

European Journal of Cancer 40 (2004) 429-435

European Journal of Cancer

www.ejconline.com

Exposure to the sun and sunbeds and the risk of cutaneous melanoma in the UK: a case–control study

V. Bataille^{a,b,*}, A. Winnett^b, P. Sasieni^b, J.A. Newton Bishop^c, J. Cuzick^b

^aGenetic Epidemiology and Twin Research Unit, St Thomas Hospital, Lambeth Palace Road, London SEI 7EH, UK

^bCancer Research UK, Statistics, Mathematics and Epidemiology Department, Wolfson Institute of Preventive Medicine, London EC1M 6QB, UK ^cGenetic Epidemiology Division, Cancer Research UK, St James's University Hospital, Leeds, UK

Received 14 April 2003; received in revised form 26 August 2003; accepted 18 September 2003

Abstract

Migration, latitude and case-control studies have clearly established a link between melanoma and sun exposure. This casecontrol study of melanoma was set up to examine the role of sun exposure and sunbeds in the pathogenesis of melanoma in the United Kingdom (UK), a country with low levels of ultraviolet radiation. The study included 413 cases and 416 controls. More than 10 severe sunburns compared with less than 10 sunburns was associated with an Odds Ratio (OR) of 1.98 (95% Confidence Interval (CI) 1.02–3.86) (P=0.04) when adjusted for age, gender and skin type. Sunburns before the age of 15 years were not associated with melanoma once adjustments for age, gender and skin were made. 31% of women and 16% of the men had used sunbeds. Sunbed users were younger than non-users (40 years versus 51 years, P < 0.0001). Ever use of sunbeds gave an adjusted OR of 1.19 (95% CI 0.84–1.68) (P=0.33). The risk of melanoma did not increase with increasing hours or years of sunbed exposure. The risk associated with sunbed use was only significant for young individuals with fair skin for whom there was a significant OR of 2.66 (95% CI 1.66–6.09) (P = 0.02) after adjustment for the sun exposure variables. Outdoor occupation and residence in hot countries were not associated with an increased risk of melanoma. The only significant associations in this study were with 10 or more sunburns and the use of a sunbed in young subjects with fair skin. Sunbed use is now becoming more prevalent in Caucasian populations and the results of this study suggest that sunbed usage may moderately affect individuals with sun-sensitive skin types. However, the magnitude of melanoma risk in association with natural and artificial sun exposure is small compared with phenotypic risk factors such as skin type and naevus counts. However, it is possible that the mean lag time of 7 years between exposure to sunbed and melanoma in this study may have led to an under-estimation of the long-term melanoma risk. © 2003 Elsevier Ltd. All rights reserved.

Keywords: Melanoma; Case-control study; Sunburns; Sunbed; Ultraviolet light; Naevi

1. Introduction

Many epidemiological studies have investigated the association between sun exposure and melanoma [1]. Latitude and migration studies provide some evidence that ultraviolet radiation exposure is important in the pathogenesis of this tumour. The highest incidence of melanoma occurs in white-skinned peoples living at low latitudes, in Queensland, Australia as well as Auckland in New Zealand [2,3] and the age/incidence curves show gradation in incidence between Australia, the United States (US) and Europe consistent with this view [4]. However, host factors are crucial in the relationship between sun exposure and melanoma and the latitude changes in melanoma incidence are significantly affected by skin type with a reduced incidence in Southern Europe [4]. Intermittent sun exposure, especially in childhood, appears to be most detrimental, whilst chronic sun exposure can be associated with diminished risks especially in good tanners [2,5–9]. Within populations with low levels of ultraviolet radiation exposure, the association between melanoma and sun exposure is more controversial and the public health messages used in Australia do not necessarily apply in Europe [6,7,10,11].

^{*} Corresponding author. Tel.: +44-207-9298-9292x2084; fax: +44-207-704-941.

E-mail address: veronique.bataille@cancer.org.uk (V. Bataille).

^{0959-8049/\$ -} see front matter \odot 2003 Elsevier Ltd. All rights reserved. doi:10.1016/j.ejca.2003.09.030

A history of sunburn as a marker of sun exposure also appears to be linked to melanoma, but this may mainly reflect the host susceptibility to ultraviolet radiation (UVR) so that associations between sunburns and melanoma vary depending on the population studied. After adjustment for skin type, some of the associations with sun exposure and sunburns often disappear [6,7,11,12]. Furthermore, some studies have found that sunburns in good tanners and chronic sun exposure can be associated with diminished risks of melanoma [7,13]. Relative risks for melanoma associated with sun exposure are usually quite moderately raised and comparable in magnitude or less than to those linked to host factors such as hair and eye colour so these associations may (in part) reflect the confounding by the host response to UVR.

Sunbed exposure has also been linked to melanoma, although this association is more tenuous and has not been established. Several case–control studies reported a small raised risk of melanoma associated with some aspects of sunbed exposure [14–19], whilst others have found no such association [6,12,20,21].

This case–control study of melanoma was conducted in the North East Thames region of the United Kingdom (UK) between 1989 and 1993 to examine the role of sun and sunbed exposure and naevi in melanoma. The results regarding the naevus phenotype have been published elsewhere in Refs. [22,23]. This study reports on the analyses relating to sun and sunbed exposure over a lifetime in relation to melanoma risk as well as the potential associations between the naevus phenotype and ultraviolet radiation exposure.

2. Patients and methods

413 newly diagnosed melanoma cases aged 16-75 years, diagnosed from August 1989 to July 1993 were recruited from hospitals and general practices in the North East Thames region of the UK. The study was approved by local ethics committees in this region. All histological subtypes of melanoma were recruited including melanoma in situ and lentigo maligna. Four hundred and sixteen controls were recruited from the same region and over the same period: 282 controls came from three major hospitals and the remaining 134 controls were recruited from general practices. Controls were recruited in hospital's outpatients and general practices from which the cases were recruited. Controls with chronic diseases which may have affected their sun exposure were excluded as well as controls treated with oral steroids and/or immunosuppressants. Controls were not recruited from skin clinics as these controls may have included subjects with skin diseases related to sun exposure. The total body examination of cases and controls was always carried out in well-lit clinical

examination rooms and interviews and/or examinations were never carried out at home. The methods for recruitment of cases and controls have been described in our previous publication in Ref. [22].

Data on sun exposure and the use of sunbeds were collected by trained interviewers using a questionnaire. For the definition of severe sunburns, cases and controls were asked: "How many times have you been sunburnt so badly that you have (i) either developed blistering of the skin, (ii) been sore for two days or more or (iii) had peeling of the skin for one week or more?" The number of severe sunburns as defined above was recorded in the following age periods: 0-14 years, 15-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years and 65-75 years. Cases and controls were asked how many weeks per year (excluding long-term residence abroad) they had spent in hot climates. Weeks abroad were recorded by age groups (0-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-60 years). For residence abroad, subjects were asked if they had ever lived abroad in a hot country with summers hotter than in the UK or in high altitudes for more than 1 month. The country, the year the residence started, the duration in months and the number of hours per day when the weather was hot was recorded. For sunbed exposure, cases and controls were asked whether they have ever used sunbeds. If yes, the type of sunbed device was recorded for each episode of exposure (small ultraviolet B (UVB) lamp at home, ultraviolet A (UVA) bed at home, small UVA bed in solarium or beauty parlour or large UVA bed in solarium or beauty parlour). The amount of exposure by episode was recorded in weeks per year and hours per week with a record of the year the exposure started and stopped. All cases and controls were examined by one of two dermatologists. All naevi 2 mm or larger in diameter on body sites other than on the genitalia, the posterior scalp, the female breast and the soles and palms were counted. Clinically atypical naevi were also counted. An Atypical Mole Syndrome (AMS) score was computed as a means of defining an atypical naevus phenotype, as described elsewhere in Ref. [24]. This score is based on the allocation of one point for the each of the following: the presence of 100 or more naevi, two or more atypical naevi, one or more naevi on the buttocks and/or dorsum of the feet, one or more naevi on the anterior scalp and one or more naevi in the iris. The maximum score is therefore 5.

2.1. Statistical methods

Comparisons between the variables were based on a retrospectively stratified analysis using unconditional logistic regression as implemented by STATA [25,26]. To control for potential confounding factors, multiple regression models were fitted. The regression equations included, when appropriate, terms for age, gender, four categories of skin type and sun exposure variables. 95% Confidence Intervals (CIs) and significance levels were based on the asymptotic approximation of the estimated logarithm of the Odds Ratio (OR) and its standard error. Chi-squared tests for trend were based on the deviance obtained from the likelihood ratio and one degree of freedom. Trend tests did not include a separate intercept parameter for level zero and were based on the linear scoring for the groups shown in the tables. The ORs presented represent the risk associated with an increase in the variable of interest by one level. Thus, for an increase of three levels, one should cube the ORs.

3. Results

3.1. Sunburns

In men, 66% of the cases reported at least one severe sunburn compared with 63% of the controls. In women, 63% of the cases and 61% of the controls reported at least one severe sunburn. At least one severe sunburn gave an OR adjusted for age and gender of 1.21 (95% CI 0.90–1.61) (P = 0.2). When further adjusted for skin type, the OR for any severe sunburn was 1.03 (95% CI 0.71-1.40) (P=0.2). More than 10 severe sunburns compared with less than 10 sunburns yielded an OR of 1.94 (95% CI 1.02–3.86) (P = 0.04) after adjustment for age, gender and skin type. Mean number of sunburns was significantly and negatively associated with skin types (trend P < 0.0001) after adjustment for age and gender. The negative association between the number of sunburns and skin type was significant in the cases and controls when analysed separately, but in view of the greater number of skin type 1 and 2 in the cases, the power of the negative association was much greater in cases compared with controls. The mean number of sunburns was 5.9 in the cases compared with 2.9 in controls (P < 0.0001). However, an increasing number of sunburns did not have a significant effect on the melanoma risk before or after adjustment for skin type (Table 1). Ever having had a severe sunburn before the age of 15 years was associated with an OR of 1.57 (95% CI 1.09-2.27) (P=0.01) after adjustment for age and gender, but the OR was no longer significant when further adjusted for skin type with an OR of 1.34 (95% CI 0.92-1.95) (P=0.12). When analysing the data by stratifying into fair skin types (skin types I and II) and darker skin types (skin types III and IV), the case-control status affected the report of sunburns. In cases with darker skin types, the mean number of sunburns was 6.3 compared with 2.3 in controls with similar skin types. In subjects with fair skin, the differences between cases and controls was not so large: the mean number of sunburns in cases with fair skin was 5.3 compared with 4.8 in controls. The mean number of sunburns was also negatively associated

Table 1

Odds Ratios (ORs) for melanoma in relation to the lifetime numbers of severe sunburns

Number of sunburns	Number of cases/controls	OR ^a (95% CI)	OR ^b (95% CI)
0	148/159	1	1
1	134/146	1.20 (0.86-1.67)	1.08 (0.77-1.52)
2–3	65/77	1.02 (0.68–1.54)	0.82 (0.54-1.26)
4–5	15/24	0.85 (0.42-1.70)	0.65 (0.32-1.33)
6–9	10/6	1.93 (0.61-6.11)	1.80 (0.56-5.62)
≥10	29/15	2.56 (1.33-4.94)	1.94 (0.99–3.80)

^a Adjusted for age and gender; test for trend Chi square (1)=2.25; P=0.1.

^b Adjusted for age, gender and skin type; test for trend Chi square (1) = 0.38; P = 0.5.

with age (P < 0.0001). Neither naevus number nor the AMS score were associated with sunburns.

3.2. Exposure to sunbeds

Amongst cases, 28% of the females had ever used sunbeds compared with 17% of male cases. In controls, 34 and 15% of females and males had ever used sunbeds, respectively. Age was negatively associated with sunbed use: in the age group equal to or under 45 years of age, 42% of the cases and 38% of the controls had ever used sunbeds compared with 14% of cases and 15% of controls in the age group aged over 45 years. Ever use of sunbed gave an OR for melanoma adjusted for age and gender of 1.19 (95% CI 0.84-1.68) (P=0.33). Further adjustment for skin type and other sun exposure variables did not affect the results. Table 2 gives the OR for melanoma in relation to the increasing total numbers of hours exposed to a sunbed before and after adjustment for the other sun exposure variables. There was no trend in risk with increasing hours of exposure. Number of years exposed to sunbeds was also not linked to melanoma (P=0.4). The mean number of years from first use of a sunbed to the development of melanoma was 6.6 years. Age at first use of a sunbed (P=0.32) and total number of hours

T	1 1		2	
1.2	nı	e		
ıu		•	-	

Odds Ratios (ORs) for melanoma associated with cumulative lifetime hours exposed to a sunbed

Number of hours	Number of cases/controls	OR ^a (95% CI)	OR ^b (95% CI)
0	314/306	0	0
1–9	54/54	1.35 (0.87-2.12)	1.37 (0.86-2.10)
10-19	17/17	1.38 (0.69-2.68)	1.43 (0.68-2.98)
20–99	16/10	0.79 (0.34–1.83)	0.76 (0.32-1.78)
≥100	19/14	0.92 (0.43–1.91)	0.89 (0.42–1.88)

^a Adjusted for age, gender and skin type.

^b Adjusted for age, gender, skin type, cumulative lifetime numbers of weeks abroad in hot countries and total numbers of sunburns.

exposed to sunbeds (P=0.53) were not associated with melanoma. However, the number of subjects exposed to more than 20 h of sunbeds was only 9% in cases and 11% in controls so the numbers were small. Table 3 shows the mean number of hours exposed to sunbeds in relation to the number of years of use in cases and controls, respectively, which shows that the mean of 20 h of sunbed use was already exceeded in subjects who only used sunbeds for up to 2 years. Amongst cases, sunbed users had a mean age at diagnosis of melanoma of 40 years compared with 51 years in the non-users, which reflects the younger age of the sunbed users. The distribution of skin type and hair colour was similar amongst sunbed users and non-users. Mean numbers of naevi was positively associated with the use of sunbeds, but this only reflected the younger ages in the sunbed users. Once adjusted for age, gender and skin type, the association was no longer significant and no trend was observed in risk of increasing numbers of naevi in relation to sunbed use (Table 4). AMS scores were not associated with sunbed use.

We examined whether skin type, hair colour and age affected melanoma risk in relation to sunbed exposure. The OR for ever having used a sunbed in fair-skinned subjects (type I or II) was 1.87 (95% CI 1.01–3.45) (P=0.04) after adjustment for age and gender compared with 0.95 (95% CI 0.62–1.45) (P=0.73) in subjects with darker-skinned types (types III–V). The OR for ever having used sunbed, adjusted for age and gender in subjects with red or blond hair was 1.26

Table 3

Mean number of lifetime hours of sunbed use in relation to number of years of use in cases and controls, respectively

Number of years	Mean number of ho	urs
	Cases (numbers)	Controls (numbers)
≤1	4 (45)	4 (43)
≤2	24 (16)	30 (18)
≤5	49 (16)	65 (16)
≤10	187 (7)	100 (9)
>10	101 (4)	89 (4)

Missing 4 cases and 3 controls.

Table 4

Risk of having large numbers of naevi in relation to ever using sunbeds in controls only

Numbers of naevi	Unadjusted Odds Ratio (OR)	OR ^a	
0–24	1	1	
25-49	2.18 (1.28-3.69)	1.49 (0.86-2.67)	
50-99	1.82 (0.98-3.34)	1.43 (0.75-2.73)	
≥100	0.78 (0.25-2.40)	0.48 (0.15–1.55)	

Test for trend: unadjusted OR: Chi square: 0.41, P = 0.52.

^a Test for trend: OR adjusted for age, gender and skin type. Chi square = 1.21, P = 0.3.

(95% CI 0.69–2.28) (P=0.44) compared with 1.08 (95% CI 0.70–1.6) (P=0.73) in subjects with brown or black hair. The OR for melanoma associated with having ever used a sunbed in subjects below the age of 45 years was 1.20 (95% CI 0.76–1.90) (P=0.42) compared with 0.96 (95% CI 0.57–1.61) (P=0.87) for subjects above or equal to 45 years of age. Table 5 shows the ORs for melanoma in relation to both skin type and age group. The risk of melanoma in relation to sunbed use was only significant in young subjects with fair skin.

The ORs for melanoma were very similar when examining the two different types or locations of UVA sunbeds (either UVA bed at home or UVA bed in solarium/gym/beauty parlour). The use of a UVB lamp was not associated with an increased melanoma risk, although the number of subjects using UVB sunlamps was small. Lentigo maligna melanoma affected 4% of sunbed users compared with 8% of non-users. There were no differences in all the other histological subtypes between sunbed users and non-users. In terms of body sites, melanoma on the face and arms were more common in non-users compared with sunbed users, but this did not reach statistical significance. The larger percentage of facial melanomas and lentigo maligna melanomas reflects the older age groups in the non-users. Melanoma at other sites were comparable between users and non-users, even when examining sites that are rarely sun-exposed. Mean thickness was comparable between sunbed users and non-users (P=0.14). Social class was not associated with sunbed use after adjusting for age and gender (P=0.36).

3.3. Residence in a hot country, outdoor occupation and holidays abroad

Total number of hours worked outdoors in the summer was 4.7 in cases and 3.9 in controls. Table 6 shows the risk of melanoma in relation to the numbers of hours spent working outdoors. There was no significant trend after adjustment for age, gender and skin type (P = 0.5).

Eighteen percent of the cases and 16% of the controls had spent 12 months or more abroad in hot climates. Gender and age were associated with residence in hot

Table 5

Odds ratios (ORs) for melanoma in association with ever use of sunbed use according to skin type and age

Skin type	Age (years)	Numbers of cases/controls	OR ^a (95% CI)	OR ^b (95% CI)
I and II	<45	60/54	2.25 (1.1-5.02)	2.66 (1.16-6.09)
I and II	≥45	109/57	1.18 (0.47-2.97)	1.16 (0.47-2.92)
III and IV	<45	83/147	0.90 (0.51-1.59)	0.91 (0.52-1.60)
III and IV	≥45	161/153	0.84 (0.44–1.56)	0.85 (0.45-1.61)

^a OR adjusted for gender.

^b OR adjusted for gender, number of weeks abroad, total number of sunburns and number of hours working outdoors.

Table 6 Trend in risk of melanoma associated with total number of hours working outdoor in the summer as an adult

Number of hours outdoors	No of cases/ controls	Odds Ratio (OR) ^a (95% CI)
0	238/235	1
1–2	112/136	0.85 (0.62-1.18)
3–6	50/35	1.30 (0.78-2.19)
>6	13/9	0.88 (0.35-2.22)

Test for trend, Chi square (1) = 0.29 P = 0.59.

^a OR adjusted for age and gender and skin type.

countries: older males had spent the longest time abroad reflecting time spent in military service. The OR for melanoma associated with having ever lived in a hot country for 12 months or more was 0.98 (95% CI 0.67-1.47) (P=0.96). The total number of months spent living in a hot country was not associated with melanoma (test for trend after adjustment for age and gender; P=0.3). The mean number of total weeks on holiday abroad in hot climates was 31 for cases compared with 32 for controls. The total numbers of weeks on holiday abroad was not associated with an increased melanoma risk (test for trend after adjustment for age and gender; P=0.66).

4. Discussion

This case-control study of melanoma did not find that exposure to natural or artificial ultraviolet radiation was significantly associated with an increased melanoma risk in the population overall. Only 10 or more severe sunburns and exposure to sunbeds for young individuals with fair skin yielded significant, but small ORs. However, the fact that no dose response was found for hours and years of exposure to sunbeds, even in young subjects, suggests that the use of sunbeds at the levels so far experienced in the study population is unlikely to be a major environmental risk factor for melanoma. The issue of multiple testing also has to be addressed. Therefore, the few significant ORs amongst multiple analyses have to be interpreted with caution. Host factors are important when analysing risks in relation to UVR exposure and most associations with sun and sunbed exposure variables in this study disappeared once adjusted for age and skin type. The lack of association with sunbed use in this study may also be explained by the lag time between exposure and risk. As sunbed exposure has increased dramatically since the 1980s, increased melanoma risk in those exposed may not yet be apparent. However, the increased risk of melanoma mainly seen in young subjects with fair skin

exposed to sunbeds does not suggest that the lag time is very long. Study design may also be a potential weakness when examining the relationship between melanoma and UVR as complex genetic and environment interactions are likely and the case-control study design may not be sensitive enough to detect these. Furthermore, the poor recall and exposure misclassification may lead to an attenuation of risk. The data reported here may suggest the presence of poor recall in view of the inverse relationship between age and number of sunburns, but this may be explained by more frequent sunburns in the younger age groups. The fact that cases with darker skin types (III and IV) reported almost twice as many severe sunburns as the controls despite similar skin types may also suggest the presence of recall bias. In fair skin subjects (I and II), the difference between cases and controls was not so marked. Alternatively, the data may suggest that the presence of high numbers of sunburns in cases is not entirely explained by skin types and that melanoma cases are more sun-sensitive, even when skin type is taken into account. Ever having used sunbeds in this study was reported in approximately a third of women and 16% of men, which is similar to levels reported by surveys carried out in Europe in the 1990s [16,27]. However, most users were infrequent users, as more than 20 h of use was uncommon. Sunbeds emit variable doses of UVA and a range of proportions of UVB, with a session on the sunbed being equivalent to 20-30 minutes sunbathing in a Mediterranean resort [28,29]. The role of UVB in cutaneous carcinogenesis is established in laboratory and animal models and laboratory data have also been published which provide evidence for a role for UVA in the causation of melanoma [30]. Furthermore, UVA has been used to induce melanomas in two species, the opossum [31] and Xiphophorus [32]. Exposure to UVA sunbeds has been shown to cause significant DNA damage in the epidermis which can be compared with that resulting from exposure to natural sunlight. However, the DNA damage is mostly attributed to the small amount of energy emitted in the UVB range [33]. There are therefore reasonable arguments to support the view that sunbed use may increase melanoma risk and that this risk will manifest itself only in those who have a poor ability to tan.

The relationship between sunbed and melanoma is tenuous and controversial. However, even in studies reporting a positive association, adjustment for potential confounders was not always carried out and the dose response was not always confirmed, which casts doubt on the interpretation of the results. Swerdlow and Weinstock [34] in a review of the published epidemiological literature, concluded that the methodological limitations precluded any conclusion regarding a causative role for sunbeds in melanoma. In the study reported here, no dose response was observed when examining years or cumulative hours of sunbed exposure and sunbed use increased the melanoma risk in only one subgroup of subjects, namely young subjects with fair skin (Fitzpatrick skin types I and II). The results presented here are in keeping with the results of Westerdhal and colleagues [19] in Sweden, who showed that the greatest risk of melanoma was found in sunbed users aged less than 36 years. However, the magnitude of the risk in young subjects was much greater in Sweden (OR of 7.7) compared with our study (OR of 1.3). This increased risk of melanoma seen mainly in younger sunbed users has also been reported previously in Refs. [14,15,17].

The increased risk in the younger age groups may be a reflection of the recent increase in sunbed use which may have a significant impact on melanoma incidence in the next 20 years. Sunbed use increased markedly from the 1980s, and it is possible that the effects of exposure on the melanoma risk would not have manifested itself in melanoma in older melanoma cases diagnosed between 1989 and 1993, which was the time period of the study reported here. The accuracy of retrospective UV exposure data is also an issue, but there are no obvious ways to improve the collection of sun exposure data over a lifetime. Financial and practical constraints, as well as mobile populations, mean that cohort studies prospectively examining and/or measuring sun exposure patterns over a lifetime are very difficult and good biomarkers of UV-induced DNA damage are not readily available. In most studies, the extent of sun exposure is assessed by recall of episodes of severe sunburns, as well as repeated and prolonged UVR exposures, but it is not yet known at what threshold ultraviolet radiation becomes detrimental in melanoma and what part of the UV spectrum is most mutagenic. Retrospective case-control studies, therefore, may have limited power to dissect the relationship between UVR exposure and melanoma risk.

Markers of sun exposure have been used to investigate further the link between melanoma and UVR. Markers of chronic sun exposure such as the presence of solar elastosis, solar keratoses and p53 staining and/or p53 mutations have been associated with melanoma in Australia (especially melanomas of the head and neck) [35]. However, for individuals with large numbers of naevi and/or with melanomas of the trunk, markers of chronic sun exposure do not appear to be substantial risk factors [35]. This led to some hypotheses that melanoma may result from genetic alterations via a p53-dependent or p53-independent pathway, the latter likely to involve the CDKN2A or p16, gene [37]. The CDKN2A gene is mutated in the germline of up to 25% of melanoma families worldwide, and has also been shown to influence the number of common and atypical naevi [36,37]. Gene-environment interactions are also likely in the expression of the naevus phenotype, as naevi are also influenced by sun exposure with higher numbers of naevi in countries with high levels of sun exposure such as Australia [38-39]. Two recent twin

studies in the UK comparing total body naevus counts in monozygotic and dizygotic twins have also shown that both environmental and genetic factors contribute to the variance in naevus counts in adults and children [40,41]. Host factors, such as large numbers of naevi, are to date much more powerful predictors of melanoma risk (with ORs as high as 20) than sun exposure and/or sun bed exposure and this is also confirmed using the same study population as the study reported here [22]. In our study, sunbed users were found to have higher naevus counts which suggests that sunbeds may have an effect on the precursor phenotype. However, once adjusted for age, gender and skin type, this association was no longer significant. In view of the relatively small proportion of sunbed users in this study, a bigger sample size may be needed to investigate the effects of sunbed exposure on naevus counts. However, this study did not find any association between the mean number of sunburns or mean numbers of weeks abroad and mean number of naevi.

Ultraviolet radiation is the main known environmental risk factor for melanoma. The overall lack of association with natural and artificial UV exposure in the UK may suggest that the average low doses of ultraviolet radiation in this country are not high enough to generate significant ORs, but the results still confirm that subgroups of fair-skinned individuals are particularly 'at risk'. By understanding which patterns of exposure to natural and artificial sources of ultraviolet radiation are most detrimental and which subgroups of the population are most 'at risk' when exposed, one may be able to design better health initiatives for the primary prevention of melanoma. Collection of large datasets from case-control, families, sib pairs and twin studies with detailed phenotypic and sun exposure data combined with genotyping may help in the future in dissecting the relative contribution of genes and environment in the causation of melanoma. The increase in sun exposure and sunbed use in Caucasian populations over the last 20 years may also have a significant effect on the melanoma risk in the years to come, so the true impact of sunbed exposure is, as yet, uncertain.

Acknowledgements

We are grateful to the patients who gave their time and goodwill. We are grateful to Elizabeth Pinney, Bee Squire and Kairen Griffiths for their help in recruiting and interviewing cases and controls. We also thank Professor Anthony Swerdlow for his help in the design of the questionnaire and the analyses of the data. This work was funded by Cancer Research UK formerly known as the Imperial Cancer Research Fund.

References

- 1. Elwood JA, Johnson J. Melanoma and sun exposure. An overview of published studies. *Int J Cancer* 1997, **73**, 198–203.
- Holman CD, Armstrong BK. Cutaneous malignant melanoma and indicators of total accumulated exposure to the sun: an analysis separating histogenetic types. *J Natl Canc Inst* 1984, 73, 75– 82.
- Jones WO, Harman CR, Ng AK, Shaw JH. Incidence of malignant melanoma in Auckland, New Zealand: highest rates in the world. *World Surg* 1999, 23, 732–735.
- Parkin M, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. *Int J Cancer* 1999, 80, 827– 841.
- 5. Weinstock MA, Colditz GA, Willett WC, *et al.* Non familial cutaneous melanoma incidence in women associated with sun exposure before 20 years of age. *Pediatrics* 1989, **84**, 199–204.
- Osterlind A, Tucker MA, Stone BJ, Jensen OM. The Danish case control study of cutaneous melanoma. II Importance of UV light exposure. *Int J Cancer* 1988, 42, 319–324.
- Elwood JM, Gallagher RP, Hill GB, Pearson JCG. Cutaneous melanoma in relation to intermittent sun exposure. The Western Canada Melanoma Study. *Int J Cancer* 1985, 35, 427–433.
- Autier P, Dore JF. Influence of sun exposures during childhood and during adulthood on melanoma risk. EPIMEL and EORTC Melanoma Cooperative Group. European Organisation for Research and Treatment of Cancer. *Int J Cancer* 1998, 77, 533– 537.
- Whiteman DC, Whiteman AC, Green AC. Childhood sun exposure as a risk factor for melanoma: a systematic review of epidemiologic studies. *Cancer Causes Control* 2001, 12, 69–82.
- Cristofolini M, Franceschi S, Tasin L, et al. Risk factors for cutaneous melanoma in a Northern Italian population. Int J Cancer 1987, 39, 150–154.
- MacKie RM, Aitchison T. Severe Sunburn and subsequent risk of primary cutaneous melanoma in Scotland. *Br J Cancer* 1982, 46, 955–960.
- Holly EA, Aston DA, Cress RD, Ahn DK, Kristiansen JJ. Cutaneous melanoma in women. I. Exposure to sunlight, inability to tan and other risk factors related to ultraviolet light. *Am J Epidemiol* 1995, **141**, 923–933.
- Dubin N, Moseson M, Pasternack BS. Epidemiology of malignant melanoma: pigmentary traits, ultraviolet radiation and the identification of high risk populations. *Recent Results Cancer Res* 1986, **102**, 56–75.
- Walter SD, Marrett LD, From L, et al. The association of cutaneous melanoma with the use of sunbeds and sunlamps. Am J Epidemiol 1990, 131, 232–243.
- Swerdlow AJ, English JSC, MacKie RM, *et al.* Fluorescent lights, ultraviolet lamps and risk of cutaneous melanoma. *Br Med* J 1988, 297, 647–650.
- Autier P, Dore JF, Lejeune F, *et al.* Cutaneous malignant melanoma and exposure to sunlamps and sunbeds: an EORTC multicenter case-control study in Belgium, France and Germany. EORTC Melanoma Cooperative Group. *Int J Cancer* 1994, 58, 809–813.
- Westerdahl J, Olsson H, Masback A, *et al.* Use of sunbeds or sunlamps and malignant melanoma in southern Sweden. *Am J Epidemiol* 1994, **140**, 691–699.
- Chen Y, Dubrow R, Zheng T, *et al.* Sunlamp use and the risk of cutaneous malignant melanoma: a population-based case-control study in Connecticut. *Int J Epidemiol* 1998, 27, 758–765.
- Westerdahl J, Ingvar C, Masback A, Jonsson N, Olsson H. Risk of cutaneous melanoma in relation to use of sunbeds: further evidence for UV-A carcinogenicity. *Br J Cancer* 2000, 82, 1593– 1599.
- 20. Gallagher RP, Elwood JM, Hill GB. Risk factors for cutaneous

malignant melanoma in the Western Canada Melanoma Study. *Recent Results Cancer Res* 1986, **102**, 38–55.

- Holman CDJ, Armstrong BK, Heenan PJ. Relationship of cutaneous malignant melanoma to individual sunlight exposure habits. J Nat Cancer Inst 1986, 76, 403–414.
- Bataille V, Newton Bishop JA, Sasieni P, *et al.* Risk of cutaneous melanoma in relation to the numbers, types and sites of naevi: a case-control study. *Br J Cancer* 1996, **73**, 1605–1611.
- Bataille V, Grulich A, Sasieni P, *et al.* The association between naevi and melanoma in populations with different sun exposure: a joint case-control study of melanoma in the UK and Australia. *Br J Cancer* 1998, 77, 505–510.
- Newton JA, Bataille V, Griffiths K, *et al.* How common is the Atypical mole Syndrome phenotype in apparently sporadic melanoma. *J Am Acad Derm* 1993, **29**, 989–996.
- Breslow NE, Day NE. Statistical Methods in Cancer Research, Vol 1. IARC Scientific Publication No. 32. Geneva, IARC, 1980.
- 26. College Station, TX, USA, Stata Corporation.
- Autier P, Joarlette M, Lejeune F, Lienard D, Andre J, Achten G. Cutaneous malignant melanoma and exposure to sunlamps and sunbeds: a descriptive study in Belgium. *Melanoma Res* 1991, 1, 60–74.
- Wright AL, Hart GC, Kernohan E, Twentyman G. Survey of the variation in ultraviolet outputs from ultraviolet A sunbeds in Bradford. *Photodermatol Photoimmunol Photomed* 1996, 12, 12–16.
- McGinley J, Martin CJ, MacKie RM. Sunbeds in current use in Scotland: a survey of their output and patterns of use. *Br J Dermatol* 1998, **139**, 428–438.
- Moan J, Dahlback A, Setlow RB. Epidemiological support for an hypothesis for melanoma induction indicating a role for UVA radiation. *Photochem Photobiol* 1999, **70**, 243–247.
- Ley RD. Dose response for ultraviolet radiation A-induced focal melanocytic hyperplasia and non melanoma skin tumours in Monodelphis domestica. *Photochem Photobiol* 2001, 73, 20–23.
- 32. Wang SQ, Setlow R, Berwick M, et al. Ultraviolet A and melanoma: a review. J Am Acad Dermatol 2001, 44, 837–846.
- Woolloons A, Kipp C, Young AR, et al. The 0.8% ultraviolet B content of an ultraviolet A sunlamp induces 75% of cyclobutane pyrimidine dimers in human keratinocytes in vitro. Br J Dermatol 1999, 140, 1023–1030.
- Swerdlow AJ, Weinstock MA. Do tanning lamps cause melanoma? An epidemiologic assessment. J Am Acad Dermatol 1998, 38, 89–98.
- Whiteman DC, Parsons PG, Green AC. P53 expression and risk factors for cutaneous melanoma: a case-control study. *Int J Cancer* 1998, 77, 843–848.
- 36. Zhu G, Duffy DL, Eldridge A, et al. A major quantitative trait locus for mole density is linked to the familial melanoma gene CDKN2: a maximum likelihood combined linkage and association in twins and their sibs. Am J Hum Genet 1999, 65, 483–492.
- Newton Bishop JA, Wachsmuth RC, Harland M, et al. Genotype/phenotype and penetrance studies in melanoma families with germline CDKN2A mutations. J Invest Dermatol 2000, 114, 28–33.
- Kelly JW, Rivers JK, MacLennan R, et al. Sunlight: a major factor associated with the development of melanocytic nevi in Australian schoolchildren. J Am Acad Dermatol 1994, 30, 40–48.
- Harrison SL, MacLennan R, Speare R, Wronski I. Sun exposure and melanocytic naevi in young Australian children. *Lancet* 1994, 344, 1529–1532.
- Bataille V, Snieder H, MacGregor AJ, Sasieni P, Spector TD. Genetics of risk factors for melanoma. An adult twin study of naevi and freckles. J Natl Cancer Inst 2000, 92, 457–463.
- Wachsmuth RC, Gaut RM, Barrett JH, *et al.* Heritability and gene-environment interactions for melanocytic nevus density examined in a UK adolescent twin study. *J Invest Dermatol* 2001, 117, 348–352.