World J. Surg. 16, 157–165, 1992

World Journal of Surgery

Melanoma and Sun Exposure: Contrasts Between Intermittent and Chronic Exposure

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The evidence relating cutaneous malignant melanoma to previous sun exposure is now very strong. Major northern hemisphere studies consistently show increases in melanoma in association with recreational and vacation activities related to intermittent sun exposure. These studies have also recorded amounts of sun exposure from such activities. Several studies suggest an increased risk related to short periods of intensive exposure in early adult life. In contrast, regular outdoor occupation confers a decreased risk in these same studies. Australian studies, in populations with much higher levels of total sun exposure, do not show such a clear distinction between intermittent and chronic exposure. The evidence is consistent with a complex relationship of melanoma risk to sun exposure, the risk being increased by intermittent exposure to levels of sun which are higher than normal for that individual, but no increased risk or even a decreased risk related to long term chronic exposure. Possible biological mechanisms for this complex relationship are discussed. In the Western Canada Melanoma Study the effects of occupational and recreational exposure are different in form and are independent. The increased risks seen with various measures of sun exposure do not appear to be systematically different for individuals who have a good tanning response as compared to individuals who do not.

The relationship between melanoma and sun exposure is now supported by strong evidence; this review will concentrate on the details of this relationship: the type of sun exposure, how much sun exposure, when and why.

There have now been over 20 published studies relating melanoma to sun exposure (Table 1) [1–9] with 7 major studies added since the excellent review by Armstrong and English in 1988 [10, 11]. There have been approximately 5,600 patients with melanoma involved in these studies. Despite these reports, the ideal study of melanoma has yet to be done. Study design involves compromises and decisions. For example, to get adequate information on nevi and dysplastic nevi in a case-control study all cases and all controls should receive a detailed skin examination, preferably from a dermatologist with a special interest in melanoma and nevi. On the other hand, to assess a common exposure such as sun exposure it is important that the control series be representative of the source population and assessed in a neutral and non-threatening manner, which is probably better done by a well trained research interviewer than by a specialist clinician. Thus a list of the best studies of sun exposure is different from a list of the best studies of, for example, the assessment of nevi. The best studies in relation to sun exposure are those which use all available incident cases of melanoma in a defined population, use population based control groups rather than other hospital patients, use detailed interviews carried out by well trained dedicated interviewers, use standard and pretested questionnaires, and are reasonably large.

This review will concentrate on 4 studies which fulfill these criteria and have reported in detail on sun exposure; those in Queensland [12–14], Western Canada [15–19], Western Australia [20–22] and Eastern Denmark [23]. The Western Canada study was the first to be started and the questionnaire developed there has been used with some modifications in both the Western Australia and East Denmark studies. The study in Turin by Zanetti and colleagues [2] has produced only a brief report thus far but unfortunately their report includes lentigo maligna and acral lentiginous melanomas in the analyses. The other high quality studies which fulfill the criteria have not yet reported in any detail on sun exposure; these are the studies in Sweden by Beitner and coworkers [5] and in Ontario by Walter and associates [8]. These studies will undoubtedly soon add to the available information.

The Western Canada study was set up specifically to test the intermittent exposure hypothesis which was developed independently by several groups, including Elwood and colleagues [24] in Canada and by Holman and Armstrong [25] in Western Australia in the mid-1970s, although many of the key ideas can be traced back to Lancaster and to McGovern in the 1950s. The intermittent exposure hypothesis is derived primarily from descriptive epidemiology. It is clear that there is enough common ground between melanoma and non-melanoma skin cancer to make it likely that ultraviolet radiation (UVR) is related to melanoma, and yet there are enough differences to make it clear that the details of the relationships must be different [26, 27] (Table 2). The epidemiological similarities include the concentration in white populations, in those with light pigmentation, and in those who live near the equator. The epidemiological

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Table 1. Case-control studies of melanoma assessing sun exposure and/or artificial ultraviolet radiation exposure.

First author	Year	Reference	Place	Period of diagnosis	Patients			Controls	
					Number	Source	Type	Number	Source
Klepp	1979	10	Norway	1974–75	78	Radium hospital		131	Other cancers, same hospital
Adam	1981	10	England	1971–76	111	Population		342	General practice lists
MacKie	1982	10	Western Scotland	1978–80	113	Hospital	SSM or NM	113	Matched hospital
Lew	1983	10	Boston	1978–79	111	Clinic patients		107	Friends of cases
Rigel	1983	10	New York	1978–81	114	Clinic patients		228	Clinic patients and staff
Elwood	1984	10	Western Canada	1979–81	595	Population	SSM, NM or UCM	595	Matched population
Green	1983	10	Queensland	1979–80	183	Population	SSM, NM or UCM	183	Matched population
Holman	1984	10	Western Australia	1980–81	511	Population	All types	511	Matched population
Graham	1985	10	Buffalo	1974–80	404	1 hospital		521	Other cancers, same hospital
Sorahan	1985	10	Birmingham	1980–82	58	2 hospitals		333	Hospital and population
Dubin	1986	10	New York	1972–82	1103	3 hospitals		585	Skin clinic patients
Elwood	1986	10	Nottingham	1981–84	83	Population	All types	83	Matched hospital
Cristofolini	1987	10	Trento, Italy	1983–85	103	1 hospital		205	Hospital
Osterlind	1986	10	East Denmark	1982–85	474	Population	SSM, NM or UCM	926	Matched population
Holly	1987	1	San Francisco	1984–85	121	Melanoma clinic	LM, AM excluded	139	Clinic patients
Swerdlow	1988	10	Scotland	1979–84	180	Hospitals	All types	197	Hospital
Zanetti	1988	2	Turin, Italy	1984–86	208	Population	All types	416	Population
Garbe	1989	3	Berlin	1987	200	1 hospital	All types	200	Skin clinic patients
Weinstock	1989	4	U.S.A.	1976–84	130	Nurses' cohort	AM excluded	300	Nurses' cohort
Beitner	1990	5	Stockholm	1978–83	525	1 hospital	All types	525	Matched population
Elwood	1990	6	Midlands, England	1984–86	195	Population	SSM, NM	195	Hospital in/out patients
Walter[a]	1990	8	Southern Ontario	1984–86	583	Population	All, including in-situ	608	Population
MacKie[a]	1989	7	Scotland	1987	280	Population	All types	280	Hospital, excluding skin

[a]Only artificial ultraviolet radiation exposure.
SSM: Superficial spreading melanoma; NM: Nodular melanoma; UCM: Unclassifiable melanoma; LM: Lentigo maligna melanoma; and AM: Acral lentiginous melanoma.

Table 2. Comparison of non-melanoma skin cancer (NMSC) and melanoma.[a]

Feature	NMSC	Melanoma
Mainly in white populations	Yes	Yes
Increased with light pigmentation	Yes	Yes
Increased nearer the equator	Yes	Yes
Strong concentration on exposed sites	Yes	No
Male excess	Yes	No
Increased in outdoor workers	Yes	No
Linear log-incidence log-age relationship	Yes	No
Easily produced experimentally by UV	Yes	No
Risk proportional to cumulated dose of UV	Yes	No
More common in higher socio-eonomic groups	No	Yes
Rates increasing rapidly	? No	Yes

[a]Excluding lentigo malignant melanoma.
UV: Ultraviolet light.

differences include the facts that melanoma does not show the very clear concentration on exposed sites, the male excess, the increase in outdoor workers, and the simple incidence to age relationship demonstrated by non-melanoma skin cancer. Both epidemiological and experimental work on non-melanoma skin cancer is consistent with the concept that its risk is proportional to the cumulative dose of UVR received. It is clear that this does not apply to melanoma [26]. Other important features of melanoma are its greatly increased risks in higher socio-economic groups in most countries, and its clear and rapid increase in incidence rates [27]. Whether incidence rates for non-melanoma skin cancer have been increasing is not clear since most data systems are inadequate. Some of the better data sources do seem to indicate a considerable increase [28].

These features of melanoma, and therefore the intermittent exposure hypothesis, apply to the more common types of cutaneous melanoma: superficial spreading, nodular, and unclassified types. Lentigo maligna melanoma shares most of the epidemiological and clinical features of non-melanoma skin cancer, and probably has a very similar relationship to ultraviolet exposure as does non-melanoma cancers [27].

The major studies are, therefore, 2 in the northern hemisphere at latitudes of around 50°N (Western Canada) [15–19] and 56°N (Eastern Denmark) [23], and 2 in the southern hemisphere at latitudes of 32°S (Western Australia) [20–22] and 15° and 27°S (Queensland) [12–14]. The northern and southern hemisphere locations are therefore very different environments. Do we expect consistency or contrasts in the results? In regard to the intermittent exposure hypothesis, Australia is perhaps not an easy place to study this aspect of melanoma because sun exposure levels are likely to be so high that few of the population have a true intermittent exposure. It is probably easier to study intermittent exposure in a northern hemisphere population where many people have little regular exposure but indulge in binge type sun exposure during holidays and recreational activities. Measurements of ultraviolet B (UVB) by

Table 3. Significantly increased melanoma risks associated with particular activities in northern hemisphere studies.[a]

Activity	Place	Relative risk
Swim-suit activities	Canada	1.7
Sunny vacations	Canada	1.5
Sunbathing	Denmark	1.9
Boating	Denmark	1.7
Swimming	Denmark	1.5
Sunny vacations	Denmark	1.7

[a]References 15 and 23. $p < 0.05$.

personal dosimeters suggest that the annual dose, measured as a number of minimal erythemal dosages (MED), varies from about 400 MED in outdoor workers to 60 MED in indoor workers living at a northern latitude such as Britain. A holiday in the Mediterranean area including a lot of sunbathing can add 100 MED, i.e., it can more than double the regular exposure of indoor workers [29, 30]. It is perhaps for this reason that the northern hemisphere studies show clearer results in terms of intermittent exposure than do the Australian studies.

Recreational Exposure

These 2 northern hemisphere studies show significant increases in melanoma associated with a range of activities which are independent of host factors (Table 3) [15, 23]. It is unfortunate that most of these activities are extremely pleasurable. There is considerable consistency between these 2 independent studies.

The Italian study by Zanetti and colleagues [2] also shows significantly increased risks of melanoma for sports involving considerable sun exposure and in relationship to the number of vacations spent beside the sea, particularly during adolescent years. In the northern hemisphere studies [15, 23], the effects are very similar for nodular melanoma and superficial spreading melanoma.

Dosage of sun exposure was estimated in the Western Canada study using a unit of "whole body equivalent hours of exposure" [15]. This was based on the recorded information on type of activity and type of clothing worn, where this took place in the world, where it was in terms of local geography, the season, and the typical hours per day or per week. Two independent questions related to intermittent exposure, one on recreational activities and the other on vacations. The analyses for both recreational and vacation activities showed that the risk of melanoma increased when exposure was >20 whole body equivalent hours of activity (Fig. 1). This amount of sun exposure is fairly typical of that received by a northern hemisphere urban dweller during a 2 week holiday in a sunny place, or during a regular recreational activity such as swimming or boating carried out most weekends during the summer.

This increased risk of around 1.8 to 2 is not all that large, although it is statistically significant. It is seen consistently in males and females, in different age groups, and for nodular and superficial spreading melanoma. It is adjusted for skin type, assessed by skin, hair, and eye pigmentation, for usual response to sunlight to assess tendency to burn or tan, and is adjusted for ethnic origin and socio-economic status [15]. Even after adjustment for sunburn history and for freckling, these risks are still significant, although such adjustment is unnecessary or may

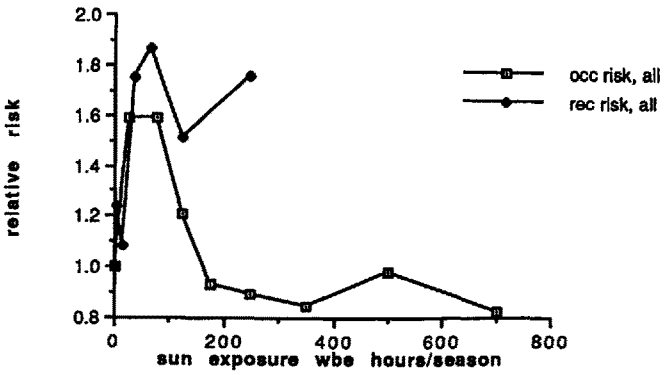

Fig. 1. Relative risk of melanoma (superficial spreading and nodular) by sun exposure in whole body equivalent (wbe) hours per summer from occupational sun exposure (occ risk) and recreational (rec risk) activities. Based on further analysis of the study by Elwood and coworkers [15].

Table 4. Reduced melanoma risks associated with occupational activities in males in northern hemisphere studies.[a]

Activity	Place	Relative risk
Occupational exposure >400 wbeh/season	Canada	0.5[b]
Farmers	Canada	0.4[b]
Construction workers	Canada	0.3[b]
Woodworkers	Canada	0.3[b]
Outdoor work	Denmark	0.7[b]
Farmers, construction workers, fishermen	Denmark	0.6 ns

[a]References 15, 18, and 23.
[b]$p < 0.05$.
ns: Not significant; wbeh: Whole body equivalent hours.

even be misleading as these are also likely outcome measures of intermittent sun exposure, as are nevi. The Canadian study does not provide data on nevi.

Thus, the northern hemisphere studies show increases in melanoma risk with recreational sun exposure >20 whole body equivalent hours per season. In these studies, the people with the highest sun exposures were those who had regular outdoor jobs, mainly men. The data for men show significantly *reduced* risks of melanoma in those with the highest measured exposures in Canada, those with outdoor work recorded in Denmark, and specific categories of workers who would be expected to work outdoors; for example, most woodworkers in Western Canada are involved in forestry and logging operations, not in indoor craftsmen work (Table 4). The detailed dose data combining both sexes shows that the decrease to risks similar or below that of unexposed people occurs with occupational exposures >200 whole body equivalent hours per season (Fig. 2). Very interestingly, however, risks in those with occupational exposure of about 20–100 units are elevated both compared to those with little occupational exposure and those with heavy exposure. This increased risk is significant and is independent of host factors. It shows consistency with the range of doses from recreational exposure which confer increased risk. The data are more striking for men, where the decrease at high exposures is significant with substantial num-

Table 5. Evidence for melanoma risk with short previous exposures.

First author	Year	Reference	Relative risk	95% confidence interval	*p* value	Measurement of exposure
Paffenberger	1978	31	3.9		0.01	Outdoor work recorded at college medical exam; prospective.
Brown	1984	32	7.7	2.8–21.3	0.0002	US service: tropics vs US/Europe
Elwood	1986	38	1.8	0.6–5.1		≥1 year tropical, subtropic living
Beitner	1990	5	1.9	1.0–3.6		Lived in Mediterrean, tropic, subtropics >1 year in last 10
MacKie	1989[a]	7	2.6	1.3–5.4		Lived 5+ years, tropical, subtropical
	1989[b]		1.8	0.8–4.0		

[a]Males.
[b]Females.

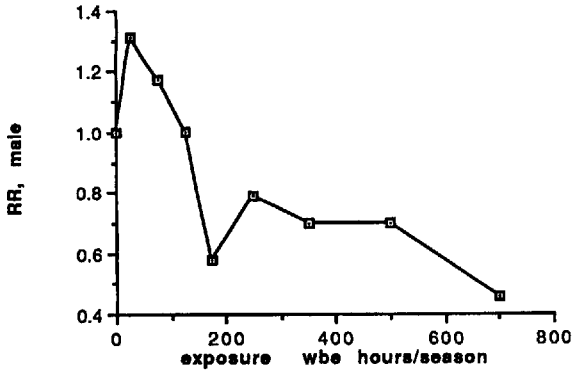

Fig. 2. Relative risk (RR) of melanoma (superficial spreading and nodular) for males by occupational sun exposure in whole body equivalent (wbe) hours per summer. Based on further analysis of the study by Elwood and associates [15].

Table 6. Melanoma risks associated with particular activities in Australian studies.[a]

Activity	Place	Type	Relative risk
Boating	Western Australia	SSM	2.4[b]
Fishing	Western Australia	SSM	2.7[b]
Swimming	Western Australia	SSM	1.1 ns
Sunbathing age 15–24 years	Western Australia	SSM	1.3 ns
Recreation >60% of total outdoor time, age 10–24 years	Western Australia	All	1.3 ns
	Western Australia	SSM	1.6 ns
Beach time >5000 hours lifetime	Queensland	Excluding LM	1.9 ns
Beach time >500 hours age 10–19 years	Queensland	Excluding LM	1.0 ns

[a]References 12 and 21.
[b]$p < 0.05$
ns: Not significant; SSM: Superficial spreading melanoma; and LM: Lentigo maligna melanoma.

bers of observations, although the increase with moderate exposure is somewhat less.

The Western Canada data were further analyzed to determine what type of exposures were characteristic of those with a moderate amount of occupational exposure to create this high risk. Most such people had a few years of seasonal outdoor work or 1 to 2 years of outdoor work often in early life, perhaps while as a student, before settling down to a routine predominantly indoor existence. Thus the data for increased risk seen with moderate occupational exposure may be another way of showing an effect of intermittent exposure.

Some information from other sources also suggests that intense exposure in late adolescence or early adult life is associated with an increase in melanoma risk many years subsequently (Table 5). The best and earliest of these observations was made by Paffenbarger and colleagues [31] on the basis of a cohort study, the only prospective study of melanoma. They showed a four-fold increase of melanoma in college students who during their entrance examination or medical examinations during their college had recorded that they had had considerable outdoor exposure. No information is available on subsequent exposures, but it seems somewhat unlikely that there was a systematic difference in later outdoor exposures which would explain the result. Several case-control studies show that individuals who have had a few years of living in a more sunny environment, often as a result of military service, have an increased risk of melanoma. Brown and associates [32] specifically studied melanoma cases and controls who were in the United States services during World War II, and showed that those who served in the Pacific region had a considerably increased risk of melanoma compared to those who served in the European theatre.

Australian Studies

Thus the northern hemisphere studies show an increase of melanoma with high recreational exposure or a small, concentrated amount of occupational exposure, but show lower risks with heavy occupational exposure. The Canadian and the Danish studies are consistent with these results.

One would not necessarily expect the Australian results to be consistent in a simple way, as different dosages of sun are received by apparently similar activities in the 2 different locations. Looking at recreational activities, the Western Australia study shows increases in melanoma with specific activities which are likely to be related to fairly moderate to high sun exposure such as boating and fishing, whereas no increase was seen with more intensive sun activities such as swimming and sunbathing. Only a small and nonsignificant increase was seen with the proportion of total outdoor time spent in recreation at what are probably the critical ages [21] (Table 6). In Queensland, the results are a little hard to interpret, as although there

Table 7. Relative risks of melanoma with sun exposure in Western Australia.[a]

Sun exposure	Type of melanoma		
	All	SSM	LM
Total outdoor summer exposure >23 hrs/week (compared to 0–10 hrs/week)	0.70	0.57	1.32
Recreational exposure >60% of total at ages 10–24 years (compared to 0–29%)	1.28	1.57	0.79
Recreational expsoure top quartile (compared to lowest quartile)		0.63	
Occupational exposure top quartile (compared to lowest quartile)		0.51	
Risks by occupational exposure and clothing exposure of site:			
<2 hrs/day	2.21	2.43	1.83
>2 hrs/day: affected site usually covered (reference group)	1.00	1.00	1.00
>2 hrs/day: affected site sometimes exposed	2.49	2.16	2.15
>2 hrs/day: affected site usually exposed	2.08	2.43	1.18

[a]Reference 21.

SSM: Superficial spreading melanoma; LM: Lentigo maligna melanoma.

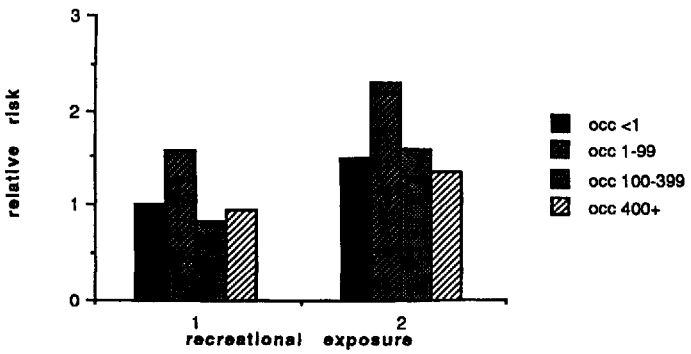

Fig. 3. Relative risk of melanoma (superficial spreading and nodular) by occupational (occ) sun exposure (<1, 1–99, 100–399 and 400+ whole body equivalent (wbe) hours per season) and by recreational sun exposure (1 = <19 and 2 = 20+ wbe hours per season). Data from Western Canada Melanoma Study [15].

was a strong and significant increase in melanoma in association with total sun exposure, a combination of recreational and occupational exposure, there was no association seen with either of these alone [12, 14]. There was an elevation of risk with total time spent on the beach during a lifetime, although it was not significant, and there was no increase seen in those with large amounts of time spent on the beach in the teenage years. These results might suggest that activities which carry moderate sun exposure carry an increased risk, whereas activities which involve greater sun exposure do not carry such an increased risk, and they suggest the possibility that extensive recreational activities in the Australian sunlight might confer similar dosages and similar sequelae as occupational exposure in the northern hemisphere.

Further, there is fairly consistent evidence from the Western Australia study that outdoor exposure through occupation with very high dosages confers, as it does in the northern hemisphere studies, a decreased risk of melanoma with significantly reduced risks being seen for total exposure >23 hours a week, and for occupational exposure in the top quartile, predominantly for superficial spreading melanoma (Table 7). Further analyses assessed the site in which the melanoma developed and showed that those patients in which the usual site was sometimes or always exposed had a higher risk than those who worked outdoors but whose affected site was usually covered. The interesting thing about these data, however, is that the lowest risk is in people who work outdoors with the affected body site covered, whereas the risk in those who work outdoors with the site exposed is actually very similar to the risk in people without any substantial outdoor exposure.

Thus there is agreement between the Western Australia and the northern hemisphere studies in terms of increased melanoma risk associated with some outdoor activities such as boating and fishing, and there is consistency in terms of the low risks seen with heavy occupational sun exposure. There are disagreements about the effect of total recreational outdoor exposure, which may be because the total dose received in Australia is so much higher than that in the northern hemisphere that it has a different effect.

Attempts have been made to express melanoma risks in terms of total sunlight. For example, Armstrong and Holman, based on the Western Australia study and consideration of other literature, initially suggested a pattern of risk increasing and then decreasing with amount of total sun exposure, and subsequently suggested an even more complex pattern with this increase and then decrease, followed by a further increase at high total amounts [1, 11, 21]. The Western Canada data, which were not used directly in the compilation of this hypothesis, are compatible with this; the risk of melanoma by total recorded sun dose in Western Canada gives a curve similar to the Holman and Armstrong suggestion, but none of the points are significantly above or below the null line.

However, any such model assumes that doses from different types of exposure are additive; thus the effect of 20 whole body equivalent hours of sun exposure from recreation would not be expected to be large in an individual with >400 hours of occupational exposure. However, the Western Canada data suggest that intermittent and constant exposure are independent in relative risk terms (Fig. 3). Therefore, an individual's total dose does not determine his/her melanoma risk. If this total dose was achieved by occupational exposure predominantly, the risk will be lower than if the same total dose were achieved by recreational exposure.

This analysis is limited by the numbers available and confirmation from the other major studies is needed. However, if confirmed, this result provides a solution to the dilemma about public education. If there is a complex curvilinear relationship with total dose, public education campaigns aimed at reducing total dose could, for some individuals with high exposures, increase the risk. However, if the effective dose is comprised of 2 independent components, then the public health impetus should be to reduce intermittent recreational exposure. This should reduce an individual's risks irrespective of occupational exposure.

Table 8. Melanoma risk with artificial ultraviolet light (UV) exposures.

First author	Year	Reference	Place	Sex	Relative risk	95% confidence interval	Measurement of exposure
Swerdlow	1988	9	Scotland	Both	2.9	1.3–6.4	Ever used UV lamps, sunbeds
Swerdlow	1988	9	Scotland	Both	9.1	2.0–40.6	Use >5 yrs before diagnosis
MacKie	1989	7	Scotland	Male	2.6	0.9–7.3	Sunbed use >3 months
MacKie	1989	7	Scotland	Female	1.5	0.8–2.9	Sunbed use >3 months
Walter	1990	8	Ontario	Male	1.9	1.2–3.0	Ever used UV lamps, sunbeds
Walter	1990	8	Ontario	Female	1.5	1.0–2.1	Ever used UV lamps, sunbeds
Walter	1990	8	Ontario	Male	2.1	0.9–5.3	Use ≥1 year
Walter	1990	8	Ontario	Female	3.0	1.1–9.6	Use ≥1 year

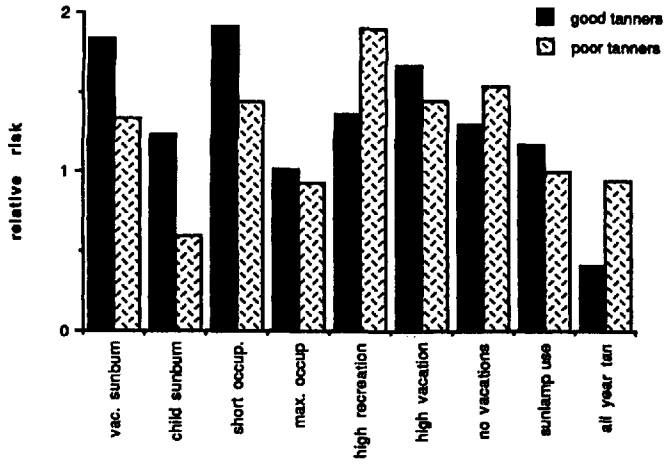

Fig. 4. Relative risk of melanoma (superficial spreading or nodular) in good tanners (n = 458) and poor tanners (n = 719) conferred by history of or exposure to: vacation sunburn (score 10–12 compared to ≤4 [16]), childhood sunburn (severe or frequent, compared to rare or mild), short term occupational exposure (1–99 wbeh compared to <1), maximum occupational exposure (200+ wbeh compared to <1), high recreational exposure (20+ wbeh compared to <1), high vacation exposure (20+ wbeh compared to <1), number of sunny vacations per decade (4+ compared to 0), sunlamp use (yes compared to no), and all year tan (all year tan compared to little or no tan). wbeh: whole body equivalent hours.

Modification of Risk

The Western Canada data have been further examined to determine if the risks associated with different sun exposures vary in different groups of people. One logical suggestion is that those who have a natural ability to tan readily are protected against the effects of excessive sun. Dubin and associates [33] have published results from a case-control study in New York which shows that those who tanned poorly have a higher risk in association with both recreational and occupational exposures. However, this study has several methodological problems. For example, the information was collected from the melanoma patients and the controls by different people under different circumstances. Moreover, although these differences are interesting, none of the differences is statistically significant. In the Western Canada study, subjects who were good tanners had a substantially lower risk of melanoma overall than those who were poor tanners [16]; Figure 4 shows the relative risks in association with other factors for each of these groups. The good tanners had a *more* pronounced increase in melanoma risk in association with vacation, childhood sunburn, and the short occupation exposures. The good tanners had a lesser increase with recreational exposure and with the number of vacations, although the good tanners had a slightly higher risk in association with total vacation exposure. Overall, there is no systematic difference between the 2 groups and no evidence to suggest that those who are naturally good tanners have any protection against the adverse effects of recreational or short occupational sun activity. The one difference between good tanners and poor tanners is that for good tanners the presence of an all-year tan, that is the presence as well as the propensity to tan, confers a substantially decreased risk of about 0.5, whereas in poor tanners, the few of them who did have an all-year tan did not have a substantially lower risk.

If among people who have similar intermittent summer sun exposures, one group also has enough winter exposure to maintain a tan and another group does not, which group would have the higher risk? Direct analysis of this question from the Western Canada study does not reveal any difference in terms of winter exposures, although again the data are very limited. Important results come from studies which directly look at the use of sunbeds. If an all-year tan is protective, those who use sunbeds would achieve a protective effect by having a regular all-year tan and therefore would avoid the acute effects of intermittent exposure such as sunburn; then they should have a lower risk of melanoma. Empirically it is fairly clear that they have a higher risk [8–10] (Table 8). The limitations of the analysis to date, even the most detailed study of Walter and colleagues [9] in Ontario, are that we do not know if those who use sunbeds regularly and those who do not have similar exposures to natural sunlight. Further analyses should address this question.

Discussion

A major conclusion from these studies is that there is something specific about intermittent recreational sun exposure which produces a different effect than chronic occupational exposure. The difference could be in the radiation itself, in the factors which go along with it, or in the biological response.

It seems reasonable to assume that occupational exposure involves exposure all day and during the whole year to sunlight, whereas recreational exposure is exposure particularly to sunlight at peak hours during the summer. During summer months, and during peak hours in the day, there is a much higher ratio of

shorter to longer wavelength ultraviolet radiation, that is UVB to ultraviolet A (UVA), and even a shorter wavelength distribution within these bands [34]. Thus for a given total dose of UVB, less UVA is received by recreational exposure compared to occupational exposure. If UVA had some beneficial effect, for example, in photorepair systems, this might explain the higher risk associated with recreational exposure. However, a major argument against the possibility that UVA or a high ratio of UVA to UVB confers a lower risk is the empirical evidence shown above that risk is increased rather than decreased by the use of sunbeds which produce predominantly UVA. However, occupational and recreational sun exposures may differ in terms of their wavelength distribution in more subtle ways, and if different wavelengths have different effects on melanoma production, this could be important.

Differences in other conditions could be relevant. Variations in temperature, humidity, and wind speed have all been shown to affect the production of non-melanoma skin cancers by ultraviolet light in experimental animals [26]. The presence or absence of clothing, sweating, and the use of sunscreens could all make meaningful differences in terms of physical conditions, chemical exposures, and immunological actions. Melanomas diagnosed today reflect occupational exposures in previous decades, which were most likely characterized by an absence of the use of sunscreens or other skin preparations, whereas recreational exposures are more likely to have been associated with considerable use of a wide range of chemical products on the skin. One study which has looked at some of these issues, including issues of washing and removing body oils, is the Queensland study which, however, did not find any significant effects [14].

In addition to these other external conditions, other sequelae of different types of sun exposure may be relevant: skin thickening, patterns of melanin disposition, patterns of temperature, and melanocyte activity. Keratin as well as melanin absorbs UVR, and skin thickening is a more important UVR blocking response to UVB than is tanning in those who tan poorly.

A major limitation of the studies described to date is that the dosages of sun exposure assessed relate only to the dosages at the skin surface. The relevant dose is presumably the dose at the level of the melanocytes and the basement membrane. It could be argued that the relatively low risk of melanoma seen in outdoor workers and presented above, in contrast to the high skin surface sun exposure dosages of these workers, occurs because these individuals have considerable natural protection against UVR due to skin thickening and melanin distribution. Thus if we had a way of assessing dose at the level of the melanocytes, these individuals might have a much more moderate dosage, particularly in comparison to individuals without heavy skin thickening or tanning who are exposed to intermittent sun exposure.

It seems quite feasible that UVR given in different dosage patterns has different effects. There is evidence that other carcinogens produce different yields if given in continuous or in intermittent dosages, and of course timing in relationship to other relevant factors is important. There does not appear to be any direct experimental evidence that in the production of non-melanoma skin tumors in animals, intermittent UVR exposure produces a different response than the same amount of UVR exposure given chronically. This would be useful information and could relate to effects on DNA damage and on DNA repair mechanisms. The newer experimental models for melanoma produced by UVR in animals may allow such experiments.

It is reasonable to suppose that intermittent exposure results in a cyclical process of stimulation of melanocytes which go through rapid proliferation and activity phases, and then go into a resting phase in the relatively unexposed period. By analogy with cancers produced in other organs ranging from breast tissue to thyroid tissue, such repeated stimulation could readily be seen as increasing the probability of carcinogenic transformation. If chronic occupational exposure produces instead one burst of rapid proliferation of melanocyte activity and then maintenance of the chronic exposed condition with proliferative activity on the part of melanocytes, the carcinogenic potential could be less. There is considerable scope, therefore, for designing animal experiments based very closely on these epidemiological hypotheses.

Exploration of the mechanism needs to assess whether the production of melanoma by sun exposure is a process restricted to the skin cells on which the UVR acts directly or is a more generalized phenomenon. Direct damage would imply localized effects, with melanoma arising in areas of skin with the most solar damage. This fits well with non-melanoma skin cancer and lentigo maligna melanoma, but not with the more common forms of melanoma. Much has been made of the association between sunburn and melanoma, but the most detailed studies available, which are those of Western Australia and Western Canada, suggest that this easily observed empirical association between history of sunburn and melanoma risk is likely to relate primarily to an increased melanoma risk in those with a tendency to sunburn, rather than being a direct consequence of the sunburn. There is, as yet, little evidence that melanomas arise particularly at body sites which have been sunburnt. It has also been pointed out for many years that the body site distribution of melanoma does not change greatly in comparison, for example, between high incidence and low incidence areas. On the basis of this, Lee and Merrell [35] suggested in 1970 that there must be a "solar circulating factor" by which UVR could increase melanoma risk throughout the body. Subsequently Rosdahl [36] showed that irradiation of one ear of a rat increased cancer production not only in that ear but in the other shielded ear, and Stierner and associates [37] have shown in humans that ultraviolet light induces an increase in the melanocyte population in shielded areas of the skin as well as directly exposed areas. The idea of a solar circulating factor has therefore considerable support. UVR could act by such indirect mechanisms, or directly, or through immunological processes. It is not difficult to imagine that different patterns of spectral distribution, threshold quantity, or fractionation of dose of UVR, could therefore have different effects.

Conclusions

The epidemiological and clinical evidence is certainly sufficient to make a firm conclusion that the more common types of melanoma are related primarily to relatively severe intermittent sun exposure on unacclimatized skin. Despite this, some recently published reviews have dismisses or regarded as merely

hypothetical the relationship between sun exposure and melanoma on logic which assesses only whether there is a simple linear relationship and concludes that there is not. The epidemiological evidence strongly suggests that the effect of long continued heavy exposure such as that received by persons with outdoor occupations is different qualitatively as well as quantitatively from the effect of intermittent exposure received typically in recreational and vacation activities. It is this latter exposure which is likely to be the major causative factor of most melanoma in developed countries and it is reduction in this exposure that public health programs should address. We must be careful about using apparently simple but possibly misleading targets for education such as sunburn, as it may well be that avoidance of sunburn is only effective if intermittent ultraviolet dosages are reduced; if they are in fact increased by using sunbed tanning or sunblockers to allow greater outdoor exposure without burning, that may not be helpful in terms of melanoma.

Further epidemiological studies of melanoma may well be useful, but have to have considerable advances in the quantitation of sun exposure and its effects to be valuable. We and others are working on these measurement problems. Opportunities to study population groups with well defined exposures could be very valuable, as they have been with other carcinogenic agents.

Résumé

La relation de cause à effet entre l'exposition au soleil et le développement d'un mélanome cutané malin est maintenant bien établie. Des études majeures provenant de l'hémisphère nord ont montré que l'exposition intermittente au soleil, pendant les vacances par exemple, augmente les risques de mélanome malin. Elles ont également enregistré les durées d'exposition suivant le type des activités au cours des vacances. Plusieurs études ont suggéré que le risque de mélanome est augmenté par de courtes périodes d'exposition au soleil chez l'adulte jeune. En revanche, dans ces mêmes études, une activité extérieure prolongée est associée à un risque plus faible. Des études, provenant d'Australie, chez des populations qui ont un niveau d'exposition élevé, ne montrent pas une telle distinction entre l'exposition intermittente et chronique. Il semble exister une relation complexe entre le risque de mélanome et l'exposition solaire, risque augmenté par le caractère intermittent et l'intensité de l'exposition. De plus, le risque n'est pas augmenté, mais au contraire diminué, par une exposition chronique. Les mécanismes biologiques responsables de ces phénomènes complexes sont discutés. Dans l'étude du Canada de l'Ouest sur le mélanome, les effets de l'exposition au soleil ne vont pas dans le même sens. Il semble que les risques ne soient pas différents, que le sujet ait ou non une bonne réponse au soleil (bronzage).

Resumen

La evidencia sobre la relación entre el melanoma maligno y la exposición a la luz solar es muy fuerte. Importantes estudios realizados en el hemisferio norte demuestran en forma consistente un aumento en la incidencia de melanoma asociado con actividades de tipo recreacional y vacacional en que hay exposición intermitente al sol; en tales estudios se ha determinado la cantidad de exposición solar relacionada con dichas actividades. Diversos estudios sugieren un mayor riesgo relacionado con períodos cortos de intensa exposición en el curso de la edad adulta temprana; por el contrario, las ocupaciones que regularmente se realizan al aire libre implican un menor riesgo, según estos estudios. Investigaciones australianas sobre poblaciones con mucho mayores niveles de exposición solar total no señalan tan clara diferencia entre la exposición intermitente y la exposición crónica. La evidencia es consistente con una compleja relación entre el riesgo de melanoma y la exposición solar, el riesgo siendo aparentemente mayor con la exposición intermitente a niveles superiores de lo normal para un determinado individuo, pero no aumentado, o aún disminuido, con la exposición crónica prolongada. En este artículo se discuten los posibles mecanismos biológicos involucrados en tan compleja relación. En el estudio sobre Melanoma de Canadá Occidental los efectos de la exposición ocupacional y recreacional aparecen diferentes en su forma, e indepdientes entre sí. Los mayores riesgos observados con diferentes medidas de exposición solar no resultan sistemáticamente diferentes en los individuos que desarrollan una buena respuesta bronceadora en comparación con quienes no la desarrollan.

Acknowledgment

This paper is based on presentations at the meeting of the Clinical Oncology Society of Australia, November 1990, Melbourne, Australia, whose support is gratefully acknowledged.

References

1. Holly, E.A., Kelly, J.W., Shpall, S.N., Chiu, S.-H.: Number of melanocytic nevi as a major risk factor for malignant melanoma. J. Am. Acad. Dermatol. *17*:459, 1987
2. Zanetti, R., Rosso, S., Colonna, S., Martina, G., Paudice, A.: Studio caso-controllo sul melanoma maligno cutaneo in provincia di torino. G. Ital. Dermatol. Venereol. *123*:461, 1988
3. Garbe, C., Kruger, S., Stadler, R., Guggenmoos-Holzmann, I., Orfanos, C.E.: Markers and relative risk in a German population for developing malignant melanoma. Int. J. Dermatol. *28*:517, 1989
4. Weinstock, M.A., Colditz, G.A., Willett, W.C., Stampfer, M.J., Bronstein, B.R., Mihm, M.C. Jr., Speizer, F.E.: Nonfamilial cutaneous melanoma incidence in women associated with sun exposure before 20 years of age. Pediatrics *84*:199, 1989
5. Beitner, H., Norell, S.E., Ringborg, U., Wennersten, G., Mattson, B.: Malignant melanoma: Aetiological importance of individual pigmentation and sun exposure. Br. J. Dermatol. *122*:43, 1990
6. Elwood, J.M., Whitehead, S.M., Davison, J., Stewart, M., Galt, M.: Malignant melanoma in England: Risks associated with naevi, freckles, social class, hair colour, and sunburn. Int. J. Epidemiol. *19*:801, 1990
7. MacKie, R.M., Freudenberger, T., Aitchison, T.C.: Personal risk-factor chart for cutaneous melanoma. Lancet *2*:487, 1989
8. Walter, S.D., Marrett, L.D., From, L., Hertzman, C., Shannon, H.S., Roy, P.: The association of cutaneous malignant melanoma with the use of sunbeds and sunlamps. Am. J. Epidemiol. *131*:232, 1990
9. Swerdlow, A.J., English, J.S.C., MacKie, R.M., O'Doherty, C.J., Hunter, J.A.A., Clark, J., Hole, D.J.: Fluorescent lights, ultraviolet lamps, and risk of cutaneous melanoma. Br. Med. J. *297*:647, 1988
10. Armstrong, B.K.: Epidemiology of malignant melanoma: Intermittent or total accumulated exposure to the sun? J. Dermatol. Surg. Oncol. *14*:836, 1988
11. Armstrong, B.K., English, D.R.: Cutaneous malignant melanoma.

In Cancer Epidemiology and Prevention, 2nd edition. D. Schottenfeld, J.F. Fraumeni, editors, Philadelphia, Saunders, (*in press*)
12. Green, A.C.: Sun exposure and the risk of melanoma. Australas. J. Dermatol. *25*:99, 1984
13. Green, A.C., Siskind, V., Bain, C., Alexander, J.: Sunburn and malignant melanoma. Br. J. Cancer *51*:393, 1985
14. Green, A.C., Bain, C., McLennan, R., Siskind, V.: Risk factors for cutaneous melanoma in Queensland. In Epidemiology of Malignant Melanoma: Recent Results in Cancer Research, R.P. Gallagher, editor, Heidelberg, Springer-Verlag, 1986, pp. 76–97
15. Elwood, J.M., Gallagher, R.P., Hill, G.B., Pearson, J.C.G.: Cutaneous melanoma in relation to intermittent and constant sun exposure: The Western Canada Melanoma Study. Int. J. Cancer *35*:427, 1986
16. Elwood, J.M., Gallagher, R.P., Davison, J., Hill, G.B.: Sunburn, suntan and the risk of cutaneous malignant melanoma: The Western Canada Melanoma Study. Br. J. Cancer *51*:543, 1985
17. Elwood, J.M., Gallagher, R.P., Worth, A.J., Wood, W.S., Pearson, J.C.G.: Etiological differences between subtypes of cutaneous malignant melanoma: Western Canada Melanoma Study. J. Natl. Cancer Inst. *78*:37, 1987
18. Gallagher, R.P., Elwood, J.M., Threlfall, W.J., Spinelli, J.J., Fincham, S., Hill, G.B.: Socioeconomic status, sunlight exposure, and risk of malignant melanoma: The Western Canada Melanoma Study. J. Natl. Cancer Inst. *79*:647, 1987
19. Gallagher, R.P., Elwood, J.M., Hill, G.B.: Risk factors for cutaneous malignant melanoma: The Western Canada Melanoma Study. In Epidemiology of Malignant Melanoma: Recent Results in Cancer Research, R.P. Gallagher, editor, Heidelberg, Springer-Verlag, 1986, pp. 38–55
20. Holman, C.D.J., Armstrong, B.K.: Cutaneous malignant melanoma and indicators of total accumulated exposure to the sun: An analysis separating histogenetic types. J. Natl. Cancer Inst. *73*:75, 1984
21. Holman, C.D.J., Armstrong, B.K., Heenan, P.J.: Relationship of cutaneous malignant melanoma to individual sunlight-exposure habits. J. Natl. Cancer Inst. *76*:403, 1986
22. Holman, C.D.J., Armstrong, B.K., Heenan, P.J., Blackwell, J.B., Cumming, F.J., English, D.R., Holland, S., Kelsall, G.R.H., Matz, L.R., Rouse, I.L., Singh, A., Ten Seldam, R.E.J., Watt, J.D., Xu, Z.: The causes of malignant melanoma: Results from the West Australian Lions Melanoma Research Project. In Epidemiology of Malignant Melanoma, R.P. Gallagher, editor, Heidelberg, Springer-Verlag, 1986, pp. 18–37
23. Osterlind, A., Tucker, M.A., Stone, B.J., Jensen, O.M.: The Danish case-control study of cutaneous malignant melanoma. II. Importance of UV-light exposure. Int. J. Cancer. *42*:319, 1988
24. Elwood, J.M., Hislop, T.G.: Solar radiation in the etiology of cutaneous malignant melanoma in Caucasians. Natl. Cancer Inst. Monogr. *62*:167, 1982
25. Holman, C.D.J., Armstrong, B.K., Heenan, P.J.: A theory of the etiology and pathogenesis of human cutaneous malignant melanoma. J. Natl. Cancer Inst. *71*:651, 1983
26. Elwood, J.M.: Initiation and promotion actions of ultraviolet radiation on malignant melanoma. In Models, Mechanisms and Etiology of Tumor Promotion, I.A.R.C. Scientific Publication No. 56, M. Borzsonyi, N.E. Day, K. Lapis, H. Yamasaki, editors, Lyon, MRC-OUP, 1984, pp. 421–525
27. Lee, J.A.H.: Melanoma and exposure to sunlight. Epidemiol. Rev. *4*:110, 1982
28. Glass, A.G., Hoover, R.N.: The emerging epidemic of melanoma and squamous cell skin cancer. J.A.M.A. *262*:2097, 1989
29. Bernhardt, J.H., Matthes, R.: Quantitative description of exposure to UV and methods of measurements. In Human Exposure to Ultraviolet Radiation: Risks and Regulations, W.F. Passchier, B.F.M. Bosnjakovic, editors, Amsterdam, Elsevier, 1987, pp. 201–212
30. Diffey, B.L., Larko, O., Swanberck, G.: UV-B doses received during different outdoor activities and UV-B treatment of psoriasis. Br. J. Dermatol. *106*:33, 1982
31. Paffenbarger, R.S. Jr., Wing, A.L., Hyde, R.T.: Characteristics in youth predictive of adult-onset malignant lymphomas, melanomas, and leukemias: Brief communication. J. Natl. Cancer Inst. *60*:89, 1978
32. Brown, J., Kopf, A.W., Rigel, D.S., Friedman, R.J.: Malignant melanoma in World War II veterans. Int. J. Dermatol. *23*:661, 1984
33. Dubin, N., Moseson, M., Pasternack, B.S.: Sun exposure and malignant melanoma among susceptible individuals. Environ. Health Perspect. *81*:139, 1989
34. McKenzie, R.L., Elwood, J.M.: Intensity of solar ultraviolet radiation and its implications for skin cancer. N. Z. Med. J. *103*:152, 1990
35. Lee, J.A.H., Merrill, J.M.: Sunlight and the aetiology of malignant melanoma: A synthesis. Med. J. Aust. *2*:846, 1970
36. Rosdahl, I.K.: Local and systemic effects on the epidermal melanocytic population in UV-irradiated mouse skin. J. Invest. Dermatol. *73*:306, 1979
37. Stierner, U., Rosdahl, I., Augustsson, A., Kagedal, B.: UVB irradiation induces melanocyte increase in both exposed and shielded human skin. J. Invest. Dermatol. *92*:561, 1989
38. Elwood, J.M., Williamson, C., Stapleton, P.J.: Malignant melanoma in relation to moles, pigmentation, and exposure to fluorescent and other lighting sources. Br. J. Cancer *53*:65, 1986