union of the faces of the injury. In such circumstances an artificial dichotomy results, the main root attaining its full length but being doubled. The mica retains its position in the highest part of the cleft, a short distance from the remains of the cotyledons. At the seat of injury each of the two divisions of the main root continues flat on the inner aspect, but, beyond, each presents a cylindrical form, and gives rise to rootlets in the usual manner; rootlets may also burst out from the pericambium in the divided surfaces themselves.

As relating to the matter under consideration, however, the point worthy of notice is the absence of epidermis and its pertaining root hairs from the surfaces of the injury.

Horizontal microscopic sections show that the whole of the parenchyma is healed by prominent cells of callus, the cells being correspondingly smaller in the situation of the pericambium and cambiform tissue of the fibro-vascular bundles; the reparative tissue is least marked and very scanty in the more peripheral portion of the cortical parenchyma; but nowhere does this give rise to root hairs. The same absence of epidermal extension is witnessed if shreds of the epidermis are stripped from the young stems of *Faba vulgaris*, or the young leaves of *Hyacinthus orientalis*; and this even when the plants

are grown in the moist atmosphere of a hothouse ; if at times division of the epidermal cells bounding an exposed surface or the edge of a gaping incision is to be met with, no extension takes place over the surface as occurs in the repair of animal textures.

It follows, also, from these facts that in tissues provided with glands derived from epidermal subdivision, there is no regeneration of such structures in the scar resulting from open wounds. In some very young lemons I sliced away the protuberant apex without exposing the pulp, and after some weeks of growth examined the parts by vertical microscopic section. In the repaired surface the general parenchyma of the rind passes into a thick phelloderm of flattened elements, to which latter succeed a muriform thin-walled phellogen, and cork in cell-series corresponding with those of the cork cambium ; the deeper cells of the cork are flat or cubical, the superficial of larger size and less orderly arranged ; finally, on the cork, lie the remains of the parenchyma killed by the injury. Now, whilst glands are abundant up to the very edge of the scar, there are none in the tissue of or beneath the scar itself, though, as microscopic examination showed, they were present in the piece experimentally removed. In the scars at times met with in the skin of the orange, too, and resulting from loss of substance, the same absence of glands is to be observed. What is more, an examination of the familiar scar of the style in the lemon or orange will reveal the same absence of glands in the tissue beneath the cork which invests it, though they occur beneath the epidermis up to the very limits of the scar itself ; whence it may be concluded that the epidermis takes an essential part in the development of the cutaneous glands of these fruits.

I tested the capacity for gland reproduction, finally, in *Ruta graveolens*, by cutting away the young leaves of growing shoots, close up to their attachment, so as to expose the cortical parenchyma, which is abundantly provided with sub-epidermal glands ; the divided surfaces healed in the usual way, and without any trace of gland reproduction.

As a deduction from these considerations there is, I believe, no development of appendages from the epidermis implanted by trauma, at least after embryonic life ; for, though improbable, it is not impossible that implantation cysts might arise in the embryo from such a cause.

Although this proposition will probably prove true, the converse does not necessarily follow, namely, that every dermoid, arising from embryonic inclusion, is furnished with cutaneous appendages.

In some cases, certainly, microscopic sections do not disclose such, though to prove a negative nothing short of an examination of the entire cyst would avail.

I have examined two dermoid cysts devoid of appendages, though, judging from their positions, they were prenatal in origin.

One¹ is a thin-walled cyst about $2\frac{1}{4}$ in. in diameter, removed with an

¹ No. 2559, St. Thomas's Hospital Museum.

ellipse of overlying skin; its contents are quite solid, though extremely friable, and consist solely of close-packed scaly epithelium, without hair or fat. Histologically the wall has an epithelial lining in which the Malpighian and horny layers of epidermis are represented, together with a well-marked stratum granulosum, but no papillæ, hairs, or glands were seen in the sections examined; it was removed from the back of the neck in the median line, and had been noticed twenty-seven years, in a man, æt. 48. The second cyst¹ was excised from the floor of the left of the mouth; it has solid friable contents, precisely like the foregoing, and in the microscopic sections examined no hairs or glands were met with; the epithelium exhibits the usual layers of epidermis including stratum granulosum; the cyst was from a girl, æt. 21, in whom a swelling was first noticed six years previously.

Although advocating this criterion, namely, the absence of eleidin-holding cells as that of distinguishing a mucosal cyst from a dermoid, I do not deny an occasional metaplasia or transmutation of mucosal epithelium to epidermis. In the tongue, when affected with ichthyosis, I have found a most pronounced stratum granulosum beneath the horny layers of the epithelium; and, similarly, in the immediate proximity of a carcinoma, the lingual epithelium may present this epidermal character, and eleidin-holding cells may occur in the growth itself.

And, under less unnatural conditions, the same metaplasia may arise;—the stratum is absent on the glans penis of the uncircumcised, present in that of the circumcised; but in the latter it is only appreciable by means of Gram's stain, which differentiates a brilliant violet zone beneath the uncoloured superficial layers of horny cells; when viewed on the flat, the coloured cells appear (under $\frac{1}{2}$ hom. immersion) loaded with the finest granules. So, too, I have observed the most pronounced granular cells in a horny papilloma growing from the glans of a circumcised adult. We may see typical granular cells mingled with the molluscous bodies in *Molluscum contagiosum*; and if the more direct evidence of the source of this lesion were still doubted, the presence of such cells is enough to disprove its origin in sebaceous glands, for in the latter no such cells occur.

Eleidin-holding cells, however, line the hair follicles to their deepest limits; hence in sebaceous cysts, which really arise in hair follicles, a stratum granulosum is to be found.

It is only occasionally that such cells occur in an obvious degree in squamous-celled carcinomata of the skin. If few they may readily be overlooked unless the staining method of Gram is adopted. Although the granules are intensely coloured by the usual dyes, the most reliable means of their demonstration is by the method named, since this removes the chance of mistaking fragmented nuclei for the granules in question, the nuclear chromatin being decolorised, whilst the eleidin retains an intense violet.

¹ No. 2558a, *ibid.*