CUTANEOUS CARCINOMA OF THE LOWER EXTREMITIES*

A STUDY OF CASES AT THE BARNES AND THE BARNARD FREE SKIN AND CANCER HOSPITALS OF ST. LOUIS, MO.

By Cesareo De Asis, M.D.
of St. Louis, Mo.

The aim of this paper is not to present any solution to any of the various aspects of the cancer problem, but to discuss the variety of carcinomata of the lower extremities and the course taken by this disease arising in this region of the body. The material was obtained at the Barnes and the Barnard Free Skin and Cancer Hospitals.

Frequency.—Of all the carcinomata found in the different regions of the body, those of the lower extremities are the most rare. Broders reports 12 cases of carcinoma of the lower extremities out of 2000 admitted to the Mayo Clinic between November 1, 1904, and July 22, 1915. The writer has obtained 7 cases out of 723 cases of carcinoma now (December 1, 1923) recorded in the Barnes Hospital, and 10 cases out of 6043 cases of carcinoma recorded at the Barnard Free Skin and Cancer Hospital. (See Table I.)

Table I

Frequency of Cutaneous Carcinoma of the Lower Extremities

Period (yrs.)	Total no. ca. cases	Ca. of lower extremities	Percentage
Mayo Clinic 10.5	2000	12	.6
Barnes Hospital 11.0	723	7	1.0
B. F. S. and C. Hospital... 18.0	6043	10	.2

Pathology.—It is claimed by Bloodgood that there are only two important types of cutaneous carcinoma; namely, the squamous-cell carcinoma and the basal-cell carcinoma or rodent ulcer. The mode of development, as well as the gross and microscopic findings in each variety, will now be dealt with.

The squamous-cell carcinoma is a growth of squamous epithelium of the skin. This growth leads to a thickening of the epidermis and an invasion of the underlying structures. This tumor growth has its origin in the Malpighian layer. On account of the intercellular spines or prickles which the cells of this tumor show, it is called a prickle-cell carcinoma. The primary growth leads to masses of cells. Growth continues at the edge of these masses, the central cells undergo cornification or pearl formation.

Many of these neoplasms develop in old or long-standing ulcer or in scars of old burns. Those occurring on scars of burns are called Marjolin's ulcers. When a chronic ulcer undergoes malignancy, the malignant change starts at

* Thesis presented to the Board of Graduate Studies of Washington University in partial fulfilment of the requirements for the degree of Master of Science in Surgical Pathology, June, 1924.

any point at the edge of the ulcer and is first manifested by the induration and thickening of the edges. This thickening is due to the overgrowth of the epithelial cells and to an increase of the connective-tissue cells. The growing epithelium spreads in all directions to involve also the cutaneous tissue outside the ulcer. The edges and bases of these ulcers become nodular and irregular in outline. The floor is irregular and is covered by necrotic cancerous tissue. This necrotic tissue is gray and opaque. The ulcer is hard and bleeds readily. The ulcer generally has a foul odor and may be very painful.

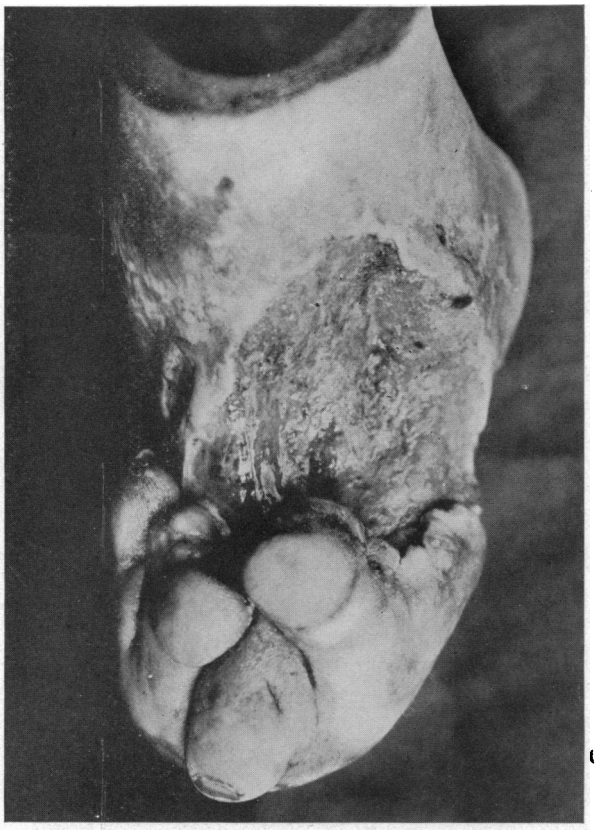

FIG. 1.—Case III. Squamous-cell carcinoma of the foot.

Basal-cell carcinoma (rodent ulcer).—After the diagnosis of carcinoma has been made on an ulcer of the lower extremities by the history and gross appearance of the lesion, it is almost impossible to ascertain in all the cases without the aid of the microscope whether the case is one of squamous-cell carcinoma or basal-cell carcinoma. However, many of the rodent ulcers have a few things in common; namely, (*a*) the margin is raised, firm, rolled, and has a glossy or mother-of-pearl appearance; (*b*) the progress is slow (five to ten years is a common duration); (*c*) the lymphatic glands are, as a rule, not involved; (*d*) the ulcer is shallow and dry, sometimes covered by a crust and bleeds readily when rubbed; (*e*) pain is absent except in the later stages. Of these, the slow progress, the translucency of the border, and the non-involvement of the lymphatic glands differentiate rodent ulcer from squamous-cell carcinoma of the prickle-cell type.

Microscopically, rodent ulcers have no epithelial pearls. The cells are round (Fig. 2b), polygonal, or even spindle in shape (Fig. 3). The cell columns are not always sharply defined from the surrounding stroma.

Distribution.—Either of these two types of cutaneous carcinoma can occur

on cutaneous or muco-cutaneous surfaces, but collected data reveal the fact that they are most common in the region from the neck up and rare on the trunk and extremities. (See Table II.)

TABLE II

Distribution of Squamous- and Basal-cell Carcinoma

Barnes Hospital (squamous- and basal-cell carcinoma)				
				Percentage
Total number of cases			361	
Neck and up			280	78
Trunk			56	15
Upper extremities			18	5
Lower extremities			7	2
Barnard Free Skin and Cancer Hospital (squamous- and basal-cell carcinoma)				
Total number of cases			1105	
Neck and up			959	86
Trunk			39	4
Upper extremities			97	9
Lower extremities			10	1
Mayo Clinic and Johns Hopkins Hospital				
	(Mayo Clinic) (Squam. cell)	(J.H.H.) (Basal cell)	Total	
Total number of cases	256	178	434	
Neck and up	200	162	362	83
Trunk	12	6	18	4
Upper extremities	32	4	36	8
Lower extremities	12	6	18	4

Etiology.—(*a*) Sex. Cutaneous carcinomata in general are more common in males than in females. Broders states that his 256 cases show a ratio of 4:1. The writer in his series has 12 males and 5 females. If injury, which is to be discussed later on, is an important factor in the etiology of carcinoma as is universally believed, then it is perfectly natural to expect that this malady would be more common in men, whose legs are more subject to injury than in women.

(*b*) Age.—Almost every writer says that cancer is rare or seldom seen before forty, or that cancer is a disease of advanced years. The writer does not wish to contradict these statements, but wants to draw the attention of the readers to the fact that his series includes four cases aged twenty, thirty, thirty-one, and thirty-two, respectively; thus 4 out of 17 are below the cancer age as it is given in text-books. Is it not safe to say that these four cases are too many to be branded "atypical"? With these cases in mind one is tempted to assume that carcinoma arising from injuries, especially those on the legs—and injuries are very common on the legs—are not very rare in persons under forty as they are commonly supposed. It seems as though malignancy arising from injuries does not show much respect for youth. It is always a good thing to suspect cancer, even if the patient is still around thirty.

(c) Trauma.—In glancing at Table III, it will be noticed that trauma

TABLE III.

Synopsis of Cases

Case	Path. No.	Age—Sex	Location of lesion	Size of lesion	Duration of ulceration	Interval between primary lesion and appearance of malignancy	Probable cause	Wassermann	Glandular involvement (inguinal)	Coexisting condition	Clinic diag.	Micros. diag.	Treatment	Result when discharged	Present status
1	1935	32–M	Lt. leg	6 x 4 cm.	1 yr.	22 yr.	Trauma	Neg.	Enlarged	Osteomyelitis of tibia	Ca.	Squamous cell ca. (prickle cell type)	Amputation	Improved	Uncertain.
2	2471	58–M	Rt. leg, post. and lat. surface of thigh knee and calf	36 x 10 cm.	56 yr.	54 yr.	Burn	Neg.	None		Ca. (Rodent) ulcer)	Squamous cell ca. (prickle cell type)	Amputation	Improved	Uncertain.
3	4568	31–M	Rt. foot	Entire foot	11 yr.	10 yr.	Trauma	None			Ca.	Squamous cell ca. (prickle cell type)	Amputation	Improved	Living and well.
4	4896	56–M	Lt. leg below knee	5 x 8 cm.	3 mo.	3 mo.	Trauma	+++	Enlarged		Ca.	Basal cell ca.	Excision in toto. Salvarsan	Improved	Uncertain.
5	6310	60–M	Lt. popliteal space	3 x 3 cm.		30 yr.	Burn	Neg.	None	Contracture popliteal space	Ca.	Squamous cell ca. (prickle cell type)	Excision of cicatrix	Improved	Uncertain.
6	6856	59–M	Lt. leg	3 x 5 cm.	1 yr.			Neg.			Ca.	Basal cell ca.	X-ray	Ulcer healed	Uncertain.
7	6885	30–M	Lt. tibia	6 x 8 cm.	25 yr.		Fracture lt. femur, osteomyelitis	Neg.	Enlarged	Osteomyelitis	Ca.	Squamous cell ca. (prickle cell type)	X-ray, later amputation	Improved	Still under treatment.

8	P–55	20–F	Lt. thigh	Multiple	1 yr.	9 yr.	Burn	None			Ca.	Squamous cell ca. (prickle cell type)	Curret. Skin graft	Ulcers healed	Uncertain.
9	None	75–F	Rt. thigh	10 x 10 cm.	3 yr.			None			Ca.	None	None	Died 4½ yrs. later	
10	P–721	62–M	Lt. inguinal flexure	7 x 7 cm.	1 yr.			None			Ca.	Squamous cell ca. (prickle cell type)	Excision and fulguration	Not improved	Uncertain.
11	None	53–M	Lt. foot	Entire foot	30 yr.		Trauma on old ulcer	None	Enlarged and suppurating		Ca.	None	Amputation. Glands excised	Left hosp. 30 da. after operation against advice	Dead. (Cause not known)
12	14–114	63–M	Rt. foot	Multiple ulcers and nodules	1 yr.	29 yr.	Burn (hot grease)	None	Enlarged but not metastatic		Ca.	None	Amputation. Glands excised	Improved	Uncertain.
13	20–47	54–M	Rt. leg and thigh	35 x 6 cm.	5 yr.	47 yr.	Burn	None	Enlarged on rt.		Ca.	Squamous cell ca. (prickle cell type)	Excision. Skin graft later	Improved	Living and well.
14	21–353	87–F	Rt. heel	4 x 3 cm.				None	Enlarged on rt.		Ca.	Basal cell ca. (?)	Excision	Improved	Died 2 yrs. later but not of ca.
15	22–180	51–M	Lt. leg and thigh	2 x 2 cm.	4 yr.	16 yr.	Psoriasis	None		Psoriasis	Psoriasis and secondary ca.	Squamous cell ca. (prickle cell type)	Cautery and radium. Skin graft	Improved	Uncertain.
16	22–213	77–F	Ball of big toe on rt.	1.5 x 2.5 cm.	8 mo.	6 yr.	Trauma	None			Ca.	Squamous cell ca. (prickle cell type)	Excision and and radium	Improved. Recurred 1 yr. later	Uncertain.
17	23–49	67–F	Lt. leg	30 x 15 cm.	1 yr.	51 yr.	Chronic ulceration	Neg.	Enlarged both sides	Varicose ulcers rt. leg	Syphilis, ca.	Squamous cell ca. (prickle cell type)	Amputation	Improved	Uncertain.
18*	7575	52–M	Rt. leg	8 x 10 cm.	1 yr.	14 yr.	Trauma	None	Enlarged both sides	Varicose veins on loth legs, metastatic nodules in liver	Ca.	Squamous cell ca. (prickle cell type)	X-ray		Still under treat. Shows some improve.

*See supplement.

plays a leading rôle in the etiology of these carcinomata. In some of these cases malignant growth started not very long after the injury, and in others years have elapsed before any manifestation of malignancy made its first appearance. In other words, the period of time elapsing between the infliction of the injury and the first appearance of the malignancy varies from a few months to years.

(*d*) Scars.—Another predisposing factor which plays an important rôle in the etiology of cancer is the scar in the site of old trauma brought about by burns. It is a common observation among surgeons that scars left by burns are very liable to become the seat of squamous-cell carcinoma, especially those situated on the lower extremities where they are more common than on the upper extremities or trunk. The malignant growth starts at the junction of the cutaneous tissue and the scar tissue. The other peculiar thing about burns on the lower extremities is that after the amputation of the limb for carcinoma, there is a tendency for the disease to recur at the stump. The five cases in the series give a history of burns of many years ago. In one of these a simple ulcer had persisted for fifty-six years. He has no history of syphilis and gives a negative Wassermann. The four others give a history of primary healing of the burned area. Later, after several years, this area broke down. The second lesions failed to heal. Broders has shown that one-fifth of his cases had arisen from scars of burns, and he, therefore, suggests that scars should be watched for a possibility of malignancy. These cases, together with those reported by others, are enough to convince one that old scars have a decided tendency to ulcerate, that the ulceration refuses to heal, and finally leads to carcinomatous growth.

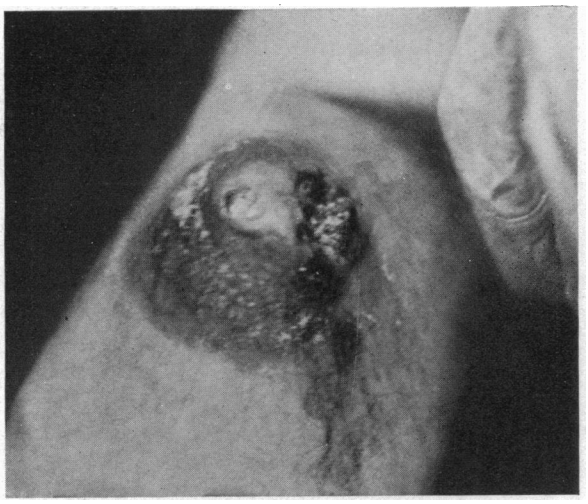

FIG. 2a.—Case IV. Basal-cell carcinoma (rodent ulcer) of the leg.

(*e*) Syphilis.—As far back as 1843, it was argued by many observers—and with convincing evidence—that syphilis is a strong predisposing factor for carcinoma. Unfortunately not all the cases in the writer's series have had Wassermann tests; several of these were treated before the Wassermann test was in general use. Of the seven that had a Wassermann test only one gave a positive reaction. This particular case gave a history of trauma at the site of the cancerous growth. Either the trauma or the syphilis might have brought about the malignancy. However, it is of interest to note here in passing that a number of observers, among whom are Fournier and

Poirier, believe that from 85 to 95 per cent. of the cases with syphilitic lesions in different parts of the body develop carcinoma.

(*f*) Varicose Veins and Varicose Ulcers.—It is a question what part varicose veins and varicose ulcers play in the etiology of carcinoma. It is, however, generally accepted that chronic ulceration is an important factor in the causation of carcinoma. In the lower extremities, the most common cause of ulceration is varicose veins. In going over the histories of cases of varicose ulcer at the Barnes and the Barnard Free Skin and Cancer Hospitals, the writer has found 310 cases, all of which were practically within the cancer age and with a chronicity of from six months to thirty-five years. He found that only one had become malignant. These figures, together with the greater predominance of cutaneous carcinoma in men than in women (about 4:1) and the greater predominance of varicose veins and varicose ulcers in women than in men (4:1 according to White, and 3:2 in the writer's 310 cases of varicose veins and varicose ulcers), seem to show that varicose veins and varicose ulcers do not play a very important part in the causation of carcinoma of the lower extremities.

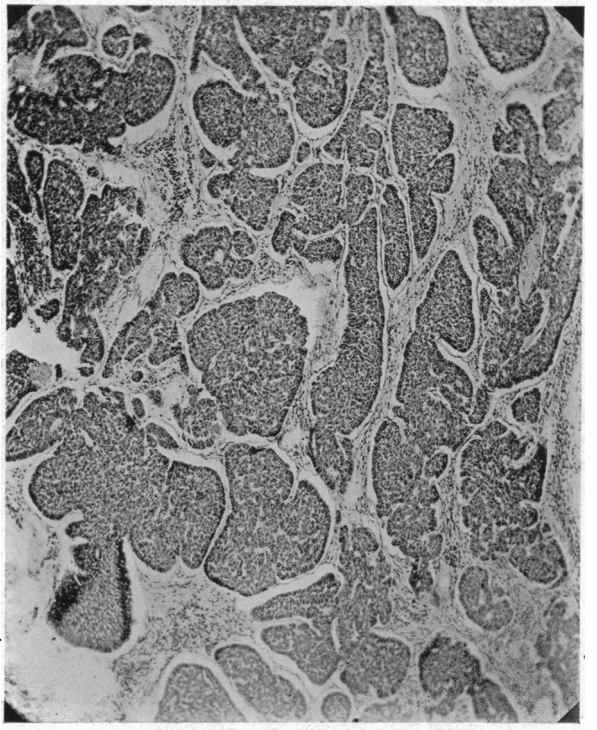

FIG. 2b.—Case IV. Basal-cell carcinoma (rodent ulcer). Microscopic section of specimen shown in Fig. 2a. The cells are mostly spherical in shape.

Metastasis.—Cutaneous carcinoma of the lower extremities in particular, and cutaneous carcinoma of other regions in general, metastasize rather late. Many of them do not show any sign of metastasis at all in the inguinal glands at the time the patient applies for treatment. This slow or late metastasis is explained by the fact that the edges of the ulcer undergo thickening and induration which are believed to squeeze the lumen of the lymphatic vessels. This prevents the flow of lymph which ordinarily carries the cancer cells. In the cases here presented only two had the inguinal glands excised for some reason or other. Our only reason for suspecting metastasis in some of them is the presence of the enlarged inguinal glands. The enlargements of the glands may have been due to other causes. As to how long these inguinal

glands have become enlarged is a difficult matter to decide, for the clinical clerk seldom, if ever, asks the patient that question. Answers given by patients are also of doubtful importance. The fact remains, however, that some of these cutaneous carcinomata metastasize rather late for the inguinal glands in some of them are not even palpable even after the disease had grown so extensively as to justify the amputation of the limb. This fact of late metastasis, therefore, suggests that early excision might be quite sufficient to effect a cure, or at least, to avoid metastasis.

FIG. 3.—Case VI. Basal-cell carcinoma (rodent ulcer). Microscopic section of basal-cell carcinoma of the leg. Many of the epithelial cells are spindle in shape (compare with Fig. 2b). Note the palisade-like arrangement of the border cells.

Some observers have proved experimentally that metastasis in distant organs has occurred in animals simply by employing unnecessary handling or massage, during the operation. That unnecessary manipulation during the operation has caused metastasis is a well-known fact. Therefore, it behooves the surgeon to be as gentle as possible with the affected organ.

Treatment.—The choice of treatment of carcinoma of the lower extremities, like that of the other regions, is chiefly determined by the extent of the malignancy at the time the patient applies for relief, the nature of the growth (whether basal cells or squamous cells), and also by one's personal choice based on his experience with his favorite method or methods. In a short paper like this there is no place for the discussion of all the different methods of treatment, together with their merits and demerits, though each may have its place under varying conditions. It might be of interest, however, to mention a few of these methods that have the most advocates and whose advantages are least questioned.

Amputation is the first choice under a number of existing conditions. If the malignant area is large, amputation is preferred and the results are satisfactory. This method of treatment is always called for in those cases which are associated with gangrene, with elephantiasis, and in large and incurable ulcerations that extend around the limb. These conditions usually mean that

the limb is of no use to the patient. If, however, the growth is of the basal-cell type and is relatively small, less radical measures are often successful because of the more benign character of the lesion.

Excision with the cold knife or the electric cautery are, I believe, the most commonly employed. But the electric cautery is the more preferred of the two. It destroys avenues of escape for tumor cells to distant regions.

The Röntgen-ray, because of its success where other modes of treatment have failed, has rallied many supporters to its standards, most of whom are X-ray experts. But in the hands of a novice the danger of X-ray therapy lies in the resulting burn which almost never heals. The burn is exquisitely painful, and has a special predisposition to carcinoma. Radium also has been often used successfully, especially in those cases which are of the basal-cell type. But, similarly, caution must be exercised with regard to the production of a burn.

FIG. 4.—Case VII. Microscopic section of a typical squamous-cell carcinoma with epithelial pearls.

Electrocoagulation Method.—This method of treatment is advocated on the ground that it prevents reinoculation or extension of the disease. It is employed as an adjuvant to the other aforesaid modes of treatment.

The Combined Methods.—It is fully recognized that none of the above-mentioned methods may be applicable to all cases of carcinoma. On this ground, Bryant and others advocate that radium and surgery will accomplish the best results. In this case radium is to be applied before and after the operation. The idea with the former is to render the cancerous cells temporarily inert during the operation, and the latter, to destroy or encapsulate the cancerous cells left behind. The advocates of X-ray, on the other hand, also claim that the greatest good is accomplished by the combined use of surgery and the X-ray. The arguments offered in support of either of these combined methods are plausible enough, but Pfahler was not satisfied with the results obtained by either of these combined methods. His idea was to "finish" those malignant cells which for unknown reasons were recrudescent

after either of the above methods. He, therefore, suggested that perhaps the best results could be obtained by the combination of the electric cautery, radium, X-ray, and electrocoagulation methods. He, with many others, claims that these combined methods accomplish the greatest good and the lowest mortality.

REPORT OF CASES (BARNES HOSPITAL)†

CASE I.—No. 3791, E. T., male, thirty-two years old, well developed, muscular, and weighed 151 pounds. He entered the hospital on February 5, 1917, for an ulcer on the left leg below the knee. When nine years old he was hit on the hip with a clod of frozen dirt. A lump appeared which later was followed by other lumps on the leg below the knee. A physician opened the lumps on the hip and leg and bone fragments were removed. They healed. In 1911, he fell off a wagon and bruised his hip and leg again and soon after an abscess developed at the hip. Bone fragments were again removed from the hip and leg. Healing followed and the wound remained healed until 1916, when he had another injury on the shin. The wound never healed since. Three months previous to admission he suffered another injury. On examination the inguinal glands were found enlarged and firm. The ulcer was 6 x 4 cm. The edges were hard and tender but were not irregular. The base had a cauliflower appearance, and had a deep green foul discharge. X-ray examination showed osteomyelitis of the tibia. He had a negative Wassermann reaction. The left leg was amputated at the junction of the upper and middle thirds. He had improved when discharged, March 13, 1917. Efforts to locate him in order to ascertain subsequent results failed.

Pathology.—The section of the ulcer shows isolated masses of different sizes and shapes made up of squamous epithelium surrounded by scanty amount of connective tissue and cellular infiltration mostly round cells and a few polymorphonuclear leucocytes. The epithelial cells at the border of these masses have a narrower protoplasm than those at or near the centre, and the nuclei stain more deeply with hæmatoxylin. The nuclei assume a variety of shapes. Some are round, others are oval, and a very few approach a spindle shape. The cells are uniform in size and regular in shape. The border cells make up from two to six layers but mostly from two to four. The oval-shaped nuclei have a transverse diameter much less than the diameter of the round ones. The intercellular spaces are more distinct near the border than at the centre. Epithelial pearls are present in the centre of the masses. The nuclei are fewer per unit area and do not stain so sharply. Diagnosis, squamous-cell carcinoma (prickle-cell type).

CASE II.—No. 5321, J. C. J., male, fifty-eight years old, entered the hospital, March 3, 1918, for a sore on the right leg. He received a burn when two years old. Since then it never healed in spite of the efforts of two doctors. At times the sore was small, but at other times it was extensive. The ulcer had a very large area covering the posterior and lateral surfaces of the right thigh, knee, and calf. The edges were indurated, raised, and irregular. The base was red and filled with unhealthy granulation tissue which gave it a nodular appearance. A slight amount of foul discharge was present. The left leg showed a slight degree of muscular atrophy. The right leg was flexed to the knee and this was the most comfortable position for the patient. In 1916–1918, the sore had spread so rapidly that it had grown from about one-half the length of his palm (9–10 cm.) to about 36 cm. in length. At the time he applied for treatment the ulcer extended from the junction of the middle and upper thirds of the thigh to the middle of the calf. He had been treated with salves. He had a negative Wassermann

† It is unfortunate that so few of the patients could be traced later in order to get information about their condition at the time of the preparation of this paper. It would seem as if there must be a particular tendency for patients with these lesions to belong to the "floating" class of the population.

reaction. The inguinal glands were palpable but not much enlarged. An amputation was performed through the middle third of the thigh. He was much improved when discharged, May 30, 1918. It has not been possible to locate him or to hear of his condition since his discharge.

Pathology.—The microscopic section shows invasive growths of epithelial cells arranged in masses which vary in size and shape. These are surrounded by connective tissue and leucocytes. The nuclei of the border cells stain deeply with hæmatoxylin. They are round, oval, or spindle in shape. In the centre of these masses the cells are less crowded, and the nuclei exhibit no uniformity of staining quality. Some stain deeply while others stain faintly. Characteristic pearl formations are present. Many of the cells are undergoing mitotic changes. Diagnosis, squamous-cell carcinoma (prickle-cell type).

FIG. 5.—Case X. Microscopic section of squamous-cell carcinoma showing the large typical epithelial cells and the absence of epithelial pearls. (Compare with Fig. 4.)

CASE III.—No. 10,991, C. M. A., male, thirty-one years old, a mechanic by trade, entered the hospital, July 28, 1921, for a sore on the right foot. On August 26, 1900, he was run over by a truck and his big toe of the right foot was cut off and the rest of the foot was skinned. The toe was amputated at the City Hospital but the wound did not heal completely before he left the hospital. This wound was later treated by a physician. Partial healing followed but the remaining toes were in an abnormal position (Fig. 1). He was unable to walk for four years. The skin did not completely heal. In 1910, he was injured again on the right foot. Ulceration began and did not heal since. The duration of the ulcer was eleven years. The base of the ulcer was about 1.5 cm. thick on section and cut with difficulty. The history does not state the presence of enlarged glands. No Wassermann test was made on this patient. An amputation was performed through the middle third of the right leg on July 29, 1921. He was discharged on August 12, 1921. He is now (December, 1923) living and well.

Pathology.—The microscopic section shows invasive growth of the squamous epithelial cells forming columns chiefly characterized by numerous epithelial pearls. Many of these epithelial columns show signs of activity. Mitoses are seen in their border cells. Most of the epithelial pearls have undergone partial or complete necrosis. The active cells stain blue with hæmatoxylin and the necrotic areas stain pink. Diagnosis: squamous-cell carcinoma (prickle-cell type).

CASE IV.—No. 11,658, J. S., male, fifty-six years old, a miner by occupation, entered the hospital on November 6, 1921, for an ulcer on the left leg just below the knee-joint

and situated latero-posteriorly. Six months before coming to the hospital he was struck on the site of the present ulcer with a piece of coal. The skin was bruised. There was no immediate swelling but the area was slightly tender. He applied salves. Two months later he noticed a slight swelling of the size of a peanut at the site of the old trauma. The tumor grew and three months later it reached the size of a walnut (Fig. 2a). Ulceration began to take place then. There was a moderate amount of dirty, greenish-yellowish discharge and slight bleeding at times. The centre showed necrosis. He suffered no pain. The tumor (5 x 8 cm.) was excised, November 29, 1921. He refused excision of the enlarged inguinal glands. He had a four plus Wassermann and was given salvarsan treatment. He was much improved when discharged, December 8, 1921. He did not report for further treatment. He has not been heard of since.

FIG. 6.—Case XIII. Squamous-cell carcinoma of the posterior aspect of the thigh, knee and calf.

Pathology.—The mass had the shape of a hemisphere measuring 7 x 6 x 4 cm. It contained two ulcers on its outer surface. Microscopically, the section (Fig. 2b) shows irregular epithelial-cell masses surrounded by dense connective tissue. The cells in these masses stain uniformly blue with hæmatoxylin. There is no central pearl formation. The masses are composed entirely of basal cells. This is a picture of a typical basal-cell carcinoma. All the larger masses show central necrosis. In a few, the necrotic areas have liquefied in part. Cysts are thus formed. Diagnosis: basal-cell carcinoma.

CASE V.—No. 14,790, J. J. H., male, sixty years old, weighed 220 pounds, entered the hospital, March 3, 1923, for an ulcer on the left leg. Thirty years previous to admission he was burned in an oil explosion. The back and legs were burned but the left leg was worse than the right. Soon after, the left leg showed contracture at the left popliteal space and since then he experienced an inability to extend the left leg. There was no pain present until six months later. Efforts to extend the limb oftentimes resulted in the cracking of the scar tissue. At the time he reported for treatment an ulcer of the size of a fifty-cent piece (3 x 3 cm.) was found at the centre of the scar tissue. This ulcer started as a small red papule as large as a dime (1.5 x 1.5 cm.). This finally broke down and resulted in ulceration which gradually spread until it reached its present size. The ulcer was

situated just below the popliteal space. The edges were sharply defined, suggestive of syphilis, but the Wassermann test was negative. The history did not mention the presence of enlarged glands. The cicatrix was excised and he had improved. He was discharged on May 7, 1923. He has not been heard of since.

Pathology.—The section shows irregular masses of epithelial cells surrounded by connective tissue and cellular infiltration. The cells at the border of these masses are round or oval. Their nuclei stain deeply with hæmatoxylin. The centre cells show signs of degeneration. Epithelial pearls are present. Diagnosis: squamous-cell carcinoma (prickle-cell type).

CASE VI.—No. B2645, J. T. G., male, fifty-nine years old, reported at the dispensary, September 23, 1923, for a sore on the left leg which he had had for over a year. It was located at the middle of the left leg and measured 3 x 5 cm. The base was irregular and slightly translucent. He had a negative Wassermann. He had been treated with X-ray and the ulcer has healed.

FIG. 7.—Case XV. Squamous-cell carcinoma of the leg arising secondarily to psoriasis. Note the scaly character of the surrounding skin.

Pathology.—Microscopically, the section (Fig. 3) shows strands of epithelial cells which are not very well differentiated extending into the deeper tissues. Here and there are areas of necrosis. No epithelial pearls are present. The nuclei are deeply stained with hæmatoxylin and the outline of the individual cells are not easily made out because of the density of the cell masses. The cells are mostly spindle in shape. Diagnosis: basal-cell carcinoma.

CASE VII.—No. B3365, W. T. U., male, thirty years old, reported at the dispensary, September 27, 1923, for an ulcer over the left tibia. Twenty-five years previous to admission he had a fracture of the left femur. The left leg was placed in a plaster cast for six weeks. Shortly after the removal of the cast the left leg became swollen and an operation was performed for an acute osteomyelitis. Drainage sinuses persisted. At the time he came for treatment there was a granulating ulcer 6 x 8 cm. over the left tibia on the medial surface. It contained numerous papillomatous tumor growths up to 2 cm. in diameter over the surface. It bled readily. The condition suggested carcinomatous growths superimposed over an old chronic inflammatory condition. There were numerous scars marking the site of old sinuses over the leg. These indicated an old osteomyelitis. He had lost in weight from 150 to 135 pounds. The right inguinal glands were enlarged and pain was present in the right ilio-inguinal region. The left inguinal glands were also enlarged but not tender. He had a negative Wassermann. For a time he was given X-ray treatment. Later, February 4, 1924, amputation at the junction of the middle and upper thirds of the leg was resorted to. He had shown marked improvement with no recurrence (May 1, 1924) when last seen.

Pathology.—The microscopic section (Fig. 4) shows irregular masses of epithelial cells surrounded by a scanty amount of connective tissue and cellular infiltration mostly of the small round-cell variety. The epithelial cells are arranged in nests. These nests

are common throughout the section. The cells at the border of the masses are thickly distributed, and the nuclei and protoplasm stain more deeply with hæmatoxylin than those at the centre. Diagnosis: squamous-cell carcinoma (prickle-cell type).

BARNARD FREE SKIN AND CANCER HOSPITAL

CASE VIII.—No. 136, E. G., female, aged twenty, entered the hospital on January 1, 1906. Ten years previous to admission she received a severe burn extending from the upper third of the leg to about the crest of the ilium involving the lower portion of the back. There was also some excoriation on the right thigh. She was confined in bed for two years. In that time the right thigh and the lower portion of the back on the left side down to the gluteal fold entirely healed. The granulating surface remaining was sluggish in cicatrizing and very painful. It never had an offensive discharge till a year previous to admission. At about that time there was discovered a tumor mass distinctly raised from the surrounding skin on the posterior part of the thigh. Examination revealed an extensive grayish tissue typical of carcinoma covering the entire posterior portion of the left thigh. She left the hospital before a positive diagnosis was obtained. In January, 1907, she was readmitted. Examination revealed cicatrization all over the left thigh. Ulcers of the size of a silver dollar (4 x 4 cm.) were located on the posterior and lateral surfaces of the left thigh. Their base was made up of nodular grayish tissue typical of carcinoma. Extensive curettement was performed and was followed by skin graft. She was discharged on May 5, 1907, with the ulcers completely healed. She has not been heard of since.

Pathology.—The microscopic section stains blue with hæmatoxylin. Thick epithelial papillæ extend for a long distance into the connective-tissue cells which are cylindrical and stain sharply. Many mitotic figures are seen. Many epithelial pearls are present. The connective tissue surrounding the papillæ are rich in fibroblasts. They also contain scattering mononuclear cells. Diagnosis: squamous-cell carcinoma (prickle-cell type).

CASE IX.—No. 1603, F. S., female, aged seventy-five, colored, entered the hospital on June 7, 1910. Three years previous to admission a small ulcer was noticed on the outer side of the right thigh (Fig. 5). This had steadily increased in size. When she reported for treatment the ulcer had a diameter of about 10 cm. The tumor was raised from the surrounding normal tissue. The edges were fairly regular but the base was uneven with necrotic tissues and sinuses. The discharge was not profuse but purulent and foul. No operation was performed. She died on January 15, 1914. No pathological section was available but the gross picture is apparently typical of carcinoma.

CASE X.—No. 945, C. L., male, sixty-two years old, entered the hospital, September 9, 1910. About a year previous to admission a lump was noticed on the left groin. This grew slowly and without pain until three months previous to admission when it burst. The mass was cauterized. Examination revealed a mass of the size of a fist (7 x 7 cm.) at the left inguinal flexure. It was cleft deeply in the centre and had a foul sanguino-purulent discharge. Excision and fulguration of the new growth were employed. The patient was discharged but did not improve.

Pathology.—The specimen shows numerous cell nests separated by adult connective tissue. The nuclei of the cells that make up these nests show a wide variation in their size and shape and staining qualities. The large, oval, fairly deep-staining ones being in the majority. Mitotic figures are numerous. Epithelial pearls are present. There is some congestion and an enormous amount of leucocytes. There are many large atypical cells (Fig. 5). Diagnosis: squamous-cell carcinoma (prickle-cell type).

CASE XI.—No. 1314, W. W., male, fifty-three years old, entered the hospital on April 27, 1912. Thirty years previous to admission an ulcer had developed at the anterior portion of the left ankle. It never healed. Discharge was constantly present. Five months previous to admission he was traumatized at the left ankle over this sore. As a result the ulcer deepened and the discharge increased. He was treated at the City Hospital. Examination revealed a cauliflower growth involving nearly the whole foot

except the toe and heel, and a part of the sole. There was a foul discharge. The inguinal glands were enlarged and suppurating. On July 7, 1912, the leg was amputated at the knee and the inguinal glands were dissected. He left the hospital on August 7, 1912, against the doctor's advice. The patient died soon after, but the exact date and the cause of death were not definitely known. The case had been diagnosed as carcinoma, but the type was not specified and the specimen was not available to me for study.

CASE XII.—No. 13,694, C. W., male, sixty-three years old, entered the hospital on December 12, 1914. Thirty years previous to admission he stepped into some hot grease. The right foot and the lower four inches of the leg were scalded. This healed completely, leaving an extensive scar. About a year previous to admission nodules developed on the scar. Examination revealed several ulcers and nodules typical of carcinoma scattered over the foot. The inguinal glands were enlarged. The right leg was amputated on December 14, 1914. He was discharged on February 19, 1915, with the stump healed.

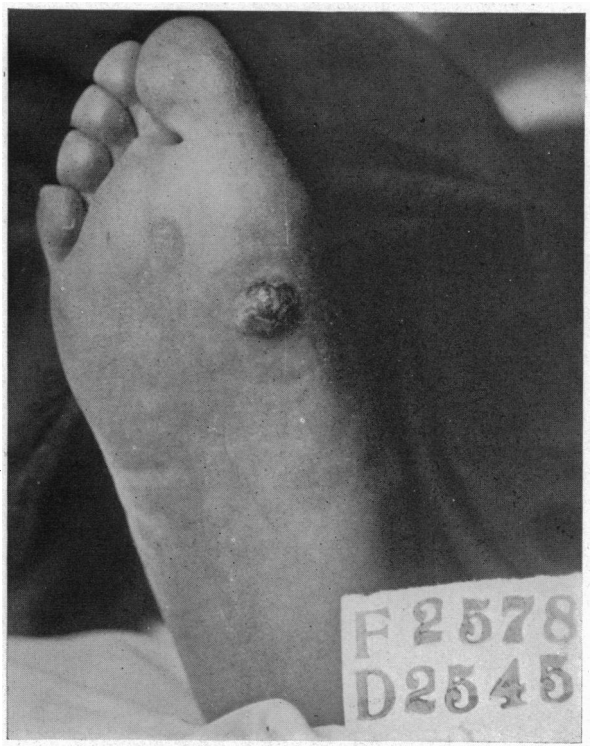

FIG. 8.—Case XVI. Squamous-cell carcinoma of the foot.

The microscopic section of the gland showed chronic lymphadenitis without carcinoma metastasis. Section of the tumor was not available, although a diagnosis of carcinoma had been made at the time.

CASE XIII.—No. 21,365. A. M., male, fifty-four years old, entered the hospital, February 23, 1920, for an ulcer on the posterior aspect of the right leg and thigh (Fig. 6). He was burned when he was two years old. Forty-seven years later (five years prior to admission) he noticed that ulceration had started at the site of the old burn. It gradually increased in size. It was not very painful. He had lost ten pounds within the two years previous to admission. The ulcerated area occupied the posterior surface of the lower third of the right thigh, back of the knee, and the upper two-thirds of the leg. The upper medial border showed areas of healing. The edges were raised, undermined, and irregular. The floor was uneven, nodular, and gave a foul discharge. The right inguinal glands were palpable. The ulcer was excised and dressed with dichloramine-T and later was given a skin graft. He had improved when discharged, May 4, 1920. He is now living and well.

Pathology.—The section shows irregular masses of squamous epithelial growths surrounded by connective tissue thickly infiltrated with small round cells. Characteristic epithelial pearls are present. The cells at the border are dense, small, not uniform in shape, have deeply staining nuclei, and show more signs of activity in contrast to the cells in the central area. Diagnosis: squamous-cell carcinoma (prickle-cell type). After

the tumor was removed, excessive growth of granulation tissue occurred. The tissue removed showed no recurrence of cancer growth.

CASE XIV.—No. 24,286, C. K., female, eighty-seven years old, entered the hospital, November 15, 1921, for a tumor under the right heel and in the groin. No satisfactory history of the duration of the disease could be obtained. The tumor mass in the heel was excised on December 13, 1921. She was very much improved. She reported for further observation on January 11, 1922. The wound was almost healed. Her daughter believed that the lump in the groin was increasing in size. She died in July, 1923, but the cause of death was uncertain.

Pathology.—The specimen is that of a tumor mass measuring 4 x 5 cm., flat and slightly pedunculated. The greater part of the surface is made up of two ulcers surrounded and separated by gray, opaque skin. On section the tumor is gray, slightly translucent material which is broken up into irregular sized parts by dense fibrous partitions. Some parts show central degeneration. The microscopic section stains blue with hæmatoxylin. The mass is made up of two kinds of epithelial cells, the round or cuboidal and the spindle. Both of these have deeply staining nuclei. The round or cuboidal cells are mostly arranged in strands separated by very scanty amount of connective tissue. The spindle cells are mostly arranged in globular masses of different sizes surrounded by a scanty amount of connective tissue. No epithelial pearls are present. Diagnosis: basal-cell carcinoma (?).

FIG. 9.—Case XVII. Front view of the legs showing varicose ulcers on the right and squamous-cell carcinoma on the left.

CASE XV.—No. 24,796, P. L. P., male, fifty-one years old, entered the hospital, February 6, 1922. Twenty years previous to admission he had a small, red, scaly papule on the extensor surface of the forearm near the elbow. It gradually spread all over the upper extremities. Later, it developed on the thigh and spread all over the lower extremities except the sole of the foot. Scales were present. He complained of itching and burning sensation. There was no pain. At times the skin cracked in places. For the last four years prior to admission there had been a growth on the anterior surface of the left leg just below the knee (Fig. 7). It measured 2 cm. in diameter. It was tender and was covered by a dark crust which was adherent. On the middle third of the thigh, on its lateral aspect, was a new growth 2 cm. in diameter. It was raised, ulcerated, and bled readily. It was indurated and tender. The floor had a grayish, slightly granulated opaque appearance. The discharge was offensive. The case was diagnosed clinically as psoriasis with secondary carcinoma. The treatment consisted in cauterization and radium application followed by skin graft. He was very

much improved when discharged, July 2, 1922. The final result of the treatment was uncertain for the patient has not been heard of since.

Pathology.—The microscopic section stains blue with hæmatoxylin. It consists of irregular masses of epithelial cells with dark staining nuclei. The cells at the margin are smaller, more dense, and possess more darkly staining nuclei than those at the centre. Few epithelial pearls are present. Mitotic changes are found mostly among the marginal cells. There is a moderate amount of cellular infiltration. Diagnosis: squamous-cell carcinoma (prickle-cell type).

CASE XVI.—No. 254,251, M. W., female, seventy-seven years old, entered the hospital on June 24, 1922. Seven years previous to admission she stepped on a needle. Eight months previous to admission she noticed a sore on the ball of the big toe of the right foot. She had picked the point of the needle out of this sore. Examination revealed a soft plantar verruca about the size of a butter bean (1.5 x 2.5 cm.), (Fig. 8). It bled readily. The lesion was excised on July 5, 1922, and soon after radium was applied. She was discharged on July 21, 1922, when the wound was showing a healthy granulation tissue. After a year she returned with an ulcer on the old scar. Silver nitrate was applied and the ulcer seemed to have improved.

Pathology.—A microscopic section of the excised lesion shows dense masses of squamous epithelial cells extending down into the underlying connective tissue. These masses are thick and placed closely together. Dense masses of small round cells fill the tissue about the deeper ends of the invading papillæ. No epithelial pearls are seen. Diagnosis: squamous-cell carcinoma (prickle-cell type).

CASE XVII.—No. 26,340, C. L., female, sixty-seven years old, poorly nourished, and poorly developed. She entered the hospital on January 1, 1923, for ulcers on both legs. The ulcer on the right leg was situated anteriorly above the ankle. It had an irregular outline and was diagnosed varicose ulcer. Since about a year previous to admission the ulcer of the left leg had grown more rapidly than ever before. It was an extensive ulceration. On admission it measured 30 x 15 cm. and was situated on the anterior surface. It extended from near the ankle to almost the level of the knee. It had a cauliflower appearance (Fig. 9). The discharge from it was foul. The base was irregular and papillomatous. In some places the base was hard, in other places it was soft. The skin below the knee and down to the ankle had a thin, gray, opaque appearance. The inguinal glands on both sides were enlarged, firm, and discrete. Amputation was performed through the junction of the middle and lower thirds of the left thigh. She was discharged on March 23, 1923. Attempts to locate the woman in order to ascertain subsequent results have proved fruitless.

Pathology.—The microscopic section shows dense masses of epithelial cells. At the outer edge the cells are pink and the nuclei stain poorly. Along the inner edge the cells stain deeply with hæmatoxylin. Mitotic changes are present. Numerous epithelial pearls are seen scattered over the epithelial growths. There is a moderate lymphocytic reaction between the epithelial mass and the underlying connective tissue. The skin shows a marked hyperæmia in the neighborhood of the tumor. Diagnosis: squamous-cell carcinoma (prickle-cell type).

SUPPLEMENT

This case is not included in this series, for it came under observation just lately. The importance of the case justifies its being reported. The following are the salient facts about the patient:

J. L., male, fifty-two years old, was admitted to the Out-patient Department of Barnes Hospital, April 12, 1924, for a tumor on the right leg. Fifteen years previous to admission he had an injury on the right leg. Repeated injuries subsequently on the site of the old trauma resulted in the appearance of the tumor one year previous to the

date of admission. Examination revealed a cauliflower growth on the right leg. It measured 10 x 8 cm. It had a purulent foul discharge. Varicose veins were present on both legs. The inguinal glands were enlarged on both sides. The liver was enlarged and presented multiple nodules which in all probability were metastatic. There was no pain. Jaundice was not evident. Up to the writing of this supplement (May 14, 1924), the patient has been under X-ray treatment for the primary growth and the tumor is gradually subsiding.

Microscopic Diagnosis.—Squamous-cell carcinoma (prickle-cell type).

SUMMARY AND CONCLUSIONS

1. Cutaneous carcinomata of the lower extremities seem to be never a primary condition. They arise on an old ulcer or some other lesion.

2. They are very rare. They comprise not more than 1 per cent. of all the carcinomata in the different parts of the body, and 1 to 4 per cent. of all the cutaneous carcinomata.

3. They are more common in men than in women, at least 2: 1.

4. They are more common above the age of fifty, but can be found even at an early age of twenty.

5. Trauma and burns play a very important part as exciting etiological factors.

6. The rôle of syphilis as a predisposing etiological factor in cutaneous carcinomata of the lower extremities is not as yet fully established.

7. Varicose veins and varicose ulcers are not the most important predisposing factor in the etiology of most of the cutaneous carcinomata of the lower extremities.

8. Cutaneous carcinomata of the lower extremities produce metastasis in the inguinal glands, either on the corresponding side alone or apparently on both sides, but mostly the former. Metastasis takes place early in some and late in others.

9. In cutaneous carcinomata of the lower extremities arising from trauma, the interval elapsing between the infliction of the injury and the appearance of the tumor varies from three months to fifty-four years.

10. Most of the cutaneous carcinomata of the lower extremities are of the squamous-cell variety (prickle-cell type).

BIBLIOGRAPHY

[1] Adami: Principles of Pathology, 2nd ed, vol. i, p. 797.
[2] Andrews and Bowlby: Surgical Pathology, p. 186.
[3] Beatty, W.: Rodent Ulcer. Boston Med. and Surg. Jour., 1918, vol. clxxix, p. 527.
[4] Broders, A. C.: Squamous-cell Carcinoma. ANNALS OF SURGERY, 1921, vol. lxxiii, p. 141.
[5] Bryant, F.: Treatment of Cancer. Boston Med. and Surg. Jour., 1921, vol. clxxxiv, p. 615.
[6] De Quervain: Clinical Surgical Diagnosis, 3rd ed., p. 821.
[7] Hazen, H. H.: Basal-cell Cancers of the Skin. South. Med. Jour., 1917, vol. x, p. 241.
[8] Hertzler, A. E.: Treatise on Tumors, p. 182.
[9] Fordyce, J. A.: Surgery of the Skin and its Appendages. Keen's Surgery, vol. ii, p. 637.

[10] Knox, L. C.: Relationship of Massage to Metastasis in Malignant Tumors. ANNALS OF SURGERY, 1922, vol. lxxv, p. 134.
[11] Kolischer, G.: Modern Cancer Therapy and its Results. Interst. Med. Jour., 1917, vol. xxiv, p. 637.
[12] Mastin, W. McD.: Ulcer and Ulceration. Am. Pract. of Surg., 1907, vol. ii, p. 164.
[13] McConnell, G.: Carcinoma, Further Studies in Metastasis. New York Med. Jour., 1916, vol. ciii, p. 785.
[14] Skillern: Carcinoma Following a Lacerated Wound of the Toe. Int. Clin., 1917, vol. ii, p. 247.
[15] Stelwagon: Diseases of the Skin, 9th ed., p. 906.
[16] Scott, A. C.: Cautery Dissection for Metastatic Cancer. Surg. Clin. of N. A., 1922, vol. ii, p. 1429.
[17] Sutton, B. J.: Tumors Innocent and Malignant, 7th ed., p. 290.
[18] Thom, B. P.: Syphilis and Malignancy. Am. Jour. of Syphilis, 1918, vol. ii, p. 140.
[19] Warbasse: Surgical Treatment, 1919, vol. i, p. 323.
[20] White, R. P.: Ulcers of the Leg Miscalled Varicose. Br. Jour. of Derm., 1918, vol. xxx, p. 138.