MALIGNANT MELANOMA*

A CLINICAL STUDY OF ONE HUNDRED SEVENTEEN CASES

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FROM the clinical and pathologic points of view melanomata are among the most important of any malignant tumors, affecting persons of all ages. They are one of the most malignant growths and the results obtained from treating them are generally known as far from satisfactory. Therefore, a special study of treatment of these lesions with more favorable outcome seems justifiable.

This is a study and analysis of a group of malignant melanotic tumors treated by surgery and showing the results of such treatment over various periods ranging from a few months to 13 years. While the number of cases analyzed is comparatively small, the end-results, where radical surgery has been employed, compare very favorably with results in treating other types of nonmelanotic malignant tumors.

The Term Melanoma.—According to scientific records, obviously, Hippocrates mentioned the appearance of melanoma first, but one may safely assume that others noted it before him because of its characteristic color and course.

F. Müller gave this type of tumor the name of "carcinoma melanodes," and the term melanoma was first used by Carswell, in 1836, and by Virchow.[1] In this paper melanoma is used as a term applying only to essentially malignant tumors.

Pigmented Naevus.—According to Kumer,[2] 32 per cent of melanomata derive from a naevus (naevo carcinoma); therefore, a brief review of the origin, pigment formation, and known causes of malignant degeneration of this type of lesion is desirable.

The pigmented naevus is characterized by the presence of naevus cells in the corium which are more or less pigmented. Soldán,[3] 40 years ago, disclosed the nervous origin of the naevus clearly and convincingly. His work remained unnoticed until Masson,[4] 27 years later, identified his discovery and supported it with his own research. They demonstrated, without any doubt, that the naevi are the neuroma of the tactile end-apparatus (Wagner-Meissner and Merkel-Ranvier). The valuable research of Soldán[3] and Masson,[4] was confirmed by Foot.[6]

Laidlaw[7] drew a philogenetic parallel between the human and animal world, pointing out that, "the pigmented hairy mole appears to be a link or transition from pigmented tactile organs of the reptilian type to the hairy tactile organs

* Read before the Third International Cancer Congress, Atlantic City, N. J., September 11, 1939. Submitted for publication February 9, 1940.

of the mammalian type." Would this be the reversion to ancestral characteristics (atavism) like the development of supernumerary breasts[8] in the milk-line or at atypical locations; normally observed only in animals?

The formation of melanin pigment is probably a specific function of the basal cell layer of the rete malpighii. Melanin is supposed to be a pyrocatechol derivative closely allied to adrenalin. In animals, the mouth is often pigmented physiologically (for example, in dogs and cats). In human beings, pigmentation may be observed in the mouth in Addison's disease, lymphogranulomatosis, pediculosis, pernicious anemia, and malaria.

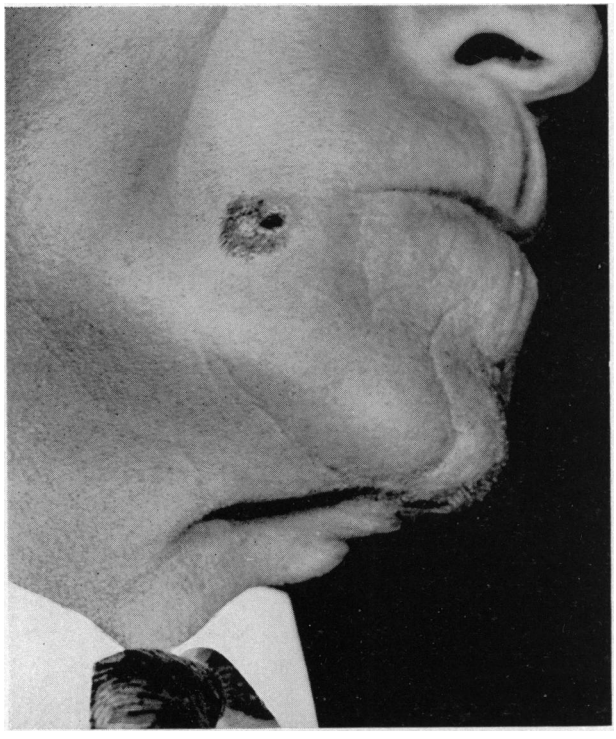


FIG. 1.—Photograph of a lesion in which repeated injury by shaving was most likely the inciting factor for the development of this malignant melanoma in a pigmented naevus. Wide local excision was performed. Patient is alive and well now for four years.

Etiology.—A melanoma often develops insidiously from a brown, black or bluish pigmented spot. Frequently, however, the wild proliferation of cells takes place after irritation or trauma, even from the unpigmented end-organs of the peripheral sensory nerves.[5] Repeated irritation over a period of years or following a single injury may be the cause, even in the very common mole with or without hair. The Cohnheim theory supposed that the pigmented mole harbors cells that are "sleepers" and after being irritated become actively growing melanoma. The cause may be friction by a corset on the back, or by the shoe in the nail bed (melanotic whitlow of Hutchinson), on the face after being cut by a razor (Fig. 1); even injection through a pigmented mole as in one of our cases seems to be the inciting cause.

Tièche[10] described a blue or bluish-black congenital macule located on the face, which is considered a persistent mongolian spot. The development of melanoma has occasionally been observed from this lesion. Infection of the surrounding skin areas of the naevus may be the irritating factor. The injudicious use of the electric needle (Fig. 2) in treating naevi was the most

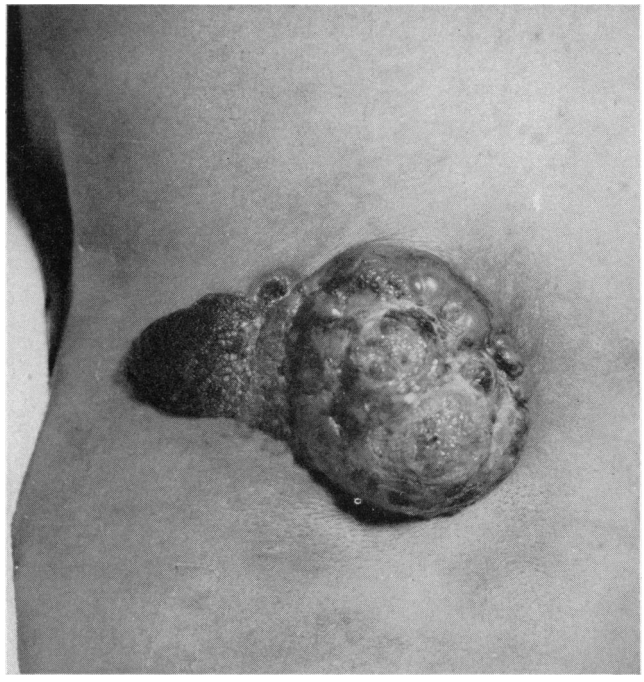


FIG. 2.—Hosp. No. J. 795: Photograph of a nonpigmented melanoma with axillary metastases, developing from a pigmented papillary naevus due to repeated irritation by electric needle. The treatment consisted of weekly desiccation over a period of 11 months. Female, age 36, died with general metastases in five months.

probable originator of melanoma in five of our cases (4.3 per cent), and in 10 per cent of the cases reported by Adair.[11] One of our patients used a corn-plaster on a congenital pigmented mole, giving rise to the development of melanoma. Trauma seemed to be the etiologic factor in 28 (25 per cent) of our cases. Daland and Holmes[46] found it in 24.8 per cent.

According to F. C. Lee,[12] Anglo-Egyptian Negroes have 100 times as many melanomata as American Negroes.[13] The reason, he ascribes, is that the wearing of shoes by the latter prevents the direct irritation of rough roads and thorns. Parkes-Weber[14] reported a newborn baby who died of liver metastases of melanoma, whose mother died, after giving birth, of generalized melanosis. He supposed that the metastasis occurred during the intra-uterine life through the placenta. The pigmented areas of xeroderma pigmentosum may give rise to melanomata, as was also observed in one of our cases.

Pathologic Classification.—From the clinical point of view melanomata have been classified as follows[15]:

(1) Naevus giving evidence of increase in size or in darkening of pigmentation.

(2) Melanoma showing well-developed tumor in local lesion.

(3) Melanoma with involvement of regional lymph nodes.

(4) Generalized melanoma—melanosis.

All of our cases were of Groups 2, 3 and 4.

Age Distribution.—The youngest patient with melanoma in our series was a 15-month-old girl, then a five-year-old boy. The oldest was a man of 78 years. Among the remaining patients there seems to be a fairly even distribution of melanomata between the ages of 20 to 70 years in both sexes. The most frequent occurrence was observed between the ages of 45 and 60, in which group 38 per cent of our patients were found. Table I shows the distribution of our 117 patients according to age:

TABLE I

AGE DISTRIBUTION

Years of age	1–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80
No. of patients	2	8	19	20	23	29	13	3

The average age according to Hintze[16] is 47.7 years for males and 54.7 for females. Darier[17] states it to be 54.4 years for both sexes, while Butterwoth and Klauder[18] found it to be 49 years. Daland and Holmes[46] found their greatest number of cases in the sixth decade.

Statistics seem to indicate that women are affected somewhat more frequently.

Anatomic Distribution.—Melanomata may develop anywhere in the skin or, rarely, in mucous membrane. According to the analysis of our cases they are most common on the head (40 per cent), lower extremities (26 per cent), and upper extremities (15 per cent). According to the available computed figures, from the literature, melanomata are observed most frequently at the extremities (40.3 per cent: upper, 10.9 per cent; lower, 29.4 per cent). Properly speaking, the head lesions are the most frequent (35.1 per cent)—with the eye, 41 per cent, considered as one unit against four extremities. The remaining 24.3 per cent are scattered all over the rest of the body.

Melanomata have rarely been primarily observed at locations other than their usual appearance on the tegument. Peters reported five cases of melanoma observed in the male urethra. There have been fewer than 100 cases of melanoma of the rectum reported (Chisholm[21]). Lenče[22] collected 43 cases of primary melanoma of the central nervous system, in addition to one case of his own, also 11 cases in the biliary tract, and 39 cases in the oral cavity. They are seldom found in the nasal cavity, esophagus, or intestines. Tučzek[23] and Goldzieher[24] have described bilateral primary melanomata of the suprarenal glands.

Modes of Spread.—After the malignant changes have occurred in the tumor, they infiltrate the surrounding tissues, spreading first by *direct extension.* Handley[25] demonstrated the involvement of the lymphatic channels, which may result in the formation of numerous subcutaneous nodules proximally

or toward the periphery from the original growth. The tumor cells reach the *regional lymph nodes* through the skin lymphatics, causing their enlargement. It is rare to observe fungating lymph nodes because death occurs as the result of general metastases before this may happen. Pigmentation is often marked in the metastatic lymph nodes, even where the original lesion contained little or no pigment. The tumor gradually invades the capillaries of the invaded nodes, ruptures the blood vessels, and makes way for the invasion of the

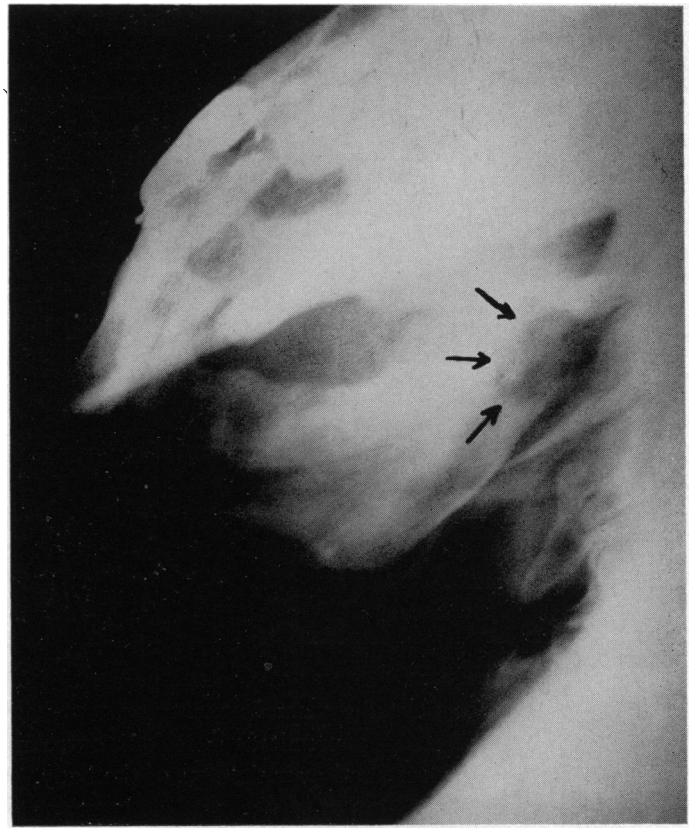


FIG. 3.—Roentgenogram showing metastasis to the lower jaw from a malignant melanoma of the toe, which was cauterized, then excised by a chiropodist, later treated by an electric needle. Excision and resection of involved inguinal lymph nodes did not arrest the disease. Patient died three months later.

blood stream by the melanotic cells, which results in generalized metastases. Blood stream invasion may also occur directly.

Metastases—The Principal Organs Involved.—Among our cases, involvement of the regional lymph nodes at the time of the first examination was noted in 31 cases (27.4 per cent). Diffuse local, multiple involvement of the skin was present in two cases, and there were recurrent lesions in ten. Generalized metastases were observed in 11 cases, and these were considered inoperable (10 per cent).

Among Adair's[11] 400 cases there were 245 recurrent lesions, of which 141 were far advanced; he found only 26 per cent (that is, 105 cases) with primary tumors in operable condition.

According to Geschickter and Copeland,[26] bone metastases have been observed in only 1.07 per cent, which is about the same incidence as among our cases where we found only one metastasis of the lower jaw (see Fig. 3). This incidence, however, is possibly higher (Daland[46]).

Metastases usually appear in the regional lymph nodes of the drainage area. Lymph node metastases may occur early or it may appear only after the disease has become generalized. In generalized melanoma all organs may be involved. Diffuse and distant skin metastases are observed which vary in their course. Spontaneous regression[46] or sudden arrest of the evolution has been observed, which again may flare up with rapid growth. The liver is frequently invaded. The lungs, brain, heart, intestine, and the whole lymphatic system have been found involved.

Metastasis in the majority of cases appears within from six months to two years after the original tumor was noticed. It may, however, develop years after the original lesion has been removed or left untreated. In some cases the growth is slow and metastasis occurs late—in exceptional cases as late as from five to 15 years. Late, distant metastases are seen most often in the melanomata of the eye.[46] General metastases developed 27 years after operation in a case described by Balčerek.[27]

Symptomatology.—The first signs of the malignant proliferation are variable. It is common to observe that a hitherto symptomless naevus feels to the patient irritated, inflamed, and it may itch or even hurt slightly. It may ooze, weep or bleed, or adhere to the clothing. It increases in size, becomes more prominent, raised, and turgescent. A black spot may appear in the middle or at the periphery of the dark pigmented area (Fig. 1). The soft, cellular naevus becomes resistant, infiltrated, and firm. These changes are usually slow, taking several months; they are rapid only if irritation or trauma (especially if repeated) is the inciting factor.

Occasionally the original region is surrounded by small metastatic nodules which may be felt rather than seen. The lesion soon ulcerates, and becomes partly covered with a scab; it has the tendency to fungate and bleed easily. It is vegetant, gray-rose or dark red, and may be mistaken for a pyogenic granuloma. Regional lymph nodes are invariably enlarged after the disease advances. There can be no rule as to the time which has elapsed since the original lesion appeared. There seems to be no direct relation between the size of the tumor and the appearance of involved regional lymph nodes, which may occur earlier if ulceration has developed. General metastases may rarely occur simultaneously with regional lymph node involvement.

Melanuria, according to Kumer,[2] was present in 28 per cent of his cases. This may occur more often in the advanced lesions. The urine usually turns a darker color after standing in air, after the secreted melanogen becomes oxidized. Rarely, the urine is black from the secreted melanin.

There are some instances where the malignant degeneration of the pigmented mole is indicated by the enlargement of the regional lymph nodes,[15] and in some cases the original lesion may be so insignificant that it may not be detected even by careful investigation.

Time When Patients Apply for Treatment.—Less than 10 per cent of our patients came within one month following the first sign of malignant degeneration. The average time was eight months, which may be considered an unnecessary delay of six months, caused by lack of information or by fear.

Size of Melanomata.—Among our patients, at the time of applying for treatment, the size of the melanomata varied from 2 Mm. to 11 cm. in diameter. About 15 per cent of them had lesions measuring less than 1 cm. in diameter. The majority had lesions of from 1.5 to 2 cm. (55 per cent); the remaining 30 per cent had lesions averaging 3.5 cm. in diameter. No direct relation between the size of the lesion and regional lymph node involvement or general metastases could be established with any accuracy.

Clinical Types of Melanoma.—Usually, a melanoma is a flat or nodular, papillary, warty, raised lesion, but it may be a pedunculated, ulcerated, and less frequently a subcutaneous nodular lesion. It may be associated with neurofibromatosis or xeroderma pigmentosum. As has been mentioned, lymph node involvement may be the first symptom. Melanoma appears singly, and is seldom multiple.

Prognosis.—Melanoma is invariably fatal if not controlled by surgery or, possibly, by irradiation. It is not yet possible to depend entirely on the microscopic picture of the lesion regarding prognosis. General metastases occur more rapidly from an irritated lesion than from an untreated one. Some may live with untreated lesions for years, but the average duration of life is between one and one-half and three years. Younger people seem to die of the disease more quickly than do the more elderly.

A great number of patients who survive the five-year period develop recurrences later, and, according to Wilbur and Hartman,[28] all patients with melanoma of the eye die of general metastases (liver) if no other cause of death intervenes. One of our patients died six and one-half years after the operation, and one after 11 years from generalized melanoma.

Some recurrent lesions, however, may also be controlled and arrested by extensive radical surgery. Daland and Holmes[46] reported a patient with recurrent, diffuse, nonpigmented melanoma with inguinal lymph node involvement who, after the resection of the diffusely recurrent nodules of the thigh and leg, was well for six and one-half years.

Prophylactic Treatment.—Though the results obtained by surgery are encouraging, it seems to be equally important to prevent improper treatment or irritation of pigmented lesions. Collaboration between the public, practitioners, and surgeons is desirable with a view to eliminating those pigmented areas which may undergo malignant degeneration.

Beauty parlors, chiropodists, *etc.*, need to be warned about the possible consequences of insufficient treatment of the dark pigmented moles. It is

advisable to excise or coagulate those darkly pigmented naevi which are subjected to irritation (for example, by shoes, clothing, combing, and shaving). It is important to avoid the use of chemical irritations—caustics and electric methods which do not destroy the lesion in its entire extent.

FIG. 4 A FIG. 4 B

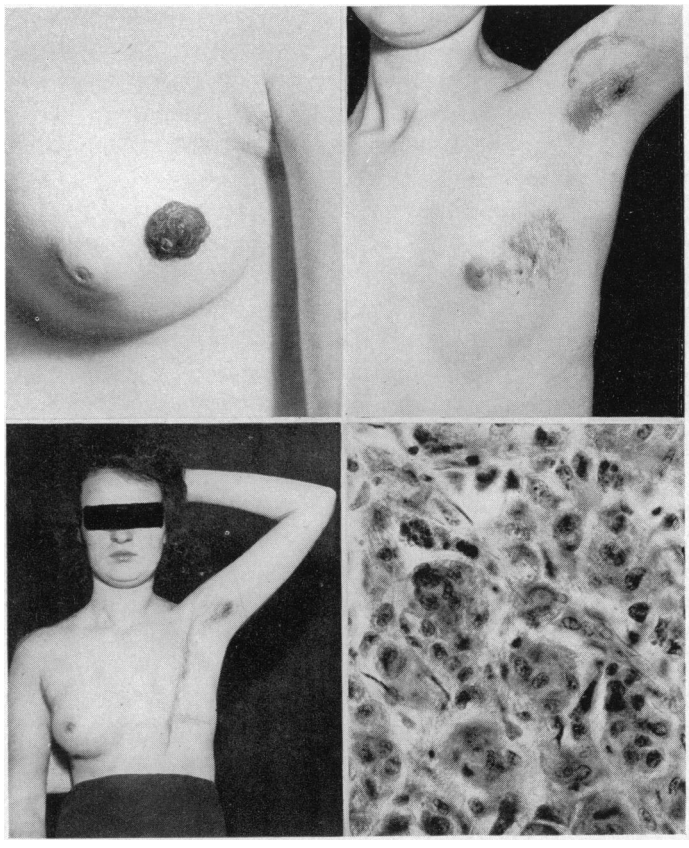


FIG. 4 C FIG. 5

FIG. 4 A.—Patient a 15-year-old girl: Malignant melanoma of three months' duration developing in a congenital naevus. Two months after local excision axillary lymph node dissection was performed. Several nodes were involved.

FIG. 4 B.—Local recurrence in ten months. Operative scar indicating previous excision and lymph node dissection in the axilla.

FIG. 4 C.—Good functional result after radical breast amputation for recurrence. Operative scar at the side of the chest indicates an electrosurgical excision for a third recurrence three months after radical operation. Prompt radical operation at the first intervention probably would have prevented repeated recurrences. Patient is well after one and a half years.

FIG. 5.—Path. No. S. C. 79660: Photomicrograph of tumor showing cells in distinct groups. Hyperchromatism and anaplasia. Dark brown pigment in many cells. (×570)

Pigmented moles occur at an average number of 20 on the body of each individual (Block[9]); therefore, it is easy to see how frequently intervention may be abused.

Especially dangerous, clinically, are the black, glistening or deeply pig-

mented moles; however, there are observations of numerous darkly pigmented moles which have been quiescent for an entire lifetime.

Surgical Treatment.—The generally accepted treatment is surgical. Early, radical excision alone gives satisfactory results at present, but dissection of the regional lymph nodes, even if there are none palpable nor enlarged, is advocated. In a melanoma of the breast of a 15-year-old female (Fig. 4 A), in whom, in spite of the fact that there were no palpable or axillary lymph nodes, dissection was performed, but pathologic examination showed secondary involvement with heavy pigmentation (Fig. 5). Although, one year later (Fig. 4 B), and, again, 18 months later, local recurrences developed. Removal of the breast, and wide excision of recurrent nodules, was undertaken. The patient has been well for the past 18 months (Fig. 4 C). Local recurrence may be more effectively controlled when there has been a previous lymph node dissection.

Administration of Coley's serum is disappointing, as is the use of colloidal lead (Adair[11]). Amadon[29] and Adair[11] condemned electrocoagulation, but Pfhaler and the French school[30] rely entirely upon it. At the Radiumhemmet in Stockholm, electrosurgery is recommended, followed by irradiation.[41] Recent literature advocates electrosurgery as the most effective method to treat local lesions.

In our opinion, wide, radical excision of the primary lesion with the underlying fascia and surrounding subcutaneous tissues including its lymphatic area, followed by regional lymph node dissection, is the choice of treatment. If biopsy is necessary to establish the diagnosis, it should preferably be accomplished by an electric loop, followed by coagulation of the lesion, in order to prevent dissemination.

Amputation is advocated in melanomata of the fingers, toes and foot, if lesion is on the heel (Fig. 6), for anatomic reasons where the connective tissue bands going from the skin perpendicularly to the underlying bone form closed spaces filled with fat tissue. This arrangement directs any inflammatory process or new growth formation toward the periosteum. The same thing happens in cases of pyogenic infection of the fingers, especially on the volar surface. The infection, if not drained, generally involves the tendon sheath, periosteum and bone. Therefore, melanomata of the fingers, toes and heels, presumably, can be effectively eradicated only by amputation followed by regional lymph node dissection.

Among the reported cases, amputation was performed in six instances followed by inguinal lymph node dissection, in which involvement was found in three cases. Of the 25 cases reported by Williams[31] (including eight non-pigmented melanomata) the only one which survived had had amputation performed.

Regional lymph node dissection appears to be indicated especially in lesions of the extremities (particularly the foot) where constant irritation seems to predispose to earlier lymph node involvement. Melanomata of the face would seem to have, therefore, a better prognosis, as they are treated earlier and are

less subject to trauma, which may delay regional lymph node involvement. Daland and Holmes[46] reported three cases surviving the five-year period; after the involved regional metastatic lymph nodes were dissected. Table II shows an analysis of our 24 cases with lymph node dissection:

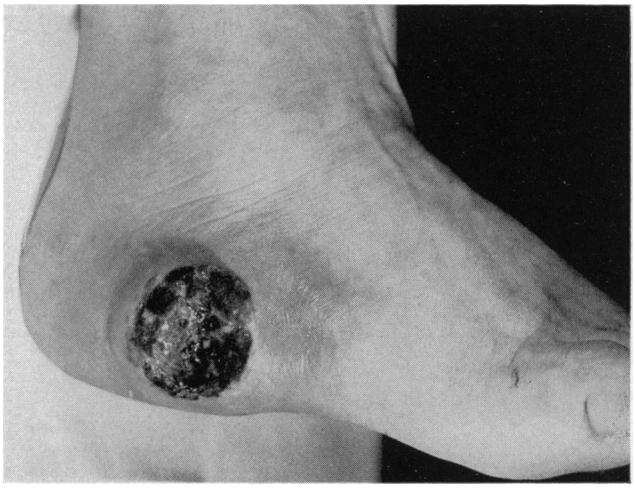


FIG. 6.—Photograph of a malignant melanoma of the right heel of two years' duration. Previous cauterization. Excision by the high frequency current, followed by inguinal lymph node dissection failed to arrest the disease. Six months later, recurrent nodules were excised from the leg, then from the thigh. This patient, male, age 56, died one year after the operation. Lived three years with the lesion. Amputation might have been a life-saving procedure.

TABLE II

ANALYSIS OF 24 CASES WHICH HAD REGIONAL LYMPH NODE DISSECTION

16 cases with involved lymph nodes..... 62.5 per cent
8 cases with hyperplasia..... 37.5 per cent

SURVIVAL AFTER LYMPH NODE DISSECTION WITH INVOLVED NODES

2 cases —No follow-up
6 cases*—Died after average period of 2 years
1 case —Died after 6½ years
7 cases —Alive (2, for 6 months; 1, for 2 years; 1, for 3 years; 1, for 5 years; 1, for 9 years; and 1, for 11 years)

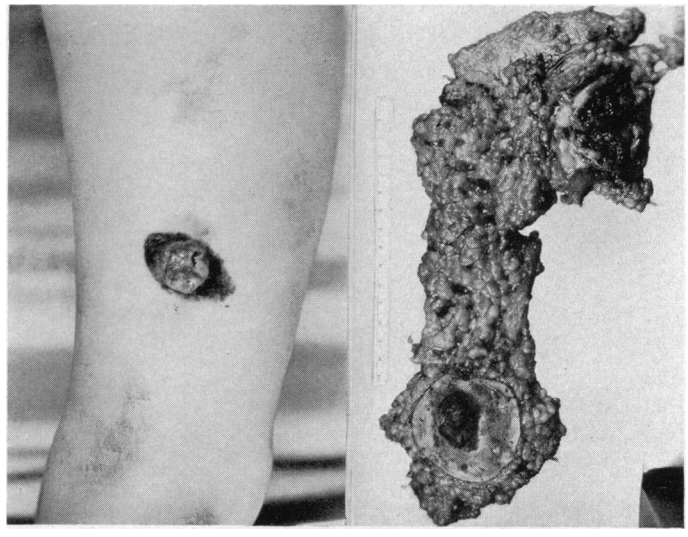
* Advanced lesions.

SURVIVAL OF CASES WITH HYPERPLASIA

1 case —No follow-up
1 case —Recurrence 2 years later
4 cases—Died (1, after 10 months; 1, after 1 year and 10 months; 1, after 2½ years; and 1 after 6½ years)
2 cases—Alive (1, after 8 months; and 1, after 3 years)

To prevent local recurrences, more radical surgery, according to the principles of Handley[25] and Pringle,[32] seems to be justified. This consists of a wide dissection of the lymph channels, not only around the lesion but also up to the nearest lymphatic nodes. The skin is reflected on each side between

the lesion and corresponding regional lymph nodes, and the subcutaneous tissue removed with the subcutaneous fascia in one continuous strip. A specimen (melanoma of the upper arm, obtained from an operation in accordance with this principle), is shown in Figures 7 A and B. With such a method, Pringle operated upon two cases—one, a woman with axillary lymph node involvement, who has been well for 38 years; and the other, a man with inguinal lymph node involvement, who has been well for 30 years. He further stated that these two were the only cases he had ever operated upon. How much the



A B

FIG. 7 A.—Photograph of a malignant melanoma of the right upper arm, with axillary lymph node involvement, which developed in a naevus. First sign one year previously.

B.—Gross specimen removed by wide incision, with surrounding subcutaneous fat tissue ad fascia, block dissection of lymphatics from lesion to axilla, and axillary lymph node dissection. One lymph node showed involvement (with heavy pigmentation).

In this advanced lesion even such a radical operation failed to arrest the disease. Patient died one year later of pulmonary involvement.

more radical approach will improve the result can be answered only in the future, after more experience and follow-up observation.

Roentgen Ray and Radium Therapy.—According to Adair,[11] irradiation is of questionable value, and Stewart[34] states that only 2 per cent of melanomata have some degree of radiosensitivity. Darier even states that roentgen ray and radium treatment is harmful. Francis Carter Wood expresses his belief in its inefficacy. Meland[35] states that roentgenotherapy may destroy the local lesion but that all the patients die of general metastases. Holfelder[36] treated 18 patients, 14 per cent of whom had previously been operated upon, and 40 per cent died within the first year. Chaoul[37] (using daily doses of 300 to 500 r to a total of 8 to 15,000 r) treated 14 cases, and failed in only two instances. However, only one case survived four years, and the majority less than one year. McEuen[38] reported two cases out of six, well over five years after radiotherapy.

We may conclude that irradiation under the present technic is not recommended as the sole treatment of melanomata, although one may conceive that early, localized lesions may be destroyed with heavy radiation, which of course may be more conveniently excised radically with better ultimate and cosmetic results.

Analysis of Available Material.—There were 117 cases available for study from the records of the Skin and Cancer Unit of the New York Post-Graduate Hospital. In these cases the clinical diagnosis of melanoma was made. Of this series, only 81 have been verified by pathologic examination.

Six cases were admitted with general metastases for palliative treatment. In these cases only biopsies were taken.

Operations were performed upon 75 patients.

There was no operative mortality. Among these 75 cases, there were 15 patients woh did not return for follow-up examinations. The analysis of these cases is shown in Table III:

TABLE III

ANALYSIS OF 81 HOSPITALIZED PATIENTS

Total No. of patients admitted to hospital		81	
Inoperable, biopsy only		6	
No. patients operated upon		75	92.5%
Operative Cases:			
Postoperative deaths	0		
Died (with follow-up)	24		
Alive (with follow-up)	36		
No follow-up (lost)	15		
Total	75		
Cases with Follow-Up;			
Alive (after from 3 months to 13 years)	36		
Dead (after from 6 months to 11 years)	24		
Total	60		

GROUP A.—TIME-PERIOD OF POSTOPERATIVE FOLLOW-UP OF 36 PATIENTS FREE OF RECURRENCE OR METASTASIS

5— 3	months:	Toe, ear, cheek, foot, forehead
5— 6	months:	Breast, arm, temporal region, 2 on the foot
5— 1	year:	2 foot, back, 2 eye
7— 1½	years:	3 cheek, scalp, 2 arm, foot
1— 2½	years:	Toe
3— 3	years:	Forehead, foot, arm
1— 4½	years:	Arm
1— 5	years:	Forehead
2— 8	years:	Cheek, back
1— 9	years:	Forehead
2—10	years:	Arm
1—11	years:	Lip
1—12	years:	Arm
1—13	years:	Arm

Summary of the above: Head, 16 cases; extremities, 16 cases; elsewhere, four cases.

GROUP B.—TIME-INTERVALS BETWEEN OPERATION AND DEATH OF 24 PATIENTS WHO DIED OF THE DISEASE

1	died	in	6 months
1	"	"	9 months
1	"	"	1 year
3	"	"	1½ years
4	"	"	2 years
6	"	"	2½ years
3	"	"	3 years
1	"	"	4 years
1	"	"	4½ years
1	"	"	4¾ years
1	"	"	6½ years
1	"	"	11 years

GROUP C.—CASES FOLLOWED FIVE YEARS OR MORE, INCLUDING FIVE CASES WHICH WERE NOT TRACED AS ASSUMED DEATHS

Postoperative deaths	0
Known deaths	10
Assumed deaths (cases lost)	5
Well without recurrence	9
Lived with recurrence, until death 6½ and 11 years after operation	2
Total	26

5-year survival—42.3%
10-year survival—19.2%

These statistics are given with the lost (not followed-up) five cases which are considered as dead.

None of our cases lived free of disease over the five-year period having melanomata on the foot. In one case it was on the toe, which was amputated after a recurrent lesion, but the patient died 11 years later. Therefore, according to our small series of cases, we may reaffirm our previous statement that these malignant pigmented lesions are more benign in their clinical course on the head than when situated on areas such as the foot, where they are subjected to more trauma.

Among the patients in Group C, five had regional lymph node dissection; three of these five have survived for eight, nine and 11 years, respectively, with no evidence of disease, in spite of the fact that the regional lymph nodes were secondarily involved.

Five patients have been well for over ten years (one each for 13, 12, and 11 years, and two for ten years), one for nine years, two for eight years, and one for over five years. One died from general metastases 11 years after operation, following a symptomless period of eight years, and another died suddenly with general metastases after six and one-half years.

Statistics from Other Authors.—Darier[17] reported 43 cases, with follow-up on 23 of them. He employed electrosurgery, and had nine patients living for periods ranging from one to 12 years after operation. Miescher and Schürch[19] reported on 41 cases of melanomata on the head and extremities, treated by surgery and electrosurgery, and stated that 19 patients survived for periods varying from one to 11 years after operation (Table IV).

TABLE IV

SUMMARY OF CASES REPORTED BY OTHER AUTHORS WITH DEFINITE ARREST OF THE DISEASE FOR FIVE YEARS OR LONGER

Reported by	No. of Cases	Location of Lesion	Kind of Therapy	Survival: No. of Cases	Survival: Time	Percentage of 5-Year Arrest	Percentage over 10 Years
Adair[11]	70	Head, body and extremities	Surgery	23	5 yrs.	33	
Affleck[20]	170	Head, body and extremities	Surgery	20	5 yrs.	11.1	
Bloodgood[39]	200	Head, body and extremities	Surgery	1	5 yrs.	0.5	
Daland and Holmes[46]	82	Eye, head, body, and extremities	Surgery	15	5 yrs.	18.3	
de Cholnoky	26	Eye, head, body, and extremities, except eye	Surgery	11	5 yrs.	42.3	
				5	10 yrs.		19.2
Gleave[40]	18	Eye	Surgery	9	5 yrs.	50	
				5	15–19 yrs.		27
Hintze[16]	54	Head, body and and extremities	Surgery and x-ray	15	5 yrs.	27	
				5	13 yrs.		9.2
Meland[35]	50	Head, body and extremities	Surgery	9	5 yrs.	18	
Scharnagel[41]	70	Head, body and extremities	Electro-surgery and x-ray	27	5 yrs.	39	
Scott[42]	53*	Head, body and extremities	Electro-cautery	11	5 yrs.	37.9	
Total	793			156			
Average per cent of five-year arrest						19.2	

Differential Diagnosis.—Differentiation of melanoma from epithelioma is not difficult if pigmentation is present. The classic symptoms are well known. However, as Ewing has pointed out, there are pigmented epithelial tumors that are not identical with melanomata, and it is sometimes difficult to distinguish between them. These lesions are the pigmented epithelial papillomata, pigmented basal cell tumors, pigmented carcinoma in xeroderma pigmentosum.

Ulceration of the nail bed should be regarded with suspicion, especially above the age of 40, according to Womack.[43]

Ulcerated hemangiomata, warts, frequently granulation tissue, and above all pyogenic granuloma may closely simulate rapidly growing melanoma of the skin and mucous membrane. According to MacKee and Cipollaro,[44] the pyogenic granulomata, sometimes dry but mostly with mucopurulent exudate present, are soft (boggy), of various shades of red, often encrusted, and vary in diameter from 2 Mm. to 1 cm. They bleed readily and may be pedunculated. Melanomata grow relatively slowly; they are firmer, and discharge only if ulceration is present. Often, there is a history of an antecedent naevus with more or less pigmentation.

Histologic examination should confirm the diagnosis.

Nonpigmented Melanomata.—These are only rarely diagnosed clinically (3 per cent of our cases). The absence of pigment may be explained by their rapid growth—with bad prognosis. These melanomata are observed in patients past middle life. More than 50 per cent of them are at the lower extremi-

ties. Horwitz,[45] among his 49 cases, found that their life average was 18.8 months, and that the postoperative arrest in 10 per cent of his cases ranged from two weeks to six and one-half years. Of his cases, 80 per cent died in from seven to 25 months (average, 16.8 months) when only irradiation was resorted to (six cases). Of eight cases, in which surgical excision was followed

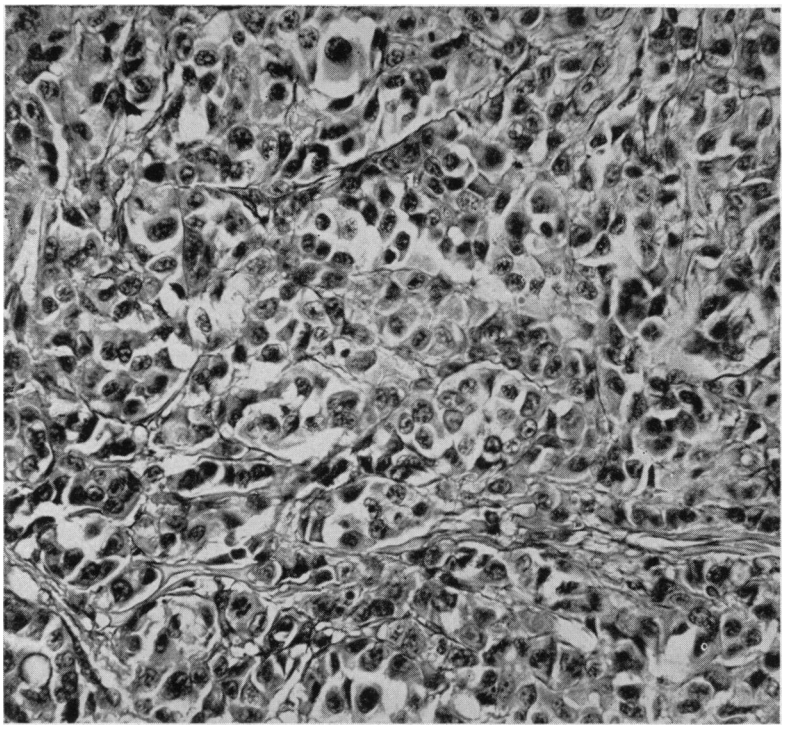


FIG. 8.—Path. No. S. C. 18683: Photomicrograph of a nonpigmented melanoma beneath skin of sole of foot. Female, age 68. Duration one year. (×250)

by roentgen ray and radium therapy, three were alive (for two years and 11 months, three years and eight months, and five years and nine months after operation).

Among our cases, there was a 55-year-old female with a nonpigmented melanoma. In this case, after amputation had been refused, 30 superficial, recurrent lesions were removed by an electric loop, at nine different intervals. The duration of the disease from beginning to end was three years. Only after two years was a lesion noted at the popliteal region, followed by others along the lymphatic path at the middle of the thigh within six weeks. The inguinal lymph nodes were involved for only a few months before the disease became generalized. Apparently, the tumor was spreading through the lymphatics of the subcutaneous tissues, and it could be clearly observed, clinically, that its propagation followed the lymphatics before the disease became generalized.

The study of this case and others suggest that amputation might have been a life-saving procedure.

SUMMARY AND CONCLUSIONS

Melanomata are pigmented or nonpigmented tumors of the skin and mucous membrane, supposedly of nervous origin. These extremely malignant lesions frequently arise from pigmented moles. They are observed at all ages, but predominantly between 45 and 60 years, and in both sexes.

Trauma and chronic irritation are evident in their development, as etiologic factors, in 25 per cent of cases. Lack of information is responsible for the fact that patients apply for late treatment. In the majority of cases there is an average of six months' delay. Since we are dealing with a superficial lesion that is easily discoverable, this dangerous delay could be prevented by disseminating information to the laity. Prophylactic treatment is advocated.

A clinical study and analysis of 117 cases of malignant melanoma are reported. Modes of spread, metastasis, symptomatology and prognosis are discussed.

Roentgen ray and radium therapy may destroy a local lesion, but authenticated cures under this treatment are rare; therefore, in operable cases it is not recommended in its present form.

In destroying the local lesion, electrocoagulation followed by lymph node dissection may be a desirable procedure.

In our opinion, radical surgery is the treatment of choice, and should consist of wide local excision including surrounding subcutaneous fat tissue and underlying fascia, followed by regional lymph node dissection. More radical intervention, consisting of removal of the lymphatic vessels in the subcutaneous fat tissues around the lesion and between the lesion and the regional lymph nodes, may also be desirable in irritated lesions. Amputation of the fingers, toes, and foot is advocated for anatomic reasons. This may give us improvement of the percentage of "five-year arrest," which to-day occurs in about one-third of the cases. The author's statistics of a relatively small number of cases show five-year arrest in 42.3 per cent, and ten-year arrest in 19.2 per cent of the cases; not including the cases untraced which are reported as deaths. In the New York Skin and Cancer Unit of the New York Post-Graduate Hospital, the tendency is to undertake radical surgery in treating melanomata.

The author wishes to acknowledge the kind cooperation of Dr. D. S. D. Jessup, Associate Consulting Pathologist of the New York Post-Graduate Hospital, who not only reviewed the slides of the cases studied but also gave many valuable suggestions in the preparation of this paper.

DISCUSSION.—Dr. D. S. D. Jessup (New York): There are some features of the pathology of melanotic tumors which are in contrast to the course pursued by other malignant tumors:

(1) The small and often insignificant size of the primary growth: One of our last treated cases had a tumor of short duration, 1 cm. in size, on the toe, which had already metastasized to the inguinal nodes. Another tumor, 3x5

Mm., under the nail bed of a finger, present for two months, showed invasion of the axillary nodes.

(2) The relatively benign appearance of the tumor cells in many melanomata: There are very few if any mitoses, anaplasia is absent, and in bleached sections, after removal of the pigment, the tumor appears relatively benign compared to what we are accustomed to see in metastasizing carcinoma or anaplastic sarcoma.

(3) In the metastases, we often find mere streaks of pigment in small cells as the only indication that the tumor is spreading from its primary site.

(4) Naevocarcinoma: While many believe that a large percentage of melanocarcinomata develop from pigmented naevi, it has been very seldom that we have been able to find traces of naevus cells alongside the developing melanocarcinoma. There is often the history of a pigmented birthmark but many of the deeply pigmented flat growths contain no naevus cells and show only pigmented cells in the corium. Where such pigment is deep in the corium we have the blue naevus, and if it is in the sacral region, the mongolian spot. Such pigmented areas may develop into melanocarcinoma, but we have followed many of the cases for years after removal of the tumor and they have shown no tendency to recurrence or spread. There does not seem to be any distinguishing feature in these flat melanomata which enables us to say whether they are potentially malignant. We see remains of flat melanomata alongside of more recent melanocarcinoma developing in the melanomatic bed, and we cannot differentiate the remains of the original growth from the clinically benign melanomata which have been treated by simple excision, and followed for years.

(5) Treatment: In following these treated cases for years, we have been impressed by the fact that surgery proves effective, often for long periods, and that regional node block dissections should be employed in the same way as in other forms of metastasizing carcinomata.

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