

The Treatment of Malignant Melanoma — Report of 862 Cases*

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THIS report embodies our experience on the Mixed Tumor Service of the Memorial Hospital for Cancer and Allied Diseases of New York City from 1917 to 1946. We reviewed 951 cases of malignant melanoma, of which 862 were available for critical analysis and 595 for determination of five-year end-results.

The term melanoma is used to designate the malignant tumor. We have discarded synonyms which are morphologic or genetic in purpose. Pigmented nevus or neuronevus is used to designate the benign precursory lesion rather than the confusing term, benign melanoma. The analysis is confined entirely to the malignant tumor, melanoma.

ETIOLOGY AND INCIDENCE

More than 50 per cent of our patients related a history of pre-existing nevus. The early signs of malignant degeneration were alteration in color, increased blackness, elevation, itching, pain or bleeding.

Trauma was alleged to have initiated these changes in not over one-fifth of the cases. Even this was a doubtful factor in most instances as the trauma appeared to be insignificant and probably served only to focus the patient's attention to a pre-existing nevus which was already beginning to show malignant change. Chronic irritation, as in the collar or belt-line, or from a shoe, on the other hand, should be given serious consideration as a possible stimulant.

Table 1 reveals the incidence of various primary sites in this series. It shows that there was a preponderance of involvement of the lower extremity as compared with the upper extremity, whereas the incidence of pigmented nevi is exactly the opposite. Also it discloses that the feet are a common site, almost as many occurring there as in the entire upper extremity. The nail bed is a favorite location. The group of 13 ano-rectal melanomas is probably the largest single collection as yet reported. The oro-nasal mucosal series represented about 3 per cent of all of our cases—about equally distributed in the gums, palate, nasal cavity and paranasal sinuses. There were 29 malignant melanomas of the vulva and two in the vagina. We found no primary visceral melanoma, all of our cases being confined to the skin, the mucocutaneous junctions and adjacent mucosa, and the eye (choroid and conjunctiva).

TABLE 1.—Primary Site of Melanoma from 1917 to 1946

The Memorial Hospital for Cancer and Allied Diseases, New York, N. Y.		
Site		Per Cent
Lower Extremity:		27.0
Exclusive of feet	12.7	
Feet, exclusive of nails	12.2	
Subungual	2.2	
Head and Neck		23.1
Trunk		17.9
Upper Extremity:		13.7
Exclusive of hands	10.1	
Hands, exclusive of nails	2.3	
Subungual	1.2	
Eye		8.6
Vulva and Vagina		3.6
Oro-Nasal Mucosa:		2.6
Lip	0.6	
Gingivae	0.6	
Palate	0.4	
Paranasal sinuses	0.5	
Rectum and Anus		1.5
Genitalia, Male		0.4
Unknown Primary Site		1.5

Distribution according to site is based upon 851 cases, since the site was not stated in 11 of 862 cases reviewed.

Chart I reveals that the cases were almost equally divided between the sexes, not only as a group, but also in the various age-groups. The majority of cases appeared in the 35- to 70-year period. The youngest patient was four months, the oldest, 86 years. There was a female preponderance in the extremities and ano-rectal area, but this was not significant.

There was a series of 15 patients of prepubertal age who had tumors histologically classified as malignant melanomas. Although the microscopic appearance of these pigmented tumors is so iden-

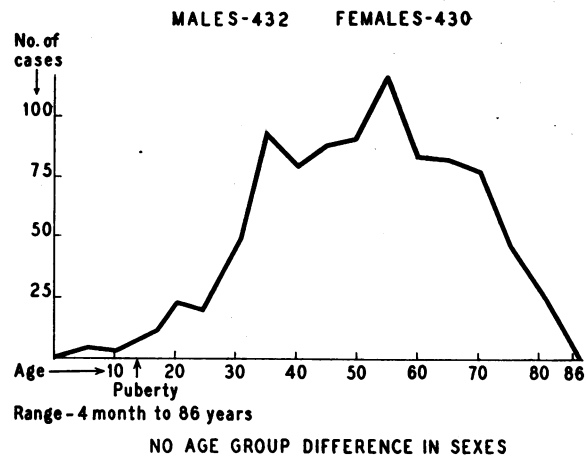


Chart I.—Age distribution in 862 patients with melanoma.

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tical with their congeners of adult life that pathologists cannot distinguish between them, their behavior is not in keeping with their anatomical structure. None of these melanomas metastasized and all of the patients have survived indefinitely. It must be accepted that this tumor has a most definite etiologic relationship to hormonal factors originating in pituitary, gonads and adrenal cortex. Inasmuch as the behavior of this tumor is so benign and the prognosis is so good, it would be well to classify it separately as prepubertal melanoma. One important conclusion to be drawn from

this observation is the wisdom of removing deeply-pigmented moles in infancy and childhood.

Only ten (1.2 per cent) of the 862 patients with malignant melanoma were Negroes and the majority of these were mulattoes. Melanoma in the Negro seems to occur more commonly in the mouth, nail bed and on the soles of the feet.

END-RESULTS OF TREATMENT

Of our 862 patients, 552 or 64 per cent had recurrent melanomas, i.e., had received prior treatment elsewhere. All of these patients are included in our statistics. We have listed every patient with melanoma who reported to our clinic, regardless of whether they were beyond help through treatment, or did not return after the initial visit.

In Table 2, it is evident that patients in the age group of puberty through 24 years had the poorest prognosis. The curability in these young adolescent patients was equivalent to about one-half of the over-all five-year salvage of 10 per cent. If we exclude the patients of the prepubertal age, the over-all five-year salvage would be about 9.5 per cent. There is no significant difference between the sexes.

The five-year end-results by primary site are presented in Table 3. It shows that the best end-results were obtained for malignant melanoma involving the hands, feet, eye and skin of the trunk. It is realized with dismay that none of the patients with mucosal melanoma survived five years. Malig-

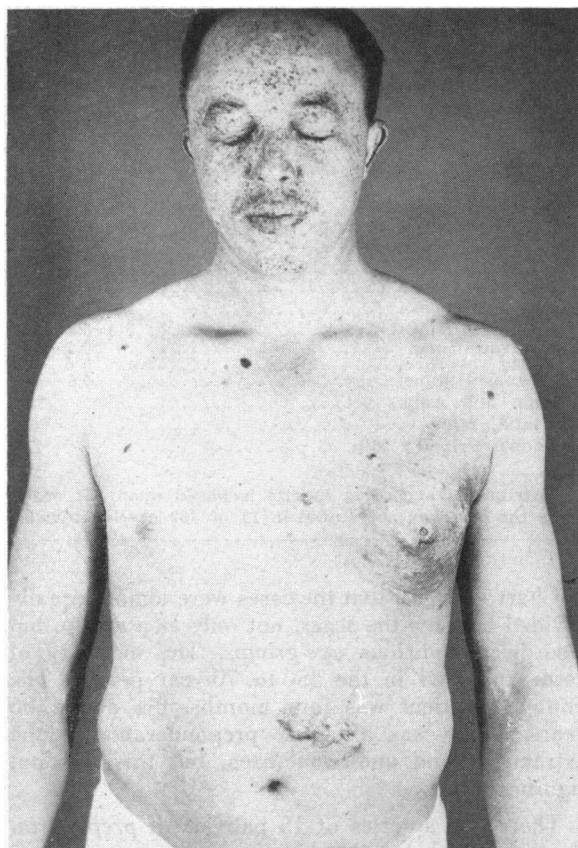


Figure 1.—Melanoma of skin of left upper abdominal wall in a mulatto male with satellite and left breast skin lesions and metastases to left axillary lymph nodes.



Figure 2.—Showing the very extensive area remaining for skin grafting following a very radical excision "in continuity" of the involved skin and underlying fascia, combined with a radical mastectomy.

TABLE 2.—Five-Year End-Results in 595 Cases of Melanoma In Relation to Age Groups

Age Period	Total Cases	Per Cent of Five-Year Survivals
Prepuberty	10	100.0
Puberty through 24 years	145	5.3
25 through 39 years	145	8.2
40 through 59 years	250	9.6
60 years and over	168	10.0

TABLE 3.—Five-Year End-Results in 595 Cases of Melanoma In Relation to Primary Site of Tumor

Site	Number	Per Cent
Lower Extremity:		
Leg, exclusive of feet	73	4.8
Feet, exclusive of nails	77	14.5
Subungual	9	11.0
Head and Neck	138	8.8
Trunk	98	9.8
Upper Extremity:		
Arm, exclusive of hand	59	6.3
Hand, exclusive of nails	16	42.0
Subungual	9	11.0
Eye	58	12.8
Vulva and Vagina:		
Vagina	2	None
Vulva	23	4.5
Oro-Nasal Mucosa:		
Lip (muco-cutaneous)	3	66.7
Gingivae	4	None
Palate	3	None
Paranasal sinuses	6	None
Rectum and Anus	5	None
Genitalia, Male	3	None
Unknown Primary Site	8	12.5

Over-all five-year survival-rate, 9.7 per cent; no sex difference.

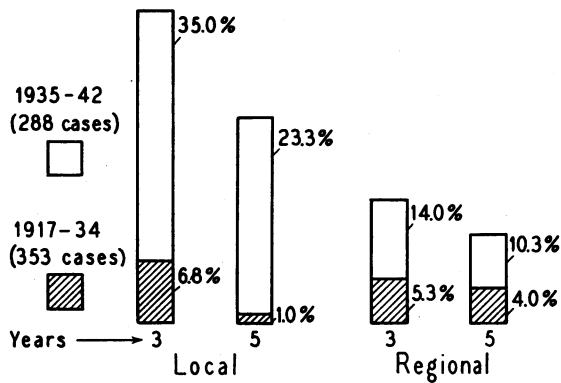


Chart II.—Three- and five-year end-results in the treatment of melanoma, in relation to the time period and the extent of the disease.

nant melanoma of the extremities, exclusive of the hands and feet, yielded about one-half of the overall survival rate of 10 per cent.

Chart II offers a comparison of non-selected groups of patients with malignant melanoma treated by surgical excision and/or by radiation therapy. Before 1935, irradiation was the primary mode of treatment. The modalities employed were low and high voltage x-rays, telecurie therapy by a large radium bomb or pack, superficial radon plaques, and the interstitial deposition of gold radon seeds. In 1935 surgical measures were established as the primary therapeutic agent. We, therefore, have two groups of unselected cases suitable for comparing the results obtained with irradiation and surgery. For localized melanoma, the later surgical treatment secured five times the salvage for three years and 23 times the salvage for five years, than was obtained by primary radiation therapy. Whenever metastases to regional lymph nodes had occurred, the salvage at three years was nearly three times greater and at five years two and one-half times greater as a result of predominantly surgical treatment. It could be stated more simply and conclusively that radiation therapy of any type and degree was completely ineffective.

In Chart III a comparison is shown between all of the patients treated by irradiation and by surgery, regardless of the time period. For localized melanomas, surgery yielded 38.4 per cent salvage at three years, as against 1.6 per cent for irradiation; and 17.7 per cent as against none for five years. The same proportionate increase in salvage is revealed in the treatment of patients with metastases to the regional lymph nodes. Included in the analysis are 18 patients surviving from ten to seventeen years, all of whom had undergone surgical treatment, with or without irradiation. No patient was treated solely by irradiation. These patients all had dissection of the regional lymph nodes and in seven patients the nodes were positive for metastatic melanomas.

The most important surgical principle in the treatment of melanoma is wide and deep excision of the primary lesion. This is based on the known frequency of local recurrence after conservative surgical removal and the tragic development of

associated satellite lesions due to early permeation of the subdermal and deep fascial lymphatic channels, with retrograde local metastases vertically back toward the skin along the connecting fibrous septa and centrifugally in the immediate vicinity of the local lesion. Regardless of the size of the primary melanoma, at least six to ten centimeters of skin border and a still wider circle of deep fascia should be removed *en masse* with the primary tumor. The skin margins should be undermined laterally as very thin, almost full-thickness flaps, so that the subcutaneous fat overlying the wider circle of fascia will be removed with it from the underlying muscles. In the majority of cases primary skin grafting is required to close the defect.

If the regional lymph nodes are not palpable, the question of elective dissection of these node-bearing regions depends on many factors, such as the location of the primary melanoma, the his-

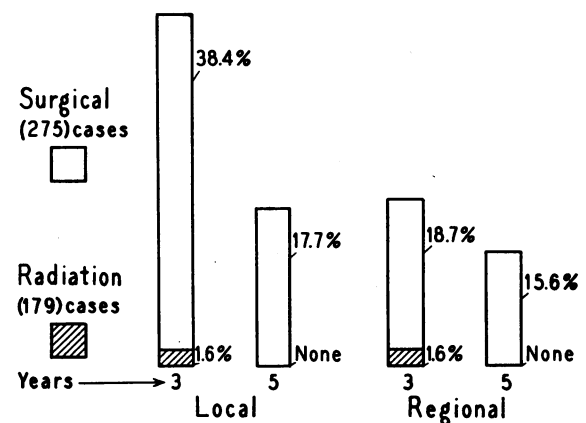


Chart III.—Three- and five-year end-results in the treatment of melanoma, in relation to type of treatment and the extent of the disease.

tologic picture, the age of the patient, and the ability of the patient to return for regular follow-up examinations. If the regional lymph nodes are positive for metastatic melanoma, they are removed by radical dissection about two weeks later, or preferably "in continuity" at the time of the initial operation.

The operation which we call "wide excision of the local melanoma with radical dissection of the regional lymph nodes in continuity" is based on the soundest oncologic principle as yet evolved. It is the same principle as the one underlying the operation of radical mastectomy for cancer of the breast and the one-stage Miles operation for cancer of the rectum. It is an attempt to remove the primary melanoma and all of its lymphatic drainage basin, including the first group of regional lymph nodes, *en masse*. Unfortunately, this is not always possible in cases where the primary lesion is at a great distance from the regional nodes, as in the hand or foot. In these cases one may have to perform a very radical procedure as an interscapulothoracic amputation of the upper extremity, removing the scapula and most of the clavicle while encompassing the entire axilla. In the lower extremity

for primary melanoma of the foot metastatic to inguinal and femoral lymph nodes, we resort to a hip joint disarticulation combined with a retro-peritoneal dissection of the iliac and obturator

lymph nodes. One of us (G.T.P.) has recently performed two hemipelvectomies for melanoma in which the innominate bone was removed, together with the lower extremity.

Chart IV is based on too few cases in several of the categories, but is presented only because we feel it shows a definite trend toward greater salvage in keeping with the institution of more radical surgery. It reveals that the more radical surgery of local excision plus regional node dissection for localized melanoma offers a better three- and five-year salvage, and that the same applies to regional metastatic melanoma when comparing the "continuity" operation with separate local excision plus regional node dissection.

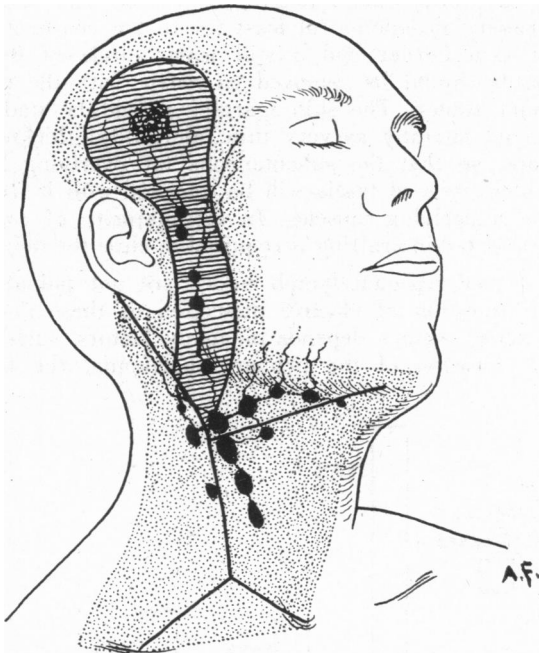


Figure 3.—To illustrate the principle and scope of the excision and dissection in continuity of a primary melanoma situated on the temple with metastases to the cervical lymph nodes.

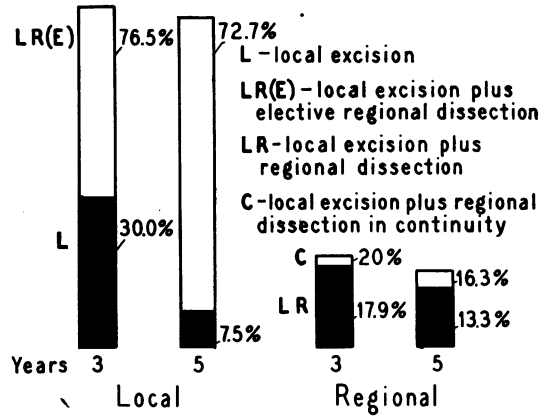


Chart IV.—Three- and five-year end-results in the treatment of melanoma in relation to the type of surgical treatment and extent of disease.

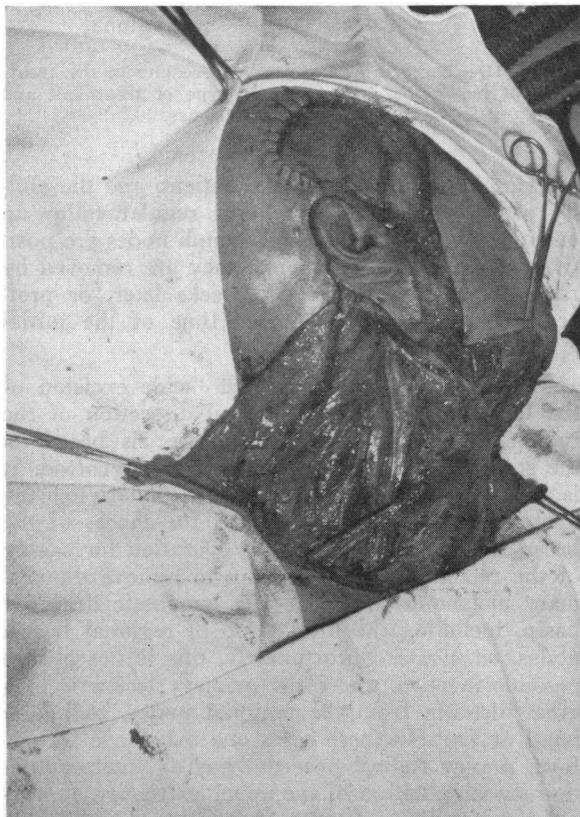


Figure 4.—Photograph taken at operation.

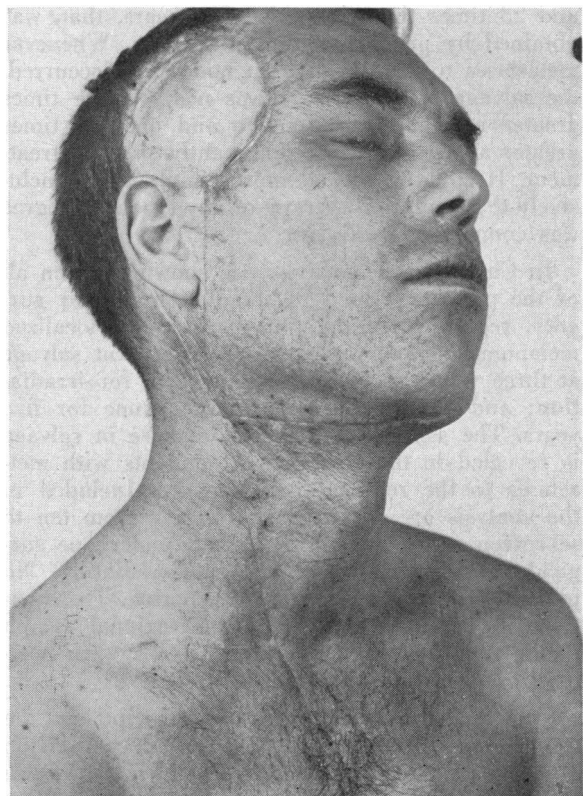


Figure 5.—The same patient ten days after the operation.

In the last two years, in 147 patients with malignant melanoma, we performed the "continuity" operation in 34 cases; 23 are still alive without evidence of disease and three are living with residual melanoma. Of six patients undergoing radical amputations, four are living without evidence of disease, and two are alive with recurrent melanoma.

SUMMARY AND CONCLUSIONS

We have presented an analysis of 862 cases of malignant melanoma, of which 595 were available for five-year end-result study, with an over-all salvage of 9.7 per cent. Radiation therapy alone in all its forms and combinations has yielded no five-year survivals. Surgical attack has resulted in 38.4 per cent three-year and 17.7 per cent five-year salvage for localized melanomas, and 18.7 per cent three-year, and 15.6 per cent five-year salvage of patients with melanoma metastatic to regional lymph nodes. In addition, we have presumptive

evidence of a trend toward greater saving of life by widening the scope of our radical surgical attack through the institution of one fundamental principle of cancer surgery, namely, the *en masse* excision of the primary lesion with its entire lymphatic drainage basin and the dissection of the regional nodes, "in continuity."

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Rupture of the Heart

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CARDIAC failure is a condition which may kill a person instantly.² Such sudden failure may be due to a thrombosis of a coronary artery, rupture of the interventricular septum,¹ rupture of the ventricles, or hypertension with myocardial failure. Myocardial infarction results from ischemic necrosis of heart muscle. The necrotic muscle is gradually removed and replaced first by open granulation tissue rich in vessels, and later by fully formed scar tissue. This scarring of necessity develops slowly from the periphery of the necrotic area, leaving a central area of flabby, necrotic tissue which has very little tensile strength. The weakened area may give way and bulge outward so that aneurysm of the heart is formed with marked thinning of the wall, and rupture may occur through the center of the necrotic tissue. Rupture of the left ventricle through a recent infarct is unusual⁴ but may occur, particularly when the necrosis of the muscle is at its height and before significant replacement by scar tissue has taken place. It leads to very rapid death by cardiac tamponade, but if the tear is very small, bleeding may be so gradual that death is delayed for hours.

Friedman and White⁵ found ten cases of cardiac rupture in 270 instances of myocardial infarction among nearly 3,000 autopsies at the Massachusetts General Hospital. All were found in patients with acute infarction. However, in a series of cases of patients in mental institutions, Jetter and White⁶ report an incidence of 73 per cent of rupture of the

heart with cardiac tamponade in cases with recent myocardial infarction. In spite of the fact that rupture of the heart is not a rare condition, many physicians and coroners still neglect to consider this condition as a cause of death, and are usually satisfied with a customary diagnosis of coronary heart disease or hypertension with myocardial failure. This fact was admirably brought out by Simberg⁹ and Levine⁷ who pleaded for a more accurate appraisal of all sudden deaths attributed to heart disease. Correct diagnosis can be obtained in only one way: all physicians and coroners should insist on postmortem examinations in every case of sudden death, and if no adequate cause is determinable by examination of the chest and abdomen, then the skull should be opened and the brain carefully examined. This will obviate the common practice of routinely signing a death certificate giving apoplexy or coronary occlusion as the cause of death.

Rupture of the heart with or without classical signs or symptoms suggesting myocardial infarction is a condition which the general practitioner either believes does not exist or which is so rare that it can be overlooked entirely as a cause of sudden death. Yet, in cases of sudden death, postmortem examination will not infrequently disclose a rupture of one of the ventricles through the area of a recent infarction. Clinical symptoms may be entirely lacking as in those cases of so-called "silent coronary." That this condition is far from rare is evidenced by the following four case reports of patients who died suddenly, with autopsy revealing rupture of the anterior surface of the left ventricle.

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