

FORDYCE (J. A.)

MULTIPLE BENIGN CYSTIC EPITHELIOMA  
OF THE SKIN

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Dr. Fordyce's Case of Multiple Benign Cystic Epithelioma of the Skin.

MULTIPLE BENIGN CYSTIC EPITHELIOMA OF THE SKIN.<sup>1</sup>

BY

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THE limited number of cases of this curious affection which have been observed together with its very interesting pathological anatomy have prompted me to present to this Society a report of two cases,—mother and daughter—which have been under my observation for some months.

*Daughter's Case.*—The case which first came under my care affected a girl 19 years old. She is of German parentage, and has four brothers living, none of whom have any skin trouble.

Her mother, she states, has had an eruption on her face and neck for many years. Her father's skin is free from disease.

The patient is a blond, well developed and of average intelligence. She has always enjoyed good health and has been regular in her menstrual function.

Her mother says that no eruption was present on her skin at birth. As nearly as the mother and daughter can recollect, small pimples were noticed on the left temple and forehead about six years ago. At first they were small, about the size of a pin's head; they have gradually enlarged until many of them have attained the size of a split pea. She thinks during the past two years no increase in the number or size of the tumors

<sup>1</sup> Read before the Sixteenth Annual Meeting of the American Dermatological Association, New London, Conn., September 14, 1892, and the New York Pathological Society, Nov. 23, 1892.



has taken place. Shortly after the outbreak of the disease on the left temple similar papules appeared behind the left ear, then over the face and neck.

The statements of the patient regarding the time the eruption was first noticed as well as the order in which it developed cannot be regarded as strictly accurate.

*Present Condition.* (See chromo-lithograph.)—Numerous translucent, pearly-looking tumors, from the size of a pin's head to that of a split pea, are seen scattered over the forehead, temples, eyelids, cheeks, nose, behind and below the ears, back of the neck and through the hair. In the interclavicular regions from fifteen to twenty tumors are seen, and a few over the upper portion of the chest. The tumors are grouped on both temples and behind the ears, otherwise disseminated. On the left temple a circle is formed by half a dozen tumors.

In general the growths are discrete; in one or two places, however, masses were formed by the confluence of three or four tumors. They are imbedded in the skin and project beyond its surface. To the touch they are firm and painless; the larger tumors are tense, shiny and are freely movable. The lesions are dome-shaped, flattened and some of the smaller ones acuminate.

A central depression was noted in a number of the growths causing them to simulate very closely the lesions in molluscum contagiosum.

In color the tumors differ little from that of the surrounding skin; the smaller ones are a trifle darker while the stretching of the epidermis by their growth imparts a shiny appearance to the larger ones.

A few of the lesions presented a pale yellow tint, not sufficiently pronounced, however, as to suggest xanthoma.

The pearly translucent appearance of many of the tumors, caused them on casual examination to simulate vesicles, so that I was led to puncture one of them for fluid. The puncture was followed by slight bleeding only and revealed a solid formation.

The majority of the larger growths were covered with minute capillaries and intermingled with the lesions telangiectases and black pigment spots were found.

Scattered among the smaller translucent lesions a great number of white papules of the same size and shape as the characteristic lesions of the affection were noted, which differed in no respect from the ordinary milia. Many of the larger tumors also contained one or more white bodies like milia. The mucous membranes were normal.

The patient's face has an oily appearance; she perspires freely.

*Mother's Case.*—At my suggestion the mother of the patient presented herself for my inspection.

At first glance the identity of the eruption in the two cases was evident. (See Fig. 1 in text.)

In size, appearance, and general distribution the lesions were almost the counterparts of those on the daughter's face. She stated that her attention was first attracted to the eruption when she was about 15 years old. Her father had a group of tumors like those on her daughter's temple, and in the same locality, she recollects that they were always present and that no attempt was made to remove them. In her own case the tumors have increased in number from year to year. She experiences no inconvenience from them except a slight itching during the summer. At the inner angle of the right eye a large semi-translucent looking tumor containing a number of white milium-like bodies and covered with dilated capillaries is present. This tumor is about the size of two peas, double the size of any other growth on her own or her daughter's face. She thinks this lesion has grown during the past year. The other tumors with the exception of one below and to the right of the outer angle of the mouth are of pretty uniform size.

The eruption extends over the forehead, face, auricles, the anterior, lateral, and posterior aspects of the neck, and over the upper portions of the back and chest and has existed for over 30 years.

Numerous telangiectases are present over the cheeks and a few comedones are scattered here and there over the face. The clinical description of the eruption in the daughter's case applies equally well to the mother's.

As a similar eruption had never presented itself to me it was not possible to arrive at a diagnosis unaided by the microscope. Dysidrosis was readily excluded by the absence of fluid in the lesions. Hydradenoma (Darier), adenoma sebaceum, and colloid milium suggested themselves to me as possible diagnoses.

*Histology.*—For microscopic examination six tumors were excised from the face and back, placed for half-an-hour in a corrosive-sublimate solution and afterwards hardened in alcohol.

Sections were cut in celloidin, and stained with hæmatoxylin, safranin, and borax-carmin. Under low amplification or with the naked eye the derma is seen to contain a number of irregularly rounded, oval, and elongated masses which take a



Fig. 1.

deeper stain than the surrounding tissue. In some sections these cell masses are quite distinct while in others they intercommunicate in the most remarkable manner. These masses extend from just beneath the epidermis to, in some cases, the region of the coil glands. (See Plate, Figs. 1 and 2.) With moderate enlargement the resemblance which these cell heaps bear to an adenoma is very striking, suggesting at once the case described by Perry as an adenoma of the sweat glands and apparently justifying the name *hydradenoma*, given to this affection by some of the first observers. With stronger amplification these darkly stained masses are seen to consist of epithelial cells hav-

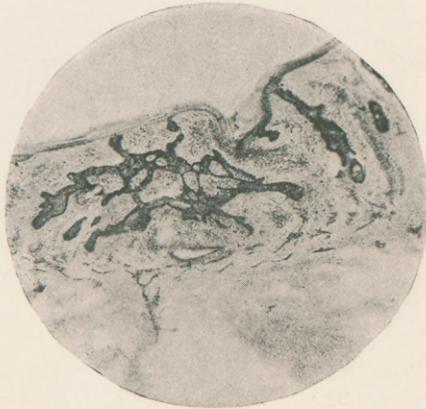


Fig. 2.

ATYPICAL EPITHELIAL CELL PROLIFERATION IN  
LUPUS ERYTHEMATOSUS.

ing the same appearance as the cells in the lower layers of the epidermis. They are inclosed in connective tissue which has undergone considerable thickening and condensation.

While in some of the sections the epithelial cells are densely packed together without a distinct structure, in others they are made up of tracts two or more cells wide, which are twisted and intermingled among themselves in the most complicated way. (See Plate, Fig. 2.) Linear tracts, two or more cells wide, ramify throughout the derma, connecting the cell masses and occurring independent of them; the narrower ones closely resemble coil-gland ducts although no distinct lumen can be made out. The tracts are not well shown in the photographs, but they are a

noticeable feature of many of the sections, recalling the atypical cell proliferation in true epithelioma and in sections from a case of lupus erythematosus which I prepared from a patient of Dr. Piffard. (See Fig. 2 in text.) The downgrowth and proliferation of epithelium seen in that case is of the same character and appearance as in the case which I am describing, and presented such an unusual departure from the histology of lupus erythematosus, that it is introduced here for comparison and to show that identical histological appearances may accom-

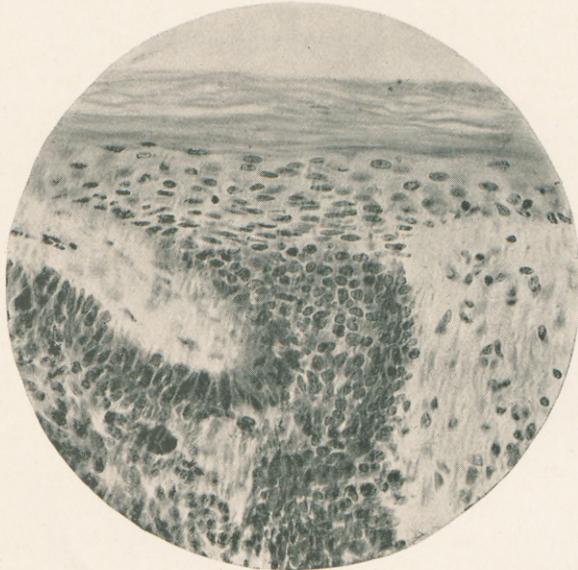


Fig. 3.

ENLARGED VIEW OF AN EPITHELIAL DOWNGROWTH FROM FIG. 2, SHOWING THE CHARACTER OF THE CELLS. (PHOTOMICROGRAPH BY DR. PIFFARD. SPENCER  $\frac{1}{6}$  IN. X 300.)

pany so widely dissimilar processes. Figure 3 in the text, an enlarged view from the same section, as in Fig. 2, shows the character and origin of the cells from the basal layer of the epidermis.

While the cell masses in the sections from some of the tumors are composed almost exclusively of densely packed epithelial cells, in other tumors the intricately intertwined bands and tracts predominate in their formation.

In other tumors, again, these cell heaps are more compli-

cated in their structure and show the "pearls" and cell "nests" of malignant epitheliomata. These cell nests are seen in all stages of development—centrically arranged and nucleated cells which show no horny degeneration, well defined imbricating horny cells (see Plate, Fig. 4), stratified corneous tissue and amorphous matter with here and there a stained nucleus present.

Cysts are seen surrounded by laminated cells containing kerato-hyaline enclosing dark brown or almost black granular pigment and detritus (see Plate Fig. 5), or entirely empty.

While in many of the sections the individual cells in the masses take the stain with equal facility, in others the centrally located cells are much paler in color or show only a few nuclei or imperfectly stained cells. (Plate, Fig. 7.)

Again the cell tracts are so arranged as to form an alveolar like structure enclosing nuclei and such lightly stained cells that a high power is necessary to reveal their presence. The walls of the alveoli, however, instead of being made up of fibrous tissue consists of epithelial cells so arranged as to resemble the columnar cells of a cylindroma. The striking resemblance which some of these cell masses bears to glandular tissue is well shown in Figure 6 of the plate. In one of my preparations it is difficult to resist the belief that an abortive attempt at the formation of a sweat gland was present, for a distinct lumen containing no nuclei or degenerated cells can readily be seen surrounded by regularly arranged cylindrical-like cells. The absence of an external limiting membrane is, however, opposed to the view that the structure is glandular.

In addition to the cysts lined with stratified epithelium containing corneous matter and debris included in the cell masses, identical cysts are found occurring in the connective tissue apparently unconnected with other structures. Small cysts with homogeneous contents were noted in the cell collections probably produced by the degeneration (colloid) of single cells.

The colloid degeneration seemed, in the tumors examined by me, to be confined to the centrally located cells in the cell masses rather than to the epithelial nests. These latter structures contained almost exclusively corneous tissue and dark granular pigment.

A few large cavities were noted throughout some of the sections surrounded by condensed connective tissue from which the cell contents had been detached probably in the methods of preparation.

Sections from the first tumors examined by me failed to show any connection between the new growth and the epidermis or glandular appendages. Further investigation, however, of the tumors in which a central depression was macroscopically visible revealed a direct downgrowth and proliferation of the epidermis and also of the external root sheath of the hair follicle. (See Plate Figs. 1 and 3.) In these preparations the proliferated basal layer of the epidermis can be seen forming

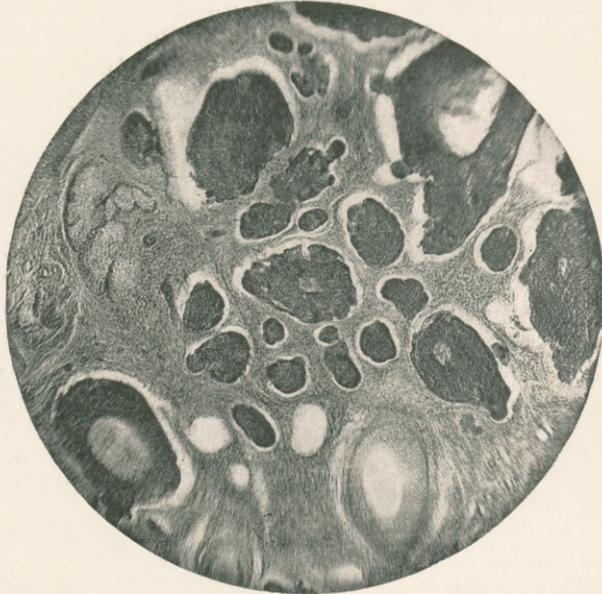


Fig. 4.

SECTION FROM RODENT ULCER OF THE FACE, SHOWING MASSES OF EPITHELIAL CELLS RESEMBLING THOSE MET WITH IN BENIGN EPITHELIOMA. (PHOTO-MICROGRAPH BY DR. PIFFARD. GUNDLACH,  $\frac{1}{2}$  IN. X 50.)

the peripherally situated cells of the masses and retaining the same palisade arrangement of the cells as in normal epidermis.

The bands, tracts and alveolar like structures of the cell heaps are evidently the result of a proliferation of this layer, while the horny masses represent the physiological tendency of the epidermis to form corneus tissue.

The cell heaps in many sections approach the hair follicles so closely that the hair is deflected from its normal course. In



Fig. 1.



Fig. 4.

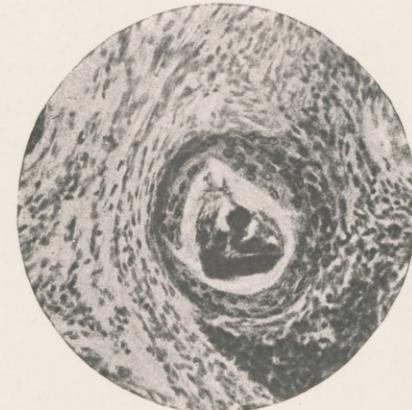


Fig. 5.



Fig. 2.



Fig. 3.

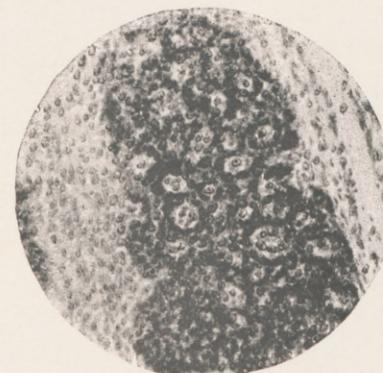


Fig. 6.

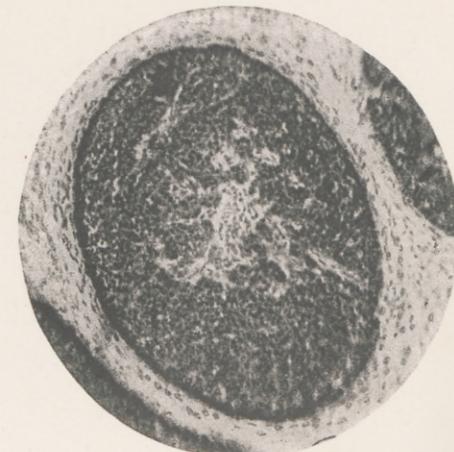


Fig. 7.

THE HISTOLOGY OF BENIGN CYSTIC EPITHELIOMA OF THE SKIN.  
(Photo-micrographs by the Author.)



Fig. 1 a direct out-growth from the external root sheath of the hair can be seen. Numerous sebaceous glands were observed throughout the sections which were in every respect quite normal and independent of the cell groups described. Normal coil glands and ducts were seen in a few of the sections; they were, however, less numerous than in an equal number of sections from normal skin, while in some of the tumors none were found.

The accompanying photo-micrograph from a section of rodent ulcer is introduced at this place to show the intimate resemblance which the epithelial processes in this affection bear to those of the disease under consideration. (See Fig. 4 in text.) A cut representing the clinical appearance of the lesion from which this section was taken can be found in Dr. Piffard's *Elementary Treatise on Diseases of the Skin*, page 101.

While it has been the almost universal custom to regard such histological appearances as seen in my case as pathognomonic of malignant epithelioma the clinical appearance and natural history of the affection differ widely from the classical epithelial new growths. We are compelled to enlarge the conception which attaches to the term epithelioma or to search for a more appropriate designation for this disease.

The few cases which have been observed and investigated are the following:

Jacquet and Darier in 1887 under the title of *Hydradénomes éruptifs*, describe the case of a young man aged 26, in the service of M. Besnier, whose chest and arms were the seat of a number of small tumors varying in size from a pin's head to a small pea. The first appearance of these tumors was noted when the patient was eight years old.

From a histological standpoint Darier looked upon the growths as epithelial adenomata originating in the sweat glands or briefly hydradenoma with colloid cysts.

Darier subsequently abandoned the theory which regarded the tumor as glandular in origin in favor of the view which is now held by Jacquet, to be referred to later on.

Török in 1889, carefully examined a similar case affecting a man aged 33, on whom the tumors had existed for fifteen or sixteen years.

The result of his microscopic examination yielded quite analogous results to Darier's, although he interprets his observations differently. While Darier believed that the normal sweat glands had proliferated in such a manner as to form the tumors,

Török thinks that they developed from misplaced embryonic germs of these glands which failed to develop in a normal manner. As reasons for this belief he refers to the fact that few sweat ducts are found in the affected area, and also that the coils beneath the tumors are correspondingly diminished in number.

The presence of the cysts and cell masses in the middle region of the corium leads him to believe that they are formed from cells originally destined to develop into sweat glands, but which were cut off from the surface epidermis and prevented from descending to the normal depth of the coils. He furthermore found cysts in the *arrectores pilorum* which he believes could only have found their way there in foetal life.

The limitation of the cell masses to the middle area of the corium was noted in a number of the tumors examined in my own case while the diminished number of coil glands in the lower dermal region was a noteworthy feature. The direct origin of many of the cell masses from the surface epidermis and the hair follicles with their formation of horny tissue is opposed, however, to Török's theory unless we have to do with a complex process affecting both the indifferent epidermic cells and those destined to form sweat glands.

Quinquaud and Jacquet at the International Dermatological Congress held in Paris in 1889, each presented a case of this interesting disease.

Quinquaud proposed the name "Eruptive cystic epithelial celluloma" for the affection, while Jacquet preferred to call the neoplasm "Benign cystic epithelioma of the skin."

Both of these cases were acknowledged to be identical with those previously reported.

These authors deny the relationship of the new growth to the sweat glands; they look upon it as developed from embryonic epithelial germs of indifferent nature misplaced during foetal life and remaining in a latent condition until excited by some influence into active proliferation.

This view is also adopted by Philippson who has at Unna's clinic observed and investigated a fifth case of the disease and studied its relationship to colloid milium (Wagner) and colloid degeneration of the skin (Besnier). He concludes that this affection and colloid milium are identical, and that "anatomically they belong to the class of benign epitheliomata with colloid degeneration and arise from embryonic epithelial germs in the cutis."

The case described by Philippson is without doubt identical with the others quoted and with my own, but his attempt to prove its identity to colloid degeneration of the skin seems to have signally failed, for Besnier <sup>1</sup> who is familiar with the clinical appearances of both affections denies their relationship, and quotes Balzar, who made the microscopic examination in his original case <sup>2</sup> of colloid degeneration of the skin, and who has since compared its pathological anatomy with that of benign epithelioma, as saying that it never occurred to him to attempt to establish a relationship between the two affections.

It is highly probable that many of the milia usually met with are of the same nature and have a similar origin to that of the tumors under consideration. One of the smallest papules met with in my patient having the exact appearance of a milium was excised and examined. It was composed of a single collection of epidermic cells, of the same character as in the larger growths and surrounded by thickened connective tissue.

This origin of milia from embryonic deposits in the cutis has been referred to by Robinson, <sup>3</sup> Epstein and later by Philippson (*loc. cit.*). The colloid degeneration of the skin first described by Besnier and Balzar, however, is a colloid degeneration of the connective tissue and vessels of the derma which may spontaneously disappear while the benign epitheliomata have never been observed to do so.

Perrin <sup>4</sup> recently investigated a case of colloid degeneration of the skin and found substantially the same lesions as in the original case of Besnier's.

The case described by Perry as an adenoma of the sweat glands and so beautifully shown in the chromo-lithograph accompanying his article, is undoubtedly identical with the other cases of benign epithelioma although his histological description is too brief to be satisfactory on conclusion.

It is now generally believed that the affection described by Kaposi <sup>5</sup> under the name *Lymphangioma tuberosum multiplex* is at least clinically and probably in all respects the same disease as benign epithelioma.

<sup>1</sup> Pathologie et Traitement des Maladies de la Peau, par Kaposi. Traduction par Basnier et Doyon. II Edition française, Tome II p. 368.

<sup>2</sup> Sur un cas de dégénération colléid du derme, par M. Ernest Besnier. *Annales de Dermatologie et de Syphilographie.* Tome X. 461.

<sup>3</sup> Manual of Dermatology, 1885, p. 73.

<sup>4</sup> Colloid Degeneration of the skin. Second International Dermatological Congress, held in Vienna, 1892.

<sup>5</sup> Pathologie und Therapie der Hautkrankheiten. Dritte Auflage, 1887, page 742.

Hoggan<sup>1</sup> first denied the correctness of Kaposi's anatomical description and Besnier (*loc. cit*), Török<sup>2</sup> Jacquet and others have made out a strong case in favor of the view that Kaposi's disease is in reality one of benign epithelioma.

The case described by Lesser and Beneke<sup>3</sup> as one of *lymphangioma tuberosum multiplex* has been identified by Dr. Lukasiwicz,<sup>4</sup> Professor Kaposi's assistant, as an example of the disease, described by Kaposi under that name. Beneke who made the anatomical investigation of Lesser's case regarded it as more closely allied to an endothelioma than a lymphangioma, although because of the pronounced development of the lymphatic capillaries he preferred to retain Kaposi's original name.

Török<sup>5</sup> and Philippson<sup>6</sup> in criticising this case hold strongly to the opinion that it was a true case of benign epithelioma.

The case of congenital adenoma sebaceum<sup>7</sup> described by Pringle is, according to that author's description and opinion, closely allied in origin and clinical appearance to "hydradenoma" representing an analogous condition of the sebaceous glands.

A differential diagnosis of the two affections seems to be impossible without invoking the aid of the microscope, for the telangiectases regarded by Perry as peculiar to adenoma sebaceum were also found present in my case.

As nearly as I am able to form an opinion from the cases quoted by Pringle, from Balzar, Vidal and Hallopeau there seems to be as good reasons for regarding them as examples of benign epithelioma as of adenoma sebaceum.

It is quite probable that the two diseases may have an analogous origin in foetal life, for as all the appendages of the skin are formed by the ingrowth of the deep cells of the stratum Malpighii during foetal development, it is rational to conceive that under the influence of certain conditions not understood,

<sup>1</sup> On multiple lymphatic naevi of the skin, and their relation to some kindred diseases of the lymphatics, Plate XVI. *Journal of Anatomy and Physiology*, Vol. XVIII. p. 304.

<sup>2</sup> *Annales de Dermatologie*, 1891, No. 2. *Monatshefte für prakt. Dermat.* Bd. XIV. 1892, page 184.

<sup>3</sup> Ein Fall von Lymphangiosum tuberosum multiplex (Kaposi), *Virchow's Archives*. Heft 1. 1891, page 86.

<sup>4</sup> *Archiv für Dermatologie u. Syph.*, 1892, 1.

<sup>5</sup> *Monatshefte für prakt. Dermat.* Bd. XII. No. 6, 1891. *Ibid.* Bd. XIV. No. 5, 1892, page 184.

<sup>6</sup> *Ibid.* Bd. XII. No. 5. 1891.

<sup>7</sup> *British Journal of Dermatology*, January, 1890.

at one time cells destined to form sweat glands, at another those intended for the formation of sebaceous glands, and again those of an indifferent nature, might be cut off from the germinal layer or retain their embryonic nature until brought into activity through some influence during the development of the individual.

It is a noteworthy fact that the majority if not all of the few cases reported, appeared about the age of puberty when we would expect the skin and its glandular appendages to take on increased activity.

After the foregoing portion of my paper had been prepared and read at the last meeting of the American Dermatological Association I received the September number of the *British Journal of Dermatology* containing Dr. Brooke's most excellent article which covers essentially the same ground as I had gone over independently.

By a curious coincidence three of his cases occurred in one family, affecting a mother and her two daughters. The lesions in these cases as in my own affected principally the face.

In the time the tumors appeared, their clinical behaviour, and in their anatomical structure, Brooke's cases are identical with my own. They differ, however, from the other reported cases in their apparent hereditary origin, in affecting chiefly the face, and from the fact that anatomically a connection was traced between the tumor elements and the overlying epidermis. This histological difference from the other cases is not inconsistent, as stated by Brooke, with their supposed embryonic origin.

*Clinical Course.*—As stated previously the tumors appear about the age of puberty and increase slowly in size until they attain the size of a split pea. Their surface remains quite smooth, and neither ulceration nor spontaneous involution have been observed. No impairment of the general health results; nor do the growths give rise to any subjective sensations. The entire course of the affection is so free from any evidence of malignancy that the word benign seems an especially happy one to qualify the term epithelioma which custom has associated with malignancy.

The clinical course of rodent ulcer is so different from that of the classical epithelioma that many writers hesitate to class it with that growth, and now that atypical epithelial proliferation is not confined to malignant tumors their position is still further strengthened. The use of epithelioma molluscum for molluscum

contagiosum affords a precedent for enlarging the meaning of epithelioma, and no valid argument can be brought forward against the use of that term for this affection which is so clearly demonstrated to be of an epithelial nature. A question which has suggested itself to me and to others is what is the dividing line between the benign and malignant epitheliomata? Should a parasitic element be demonstrated in the malignant disease, this question might be readily answered.

*Treatment.*—Up to this time no application or internal medication has met with any success in removing the growths. I have succeeded in removing the majority of the larger tumors in my case by means of the dermal curette and have expressed some of the smaller ones with Dr. Fox's comedo extractor. They are loosely attached to the surrounding tissues and when the epidermis is broken are readily separated. The little wound which is left readily heals with a slightly depressed scar.

#### EXPLANATION OF THE PLATE.

Fig. 1. Section of the nodule from the face showing the depression of the surface of the skin and the general arrangement of the cell masses in the cutis. At the extreme right of the section a downgrowth of the surface epidermis is seen while to the left of this a proliferation from the hair follicle is visible. Wales 1 in. No ocular—x 25.

Fig. 2 represents a section through a nodule from the back showing the cell masses surrounded by condensed connective tissue. Here the collection of cells is composed of inter-communicating tracts which simulate with a low power hypertrophied glandular tissue. Wales 1 in. No ocular—x 25.

Fig. 3. A more highly magnified view from the right of Fig. 1 showing the origin of the new growth from the epidermis. Zeiss apochromatic 16mm. Projection ocular 4—x 60.

Fig. 4 shows a cell "nest" consisting of imbricating horny cells surrounded by compressed nucleated cells. Zeiss apochromatic 4mm. Projection ocular 4—x 250.

Fig. 5 represents a similar appearance to Fig. 4. The contents of the cyst, however, are dark amorphous granular matter. Zeiss 4mm. Projection ocular 4—x 250.

Fig. 6 shows the cylindroma-like arrangement of the epithelial tracts enclosing more faintly colored cells. Zeiss 4mm. Projection ocular 2—x 125.

Fig. 7. A collection of cells with central (colloid) degeneration. The peripherally situated cells are arranged as in the basal layer of the epidermis. Zeiss 8mm. Projection ocular 4—x 125.

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