The title "Metastasis of a Basal-cell Epithelioma" might be considered a "contradiction in terms," as absence of metastasis is generally considered one of the cardinal characteristics of basal-cell epithelioma. Sutton (1) defines basal-cell epithelioma as "a comparatively benign variety of carcinoma of the skin which probably develops from the basal layer of the epidermis or from the skin glands, does not metastasize, and is composed of small, deeply staining cells of various forms." Delafield and Prudden (2) state that "lymph glands are seldom involved by basal-cell epithelioma, and if so, there is a change in the structure of the growth." Hazen (3) advises that "all surgeons should become familiar with this class of tumors, for they do not metastasize and hence it is not necessary to remove the adjoining lymph glands. When glandular involvement is spoken of as occurring in this group of tumors, it is probable that there is an error in diagnosis and that the growth is really of cuboidal cellular origin." This view is shared by H. Montgomery (4), who says that "careful examination will prove practically all such metastatic tumors to be either transitional or squamous-cell in character."

Several cases of metastasis of this transitional or basal-squamous-cell epithelioma have been reported, and a small number of cases of pure basal-cell epithelioma in the original growth, with the mixed type or pure squamous-cell epithelioma in the involved gland, are on record. A thorough search through the literature has revealed only five histologically proved cases of metastasis of a pure basal-cell epithelioma in which both the original growth and the metastasis were of pure basal-cell type.

The first case of this kind was reported by Beadles (5) in 1894.
His patient was a man aged forty-six, who died from septic pneumonia due to absorption of discharge from a rodent ulcer of the face. A gland the size of a pea, in the submaxillary region, removed at autopsy, showed one-third of its area involved by a new growth of epithelial masses resembling glandular carcinoma, showing no "cell nests" or keratinoid changes and separated by fibrous stroma. Janeway (6), in 1910, had a patient with a primary tumor involving the skin of the bridge of the nose. After various forms of therapy and recurrences for seventeen years, a new tumor developed under the mucous membrane of the hard palate. Both tumors on histologic examination showed typical basal-cell epithelioma.

Körbl (7), in 1912, reported a case (Case 61) of rodent ulcer developing from a seborrheic keratosis, on the right temple of a woman of sixty-six. Biopsy showed a typical basal-cell epithelioma. In two months, following eight x-ray treatments, the tumor was completely healed. One year later no evidence of local recurrence or glandular metastasis was noticed, but five months after this the patient returned with a massive glandular swelling under the jaw, involving the entire length of the right sternomastoid muscle and the supraclavicular space, without any change at the site of the original growth. The tumor was inoperable. Within three months it had grown from a small pre-auricular gland to its present size. Histological examination of a section from beneath the scar tissue and from the swollen glands showed a basal-cell epithelioma completely identical with that found in the biopsy from the ulcer before radiation.

Finnerud (8), in 1924, reported two cases of basal-cell epithelioma of the face with metastasis to the submaxillary lymph glands. One of these was the first case reported showing cyst formation in epithelial clusters in a gland. Finnerud's first patient was a man thirty-nine years of age, with a tumor on the left side of the face of thirteen years' duration. This had recurred three times in spite of excision and two temporarily successful x-ray treatments, and at the time of the last recurrence a hard nodule the size of a pea was palpable in the left submaxillary region. A second gland, the size of a walnut, fluctuating and cystic, appeared three and one-half years later, and a third gland of the same type appeared one and one-half years after this. Histologic examination of a section from a recurrent nodule in the face lesion showed basal-cell epithelioma in branching tubular processes separated
by dense, fibrous tissue, marked round-cell infiltration, acanthosis, and slight parakeratosis in the epidermis. The cells had heavily stained, large nuclei and little protoplasm. There were no prickle cells. Histologic examination of each of the three glands involved showed the same picture, with the addition of a successively greater amount of cyst formation and tendency to necrosis of the epithelial masses.

Finnerud's second patient was a man aged fifty-six, who had had a tumor on the right cheek and upper lip for thirty years, which had been unsuccessfully treated by excision, x-ray, and radium. He had also a nodule in the right submaxillary region. Histologic examination of a section from this nodule showed islands of basal-cell epithelioma in the lymph glands and strands of similar cells invading the adjacent fat and connective tissue. A section previously taken from the tumor of the face gave the same histologic picture except for a greater amount of intervening fibrous tissue.

I have found four additional cases of possible but, in my opinion, not proved metastasis of a basal-cell epithelioma. D. W. Montgomery (9), in 1898, reported the case of a woman fifty-six years of age, with a superficial epithelioma of the bridge of the nose near the right inner canthus, which was twice excised. Eight years after the second excision a pre-auricular and three submental lymph glands enlarged. The patient died eighteen months later. A drawing of the section of the nose lesion resembled basal-cell epithelioma but was not stated to have been such and may have been a mixed type of tumor. No section was taken of the metastases.

Dubreuilh and Auché (10), in 1901, had a patient with a deep ulcer in the center of her face. Twelve ganglia with wrinkled and retracted overlying skin, suggestive of scirrhous carcinoma of the breast, later developed on the face and neck. No histologic report of the case was given.

Fordyce (11), in 1902, reported the case of a patient sixty years of age, with a rodent ulcer of ten years' duration on the side of the nose, extending to the inner canthus, and another lesion behind the ear, which had been improperly treated, with recurrence in the scar. The lymph gland near the mastoid on the same side was enlarged, and histologic examination of both the lesion in the derma and the lymph gland showed typical embryonic epithelial processes separated by fibrous stroma. The involve-
ment of the lymph gland in this case appears to me to have been
due to the effects of trauma from the incomplete operation and to
local extension of the lesion rather than to metastasis.

Marassovich (12), in 1910, saw a man sixty-four years of age
with a flat tumor, the size of a dime, in the right ala nasae, of three
years' duration. A few months later a hard tumor, the size of a
bean, appeared on the lower lip, which soon ulcerated, with en-
largement of the retro-mandibular and submaxillary glands. The
ulcer clinically resembled basal-cell epithelioma. This and the
glands were excised, and no recurrence was noted four and one-
half years later. No complete pathological report was given with
this case. The evidence here is very weak, especially on account
of the rarity of basal-cell epithelioma of the lower lip.

REPORT OF A CASE

T. E., a white American, a chauffeur, aged thirty-seven and single,
entered the New York Post Graduate Skin Clinic Sept. 9, 1927. His
family history showed nothing especially significant. His father, sixty-
two years of age, was well except for dyspepsia of several years' duration.
His mother had died at the age of fifty-eight, of Bright's disease. There
was no history of cancer or tuberculosis in the family. The patient had
always been in excellent health until the onset of the present illness.

Fifteen years earlier (1912), a slightly scaly area, the size of a pinhead,
had appeared on the radial side of the proximal phalangeal joint of the
patient's right ring finger. The scale was thin, white, and shiny and
dissolved readily in water, but soon reappeared. There were no signs of
inflammation nor any subjective symptoms. Nothing further was
noted for five years. After this time a small crack occasionally appeared
in the scale, through which minute quantities of pus and blood oozed.
About ten years after onset, a salve containing some strong acid was
applied. This produced severe itching, frequently disturbing the
patient's sleep, and gradual extension of the lesion toward the knuckle
was noticed. Three years later a warty growth the size of a pea, appeared
above the scaly patch near the knuckle, and an ulcerated area developed
in the intervening space. After a year the itching ceased, and the
affected area became red and tender, followed by a purulent discharge.
Motion of the distal joints became more and more limited, ending in
complete ankylosis.

On Aug. 15, 1924, the patient visited the Cornell Skin Clinic. At
this time he presented a painless, infiltrated area 2 x $\frac{3}{4}$ in. in diameter
on the outer side of the base of the right ring finger. This was slightly
nodular at the base and had shallow indolent ulcerations. No other
lesions were found. A tentative diagnosis of dermatophytosis or tubercu-
losis verrucosa cutis was made and full strength Whitfield's ointment
was given. This application irritated the lesion and caused bleeding
in the center of the crusted area, so that a half strength ointment in
conjunction with wet dressings of *eau d'Alibour* was prescribed, bringing about slight improvement. The presence of a superficial ulcer with a granulating center aroused a suspicion of syphilis, and a Wassermann test was done, which proved negative. A biopsy was performed on Oct. 17, 1924, and histologic examination by Dr. J. Frank Fraser showed a basal-cell epithelioma originating from the inner sheath of the hair shaft (Huxley's layer) (Fig. 1).

On Dec. 1, 1924, Levin (13) presented this patient, with a diagnosis of basal-cell epithelioma of the finger, before the Section on Dermatology of the New York Academy of Medicine. He showed a superficial, flat ulcer, 3 in. long, and 1½ in. wide, between the base of the right ring and middle fingers. The lesion was bright red, moist, sharply defined, tender on palpation, and fixed to the underlying tissues and bone. The proximal part was stony hard. There was some scarring.

Surgical diathermy or, preferably, amputation was advised, but the patient left the clinic before either procedure could be performed. Later he received four or five intensive roentgen-ray treatments from a private physician and used various salves prescribed by druggists, without any improvement in the lesion.

On April 11, 1926, the patient entered the surgical service of Dr.
Moorehead at New York Post Graduate Hospital with a red, raw, indurated area with a white margin, on the radial side of the right ring finger, and ankylosis of both interphalangeal joints. Physical examination was negative except for the local condition. A diagnosis of lupus vulgaris was made, and amputation at the metacarpophalangeal joint was done.

Histologic examination by the general pathologist showed a basal-cell epithelioma originating in the skin and deeply invading the tissue on the flexor side of the finger. There were irregular nests of basal-cell epithelioma composed of slightly cornified basal cells, some of which had degenerated nuclei with chromatin granules and mitotic figures. The stump healed completely eleven weeks after operation. A roentgenogram of the right hand and arm was entirely negative.

On Sept. 1, 1926, the patient again entered the surgical service of Dr. Moorehead at New York Post Graduate Hospital, complaining of a painless swelling in his right axilla, which had gradually increased in size, beginning three weeks after amputation of the finger. The physical examination was entirely negative except for a hard, movable, nontender, non-inflammatory, fairly uniformly outlined swelling, the size of a chestnut, in the right axilla. This was removed surgically and the histologic report of the general pathologist, Dr. Ward J. MacNeal, was "advanced metastatic squamous-cell carcinoma."

Eight months after the amputation of the finger the stump broke open and began to ulcerate. The wound was dressed in the New York Post Graduate Hospital Fracture Clinic for six months, but failed to heal, and on Sept. 6, 1927, the patient was transferred to the skin clinic, with a diagnosis of tuberculide. At this time he showed an indolent, granulating ulcer, the size of a quarter, at the site of amputation, and was given a 1 per cent balsam of Peru ointment and two erythema doses of Grenz rays to the palmar surface of the lesion. A mild reaction occurred two weeks later, and another erythema dose of Grenz rays was administered. On Oct. 4, 1927, three elevated, dime-sized, violaceous, sarcoid-like nodules developed on the flexor surface of the middle of the right forearm (Fig. 2). A month later sections were taken from two of these lesions, and microscopic examination of the tissue showed typical basal-cell epithelioma. Four and two-thirds erythema doses of Grenz rays during the following month failed to cause any change in the arm lesions, nor did seven and one-half units of Grenz rays affect the ulcerating stump of the finger. The nodules on the arm enlarged and became bright red but were never painful. Three more nodules appeared, which were also histologically basal-cell epitheliomas.

Dr. David Satenstein examined the section from the excised gland which the general pathologist had diagnosed as "advanced metastatic squamous-cell carcinoma" and reported "metastatic basal-cell epithelioma" (see histologic examination), although others who examined the section thought that an undifferentiated squamous-cell carcinoma should be considered.

The right axilla had been swollen since three months after the gland was removed. This swelling now increased, and the arm and forearm...
also became swollen. The patient was given two deep roentgen-ray treatments, one month apart, to the anterior and posterior surfaces of his axilla and chest without any reduction of the swelling.

On March 15, 1928, he entered the same surgical service of the New York Post Graduate Hospital for the third time, complaining of swelling of the right axilla, arm, and forearm, of fourteen months' duration. Physical examination revealed several hard, adherent, immovable masses in the right axilla, with marked pitting edema of the arm and forearm. Histologic examination of the glands showed an atypical squamous-cell epithelioma. The arm finally became so swollen that it could not be raised, and there was throbbing pain in the right axilla.

On May 8, 1928, Dr. J. J. Eller (14) presented this patient before the Manhattan Dermatological Society. At this time his right arm was very much swollen, but he seemed better after having received deep radiation to the chest, neck, and axilla. In the discussion Dr. G. Frank Fraser said that only five cases of metastasis of a basal-cell epithelioma had been reported and that the present case might be of the undifferentiated type of epidermoid carcinoma, but the histologic picture suggested basal-cell epithelioma, although the location was unusual.

Dr. George M. MacKee said that 12 to 15 per cent of sections of basal-cell epithelioma show keratinization and prickle cells, and that these should be classified by the highest type of cell present. Dr. Oulmann had seen a patient with a squamous-cell epithelioma on the hand, and flat, red, basal-cell epitheliomas on the arms, and also a patient with a basal-cell epithelioma of the skin and a squamous-cell epithelioma of the glands. He stated that in the present sections the epithelium was intact and that the tumors might be from glandular structure.
In June 1928, the patient was referred to the Memorial Hospital, where an intrascapular thoracic amputation was done, and the wound healed in two months. A roentgenogram of the chest, taken before the amputation, was entirely negative. In October 1928, Dr. Eller again presented this patient before the Manhattan Dermatological Society and reported that the right arm had been amputated the previous June and that histologic examination of the tissue revealed mixed basal-cell and squamous-cell epithelioma. The skin lesions and some of the glands showed true basal-cell epithelioma, while other glands gave a histologic picture of typical squamous-cell epithelioma. Dr. James Ewing had examined the sections and said that undifferentiated cells were present. The patient had gained fourteen pounds from June to October 1928.

Following this last operation the patient went along comfortably until February 1929, when a metastatic node, which was infiltrating beyond its capsule and was broken down in the center, appeared in the right supraclavicular fossa. No other nodes appeared to be involved. The affected area was radiated, and a wide removal was done, leaving a clean surgical field. The tissue showed an epidermoid carcinoma. On Dec. 6, 1929, Dr. Eller presented the patient and demonstrated a slide...
of a section from the axilla before the Atlantic Dermatological Conference in New York City. In the discussion, Hazen stated that in over 800 cases in Bloodgood's pathological laboratory only one case of metastasis of a basal-cell epithelioma to a lymph gland was found. Dr. Fraser considered the tumor of basal-cell type, arising from sweat duct epithelium, and he could find no histologic evidence that the section was from a lymph node. Weidman agreed with Fraser and thought that the whorling tendencies in some of the nests indicated pearly traits, although no true pearls were seen.

FIG. 4. HIGH-POWER MAGNIFICATION OF AREA IN FIG. 3, SHOWING WHORL ARRANGEMENT OF NEOPLASTIC CELLS AND SPINDLE-SHAPED CELLS WITH ELONGATED NUCLEI AT THE MARGINS OF SOME OF THESE FOCI

Many mitotic figures, but no prickles, are seen.

Since the patient's admission to the Memorial Hospital many sections had been taken. These varied greatly, depending upon the location of the tissue examined. Some showed epidermoid carcinoma of adenoid basal-cell type, others a plexiform basal-cell structure, and some a plexiform squamous carcinoma, Grade II. The histologic course continued, as at the onset, to show these wide variations in structure.

The patient made favorable progress for a while, but the supraclavicular node recurred. Repeated efforts were made to control this local recurrence, but a few months later the patient developed secondary involvement of the chest, and died on Jan. 20, 1930.
Histologic Examination

Dr. David Satenstein of the New York Post Graduate Hospital examined the sections and gave the following report:

"Lesion from forearm (Fig. 3), tissue submitted with clinical diagnosis of sarcoid, Oct. 4, 1927: Throughout the entire cutis there are variously sized and shaped foci of cellular elements. They are in no relation to the vessels or to any of the appendages of the cutis. There is very slight inflammatory reaction about these cellular masses. The remaining cutis is unaltered, and the epidermis only shows changes due to stretching. The cellular masses apparently have no connection with the epidermis.

"These foci are composed of cells containing vesicular nuclei similar to those of the basal cell layer of the epidermis (Fig. 4); for the greater part the cell body cannot be seen. Within these foci are numerous whorl formations. At the margin of some of these foci the cells are arranged in layers; the nuclei are elongated and the outlines of the cell bodies are spindle-shaped. There are spaces between these spindle-shaped cells, but no prickles are to be seen. In various parts numerous mitotic figures are present. While there are numerous portions of this

Fig. 5. Axillary Tissue, Showing Sharply Outlined Cellular Masses in Dense, Cellular Connective Tissue

Note cavities containing cellular débris in center of some of these masses. No lymphoid structure visible.
section suggestive of prickle-cell epithelioma, taken altogether it should be considered as a basal-cell epithelioma of the intermediary type.

"Nodular lesion of forearm very close to location of section just described, tissue submitted Nov. 1, 1927, for corroboration of diagnosis of first piece of tissue: The features of this tissue, as far as the cytology is concerned, are identical with those shown in Fig. 4, but mitotic figures are more numerous. The cellular masses are somewhat small, widely spread in the upper portion of the cutis; some extend down to the fat. Similarly,

FIG. 6. HIGH-POWER MAGNIFICATION OF AREA IN FIG. 5, SHOWING FOCI COMPOSED OF MANY Densely Packed Cells with Ill-defined Outlines and Vesicular Type Nuclei

There are many mitotic figures, but no whorl nor pearl formations. Note intact margin of cellular masses, consisting of flat cells with spindle-shaped nuclei.

in this tissue, there is no other change in the cutis aside from a moderate inflammatory reaction in the upper cutis. Diagnosis similar to that of previous specimen.

"Tissue from axilla, March 15, 1928 (Fig. 5): Within a densely cellular fibrous stroma are irregular, large and small, sharply margined, cellular masses. There are no connective-tissue elements between the cells comprising the masses. In the center of some of these masses are cavities containing broken down cellular elements.

"These foci are composed of densely packed cells; the nuclei are all of the vesicular type and vary in size; the outline of the cell body is
difficult to establish. At various points there are groups of two to five nuclei within a single cell. Some of these nuclei have become hyalinized. At various points are mitotic figures. In a few places the outlines of the cells can be definitely seen, especially at the margins of the masses, but nowhere can definite prickles be established. There is very little tendency toward whorl formation and nowhere is there any pearl formation (Fig. 6). Diagnosis: Metastatic deposit in the axilla. Basal-cell epithelioma of the intermediary class.

"Remark: There is nothing definite in this tissue except for a few isolated spots that would justify the diagnosis of a prickle-cell epithelioma or that there is a transition from a basal-cell epithelioma to a prickle-cell epithelioma."

**Comment**

In this case we have an illustration of the fact that a basal-cell epithelioma should not be regarded as a harmless lesion. It is always potentially dangerous because of its ability to assume a malignant character and metamorphose to the squamous-cell type. The types of epithelioma intermediate between the established basal-cell and spinal-cell have been much neglected, and little is known about them, probably largely because of their relative rarity. Jadassohn (15) says: "Between basal-cell and spinal-cell epitheliomas are mixed forms, in which the two histological characteristic pictures exist side by side, and the intermediary forms, in which the cells are neither typically basal nor typically spinal. These non-classical forms incline more to the basal-cell type but are more malignant and resistant to radiotherapy."

In discussing the mixed and intermediary prickle-cell epithelioma, Darier and Ferrand (16) state that this epithelioma shows a mixture of characteristics of prickle-cell and basal-cell types clinically and histologically; is not rare; and comprised 15 per cent of their group of prickle-cell epitheliomas. It occurs especially on the face, but may involve any part of the body. It may remain stationary for years and then suddenly grow rapidly and possibly involve the lymph glands. It responds poorly to radiotherapy. Darier (17) was the first to describe the so-called "metatypical" type of epithelioma and said that it comprised 10 to 15 per cent of all epitheliomas. These epitheliomas resemble the basal-cell type and may remain quiescent for years and then involve the lymph glands. Histologically there are two types, in both of which there are some features of both basal-cell and prickle-cell epithelioma.
That this type of epithelioma sometimes metastasizes is shown by the following cases: At the meeting of the Manhattan Dermatological Society on Oct. 11, 1922, Oulmann (18) said that he had had a patient over seventy, with numerous sebaceous warts showing carcinomatous degeneration, who developed glandular metastases showing basal-cell as well as squamous-cell epithelioma.

Ormsby (19) presented before the Chicago Dermatological Society a man aged seventy-seven, who had an eruption of twenty-four years' duration. This consisted of ten plaques of various sizes situated on the neck, chest, back, and dorsum of the left hand. The largest was on the right shoulder and measured $10 \times 30$ cm. This was erythematous, scaly, and crusted, and contained in the center a vegetating, crusted mass the size of a hazelnut. The eruption had always before been treated as psoriasis. In November 1925, this patient was again presented. Nine plaques were practically cured with roentgen ray and carbon dioxide snow. Histologic examination of the vegetating lesion in the center of the big patch showed marked dyskeratosis, and sections from other plaques showed some characteristics of prickle-cell epithelioma. Metastases had occurred in the axilla and upper chest cavity, and the arm and forearm were hard, swollen, and painful. The interesting point was that from a superficial patch of twenty-four years' duration a nodule developed and metastasized. It was agreed that many years' irritation of a basal-cell epithelioma may cause it to simulate a spinal-cell epithelioma, and that cancer is a biological reaction to many forms of irritation. It was assumed that mutation of cell type had occurred in this case. There was present nuclear division, usually associated with basal-cell growth, and amitosis, as well as indirect cellular division.

One must also consider epitheliomas of sudoriparous origin, to which class Dr. Fraser considers this case belongs. According to Crosti (20), these tumors are rare and can be diagnosed only by thorough study of their histologic structure. They usually develop spontaneously, or after slight trauma, as a small, slowly growing nodule; rarely ulcerate; and may cause a lymph metastasis and death.

The histologic picture is polymorphous, with tubular or cystic cells predominating and basocellular and spinocellular cells present, and is characterized by frequent hyaline and mucous degeneration of the cells and the deep site of the mass, with no relation to the epidermis, hair follicles, or sebaceous glands. The tubular or tubulocystic epithelium at times recalls hydro-adenoma.
Diss and Peterschmidt (21) reported a tumor occurring on the lower eyelid of a man aged sixty-seven, which showed cells of the type and arrangement of sweat duct epithelium, and Hufschmitt and Diss (22) described a tumor in the scalp composed of cells of sweat duct origin. Bechet (23) presented a patient showing a squamous-cell epithelioma superimposed on a pre-existing basal-cell epithelioma. The occurrence of intermediary types can rule out this rare possibility in the present case. Histologic examination of two sections of the original growth showed only basal-cell epithelioma, although the slight cornification of the basal cells in the second section might be regarded as the earliest sign of the subsequent gradual transition to the prickle cell type. The histologic structure of the nodules on the forearm was that of basal-cell epithelioma and the feature most suggestive of prickle-cell epithelioma was the tendency toward whorl formation. The malignant activity of the neoplasm was evidenced by the numerous mitotic figures.

In the tissue from the axilla the microscopic picture more closely resembled that of squamous-cell epithelioma, on account of the hyalinization of many of the nuclei and the large number of mitotic figures, although even here no prickles nor pearl formations could be found. In the tissue obtained at the time of amputation some areas still showed only basal-cell epithelioma although most of them showed both basal-cell and squamous-cell epithelioma or only squamous-cell epithelioma. In the supraclavicular gland metastasis, squamous-cell epithelioma alone was present.

In this case a mutation of cell type, possibly caused by long continued irritation, probably occurred. It is significant that a lesion starting as a basal-cell epithelioma and remaining inactive for many years can suddenly assume malignant character and cause death in three years through metastasis.

**Summary**

1. Metastasis of a pure basal-cell epithelioma as such to a lymph gland is an extremely rare event, and only five instances have been reported.

2. A basal-cell epithelioma may change to a basosquamous epithelioma and metastasize in this form or as a pure squamous-cell epithelioma.

3. A case is reported of a pure basal-cell epithelioma remaining quiescent in the finger for years, and finally assuming malignant
character and metastasizing to nodules in the forearm and to the axillary and supraclavicular glands and to the chest, causing death. The histologic picture varied from pure basal-cell epithelioma in the original growth through the intermediary form of basal-cell epithelioma and the mixed type to pure squamous-cell epithelioma in the supraclavicular glands and chest.

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