Effect of Intermittent Exposure to Sunlight on Melanoma Risk Among Indoor Workers and Sun-Sensitive Individuals

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Intermittent exposure to sunlight is considered to be an important risk factor for melanoma, but the associations reported in most case–control studies are surprisingly weak. The aim of this study was to evaluate whether the incorporation of a subject's background exposure to the sun and pigmentation characteristics (which are assumed to influence a person's susceptibility to sunlight exposure) could produce stronger associations between sunlight exposure and the risk for melanoma. A population-based case–control study was performed in the mid-eastern part of the Netherlands. The study group comprised 141 patients with a histologically verified melanoma and 183 controls with other malignancies who were registered by the same cancer registry. Patients with a lentigo maligna melanoma or an acrolentiginous melanoma were excluded. Information was collected by interviews and physical examination. We categorized subjects as indoor or outdoor workers on the basis of occupational exposure to the sun. Pigmentation characteristics, which are known to be risk indicators for cutaneous melanoma, were summarized as one sun sensitivity score. We used this score to distinguish between sun-sensitive and sun-resistant persons. The odds ratios associated with sunbathing, vacations spent in sunny countries, and sunburns were higher among the indoor workers than among the outdoor workers. After stratification by the sun sensitivity score, the effect of sunbathing, participating in water sports (swimming excluded), vacations to sunny countries, and a history of sunburn was largest for the sun-sensitive persons. The data show a general trend toward higher relative risks among indoor workers and sun-sensitive individuals. The results of this study support the intermittent sunlight hypothesis. *Key words*: melanoma, pigmentation, sunbathing, sunburn, sunlight exposure, tanning. *Environ Health Perspect* 101:252–255(1993)

As a result of the dramatic rise in the incidence of cutaneous melanoma in the past decades, this tumor has become a growing threat to public health. Nowadays, sunlight exposure is widely accepted as an important risk factor; however, most case–control studies report inconsistent and surprisingly weak associations (*1*). One of the reasons for this weak association may be that the association between sunlight exposure and melanoma risk was not evaluated in the most relevant subgroups. The maximum effect of sunlight exposure is expected to occur in individuals who do not tan easily. Such individuals are mainly indoor workers and persons who have sun-sensitive skin.

The "intermittent sunlight hypothesis" states that the relationship between sunlight exposure and melanoma is not directly proportional: short bursts of intense exposure to the sun (intermittent exposure) carry extra risk, whereas more regular, chronic exposure is believed to have a neutral or even protective effect (*2,3*). The principle underlying this theory is that ultraviolet radiation only leads to an increase in melanoma risk if the skin has not yet become accustomed to the sun. Tanning gives protection against sunlight and thereby decreases the melanoma risk.

The aim of this study was to evaluate the association between intermittent sunlight exposure and melanoma risk in subgroups of people who differed with respect to their opportunity to tan gradually. The associations were expected to be stronger among indoor workers than in outdoor workers and stronger among sun-sensitive subjects than sun-resistant subjects.

Methods

We performed a case–control study on risk factors for the most common types of melanoma (i.e., superficial spreading melanoma), and nodular melanoma, in the Netherlands. Information on sunlight exposure and other risk factors was collected by professional interviewers using a modified version of the questionnaire designed in the Western Canada Melanoma Study (*2*). The questionnaire inquired about exposure in three periods of life (before 15, between 15 and 25, and after 25 years of age). Results from other studies have suggested that exposure during early life is important in the etiology of melanoma (*2,3*); therefore, exposure during childhood and adolescence was considered to be the relevant exposure time in this study. We measured intermittent sunlight exposure by four indices: participation in sunbathing; participation in water sports, such as boating and fishing (swimming excluded); the number of vacations spent in sunny countries; and a history of sunburn. We decided to use data on sunlight exposure that occurred between 15 and 25 years of age because the number of persons who reported sunbathing, participating in water sports, or spending vacations in sunny countries before the age of 15 was too small to provide meaningful results in a stratified analysis.

We categorized subjects as indoor or outdoor workers on the basis of occupational sunlight exposure between 15 and 25 years of age. The subjects were asked about any jobs they had held for more than 6 months. Information was recorded on the average number of hours per week spent outdoors for each job. Based on this information, we distinguished between subjects who had ever worked outdoors and those who had never worked outdoors.

Information was also obtained about demographic variables such as age, sex, and educational level and about several pigmentation characteristics known to be associated with melanoma risk. Subjects were asked about their tendency to burn in the sun and their ability to tan. A physician trained in dermatology examined the respondents to obtain information about skin, hair, eye color, and the degree of freckling.

We also stratified subjects as sun-sensitive and sun-resistant individuals because pigmentation characteristics are supposed to modify the effect of intermittent exposure to the sun. Several pigmentation characteristics are indicative of sun sensitivity, but it is not yet clear which characteristic gives the best description of sun sensitivity. Furthermore, the pigmentation characteristics are highly associated. Individuals with blond or red hair often have blue or gray eyes, a fair complexion, many freckles, are susceptible to sunburn, and do not tan easily. Therefore, we decided to use a multivariate model to combine pigmentation characteristics into a single measure: a sun-sensitivity summary score. The score was

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obtained using the logistic regression function described by Miettinen (4). The presence or absence of a melanoma was the dependent variable in this function, and pigmentation characteristics such as tendency to burn, the ability to tan, the color of the skin, hair, and eyes, and the degree of freckling were the independent variables. The function was fitted to data from the entire set of subjects, and the sunlight exposure was set at the nonexposed value for all the subjects. After deriving the fitted scoring function, we computed a score for each subject. The score was used to distinguish between sun-sensitive and sun-resistant persons. We selected 0.265 as cut-off point because this value represented the median value for all the subjects.

The melanoma cases and the control patients were selected from a regional cancer registry, the Comprehensive Cancer Centre IKO, which covers the mid-eastern part of the Netherlands. Controls were patients with other types of malignancies: urogenital cancer, laryngeal cancer, or (non-)Hodgkin's lymphoma. All the patients were diagnosed between 1988 and 1990. The Netherlands Cancer Registry covers more than 95% of all cancers that are diagnosed in the Netherlands (5).

In the Netherlands privacy rules are strict, so eligible patients could only be contacted in an indirect way. The Comprehensive Cancer Centre asked the specialists who were treating the patients to invite them to participate in the study. From the eligible patients, 175 subjects with a melanoma (80%) and 188 controls (47%) agreed to participate. Based on a histopathological review by one pathologist, 31 cases had to be excluded: 4 lesions were not considered to be melanomas, and 27 melanomas were classified as lentigo maligna melanoma or acrolentiginous melanoma. Furthermore, physical examinations to determine the skin complexion and to make nevus counts could not be performed in three cases and three controls. Two controls were not Caucasian. Thus, 141 cases and 183 controls remained for analysis.

To evaluate the interaction between the type of work and intermittent sunlight exposure and sun sensitivity and intermittent sunlight exposure, we used multiple logistic models. The models were constructed with indicator terms for each category of joint exposure (6). The reference category was defined as 1) outdoor workers without intermittent sunlight exposure and 2) persons with a probability <0.265 for developing a melanoma based on pigmentation characteristics and without intermittent sunlight exposure. Each model included three indicator terms: two for the presence of each type of exposure in the absence of the others and one indicating the presence of joint exposures. The odds ratios to estimate the effect of each category of joint exposures was obtained as the antilogarithm of the corresponding term (6).

The model for the evaluation of the interaction between the type of work and intermittent sunlight exposure also included the variables age, sex, educational level, tendency to burn, hair color, and freckling. The model for the evaluation of the interaction between sun sensitivity and intermittent sunlight exposure included the three indicator terms and age, sex, and educational level.

Results

Table 1 presents the distributions among cases and controls of intermittent exposure indices and occupational exposure. More of the patients with a melanoma had participated in sunbathing, water sports (boating, fishing), had spent vacations in sunny countries, and experienced sunburns than the controls.

The majority of the cases had never worked outdoors between 15 and 25 years of age. The odds ratios (OR) associated with intermittent sunlight exposure, adjusted for age, sex, educational level, tendency to burn, hair color, and freckling, varied from 1.43 to 2.16. Outdoor workers had a significantly decreased melanoma risk compared to indoor workers (OR=0.57).

The sun sensitivity score represents the probability of developing a melanoma given the pigmentation characteristics of the individual. Based on the score, the subjects were divided into two groups: sun-sensitive persons with a score of >0.265 and sun-resistant persons with a score of ≤0.265. Among the cases, 68% were classified as sun sensitive versus only 37% of the controls. The distribution of pigmentation characteristics among the two groups is presented in Table 2.

Table 3 shows that the odds ratios associated with the indices for intermittent exposure were higher for the persons who never worked outdoors than for the outdoor workers. The odds ratio for sunbathing among the indoor workers was 3.00 (95% CI: 1.43–6.30), while for the outdoor workers the odds ratio was 0.76 (95% CI: 0.32–1.80). For vacations in sunny countries and a history of sunburn the same pattern was found (indoor workers: OR=2.44, 3.90; outdoor workers: OR=0.77, 1.90, respectively). For water sports the odds ratios were increased for both indoor and outdoor workers.

Table 4 presents the results of stratification by sun sensitivity. Sun-sensitive persons had higher odds ratios for all the indices of intermittent exposure than sun-resistant persons. The odds ratios for the sun-sensitive individuals were 7.69 for sunbathing, 22.65 for watersports, 5.10 for vacations in sunny countries, and 8.67 for a history of sunburn. There were significant differences between sun-sensitive and sun-resistant persons for sunbathing and history of sunburn, as indicated by the 95% confidence intervals, which did not overlap.

Table 1. Distribution among 141 cases and 183 controls of intermittent sunlight exposure indices and occupational sunlight exposure

Exposure	% Cases (*N*)	% Controls (*N*)	Crude odds ratio (95% CI)	Adjusted odds ratio[a] (95% CI)
Intermittent exposure indices				
Sunbathing	45.3 (63)	26.8 (49)	2.27 (1.42–3.61)	2.16 (1.22–3.81)
Water sports	13.0 (18)	6.0 (11)	2.33 (1.08–5.03)	1.60 (0.66–3.87)
Vacations in sunny countries	36.4 (51)	20.8 (38)	2.19 (1.34–3.57)	1.43 (0.75–2.74)
Sunburns	58.9 (83)	32.2 (59)	3.01 (1.92–4.72)	2.10 (1.23–3.56)
Occupational exposure (ever vs. never outdoors)	38.3 (54)	51.4 (94)	0.59 (0.36–0.97)	0.57 (0.33–0.98)

[a]Adjusted for age, sex, educational level, tendency to burn, hair color, and freckling.

Table 2. Distribution of pigmentation characteristics among cases and controls within strata of sun sensitivity

	Sun sensitivity score[a]			
	≤0.265		>0.265	
Pigmentation characteristic	% Cases (*N*=44)	% Controls (*N*=115)	% Cases (*N*=97)	% Controls (*N*=68)
Light skin color	2.2	4.4	37.5	28.4
Red or very fair hair	2.2	0.0	22.9	19.4
Blue eyes	40.0	51.3	39.6	40.3
Many freckles	6.7	6.1	64.6	50.8
Tendency to burn	15.6	11.3	66.7	65.7
Ability to tan	26.7	20.0	57.3	49.3

[a]A score ≤0.265 means that the probability of melanoma, given the individual pigmentation characteristics, is lower than or equal to 0.265.

Table 3. Odds ratios with (95% confidence intervals) associated with indices of intermittent sunlight exposure between 15 and 25 years of age according to occupational exposure

Index of exposure	Never worked outdoors[a] OR (95% CI)	Ever worked outdoors[b] OR (95% CI)
Sunbathing	3.00 (1.43–6.30) (49/26)[c]	0.76 (0.32–1.80) (14/23)
Water sports	2.20 (0.75–6.49) (11/7)	2.61 (0.65–10.49) (7/4)
Vacations to sunny countries	2.44 (1.09–5.42) (38/20)	0.77 (0.31–1.93) (13/18)
History of sunburns	3.90 (1.82–8.33) (54/28)	1.90 (0.89–4.06) (29/31)

The odds ratios were adjusted for age, sex, educational level, tendency to burn, hair color, and freckling.
[a]Never worked outdoors: 87 cases, 89 controls.
[b]Ever worked outdoors: 54 cases, 94 controls.
[c]Number of cases/number of controls.

Table 4. Odds ratios with (95% confidence intervals) associated with indices of intermittent sunlight exposure between 15 and 25 years of age according to sun sensitivity score

Index of sunlight exposure	Sun-sensitive individuals[a] OR (95% CI)	Sun-resistant individuals[b] OR (95% CI)
Sunbathing	7.69 (3.53–16.78) (42/15)[c]	1.48 (0.68–3.22) (21/34)
Water sports	22.65 (4.81–107.7) (16/2)	0.44 (0.09–2.18) (2/9)
Vacations to sunny countries	5.10 (2.34–11.13) (36/17)	1.57 (0.66–3.71) (15/21)
History of sunburns	8.67 (4.34–17.29) (63/23)	1.63 (0.78–3.42) (20/36)

The odds ratios were adjusted for age, sex, and educational level.
[a]Sun-sensitive individuals: 97 cases, 68 controls.
[b]Sun-resistant individuals: 44 cases, 115 controls.
[c]Number of cases/number of controls.

Table 5. Distribution of demographic and pigmentation characteristics among 141 patients with melanoma and 183 control patients

Variable	% Cases (*N*)	% Controls (*N*)
Age		
≤40	34.8 (49)	24.6 (45)
41–50	24.1 (34)	14.8 (27)
51–60	22.0 (31)	27.9 (51)
>60	19.2 (27)	32.8 (60)
Sex		
Men	48.9 (69)	54.1 (99)
Women	51.1 (72)	45.9 (84)
Educational level		
Low	35.5 (50)	47.6 (87)
Intermediate	36.9 (52)	30.6 (56)
High	27.7 (39)	21.9 (40)
Skin color		
North European	26.2 (37)	13.2 (24)
Middle European	73.8 (104)	86.8 (158)
Hair color		
Red/fair	16.3 (23)	7.1 (13)
Blond	63.8 (90)	55.2 (101)
Brown/black	19.9 (28)	37.7 (69)
Eye color		
Blue	39.7 (56)	47.5 (87)
Grey/green	46.1 (65)	38.8 (71)
Brown	14.2 (20)	13.7 (25)
Freckles		
None	27.7 (39)	38.8 (71)
Few	51.8 (73)	55.7 (102)
Many	20.6 (29)	5.5 (10)
Tendency to burn		
None	9.2 (13)	29.0 (53)
Light	40.4 (57)	39.3 (72)
Fair	44.0 (62)	25.7 (47)
Severe	6.4 (9)	6.0 (11)
Ability to tan		
Good	7.8 (11)	12.0 (22)
Fair	44.7 (63)	57.4 (105)
Little	43.3 (61)	23.0 (42)
None	4.3 (6)	7.7 (14)

Discussion

Our study data show a general trend toward higher relative melanoma risks associated with intermittent sunlight exposure among indoor workers and sun-sensitive individuals. This modification of the melanoma risk by the ability to tan and the opportunity for gradual tanning has only been addressed in a few studies (*2,3,7,8*). To our knowledge, the effect of occasional sunlight exposure has never been evaluated separately for indoor and outdoor workers. Holman et al. (*3*) and Weinstock et al. (*7*) measured periodicity of exposure by restricting the analyses to melanomas on the trunk. They reasoned that in comparison with other body sites, exposure to the trunk was more likely to occur in concentrated bursts. Holman et al. (*3*) found an odds ratio of 12.97 (1.95–83.94) associated with the use of two-piece bathing suits or sunbathing in the nude between 15 and 24 years of age compared to the use of one-piece bathing suits. Weinstock et al. (*7*), however, failed to confirm this strong site-specific association between trunk melanoma risk and the use of two-piece bathing suits; they reported an odds ratio of 0.8. Holman et al. also considered the variable "recreational exposure as proportion of total outdoor exposure." This variable, which measured the concentration of outdoor exposure in leisure time, showed little evidence of an association with melanoma risk (*3*).

Modification of sunlight exposure by sun sensitivity was considered in four studies (*2,3,7,8*). Both Weinstock et al. (*7*) and Dubin et al. (*8*) found higher risks of melanoma among sun-sensitive persons than among more sun-resistant persons. Holman et al. (*3*) found interactions between sun exposure habits and skin reaction to sunlight that were difficult to interpret. Elwood et al. (*2*) reported some results that were similar to those observed in the present study: increased risks associated with sunbathing and participating in water sports in high-risk groups. However, their association with the number of vacations in sunny countries was higher in low-risk subjects.

The melanoma patients in our study were younger than the control patients, were more highly educated, a larger proportion were blond/red and freckled, and they were more susceptible to sunburn (Table 5). Therefore, the odds ratios for indoor and outdoor workers were adjusted for these confounding variables.

To evaluate the modification of the effect of sunlight exposure, Dubin et al. (*8*) evaluated odds ratios according to various pigmentation variables. Tanning ability was the only variable for which consistent patterns were observed. Elwood et al. (*2*) divided the subjects into groups on the basis of their melanoma risk as derived from hair color, skin color, and history of freckles (*2*). We used a multivariate summary score to represent various important pigmentation characteristics and checked whether the scoring function was adequate and the stratification tight enough. Table 2 shows that within each stratum of sun sensitivity, cases and controls were comparable with respect to the pigmentation characteristics incorporated into the sun sensitivity score. For example, among the category with a score of >0.265 there was close similarity between the frequency of red or very fair hair in the cases and controls: 22.9% versus 19.4%, respectively. A difference in proportions of more than 10% was only observed between sun-sensitive cases and controls with respect to the presence of many freckles. Thus, the higher odds ratios among the sun-sensitive group cannot be explained by residual confounding due to large differences in pigmentation characteristics between cases and controls within the strata.

Drawbacks of the present study were the low response rate among controls

(47%) and the lack of statistically significant results. The control patients or the specialists who were treating them were less motivated to participate, probably because the study was presented as a study on the risk factors for skin cancer. The consequences for the risk estimates depend on the reasons for nonresponse. If the main reason was that the specialists failed to invite their patients to participate, then selection did not depend on previous sunlight exposure. On the other hand, if selection did depend on previous sunlight exposure, it would bias the risk estimates for all the subgroups in the same direction. Therefore selection bias does not seem to be a plausible explanation for the higher odds ratios for the indoor workers and sun-sensitive individuals. However, such bias cannot be definitely ruled out.

Another possible problem in this study may have been that the public is well aware of the possible relationship between sunlight exposure and skin cancer. The melanoma patients may have had a stronger tendency than controls to recall previous sunlight exposure because they and/or the interviewers thought that their disease was related to sunlight exposure. In an attempt to prevent such recall bias, the interviewers were kept blind to the case–control status of the respondents, but the interviewers could not always prevent the respondents from revealing the nature of their disease during the interview. However, the potential for recall bias does not explain the higher odds ratios in the indoor workers nor the higher odds ratios in the sun-sensitive persons.

Measuring intermittent sunlight exposure is complicated. Until now many studies have used recreational activities such as sunbathing, swimming, boating, and fishing as indices for intermittent sunlight exposure. These activities were supposed to represent a pattern of irregular, intense exposure to the sun. However, we have reservations regarding the adequacy of these intermittent exposure indices. One question, for example, is whether participation in water sports is specific to intermittent exposure or whether it measures another phenomenon; for example, exposure to carcinogens in water (*9*). For this reason we distinguished between swimming and other water sports. Swimming was defined as involving contact with water rather than exposure to sunlight and was therefore not included in the water sports as a measure for intermittent sunlight exposure. Another reason why the use of recreational activities as indices for intermittent sunlight exposure may have been inadequate is that sunbathing and vacationing in sunny countries only add to an already continuous pattern of exposure in persons who are exposed regularly. The results of this study appear to confirm the idea that recreational exposure of persons who work indoors is a better representation of intermittent exposure to the sun.

The objective of this study was to address a number of the factors that Dubin et al. (*8*) considered to be partly responsible for the inconsistency in the results published in the literature. We distinguished chronic and intermittent sunlight exposure, host characteristics that influence susceptibility to sunlight exposure, the age at which exposure is believed to be the most critical, and histological subtypes (lentigo maligna melanomas and acrolentiginous melanomas were excluded). Consequently, this study can be regarded as a serious attempt to clarify the intermittent sunlight theory. The results confirm the expectations that are raised by this theory: the associations between occasional sunlight exposure and melanoma risk are stronger among indoor workers and subjects who have a sun-sensitive skin.

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