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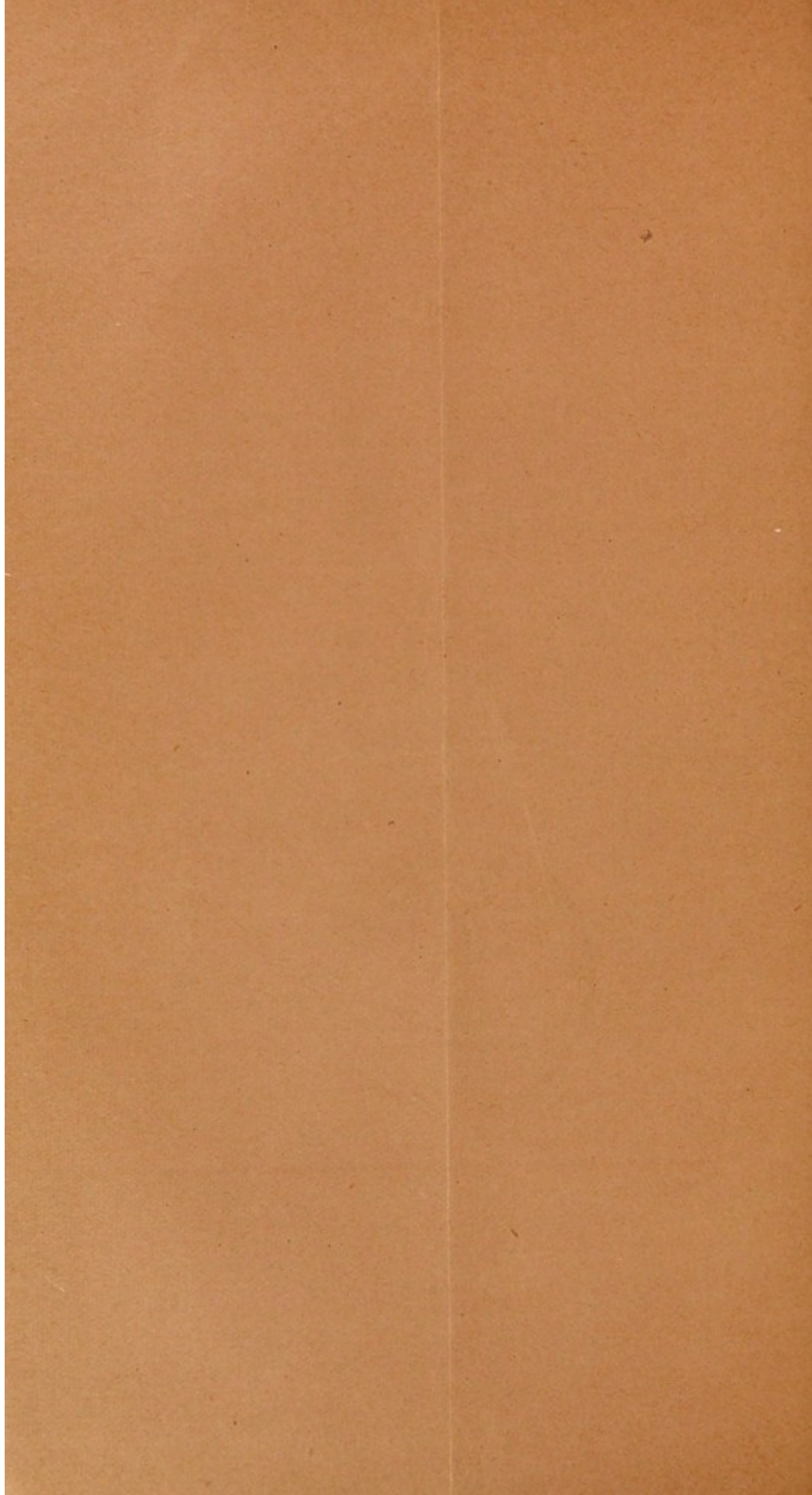
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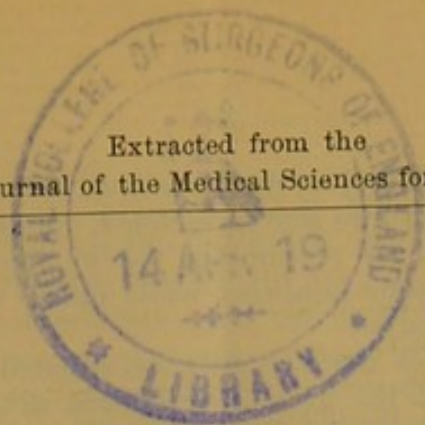
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PSORIASIS—VERRUCA—EPITHELIOMA; A SEQUENCE.¹

By JAMES C. WHITE, M.D.,
Professor of Dermatology in Harvard University.

It is my purpose in this paper to present brief notes of two remarkable cases of disease—cases extraordinary, not for the rarity of the pathological processes they represent, but for the very unusual sequence of tissue-change exhibited in their course.

CASE I.—In 1866, a gentleman, æt. 27, consulted me on account of psoriasis. It had first manifested itself six years previously, and had remained constantly present in some degree up to this date, nearly disappearing each summer, but increasing again in intensity in the winter, in spite of considerable doses of Fowler's and Donovan's solutions, which had been taken from time to time. The disease had not been known in the family in other generations, and the patient's health had otherwise been uniformly excellent. At this time the only portions of the integument affected were the forehead, chest, and arms. The type of the disease was *guttata* and *nummularis*, and the patches presented a marked degree of hyperæmic activity, to such a degree in fact that they were greatly excited by such stimulating applications as Vleminckx's solution, and tincture of German soap and oil of cade, which were at that time employed; and in fact the skin then and subsequently showed itself unusually intolerant of active external remedies, to such a degree that Fowler's solution was again advised as the only hopeful or possible means of relief. The case remained under my occasional observation for ten or twelve years without marked features of interest, but during all this time it retained an extraordinary obstinacy to all methods of treatment, external or internal, which were employed, many of them the new remedies introduced into the materia medica of the disease in that period. The disease in the mean time manifested its own independent vagaries of advance and retrogression, now and then covering large areas of the general surface of the body, but never wholly disappearing from certain localities, as the scalp and backs of the hands.

Ten years ago several of the patches upon the latter parts and the lower forearms especially, began to undergo a change. Their bases became less

¹ Read before the Boston Society for Medical Improvement, November 24, 1884.

hyperæmic, and they themselves more elevated and less scaly, until they were gradually converted into sharply-defined, prominent, firm, and horny outgrowths, some of them resembling the unpigmented formations of keratosis senilis in the same localities, while others were more like callosities or some form of warts.

Three years ago one of these outgrowths, situated upon the right palm near the wrist in one of the great longitudinal dividing furrows of the skin, became excoriated either by abrasion or fissuring, which refused to heal by the simple measures employed, and terminated in a small ulcer. It remained in this condition many months, sometimes nearly filling up and protecting itself with a thin epithelial cover, sometimes breaking down again and remaining in an open, indolent condition, but the destructive process gradually extended more deeply into the cutaneous tissues and widened its borders. After a time the peripheral portions of the integument became indurated and thickened, forming a dense and elevated circumvallation about the central ulceration. During this long period the efforts to restore the part to a healthy condition were persistent and various; at first simply soothing applications combined with restraint to the movements of the part, afterwards more stimulating applications, then cauterizing agents, as chromic and concentrated nitric acids, and later the curette. Finally, as the ulcer enlarged and deepened, so that the integument involved in the destructive process and surrounding induration was one-half inch in area, the whole growth in August, 1883, was deeply scraped. At the same time another lesion identical in history and character, but of much smaller size, which had more recently and gradually established itself upon one of the warty hypertrophies situated upon the palmar fold of skin between the fore and middle fingers of the left hand, was also thoroughly curetted.

These more radical operations were, however, as unsuccessful as the measures previously employed. The wound closed up, and some sort of epidermal covering was established, but the areas primarily affected became the seat of a much more rapidly progressive induration and thickening, so that the integument of the right palm became involved in the process to the extent of more than an inch in circumference, and presented subsequently, at the beginning of this year, at a consultation held by Prof. Henry J. Bigelow, and Dr. R. M. Hodges, under whose skilful and constant surgical care the case had been for a long time, with the writer, a reddened prominence, largely occupying the lower third of the palm, of somewhat uneven surface, in the centre of which a new ulcer had established itself with an everted edge of exuberant fungoid granulations. To the touch the rest of the mass was deeply resisting, except in one or two parts, where boggy-feeling globular elevations the size of a large pea, and somewhat translucent, existed. These had also formed in the neighborhood of the ulcer before the last operation. Upon the other hand, too, the tissues surrounding the seat of the curetted ulcer were becoming rapidly indurated to a much greater extent than previously. The brachial and axillary glands remained unaffected. The parts had been excessively painful for a long time, and the patient's strength was giving way under his suffering and anxiety. His medical attendants had long previously formed an opinion that the disease had become epitheliomatous in character, and were then of the unanimous conclusion that it could be overcome only by thorough removal of the affected tissues. The growth had penetrated so deeply that a radical local excision of the diseased parts

alone was no longer possible, so that amputation of the right hand and of as much of the left as was involved in the diseased process was advised. Before resorting to such extreme measures, however, it was thought advisable by them, considering the rare, or even unparalleled, history of the case, that the patient should have the benefit of the opinion also of certain distinguished dermatologists and surgeons in Europe, and accordingly he proceeded thither in January of this year and consulted Mr. Hutchinson and Sir James Paget, of London, and Professors Kaposi and Billroth, in Vienna.

On his return, after an absence of six or seven weeks, during which he had the personal attention of Dr. G. W. West, the disease was found to have made great advance. The skin of the whole palm of the right hand had apparently become implicated in the process, and the lower half was fully occupied by a deep ulcer with dense, enormously everted edges in a state of flamboyant granulation, encroaching at its inferior part upon the wrist. The ulcer upon the left hand had also extended rapidly, and was assuming the same fungous, exuberant appearance as the other. The patient's general condition had naturally become decidedly worse, for the prognosis had not been lightened by the opinions he had obtained from the eminent professional gentlemen above named, and the affected parts were excessively painful, so that sleep was obtained only by the aid of narcotics. As it was decided by his medical attendants after repeated consultations that nothing was to be gained by further delay he consented to submit to the measures previously advised, and in April last the right hand was amputated above the wrist, and the fore and middle fingers of the left hand were excised through the middle of the metacarpal bones by Dr. Hodges. The wounds healed quickly and properly, and the long-continued sources of mental and physical irritation having been thus wholly removed, the patient regained his old condition of good health, and the tissues bordering upon the former seats of disease have remained in their normal state.

The parts removed were given to Prof. Fitz for examination, who makes the following report: "The palm of the right hand presented an elevated, rounded, ulcerating mass with dense everted edges and irregularly scalloped outline. The surface for the most part was smooth, reddish-gray, and translucent, but showed an irregular deep, sinuous depression at the upper and outer fourth. It measures two and a quarter by three and a third inches, and the mass projected two-thirds of an inch above the cutaneous surface.

"On section the superficial ulcer corresponded with a circumscribed new formation, one and a quarter inches in thickness, extending through the skin and subcutaneous fat tissues to the deep fascia, being intimately united to the tendinous sheaths, which were not perforated. The growth was continued into the substance of the unciform bone and into the abductor minimis digiti. The cut section was in general relatively homogeneous, gray, and translucent. Minute ecchymoses were present near its free edge, and occasional opaque lines extended upwards and outwards from the base. Pressure caused the escape of small, soft, opaque, white plugs.

"The microscopic examination showed that the structure was composed of variously shaped, anastomosing bands of cells, resembling the deeper layers of the epidermis, and separated by a framework of fibrous tissue. The bands contained numerous onion-shaped bodies of laminated epidermoid cells, and extended irregularly in all directions.

"At the palmar base of the fore and middle finger of the left hand was a small, superficial ulcer upon the surface of a dense rounded and flattened nodule, one by one and a half inches in length and breadth, and three-fourths of an inch in depth. The cut section of the nodule showed a gray, slightly translucent new formation traversed by occasional fibres. The growth extended into the subcutaneous fat tissue, and the tendons beneath were freely movable. The structure was like that of the growth on the right hand, though the fibrous portion was relatively more abundant, and in both the characteristic appearances of flat cell, epidermoid cancer were presented."

This case presents, therefore, three distinct pathological affections of the cutaneous tissues; psoriasis, verrucous hypertrophy, and epitheliomatous new growth; not occurring independently of each other, but as successive, mutual transformations in the above order. It is this sequence which constitutes its peculiar features. I cannot find its like recorded in dermatological literature. Psoriasis has in very rare instances developed into warty growths in certain localities; verrucæ, as is well known, not unfrequently degenerate into epithelioma; but no case is on record, so far as my knowledge extends, of psoriasis terminating in cutaneous carcinoma through this or other intermediate transformation. Psoriasis is among the more common affections of the skin, 1924 cases having been recorded in the 58,617 cases of cutaneous disease reported by members of the American Dermatological Association in its combined returns of five years, a ratio equal to 3.28 per cent. It is, therefore, a matter of frequent observation, and no disease of the integument presents a more regular course, a greater uniformity and simplicity of lesions, and a more indifferent relation to the economy as a whole than it. It might have been predicted in every individual case before this, as far as the recorded experience of dermatologists reaches, that the disease could lead to no serious results directly or indirectly.

Let us consider what is the nature of this affection, and what connection there may be between it and the other two processes with which it is so intimately associated in this case. Psoriasis has been generally regarded as an inflammatory process of the skin, and in most works on dermatology it is placed among the inflammatory or exudative affections. Hebra, however, in his latest edition, laid greater stress upon its relation to simple epidermal hyperplasy, and his son, in his recent work—*Die krankhaften Veränderungen der Haut*—describes it as a local epithelial hyperplasy produced by the quantitative increase and qualitative (alienation) change in all the epidermal strata. Dr. A. R. Robinson, of New York, was among the first to recognize the essential anatomical nature of the disease, and to show by thorough microscopical study that it is not primarily an inflammatory affection of the papillary layer of the corium. In the beginning the process is simply one of hyperplasy of the Malpighian layer, and the apparent hypertrophy of the papillæ is the result of the extension

downwards of the newly-formed rete cells, the intermediate papillæ not being elevated above the general level of their tips in the surrounding healthy skin. Later the bloodvessels of the papillæ become dilated, serum and white corpuscles exude, and these conditions with the great increase of epidermal development give rise to the redness and thickening of the skin. The important points established by Dr. Robinson's investigations are that the hyperplasy precedes the hyperæmia, so that any inflammatory phenomena in the tissues of the cutis are to be regarded as secondary and not essential features of the disease.¹ Of the reality and intensity of the inflammation of the cutaneous tissues which not unfrequently accompanies the disease there can be no question. This is of most common occurrence in the early stages of universal psoriasis of rapid evolution, but occasionally accompanies individual cases throughout their course. The dermatitis at times amounts to a true eczema, and often demands special treatment for its relief before the proper and more stimulating applications for the psoriasis can be employed.

Auspitz, in his *System der Hautkrankheiten* (Wien, 1881), has contributed a valuable chapter to our knowledge on the classification of affections of the epidermis, among which he places psoriasis. This seventh class of his system contains the following subdivisions, which in their mutual relations are of especial interest in connection with the cases under our consideration, as shown in the accompanying table:—

7th Class.—Epidermidoses = Anomalies in the growth of the cuticle.

A. Keratonoses = Anomalies of formation of the horny layer.

Family II. Parakeratoses = Quantitative anomalies in the process of cornification.

Psoriasis.

C. Akanthoses = Anomalies of the prickle layer of the epidermis.

Family I. Hyperkanthoses = Simple akanthoma.

Verruca = Warty akanthoma.

Family II. Parakanthoses = Alveolar akanthoma.

Epithelioma. With cornification of the cells of the new growth.)

He recognizes the following anatomical changes as of constant occurrence in *psoriasis*; an increased thickness of the horny layer; certain changes in the stratum granulosum and stratum spinosum indicating more rapid transformation in their development than is natural, as shown by an increase of the nuclei in the deeper layers of the prickle cells and a more abundant granulation in the uppermost, in those undergoing transformation into the true granular cells, together with a more rapid loss of their spines, and a thicker superposition and change in form of the cells of the cylindrical layer; and, finally, an overfilling of the papillary capillaries. He regards the disease, therefore, not as an inflammatory affection, but as an anomaly of the process of cornification of the epidermis, and im-

¹ New York Medical Journal, July, 1878.

perfect transformation, that is, of its cells, so that those of the horny layer do not adhere closely, and form dry and scaly elevations, while the younger, deeper layers are also less adherent, so that the cylindrical layer is easily laid bare above the hyperæmic tips of the papillæ, which bleed readily on such denudation.

In *verruca* we have a quantitative change in the formation of the stratum spinosum, an excessive formation of the prickle cells, extending in some forms far downwards into the corium between the papillæ, thus simulating a marked prolongation or hypertrophy of these bodies. The down-growth of the epidermal cells is always continuous, however, and nipple-shaped in its encroachments upon the cutis. The cornified cells of the upper layers are magnified in quantity in the same proportion.

Whenever this uniformity or continuity of epithelial hypertrophy or new growth is interrupted in its invasion of the tissues of the corium, and the epidermal cells are found seemingly developed in separate foci below the general line of the rete, we have another condition to which we apply the title *epithelioma* or carcinoma. In it the prickle cells are arranged in no orderly manner, but permeate the tissues of the corium in all directions it may be, or congregate in nests or alveoli, taking their origin either from the cells of the epidermis or from their continuations along the glandular structures of the cutis.

We see, therefore, that these three dermatoses which enter into the clinical history of our case, and which are in their nature apparently as unlike as their companionship is rare, have a close affiliation in their anatomical relations. The transformation of patches of psoriasis into horny or warty permanent growths is not referred to in most works on dermatology as of possible occurrence even; the transformation of verrucous growths into epithelioma is of not very infrequent occurrence; but the sequence followed in our case, psoriasis—verruca—epithelioma, is extremely rare or unparalleled in dermatological history. Milton says¹ "there is a form of wart so like lepra,² or of lepra so like wart, that I am at a loss to know which it is," and in one of the three cases observed by him the growth "began as lepra-spots;" and Gaskoin³ states that "psoriasis often displays a condition which shows a near approach to warts."

With the difficulty of distinguishing palmar psoriasis at times from syphiloderma of this part, the resemblance of these secondary callosities to the latter, or the syphilide cornée of French writers, is worthy of special mention in connection with our case. To one who had not observed the disease from its early manifestations and watched the local changes above referred to step by step, the appearances of the hands alone, while the disease was in a quiescent state as far as the general surface was

¹ Pathology and Treatment of Diseases of the Skin, London, 1872, p. 329.

² The word lepra is here used in the British sense, synonymous with psoriasis.

³ On the Psoriasis of Lepra, London, 1875, p. 87.

concerned, might have suggested the question of their syphilitic character. They were, however, well marked horny concretions, rising above the general surface in the form of prominent, more or less conical elevations. They had not that appearance of being embedded or encapsuled in the skin, as if they could be easily enucleated, nor were they seated upon a hyperæmic base or surrounded by a scaling ring or wall-like edge. They were in reality, what close observation and their history demonstrated, horny concretions, true warty growths springing up from the seats of old patches of psoriasis. In other words, a long-continued process of modified epidermal formation had upon parts spontaneously prone to such development transformed itself into a permanent hypertrophy of the same cell tissue.

The subsequent change is of far less uncommon occurrence, that namely of so-called benignant epidermal growths into those entitled malignant. Epithelioma may follow simple prolonged inflammation of the cutaneous tissues, as in the so-called Paget's disease of the nipple, or protracted granulation formation, as in the exuberant outgrowths of elephantiasis, chronic ulcers of various origin, in lupus, old fissures of the lip and elsewhere, etc.; but even in these cases, where the primary disease is seated in the deeper layers of the skin, the epidermal tissues become involved in the perverted development only after prolonged efforts to reproduce themselves in proper place and form. It is, however, in the course of affections of the epithelial structures of the skin that this malignant transformation is most frequently observed. The most common starting point of epithelioma of the face in all its clinical varieties from the flat, superficial forms to the "rodent ulcer," or stages of deep penetration, is that very frequent condition of imperfect epidermal formation after middle life called keratosis senilis. The cutaneous horn, the sebaceous cyst, both modifications of the epithelial structures, may eventually, as is well known, undergo transformation into this disease, and, to approach more closely to the anatomical conditions in this case, the pointed condyloma and the ordinary verruca, essentially identical in structure and primarily an epidermidosis rather than a papilloma, may also terminate in it. Epithelioma of the skin may be said not only to follow all these affections above described, but to rarely occur without some similar precedent process.

In this instance two factors may have been operative in the development of the final condition, not only the verrucous hypertrophy with the possibilities of epitheliomatous transformation essentially incident to it, but the prolonged ulceration and granulation of the cutaneous tissues, which may at first have been simply the expression of futile reparative efforts in a part of less vitality than the surrounding structures and terminating in a perversion of cell development. Whether one or both of these agencies were active and just when the epitheliomatous transforma-

tion was established in this case, cannot be definitely determined. Eventually there were observed, in addition to the slowly progressive infiltration and destruction of the surrounding tissues, the development of encysted centres of secondary metamorphosis (colloid) beyond the visible bounds of the disease, and finally a most rapid outburst of exuberant fungoid outgrowth.

Thus we have established an uninterrupted sequence of psoriasis through verruca into epithelioma, or, in other words, psoriasis as a cause of carcinoma. Of so serious a termination of so common an affection I could find no record, and believed that the case would remain in my experience, as long in the future as in the past, unique.

CASE II.—On the first of August of this year a gentleman, fifty-two years old, consulted me on account of a sore upon his hand of several years' duration. He showed me an ulcer occupying the anterior surface of the right wrist, extending slightly into the palm of the hand, about two inches in length and one and a half inches in transverse diameter. It was surrounded by a very prominent and indurated border, extending deeply beneath the skin, and was very painful. I noticed at the same time upon his forehead several small, slightly elevated patches, red and covered with thin scales, and upon the hands and fingers a considerable number of horny, wart-like growths. I immediately recognized that I had before me one of those extraordinary coincidences of the simultaneous occurrence of disease of extreme rarity. Here was again a patient who presented general psoriasis, warty growths upon the hands, and unmistakable epitheliomatous disease. What was their connection in this case? I found that he had had psoriasis nearly constantly since early manhood, and had tried various methods of cure, including arsenic, mostly in vain as far even as temporary results. Some ten years ago several of the chronic patches of psoriasis upon his hands began to assume a thickened, horny appearance, and transformed themselves into true warty outgrowths. Some time since one of these upon the palmar surface of the wrist softened and became a sore, which could not be made to heal, and gradually developed into its present condition in spite of repeated efforts to cure it by caustics and scraping.

Such was the history in brief of the ulcer. In addition, one of the warty formations between the fingers was beginning to soften, and revealed on pressure a boggy consistence. There were also a small, prominent, ulcerating patch upon the inside of the buttock near the anus, and two small excoriations covered with crusts of doubtful character upon the penis and in the groin, none of which were of long duration. The general surface presented a sparsely scattered psoriasis of *guttata* variety. The patient was somewhat feeble from the suffering caused by the disease in the palm. There was no affection of the brachial glands. He was advised to have the diseased tissue removed by thorough excision, and for this purpose he entered the Massachusetts General Hospital, under the care of Dr. R. M. Hodges, who had seen the patient with me, and recognized the remarkable identity of the case with that first reported. Dr. Hodges has kindly prepared the following account of its subsequent history: "The operation performed on Mr. —'s wrist, August 18th, was an excision of the diseased tissues, without regard to the extent of surface sacrificed, or the depth or character of the parts involved. This extent

represented superficially the area of a circle two and one-eighth inches in diameter, and in depth penetrated to the flexor tendons and the anterior surface of the carpal bones. The ulnar artery and nerve, the palmaris longus tendon, portions of the muscles of the thumb and of the little finger, and the anterior annular ligament were divided or removed. The patch near the anus was also dissected out. September 12, a necrosis of the tendons and fasciæ along the ulnar side of the forearm, which had slowly taken place, required an incision and the removal of the dead tissues. The healing processes following these two operations having been nearly completed, the patient, without apparent reason, on September 18th, suffered sudden and extreme pain at the inner side of the upper arm. On the 20th the red lines of a lymphatic inflammation were visible, the axilla gradually became swollen and infiltrated without any focal centre, and a deep cellulitis with grave constitutional symptoms developed itself. In spite of free incisions and active supporting treatment, the patient's strength gave way, and on October 4th death occurred from exhaustion. It is needless to say that from first to last, the most painstaking antiseptic dressings were used." This unfortunate termination had, of course, only an incidental connection with the operation, which promised to be as successful as that in the first case.

An examination of the tissues removed by excision was made by Prof. Fitz, who furnished the following report: "The specimen was characterized by the presence of large masses of epithelioid cells of irregular shape and size, separated by narrow bands of fibrous tissue, and extending deeply downwards into the subcutaneous fat tissue. The appearance and grouping of the epithelioid cells suggested that all the epithelial constituents of the skin were involved, rete and epidermis, hair and sebaceous follicles, likewise the sweat glands. An atypical new formation, simulating the last-mentioned structures, with a central cavity, was abundantly present in the main tumor. The smaller nodule (from anal region) of more superficial growth simulated in its new formation rather the other cutaneous structures.

"A comparison of the specimens from the two cases showed a marked difference of composition. That from Case I. presented an abundant, dense, fibrous stroma, with narrow and sparse anastomosing bands of small, round epithelioid cells. The shape, size, and junction of these bands directly suggested the distribution of the lymph-vessels of the skin. Indeed, the question directly arose, whether the new growth may not have affected primarily the lymphatics, representing what has been called catarrhal lymphangitis. The specimen from Case II. showed an abundant, luxuriant growth of large epithelioid cells with but a scanty fibrous stroma between the masses. Epidermoid pearls were numerous in the small nodule, and cavities of considerable size with irregularly projecting and abundantly cellular walls suggested the dilatation, as well as new formation, of an adenoid structure resembling the sweat-gland."

[During the preparation of this paper for the Society, I discovered in *Ziemssen's Handbuch*, Band xiv. (Hautkrankheiten), a reference to a case, the following brief account of which is published in the *Gaz. des Hôpit.*, 1878, p. 750. Dr. Cartaz presented to the Anatomical Society the report of a healthy man, 40 years old, who had never had any other disease excepting a psoriasis, which began twenty-three years previously,

and had invaded among other regions the palms and soles. In consequence of scratching, the scales upon one of these processes, situated upon the palmar surface of the second phalanx of the ring finger of the right hand, was removed, and there remained a little ulceration, which gradually extended to the size of four centimetres. The callous borders and the deep-seated granulations, bleeding at the slightest touch, established the diagnosis of *cancroide*. Amputation at the metacarpo-phalangeal joint was performed, and there was no return of the disease.

Although no mention is made in this very brief report of the intermediate formation of warty growths, there can be no doubt at least of the close resemblance of the case to those above reported in the connection of its initial and final processes, probably none of its complete identity.]

We have thus the record of three cases of psoriasis terminating in carcinoma of the cutaneous tissues. There are no peculiarities in the history or character of the primary dermatosis in the first two, at least, to suggest even an explanation of so rare and grave a transformation of process. Innumerable cases of as long duration and intractable type occur with no such termination, and it is unlikely that psoriasis is capable of such a direct change. The lesson to be drawn from their study is, that the transformation of patches of psoriasis into verrucous hypertrophy must be regarded as an ominous occurrence, and that the softening or other change of such horny growths demand thorough excision without delay.

