Incidence of Cutaneous Melanoma in the United States by Histology with Special Reference to the Face

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ABSTRACT

Cutaneous melanoma has been classified into three distinct histological subtypes based on histopathological and clinical features. The incidence of the least common type, lentigo maligna melanoma, has been most strongly associated with chronic sunlight exposure as its cause, especially lesions presenting on the face area. The relationship of sunlight exposure to the other two major subtypes, superficial spreading melanoma and nodular melanoma, is unclear. Based on over 13,000 cases of cutaneous melanoma collected by the Surveillance, Epidemiology, and End Results (SEER) program of the NCI, we report histological-specific incidence findings strongly support the importance of considering histological subtypes of the age-incidence curves suggest that different histologies than the North and for males it increased with age. There was a smaller increase for females. This study documents the incidence of cutaneous melanoma by histological subtype within four anatomic sites. The different shapes of the age-incidence curves suggest that different histologies may react differently to sunlight exposure as an etiological factor. Our findings strongly support the importance of considering histological subtypes of cutaneous melanoma in future etiological studies.

INTRODUCTION

Clark and his associates classified melanomas into three distinct subtypes based on histological appearance and biological behavior (1). Hutchinson's freckle or LMM4 was associated with exposure to sunlight and occurred principally in elderly persons (2). LMM was concentrated on the head and neck whereas SSM and NM occurred more frequently on other parts of the body (3). LMM was noted to have features similar to squamous and basal cell carcinomas which are strongly associated with exposure to the UV component of sunlight (4). More recently, different risk factors have been reported for LMM than for SSM and NM (5) and a less consistent relationship between cumulative sunlight exposure with SSM or NM has been found (6). In addition, evidence suggests that SMM may have ultrastructure characteristics which set it apart etiologically from LMM (7).

Received 10/15/87; revised 4/7/88, 5/26/88; accepted 5/31/88.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact. 1 Supported by a grant from The Meadows Foundation. To whom requests for reprints should be addressed, at Department of Cancer Prevention and Control, P. O. Box 189, The University of Texas M. D. Anderson Hospital, 1515 Holcombe Boulevard, Houston, TX 77030.

The abbreviations used: LMM, lentigo maligna melanoma; SMM, superficial spreading melanoma; NM, nodular melanoma; SIIR, standardized incidence ratio; 95% CL, 95% confidence limits; NOS, not otherwise specified.

One purpose of this study was to describe the distribution of the three major histological subtypes of cutaneous melanoma within four major anatomical sites based on incidence data. The second purpose was to test the hypothesis that other histological subtypes might have age-incidence curves similar to LMM, implying they might also be associated with chronic, cumulative sunlight exposure. A third purpose was to test the hypothesis that the incidence of melanoma of the face5 is greater in areas of the U. S. with high levels of UV exposure compared with areas of low UV exposure, since melanoma incidence had been previously related to the levels of UV radiation in the areas of residence (8).

To conduct the study, we utilized the unique resource provided by the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (9). The SEER program has ascertained enough patients with cutaneous melanomas to allow for meaningful analyses of some subgroups of melanoma by anatomic site, histological subtype, and geographic area of residence.

METHODS

A data tape for the years 1973–1981 was provided by the staff of the SEER program. The initial study group consisted of patients who had malignant melanoma of the skin diagnosed during 1973–1981 and were residents of populations served by SEER registries located in the following areas: San Francisco-Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle (1974–1981), Utah, and Atlanta (1975–1981) (9). Although Puerto Rico is included in the SEER areas, it was not included in this study since all residents are classified as Hispanic; likewise, Hispanics residing in New Mexico and all other areas were excluded. This report is limited to Anglo patients (non-Hispanic Caucasians) heretofore referred to as "white." The areas covered by the SEER program may not be representative of the whole U. S. population, however, they include a spectrum of different geographic areas and encompass over 20,000,000 persons or about 10% of the U. S. population. Whites are more representative of the general U. S. white population than are other ethnic groups (9) and are the subject of this report.

The data were analyzed separately for patients who had one of five histological subtypes of melanoma as classified by the International Classification of Diseases for Oncology (ICD-O) (10): superficial spreading (8743), nodular (8721), lentigo maligna (8742), NOS (melanoma, histology not otherwise specified); and Other (other, rare, specific histological types). The ICD-O morphology codes correspond to the histological types originally classified by Clark (1) and later by McGovern (11). The ICD-O groups anatomical sites into head (173.0–173.4), which includes lip, eyelid, ear, other face, and scalp and neck; trunk (173.5); arm, shoulder (173.6); and leg, hip (173.7).

Population denominators provided by the staff of the SEER program for 1973–1981 were used in computing sex- and age-specific incidence rates. To correct for differences in age distributions between groups, rates for all ages were adjusted using the 1970 standard U. S. male or female population based on 5-year intervals. Since numerators in some age and sex strata were small, instability of rates was a concern. To provide larger numbers of patients in some subgroups, age-specific rates

2 Face, includes lip, eyelid, ear, other face, and scalp and neck; arm, includes shoulder; leg, includes hip.
were combined into 10-year age groups beginning with age 30–39.

In order to evaluate geographic risk gradients, we grouped the SEER areas into three regions, based on previously published indices of solar radiation as measured by Robertson-Berger (R-B) meters (8). These meters provided counts of the erythemal effectiveness of UV radiation, predominantly the wavelengths between 290 and 320 nm (UV-B). Measurements were recorded at airports in metropolitan areas. For states participating in SEER, measurements were taken in Albuquerque for New Mexico, Des Moines for Iowa, Salt Lake City for Utah, and Mauna Loa for Hawaii. Annual UV-B measurements have been published for all SEER areas except Connecticut (8, 12). Counts for Concord, NH were used as a surrogate for Connecticut.6

The nine areas were grouped into North, Central, and South based on the following considerations. The UV indices clustered into three arbitrary groupings. The North with lowest indices ranged from 98 for Connecticut to 125 for Iowa. Indices for Utah, San Francisco, and Atlanta ranged from 147 to 160. The grouping of two areas (New Mexico and Hawaii) with the highest UV indices, (197 and 277, respectively), each having distinct ethnic compositions and geophysical features, were placed in the South. Thus, we grouped Connecticut, Seattle, Detroit, and Iowa into “North;” Utah, San Francisco, and Atlanta into “Central;” and New Mexico and Hawaii into “South.” The percentage of unclassified cases did not differ significantly among the three geographic groupings. We calculated age-specific incidence for North, Central, and South by gender and overall rate ratios for Central/North and South/North.

Ninety-five percent confidence limits for age-adjusted incidence rates were calculated by the method of Keyfitz (13). To assess level of significance of rate ratios among North, Central, and South, weighted averages of stratum-specific rate ratios with test-based 95% CL were computed. This method of comparison is based on the Mantel-Haenszel summary chi-square statistic for density data, which controls for age (14). If the 95% CL do not include unity, they are statistically significant at the equivalent $P$ level of 0.05 or less.

RESULTS

There were a total of 13,255 white patients with cutaneous melanoma residing in all SEER areas (except Puerto Rico) during the 9 years ending in 1981. In 93% of males and 96% of females the primary tumors were designated as occurring in one of four anatomical site groupings. Among males 45% and among females 48% of cases were histologically subclassified as LMM, SSM, or NM. The remainder of cases were grouped into NOS or Other categories. The potential bias because of the large proportion of cases not classified by histological subtypes was of pertinent concern.

Classification by Histological Subtype. To address the potential bias due to the nonclassification by histological subtype of a large proportion of cases, we compared the age-specific incidence curves for the unclassified cases (NOS and Other combined) with the remainder of cases classified by the three histological subtypes combined, for each of the four anatomical sites. There were no differences in the shapes of the curves for the histologically unclassified cases compared to the classified cases among any anatomical site. Fig. 1 shows the curves for the face for LMM, SSM, and NM combined by gender (831 males; 637 females) and Fig. 2 for NOS and other combined by gender (749 males; 469 females). The similarity of the curves provided reassurance that those patients whose melanomas of the face were histologically subclassified were representative of those who were not subclassified, at least for the major variables of age and gender. For this reason we deleted the not classified from further analysis.

Incidence by Histological Subtype and Anatomic Site. The

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* J. Scotto, personal communication.

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12.

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13.

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14.
HISTOLOGY OF MELANOMA OF THE FACE

Table 1 Number of cases and average age-adjusted incidence of cutaneous melanoma for all SEER areas, 1973-1981, by anatomic site and histological subclassification

<table>
<thead>
<tr>
<th>Anatomic Site</th>
<th>LMM</th>
<th>SSM</th>
<th>NM</th>
<th>NOS</th>
<th>Other*</th>
<th>Total No</th>
<th>Overall Inc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>392</td>
<td>0.5</td>
<td>289</td>
<td>0.4</td>
<td>150</td>
<td>0.2</td>
<td>685</td>
</tr>
<tr>
<td>Trunk</td>
<td>88</td>
<td>0.1</td>
<td>897</td>
<td>1.1</td>
<td>303</td>
<td>0.4</td>
<td>1329</td>
</tr>
<tr>
<td>Arm</td>
<td>70</td>
<td>0.1</td>
<td>376</td>
<td>0.5</td>
<td>150</td>
<td>0.2</td>
<td>636</td>
</tr>
<tr>
<td>Leg</td>
<td>25</td>
<td>0.03</td>
<td>159</td>
<td>0.2</td>
<td>69</td>
<td>0.1</td>
<td>379</td>
</tr>
<tr>
<td>Other*</td>
<td>8</td>
<td>0.009</td>
<td>12</td>
<td>0.02</td>
<td>3</td>
<td>0.003</td>
<td>409</td>
</tr>
<tr>
<td>Total</td>
<td>583</td>
<td>0.8</td>
<td>1733</td>
<td>2.2</td>
<td>675</td>
<td>0.9</td>
<td>3438</td>
</tr>
</tbody>
</table>

Females

<table>
<thead>
<tr>
<th>Anatomic Site</th>
<th>LMM</th>
<th>SSM</th>
<th>NM</th>
<th>NOS</th>
<th>Other*</th>
<th>Total No</th>
<th>Overall Inc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face</td>
<td>328</td>
<td>0.4</td>
<td>226</td>
<td>0.3</td>
<td>83</td>
<td>0.1</td>
<td>427</td>
</tr>
<tr>
<td>Trunk</td>
<td>45</td>
<td>0.1</td>
<td>546</td>
<td>0.6</td>
<td>137</td>
<td>0.2</td>
<td>663</td>
</tr>
<tr>
<td>Arm</td>
<td>79</td>
<td>0.1</td>
<td>554</td>
<td>0.7</td>
<td>155</td>
<td>0.2</td>
<td>818</td>
</tr>
<tr>
<td>Leg</td>
<td>67</td>
<td>0.1</td>
<td>728</td>
<td>0.9</td>
<td>192</td>
<td>0.2</td>
<td>1127</td>
</tr>
<tr>
<td>Other*</td>
<td>5</td>
<td>0.01</td>
<td>12</td>
<td>0.01</td>
<td>1</td>
<td>0.001</td>
<td>247</td>
</tr>
<tr>
<td>Total</td>
<td>524</td>
<td>0.6</td>
<td>2066</td>
<td>2.5</td>
<td>568</td>
<td>0.7</td>
<td>3282</td>
</tr>
</tbody>
</table>

* Other, rare tumor histologies.
* No, number of cases.
* Incidence per 100,000 age-adjusted to the 1970 U. S. male/female population.

Table 2 Male-to-female incidence ratios by histological subtype and anatomic site

<table>
<thead>
<tr>
<th>Anatomic Site</th>
<th>LMM</th>
<th>SSM</th>
<th>NM</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face</td>
<td>1.3</td>
<td>1.3</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Trunk</td>
<td>1.0</td>
<td>1.8</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Arm</td>
<td>1.0</td>
<td>0.7</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Leg</td>
<td>0.3</td>
<td>0.2</td>
<td>0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Overall</td>
<td>1.3</td>
<td>0.9</td>
<td>1.3</td>
<td>1.1</td>
</tr>
</tbody>
</table>

* All ratios that are different from unity are significant at P = < 0.05.

expected, there was a male excess of melanomas of the face (M:F = 1.5) and trunk (M:F = 2.0), and a female excess of the arm and shoulder (M:F = 0.8) and leg and hip (M:F = 0.3). Those male-to-female incidence ratios that were not unity, were statistically significant at P = <0.05. LMM reflected the male preponderance of the face (M:F = 1.3) and female preponderance of the leg (M:F = 0.3); for the trunk and arm the male-to-female ratio was unity. SSM showed a male preponderance of the face (M:F = 1.3) and trunk (M:F = 1.8) and a female preponderance of the arm (M:F = 0.7) and leg (M:F = 0.2). Males had an excess of NM on the face and trunk and females an excess on the leg; the male-to-female ratio for the arm was unity.

Geographic Distribution and UV Index. One of the arguments for the strong etiological role of cumulative sunlight exposure in melanoma of the face is its progressive increasing incidence with advancing age. This characteristic age-incidence curve was manifested for melanomas of the face when all three histological subtypes were combined (Fig. 1). Age-specific incidence curve was manifested for melanomas of the face when all three histological subtypes were combined (Table 1) and histologically classified as LMM, SSM, and NM combined by gender.

Table 3 from the lowest to the highest, along with the numbers of cases, age-adjusted incidence, and 95% CL by gender. The incidence rates for Hawaii were disproportionately higher than for other areas. The occurrence of melanoma in Hawaii has been described (15) and tends to be anomalous in Hawaiian whites compared with whites residing in the continental U. S. The numbers of cases among the South were small in comparison with the numbers contributed by the other areas.

SIR for Central and South based on the North are given for LMM, SSM, and NM of the face by gender in Table 4. The SIR was elevated in both the Central and Southern regions relative to the North for both males and females for all his-
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Table 3 UV index and average annual incidence of cutaneous melanoma by SEER area, 1973–1981, for all anatomic sites and all histologies

<table>
<thead>
<tr>
<th>Region/area</th>
<th>UV index</th>
<th>No*</th>
<th>Inc*</th>
<th>95% CL</th>
<th>No</th>
<th>Inc</th>
<th>95% CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>North</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connecticut</td>
<td>98</td>
<td>1195</td>
<td>8.7</td>
<td>8.2</td>
<td>9.2</td>
<td>1149</td>
<td>7.8</td>
</tr>
<tr>
<td>Seattle</td>
<td>101</td>
<td>802</td>
<td>8.2</td>
<td>7.6</td>
<td>8.8</td>
<td>814</td>
<td>8.0</td>
</tr>
<tr>
<td>Detroit</td>
<td>110</td>
<td>960</td>
<td>6.6</td>
<td>6.2</td>
<td>7.0</td>
<td>879</td>
<td>5.6</td>
</tr>
<tr>
<td>Iowa</td>
<td>125</td>
<td>829</td>
<td>6.2</td>
<td>5.7</td>
<td>6.7</td>
<td>962</td>
<td>6.7</td>
</tr>
<tr>
<td>Central</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Utah</td>
<td>147</td>
<td>396</td>
<td>8.3</td>
<td>7.5</td>
<td>9.1</td>
<td>425</td>
<td>8.4</td>
</tr>
<tr>
<td>SF</td>
<td>151</td>
<td>1317</td>
<td>10.5</td>
<td>10.1</td>
<td>10.9</td>
<td>1299</td>
<td>9.8</td>
</tr>
<tr>
<td>Atlanta</td>
<td>160</td>
<td>490</td>
<td>11.6</td>
<td>10.6</td>
<td>12.6</td>
<td>496</td>
<td>10.0</td>
</tr>
<tr>
<td>South</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Mexico</td>
<td>197</td>
<td>364</td>
<td>7.7</td>
<td>6.9</td>
<td>8.5</td>
<td>395</td>
<td>8.3</td>
</tr>
<tr>
<td>Hawaii</td>
<td>277</td>
<td>283</td>
<td>24.8</td>
<td>21.9</td>
<td>27.7</td>
<td>200</td>
<td>17.6</td>
</tr>
</tbody>
</table>

* Number of cases.
* Incidence per 100,000 age-adjusted to the 1970 U.S. male/female population.

Table 4 SIR* by region, histology, and gender of the face

<table>
<thead>
<tr>
<th>History</th>
<th>Central</th>
<th>South</th>
<th>95% CL</th>
<th>95% CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMM</td>
<td>145</td>
<td>1.81</td>
<td>1.47</td>
<td>2.23</td>
</tr>
<tr>
<td>SSM</td>
<td>95</td>
<td>1.66</td>
<td>1.28</td>
<td>2.15</td>
</tr>
<tr>
<td>NM</td>
<td>49</td>
<td>1.48</td>
<td>1.05</td>
<td>2.10</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMM</td>
<td>123</td>
<td>1.77</td>
<td>1.41</td>
<td>2.22</td>
</tr>
<tr>
<td>SSM</td>
<td>68</td>
<td>1.54</td>
<td>1.14</td>
<td>2.09</td>
</tr>
<tr>
<td>NM</td>
<td>31</td>
<td>1.97</td>
<td>1.25</td>
<td>3.12</td>
</tr>
</tbody>
</table>

* SIR compared to the North region.
* Significant at P < 0.05.

tologies. The SIR was statistically significant for each histological subtype in the Central regions compared to the North for both genders. In the South relative to the North, the SIR for LMM was also significantly elevated for males and SSM was significantly elevated for females.

Age-specific incidence curves for LMM are shown for North and Central (Fig. 4A) and North and South (Fig. 4B) by gender. Incidence of LMM was higher in the Central region than the North in virtually every age group over age 50. The shapes of the LMM curves are remarkably similar for the North/South. Age-specific incidence curves for SSM are shown for North and Central (Fig. 5A) and North and South (Fig. 5B) by gender. Incidence of SSM of the face among men was higher for Central than for North with the exception of age group 50–59 in which the incidence was the same. In the Central region, the curve increased in age groups 60–69 and 70–79 and decreased in the oldest age group. For females, rates in the Central region were higher in the two younger and the two older age groups. The same general pattern for SSM prevailed in the North/South. For NM in both genders, incidence rates increased sharply in both regions in the oldest age group only.

DISCUSSION

The potential bias because of the many unclassified cases into histological subtypes was of concern. There is no pathology reference center serving all of the participating SEER areas, thus classification by histological subtype would be expected to vary. There could have been a tendency to classify some melanomas by histological subtypes that were known to have an association with certain anatomic sites, gender, and even solar exposure. This tendency would probably occur among all participating SEER areas to a greater or lesser extent. Because of local expertise in melanoma diagnosis and treatment, classification by histological subtype might also vary. Although we present incidence rates by histological subtypes, it should be kept in mind that less than half of the data was included. Thus, the incidence rates may not reflect the entire morbidity for these site-specific combinations. The combining of nine SEER areas into three regions would tend to minimize any systematic bias in histological classification among SEER areas. We can think of no other observer bias that would unduly affect the stability and trends of the incidence rates we report here. Schwartz et al. were also concerned about the effects of unclassified and misclassified melanomas in their study of seasonal incidence by histological subtype and body site (16). They concluded that classification either by histology or body site was not severe enough to mask seasonal differences in melanoma occurrence should they be found. Therefore, we believe that the characteristics of the histologically unclassified cases would not introduce sufficient bias to preclude further analysis and interpretation of the results we report, provided these limitations are kept in mind.

Despite the large volume of epidemiological, clinical, and...
experimental literature on cutaneous melanoma, the etiology of this commonly occurring malignancy is not well understood. Until recently, most studies considered cutaneous melanoma as a single entity, although its morphological diversity was described by Clark and his associates in 1969 (1). The different histological entities have different presentations, clinical histories, prognoses, and epidemiological features. McGovern et al. in 1980 specifically suggested that the different histological subtypes may also have different etiologies (17).

There are currently two competing hypotheses regarding the etiological role of sunlight and cutaneous melanoma. One suggests that cumulative or chronic exposure is important and the other that intermittent, strong exposure at an early age is important. The two hypotheses need not be mutually exclusive. One of the arguments for the strong etiological role of cumulative sunlight exposure in melanoma of the face is its progressive increasing incidence with advancing age. This characteristic age-incidence curve was manifested for melanomas of the face when all three histological subtypes were included, whereas it was not manifested for melanomas occurring on the trunk, arm, and leg.

Exposure of the facial area to sunlight is described as both intermittent and chronic. In our society, facial exposure to sunlight is constant, whether intermittent or chronic, subject to changing customs such as makeup use and hair length. Elwood and Hislop postulated that the effects of UV radiation differ for various subtypes of melanoma (3). This is the hypothesis we set out to test, using LMM of the face as the model for chronic, cumulative exposure. Deviations from the LMM model imply other than chronic, cumulative exposure.

Sunlight exposure, specifically the UV-B wavelength from 290 to 320 nm, is believed to have a direct, etiological association with squamous and basal cell carcinomas (18) but the extent of its association with cutaneous melanomas is still uncertain. The correlation between UV exposure with melanoma mortality (19) and incidence (20) have been known for years. LMM is said to be closely analogous to squamous cell carcinoma of the skin with regard to its pathogenesis and effects of UV radiation (4). Cumulative sunlight exposure has not been consistently associated with SSM and NM (6).

For each histological subtype of melanoma of the face, incidence ratios were consistently higher among the Central and South regions than the North. This finding was predicted under the hypothesis that constant UV exposure is associated with melanomas of the face. For LMM occurring among both males and females, the incidence increased progressively with age, whereas the age-incidence patterns were different for SSM and NM. The shape of the SSM curves was also different between males and females. Among males, the curve increased sharply in only two age groups and was more pronounced in the Central region than in the North. Among females, the shape of the curve in the Central region assumed a bimodal shape. Bimodal age curves in adults are unusual and imply either an admixture of disease classifications, different etiological mechanisms exerting their effects at different ages, or the same etiological mechanism with the effects tempered by age-related host factors. These data generally do not provide information about the nature of biological mechanisms, but can reinforce mechanisms generated by other kinds of studies and can add to the biological plausibility of a hypothesis. The level of male/female differences for SSM in the older ages is noteworthy. The age curves are markedly different for NM than for LMM and SSM. The contribution of NM to total melanoma of the face occurs only in the oldest age groups and is similar for men and women. The precipitous increase in NM in these older groups deserve further study. For all histological types of melanoma, Gallagher et al. found hair color (blonde or red) had the strongest association with melanoma, followed by light skin color. Light eye color was not a risk factor independent of hair and skin color (6). They also found that freckling was an independent risk factor. The person's tendency to burn and inability to tan, rather than actual frequency of sunburn in the past were additionally important factors. They consider it unlikely that total risk of melanoma was directly related to cumulative sunlight dose.

Recently, different risk factors have been reported for LMM than for SSM and NM. Holman and Armstrong reported that LMM had the strongest association with indicators of sunlight exposure whereas for SSM age at arrival before age 10–14 to Australia was a greater risk factor than length of residence (5). They suggested that LMM resulted from an accumulation of UV radiation-induced damage to melanocytes in exposed areas of the skin. Initiated nevus cells may develop into SSM as a
result of promotion by intermittent sun exposure. NM was considered to be a common end stage of melanoma arising from either of the other two pathways. Elwood et al. reported risk factors by SSM and NM and for the four main anatomic sites (21). Among 595 subjects and population-matched controls, relative risks for hair color, skin color, freckles, and sun reaction were not significantly different between persons with SSM or NM. Similarly, there were no differences among the four anatomic sites.

It has been suggested that the effect of sunlight may be to increase the number of abnormal target melanocytes that are susceptible to malignant transformation by exposure to environmental carcinogens (22). Although our findings do not relate directly to mechanisms of carcinogenesis, they strongly support the importance of considering histological subtype of cutaneous melanoma in future studies and that the different histologies may react differently to sunlight as an etiological factor. The different shapes of the age-incidence curves by histology are consistent with different biological mechanisms as suggested by other studies described above.

REFERENCES

Incidence of Cutaneous Melanoma in the United States by Histology with Special Reference to the Face


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