

CANCEROUS AFFECTIONS
OF THE SKIN

GEORGE THIN

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ON
CANCEROUS AFFECTIONS OF THE SKIN

A TREATISE ON EPITHELIOMA AND RODENT ULCER

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MEDICO-CHIRURGICAL SOCIETY

By GEORGE THIN, M.D.



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PREFACE.

IN writing the following monograph, the author has drawn freely on the available German, French, and English works which bear on the subject. The source of the information given in the introductory historical retrospect in reference to Epithelioma is Thiersch's "Epithelialkrebs namentlich der Haut." In the descriptions of Epithelioma and Rodent Ulcer he has used freely the classical pictures of these diseases given in Paget's "Lectures on Surgical Pathology."

He is indebted to Mr. Henry Morris, who was so good as to read the manuscript, for several suggestions.

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ON
CANCEROUS AFFECTIONS OF THE SKIN.

EPITHELIOMA.

Synonyms: Epithelial Cancer; Cancroid.

BEFORE the time when the microscope began to be used in examining the tissues which constitute tumours, the history of epithelioma is inextricably mixed up with the history of cancerous growths in general. Earle and Astley Cooper had observed that cancer of the lip frequently returned after operation, and that the neighbouring lymphatic glands became the seat of cancerous disease; but it was only after the appearance of Johannes Mueller's work on the finer structure of morbid growths that the nature of epithelioma formed the subject of discriminate investigation. Mueller himself was the first to find epithelial structures and nucleated cells on the surface of a cancer of the cheek. At the same time, certain differences between cancer of the skin and cancer of other organs did not fail to strike him, and he remarked "that, in the skin, cancer elements similar to those found in other organs were not frequently observed."

Lebert, Hannover, and Ecker were the first to point out the structural characteristics which define epithelioma as a specific disease.

DESCRIPTION.

Epithelioma of the skin frequently begins in the form of small, closely set, irregularly defined papules, covered with minute epithelial scales, which are being continuously shed and reformed. On examination the affected spot is found to be hard and nodular, and, if the partially detached epidermis is removed, the exposed surface is found to be red and granular. After a period more or less long (the process being essentially a chronic one), the thickened and raised area extends gradually on every side, and a superficial hard tumour results, the swelling being elevated above the level of the surrounding skin, and limited by an abrupt margin. At first movable with the skin in which it has developed, the tumour gradually becomes fixed to the subjacent tissues, and there is eventually formed an elevated, hard, uneven, vascular growth in the skin, sometimes small and limited, and at other times involving an area of considerable extent. Eventually ulceration takes place.

At other times ulceration occurs so early as to appear to be the initial stage of the lesion, the preceding induration passing unobserved. A small, dry, yellow or blackish crust, covering a fissure in the epidermis, is in these cases all that is at first observed.

Or the first breach of surface may take place on a warty growth. A wart becomes fissured, the epidermis covering it appears to be thicker, and

eventually the wart becomes hard, then ulcerates, and is transformed to epithelioma.

The epitheliomatous ulcer has an uneven surface, and is irregularly bounded by hard, livid, everted edges. It is covered by minute granulations, or by a dry, greyish crust, which if removed is quickly renewed.

The discharge from the ulcerated surface is a thin, scant, sanious ichor, which is usually inoffensive. The ulcer bleeds easily when touched. The sensations to which it gives rise vary in different cases. Sometimes there is severe, lancinating pain; at other times stinging or pricking sensations, which lead the patient to increase the irritation by frequent scratching. In the intervals there may be a disagreeable sensation of heat. In some cases there is little or no pain.

In the onward course of the disease the ulceration extends downwards to the subcutaneous tissues, and causes destruction of the muscles and bones. Whilst in the centre and in the earlier-affected parts of the diseased area ulceration and destruction of tissue make steady progress, the disease is found in its primary stages on the circumference of the sore. In the border of the ulcer small papillary nodules are formed, with a scaly surface; and frequently these advance to the formation of tubercles or small tumours before they are involved in the extension of the original lesion.

Eventually the lymphatic glands corresponding to the affected part become enlarged. They are at first felt as small, hard, movable, isolated tumours, producing little inflammatory reaction. As they

increase in size they become incorporated in a single somewhat lobulated mass, which eventually softens. The skin which covers it becomes adherent, then red, and finally ulceration occurs.

Examined more in detail, the cancerous ulcer is found to be usually round or oval, or elongated in shape. The infiltration, which is the essential feature of the disease, produces hardness in its base and borders. The indurated boundary of the ulcer can be felt as a distinct mass, which prevents movements over the subjacent tissues, and its borders are generally raised, sinuous or nodulated. They are frequently everted, and sometimes undermined. The surface of the ulcer itself is usually concave, unequal, nodular, or warty. The characters of the ulcer depending on the combined effects of simultaneous new growth and absorption, destruction of tissue and inflammation are maintained more or less constantly in any tissue to which the disease extends.

In proportion to the rapidity of the cancerous process follows the epithelial infection of the lymphatic glands. From those nearest the primary seat of the disease the infection gradually extends towards the trunk, but more frequently the proximate glands alone become cancerous. The parts between the seat of the cancer and the affected glands may exhibit no appearances of disease. The nature of the glandular affection is indicated more by their hardness than their size. The peculiarities of the disease are reproduced in the glands.

The diseased skin covering the glands may become acutely inflamed and suppurate, and cancerous ulcers result from this process.

Although epithelial cancer takes its origin from the normal investing epithelial structures, in the course of its progress it invades all the tissues. Muscles, bones, and fibrous tissue are alike invaded and destroyed by it. As a secondary disease, or in its recurrence after operation, it may be seated in any of these tissues, or near its primary seat. Usually it affects the nearest lymphatic glands, and occasionally, but not frequently, it is found in the internal organs.

Sir James Paget has very clearly described how the appearances presented by different cases of epithelioma depend on the part of the integument in which the growth most freely takes place. If the epithelial structures are mostly limited to the thickness of the corium, the resulting cancer is little elevated above the normal level of the skin. If the development is chiefly in the papillary layer, the growth is prominent and warty. If it grows chiefly in the subcutaneous tissue, we have a deep-seated flat or rounded mass. (These distinctions chiefly belong to the earlier stages of the growth.)

If an epithelioma is examined previous to ulceration, the affected part is found to be unnaturally firm, hard, and enlarged. The lip, for example, if it is the seat of the disease, pouts and projects like one overgrown. The swelling is slightly elevated, rising gradually or abruptly from its borders, and having a round or oval sinuous outline. The firmness or hardness of the diseased part varies in different cases, and, however firm, it is usually flexible and pliant, and feels moderately tense and resilient on pressure. It extends at this stage more in length than in breadth or depth.

Paget states that "an epithelial cancer is occasionally met with, having the shape of a sharply bordered circular or oval disk, upraised from one to three lines above the level of the adjacent skin or mucous membrane, and imbedded in about the same depth below it. The surfaces of such disk-shaped cancers are usually flat, or slightly concave, granulated, spongy, or irregularly cleft; their margins are bordered by the healthy integuments, raised and often slightly everted by their growth. Such shapes are not unfrequent among the epithelial cancers of the tongue, of the lining of the prepuce, and of the scrotum." He had removed such a one from the perinæum, and had seen one in the vagina.

The epithelial cancer may grow out in the form of a cone. Paget removed one from the lower lip, which was half an inch high, and nearly as much in diameter at its base. In another instance, an exactly similar cancer was situated in a chimney-sweep's neck. In both cases, Paget observes, the growth was covered with a thick, laminated, black and brown scab, not easy at first to distinguish from syphilitic rupia. Other instances are on record. Mr. Henry Morris informs me that he has seen one on the outer side of the dorsum of the foot of a man aged fifty-six.

Epithelial cancer may exist in the form of pendulous growths from the cutis. Paget has seen such growths on the lower lip, and, as occurring at the anus, refers to masses of very firm exuberant granulations, some two inches in diameter, springing from narrow bases of the cutis or deeper tissues, and far overhanging the adjacent healthy skin.

But, whatever form the cancerous swelling may

assume, the final results are the same, unless relief is afforded by early operation. The pain and fever which accompany the later stages of the malady, the exhaustion associated with the ever-increasing discharge from the ulcerated surface, and the disturbance of function inevitably produced when the disease affects the outlets of the body, combine to induce a condition of exhaustion and cachexia, which progresses until the patient dies.

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VARIETIES OF EPITHELIOMA. MEDICO-CHIRURGICAL SOCIETY

The resistance of the *pars reticularis corii* to the extension of the epithelial growth, which constitutes an essential feature of the disease, is so much greater in some cases than in others that it has led to two chief varieties of epithelioma being described by authors, viz., the deep-seated or infiltrating form, and the superficial form. Although the results of these two forms are very different as regards the fate of the patient, the nature of the process is in both cases the same. In the superficial form the advancing epithelium is for a long time unable to penetrate the strong, firm bundles of the corium, and, as Erasmus Wilson has expressed it, contents itself with cropping off the highly organized *corpus papillare*, healing taking place, apparently, as soon as that effort is accomplished. These are the cases in which the disease presents the appearance of an extending cicatrix like that of a burn. The centre of the ulcer appears to be healed, while the extending border which surrounds the cicatrix is in a state of slow ulceration.

When, either from the greater destructive power of

the cancerous epithelium in any given case, or from an inherent weakness of the fibrous tissue of the corium, the growing epithelium pierces the *pars reticularis corii*, the clinical aspects of the case are very different. The epithelial columns having once penetrated the true skin, the course of the disease advances with comparative rapidity. The fat and subcutaneous tissue offer a feeble opposition to the neoplastic growth, and the great destruction which ensues justifies the name of "deep-seated epithelioma."

The fact that in rodent ulcer the destructive course of the disease also follows that of the *corpus papillare*, and usually spares the deeper parts, has led to a complete confusion between this form of cancer and the superficial form of ordinary epithelioma.

Two other varieties of epithelioma are met with—papillary epithelioma or malignant papilloma, and melanotic epithelial cancer; the latter being rare.

When an epithelioma occurs in such a form that the chief feature is in the projecting papillary growth, it is spoken of as a papilloma. It may assume this form from the beginning, and is very likely to do so when it begins, as it not unfrequently does, in a wart of old standing; or the papillary growth may develop subsequently on a superficial, or more frequently on a nodulated, ulcerating epithelioma. The growth may project considerably above the level of the surrounding skin, and may be seated on a broad base, or on a constricted neck, assuming the form of a fungus. The surface is formed of clusters of enlarged papillæ, which are cylindrical, pyriform, or conical. They are single or in clusters. They are very vascular; the surface, thinly covered with an opaque white cuticle,

is of pink, vermilion, or brightly florid hue. In some cases, when the loose epidermic cells are washed away, the surface is seen to be largely granulated and lobulated, producing a cauliflower-like excrescence. The granulations of which the surface is composed are bare, and bleed on slight contact.

Melanotic epithelial cancer is met with, although very unfrequently. In this case the epithelial cells contain melanotic matter, and a similar substance is found abundantly between the cells.

The variety of form in which epithelial cancers are found depends on the varying relations of the growth of the epithelium to the concomitant growth of the connective tissue. For at the same time that there is destruction of the connective tissue by the neoplasm, there is also, more or less, new growth of fibrous tissue, and the varying comparative rapidity of growth of the epithelium and the fibrous tissue in different cases affords the conditions of many varieties of cancer. We have, indeed, the conditions of an almost unlimited variety of form.

The appearances which may be observed by the naked eye in sections of epitheliomatous tissue have been thus described by Paget:—

“The vertical sections of the superficial epithelial cancers of the integuments,” he remarks, “display many important differences in relation to the depth to which the cancer-structures occupy the proper tissues of the skin or mucous membrane.

“In some, only the papillæ, or the papillæ and the very surface of the tissue on which they rest, appear to be involved. The enlarged papillæ in such cases usually retaining their direction and their cylindrical

or slenderly conical shape, appear like fine grey stripes or processes vertically raised on the healthy white tissue of the integument, or on its surface rendered similarly grey by cancerous infiltration. And the outlines of the papillæ are commonly the more marked because of their contrast with the opaque white substance formed by the epidermoid scales which cover them and fill up all the interstices between them. In such cases the cancerous material may be more abundant on the surface than in the substance of the papillæ or corium; and often the whole morbid substance is brittle, and may be separated from the corium which bears the papillæ.

“But more frequently, and almost always in such cases of epithelial cancers when they are removed in operations, the cancerous structures are more deeply set. They occupy the whole thickness of the integument, or reach to a level deeper than it. The base or lower border of the diseased mass rests on, or is mingled with, the subcutaneous or submucous tissues. The lateral borders usually extend outwards for some distance, on each side, beneath the healthy integument which bounds the upraised part of the diseased growth, and which is usually raised and everted so as to overhang the adjacent surface. In nearly all these, also, while the surface and central parts of the cancer are being destroyed by ulceration, its base and borders are, at a greater rate, extending more deeply and widely in the subcutaneous or submucous tissues.”

HISTOLOGY OF EPITHELIOMA.

The essential feature in the histology of epithelioma is expressed by the word itself. The disease is a

neoplasm, and the constituent elements of the new growth are epithelial cells. That the objective characters of the affection are chiefly those of loss of substance, and not of actual tumour, is due to the circumstances under which the new growth extends, the increase of volume caused by the formation of new epithelium being more than compensated by the destruction of vascular tissue which attends the epithelial development.

But there is more than a simple hypertrophy of epithelium at certain given points. There is more even than a simple loss of balance or proportion in the relations of the epithelium to the connective tissue. The epithelium of the neoplasm acts as an irritant on the adjacent vascular structures, and inflammatory changes are the result. This is the cardinal fact that distinguishes cancerous from normal epithelium, and which is inexplicable on the hypothesis put forth by Boll, to the effect that epithelioma is caused by a disproportion between the vital energy of the epiplastic and the mesoblastic elements. There is a perfect toleration of normal epithelium on the part of the mesoblastic tissues ; and the epidermis may undergo various hypertrophic changes without exciting inflammation in the connective tissue which it covers. Not so when an epithelium is cancerous. The parts surrounding the new epithelial formation are in the latter case infiltrated more or less thickly with exudation cells, and the condition of the connective tissue gives evidence of the existence of serous effusion. The redness of the parts, as seen by the clinical observer, finds its explanation in the engorged blood-vessels observed by the pathologist.

The classic symptoms of inflammation—*tumor, calor, rubor, dolor*—are present, and are the objective signs of a destructive effect exercised on the blood-vessels of the part by an epithelium which has acquired characters that make it comparable to a foreign body.

The cancerous epithelium of the skin may thus be studied under two aspects—the remarkable quality which it acquires of growing downwards into the connective tissue; and the equally, if not more, remarkable quality by which it leads to inflammatory, and consequently to destructive, changes in that tissue.

The growth of a cancerous epithelium downwards into the connective tissue is observed when we examine vertical sections through the border of an epitheliomatous ulcer, or through an epitheliomatous growth in its early stages. In sections of this kind the neoplastic epithelium is observed in isolated masses in the midst of the connective tissue; but, if the section is favourably chosen, downward projections from the rete mucosum are also seen (Fig. 1).

A comparison of a number of sections shows that the downward growths of the rete, after they attain a certain depth, assume usually a more or less horizontal course. The direction of their development is then dependent to some extent on the natural formation of the connective tissue. They grow in the direction of least resistance, and we thus find narrow epithelial columns pushing their way in the vascular tracts that separate the large groups of bundles. In the parts where the growth is luxuriant the destructive effect on the bundles of connective tissue permits the epi-

thelium to develop as large spherical masses or as groups of cylinders, amongst which it is no longer



FIG. 1.—VERTICAL SECTION THROUGH AN EPITHELIOMA OF THE SKIN OF THE HAND.

A, the rete Malpighii, from which projections downwards are observed penetrating the tissue of the cutis ; B, a laminated capsule which has formed in the rete Malpighii ; C, downward growth of cancerous epithelium, the connection with the rete Malpighii being preserved in the section ; D, column of cancerous epithelium growing deeply in the cutis ; E, vascular tracts indicated by thickly set infiltration of leucocytes. (There is a great deal of small-cell infiltration throughout the whole thickness of the corium.)

possible to find any trace of the natural formation of the cutis. It is this peculiarity of growth that has

led to so much difference of opinion as to the origin of the epithelial masses which form the most characteristic elements in cancer of the skin. Although it is possible by careful examination to detect cancerous epithelium growing direct from the pre-existing normal epithelium of the part, yet by far the most luxuriant growth takes place in directions more or less parallel to the surface of the integument, and thus most of the cell-masses which are observed in a vertical section do not appear to be in direct continuity with the normal structures that in the first instance gave origin to the masses from which they sprang. In some cases, indeed, it seems very difficult to trace the exact continuity of the normal epithelium. Round isolated groups of epithelial cells are seen at various depths in the substance of the cutis, surrounded by connective tissue, and apparently having no connection with any other epithelium. It was this appearance that gave so much support to the doctrine of Virchow, that the epithelial elements of cancer are developed from connective-tissue cells. When small clusters of two or three epithelial cells were seen deeply situated in the cutis, exactly in the position in which the stellate appearances are found, which were long considered to be the cells of connective tissue, it was very natural to suppose that they took their origin in some diseased condition of the so-called plasma-cells.

This doctrine received a damaging blow from two distinct lines of investigation. The discoveries of Schweigger-Seidel, Ranvier, and Boll, verified by other trustworthy histologists, showed that the connective-tissue corpuscle of Virchow is nothing but a

space existing between the bundles of connective tissue, and that the real connective-tissue cell is a flat endothelium, which in ordinary circumstances usually escapes observation. Parallel to these histological discoveries stands the great work of Thiersch, who showed in a masterly monograph that in cancer of the lip the diseased epithelium takes its origin from the normal epithelial structures of the part. After Thiersch, Waldeyer showed that in cancer of the breast the diseased epithelium takes its origin in the morbid development of the acini of the mammary gland. Since then, the doctrine that all cancerous epithelium takes its origin from normal epithelium has been gradually and steadily gaining ground. The distinction that has been made between epithelioma as a morbid development of pre-existing epithelium, and carcinoma as a new development of epithelium in tissues in which it did not before exist, is not, in our opinion, supported by sufficient evidence. In some cases it is more difficult than in others to demonstrate the origin of the morbid epithelium; but in the great majority of cases, sufficiently patient observation will show what the origin has been, and in a small number of cases only has it been found impossible to demonstrate the connection. We are warranted by analogy in concluding that, although certain links in the chain may have been lost in a few exceptional cases, the development has in them also taken place according to the general law.

Indeed, the view that the epithelium in cancer of the skin takes its origin from the pre-existing epithelium, was a very early one. Thiersch has given in his monograph a complete account of the opinions held

regarding the origin of cancer, and of cancer of the skin more especially, from the time the microscope was first used in the study of pathology. We learn from him that, in 1844, Ecker found in three cases of cancer of the lower lip that the disease was nothing else than an hypertrophy of the papillæ of the lip. His description of the appearances identifies his cases as examples of the papillary form of cancer, although Ecker, believing, in accordance with the doctrine generally held at that time, that cancer was an heterologous growth, for the very reason that he found in his cases that the elements did not differ essentially from those found in normal tissues, concluded that they could not be cancerous. In the same year, Mayor *fits*, of Geneva, examined a part of the lower lip, removed by operation from a man fifty-eight years of age. Sections of the growth contained alveolar structures, and in the alveoli were found masses of regularly formed nucleated epithelium. He afterwards published another case of a similar kind, and came to the conclusion that these epidermal tumours were to be ranked with cancerous growths, although characteristic so-called cancer-cells were not found in them. In 1845 we find Lebert distinguishing three kinds of epidermal growths which could be considered cancerous: first, papillary growths with an inflamed hardened base and superficial ulceration; second, a papillary cauliflower-like excrescence with enlarged sebaceous glands; third, epidermal growths consisting of a fibrous stroma, the meshes of which were filled with epidermic *débris*. Rokitansky, in 1846, advanced the doctrine that these epithelial growths were simply cancerous. But while Ecker, Mayor, and Lebert

believed that the epithelial cells took their origin in the immediate proximity of pre-existing epithelium, Rokitansky, on the contrary, was of opinion that the epithelial cells took their origin independently in the substance of the vascular stroma distinct from normal epithelium. In 1852, Hannover published a monograph on epithelioma, in which he maintained that epithelial cells can only be developed from pre-existing epithelium. He describes how epithelial growths with numerous undermining roots penetrate the subjacent cutis. He regarded the rete Malpighii as the origin of these growths. In 1855, Virchow advanced the doctrine that in epithelioma or canceroid diseases epidermoid cells are developed from connective tissues; and from that time the doctrine that in epithelial cancer the epithelial cells are produced by proliferation of connective-tissue corpuscles received general assent. This view was the prevailing one until the appearance of Thiersch's monograph in 1865. The object of this work was to show, by numerous and careful anatomical observations, that the epithelial masses to which epithelial cancer owes its name are not derived from connective tissue. "I believe," he says, "that the origin from connective tissue has never yet been proved by direct observation, that the inference is not justified that such an origin is either certain or probable; but that, on the contrary, all the circumstances speak for the derivation of the epithelial masses from the epithelial structures of the part in which the disease arose." This doctrine of Thiersch's has now been almost universally adopted.

It may seem strange, when we consider the number of excellent observers who have worked at this subject,

that it should still be a matter of uncertainty as to whether all or only one of the normal epithelial structures of the skin give rise to the epitheliomatous growth. Such is, however, the case. Billroth remarks that the proof of epithelial ingrowths is always easiest shown for the rete Malpighii, and although the sebaceous glands are often described as affording an origin for cancer-epithelium, satisfactory proof that such is the case does not seem to be forthcoming. Boll, in a monograph bearing on this subject, has stated that in a considerable number of cases of epithelioma which he minutely examined, he found no proof that the sebaceous glands took part in the new growth. Our own experience leads us gradually to adopt this view more and more strongly, and we are disposed to believe that appearances which we observed in our earlier investigations, and that led us to believe that the sebaceous glands took their share in producing cancerous epithelium, merely indicated that these glands underwent considerable enlargement. This condition is, however, not limited to cancer of the skin. In other diseased states, in which the cutis is the subject of chronic inflammatory conditions, the sebaceous glands become large and distended, but the enlargement is not such as can be identified as cancerous. On the other hand, the rete Malpighii can be shown not only to penetrate directly and deeply into the cutis, but in the penetrating portions individual cells undergo forms of abnormal growth and change which are characteristic of unmistakable cancerous epithelium found in isolated masses deeply in the cutis. These changes are alike found in the altered rete and in the apparently isolated cancerous

elements, and show that the rete Malpighii not only becomes abnormally developed in extent (a condition found in many chronic changes of the skin), but that it acquires a specific and distinct cancerous development.

When we examine the epithelial formations in cancer of the skin more closely, we find that they present differences of a marked character. Indeed, it may be said that each individual case is stamped with its own physiognomy. These varieties are due to the size of the individual epithelial elements in different cases, and the degree to which they take on the horny development. In the natural evolution of an epidermic cell there are certain well-defined stages. The small cell, in which the protoplasm stains deeply with certain colouring agents, and in which the nucleus more particularly is easily and deeply stained, may be taken as representing the first stage. The large, flat, horny cell, which does not stain deeply with carmine or logwood, and in which the nucleus scarcely stains at all, may be taken as the last stage. It is characteristic of certain cases of epithelioma that, in the new formation, cells representing both these stages, and all intermediate ones, are found throughout the growth. In others the epithelial development does not pass beyond an intermediate stage, all the cells readily staining with the ordinary dyes, and none of them attaining the stage of extreme horny metamorphosis. Individual cases are again characterized by the mode in which the epithelial elements are arranged in respect to each other. In some the cells are clustered in concentric laminae—the laminated capsules of Paget,—and in these cases we usually find the cells taking on the extreme epidermic

formation. (See Figs. 2 and 3.) In other cases the cells remain comparatively small, and are grouped in

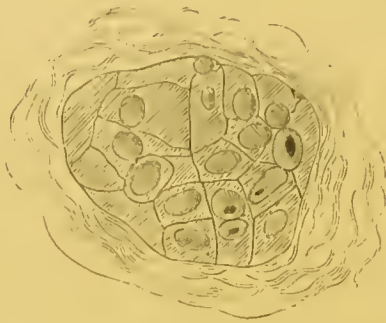


FIG. 2.—TRANSVERSE SECTION OF A COLUMN OF CANCEROUS EPITHELIUM IN THE DEEPER LAYER OF THE CUTIS.

Showing the epidermic type of the epithelium. (From an epithelioma of the hand.)

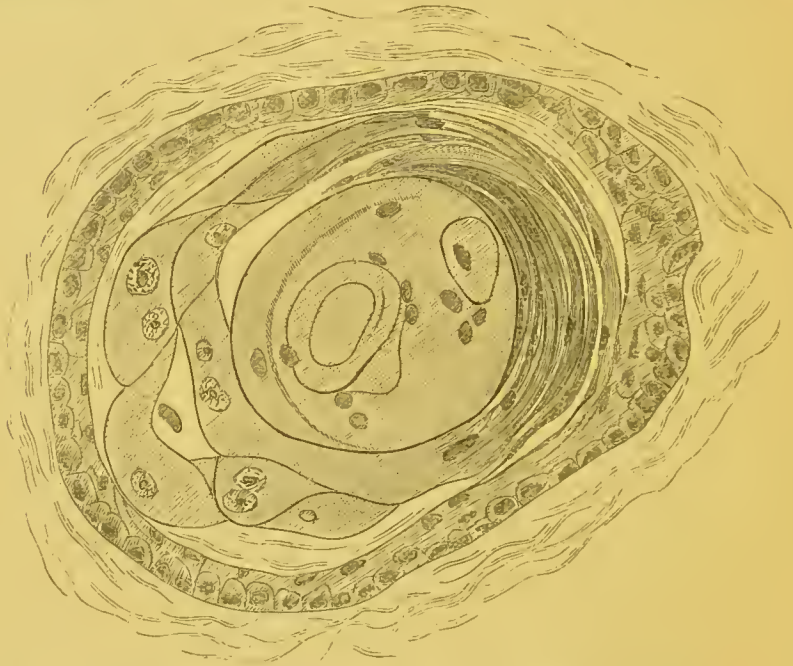


FIG. 3.—A LAMINATED CAPSULE, OR "NEST," FROM AN EPITHELIOMA OF THE FINGER.

Showing the transition from the small, newly formed epithelial cells on the outer surface, to the large, flat, intermediate cells and the fused horny mass in the centre.

small cylinders, which ramify luxuriantly in the skin, and contain no laminated capsules. Between these two

varieties intermediate forms are found. The difference seems to depend on the fact that in some cases of cancer the impetus to the formation of horny epithelium is stronger than in others. In one case the tendency is to the formation of cells partaking more or less of the type of the horny layer of the epidermis. In the other the cells retain the characteristics which are distinctive of the cells of the rete Malpighii.

Although laminated capsules are found luxuriantly developed in many cases of epithelioma, they are not distinctive of this disease. Not only in some forms are they wanting, but they are sometimes found in conditions which are not allied to cancer, as, for example, in lupus and in the hyperæmic zone of cicatrices.

The existence of a morbid element in cancerous epithelium is shown by the occurrence of a change which is never found in healthy epithelium. In the midst of a mass of cells, which are apparently normal in their characters, a single cell may sometimes be found presenting appearances which are suggestive of colloid degeneration. The substance of the cell is swollen, and has a special reaction to colouring agents. It is around such a cell that the characteristic grouping of a laminated capsule frequently takes place.

In the midst of cancerous masses small cavities are sometimes found, containing numerous nuclei; and the idea has been conceived, and has found its way into many text-books, that certain cells enlarge, become so-called "mother cells," and that in them are originated numerous small or so-called young cells ("daughter cells"). This opinion is more supported by its harmony with certain preconceived

theories than by actual observation. In the midst of cancerous epithelial cells (as in all actively growing epithelium in the skin) it is easy, especially by log-wood staining, to demonstrate the existence of numerous nuclei, which evidently do not belong to the fully developed epithelial cells. It can frequently be made out that these nuclei are situated in spaces or angles between the cells, and it is also an undoubted fact that in the meshes of a broken epithelial cell such nuclei may be found. When we consider that it has been reliably shown that white blood-corpuscles, or so-called lymph-cells, can and do make their way into the centre of broken epithelial structures, and that their nuclei are not to be distinguished in size or colouring qualities from the nuclei previously referred to, it is evident that the theory of so-called "mother cells" and "daughter cells" cannot be considered as established. All the appearances, on which this theory has been founded, are equally explained by the fact that white blood-corpuscles wander into all the various spaces which are formed in the midst of cancerous masses. The fact that they do so may be conceded by observers who would not agree as to their ultimate fate or development.

Although the problem of the mode of origin of epithelial structures in cancer of the skin may now be considered as definitely settled, another problem of great scientific interest, and intimately associated with it, still forms the subject of much difference of opinion. Theoretically it may be considered that the mode by which new cells are added to pre-existing epithelium would not be very difficult of observation, yet it is practically one that has eluded the most careful in-

vestigations of pathologists. But the question is not limited to pathology. There can be little doubt that the growth of cancerous epithelium takes place in a manner similar to that in which epithelium grows in normal conditions. As a matter of fact, it is not yet definitely settled where the new cells come from that go to build up the rete Malpighii, and which are continually replacing the cells that are shed by the ordinary desquamation of the superficial layers of the epidermis. The term "proliferating epithelium" is in common use, but when analysed it will be found to suggest more the results of a physiological process than to describe the steps by which this process is accomplished. No doubt a definite idea is attached to the term. In accordance with long-received doctrines regarding cell-growth, it is understood that the rete Malpighii continually regenerates itself by a simple process of cell-division, although authors who implicitly receive and teach this doctrine not unfrequently remark that evidences of the process are very difficult to observe. As a matter of fact, division of the cells of the rete Malpighii is not seen. The appearances on which this belief rests are connected with certain phases observed in the nucleus of the cells. Although, as a rule, the nuclei of the cells of the rete are seen to be entire, yet occasionally appearances are observed which seem to indicate a division of the nucleus. This division of the nucleus once unsuspected, by an effort of the imagination the process of division was extended to the whole cell. But weighty arguments might be brought against the theory that these appearances in the nucleus indicate division of the cell. In all tissues in which nucleated

cells are found, a small proportion of the cells are seen to contain two nuclei. But a process of cell-division in cells that have once reached their fully developed stage is so rarely observed in the rete, that it is quite open to doubt whether it occurs at all. When, instead of one nucleus, two or more nuclear elements are observed in an epithelial cell in the skin, it will usually be found that these elements do not occupy a greater space in the cell than would have been occupied by an ordinary undivided nucleus. To an observer not influenced by any preconceived theory regarding cell-division, it suggests a breaking up of the nucleus quite as readily as a process of physiological division. Both in the healthy rete Malpighii and in the cancerous epithelium these appearances of divided and broken-up nuclei are observed in some of the cells, but neither in the one case nor the other do they afford evidence that the cells multiply by division.

It must be borne in mind that the processes of cell-division which can actually be observed, and which are beyond misinterpretation, have been seen in young cellular elements, in which the process of growth has not carried them to their full physiological development. The doctrine of cell-division in an undifferentiated cell is one thing; in a differentiated cell it is another. If the cells of the rete Malpighii multiply by division, it is almost incomprehensible how the subject should still have been open to dispute. No tissue comes more frequently under the direct observation of histologists and pathologists than the epithelial structures of the skin, and in no tissue is cell-multiplication more actively and more continually

going on. Surely, if cell-fission were constantly taking place, the fact would be so frequently observed that no room could have been left for regarding it as open to doubt.

What is seen in sections through actively growing epithelium in the skin is as follows:—The epithelial cells are found entire; their nuclei are found mostly entire. Lodged in clefts between the cells, small, deeply stained nuclei of irregular shape are found, which are regarded by competent observers as nuclei of white blood-corpuscles or “wandering cells.” These nuclei are found in considerable numbers between the cells of the columnar layer in all so-called active proliferating processes in the skin, and sometimes a nucleus is found partially inserted between the deep borders of two cells and partly still in the sub-epithelial connective tissue. It is beyond doubt that there is a constant influx of these “wandering cells” from the connective tissue into the epithelium. Whether these “wandering cells” eventually develop into epithelial cells is a matter that is considered still uncertain. Observations which have been published, tending to support this view, have not yet received universal or even common assent. Yet the view is by no means a new one, and, during the last decades, investigators have from time to time come forward maintaining the view that from these “wandering cells” the epithelium is formed. This is the view which has been adopted by the author. Whilst he has been unable to discover any evidences of multiplication by cell-division or endogenous cell-growth in the cancerous epithelium, he has observed appearances which seem to him to indicate that the

“wandering cells” take on the epithelial characters; and he adopts the view which has been suggested, that a wandering cell or lymph corpuscle brought under the influence of an epithelial cell may itself become epithelial. According to his observations, in the cells which are about to undergo the epithelial change the nucleus becomes larger and the granular appearance of the protoplasm of the cell is gradually lost, and cells are found which combine appearances indicative of the character of “wandering cells” and of cells of an epithelial type.

Whilst the epithelium is undergoing the process of development which we have described, the connective tissue, on the other hand, is undergoing characteristic changes. These may be conveniently divided into three stages, although all the three conditions are frequently found in the same parts of the growth. The first effect of the morbid epithelial development, so far as it is made evident, consists simply in an increased migration of white blood-corpuscles. There is a more or less pronounced so-called small-cell infiltration. In the part where the disease is more advanced, the small-cell infiltration has increased to such an extent that the connective tissue is obscured. If, however, we examine the connective tissue carefully, we find that it has become more or less disintegrated, and has partially disappeared. The large, strong bundles of white fibrous tissue are split up into small elements—which are really finer component bundles not usually evident in sections of the cutis. Between these smaller component bundles thus brought into evidence, rows of white blood-corpuscles are found. In a further advanced stage of disintegration the small

component bundles disappear, but their outline can still be made out, being indicated by minute elastic fibres and *débris* which indicate the direction of the disintegrated bundles. In a still further advanced stage the connective tissue elements have lost all traces of their ordinary distribution, and their place is taken by dense masses of small cells, dilated blood-vessels, and masses of red corpuscles which have escaped from the vessels. This state of connective tissue is closely allied to that of ulceration, and is that which is found forming the base of the ulcers from which the undermined epithelium has disappeared. The breaking down of epithelium, which leads to ulceration, is, in fact, preceded by disintegration of the sub-epithelial connective tissue.

If we take a general survey of the process which we have been describing in detail, we shall observe that the chief elements in the morbid process consist in an abnormal condition of the epithelium of the skin. This abnormal condition is characterized, in the first place, by a diseased activity of growth; in the second place, by a diseased state of the epithelium itself; and thirdly, by effects on the subjacent tissue which lead to disruption and disintegration. This diseased epithelium possesses the faculty of destroying connective tissue, and of finding its way into lymphatic vessels, and by lymphatic vessels into lymphatic glands, and occasionally through the lymphatic system into the viscera, and there exercising the fatal power of multiplying at the expense of the normal elements amongst which it has passed.

In endeavouring to estimate the nature of the diseased activity which characterizes this epithelium,

it is instructive to observe its effects in the first stage. The first effect on the sub-epithelial connective tissue is an injury to the walls of the capillary blood-vessels, which leads to the escape in considerable numbers of the white corpuscles of the blood. The process is analogous to that which is observed in the blood-vessels of the conjunctiva when a wound is inflicted on the cornea. If the centre of the anterior surface of the cornea is touched with a point of lunar caustic, an influence is transmitted from the cauterised spot to the walls of the blood-vessels in the conjunctiva, which so far injures them that an escape of plasma and the formed elements of the blood takes place. Something analogous occurs in cancer of the skin. So soon as the epithelium has lost its normal character, it becomes capable of transmitting an influence to the blood-vessels by which the integrity of their walls is impaired. Cancerous epithelium is evidently a connective-tissue poison. This is still further shown by the disintegration and disappearance of the bundles of white fibrous tissue. Simple inflammatory œdema of the skin does not lead to the destruction of the white fibrous tissue, and in the case of cancer the direct action exercised by the morbid epithelium must be of a very destructive character.

It is usual to refer the destruction of connective tissue to the cutting off of the blood-supply by the encroachment of growing masses of epithelium. This mechanical action certainly takes place, but it is not difficult to observe that the inflammatory œdema and the destruction of the white fibrous tissue occur in parts in which the direct mechanical action of the epithelium has not begun. The destruction is due

more to the poisonous action exercised by contiguous cancerous elements than to strangulation.

Speculation as to the possible nature of the new power which is generated by cancerous change of the epithelium naturally leads us to consider what is known regarding the etiology of the disease.

ETIOLOGY.

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Those who consider that epithelioma is simply caused by a difference in the physiological activity of the epithelium and of the connective tissue naturally lay great stress on the fact that cancer is usually a disease of advanced life. According to this view, by advancing age and the impaired vigour of the circulation the connective tissue becomes less able to resist the encroachments of an epithelium which they suppose is ever ready to grow downwards, and which is only kept in check by the physiological energy of the subjacent connective tissue. But if it be granted that the essence of the process does not lie simply in excessive growth of epithelium, but that it is to be found in the formation of a poisonous epithelium, the problem becomes more complicated. If cancer is in most cases a disease of advanced age, that is because it is one of those morbid processes that are usually associated with impaired vital energy. This impairment may probably in the first instance lie not in the connective tissue, but in the epithelium itself, and the abnormal activity of growth which eventually characterizes it may not improbably take its origin in a weak vitality.

Epithelioma is a disease of advanced life, mostly

occurring after the age of forty, although it is also found in youthful and, in rare instances, even in very young individuals. Epithelioma of the skin is more common in men than in women. In 102 cases referred to by Thiersch, 80 were males and 22 females. Dr. Marsden states that in 1,467 patients admitted into the Cancer Hospital in London, 1,022 were males. Koch, in 145 cases, found 132 cases in males and 13 in females. The disease is not usually considered hereditary, although an instance was reported to Professor Gross by Dr. Foster, of Indiana, in which the disease occurred in three members of the same family. Certain local (congenital or acquired) histological conditions of the skin are, it is well known, favourable to the development of epithelial cancer. It is notorious that the disease often begins in a wart, and it has been stated that the irritation of shaving gives rise to cancer.

The most remarkable facts connected with the development of cancer of the skin are those which have been described in connection with the disease termed xeroderma by Kaposi, and which will probably be known in future as "Kaposi's disease." In this affection, of which a considerable number of examples have now been collected in Germany, France, and in England, the usual mode of termination seems to be the formation of great numbers of cancerous tumours in the skin. Preceding the development of the cancerous change is an abundance of pigment, in itself probably indicating an abnormal condition of epithelium. One of the most extraordinary circumstances connected with this disease is its occurrence in several members of the same family.

Local irritation of the skin, of long duration, predisposes to epithelioma. The disease may develop in chronic ulcers of the leg, in lupus, and even in syphilitic infiltration. Long-continued irritation of any excoriated surface by mechanical or chemical agencies may also give rise to the affection. It is well known that the most frequent cause of cancer of the lower lip in men is the tobacco-pipe, and that the irritation which caused chimney-sweep's cancer was due to the soot which chimney-sweeps allowed to remain in contact with the skin. A simple wound may provoke the development of the disease. Agnew refers to a case in which a healthy man, while lurching in a train, wounded his cheek with a fork in consequence of a sudden lurch of the carriage while rounding a curve. In a few weeks the wound assumed all the characteristics of carcinoma, from which in the course of eighteen months he died. The same author refers to a case in which a cancerous ulcer followed a wound made by a mowing machine. In this connection Mr. H. Morris has called my attention to the frequency of epithelioma of the glans penis in tight prepuce or phimotic conditions.

LOCALIZATION.

Epithelial cancer may appear on any part of the surface of the body, but it occurs with greatest frequency on the face. After the face the genital organs appear to come. In 102 cases, Thiersch found 78 were on the face, 48 of these being in the lip; 4 were on the extremities, and 10 were on the mucous membrane of the mouth.

On the face it may inflict the most terrible destruc-

tion before the patient's life comes to an end. The whole cheek, nose, lip, and part of the forehead may break down. When the disease extends superficially, cicatrization may take place in the centre. Eventually, however, the disease extends inwards: the bones become affected, the teeth are lost, and the fauces are laid bare; portions of the skull may be completely destroyed, the dura-mater exposed, and the pulsation of the brain may become visible.

In the lip it commences either as a warty growth, which gradually ulcerates, or as a crack or fissure, the edges of which have a tendency to spread; the lip becomes thickened, hard, ulcerated on the surface, projects outwards, and allows the saliva to flow out of the mouth. The mucous membrane of the cheek eventually becomes involved, and ulcerates, the disease extending at last towards the throat and the bones.

On the penis, epithelioma commences frequently as a tubercle on the prepuce, which after a time gives rise to a large, irregular, spreading mass. In other cases it develops as a hard scirrhus mass, of a pale reddish or white colour, on the glans or between the prepuce and glans. On the scrotum, where it has been chiefly observed as chimney-sweep's cancer, it commences usually as a tubercle or wart, from which it rapidly spreads superficially, the testicles and inguinal glands being frequently not affected. In epithelioma of the glans and sulcus coronarius the thickening of the dorsal lymphatic vessel of the penis early takes place, and is detected as a thick, hard, nodulated tract stretching along the back of the member towards the tissue of the *mons veneris*, where

it diverges towards the glands of the inguinal region. The latter swell into hard nodulated masses. The corpus cavernosum thickens, the prepuce becomes indurated, and the glands enlarge. An abscess eventually forms, and ulceration takes place.

In the female genital organs the disease mostly springs from the labium majus [generally beginning on the mucous membrane aspect, or at the junction of the mucous membrane with the skin, and, like epithelioma of the tongue, lips, and cheek, being often preceded for a long time by the condition termed by English surgeons ichthyosis.—H. M.] It develops sometimes early as a papilloma, but more frequently as a hard thickening of the labium, over which the skin retains its natural colour, but is thick and unyielding. As a rule, however, a flat, moist part is found, presenting a granular surface on the hard base, resembling in some respects the appearance found in certain stages of chancre. The development of severe lacerating pains and the extension of the ulceration remove all doubts. A characteristic malignant papilloma is developed, and the lymphatic glands become affected.

The disease first noticed by Huguier, and to which attention has been called by Dr. Matthews Duncan, who describes it as lupus of the vulva, is probably frequently mistaken for epithelioma. We have had the privilege of seeing cases which have been under Dr. Duncan's care in St. Bartholomew's Hospital, and have had the opportunity of verifying the diagnosis by histological examination. This observer has shown that a class of cases, which have been referred to as syphilis on the one hand, or as cancer

on the other, are distinguished from both, and belong to a specific affection peculiar to the genital organs of the female. The enormous swelling which sometimes characterizes these cases, and the long duration of the disease, distinguish it clinically from epithelioma. In some cases ulceration takes place in the form of a sharp, clean-cut hole of considerable depth, which exhibits none of the special characteristics of either cancer or syphilis. The course of the disease is uninfluenced by anti-syphilitic remedies, and enormous and progressive destruction of parts may take place over a period of years, without any symptoms of general cancerous infection.

Epithelioma of the anus is rare. When it occurs it is met with at the anal orifice as a somewhat notched and protuberant growth. It extends into the interior of the gut, where there is more or less ulceration. Epithelial cancer is also, although not frequently, found in the shoulders, neck, and thorax. When it occurs in the extremities it is very seldom idiopathic, but develops almost exclusively on the leg, taking its origin in cicatrices, varicose ulcers, syphilis, lupus, &c. Epithelioma of the face not very unfrequently takes origin in syphilitic and lupoid scars.

DIAGNOSIS.

Before the ulcerative period, epithelioma is liable to be confounded with acne sebacea, warts, and certain forms of lupus. The most frequent source of error at this early stage is probably acne sebacea. This affection may be of long duration, and is attended with black adherent crusts, which desquamate and are

renewed unceasingly. If the physician, relying on this appearance, believes that he has to do with epithelioma, and applies caustics, he creates an ulcer, changes the nature of the lesion, and renders it impossible for some time to come to a correct diagnosis. In order to avoid this error, it must be remembered that in acne sebacea the crusts are formed by a mixture of fatty matters and epidermic *débris*. When this is removed, healthy skin is found under the crusts, the orifices of the sebaceous follicles distended by excessive secretion are observed, and nearly always certain points are found free from this exudation, and in them the characteristic features of the lesion are unmistakable. At the same time it is to be borne in mind that acne sebacea may give rise eventually to epithelioma.

At this stage it is possible to confound epithelioma with the tubercles of lupus. In the latter affection the characteristic lupus-infiltration will be found on or near the borders of the affected part. Further, in lupus the patient is either young or has a history and traces of having been affected by the disease at an early age.

A tubercular syphilide will be recognized by the colour and the grouping of the tubercles. Epithelioma begins, in general, by a single tubercle; its course is slower and its duration longer.

The early stage of epithelioma may be mistaken for a wart, and the diagnosis between the two is often exceedingly difficult. If a tumour is developed in an old person, and shows a tendency to increase, if it is the seat of frequent desquamation, and if immediately surrounding it there is a tendency to hypersecretion

of epidermis, the probability is that we have to do with an early stage of an epithelioma.

After the stage of ulceration, epithelioma may be confounded with syphilis or lupus. If it is situated on the genital organs it may possibly be mistaken for a chancre; but if attention is paid to the history and to the duration of the ulcer it will not be difficult to arrive at a correct diagnosis. In an epitheliomatous ulcer of the penis there is rapid swelling of the corpus cavernosum. In the later stages the recognition of the cancerous nature of the affection cannot be attended with any difficulty.

In the case of tertiary syphilitic ulcers it must be remembered that their course is much more rapid than that of cancerous deposits. The nature of the ulceration will also throw light upon the case. In syphilis the ulcers are generally multiple, whilst in cancer the ulceration is usually, although not invariably, single. The tissues surrounding an epitheliomatous ulcer are more or less infiltrated and hardened, whilst in syphilis the diseased surface is usually bounded by apparently healthy skin. The pain which is frequently present in cancer is not found in syphilis. The pain of an inflamed syphilitic sore is more amenable to palliatives, and is not so persistent.

The quality of nodulation is sometimes useful in distinguishing lupus from epithelioma. In lupus the edges of the ulcer are yielding and regular, and not everted; the ulceration extends more on the surface than in depth; characteristic lupus-tubercles are found near the border of the ulcer; and again, the age of the patient comes to our assistance. Lupus is a disease of early life; epithelioma usually commences

after middle age. It is to be remembered that epithelioma may develop in the seat of lupus.

PROGNOSIS.

The prognosis in epithelioma must be always grave, although it is not so grave as in other forms of cancer. Its course is usually slow. After operation it may not return, and when it does return there has often been in the interval a considerable period of relief. Metastasis to the internal organs occurs, but it is by no means the rule.

The gravity of the disease in any particular case depends on whether the ulceration attacks the deeper tissues or remains localized on the surface of the skin. In the deep-seated or penetrating form of the disease the patient's life is more rapidly endangered. The disease often lasts for a considerable time, sometimes for years, without the patient's health being much affected, or even without much pain being suffered. But eventually the constitutional power of the patient becomes impaired; the characteristic pain of cancerous affections makes itself felt; and the patient finally sinks from exhaustion,—occasionally, although rarely, from hæmorrhage caused by the process attacking the blood-vessels in the course of its progress.

TREATMENT.

The treatment of epithelioma is entirely surgical. No internal medication is of the slightest effect against the disease. The methods by which the patient's strength must be supported, his pain re-

lieved,* and the disturbance of his general health by the disease so far as possible mitigated, are in accordance with the ordinary principles of medicine. The treatment of the disease itself leaves us only the alternative of two remedies: caustics and the knife. The choice of these two measures is influenced necessarily by the extent and situation of the disease, and very considerably by the predilections of the medical attendant. The surgeon will, where it is possible, have recourse to the knife; and there are surgeons of great experience who consider that caustics are to be entirely avoided. The specialist in dermatology, however, probably in most cases, where they are not particularly contra-indicated, has recourse to caustics. For our own part, we believe that in cases in which the disease is somewhat advanced, but may be still regarded as within the reach of remedies, a cutting operation is generally to be preferred. In the very early stages, caustics and the curette are sometimes sufficient to remove the disease; and in cases in which we have diagnosed what we believed to be a very early stage of epithelioma on the face, we have by this means succeeded in effecting what has seemed to be a satisfactory cure, with a very insignificant cicatrix.

When an ulcer with hardened borders and evident infiltration has formed, complete excision of the whole diseased tissues, if the operation can be accomplished, is the most effectual method of dealing with the disease. Any application of caustics which could

* Mr. H. Morris informs me that he has found that cocaine applied, compounded with vaseline or in aqueous solution, has a very pain-killing influence.

approach such an operation in thoroughness requires to be severe, and probably to be repeated. In such cases the treatment by excision is steadily gaining favour in London.

As regards relapses, the evidence does not appear to justify the preference of one of these modes of procedure to the other; but it is claimed on behalf of caustics that they secure a thinner and finer cicatrix than can be obtained by a cutting operation. Of course, the cicatrix obtainable after operation will depend to some extent upon the skill of the surgeon, and also on the part on which he operates. It is claimed for cauterization that it has special advantages with regard to the cicatrix when the disease is situated near the eyelid or on the nose or cheek. The argument for caustic becomes still stronger when a superficial epithelioma occupies a large extent of surface, is partially cicatrized in the centre, and the neoplasm seems to exist only on the border of the ulcer, or on isolated points of the affected surface. Kaposi considers that in such a case it is more reasonable to attack each individual nodule with caustic than to dissect out a large portion of tissue. He claims that even large nodular masses of epithelial cancer can be destroyed with great ease, the cancer tissue breaking down readily under the caustic, which is resisted by the healthy tissue.

The caustic recommended by Kaposi in these cases is nitrate of silver or chloride of zinc. As cauterization is largely employed by the Vienna school, it will be useful to quote Kaposi's remarks on the subject. He affirms that "under arsenical paste nodular epithelial cancer shrinks, whilst the healthy surrounding tissues remain completely intact. Only,"

he adds, "a single eyelus of three days will not always suffice, and, after the slough has fallen off, a second and even a third eyelus must sometimes be had recourse to in order to destroy all the deeply situated cancer masses. Whilst nitrate of silver, ehloride of zine, and arsenical paste are indicated where it is desirable to spare as much as possible the healthy structures, the more destructive caustics—potassa fusa, Vienna paste, ehloride of zine paste, &c.—must be used where it is necessary to destroy large masses of diseased tissue, and where some of the healthy tissues may be destroyed at the same time without any great disadvantage. Feebler caustic agents, such as solutions of nitrate of silver and ehloride of zine and creosote, may be used to destroy very thin layers of cancer tissue—for example, single thin specks of cancer which have been left behind in the midst of a healthy granulating wound. In epitheliomatous degeneration of the conjunctiva, of the mucous membrane of the nose, &c., whatever form of caustic is ehosen, it is necessary that it shall be used with sufficient energy, and repeated when and where necessary. Caustics are especially useful in the treatment of relapses, and in cases where the cancerous infiltration has so far progressed that the question of extirpation can no longer be entertained.

"Whether epithelial cancer is removed by extirpation or by caustics, relapses frequently occur after shorter or longer intervals. These appear mostly single, in the form of the well-known small vesicular transparent nodules, which are sometimes for many years limited only to the upper layers of the skin. Each new nodule as it appears can be attacked with

fresh cauterization. By this means," Kaposi remarks, "permanent cure may be attained, or the malady restrained within small limits. So frequent operations with the knife," he considers, "would be impracticable.

"In cases where an operation with the knife cannot be entertained, systematic continued cauterization is still attended with unmistakable advantages. The extension of the evil on the surface and in the deeper tissues is for a time restrained in some parts, and even cicatrization secured. The sloughing, offensive condition of the ulcerated surface is improved, with the result that fever, sleeplessness, loss of appetite, and pain are diminished, the general condition ameliorated, the discomforts of the patient's condition lessened, and life prolonged over many months, and even years. On the other hand," Kaposi continues, "there are forms and conditions of epithelial cancer in which the necessity for operation by the knife is clear. Such are cases in which infiltration penetrates the deeper layers of tissue, the progress being more inwards than on the surface. Also in cases in which the return of the malady is not in the form of superficial nodules, but in quickly growing, deeply situated nodules, covered either with unaffected skin or with an unbroken cicatrix which has been left as the result of the previous operation."

As few writers have had so much experience as Kaposi in the treatment of epithelioma by caustics, we have felt it our duty to quote his words in full. But we believe the generally accepted rule of treatment to be that caustics should only be preferred to the knife in exceptional cases; for example, in com-

ination with the curette in very early stages, or, if the disease is developed, when patients are unwilling to permit a cutting operation, or when such an operation is impossible. It is doubtful whether, in deep-seated cancer, when the diseased tissues are beyond the reach of the knife, much good can be obtained by cauterization, as in such cases the widely ramifying epithelial growths generally extend too deeply into the healthy tissues to be followed up by caustics.

Dr. Duhring lends his high authority on the side of caustics. "Superficial epitheliomata," he remarks, "are in the majority of cases best removed with caustic. Among the various remedies, caustic potash in stick form or in solution occupies a high position. It causes much less pain than other powerful caustics, which, moreover, does not continue after the cauterization, and by means of acids may be at once removed. The growth should be thoroughly cauterized, no part of it being permitted to remain undisturbed."

Kaposi has latterly strongly advocated pyrogallie acid as an application in epithelioma, his recommendation being endorsed by Dr. Duhring. It is used in the form of an ointment (one or two drachms to the ounce), which is spread upon muslin and applied from two to six days constantly. It is preferred on account of its painlessness, contrasting in this respect with the chloride of zinc, which, although effective, is very painful. Chloride of zinc is used as a paste in the proportion of one part to three parts of gum, mixed and moistened with a little water. The paste is laid over the diseased surface, which must be blistered if the skin is entire, the surrounding healthy tissues being protected by adhesive

plaster. A strip of plaster cover should be placed over the whole. The paste will destroy structures equal to three or four times its own thickness. In using arsenical paste, the possibility of absorption with poisonous results must never be forgotten. The formula for arsenical paste (*Pulvis Cosmi*) is given by Kaposi as follows:—

℞.—Acid. Arsenici albi	1·0
Cinnabar. fact.	3·0
Ungu. Emoll.	24·0

The paste should be applied only to a limited extent of surface. On account of the danger of poisoning it is now rarely used.

The zinc paste of the Middlesex Hospital, which is widely known and used, is: *Zinci chloridi*, liquoris *opii*, āā; flour q.s. to make a paste.

The thermo- and galvano-cautery may also be used in accordance with the rules of ordinary surgical practice, and are by some surgeons preferred to caustics.

Wherever a cauterizing operation is chosen in the treatment of epithelioma, thoroughness is essential; and in cutting operations the surgeon should carry his knife, where it is possible, wide beyond the apparent disease. Returns of the malady are not to be wondered at when we consider how often isolated cancerous epithelium may be found in the tissue adjoining the line of excision by which the diseased part has been removed. It suffices only that a few of these epithelial elements should be left (too few in number, it may be, to permit their affecting the appearance or consistency of the tissue) in order to

form the seeds of another inevitable outbreak of the disease at some future time. Early and thorough operation is the key to success in the treatment of epithelioma.

Small warty growths or suspicious-looking isolated tubercles in the skin of elderly people should be carefully watched, and if there is any sign of growth or increased vascularity the patient should have the benefit of the-doubt. In such cases, thorough scraping with a sharp spoon and the firm application of caustic will probably save the patient from future malignant disease; and an operation of this kind may be permitted at an early stage, when a proposal for excision would not be entertained.

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RODENT ULCER.

Synonyms :—Canceroid ulcer, Ulcère rongéant, Ulcère chancreux, Der Flache Krebs, Ulcus exedens, Noli me tangere.

HISTORY.

The history of the recognition of rodent ulcer as a specific disease, and of the various views formerly and still held regarding its nature, presents some features of unusual interest. Clinically, it may be said to have been discovered by English surgeons; pathologically, its special characters were first recognized in Germany; while more recently the tendency has been to ignore that the affection has specific characters, either clinical or pathological. The earlier clinical observers were specially occupied in showing that, although capable of no spontaneous cure, it was not a cancer; Thiersch showed that its clinical peculiarities are due to the fact that it is a form of cancer, but that it is a form associated with certain histological peculiarities; whilst later writers have either lost sight of, or have never grasped the import of, the histological inquiry of Thiersch, and have refused to see more than one kind of epitheliomatous growth in the skin, believing that the greater or less activity

and extent of the growth account for all the varieties observed by the clinician.

As it is impossible to understand the views now entertained by various authorities in reference to the nature of the affection usually known as rodent ulcer, or rodent cancer, without a certain familiarity with the phases of opinion which have prevailed regarding it during the last forty years, it will be convenient to enter into a somewhat extended historical retrospect of the subject.

The first notice of the disease was published in the "Dublin Hospital Reports" for 1827, by Dr. Jacobs. This observer remarked as follows:—

"I allude," he states, "to destructive ulcerations of a peculiar character, which I have observed to attack and destroy the eyelids, and extend to the orbit, eyeball, and face. The characteristic features of this disease are the extraordinary slowness of its progress, the peculiar condition of the edges and surface of the ulcer, the comparatively inconsiderable suffering produced by it, its incurable nature, unless by extirpation, and its not contaminating the neighbouring lymphatic glands. The slowness with which this disease proceeds is remarkable.

"This disease may be observed under two very different conditions, either in a state of ulceration or in a fixed state, in which its progress is made towards healing. In the latter condition, the parts present the following appearances:—The edges are elevated, smooth, and glossy, with a serpentine outline, and are occasionally formed into a range of small tubercles or elevations. The skin in the vicinity is less thickened or discoloured. The part within the edges

is, in some places, a perfectly smooth, vascular, secreting surface, having veins of considerable size ramifying over it, which veins give way, causing slight hæmorrhage; in other places, the surface appears covered by florid, healthy-looking granulations, firmer in texture and remaining unchanged in size and form for a great length of time. The surface sometimes heals over in patches, which are hard and smooth and marked with the venous ramification to which I have alluded.

“I have not observed that the lymphatic glands were in the slightest degree contaminated, the disease being altogether extended by ulcerations from the point from which it commences.”

Mr. Cæsar Hawkins, in a clinical lecture published in 1842, wrote as follows:—

“It differs, in fact, from the ordinary progress of cancer by its great slowness, so that I have repeatedly seen it after it had existed twenty or thirty years without having materially affected the health; it is generally characterized by the little pain attending it, though occasionally this is severe. It has very little disposition to hæmorrhage, or to the formation of fungus of any size. The discharge has none of the fœtor which that of ordinary cancer possesses, neither does it affect the glands or the rest of the body, as far as I have seen it, being throughout a local disease.”

Meanwhile, the peculiar nature of the ulcer was recognized in France.

Nélaton, in his Text-book of Surgery, published in 1844, gives an excellent account of rodent ulcer under the name of *ulcère chancreux*. He states “that it sometimes begins by a simple nodule in the form

of a wart, to which the name of *tubercle malin* has been given ; sometimes by a small hard tumour of a yellowish and slightly opaque colour, a smooth shining surface, never being the seat of hairs, often thickly covered with red lines, which result from dilatation of blood-vessels. Its base is broad and its structures compact." This nodule may, he remarks, "long be innocent in character if it is not irritated. But if the patient cut it in shaving, or if he scratches it, the wart becomes painful, swells, and ulcerates. The thickening in which it took its origin being once destroyed, the disease extends with more rapidity." Sometimes, he adds, "the primary induration is so slightly pronounced that it passes unobserved." Whatever be its mode of origin, he continues, "the ulcer presents an unequal rugged surface, irregularly bounded by livid, hard, and rolled-over borders. Sometimes it takes a fungous form with a broad pedicle. The skin surrounding the ulcer often preserves at the beginning its natural appearance, and later on it becomes of a livid red." He also remarks "that these ulcers are never accompanied by enlargements of the neighbouring lymphatic glands, and that the general health of the patient is often perfect." He observes "that sometimes the process of ulceration may be resisted for several years, or even for the rest of the patient's life, without derangement of health. At other times," he remarks, "the ulceration exercises rapidly its corrosive action in depth, as well as on the surface ; it destroys not only the skin and subcutaneous connective tissue, but reaches the muscles, cartilages, and even the bones."

Nélaton was evidently familiar with the distinctive characters of rodent ulcer as a special affection.

Brodie ("Lectures," 1846) described the affection in the following words:—"A man has a soft tubercle upon the face, covered by a smooth skin. He may call it a wart, but it is quite a different thing. On cutting into it you find it consists of a brown solid substance, not very highly organized. A tumour of this kind may remain on the face unaltered for years, and then, when the patient gets old, it may begin to ulcerate. The ulcer spreads slowly but constantly, and if it be left alone it may destroy the whole of the cheek, the bones of the face, and ultimately the patient's life; but it may take some years to run this course. So far these tumours in the face, and these ulcers, are to be considered as malignant. Nevertheless, they are not like fungus hæmatodes or cancer, and for this reason, that the disease is entirely local. It does not affect the lymphatic glands, nor do similar tumours appear in other parts of the body."

Paget, in his "Lectures on Surgical Pathology," thus describes the disease:—

"It has been confounded," he remarks, "by many with different forms of cancer; yet it is distinct from them in structure as well as in history, and had better be described by some name which may not add to the yearly increasing confusion that arises from the use of terms expressing likeness to cancer.

"The constantly progressive ulceration is a character in which the disease represents cancer, especially epithelial cancer. The likeness in this respect may indicate some important affinity between them, but the differences between them are greater;

for not only is the rodent ulcer usually unlike that of any cancer in its aspect, rate and mode of progress, but the tissues bounding it, and forming its base and walls, never contain any epithelial or other cancerous structure—they are infiltrated with only such structures as may be found in the walls of common chronic ulcers.

“The most usual characters of the rodent ulcer, whether on the cheek, the eyelids, upper lip, nose, scalp, vulva, or any other part, are as follow:—It is of irregular shape, but generally tends towards oval or circular. The base, however deeply and unequally excavated, is usually, in most parts, not warty or nodular, or even plainly granulated; in contrast with cancerous ulcers, one may especially observe this absence, or less amount, of up-growth. It is also comparatively dry and glossy, yielding, for its extent, very little ichor or other discharge, and has commonly a dull reddish-yellow tint. Its border is slightly, if at all, elevated; if elevated, it is not commonly or much either everted or undermined, but is smoothly round or lowly tuberculated. The immediately adjacent skin usually appears quite healthy. The base and border alike feel tough and hard, as if bounded by a layer of indurated tissue about a line in thickness. This layer does not much increase in thickness as the ulcer extends; and herein is another chief contrast with cancerous ulceration: in the progress of the rodent ulcer we see mere destruction, in the cancerous we see destruction with coincident, and usually more than commensurate, growth. It is only in the rarest cases that a growth is associated with rodent ulcer.”

A very important “Clinical Report on Rodent Ulcer” was published by Mr. Jonathan Hutchinson

in the "Medical Times and Gazette" for 1860. In this report Mr. Hutchinson collected materials for a complete history of forty-two cases, and accompanied it with a valuable tabular statement of the more important facts connected with them. To the "Report" Mr. Hutchinson appended a number of "Aphorisms," from which we extract the following:—

"That there occurs not infrequently on one or other part of face a form of ulceration which is characterized by an indurated edge, and by a tendency to spread to adjacent structures, without regard to difference of tissue, which is very slow in its progress, does not cause much pain, does not induce cachexia, and is never followed by large glands or deposits in the viscera.

"Sections of the indurated edge of this ulcer (or of the portions of the new growth, which are sometimes produced about it) do not exhibit the cell-structures met with in epithelial or scirrhus cancer, but only those of organizing fibrous tissue.

"This ulcer differs from lupus exedens in that it never occurs in the young, and never gets well spontaneously, while lupus exedens but rarely begins after the age of thirty, and usually tends, after the lapse of time, to cicatrize spontaneously. The two also further differ, in that lupus has a tuberculated, inflamed border, without any great degree of induration, while the edge of the ulcer in question presents an extremely indurated ridge, without tubercles, and comparatively free from inflammatory congestion.

"The ulcer in question differs from cancer in that there is but seldom any tendency to the production of new material, that it never causes the glands to enlarge, or induces morbid growths in the internal viscera.

“The rodent ulcer is most commonly met with between the ages of fifty and sixty, and is equally frequent in the two sexes.

“It occurs but very rarely on any other region than the integument of the face, and is most common in the eyelids.

“It is a singular and very significant fact that no case has yet been recorded in which the rodent ulcer attacked the lower lip, either primarily or by extension, while that part is well-known to be a very frequent seat of epithelial cancer.

“The diagnosis of rodent ulcer is usually easy. An ulcer with a hard sinuous edge, situated on some part of the upper two-thirds of the face, of several, or perhaps many, years’ duration, almost painless, and occurring in a middle-aged person of fair health and without enlarged glands—such a sore is almost certain to be of the rodent type.”

The first stage in the history of rodent ulcer may be said to have finished with Mr. Hutchinson’s “Report.” It seemed to be definitely settled that rodent ulcer was not cancerous in its nature, and that the structural elements of epithelial cancer were not to be found in its base or borders. This latter belief was soon afterwards shown to be incorrect.

Thiersch in 1865 directed attention to the fact, that the rodent ulcer of English writers had been correctly considered by Schuh as a form of epithelial cancer. The German writers have adopted his term, *Flacher Krebs*—superficial cancer.

Thiersch states that his investigations had led him to form the opinion “that epithelioma is to be divided into two classes, which, in spite of occasional transitions

from one to the other, can, as a rule, be easily distinguished on clinical grounds." These classes were the superficial and deep-seated or penetrating varieties.

"Superficial epithelial cancer or rodent ulcer," he remarks, "is always characterized by a superficially situated epithelial neoplasm a few millimetres in thickness, which, in a vertical section, is seen to be always sharply demarcated from the connective-tissue stroma.

In penetrating epithelial cancer, on the other hand, a sharp limitation is not to be observed. The epithelial neoplasm does not form a superficial layer, but extends to a considerable depth in the form of irregular masses." "Superficial epithelial cancer," he continues, "he recognized only as a shallow ulcer with thin, or slightly thickened, borders, whose immediate surroundings present nothing abnormal in colour, resistance, or form. Deep-seated epithelial cancer, on the other hand, forms, as a rule, ulcers of a very irregular kind, and there are always to be found, partly in the vicinity, and partly in the base, of the ulcer, hard nodules from the size of a pea to that of a walnut. Both forms act destructively from the surface downwards in so far as they both extend in circumference. The superficial cancer does this more slowly than penetrating cancer. Both forms may or may not be attended with papillary vascular growths. But in the superficial form these papillary growths are the exception; in the penetrating form they are the rule. Both forms may become infiltrating cancers, insomuch as in the superficial form, the epithelial growth may deepen, and the sharp delimitation from the stroma may disappear." Cancerous infiltration he looks upon as the final stage of the disease, which

in the superficial form arrives more seldom and later, in the penetrating form more frequently and earlier.

He remarks emphatically, "that the rodent ulcer of Paget and Foerster, and the so-called Jacob's ulcer," is identical with his *Flacher Krebs*—superficial epithelioma.

Thiersch's views have found universal acceptance in Germany, and form the basis of most of the descriptions of cancer of the skin that are found in the various text-books. In Hebra's Text-book of Skin Diseases, for example, we find Kaposi accepting the view that rodent ulcer and ordinary epithelioma are identical. In his own text-book, recently published, he describes *ulcus rodens*, or superficial epithelial cancer, "as a rounded, yet, when of great extent, triangular or polygonal, shallow ulcer, with sharply marked edges, whose brown or yellowish-red, finely granular surface secretes a viscid fluid, which, when it is dry, forms a varnish-like covering. The base and border of the ulcer are hard, not easily moved, the latter sometimes smooth, sometimes beset with firm, vesicular-looking, shining, nodules." His observations have led him to agree with other observers as to the length of time that the rodent ulcer may last without affecting the general health. Ten to twenty years it may so last, producing no swelling of the neighbouring lymphatic glands, its action being entirely limited to the cutis, ending sometimes in the destruction of the undermined cartilage, sometimes in the cicatricial contraction of the surface of the sore. But Kaposi is of opinion that the clinically "superficial" cancer may, in its further development, give rise to a nodular or "deep-seated" epithelial

cancer. Apparently he considers the difference to be one of degree and not of kind, the rodent ulcer being only a less virulent form of epithelioma.

German surgeons and pathologists have not followed up successfully the indications which are found in Thiersch's work, and under the term superficial cancer (*Flacher Krebs*) we find that they mix inextricably cases of superficial epidermic epithelioma and rodent ulcer. The later German writers on dermatology have entirely failed to grasp the distinction.

We recognize rodent ulcer in the *epithéliôme tubulé* of Cornil and Ranvier.

Whilst Thiersch, in 1865, had already demonstrated that rodent ulcer was histologically a form of epithelioma, we find, in England, that Moore, in 1867, endeavoured to show, on clinical grounds, that there is a more real identity of the rodent disease with cancer than had been assigned to it in published accounts. The influence of Thiersch's work had not yet made itself felt in England. Although Moore did not do much by histological methods to establish the claim of rodent ulcer to be a cancer, yet on clinical grounds his observations were of first-rate importance. He laid stress upon the fact that the first stage of the disease is a solid growth. The disease, he says, "spreads by the growth of the original solid pimple advancing upon and involving the adjoining healthy structures—the central crack or excoriation, too large to be sealed by a scab, becomes a distinct ulcer." "Thus the aspect of the disease changes, though not its nature. It is a cutaneous nodule with a superficial and central ulceration. The

solidity claims most attention—it was named a pimple; but as the growth spreads deeply and broadly, its thickness not increasing with its area, while the scab excoriation widens into a cavity, the loss of substance causes most attraction, and the disease is miscalled an ulcer.” He also remarks “that although the disease originated in the skin, it is not limited to that texture, but corresponds with cancer eminently in the particular faculty of indiscriminately invading the tissues of all it meets.” Added to this, he says, “there are further indications of this cancerous nature in the occasional identity by its microscopical elements with those of epithelial cancer, and since, so far as we know, it is never spontaneously curable, in its tendency to produce a fatal result.”

Soon in England also the epithelial nature of rodent ulcer began to be recognized. In a paper presented to the Pathological Society in 1871, Mr. Hulke stated that the “minute structure of the morbid tissue forming the hard edge of a rodent ulcer consists exclusively of cells without the admixture of an intercellular substance. The cells are small and round; they resemble those of the epidermal rete mucosum. At the periphery of the hard edge and base they form cylinder and bud-like masses, which intrude into normal tissues underlying the ulcer. Near those invading buds the connective-tissue corpuscles are unusually numerous, and in some situations appearances indicating proliferation of these corpuscles, and evolution of the morbid tissue out of them, were observed.”

Dr. Collins Warren, in the “Boylston Prize Essay” for 1872, confirmed the observations of

Thiersch and Hulke, and showed that in cases diagnosed as rodent ulcer not only was an epithelial neoplasm present, but laid stress on the observation that in this neoplasm the cells differed in size from those which are characteristic of epithelioma.

Since the appearance of this work, all difference of opinion as regards the existence of an epithelial neoplasm may be considered as having ceased. Subsequent observers have directed their attention to the special characters of the morbid epithelium, and to the source from which it takes its origin.

We have illustrated the history of this disease by copious quotations with a definite purpose. Whilst there is no form of neoplasm that is more easily detected on microscopical examination than that of ordinary epithelioma, it must seem strange that skilled observers for so long a time should not have been able to recognize in rodent ulcer the characters of an epithelial growth. The keen clinical eye of Jacobs and others had early distinguished a form of ulceration possessing special and peculiar characters, more destructive than an ordinary ulcer, and yet differing from growths recognized as cancerous by sparing the lymphatic glands. Clinical observation, and microscopic examination, at that time, alike combined to separate rodent ulcer from epithelioma of the skin. How was it then, that it was reserved for Thiersch to establish on an irrevocable basis the doctrine that rodent ulcer is, after all, an epithelioma? The answer to this question will appear in the sequel. In the meanwhile it may be remarked that we seem at the present time to have arrived at a retrograde stage in the history of this disease. Whilst the

earlier writers failed to recognize it as a cancer, whilst Thiersch pointed out that it was a cancer of peculiar anatomical characteristics, the tendency recently has been, both by clinical observers and by pathologists, to consider rodent ulcer and ordinary epithelioma as one disease. Whilst trained and excellent observers, not so long ago, could not recognize cancerous elements in the disease at all, it would appear now that it is impossible to distinguish it from any ordinary cancer. In accounting for this paradox, something may be set down to histological methods; but assuredly this is not a sufficient explanation. Histological methods have been sufficiently advanced for forty years for the recognition of the epithelial neoplasm in cancer of the skin, and if trained observers at any time during this period failed to notice epithelial growths in rodent ulcer, the presumption is very strong that in that disease the neoplasm is of such a nature that its detection is more difficult than usual. This difficulty will be partly accounted for when we have considered the histology of rodent ulcer.*

**Mode of Examination of the Rodent Ulcer.*—In examining rodent ulcers histologically, it is very important that special care be taken in hardening the tissues. The cells of the neoplasm have so little power of resistance that if they are not carefully hardened nothing is seen of them but a mass of nuclei. Even the limits of the cell-mass are liable to be lost, and it is sometimes impossible to tell where a cluster of the new growth ends and the surrounding small-cell infiltration begins. We are satisfied that there would have been less difference of opinion in regard to the nature of this disease if careful and slow hardening had been used. We have found hardening in a solution of bichromate of potash much more reliable than any other method. If the tissue is allowed to remain in the solution for six to eight weeks, and if the sections are stained with logwood and eosin, preparations will be obtained of a very demonstrative character, and the difficulty of distinguishing epidermic epithelioma from

DESCRIPTION AND COURSE.

Rodent ulcer, undoubtedly occurring most frequently in the upper parts of the face, but found also on other parts of the body, begins, in the great majority of cases, if not always, as a small pimple or tubercle situated in the substance of the cutis. The swelling is circumscribed, hard, and uneven (if its size allows the condition of its surface to be appreciated by the finger), and is not painful. The cutaneous pimple or tubercle grows towards the surface, and as it becomes prominent leads to the formation of epidermic scales, which are being continually removed and replaced. Under the scales the swelling is seen to be dark in colour and surrounded by small veins. In course of time the epidermis gives way and the ulcer is formed.

The papular stage is usually sufficiently well marked, and lasts sufficiently long to be a prominent feature in the history of the ulcer in a large number of cases, but sometimes, although rarely, it escapes notice. Patients occasionally describe the first appearance of disease as a scab, and instances are recorded in which the ulcer has formed in a scar, and as the direct result of a wound or a blow.

The time that elapses before the pimple ulcerates varies greatly, but it is usually a considerable time, several years often passing before the small tumour breaks down. Indeed, the process may be extremely chronic, many years intervening between the formation

the epithelial growth of rodent ulcer will be very greatly diminished. Chromic acid, and even osmic acid, give preparations which are much less reliable.

of the tubercle and that of the rodent ulcer which results from its disintegration.

In exceptional cases the tumour may develop to a considerable size, growing subcutaneously to be as large as a pigeon's egg, the skin remaining entire; or it may project as a dark vascular mass to a considerable extent above the level of the surrounding skin.

Sometimes, near the ulcer, but separated from it by apparently healthy skin, one or more subcutaneous tumours are observed, which, on examination, are found to be composed of the cell-growth that is always found in the border of the ulcer.

The characters of the ulcer itself are not uniform. The edges may be hard, elevated, and rounded or "rolled over," or they may be abrupt and hard at only one or two points. The surface of the ulcer may be dry and without granulations, or may be vascular, secreting, and granulating.

As a rule the discharge has little odour.

It has been laid down by all the English authorities on this disease that the glands are never affected.

During the course of the disease attempts are made at cicatrization.

Although the ulceration may remain superficial for many years, it may, and usually does, eventually penetrate the subcutaneous tissues and the bones. In the face (the common seat of the disease), the nose may become destroyed, the eye may be lost, and the ulcerative process may extend deep into the orbit, and thence, by perforating the floor, it may reach the antrum. The essentially local nature of the disease, and the immunity of the lymphatic glands, sometimes

allows the destructive process to progress to a hideous extent before the patient's life is put in jeopardy. In a case of Paget's, a man, in whom the disease had lasted eighteen years, lost, before he died, the greater part of his tongue, the right cheek, the right eye, and right upper maxilla.

The patient sometimes dies of repeated hæmorrhages.

As a rule, the destructive process goes slowly on over a considerable term of years, with little apparent injury to the patient's general health.

The amount of pain felt varies in different cases, but, generally, very little suffering is experienced.

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In some rodent ulcers a "ridge," more or less pronounced, encircles the edge of the sore. The "rolled-over" appearance of the ridge or border is so marked that a sulcus is formed between the projection and the skin. Sometimes the ridge is undermined on both sides, remaining attached to the skin by a narrow pedicle.

When in a rodent ulcer of this kind a section is made through the whole thickness of the skin, from the healthy tissue to the surface of the ulcer, the ridge is seen to be caused by an exuberant growth of peculiar small epithelial cells, arranged in well-defined groups. Groups of similar cells are found in the tissue of the cutis immediately under the ridge, and in the upper strata of the ulcer adjacent to the margin. After the ulcer has lasted many years, and involved a considerable extent of surface, the cell-groups may be still limited to the superficial part of

the cutis. They do not extend outwards towards the healthy skin much beyond the line of the sulcus formed by the outer edge of the ridge and the skin.



FIG. 4.—VERTICAL SECTION THROUGH THE MARGIN OF A RODENT ULCER OF THE BACK.

a, surface of the ulcer; *b*, healthy skin external to the “ridge” or “rolled-over” border. The dark objects in the figure represent the cell-groups as seen slightly magnified. The ridge, *d*, is divided through the centre by a septum of epidermis. At *c* the connective tissue is healthy, no cell-growth being found at this depth.

In those cases in which there is no ridge the characteristic groups of small epithelial cells are found in the superficial parts of the cutis immediately under the border of the ulcer, and extending only a very short distance outwards beyond the margin. Small isolated groups are also found in the surface of the ulcer, but, as a rule, not extending into the thickness of the middle layer of the corium.*

The forms assumed by these cell-groups can be classified as belonging to one of two kinds. The ridge is composed of groups which uniformly tend to assume a cylindrical form, and they are, therefore,

* The description which follows is condensed and extracted from papers by the author, published in volumes xxix. and xxx. of the “Transactions of the Pathological Society of London.”

seen in section to be cylindrical, pyriform, ovoid, or circular. From the cylindrical mass thus formed, similarly shaped buds are thrown out; the connective tissue between them becomes more and more encroached upon, until, finally, adjacent groups join and form large cylindrical masses. When the masses have acquired a certain size they begin to break down in the centre by a formation of small cavities, the largest of them being literally honeycombed. At the same time the connective tissue between these masses and the rete mucosum becomes thinner and thinner, until the new epithelial growth and the lowermost stratum of the rete cells are in contact, and the vascular supply is thus completely cut off.

Many of the cells of the rete mucosum, over the most projecting of these cylindrical columns, show the usual appearances of nuclear degeneration. In some the nucleus has disappeared, leaving a vacuole in its place; in others a crescent-shaped remnant still stains with logwood. In others, again, a small round nucleus, staining deeply in logwood, or two, more rarely three, still smaller nuclear bodies, also staining deeply, are found in the cavity left by the destruction of the old nucleus. Similar small nuclear bodies are found between the palisade-cells which form the lower boundary of the rete, and in spaces between cells which are more or less broken down. Where the cell-masses of the new growth are in contact with the rete, the number of these nuclei is greater, and towards the border of the ulcer, as the rete becomes more broken down, the number of these small cellular elements increases. Finally, the epidermis proper is, for a short distance, represented by the horny layer

alone, until at last the exposed surface of the ulcer is reached.

The other form assumed by the cell-groups is in marked contrast to that just described. Whereas in the superficial parts of the cutis the connective tissue yields to the growing masses, in the deeper stratum the resistance is so great that the direction of the new growth is everywhere determined by the arrangement of the bundles of connective tissue. The new cells are found in clusters of indefinite shape, situated in spaces formed by separation of the bundles, and the groups grow by the cells extending (at first in single file) between the bundles. They do not penetrate to the deeper layers, where the bundles are thick and strong, and the elastic fibres very large.

The external or bounding cells of the cylindrical groups have sometimes a columnar form. The other cells of these groups, and all those in the cutis tissue, are composed of a spherical nucleus, which stains deeply with logwood, and a scant amount of yielding cell-substance, which resists badly the action of the ordinary hardening solutions. All the groups of cells are penetrated freely by elastic fibres, which pass straight through them unaltered. The connective tissue between the groups is well supplied with blood-vessels.

The sebaceous glands and hairs in the adjacent skin degenerate before they come in contact with the cell-growth.

The cells of the new growth have distinctive characters, and differ from those found in epithelioma in other respects than dimensions. The nucleus is of a fairly uniform size. The different forms in which

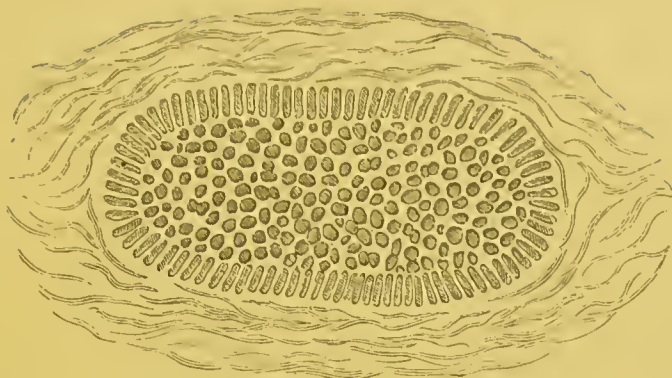


FIG. 5.—SECTION THROUGH A CELL-MASS (BEING ONE OF THOSE SHOWN AS SLIGHTLY MAGNIFIED IN FIG. 4) FROM A RODENT ULCER OF THE BACK.

The engraving shows the characteristic palisade-like cells which sometimes form the border of the cell-masses in rodent ulcer, and the relative size of the nuclei. The nuclei should be compared with the nuclei of the cells in Figs. 2 (page 24) and 7 (page 70), which are drawn to the same scale. It will also be observed that no distinct cell-substance or cell-wall is visible, the nuclei appearing as if imbedded in an amorphous matrix. Magnified 250 diameters.

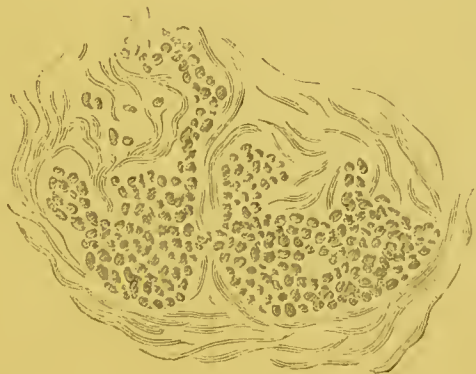


FIG. 6.—CELL-MASSSES FROM A SECTION OF A SMALL RODENT ULCER OF THE UPPER PART OF THE FACE.

The cell-substance or cell-wall is quite indistinguishable, the nuclei alone being visible. (Contrast with Fig. 7 in order to observe the difference between the cells of rodent ulcer and the cells of ordinary [epidermic] epithelioma when the latter is characterized by cells of a small type.) Magnified 250 diameters.

it is found probably depend on the varying effects produced in different cases by the hardening fluids employed to prepare the tissue for examination. In our preparations the nuclei were invariably found entire.

The cell-protoplasm is comparatively scant in amount, is scarcely or not at all granular, and if it has a cell-wall, the latter, except in the border columnar cells, is, as a rule, too delicate to resist even the most careful treatment by solutions of bichromate of potash. In an ulcer given us for examination by

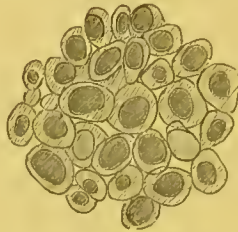


FIG. 7.—PORTION FROM THE CENTRE OF A LARGE CELL-MASS IN AN EPITHELIOMA (EPIDERMIC EPITHELIOMA) OF THE UPPER PART OF THE CHEEK.

To contrast with Figs. 5 and 6, being drawn to the same scale. The position of the ulcer shows that an ordinary epidermic epithelioma may attack the same parts as those on which rodent ulcer is common. In this case a correct diagnosis between the two forms was not made before excision, but there was no difficulty in making the diagnosis after the microscope was used. Although purely of the epidermic type, the neoplastic epithelium consisted entirely of cells similar to those shown in the engraving, and no "nests" were formed. Magnified 250 diameters.

Sir James Paget, we hardened portions in osmic acid. The nuclei in the sections made from this portion were in excellent preservation, but the cell-substance was not better preserved than in the bichromate preparations of the same ulcer. The resisting power of the cells appears to vary in different cases. Although all the specimens we have examined were hardened in the same manner, the cells in the pre-

parations from Sir James Paget's case were better preserved than in any of the others. This difficulty in hardening the cell-substance has induced Dr. Collins Warren to entertain the erroneous idea that the cell-masses are constituted by nuclei imbedded in an undivided mass of protoplasm. If care is taken it is possible (although with great difficulty) to isolate some of the cells, and it is then seen that there is a thin transparent plate of cell-substance, with a well-defined border round the nucleus.

These remarks apply to the ordinary cells of the masses. The columnar cells which sometimes form the border row are more resistant, but in most preparations their size and shape are only indicated by the faint regular lines seen in deeply stained sections.

The cells have certain negative qualities which distinguish them from the cells of epidermic epithelioma, and which are independent of their relative size. They never enlarge into the flat horny cells characteristic of the latter disease, never become "prickle" cells, at least as observable after the use of ordinary reagents, and never form the so-called "nests" or *globes épidermiques* (so long as this term is limited to the special changes in newly formed cancerous epithelium). A chemical difference is brought out by the employment of eosin. The readiness with which the cells of the epidermis are coloured a deep orange red by this staining agent, proves that they contain a substance for which it has a special elective affinity. The newly formed cells in epithelioma are similarly stained by eosin, but the substance which is so rapidly and deeply stained by

this dye in cells of the epidermic type does not exist in the epithelial cells of rodent ulcer.*

The softening which takes place in the centre of the larger cell-masses is produced by mucoid disintegration and liquefaction of the cells.

When the ascending edge of the new cell-growth has come in contact with the small cells of the lower layer of the rete mucosum or the border of the external root-sheaths of the hairs, it is sometimes difficult to detect the line of separation; and scattered through the various works and memoirs on cancer, drawings are found in which the cell-growths of what is evidently rodent ulcer are made to show a continuity with the epidermis. With sufficient care this confusion of the line of contact of the two elements can be avoided.

Another peculiarity in these cases seems to be the small amount of cell-infiltration and disorganization in the connective tissue of the corium, as compared with what occurs in epidermic epithelioma. Sometimes the amount of cell-exudation in the neighbourhood of growing masses of even considerable size is very slight, especially in the deeper strata of the cutis; and when, in the connective tissue between the exuberant growths in the papillary layer, an abundant cell-infiltration is found, the area so affected does not extend far beyond the limits of the new cell-growth.

The nucleus of the ordinary exudation-cell does not differ very greatly in size and staining capacity from that of the specific cell in question, but the want of a well-defined border in the masses of exudation-cells,

* By capacity of staining by eosin the power of *retaining* the dye is understood.

and their irregular arrangement, ought to be sufficient to prevent their being confounded with the epithelial masses.

In a case of rodent ulcer of the cheek we found a distinct membrana propria surrounding and enclosing the cell-masses of the neoplasm.

Drs. Tilbury and Colcott Fox* communicated a paper to the Pathological Society of London in 1879, in which they stated that "the epithelial growth in rodent ulcer starts from the external root-sheath of the hair, from any part of it, and from one or more foci. Buds sprout out from the hair-follicles in solid processes, pushing the tissues *en masse* and indiscriminately before them. Some of the masses grow downwards and others horizontally, or even upwards, in close proximity to the rete, and then spread along its under surface."

Dr. Sangster, who has devoted much attention to the histology of rodent ulcer, read, at the meeting of the British Medical Association in 1882, an able paper in which he seemed to support the view that the neoplasm takes its origin from the external root-sheath of the hairs.†

By the great goodness of Dr. Colcott Fox and Dr. Sangster, who have placed their microscopical preparations at our disposal, we have been able to examine the sections on which the views published by these authors have been based. We have not been able to

* "Transactions of the Path. Soc. of London," vol. xxx.

† Dr. Sangster (oral communication) informs us that his investigations have not satisfied him regarding the origin of the cancerous epithelium in rodent ulcer. He has not been able to trace the origin definitely to any epithelial element in the skin, although it seems to him that the origin from the root-sheaths of the hairs is a probable one.

satisfy ourselves that there is in their preparations any evidence which would justify us in adopting the opinion that in rodent ulcer the neoplasm takes its origin in the external root-sheaths. In no case of our own, or in any of those submitted to us, have we found any neoplastic growth in a case of unmistakable rodent ulcer taking its origin from those structures. The chief difficulty in securing a uniformity of opinion in regard to the origin of the epithelium in rodent ulcer lies in the fact that there is no unanimity amongst observers as to what histologically constitutes a rodent ulcer, and on the part of some an inability to appreciate the histological differences between it and epidermic epithelioma. So long as the diagnosis of rodent ulcer rests solely on clinical evidence, so long will the mistakes that are made in diagnosis prolong the confusion that reigns with regard to the pathology of the disease. We are satisfied, and we are borne out in our view by experienced surgeons, that ulcers are found in which it is at a given time impossible to tell with certainty, on clinical grounds alone, whether we are dealing with rodent ulcer or with epidermic epithelioma. It has come within our own knowledge and observation that ulcers diagnosed as rodent ulcers have, when examined histologically, been found to be examples of typical epidermic epithelioma. If, in a case diagnosed as rodent ulcer, sections examined by the microscope show neoplastic growths developing from the hair-sheaths, or from the rete Malpighii, that is not sufficient to establish the fact that pathologically true rodent ulcer takes its origin in this way. If histologically the case is found to be epidermic epithelioma, it only shows that

the surgeon has failed to recognize clinically the variety of cancerous disease with which he was dealing. The diagnosis for the present purpose must be founded upon the histological examination, not on the clinical appearance, and only if the microscopic appearances show that the neoplasm consists of cells having the characteristic appearance of those of rodent ulcer can any weight be attached to the fact that certain structures in the skin give rise to epithelial growths. Sections have been submitted to us, on which opinions regarding the origin of the neoplasm in rodent ulcer have been based (and given and accepted authoritatively), that exhibited under the microscope the appearances that are characteristic of pure epidermic epithelioma. Another source of error as regards the alleged growth from the hair-follicles appears to us to lie in the fact that sufficient weight has not been assigned to the deformities of the hair-follicles which are found near the border of the ulceration. Close to the advancing masses of cells in rodent ulcer the hairs drop from the follicles, and the hair-sheath sends out knobs of bud-like formations which are neither more nor less than attempts to form a new hair. At the same time the position of the follicle itself becomes altered by the pressure of the swelling, and assumes frequently an oblique and even horizontal position in the skin. It is these distorted hair-follicles, with futile attempts to develop new hairs, that have been described and figured as examples of rodent epithelial structures taking their origin in hair-follicles.

Were observers, first of all, to train themselves to distinguish the cell-clusters in rodent ulcer from

those in epithelioma, without regard to the clinical or previous diagnosis, and if they would give sufficient weight to the distorted conditions of the hair-follicles, which are frequently found in various pathological conditions, and to the thickening of the rete Malpighii, which is usually found in all conditions of the skin attended with congestion, we are confident that the histology of rodent ulcer would come to be recognized as being specifically distinct from that of epithelioma.

No evidence has, up to this time, been published which gives satisfactory proof that the neoplasm in rodent ulcer springs from either the rete Malpighii, the hair-follicles, or the sebaceous glands.

Thiersch recognizes the cell-growth of rodent ulcer as composed of groups of cells of uniform size, arranged in alveoli. In regard to their source, he states that they are found in connection with the rete Malpighii, and in the situation and of the form of the sebaceous glands. On the latter point we have been unable from our preparations to verify his statements, and have, therefore, all the more carefully sought for evidence in his "Atlas" to confirm them. Such evidence is, in our opinion, not to be found there. There is no appearance figured which connects either the rete Malpighii or the sebaceous glands with the cell-masses. Mere contact, such as we have frequently found in our own preparations, between a cell-mass and a part of the rete mucosum in itself proves nothing. The position and form of the masses which are supposed to identify them with the sebaceous glands are simply the position and form which any luxuriantly growing cell-mass in the papillary layer of the cutis must necessarily assume. Not only is there no direct

transition between a sebaceous gland and a cell-mass figured, but there is no drawing which shows any active change at all in the sebaceous glands. The failure to detect a homogeneous membrane between the cells and the connective tissue is, perhaps, to be attributed to the methods he employed.

But although Thiersch's "Atlas" does not afford positive proof of the origin from the rete mucosum or sebaceous glands, it affords unmistakable evidence to the effect that the cell-growth of rodent ulcer can take its origin in the sweat-glands. He publishes a case* in which transitions were observed from normal sweat-glands to coils with an exaggerated lumen. Nearer to the diseased mass the lumen of the glandular structures becomes scarcely observable, and there is an unbroken transition from these latter to cylindrical and rounded masses of cells without any lumen at all.

That an epithelial growth in the skin may originate in the sweat-glands—(that there is a veritable adenoma of the sweat-glands)—was first shown by Verneuil, who published a remarkable case of this kind in 1854.† In this case the histological characters, so far as they can be inferred from Verneuil's figures and description, have a strong resemblance to those which are distinctive of rodent ulcer.

The results of our own attempts to trace the origin of the neoplasm have been almost entirely negative. But although we have never been able to observe any continuity with the rete mucosum, or hair-sheaths, or sebaceous glands, we have twice, in our own cases,

* In Plate IX., Figs. 1 and 2, of his "Atlas."

† "Archives Générales de Médecine," vol. ii. p. 458.

observed appearances in the sweat-glands that strongly suggest that they afford the first point of departure of the growth. In the cases referred to, the lumen of the gland had become much enlarged, and was filled with a mass of neoplastic cells. The cell-masses of the new growth were not, however, traced in direct continuity with the abnormal sweat-glands.

Cornil and Ranvier, who, under the term *tubular epithelioma*, describe a growth that in its main features can be identified with the neoplasm of rodent ulcer,

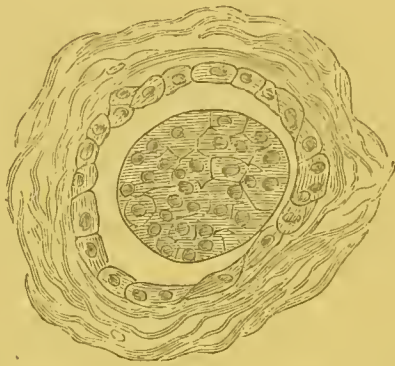


FIG. 8.—SECTION THROUGH A SWEAT-TUBE IN A CASE OF RODENT ULCER OF THE BACK.

Showing the lumen of the tube enlarged, and containing a mass of newly formed epithelial cells of the rodent ulcer type.

state that when this growth takes place in the skin it takes its origin in the sweat-glands; and it is worthy of note that these observers also state that the growth occurs on the trunk and limbs as well as on the face.

The question of the histology of rodent ulcer cannot be left without reference to the excellent monograph of Dr. Collins Warren. This observer has reported on five cases of rodent ulcer. He concludes that the cases of rodent ulcer were forms of epithelial cancer, and that they differed from the forms of epithelial cancer of which cancer of the lower lip is the type,

in the small size of the epithelial cells: so far following Thiersch. He, however, makes statements which receive no support from the cases examined by Thiersch, Mr. Hulke, and ourselves. He found that the cells of the growth have a tendency to form themselves in the centre of the masses into the well-known epidermic balls, and that the edges of the masses were lost in smaller cells of an indifferent character, and this, although he states that "at certain parts of the edges of these cell-structures the cells resemble cylinder-epithelium, reminding one of the shape and arrangement of the epithelium immediately surrounding the papillæ of the skin." "As we approach," he remarks at another place, "the periphery, cells of an epithelial character become fewer in number, and those which predominate here resemble the small round cells which are so frequently found in morbid growths."

No such epidermic balls were to be seen in our sections, nor are they to be found in those figured by Thiersch and Hulke, although in some of our sections partially broken down epithelial structures belonging to the normal tissue (usually the remains of a hair-follicle) at first sight seemed to resemble them. We cannot help thinking that this must be the explanation of the "balls" in Dr. Warren's cases.

Dr. Warren seems further to have been unsuccessful in preserving the well-defined border of the masses, and in distinguishing between the occasional clusters of exudation-cells and the true morbid growth. The limits between the two are, in reality, strictly defined—leaving out of account the occasional leucocytes which are found in and about the membrana

propria,—and there is no such transition in the character of the cells towards the centre of the masses as Dr. Collins Warren describes. With the exception of the columnar border cells, all the others retain a fairly uniform size and appearance until they break down.

ETIOLOGY.

The etiology of the disease is involved in mystery. To speak of constitutional proclivity does not advance our knowledge regarding the point. It is an affection of advanced life, being very rarely seen under the age of forty.* In the greater number of cases it begins between the ages of fifty and sixty, and is somewhat more common between the ages of sixty and seventy than between forty and fifty. It develops in persons who in other respects are in the enjoyment of excellent health.

DIAGNOSIS.

The points in diagnosis between rodent ulcer and syphilis and lupus are the same as those by which epithelioma is distinguished. Syphilis and lupus excluded, the question presents itself as to whether we have to do with epidermic epithelioma or rodent cancer. For those who hold that there is an identity between rodent ulcer and superficial epidermic epithelioma, this question does not exist. But for those who believe that superficial epithelioma is produced by one form of morbid epithelial cell, and rodent ulcer by

* The limitation as regards age is not absolute. We have seen a case, under the care of a friend, in a young woman; and Mr. H. Morris informs me that he has had a case for three years under observation, which began in the fourteenth year of life, and has now (1886) lasted fifteen years.

another, it becomes a matter of much interest to ascertain whether there are any fixed diagnostic signs by which the one form can be definitely, and in all cases, distinguished from the other.

While there are some cases in which the distinction appears to us not to present great difficulty, there are others in which the differential diagnosis between these two forms appears impossible. That greater certainty in making this diagnosis may be hoped for, as an advance of the future, seems probable. In examining sections from so-called rodent ulcers that have come under our observation, we have been struck by the fact that some surgeons have arrived, on clinical grounds in the majority of cases, at the same result to which we were led by microscopical examination. The rodent ulcer of these surgeons presented in sections the appearances which we have described as characteristic of rodent ulcer. Other surgeons have been less fortunate, and it has fallen to our lot to examine microscopically several examples of this disease which were diagnosed by the surgeon as rodent ulcer, but which, on microscopical examination, we found to be typical epidermic epithelioma. We are borne out in our opinion, by surgeons in whose capacity to distinguish the two forms clinically we have great confidence, that there are cases in which a diagnosis is impossible.

It has been laid down by authors that the locality on which the ulcer is found facilitates the diagnosis. Mr. Moore states that whilst rodent ulcer springs up on the free surface of the skin, epithelioma almost exclusively originates where that structure is continuous with the mucous membrane, or on the mucous membrane itself.

Mr. Hutchinson considers that rodent ulcer occurs on the upper part of the face, and ordinary epithelioma on the lower. We have met with facts that do not bear out either of these opinions. We have found rodent ulcer on the trunk, and ordinary epithelioma on the upper part of the cheek. Although it is well known that the upper part of the face is the favourite habitat of the rodent form, it is not so exclusively. Epidermic epithelioma and rodent ulcer may equally occur on any part of the body, although there are certain parts on which one or the other is very rarely found.

The small solid growth in which rodent ulcer frequently originates produces less inflammation in the surrounding tissues—is longer tolerated—than is generally the case with ordinary epithelioma. After ulceration occurs, it usually takes place at first very slowly and very superficially. If the glands become affected, we almost certainly have to do with epithelioma; but if the disease lasts over a longer period of time, and the glands do not become affected, the probability that we have to deal with a rodent ulcer becomes more and more of a certainty. At a later period of the disease the diagnosis is easier. Mr. Moore observes “that there is more solid substance of the epithelioma, and the gaps which it makes by destroying the normal parts, though equally great, are less openly cavernous, than in rodent ulcer; which latter, moreover, after excavating the features, contributes nothing in the way of contraction to close the gap. The extension of rodent ulcer is pretty equal in all directions, except for the inequalities in the edge, from which it bears its name. If

it began in the face, it will therefore remain limited to the face; but epithelial cancer tends downwards, and encroaches on the neck.”

In our description of the disease, and in the various quotations which we have given from very experienced observers, our readers will find indications that will be useful in assisting them to make the diagnosis. But we feel bound to add that, to ourselves, the diagnosis does not seem so easy as it would appear to be from reference to the classical works on the subject. While it seems to us to be beyond doubt that we have two distinct forms of epithelioma producing cancerous ulceration in the skin, and while it appears certain that the gravity of the disease largely depends upon the particular morbid epithelium concerned in the process, and that the typical rodent ulcer can be diagnosed as such, there are cases in which the diagnosis between superficial epithelioma and rodent ulcer is for a time impossible. Probably in the future, when a more accurate knowledge is possessed of the distinguishing histological differences between these two forms, and when clinical and pathological observation are brought to bear on a considerable number of individual cases, diagnostic marks may be discovered which will enable us before excision to tell with greater certainty with what form we have to deal.

PROGNOSIS.

If the disease is allowed to follow its course unchecked by treatment, or if the treatment consists in simply increasing the irritation by insufficient

eauterization, the ulceration will gradually extend. After a time, pain may become a prominent symptom, and as the ulceration extends, vital parts may become involved in destruction. Death is eventually caused by exhaustion or hæmorrhage. In one of the cases reported by Mr. Cæsar Hawkins, the ulcer had existed twenty-five years, and had destroyed a large part of the face, without affecting the patient's health. In other cases the disease has lasted an equal or longer time. In a case in which we examined the ulcer, the affection had lasted forty-three years, during which time it had been continually growing. When removed by Paget, the ulcer covered the whole of the scapula from top to bottom, and from side to side. In this case there was no recurrence. If the ulcer is small, or can be entirely removed, the prognosis is favourable. The disease can be completely removed, and if none of the morbid growth is left, it does not recur.

TREATMENT.

Rodent ulcer should be treated on the principles that have been laid down for the treatment of epithelioma in general. It should be borne in mind that the disease is not the ulcer, but the solid growth that leads to ulceration. If the whole of this growth is removed there is little reason to fear a recurrence of the disease, which may be effectually eradicated. There is no other form of cancer in which a cure may be so confidently looked for, provided the treatment is undertaken in time. The disease is not only a local disease, but remains localized. For a long time

it does not even penetrate the cutis, but slowly extends along the papillary layer, to which its destructive action is confined. As compared with the other form of epithelioma (epidermic epithelioma), there is not only no infection of the lymphatics, but there is no widespread infection of cellular elements in the vicinity of the neoplasm. In epidermic epithelioma, amongst the numerous cells which infiltrate the connective tissue beneath and beyond the borders of the diseased epithelial elements, there are some which have come under the influence of the morbid action, and afford a nidus for a recurrence of the cancerous growths. In rodent ulcer this widespread influence does not exist. The only cellular elements that acquire the power of reproducing the disease are those which are in direct contact with the neoplastic growths. If the whole of these growths are removed, there is no focus of re-infection left. In epidermic epithelioma the surgeon can never be sure that he has removed every diseased element, even when his knife has been carried apparently well beyond the disease: in rodent cancer, so long as the deeper layers of the corium have not been penetrated by the neoplasm, it is possible to remove every diseased element.

Since timely operation is of so much consequence, it is of great importance that the nature of the affection should be recognized at an early stage. If left to itself there is no cure, but there is the certainty of increased destruction. So soon, therefore, as it is evident that we have to deal with a rodent ulcer, or with a growth that contains the elements that will lead to the formation of a rodent ulcer, it becomes our

duty to advise a radical operation. Palliatives or constitutional treatment waste precious time.

The operation that is in every respect most satisfactory is excision. The growth or ulcer should be entirely removed, the knife being carried well beyond the diseased tissues.

In very early stages there is no doubt that a cure may be obtained by scraping out the growth and subsequent cauterization, and this plan may be safely adopted if for any reason excision is rejected. We have not hesitated in very early cases to adopt this method, although on general grounds we still think excision preferable.

Cauterization alone will completely destroy the growth and secure cicatrization, but if caustics are employed they should be used effectually. The indications for their use have been given in our remarks on the treatment of ordinary epithelioma. Potassa fusa, Vienna paste, or chloride of zinc are the caustic agents which will be found most useful. Mr. Moore, whose experience was very large, recommends the chloride of zinc in preference to the others, believing that the temporary wasting of the natural textures adjoining those which its action destroys, tends to exhaust the vitality of any morbid fragments which may remain in them, and thus to diminish the probability of a return of the disease.

In more advanced cases, when the morbid growth has attacked the muscles and bones, the results of treatment are much less hopeful than in the earlier cases. The neoplasm ramifies freely amongst the delicate connective tissue in which the muscular fibres are imbedded, and in the canaliculi of the

bones. Yet even in such cases the results are more hopeful than in ordinary epithelioma. If the surgeon, by the combined use of the knife and caustics (more especially the chloride of zinc), can succeed in removing the whole of the neoplasm, the wound may heal. In such cases the bone itself must be taken away to a depth exceeding that which has yielded to the disease. Where this is possible the subsequent use of a vulcanite mask, to conceal the hideous deformity that results from the destruction of the nose and part of the bones of the face, enables the unfortunate victim to appear amongst his fellows, and to obtain some enjoyment from life.

In all cases in which there is a chance of success the patient should have the benefit of it, and if the neoplasm is known to be of the rodent variety, the surgeon should feel more encouraged to undertake an operation than if he were dealing with an epidemic epithelioma.

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