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END RESULTS IN THE TREATMENT OF MALIGNANT MELANOMA

A REPORT OF 1190 CASES*

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THE PRESENT REPORT is based upon an experience with 1190 cases of malignant melanoma treated and followed at the Memorial Cancer Center and the Pack Medical Group, covering the period from January, 1917, through December, 1950. This analysis is unique because of the following reasons: it is the largest series of malignant melanomas ever analyzed and reported; the entire group of patients were under the management of one department with group judgment and control; the span of years during which diagnosis and treatment were done was long, affording an unusual opportunity to evaluate the changing and improving principles of therapy.

The term "melanoma" is used to signify the malignant tumor only and does not include the compound or junctional nevus. Prepubertal, or juvenile melanoma is not incorporated in this discussion or presentation of statistical data inasmuch as its clinical behavior is usually benign. All of the cases in this study have had histologic confirmation of the clinical diagnosis of malignant melanoma. The study of malignant melanoma is important because (1) the majority of these "black cancers" originate from long-standing pre-existent nevi, (2) the majority of melanomas would be pre-

vented by the judicious excision of dangerous nevi, (3) the constant visibility of the tumor should enable an early diagnosis to be made, and (4) although the melanoma is the most accessible of all major forms of cancer, it has the unwelcome distinction of the lowest curability.

The total number of cases is divided into two groups: the determinate and the indeterminate. The indeterminate group includes the following: (a) patients who are lost to follow-up within a five-year period after treatment, (b) patients who refused treatment or palliative care, and (c) patients who, within a five-year period after treatment, die of other causes not related to melanoma *e.g.*, coronary occlusion, cerebrovascular accident, etc. All other cases are determinate, including patients with either operable or inoperable melanoma: this determinate group forms the basis for our end-result analysis.

END RESULTS OF TREATMENT OF MELANOMA BY FIVE-YEAR PERIODS 1917-1950

In Table I are listed the total figures for definite cures according to five-year periods. The first period includes the years 1917 through 1925 because of the small number of cases in the early years. The total number of patients treated during the 33-year period is 1190, of which 957 are determinate (80 per cent). Of these, 381 patients are living with or without evidence of melanoma, as of January 1, 1951. The remain-

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ing 809 patients are dead or lost to follow-up observation. Therefore, the total percentage of survival is 32.0. This percentage of survival is not a five-year figure since it includes those living with recurrent melanoma as well as those living free of evidence of recurrence less than five years. The steady increase in the number of patients in each five-year period is evident in Table I; for example, 446 new patients, or more than one-third of the total number, were seen during the last five-year period, 1946-1950. The results of treatment of these patients are not yet available for end-result analysis.

Thus we are limited in an evaluation of end results to the 744 patients treated in the period 1917-1945, and of these 575 are in the determinate group. The number of patients free of evidence of melanoma five years or more is 123. This number represents 21.4 per cent five-year definitive cures based on the 575 determinate cases, or 16.5 per cent based on the 744 total cases. The steady improvement in end results in the five-year periods from a low of 10.0 per cent in the 1917-1925 period to a high of 27.6 per cent in the 1936-1940 period is encouraging. The slight decline to 26.0 per cent in the 1941-1945 period may not be significant, but World War II, with its loss of civilian doctors to the military service, could have been a factor. The apparent discrepancy between the number of living patients and the number of five-year definitive cures is explained by the fact that the latter series includes those patients who, after living five years or more without melanoma, died of a heart attack or other unrelated cause. In melanoma, probably more than for most other malignant tumors, a five-year postoperative period without evidence of recurrence is quite valid as a criterion of cure, although there are a few unusual instances of patients who survived more than five years with residual melanoma present. One such patient lived 17 years following local excision of melanoma, with repeated sur-

gical removal of recurrences, and finally died with widespread metastases.

INCIDENCE OF MELANOMA ACCORDING TO LOCATION

In Table II we present the incidence of melanoma according to anatomical location, from 1917-1950. The head and neck group includes the skin area above the level of the clavicles but excludes melanoma of the eye and oronasal mucosa, which are listed sep-

TABLE I.—End results in the Treatment of Melanoma by Five-year Periods, 1917-1950.

Period	Total Cases	Determinate Cases	Living	5-year	
			as of January, 1951	Number	Percent
Total 1917-1945 for Five-Year Evaluation.....	744	575	121	123	21.4
1917-1925.....	74	50	5	5	10.0
1926-1930.....	85	73	6	9	12.3
1931-1935.....	145	114	18	19	16.7
1936-1940.....	166	123	32	34	27.6
1941-1945.....	274	215	63	56	26.0
1946-1950.....	446	382	257	—	—
Grand Total 1917-1950.....	1190	957	381 (32%)	—	—

arately. There have been two patients with primary esophageal melanoma. The palm is considered separate from the arm, and the sole separate from the leg because of the difference of epidermal density and the distinctive natural history of the disease in these locations. The subungual group is separate from both extremities in order to evaluate lesions in this particular anatomical location. The anorectal melanomas include lesions arising mostly from the skin of the anus and extending into the rectum, but there were several neoplasms which appeared to originate in the mucosa of the rectum several centimeters above the mucocutaneous junction. The only figures of especial significance in Table II seem to be the incidence of melanoma in the head and neck, 22.1 per cent, and on the sole, 9.0 per cent. Both are proportionately higher than one might expect on the basis of percentage of total skin surface. The head and

TABLE II.—Incidence of Melanoma According to Location, 1917-1950.

Location	Number	Percent
Total cases	1190	100.0
Head and neck	263	22.1
Eye	56	4.7
Oronasal, esophagus	21	1.8
Arm	101	8.5
Palm	16	1.3
Subungual	35	2.9
Leg	218	18.3
Sole	107	9.0
Trunk	288	24.2
Genitalia	37	3.1
Anorectal	19	1.6
Primary site unknown	29	2.4

neck figure may be explained by the fact that the case load of this department at the Memorial Cancer Center is unusually large, and thus more melanomas of the head and neck are seen at this Center than at the average clinic. The possibility exists therefore that 22.1 per cent does not represent the true incidence of melanoma in this location. The 9.0 per cent in the sole is probably a reflection of its true incidence and is proportionately high considering the area of skin surface of the sole.

END RESULTS IN THE TREATMENT OF
MELANOMA ACCORDING TO LOCATION

Table III shows the five-year end results according to the regional location of the melanomas. Both the total and determinate causes are listed in order to appreciate the number lost to follow-up and thus unavailable for end-result analysis. Since the five-year survival without recurrence is 21.4 per cent over-all, the significantly different results according to location are the following: (a) Low—primary location unknown, only one five-year cure; anorectal, no five-year cures; oronasal, 9.1 per cent; and trunk 13.7 per cent. (b) High—subungual, 38.9 per cent; and palm, 87.5 per cent. The low percentage survival group is explained as follows. The patients whose primary site for the melanoma was never discovered could really expect no survival in-

asmuch as the primary tumor could not be excised. Yet there is one amazing case in this group wherein axillary dissection for proved metastatic melanoma was done and in the ensuing 14 years, vigilant search has never discovered a primary site. The patient defies all laws and expectations by continuing to live. In the anorectal lesions, as well as the oronasal group, discovery and diagnosis of the tumor is unusually delayed because these regions are seldom examined thoroughly in a routine physical examination. Furthermore, surgical treatment of melanomas in these two regions is apt to be too conservative. This reasoning might also be applied to the management

TABLE III.—Five-year End Results in the Treatment of Melanoma According to Location, 1917-1945.

Location	Total Cases	Determinate Cases	5-year Definitive Cures	
			Number	Percent
Total Cases	744	575	123	21.4
Head and neck	173	128	23	18.0
Eye	47	35	9	25.7
Oronasal	17	11	1	9.1
Arm	58	46	8	17.4
Palm	11	8	7	87.5
Subungual	24	18	7	38.9
Leg	125	98	30	30.6
Sole	59	48	15	31.2
Trunk	162	131	18	13.7
Genitalia	31	25	4	16.0
Anorectal	16	10	0	0.0
Primary site not determined	21	17	1	5.9

of malignant melanomas of the genitalia, although a 16 per cent five-year definitive cure is not far below the general average of 21.4 per cent. In the case of melanomas of the head and neck one might blame the slightly low curability on reluctance of the patients or surgeons to perform an adequate excision because of cosmetic reasons. In the case of melanomas of the trunk a probable explanation is that the regional lymphatic drainage is potentially widespread, the metastases from a malignant melanoma of the abdomen, for example, may spread to either groin, either axilla, either side of the

neck, or to all six regions of lymphatic drainage. The results for melanomas of the extremities are much better because the regional metastases spread initially usually to one lymph node bearing region.

In these locations in which melanomas enjoy a higher cure rate the subungual lesions are examples; their curability can be

TABLE IV.—Five-year End Results in the Treatment of Melanoma in Relation to Sex and Age, 1917-1945.

Sex	Total Cases	Determine Cases	5-year Definitive Cures	
			Number	Percent
Male.....	372	294	46	15.6
Female.....	372	281	77	27.4
Age				
Pubertal*.....	86	71	16	22.5
Adult†.....	641	495	105	21.2

* Age: 11 through 30 years.
† 31 years and over.

explained by the fact that the usual treatment is amputation of the entire digit. This results in a margin of excision of approximately 8 cm., which is probably wider than the margin around many excised melanomas. The remarkable end result for melanomas of the palm is difficult to understand except that the number of patients is so small that the results probably have no statistical significance. It demonstrates the fallibility of statistical analysis in a small number of cases. Of those with melanomas of the palm living and well five years or more, only one had a radical amputation of the upper extremity; the other six had wide local excisions with or without axillary lymph node dissection.

END RESULTS IN THE TREATMENT OF
MELANOMA IN RELATION TO
AGE AND SEX

Table IV shows the five-year end results according to sex and age. A surprising coincidence is that the total number of cases up to 1946 was exactly divided between the sexes. Of more interest is the

difference in five-year survival without recurrence, 15.6 per cent for the males and 27.4 per cent for the females. This difference may be explained hypothetically in several ways. It could be an endocrinological difference inasmuch as we know that hormonal changes have some influence on the clinical behavior of melanoma, as seen in the prepubertal melanoma and in the pregnant female. It is doubtful, however, that there is a real sex difference in the prognosis for melanoma, but more probably is it due to the fact that women as a group are more "cancer conscious" than men and tend to see their doctor earlier because of a "mole" which is changing in appearance. It is true that women make

TABLE V.—Five-year End Results in the Treatment of Melanoma According to Delay in Definitive Surgery, 1917-1945.

Type of Case	Determine Cases	Percent of Determine Cases	5-year Definitive Cures	
			Number	Per cent
Operable—Total..	415	73.3	117	28.2
Immediate*.....	203	35.9	81	39.9
Delayed†.....	212	37.4	36	17.0
Inoperable.....	151	26.7	0	0.0

* No previous operation or local excision within one month of definitive surgery.

† Local excision more than one month prior to definitive surgery.

more frequent visits to the doctor for routine physical examinations than do men. In the Strang Clinic for Cancer Detection women outnumber men two to one.

Age. Our earlier report on melanoma gave an impression that melanoma was more malignant in the young adult during the years of puberty than in the older age group. There seemed to be no significant difference in survival according to decades after the age of 30. Prepubertal melanoma is not included in this study. Therefore, only two groups were analyzed: (a) Pubertal, and (b) Adult. Since the age of onset of puberty is rather indefinite, 11 years was arbitrarily chosen as the base

line. Since skeletal growth may continue until the age of 30, this age was taken as the dividing line between puberty and maturity. Our results do not show any significant difference in survival between the pubertal and the adult groups.

END RESULTS IN THE TREATMENT OF
MELANOMA ACCORDING TO DELAY
IN DEFINITIVE SURGERY

Of the determinate cases prior to 1946 there were only 566 in which operability was stated in the clinical record. Of these, 415, or 73.3 per cent, were operable. These operable melanomas are divided here into

sion of a lesion considered to be a nevus, the specimen is too often discarded or the lesion has been cauterized beyond histologic recognition, instead of being submitted to a competent pathologist for correct diagnosis. The first knowledge of the true nature of the tumor comes with the return of the patient several months later with palpable metastases in the lymph nodes of the neck, axilla or groin. The best chance for cure is in the first excision. There were 151 patients, or 26.7 per cent, who had inoperable melanoma at their initial visit, many of whom had been treated by inadequate local excision by practi-

TABLE VI.—Five-year End Results in the Treatment of Melanoma According to Surgical Procedure, 1917-1945.

Period	Wide Local Excision			Wide Local Excision and Dissection of Regional Lymph Nodes			Wide Local Excision in Continuity with Dissection of Regional Lymph Nodes			Amputation		
	Determinate Cases	5-year Definitive Cures		Determinate Cases	5-year Definitive Cures		Determinate Cases	5-year Definitive Cures		Determinate Cases	5-year Definitive Cures	
		Number	Per cent		Number	Per cent		Number	Per cent		Number	Per cent
Total Cases	204	76	37.3	162	32	19.8	62	9	14.5	16	5	31.2
1917-1925	26	3	11.5	14	2	14.3	0	0	0.0	2	0	0.0
1926-1930	28	9	32.1	11	0	0.0	0	0	0.0	1	0	0.0
1931-1935	41	12	29.3	36	6	16.7	0	0	0.0	4	1	25.0
1936-1940	39	17	43.6	53	14	26.4	7	1	14.3	3	2	66.7
1941-1945	70	35	50.0	48	10	20.8	55	8	14.5	6	2	33.3

two groups according to the time of surgery, namely, immediate or delayed. The immediate, or early operable group includes those patients who were untreated at their initial visit, or who had definitive surgery within one month after local excision for diagnosis. The delayed operable group comprises those patients who had a delay of one month or more between treatment elsewhere and definitive surgery. As can be seen in Table V, the five-year survival without recurrence of patients in the delayed group is less than half that of the immediate group. The importance of avoiding delay in proper treatment cannot be overemphasized. The culpability for this delay is attributable often to the doctor, whether he be dermatologist, general practitioner or surgeon. After inadequate exci-

tioners unaware of the serious nature of the lesion.

END RESULTS IN THE TREATMENT OF
MELANOMA ACCORDING TO SURGICAL
PROCEDURE

As to the management of melanoma, it is a well-accepted principle that surgical treatment offers the best chance for cure. Radium and external irradiation are no longer used as primary forms of therapy at the Memorial Cancer Center. In Table VI the surgical procedures have been divided into four groups: (1) wide local excision; (2) wide local excision plus radical dissection of adjacent regional lymph nodes; (3) wide local excision in continuity with radical dissection of adjacent lymph nodes;

and (4) radical amputation of an extremity. The amputation of a finger or toe is classified as a wide local excision rather than a radical amputation. What is meant by the term "wide local excision?" It cannot be definitely stated how wide a margin of normal skin around the melanoma is necessary to be adequate and safe. But the term is used to distinguish it from the usual local excision of a benign skin lesion with only a few millimeters of normal skin margin. At

to be of any significance. Furthermore, the relatively poor results obtained following wide local excision in continuity with dissection of regional lymph nodes are due to the fact that the more advanced melanomas were so treated and 62 cases are not enough to evaluate this procedure completely. From 1946 through 1950 there were 107 cases treated by this procedure and a better evaluation will be possible in the near future.

TABLE VII.—Five-year End Results in the Treatment of Melanoma in Relation to Metastasis to Lymph Nodes, 1917-1945.

Period	Lymph Nodes Positive			Lymph Nodes Negative		
	Determine Cases	5-year Definitive Cures		Determine Cases	5-year Definitive Cures	
		Num-ber	Per cent		Num-ber	Per cent
Total Cases	199	28	14.1	37	15	40.5
1917-1925	15	2	13.3	0	0	0.0
1926-1930	11	0	0.0	1	0	0.0
1931-1935	36	5	13.9	4	2	50.0
1936-1940	52	9	17.3	10	6	60.0
1941-1945	85	12	14.1	22	7	31.8

Totals represent number of patients having radical surgical treatment not including wide surgical excision.

the Memorial Cancer Center the excision is always three dimensional, referring to a wide removal of skin, subcutaneous tissues and fascia to such an extent that closure of the wound by skin grafting or transposed skin flaps is often necessary.

In Table VI is shown the improvement in end results by successive quinquennial periods based on our experience with the various surgical procedures. Wide local excision shows the best results. This paradox is, of course, due to the fact that the early lesions were so treated. The more advanced melanomas, some with palpable metastases, were treated by the other three more radical procedures, the best results being in the radical amputation group. However, there were only 16 radical amputations done up to 1946 and this number may be too small

END RESULTS IN THE TREATMENT OF MELANOMA IN RELATION TO LYMPHATIC METASTASES

The results in Table VII are based on the three more radical surgical procedures and do not include wide local excision because the latter procedure does not involve lymph node dissection. There is a striking difference between the five-year end results in patients with metastases (14.1 per cent) and without metastases (40.5 per cent) in lymph nodes. The five-year results do not seem to vary much according to five-year periods. In the group with positive metastases in lymph nodes, this probably implies that once metastases spread to the lymph nodes, only about 14 per cent will be cured even by radical surgery. If the group in which the lymph nodes were negative for metastasis is large enough to be significant, it would imply that in spite of elective lymph node dissection, one can only hope to salvage 40 per cent, the other 60 per cent having already metastasized by the blood stream.

SUMMARY

1. A total of 1190 cases of malignant melanoma is reported covering a period from 1917-1950; 744 patients were seen up to 1946, of which 575 records are available for analysis. Of these, 123 patients, or 21.4 per cent, were free of evidence of melanoma five years or more, as of January 1, 1951. This incidence and the five-year end results of melanoma according to anatomical location is presented.

2. The five-year end results according to sex is 15.6 per cent definitive cures for men and 27.4 per cent for women.

3. There is practically no difference in prognosis according to age after the onset of puberty.

4. There were 73.3 per cent of malignant melanomas in the operable group, and delay in obtaining definitive surgery more than a month after adequate local excision reduced the five-year cures from 39.9 per cent to 17.0 per cent.

5. The five-year end results according to type of surgical procedure is presented. The five-year end results in relation to metastases in regional lymph nodes are 14.1 per cent for patients with nodes positive for metastases, and 40.5 per cent for those with lymph nodes free of metastatic melanoma.

6. The ten-year definitive cures of patients treated prior to 1940 was 12 per cent (33 patients). Radical surgical treatment was routinely adopted after this date.

7. The importance of obtaining proper

surgical treatment of melanoma without delay cannot be over-emphasized. The best chance for cure is at the time of first excision.

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