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Sun Exposure and Malignant Melanoma among Susceptible Individuals

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The purpose of this case-control study was to identify susceptible subgroups, primarily based on pigmentary characteristics, at higher risk of developing melanoma when exposed to the sun. The study group, which was interviewed from 1979 to 1982, consisted of 289 consecutive patients with melanoma and 527 randomly selected controls without cancer. In general, the risk of melanoma associated with sun exposure was greater for individuals expected to be susceptible on the basis of poor ability to tan, but not other pigmentary traits. There were, in addition, some noteworthy interactions between age and sun exposure.

Among subjects with poor tanning ability, the risk of melanoma associated with outdoor occupation was more than 3-fold [odds ratio (OR) = 3.3] compared to indoor occupation. In contrast, the analogous OR was much less elevated among subjects with a good ability to tan (OR = 1.5). Mixed indoor and outdoor job exposure was protective among good tanners (OR = 0.80), but not among poor tanners (OR = 1.5). A similar pattern was seen for recreational sun exposure and, when applying multiple logistic regression, for the patient's overall subjective assessment of his lifetime sun exposure. However, quantitative assessment of average hours of sun exposure did not prove to be a good indicator of melanoma risk, even among susceptible individuals. A history of severe sunburn with blistering was associated with nearly 3-fold risk among poor tanners (OR = 2.9) but was protective among good tanners (OR = 0.79). A history of nonmelanoma skin cancer or solar keratosis was a very strong risk factor (OR = 7.3), which, however, did not significantly differ in magnitude among susceptibility subgroups.

Introduction

Epidemiologic evidence for an etiologic role of solar radiation in malignant melanoma of the skin is derived principally from geographic studies and anatomical site analyses. Geographic studies have linked melanoma to latitude gradients, mean annual ultraviolet light (UV) exposure, measurements of UV flux, and migration patterns, although not consistently in all reports (*1–3*). Analyses of anatomical site have related increases in incidence rates over time and higher relative tumor densities to exposed sites (*1,4*).

Several case-control studies, including one of our own, have attempted to relate lifetime cumulative and intermittent sun exposure to the risk of developing malignant melanoma (*5–15*). However, although at least two of these studies have provided evidence of a positive dose-response relationship with cumulative sun exposure (*7,15*), several studies have found no relationship or even an inverse association (*5,8,9,12,13*). Conflicting results have also been reported for recreational or intermittent sun exposure (*5,11,12*).

The purpose of the present study was to try to clarify our understanding of the relationship between sun exposure and melanoma by taking into consideration host susceptibility factors. The susceptible subgroups we investigated were primarily based on pigmentary characteristics, which were expected to result in an individual being at greater risk of skin damage by UV radiation. In addition, we sought to identify the kind of sun exposure, whether chronic or intermittent, which most increases the risk of melanoma among susceptible individuals.

Materials and Methods

Subjects

Cases and controls for this study essentially comprise a 1979–1982 subset of subjects from our earlier study (*13*). For this subset, interview questions were added that elicited quantitative sun exposure in average hours per day up to 20 years prior to the interview, a history of severe sunburn with blistering, a history of regular exposure to artificial UV, and parents' ethnicity.

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Patients entering University Hospital, Bellevue Hospital, or Manhattan Veterans Administration Hospital for treatment of newly diagnosed primary malignant melanoma were given an interview and physical examination by the current Melanoma Fellow. All lesions were histopathologically confirmed to be melanoma. During the case accrual period there were two Fellows serving consecutive terms; a training period between the two terms was used to standardize the interview procedure. Between October 1979 and January 1982, the total accrual of cases was 297.

Potential controls were randomly chosen from among patients 20 years of age or older appearing for a first visit to the New York University Skin and Cancer Unit general skin clinic or a first reregistration after 2 years of absence. Patients under 20 years of age were excluded because few potential cases of melanoma in this age group were expected. Restricting controls to patients appearing for first visits or reregistration was designed to eliminate bias due to the overrepresentation of long-term patients with chronic skin disease. Although it was not possible for the Melanoma Fellows to interview controls, each control interview followed the standardized procedure developed for cases. A total of 748 potential controls were interviewed concurrently with the cases between October 1979 and January 1982, approximately two and a half times as many as cases.

An additional 426 skin clinic patients refused to participate as controls. For a random sample of 100 of these, we obtained basic demographic data and dermatologic diagnoses from the clinic records. Those who refused to participate differed only negligibly with respect to age, sex, marital status, race, year of visit, or dermatologic diagnosis.

Of the total of 297 potential cases of melanoma, 8 were excluded for one of the following reasons: age less than 20 years (3), nonwhite race (1), or previous melanoma (4). Of 748 potential controls, 221 were excluded for reasons of age (1), race (77), previous melanoma (3), or diagnosis of lesions, either malignant or benign, known to be caused by sun exposure (140). After exclusions, 289 valid cases and 527 valid controls remained.

In the final study group, the mean age of cases (51.7 years) was about 10 years greater than that of controls (42.7 years). The sex distributions in the two groups were reasonably similar, the percentage male being 53% (154/289) among cases and 47% (247/527) among controls. With respect to anatomic site of melanoma, nearly 40% (110/289) of lesions were diagnosed on the trunk, more than one-quarter (84/289) on the lower limbs, almost one-fifth (56/289) on the upper limbs, and the remaining 14% (39/289) on the head and neck. Over three-quarters (223/289) of melanomas were of superficial spreading histologic type; there were no sizable numbers of other histologic types, the remainder being roughly equally divided between lentigo maligna, nodular, acral lentiginous, and unclassified radial growth-phase melanoma.

For controls, as many as four current dermatologic diagnoses were recorded, representing a wide variety of skin conditions with no single type of diagnosis predominant. The conditions include skin infections (53), other infections and parasitic diseases (81), allergic diseases (internal agents) (18), seborrheic dermatitis (41), eczema (41), contact and radiation dermatitis (40), psoriasis and other scaling dermatoses (53), pruritis and related conditions (41), diseases of the nail, hair, hair follicles, and sweat and sebaceous glands (141), nonmalignant neoplasms (94), other miscellaneous conditions (112), and unknown conditions (9). We were aware of the possibility that patients diagnosed with such skin conditions may not have had a sun-exposure history representative of the population as a whole. Those among them who have also had skin conditions in the past may have had sun exposure either recommended or contraindicated, depending on the particular condition. Consequently, an important part of the study design was to obtain a prior history of significant skin disease for both cases and controls, so as to be able to adjust for possible confounding effects.

Study Variables

Qualitative indicators of sun exposure included occupational and recreational exposure (mostly indoor, mostly outdoor, or both indoor and outdoor), overall exposure (none, little, moderate, or much during one's entire lifetime, compared to other people), severe sunburn with blistering (ever or never), and previous (but not current) nonmelanoma skin cancer or solar keratosis (yes or no). Quantitative sun exposure in average hours per day was obtained for three time intervals prior to interview (0–5 years, 6–10 years, and 11–20 years). These three variables were computed from each subject's report of average sun exposure separately for summer weekdays, summer weekends, winter weekdays, and winter weekends; the final quantity was determined as a weighted average depending on the relative number of months each subject considered as comprising summer and winter during the particular time period. For a subset of subjects younger than 45 years of age at interview, we were able to compute average sun exposure at ages 15 to 25 years.

These different measures of sun exposure represent different combinations of chronic and intermittent exposure. We assume chronic exposure to occur daily or almost daily over a period of years. Intermittent exposure is assumed to occur weekly or less often. On the basis of the wording of our interview questions, occupational sun exposure, overall sun exposure, and quantitative sun exposure can be considered as cumulative measures, that is, mostly chronic exposure with an intermittent component. Recreational sun exposure and history of severe sunburn with blistering, however, probably are indicative mostly of intermittent sun exposure. A history of skin cancer or solar keratosis is probably indicative of intense chronic sun exposure.

Other measures of UV exposure included birthplace, residential history, and whether the subject was ever regularly exposed to artificial UV (at least once a week for at least 6 months). Birthplace was recorded by state or country and subsequently recoded into major geographic groupings. Residential history included the latitude of all places lived in for a period of 2 years or more, as well as duration (years) of residence. A subject's average residence latitude was weighted according to these durations.

Potential confounders included age, sex, ability to tan, history of freckling, number of moles, hair color, eye color, parents' ethnicity, history of using photosensitizing drugs (*16*), and history of previous skin diseases. Previous skin diseases were grouped according to whether UV exposure was likely to have been recommended or contraindicated in patients with such conditions (*16*; A. W. Kopf, personal communication).

Potential susceptibility subgroups were based on tanning ability, freckling, mole count, history of nonmelanoma skin cancer or solar keratosis, history of severe sunburn with blistering, parents' ethnicity, and eye color. It is important to note that these susceptibility subgroups were used to examine effect modification rather than to assess confounding. Effect modification would be present, for example, if the OR relating sun exposure to melanoma differed across levels of a pigmentary factor. As an example, individuals who tan darkly may be less susceptible to the carcinogenic effects of sun exposure than individuals who tan poorly. Confounding, however, refers to the effect of a factor that is not necessarily an effect modifier but, when uncontrolled, results in a mistaken assessment of the relationship between the study exposure and disease. For example, if controls are chosen from among those who are likely to have had sun exposure recommended as part of therapy for another disease, the true relationship between sun exposure and melanoma would be obscured. Adjustment for confounding was accomplished by stratification and multiple logistic regression. It should be noted that a single factor can be both a confounder and an effect modifier.

Data on most of the study variables were collected for all subjects, with very small percents unknown. However, the question on the history of severe sunburn with blistering was introduced after the study had already started and was obtained only for a subset of 132 cases and 443 controls.

Statistical Methods

Statistical evaluation of epidemiologic risk factors for malignant melanoma (versus controls) employed the odds ratio (OR) (*17*). Age and sex adjustments were always included, the former by 10-year intervals. Statistical significance was determined by the two-tailed Mantel-Haenszel chi-square and pertinent tests for trend (*17,18*). The baseline exposure group for each study factor was either the unexposed category or the category most frequently reported by controls. Confidence intervals (CI) based on the adjusted risk were determined by the asymptotic maximum-likelihood method (*19*). All statistical tests were considered significant at the $p < 0.05$ level. In general, unknowns were excluded from the analysis. In the text, unless otherwise specified, OR always refers to the Mantel-Haenszel OR.

Simultaneous control of several confounding factors, in addition to age and sex, was accomplished by multiple logistic regression (*18*). OR obtained from the multiple logistic regression coefficients were included in the tables (in addition to the Mantel-Haenszel OR), but are not given in the text unless stated as such. Statistical significance ($p < 0.05$) for adding or removing from a given model the possibly several levels of a risk factor, or a set of interactions between risk factors, was derived from the likelihood ratio test. In the tables, significance levels for adding main effects and interactive effects are given in footnotes. In general, subjects with unknown values for any of the risk factors considered in the multiple logistic analysis were excluded at this point, leaving 202 cases and 378 controls. The only exception was severe sunburn with blistering, for which there was a substantial percent missing. For this variable we included an indicator for "missing" in the multiple logistic analysis (*18*) in order to retain a maximum number of subjects. Those subjects who were excluded from the multiple logistic analysis were nonetheless retained in the Mantel-Haenszel analysis.

Results

Consideration of Potential Confounding Variables

Before presenting our results relating sun exposure to melanoma, we summarize the odd ratios we obtained for pigmentary characteristics, ethnic background, and dermatologic and drug history, all of which were considered potential confounders of the relationship between sun exposure and melanoma.

Pigmentary characteristics were discussed in detail in our earlier report (*13*), so that only a brief summary of results is given for these variables (Table 1). Subjects with little or no ability to tan were at increased risk of melanoma (OR = 2.2, $p < 0.01$), compared to those with average or greater ability to tan. A history of freckling was associated with a more than 3-fold risk of melanoma (OR = 3.4, $p < 0.01$). Compared to subjects with 1 to 25 moles on the body, those with no moles were at decreased risk (OR = 0.18, $p < 0.01$), whereas those with 26 to 100 moles (OR = 1.6) or more than 100 moles (OR = 2.3) were at increased risk of melanoma. Compared to subjects with no moles, those with more than 100 moles were at 9-fold risk of melanoma (OR = 8.9, $p < 0.01$) (OR not shown in the table). Subjects with red hair (as a young adult) were at increased risk of melanoma (OR = 2.6, $p < 0.05$) compared to subjects with dark brown hair, whereas subjects with black hair were at decreased risk (OR = 0.18, $p < 0.01$). With respect to eye color, subjects with blue eyes had a greater than doubled risk of melanoma (OR = 2.6, $p < 0.01$) compared with subjects with brown eyes. On the other hand, subjects with grey, green or hazel eyes were not at increased risk (OR = 0.92) compared to subjects with brown eyes.

We considered several additional confounders that

Table 1. Relative odds of melanoma by pigmentary characteristics.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
Ability to tan					
None or little	124	147	2.20*	1.61–3.20	1.90
Average or dark[c]	149	376	1.00	—	1.00
History of freckling					
No[c]	155	402	1.00	—	1.00
Yes	129	114	3.36*	2.39–4.91	2.23
Mole count					
None	9	87	0.18*	0.06–0.32	0.14
1–25[c]	214	357	1.00	—	1.00
26–100	45	62	1.60	0.97–2.62	2.16
> 100	10	11	2.26	0.83–7.12	2.49
Hair color					
Red	23	14	2.59†	1.23–6.89	
Blond	34	61	1.06	0.61–1.87	1.00
Light brown	92	139	1.20	0.82–1.79	
Dark brown[c]	125	233	1.00	—	
Black	10	71	0.18*	0.07–0.36	0.27
Eye color					
Blue	94	77	2.57*	1.76–4.09	1.92
Green-grey-hazel	70	170	0.92	0.62–1.35	1.00
Brown[c]	120	269	1.00	—	

[a]Adjusted for age and sex. Linear trend: mole count, $\chi_1^2 = 17.1$, $p < 0.001$.
[b]Adjusted for other confounding factors by multiple logistic regression (see text). Addition of main effects to the model with other confounders: ability to tan, $\chi_1^2 = 8.61$, $p < 0.005$; history of freckling, $\chi_1^2 = 11.7$, $p < 0.005$; mole count, $\chi_3^2 = 37.1$, $p < 0.005$; hair color, $\chi_1^2 = 11.3$, $p < 0.005$; and eye color, $\chi_1^2 = 6.39$, $p < 0.05$.
[c]Baseline.
*$p < 0.01$.
†$p < 0.05$.

were not discussed in our previous analysis. Ethnic background was an important determinant of the risk of melanoma. As can be seen from Table 2, there was an approximately 2-fold risk of melanoma for subjects who reported their father's origins to be British/Irish (OR = 2.2, $p < 0.01$), Scandinavian/Germanic (OR = 1.7) or North Slavic (OR = 1.8) compared to subjects whose father's origins were in other European countries. Subjects whose fathers were at least half non-European were at decreased risk (OR = 0.76). Very similar results were obtained for mother's ethnicity but are not tabulated. When we considered mother's and father's ethnicity simultaneously, the associations were strengthened (Table 2); having both parents with northern European background was associated with a 2- to 3-fold risk of melanoma. The greatest risk among the ethnicity categories was seen for subjects with both parents of British or Irish origin (OR = 3.1, $p < 0.01$).

A prior history of skin conditions for which UV exposure was likely to have been recommended therapeutically showed a strong inverse association with disease status (OR = 0.32, $p < 0.01$), having been reported by 28% of controls (149/527) but only 10% (29/289) of cases. Prior skin conditions for which patients were likely to be told to avoid UV (other than skin cancer or solar keratosis, which is discussed below as a sun-exposure variable) were also more common among controls (4.0%, 21/527) than cases (1.7%, 5/289) (OR = 0.45), but overall these conditions were not as frequently reported as conditions for which UV was likely to have been recommended. Note that these relationships with previous skin conditions were clearly artifactual rather than causal, being the direct result of choice of the source population for controls. Use of photosensitizing drugs was not significantly associated with disease status (OR = 0.85) and was not further considered as a confounder in this analysis.

Potential confounding variables were entered simultaneously into a multiple logistic regression model. Indicator variables for levels of each factor were used exclusively. Age (in 10-year intervals), sex, history of UV-recommended skin conditions, and history of UV-contraindicated skin conditions (other than skin cancer or solar keratosis) were forced into the model regardless of statistical significance. Backward elimination was used to collapse levels of other confounders, where epidemiologically appropriate and where there was no significant decrease in log-likelihood. For example, the initial model included eight indicator variables for mother's and father's ethnic origin. Removal of the four parameters for mother's ethnicity was not significant (chi-square = 0.80, 4 df) and, further, it was found that the four parameters for father's ethnicity could be replaced with a single variable indicating whether the subject's father had a northern European ancestry (British, Irish, Germanic, Scandinavian or north Slavic) (chi-square = 2.00, 3 df). The final confounder model included indicator variables for little or no tanning ability, freckling, number of moles (none, 26–100, and > 100), black hair, blue eyes, and father with

Table 2. Relative odds of melanoma by ethnicity.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
Father's ethnicity					
English, Irish, Scotch, or Welsh	54	81	2.17*	1.28-3.88	
Scandinavian or Germanic	34	50	1.68	0.94-3.29	1.62
North Slavic	106	157	1.80	1.17-2.87	
Other European[c]	55	157	1.00	—	1.00
Half or more non-European	6	34	0.76	0.24-2.18	
Parents' ethnicity					
Both English, Irish, Scotch, or Welsh	44	53	3.06*	1.70-6.22	
Both Scandinavian or Germanic	17	26	1.77	0.82-4.38	
Both north Slavic	92	122	2.23*	1.38-3.83	
Both northern European	20	34	2.17	1.00-4.95	
Both other European[c]	38	131	1.00	—	
Both half or more non-European	2	25	0.45	0.05-2.08	

[a]Adjusted for age and sex.
[b]Adjusted for other confounding factors by multiple logistic regression (see text). Addition of main effects to the model with other confounders, $\chi_1^2 = 4.33$, $p < 0.05$.
[c]Baseline.
*$p < 0.01$.

northern European ethnic origin, in addition to age, sex, and previous skin conditions. Note that red hair was not significantly associated with the risk of melanoma after simultaneous adjustment for the other factors.

Analysis of Sun-Exposure Variables and Susceptibility Subgroups

Each sun-exposure variable was evaluated within all susceptibility subgroups, as well as for study subjects overall. However, due to limitations of space, we decided to present the results of subgroup analyses only for those pigmentary variables that provided evidence of consistent patterns across several sun-exposure variables. Tanning ability was the only pigmentary variable that met this criterion. In addition, we present selected subgroup analyses by age and sex.

Mostly outdoor occupation, compared to mostly indoor occupation, was associated with an almost 2-fold risk of melanoma (OR = 1.8) (Table 3), when considering all cases and controls. Partly outdoor occupation, however, appeared to be, if anything, somewhat protective (OR = 0.79). For average or dark tanners the overall pattern was repeated: an increase in risk associated with mostly outdoor occupation (OR = 1.5) and a slight decrease in risk associated with partly outdoor occupation (OR = 0.80). For those with no or light ability to tan, however, a pattern of increasing risk with increasing outdoor exposure was observed, with partly outdoor occupation associated with a 50% increase in risk (OR = 1.5) and

Table 3. Relative odds of melanoma by occupation type, for all subjects combined and tanning subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
All subjects					
Occupation type					
Mostly indoors[c]	242	458	1.00	—	1.00
Both indoors and outdoors	20	50	0.79	0.42-1.44	0.70
Mostly outdoors	21	19	1.77	0.86-4.03	1.85
Average or dark tanners only					
Occupation type					
Mostly indoors[c]	125	319	1.00	—	1.00
Both indoors and outdoors	12	41	0.80	0.35-1.75	0.41
Mostly outdoors	11	16	1.50	0.57-4.08	1.24
No or light tanners only					
Occupation type					
Mostly indoors[c]	106	136	1.00	—	1.00
Both indoors and outdoors	8	8	1.51	0.45- 5.22	1.89
Mostly outdoors	10	3	3.31	0.79-21.71	5.52

[a]Adjusted for age and sex. Linear trend: all subjects, $\chi_1^2 = 1.17$, not significant; average or dark tanners, $\chi_1^2 = 0.20$, not significant; no or light tanners, $\chi_1^2 = 3.96$, $p < 0.05$.
[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of main effects, $\chi_2^2 = 2.86$, not significant. Addition of interactive effects of occupation type with tanning ability, $\chi_2^2 = 4.84$, not significant.
[c]Baseline.

mostly outdoor occupation associated with a more than 3-fold risk (OR = 3.3). Adjustment for multiple confounding effects by logistic regression analysis strengthened the magnitude of these observations. However, a formal test of interaction between occupation type and ability to tan, using multiple logistic regression, was not significant (chi-square = 4.8, 2 df).

We also examined interactive effects between age and occupational exposure (Table 4). Subjects 20 to 39 years of age and subjects 40 to 59 years of age were protected when their occupation was partly indoor and partly outdoor (OR = 0.37 and OR = 0.55, respectively), whereas subjects 60 years of age and older were at increased risk (OR = 1.9). Conversely, when considering the risk associated with mostly outdoor occupations, subjects 20 to 39 years of age and subjects 40 to 59 years of age were at elevated risk (OR = 2.3 and OR = 3.5, respectively), whereas subjects 60 years and older were at slightly decreased risk (OR = 0.76). The interactive effects with age were seen even more strongly in the multiple logistic analysis; moreover, the formal test of interaction between age and occupation type, using multiple logistic regression, was statistically significant (chi-square = 15.3, 4 df, $p < 0.005$).

Recreational exposure was similarly examined (Table 5). When considering all subjects, a mix of indoor and outdoor recreation was observed to be protective (OR = 0.68, $p < 0.05$), whereas subjects who reported mostly outdoor recreation were at increased risk (OR = 1.5). When dichotomizing the population according to tanning ability, this pattern was repeated for average or dark tanners, but not for subjects with little or no tanning ability. In the latter group, there was no protective effect of mixed indoor outdoor recreation (OR = 1.0), and there was a nearly 3-fold risk associated with mostly outdoor recreation habits (OR = 2.9, $p < 0.05$). As with occupational exposure, addition of interaction terms between recreation type and tanning ability was not statistically significant (chi-square = 2.5, 2 df). Unlike occupational exposure, recreational exposure showed no noticeable effect modification by age.

Similar to occupational and recreational exposure, the subjects' overall assessment of their lifetime sun exposure, when considering the entire study group, did not show an increased risk to be associated with moderate exposure (OR = 0.99) (Table 6), but did show an increased risk for much sun exposure (OR = 1.7, $p < 0.05$). Stratification by tanning ability strengthened the latter observation: Among average or dark tanners much sun exposure was associated with a more than 2-fold risk (OR = 2.5, $p < 0.01$), and among poor tanners it was associated with a 3-fold risk (OR = 3.0, $p < 0.05$). The risk gradient for overall sun exposure was very similar in the two tanning subgroups, which suggested that tanning ability acts more as a confounder of overall sun exposure and the risk of melanoma than as an effect modifier. The results of the multiple logistic analysis, however, were supportive of a protective effect for moderate sun exposure among average and dark tanners and a strong risk gradient with increasing exposure among poor tanners, similar to the relationship described above for occupational and recreational exposure. Nonetheless, addition of interactive effects between tanning ability and overall sun exposure did not contribute significantly to the multiple logistic model (chi-square = 1.8, 2 df).

When examining age subgroups, moderate sun exposure appeared protective in the 20- to 39-year old group (OR = 0.53) (Table 7), but not among older subjects. Further, much sun exposure was only associated with a slightly elevated risk among subjects 20 to 39 years of age (OR = 1.3) and among subjects 40 to 59 years of age (OR = 1.2). For subjects 60 years and older, the risk gradient

Table 4. Relative odds of melanoma by occupation type, for age subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
Subjects age 20–39 years					
Occupation type					
Mostly indoors[c]	62	231	1.00	–	1.00
Both indoors and outdoors	3	32	0.37	0.80– 1.33	0.18
Mostly outdoors	5	9	2.30	0.62–10.22	2.81
Subjects age 40–59 years					
Occupation type					
Mostly indoors[c]	107	115	1.00	–	1.00
Both indoors and outdoors	6	11	0.55	0.17– 1.65	0.27
Mostly outdoors	11	3	3.50	0.85–17.27	4.63
Subjects age 60+ years					
Occupation type					
Mostly indoors[c]	73	112	1.00	–	1.00
Both indoors and outdoors	11	7	1.95	0.70– 6.60	4.10
Mostly outdoors	5	7	0.76	0.18– 2.91	0.74

[a]Adjusted for age and sex. Linear trend: subjects age 20–39 years, $\chi_1^2 = 0.08$, not significant; subjects age 40–59 years, $\chi_1^2 = 1.41$, not significant; subjects age 60+ years, $\chi_1^2 = 0.11$, not significant.

[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of interactive effects of occupation type with age, $\chi_4^2 = 15.30$, $p < 0.005$.

[c]Baseline.

Table 5. Relative odds of melanoma by recreation type, for all subjects combined and tanning subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
All subjects					
Recreation type					
Mostly indoors[c]	103	174	1.00	—	1.00
Both indoors and outdoors	91	259	0.68*	0.46–0.99	0.71
Mostly outdoors	86	93	1.53	1.00–2.38	1.57
Average or dark tanners only					
Recreation type					
Mostly indoors[c]	56	109	1.00	—	1.00
Both indoors and outdoors	47	191	0.56*	0.33–0.94	0.59
Mostly outdoors	46	76	1.32	0.75–2.37	1.13
No or light tanners only					
Recreation type					
Mostly indoors[c]	43	63	1.00	—	1.00
Both indoors and outdoors	41	67	1.02	0.53–1.96	0.93
Mostly outdoors	40	16	2.91*	1.37–7.18	2.82

[a]Adjusted for age and sex. Linear trend: all subjects, $\chi_1^2 = 3.19$, not significant; average or dark tanners, $\chi_1^2 = 0.54$, not significant; no or light tanners, $\chi_1^2 = 8.05$, $p < 0.005$.
[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of main effects, $\chi_2^2 = 8.33$, $p < 0.05$. Addition of interactive effects of recreation type with tanning ability, $\chi_2^2 = 2.53$, not significant.
[c]Baseline.
*$p < 0.05$.

with increasing sun exposure was clear: moderate sun exposure had an OR of 1.4 and much sun exposure had an OR of 3.8 ($p < 0.01$). Multiple logistic analysis in general produced similar results with respect to age subgroups. One exception to this was an accentuation of the risk associated with much sun exposure among subjects 60 years or older (multiple logistic OR = 6.7); another exception was the high risk obtained for moderate exposure among subjects 40 to 59 years of age (multiple logistic OR = 2.5). The formal test of interaction between age and overall sun exposure was statistically significant (chi-square = 16.0, 4 df, $p < 0.005$).

Subjects were asked to quantify their average daily sun exposure during three past time periods. Controls reported an average of 2.3 hr of daily sun exposure 0 to 5 years prior to diagnosis, 2.6 hr 6 to 10 years prior to diagnosis, and 3.0 hr 11 to 20 years prior to diagnosis. Cases reported 2.1 average daily hr of sun exposure 0 to 5 years prior to diagnosis, 2.2 hr 6 to 10 years prior to diagnosis, and 2.4 hr 11 to 20 years prior to diagnosis. During each

Table 6. Relative odds of melanoma by overall sun exposure, for all subjects combined and tanning subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
All subjects					
Overall sun exposure					
Little or none[c]	66	136	1.00	—	1.00
Moderate	111	254	0.99	0.65–1.49	1.22
Much	100	130	1.73*	1.12–2.77	1.88
Average or dark tanners only					
Overall sun exposure					
Little or none[c]	19	69	1.00	—	1.00
Moderate	57	183	1.26	0.64–2.51	0.88
Much	72	118	2.48†	1.27–5.07	1.75
No or light tanners only					
Overall sun exposure					
Little or none[c]	47	64	1.00	—	1.00
Moderate	51	70	1.15	0.63–2.15	1.46
Much	26	12	3.04*	1.25–8.76	4.41

[a]Adjusted for age and sex. Linear trend: all subjects, $\chi_1^2 = 6.92$, $p < 0.01$; average or dark tanners, $\chi_1^2 = 11.5$, $p < 0.001$; no or light tanners, $\chi_1^2 = 5.79$, $p < 0.05$.
[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of main effects, $\chi_2^2 = 10.79$ $p < 0.01$. Addition of interactive effects with tanning ability, $\chi_2^2 = 1.82$, not significant.
[c]Baseline.
*$p < 0.05$.
†$p < 0.01$.

Table 7. Relative odds of melanoma by overall sun exposure for age subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
Subjects age 20–39 years					
Overall sun exposure					
Little or none[c]	16	54	1.00	—	1.00
Moderate	22	141	0.53	0.24–1.17	0.42
Much	29	74	1.31	0.58–3.01	1.37
Subjects age 40–59 years					
Overall sun exposure					
Little or none[c]	31	36	1.00	—	1.00
Moderate	53	55	1.11	0.57–2.19	2.47
Much	39	36	1.22	0.58–2.57	1.77
Subjects age 60+ years					
Overall sun exposure					
Little or none[c]	19	46	1.00	—	1.00
Moderate	36	58	1.42	0.68–3.03	1.28
Much	32	20	3.82*	1.61–9.47	6.68

[a]Adjusted for age and sex. Linear trend: subjects age 20–39 years, $\chi_1^2 = 1.13$, not significant; subjects age 40–59 years, $\chi_1^2 = 0.31$, not significant; subjects age 60+ years, $\chi_1^2 = 9.35$, $p < 0.005$.
[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of interactive effects of overall sun exposure with age, $\chi_4^2 = 15.94$, $p < 0.005$.
[c]Baseline.
*$p < 0.01$.

time period, exposure for controls was greater than exposure for cases. Further, sun exposure in both groups consistently decreased in more recent time periods. ORs for various categories of quantitative sun exposure are given in Table 8. No consistent trends are seen for either of the two most recent time periods; however, for the time period 11 to 20 years prior to diagnosis, the risk appeared to decrease with increasing sun exposure. For subjects reporting 4 or 5 or more average daily hr of sun exposure, the risk was approximately half of that for subjects reporting 2 average daily hr of exposure. When examining subgroups based on age at interview (Table 9), the protective effect of increased average sun exposure 11 to 20 years prior to diagnosis was seen to be strongest for subjects 20 to 39 years of age ($p < 0.001$), weak for subjects 40 to 59 years of age, and absent for subjects 60

Table 8. Relative odds of melanoma by quantitative sun exposure during three prior time periods.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
Sun exposure 0–5 years ago in hr/day					
0–1	100	164	1.21	0.80–1.86	1.62
2[c]	72	176	1.00	—	1.00
3	33	101	0.81	0.46–1.42	0.99
4	16	46	0.95	0.43–2.01	1.01
5+	17	35	1.31	0.56–3.15	1.42
Sun exposure 6–10 years ago in hr/day					
0–1	89	139	1.16	0.76–1.78	1.62
2[c]	74	157	1.00	—	1.00
3	36	103	1.05	0.60–1.83	1.33
4	20	64	0.88	0.44–1.73	1.21
5+	18	47	1.32	0.60–2.87	1.24
Sun exposure 11–20 years ago in hr/day					
0–1	72	103	0.99	0.62–1.57	0.89
2[c]	78	118	1.00	—	1.00
3	45	111	0.79	0.47–1.32	0.69
4	18	80	0.45*	0.22–0.88	0.49
5+	23	78	0.59	0.30–1.11	0.42

[a]Adjusted for age and sex. Linear trend: sun exposure 0–5 years ago, $\chi_1^2 = 0.46$, not significant; 6–10 years ago, $\chi_1^2 = 0.09$, not significant; 11–20 years ago, $\chi_1^2 = 0.38$, not significant.
[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of main effects to the confounder model: for 0–5 years ago, $\chi_4^2 = 4.62$, not significant; for 6–10 years ago, $\chi_4^2 = 3.42$, not significant; for 11–20 years ago, $\chi_4^2 = 8.17$, not significant.
[c]Baseline.
*$p < 0.05$.

years and older. Indeed, for this oldest group there was some indication, both in the Mantel-Haenszel and multiple logistic analyses, that melanoma risk increased with increasing exposure, although the test for linear trend (Mantel-Haenszel) was not significant. Similar results were also obtained for sun exposure 0 to 5 and 6 to 10 years prior to diagnosis in the subgroup aged 60 years and older, but are not presented in the tables. Addition of interactive effects between age and sun exposure 11 to 20 years prior to diagnosis was significant in the multiple logistic analysis (chi-square = 28.2, 8 df, $p < 0.01$).

A history of severe sunburn with blistering was associated with a 60% increased risk of melanoma (OR = 1.6, $p < 0.01$) (Table 10) when considering all subjects. Among subjects with average or dark tanning ability, however, there was a slightly decreased risk associated with severe

Table 9. Relative odds of melanoma by quantitative sun exposure 11 to 20 years ago for age subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
Subjects age 20–39 years					
Sun exposure 11–20 years ago in hr/day					
0–1	15	13	2.37	0.93–6.95	2.20
2[c]	22	49	1.00	—	1.00
3	10	68	0.48	0.17–1.20	0.30
4	6	61	0.22*	0.08–0.70	0.20
5+	5	58	0.23†	0.06–0.74	0.08
Subjects age 40–59 years					
Sun exposure 11–20 years ago in hr/day					
0–1	36	37	1.04	0.49–2.21	0.98
2[c]	30	33	1.00	—	1.00
3	19	28	0.80	0.34–1.89	0.48
4	7	12	0.64	0.18–2.17	0.57
5+	10	12	0.81	0.26–2.49	1.04
Subjects age 60+ years					
Sun exposure 11–20 years ago in hr/day					
0–1	21	53	0.52	0.23–1.14	0.64
2[c]	26	36	1.00	—	1.00
3	16	15	1.36	0.51–3.62	1.80
4	5	7	0.94	0.20–4.25	2.20
5+	8	8	1.34	0.36–4.95	1.05

[a]Adjusted for age and sex. Linear trend: subjects age 20–39 years, $\chi_1^2 = 21.82$, $p < 0.001$; subjects age 40–59 years, $\chi_1^2 = 0.58$, not significant; subjects age 60+ years, $\chi_1^2 = 2.89$, not significant.

[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of interactive effects of sun exposure with age, $\chi_8^2 = 28.15$, $p < 0.01$.

[c]Baseline.

*$p < 0.01$.

†$p < 0.05$.

Table 10. Relative odds of melanoma by sunburn history for all subjects combined and tanning subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
All subjects					
Severe sunburn with blistering					
Never[c]	45	214	1.00	—	1.00
Ever	87	229	1.61*	1.04–2.56	0.89
Average or dark tanners only					
Severe sunburn with blistering					
Never[c]	30	169	1.00	—	1.00
Ever	26	153	0.79	0.41–1.50	0.46
No or light tanners only					
Severe sunburn with blistering					
Never[c]	15	45	1.00	—	1.00
Ever	61	73	2.93†	1.34–6.88	1.87

[a]Adjusted for age and sex.

[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of main effects, $\chi_1^2 = 0.16$, not significant. Addition of interactive effects of sunburn history with tanning ability, $\chi_1^2 = 5.56$, $p < 0.05$.

[c]Baseline.

*$p < 0.05$.

†$p < 0.01$.

Table 11. Relative odds of melanoma by sunburn history for age subgroups.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
Subjects age 20–39 years					
Severe sunburn with blistering					
Never[c]	5	124	1.00	—	1.00
Ever	22	98	5.20*	1.78–16.90	5.68
Subjects age 40–59 years					
Severe sunburn with blistering					
Never[c]	18	48	1.00	—	1.00
Ever	41	68	1.56	0.76– 3.23	0.82
Subjects age 60+ years					
Severe sunburn with blistering					
Never[c]	22	42	1.00	—	1.00
Ever	24	63	0.79	0.36– 1.73	0.31

[a]Adjusted for age and sex.
[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of interactive effects of sunburn history with age, $\chi^2_2 = 18.04$, $p < 0.01$.
[c]Baseline.
*$p < 0.01$.

sunburn with blistering (OR = 0.79), whereas for poor tanners there was an almost 3-fold risk (OR = 2.9, $p < 0.01$) associated with this type of exposure. Addition of interactive effects between tanning ability and severe sunburn with blistering to the multiple logistic analysis was significant (chi-square = 5.6, 1 df, $p < 0.05$).

When considering age subgroups (Table 11), the effect of severe sunburn with blistering on melanoma risk was greater than 5-fold among subjects age 20 to 39 years (OR = 5.2, $p < 0.01$), but more modestly elevated among subjects age 40 to 59 years (OR = 1.6), and slightly protective among subjects 60 years and older (OR = 0.79). Addition of interactive effects between age and severe sunburn with blistering to the multiple logistic regression was significant (chi-square = 18.0, 2 df, $p < 0.01$).

A previous history of nonmelanoma skin cancer or solar keratosis was associated with a more than 7-fold risk of subsequent melanoma (OR = 7.3, $p < 0.01$) (Table 12). There was a relatively small difference in the magnitude of relative risk between the tanning subgroups; subjects with little or no ability to tan had an OR = 7.1 ($p < 0.01$), whereas subjects with average or dark tanning ability had an OR = 6.5 ($p < 0.01$) (not shown in table). This was indicative of little, if any, effect modification. When males and females were examined separately, the risk associated with prior skin cancer or solar keratosis was nearly 12-fold among males (OR = 11.7, $p < 0.01$), but not even 4-fold among females (OR = 3.9, $p < 0.05$). The magni-

Table 12. Relative odds of melanoma by prior skin cancer or solar keratosis for all subjects combined and separately by sex.

Risk factor	No. of melanoma patients	No. of controls	Mantel-Haenszel odds ratio[a]	95% CI	Multiple logistic odds ratio[b]
All subjects					
Prior skin cancer or solar keratosis					
No[c]	236	515	1.00	—	1.00
Yes	53	12	7.28*	3.45–14.77	10.83
Males only					
Prior skin cancer or solar keratosis					
No[c]	115	243	1.00	—	1.00
Yes	39	4	11.66*	4.28–46.37	27.03
Females only					
Prior skin cancer or solar keratosis					
No[c]	121	272	1.00	—	1.00
Yes	14	8	3.93†	1.31–10.52	4.61

[a]Adjusted for age and sex.
[b]Adjusted for confounding factors by multiple logistic regression (see text). Addition of main effects to the confounder model, $\chi^2_1 = 26.82$, $p < 0.01$. Addition of interactive effects of prior skin cancer or solar keratosis with sex, $\chi^2_1 = 3.15$, not significant.
[c]Baseline.
*$p < 0.01$.
†$p < 0.05$.

tude of risk was even higher in the multiple logistic analysis, overall and for each sex individually. Addition of interactive effects between sex and prior skin cancer to the multiple logistic analysis was not significant (chi-square = 3.2, 1 df).

Other Measures of UV Exposure

Various other measures of UV exposure were considered but were not found to be associated with the risk of melanoma. These include years of residence at various latitudes, and medical and occupational UV exposure. Because over 70% of both cases (208/289) and controls (407/527) were born in the northern United States or Canada, and over 90% of these were born in New York, New Jersey, or Pennsylvania (198 cases and 374 controls), it was not possible to meaningfully examine birthplace as a risk factor for melanoma. Quantitative sun exposure was further examined according to summer weekday, summer weekend, winter weekday, and winter weekend exposure, in an attempt to distinguish intermittent from chronic sun exposure, but this analysis did not prove informative. Consideration of quantitative sun exposure at ages 15 to 25 years confirmed the associations reported in Table 8.

Analysis by Histologic Type of Melanoma

Because the only histologic type of melanoma for which there were sizable numbers of cases in our study was superficial spreading melanoma (223/289), it was not possible to examine differences in risk factors by histologic type. An analysis restricted to the superficial spreading type, however, confirmed the findings already presented.

Discussion

Although sun exposure is widely believed to cause melanoma, published studies have reported a great many ambiguous findings and, in general, an absence of a consistent dose-response relationship (*5-15*). A number of factors may be partly responsible for the inconsistency of published results, including the need to distinguish (a) host characteristics that influence susceptibility to UV exposure, (b) chronic from intermittent exposure, (c) how long ago exposure took place, age at exposure and duration of exposure, and (d) histologic subtypes. Although the first two of these are addressed in the present report, we were not substantially able to address the latter two.

Other authors have also attempted to distinguish between total cumulative and intermittent sun exposure (*5-15,20*). Among the measures of total cumulative sun exposure that have been employed are number of hours of lifetime sun exposure, annual summer occupational exposure of more than 16 hr per week, annual hours of sun exposure at one's place of residence, years of residence in a sunny climate, history of actinic tumors, and presence of actinic changes as graded by cutaneous microtopography. Measures of intermittent exposure have included sunburn history and a variety of recreational exposures, including amount of time spent outdoors during leisure, hours per day of vacation exposure, total number of days spent in vacations in sunny climates, number of sunny vacations per decade, proportion of total summer outdoor exposure spent in recreation, and frequency of participation in sunbathing, swimming, boating, fishing, and winter sports. In spite of these careful attempts to quantify different types of sun exposure, all too often one finds reported in case-control studies a protective effect or lack of an effect of sun exposure on melanoma risk. An important question that has remained is whether such findings are the result of measurement error, confounding by unknown factors, or interactions with host characteristics.

The influence of host susceptibility factors on the association of sun exposure with melanoma previously has been examined by some researchers. In one study (*5*) the association of a single histologic type, superficial spreading melanoma, with a number of different measures of recreational sun exposure was strongest when the exposure occurred at ages 15 to 24 years and in subgroups with more than five raised nevi on the arms. However, the reported relationship was true only for the intermediate and not for the high exposure category. The same study also reported a complex interaction, for superficial spreading melanoma, between poor tanning response and frequency of sunbathing at ages 15 to 24 years, but not other sun-exposure variables. No regular pattern was seen in other studies that assessed interactions with sun-exposure variables (*6,8,9*). It is important to note that consistent patterns across several exposure variables and among levels of exposure are required if one is to guard against the fallacies inherent in unrestrained subgroup analysis (*21*).

We, too, have considered the potential for effect modification. In the present analysis, sun-exposure variables were investigated within subgroups of host characteristics; and substantial interactions, in both number and degree, were found between sun exposure and two factors, tanning ability and age.

Tanning ability was the only pigmentary characteristic for which our subgroup analysis consistently showed effect modification between sun-exposure variables and the risk of melanoma. Moreover, taken as a whole these interactive effects are biologically plausible. Subjects with little or no ability to tan exhibited substantially higher relative risks than good tanners for qualitative measures of occupational, recreational, and overall sun exposure and for a history of severe sunburn with blistering (Tables 3,5,6, and 10). Further, poor tanners exhibited a dose-response relationship between sun exposure and the risk of melanoma, with moderate exposure resulting in no more than moderately increased (up to 2-fold) risk and much exposure resulting in much increased (3-fold) risk. For good tanners, moderate exposure was protective against melanoma, whereas much exposure resulted in increased risk, but not to as high a level as for poor tanners. One can speculate that tanning may confer a shielding effect on the skin and that moderate sun exposure may actually protect against melanoma either by promoting a tan in individuals who do so easily or in some other unknown way. These relationships hold over a wide variety of sun-exposure variables reflecting both chronic and intermittent exposure. However, excessive sun exposure may overwhelm the protective mechanism provided by tanning. This is supported by our results regarding history of previous skin cancer or solar keratosis. For this variable, the similarity of OR between tanning subgroups (7.1 for poor tanners and 6.5 for good tanners) may reflect the overriding skin damage caused by the kind of intense, long-term exposure that is believed to be associated with solar keratosis and nonmelanoma skin cancer (*22*).

Our quantitative assessment of average sun exposure in three consecutive time periods showed, as previously reported (*13*), a decrease in risk with increasing exposure. This finding, which runs counter to the hypothesis that cumulative sun exposure causes melanoma, was reevaluated in the present analysis, but could not be explained by effect modification between tanning subgroups. Consideration of age subgroups, however, suggested that this inverse dose-response relationship may be restricted to younger subjects. Among subjects 60 years and older, increased average daily sun exposure 11 to 20 years prior to diagnosis was generally associated with an increased risk of melanoma (Table 9); similar results were also obtained for average daily sun exposure 0 to 5 and 6 to 10 years prior to diagnosis (not included in table). Likewise, the deleterious effects of overall sun exposure were most pronounced in the oldest subgroup (Table 7). On the other hand, younger subjects who reported a history of severe sunburn with blistering were at very much increased risk of melanoma compared to older subjects (Table 11). Although we also saw interactive effects between age and occupational exposure (Table 4), these were not consistent with our findings for other measures of cumulative sun exposure and may be a fortuitous occurrence related to the paucity of outdoor workers aged 60 years and older.

Our finding of two types of interaction effects with age, in opposite directions, may reflect two etiologies, one involving acute effects of acute exposure usually occurring at younger ages and the other involving cumulative lifetime effects of sun exposure and usually showing up at older ages. Certainly it is biologically plausible that, among older subjects, the accumulation of UV-induced skin damage over time may leave them more susceptible to the deleterious effects of subsequent sun exposure. The interactive effect between age and sunburn history is more difficult to explain. One can speculate that young individuals who react to UV exposure with severe, blistering sunburn experience a short-term effect giving them a relatively high risk of melanoma during those years. Those among them who do not develop melanoma at young ages may subsequently tend to avoid sun exposure for their entire lifetime, resulting in their risk of melanoma decreasing over time and ultimately, at older ages, becoming similar to those who have never experienced severe sunburn with blistering.

Any interpretation of the results of our study must consider the validity of the sun-exposure variables used. As described in our previous report (*13*), we performed a reliability study that confirmed the absence of interviewer bias in recording the subjects' quantitative sun-exposure histories. Even so, this quantitative history does not include such factors as the amount of clothing worn, use of sunscreens, and sun intensity, nor does it include exposure that occurred more than 20 years prior to the interview. For example, if nonmelanoma skin cancer or solar keratosis were diagnosed more than 20 years prior to the interview, our quantitative sun exposure variable would reflect the avoidance of sun exposure that usually follows such a diagnosis rather than the heavy exposure that precedes it. Further, episodes of particularly acute exposure, when averaged over a long period of time, would be indistinguishable from a miniscule increase in continuous exposure. It seems plausible, then, that an individual's subjective assessment of his overall lifetime sun exposure, such as was presented in Table 6, may implicitly include such additional factors and so may actually be a better measure of intensity of tissue exposure.

In planning future studies, it will be important to elicit information on age at occurrence for measures of acute sun exposure, such as recreational and vacation exposures, severe sunburns, solar keratosis, and nonmelanoma skin cancer. One should also try to obtain the duration of episodes of intense sun exposure, as well as intervals between exposures, which may allow for the development of a protective tan. For chronic exposure, one should consider both the age at which exposure began and its duration. For all types of exposure, one needs to consider in sufficient detail the type of clothing worn, use of sun-blocking agents, season, altitude, latitude, and proximity to reflective surfaces such as water and snow. These factors, together with duration and intervals between different periods of exposure, should help provide a more accurate composite assessment of the intensity of an individual's exposure history (*5,6*).

Elwood has suggested that UV radiation (UVR) may act as both an initiator and a promoter (*2*). He writes, "The initiator action may be associated with traumatic sunburn in childhood or adolescence, or it may be related to the production of naeves at those ages, while continued further bursts of UVR may have a promoting action on them." Where data on age and duration of exposure are available, it would be possible to compute intervals between the period of exposure and the age at risk. These time variables could then make it possible to separate short-term effects from long-term effects and, hence, help distinguish promotional effects from initiation effects.

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REFERENCES

1. Elwood, J. M., and Hislop, T. G. Solar radiation in the etiology of cutaneous malignant melanoma in Caucasians. Natl. Cancer Inst. Monogr. 62: 167–171 (1982).
2. Elwood, J. M. Initiation and promotion actions of ultraviolet radiation on malignant melanoma. In: Models, Mechanisms and Etiology of Tumour Promotion (M. Borzsonyi, K. Lapis, N. E. Day, and H. Yamasaki, Eds.), International Agency for Research on Cancer, Lyon, 1984, pp. 421–440.
3. Lee, J. A. H. Melanoma and exposure to sunlight. Epidemiol. Rev. 4: 110–136 (1982).
4. Pearl, D. K., and Scott, E. L. The anatomical distribution of skin cancers. Int. J. Epidemiol. 15: 502–506 (1986).
5. Holman, C. D. J., Armstrong, B. K., and Heenan, P. J. Relationship of cutaneous malignant melanoma to individual sunlight-exposure habits. JNCI 76: 403–414 (1986).
6. Elwood, J. M., Gallagher, R. P., Hill, G. B., and Pearson, J. C. G. Cutaneous melanoma in relation to intermittent and constant sun exposure—the Western Canada Melanoma Study. Int. J. Cancer 35: 427–433 (1985).
7. Green, A. C., and O'Rourke, M. G. E. Cutaneous malignant melanoma in association with other skin cancers. JNCI 74: 977–980 (1985).
8. Graham, S., Marshall, J., Haughey, B., Stoll, H., Zielezny, M., Brasure, J., and West, D. An inquiry into the epidemiology of melanoma. Am. J. Epidemiol 122: 606–619 (1985).
9. Lew, R. A., Sober, A. J., Cook, N., Marvell, R., and Fitzpatrick, T. B. Sun exposure habits in patients with cutaneous melanoma: A case control study. J. Dermatol. Surg. Oncol. 9: 981–986 (1983).
10. Sorahan, T., and Grimley, R. P. The aetiological significance of sunlight and fluorescent lighting in malignant melanoma: A case-control study. Br. J. Cancer 52: 765–769 (1985).
11. MacKie, R. M., and Aitchison, T. Severe sunburn and subsequent risk of primary cutaneous malignant melanoma in Scotland. Br. J. Cancer 46: 955–960 (1982).
12. Klepp, O., and Magnus, K. Some environmental and bodily characteristics of melanoma patients. A case-control study. Int. J. Cancer 23: 482–486 (1979).
13. Dubin, N., Moseson, M., and Pasternack, B. S. Epidemiology of malignant melanoma: Pigmentary traits, ultraviolet radiation, and the identification of high-risk populations. In: Recent Results in Cancer Research, Vol. 102 (R. P. Gallagher, Ed.) Springer-Verlag, New York, 1986, pp. 56–75.
14. Green, A., Siskind, V., Bain, C., and Alexander, J. Sunburn and malignant melanoma. Br. J. Cancer 51: 393–397 (1985).
15. Holman, C. D. J., and Armstrong, B. K. Cutaneous malignant melanoma and indicators of total accumulated exposure to the sun: An analysis separating histogenic types. JNCI 73: 75–82 (1984).
16. Maddin S., and Brown, T. Current Dermatologic Management. Mosby, St. Louis, MO, 1970.
17. Mantel, N., and Haenszel, W. Statistical aspects of the analysis of data from retrospective studies of disease. J. Natl. Cancer Inst. 22: 719–748 (1959).
18. Breslow, N. E., and Day, N. E. Statistical Methods in Cancer Research, Vol. 1. The Analysis of Case-Control Studies. International Agency for Cancer Research, Lyon, 1980.
19. Thomas, D. G. Exact and asymptotic methods for the combination of 2×2 tables. Comput. Biomed. Res. 8: 423–446.
20. Holman, C. D. J., Armstrong, B. K., Evans, P. R., Lumsden, G. J., Dallimore, K. J., Meehan, C. J., Beagley, J., and Gibson, I. M. Relationship of solar keratosis and history of skin cancer to objective measures of actinic skin damage. Br. J. Dermatol. 110: 129–138 (1984).
21. Stallones, R. A. The use and abuse of subgroup analysis in epidemiological research. Prev. Med. 16: 183–194 (1987).
22. Scotto, J., and Fraumeni, J. F., Jr. Skin (other than melanoma). In: Cancer Epidemiology and Prevention (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), W. B. Saunders Co., Philadelphia, 1982, pp. 996–1011.