Sun Protection and the Development of Melanocytic Nevi in Children

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Abstract

Childhood sun exposure causes nevi (and melanoma), but there is little evidence regarding the effectiveness of sun protection strategies on the number of nevi. We previously found that boys but not girls receiving a school-based sun protection program had fewer nevi on their backs than controls. Here, we investigated whether specific program components (encouraging children to stay indoors in the middle of the day during summer, to wear clothing while outdoors, and to use sunscreen) were associated with fewer nevi. An observational analysis was done on data from a sun protection trial in 1,623 children in Perth, Australia. The outcome was number of nevi on the back 6 years after baseline, when the children were 12 years old. Information on sun protection was obtained by questionnaires 4 and 6 years after baseline. The data were analyzed by mixed-effects linear regression. The time spent outdoors between 11 a.m. and 2 p.m. and the proportion of total time outdoors that was between these hours were positively associated with number of nevi. Ratios of mean counts for doubling the respective measures were 1.09 [95% confidence interval (95% CI), 1.05-1.12] and 1.10 (95% CI, 1.05-1.14). Children whose backs were covered <70% of the time while outdoors had 1.53 (95% CI, 1.34-1.75) times more nevi than children whose backs were always covered. Using sunscreen on the back when it was uncovered was not associated with number of nevi (*P* = 0.59). Children who stayed indoors in the middle of the day and wore clothing while outdoors had fewer nevi. (Cancer Epidemiol Biomarkers Prev 2005;14(12):2873–6)

Introduction

Recognition in the 1980s that the number of melanocytic nevi strongly influences risk of melanoma prompted researchers to study the epidemiology of nevi, particularly in children, in the hope of gaining a better understanding of how to prevent melanoma. Studies of children have found positive associations between sun exposure and number of nevi (1). The usefulness of nevi as biomarkers suitable for evaluating sun protection programs in children was also recognized, and to date, two trials have been published (2-5), and several are in progress (6-9).

In our trial (''Kidskin''), children were encouraged to reduce their sun exposure by staying indoors during the middle of the day in summer (when UV radiation is at its most intense) and by protecting themselves when outdoors using shade, clothing, hats, and sunscreen, with the latter being considered as a last line of defense (10). Boys in the most intensive intervention group developed the fewest nevi on their trunks, although results for girls were inconsistent (5). The other trial, from Vancouver, Canada, was of sunscreen only; children in the sunscreen group developed fewer nevi than did children in the control group (2).

We present here results of the Kidskin study for nevi on the back in relation to three aspects of sun protection: staying indoors during the middle of the day, wearing clothing that covers the back while outdoors, and wearing sunscreen when the back is uncovered. The analysis was restricted to nevi on the back because they are common on this site and can be counted with high reliability using slide photographs (11), and assessment of the back's coverage by clothing is relatively simple. Only a few studies have addressed sun protection (as opposed to sun exposure) in relation to nevi (7, 12, 13), and none has addressed the timing of outdoor activity.

Materials and Methods

Study Design. The study was a nonrandomized trial conducted in Perth, Western Australia, with schools as the units of intervention and three groups: a control group of 14 schools, a ''moderate'' intervention group of 11 schools, and a ''high'' intervention group of eight schools (3). All children who commenced school in 1995 were recruited, but those of non-European ancestry were not included in analyses.

Because the intervention was a single, multicomponent program, it was not possible to perform an intention-to-treat analysis to examine the three components of sun protection, and the results are presented as though they are from an observational study.

The ethics committees of The University of Western Australia and Curtin University of Technology approved the study protocol. Parents of all subjects gave written consent.

Measurement of Sun Protection During Summer. In 1995, 1997, 1999, and 2001, parents completed questionnaires about their children's sun-related activities over the previous summer (December-January) vacation. Parents were asked for the average time each day that the children were outdoors between 8 and 11 a.m., 11 a.m. and 2 p.m., and 2 and 5 p.m., separately for the beach, public outdoor swimming pools, at home, and around the neighborhood (including backyard swimming pools). For each venue, questions were also asked about the proportion of time the back was covered by clothing (none or hardly any, some, about half, most, all of the time), and in the last two questionnaires, the proportion of time sunscreen was applied to the back when it was not covered by clothing.

Outcome. Nevi of any size on the back were assessed from slide photographs taken in the winters of 1995, 1999, and 2001,

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when the children were 6, 10, and 12 years old, respectively. All slides of each child's back were projected side by side onto a whiteboard. A lay observer, trained by a dermatologist, identified and marked all nevi on the projection of the baseline slide and new nevi on subsequent slides. The shoulders, which are often freckled, were excluded.

To permit estimation of inter-rater reliability, the dermatologist counted nevi from 47 randomly selected triplets of slides. The intraclass correlations from analyses comparing the counts of nevi by the dermatologist and the observer were 0.82 (95% confidence interval, 0.73-0.92) for 1999 and 0.85 (95% confidence interval, 0.77-0.93) for 2001.

Statistical Analysis. The primary analyses used number of nevi at 12 years of age. Secondary analyses of nevus counts at 10 years of age were done to assess bias due to loss to follow-up. Measures of sun protection were taken from the two most recent questionnaires because the earlier questionnaires had less detailed information about time spent outdoors around the neighborhood and about use of sunscreen on the back. Only those children who had spent some time in Perth during the summer were included in these analyses because patterns of sun-related behavior may have been different among children who spent the entire vacation elsewhere.

The data were analyzed using linear mixed-effects modeling with a random effect for school. The number of nevi was log-normally distributed after a constant of 1 was added to allow for subjects with no nevi. Time spent outdoors was analyzed as a continuous variable, whereas clothing cover and sunscreen use were categorical variables. Parental education, southern European ethnicity, sex, propensity to sunburn, hair color, inner arm skin reflectance, and study group (control, moderate intervention, high intervention) were included as confounders. Body surface area was also considered as a potential confounder but did not alter any of the regression coefficients for sun protection and was not included in the final analyses. Time spent outdoors and clothing cover were mutually adjusted. Analysis of use of sunscreen on the back was adjusted for time spent outdoors.

The association with time spent outdoors in the middle of the day was evaluated in two ways: first, without adjustment for time outdoors at other times and second, as the proportion of total time outdoors that was between those hours, adjusted for the total time spent outdoors. The second coefficient shows the association with increasing the time outdoors in the middle of the day without changing the total time outdoors.

Time spent at the beach, pool, and around the neighborhood was summed after weighting by the number of days spent at each venue. Summary indices for clothing cover and sunscreen use were created by assigning values of 0, 0.25, 0.5, 0.75, and 1 to each category and calculating an average weighted by time spent at each venue. When clothing data from the two summers were used separately, the summary index was collapsed into a binary variable (some versus all of the time). When data from the two summers were averaged, the index was grouped into approximate quartiles (<70%, 70-84%, 85-99%, 100%). Sunscreen use on the back was analyzed in approximate tertiles (<60%, 60-89%, ≥90% of the time that the back was uncovered). Sunscreen use over the two summers was not averaged because different children in each year had their backs uncovered some of the time. Children whose backs were covered at all times were included in a separate category in these analyses but were not included in tests for trend across categories of sunscreen use.

Statistical analyses were done using Stata 8.2 (Stata Corp., College Station, TX). All tests of statistical significance are two sided; $P < 0.05$ was considered statistically significant for main effects, and $P < 0.01$ was considered statistically significant for interactions.

Results

Participation and Follow-up. Consent was obtained for 1,776 (70 %) of those invited to participate, including 1,623 children of European ancestry. Nevi were counted only in children who had baseline photographs and at least one subsequent photograph; 1,406 (87%) and 1,082 (67%) had data at 10 and 12 years old, respectively. The nevus counts of those who last participated at age 10 were similar at that age and at baseline to those who continued (geometric means at baseline were 3.6 and 3.5, respectively, and at age 10, were 7.0 and 7.2). The distributions of nevi at 12 years old and time spent outdoors in the previous summer are given in Table 1.

Sun Protection Measures. Table 2 shows that the number of nevi at 12 years of age was positively related to the time outdoors between 11 a.m. and 2 p.m. ($P < 0.001$) and to the proportion of total time outdoors that was between those hours ($P < 0.001$). The associations were similar for exposure during the last summer (2000-2001) and during the summer 2 years previously (1998-1999). When exposure during the two summers was averaged, there were positive, (log) linear associations with number of nevi ($P < 0.001$ for both the time outdoors between 11 a.m. and 2 p.m. and for the proportion of total time outdoors that was between these hours; Table 3). Doubling either the time outdoors between 11 a.m. and 2 p.m. or the proportion of total time outdoors that was between these hours was associated with an ~10% higher mean nevus count. Adding a quadratic term for exposure did not significantly improve the model compared with a single linear term (likelihood ratio test, $P = 0.25$ and $P = 0.36$, respectively).

Children whose backs were uncovered at any time while outdoors during the previous summer had 1.22 (95% confidence interval, 1.11-1.33) times more nevi at 12 years of age than children whose backs were covered at all times (Table 2). Similar results were seen for exposure during the summer 2 years before (Table 2). When clothing use over the two summers was averaged, there was a positive dose-response relationship: those whose backs were covered the least often had 1.53 (1.34-1.75) times as many nevi at 12 years old than those whose backs were always covered (Table 3).

There was no association between use of sunscreen on the back when the site was exposed and the number of nevi at 12 years of age (Table 2).

Sensitivity Analyses. For all sun protection measures, similar results were obtained when study group was removed from the models and when nevi at 10 years of age were analyzed in relation to sun protection during the previous summer (data not shown). No significant interactions

Table 1. Median (20th-80th percentile) of number of nevi on the back at 12 years of age and time spent outdoors during the previous summer (6 months before)

	n	All children	Boys	Girls
No. nevi on back	1,082	10 (5-17)	11 (6-19)	8 (4-15)
Time spent outdoors between 11 a.m. and 2 p.m. (min/d)	970	22.5 (8.0-61.1)	23.0 (8.0-66.4)	22.0 (8.0-58.9)
Total time spent outdoors between 8 a.m. and 5 p.m. (min/d)	970	106.6 (44.1-220.8)	112.9 (52.5-241.1)	96.6 (39.1-204.3)
Time spent outdoors between 11 a.m. and 2 p.m. (% total time)	960	24.9 (10.6-41.7)	24.6 (10.4-39.0)	25.1 (10.9-44.4)

Table 2. Association between the number of nevi on the back at 12 years of age and measures of sun protection during the previous summer (6 months before) and the summer 2.5 years before measurement of nevi

	Summer 2.5 y before measurement				Previous summer			
	n	Ratio (95% confidence interval)*	*P*	Adjusted mean†	*n*	Ratio (95% confidence interval)	*P*	Adjusted mean
Time spent outdoors between 11 a.m. and 2 p.m.								
Actual time‡	1,013	1.07 (1.04-1.10)	<0.001		953	1.05 (1.03-1.08)	<0.001	
Proportion of total ‡,§	1,008	1.03 (1.01-1.06)	0.02		945	1.05 (1.03-1.09)	<0.001	
Back covered with clothing								
Some of the time	582	1.25 (1.15-1.37)	<0.001	11.1	598	1.22 (1.11-1.33)	<0.001	10.9
All of the time	435	1.00		8.9	355	1.00		8.9
Use of sunscreen on the back while it was exposed								
Back covered at all times	435	0.81 (0.72-0.91)	0.59∥	8.9	355	0.87 (0.76-1.00)	0.59∥	9.0
≥90% of time	178	1.00		11.0	139	1.00		10.2
60-89% of time	192	0.99 (0.87-1.14)		10.9	155	1.08 (0.93-1.26)		11.1
<60% of time	207	1.04 (0.91-1.19)		11.4	296	1.07 (0.93-1.22)		11.0

*Ratio of geometric means. Adjusted for sex, southern European ethnicity, parental education, propensity to burn, hair color, inner arm skin reflectance, and study group. Time spent outdoors was adjusted for back cover and back cover, and sunscreen use was adjusted for time outdoors.
†Adjusted geometric mean of ''nevi + 1,'' with values of covariates set to the distribution of the subjects included in the analysis.
‡Estimate corresponds to a doubling of the time outdoors.
§Proportion of the total time spent outdoors between 8 a.m. and 5 p.m.
∥*P* for trend, excluding category ''back covered at all times.''

were observed between the sun protection measures and status of follow-up at 12 years of age (present versus absent) when nevi at 10 years of age was the outcome measure (P = 0.21-0.88). Additionally, no significant interactions between the sun protection measures and gender were observed (P = 0.03-0.87).

Discussion

Children who spent the most time outdoors in the middle of the day, either in absolute terms or as a proportion of the total time outdoors, had the most nevi. Children whose backs were covered least often when outdoors had the most nevi. For both measures of sun protection, the dose-response relationships were monotonic. Conversely, using sunscreen on the back when it was uncovered was not associated with the number of nevi.

The strengths of this study include its detailed longitudinal measurements of sun protective behaviors, potential confounding variables, and nevi, with high degrees of reproducibility (3-5). Its main limitation is the loss to follow-up by 12 years of age of one third of the cohort, although our analyses in relation to this issue revealed little evidence of bias.

Because the analysis of the individual components could not be based on the original assignments to study groups, the results are equivalent to those from an observational study and should not be considered indicative of the likely effects of an intervention, which are unlikely to be so large. Indeed, children in the most intensive intervention group had only about 15% fewer nevi on the back at 12 years of age than those in the control group (5).

No other investigators have reported results pertaining to whether avoiding exposure to sunlight during the middle of the day is preferable to avoiding exposure at other times of the day. Advice to avoid exposure during the middle of the day is based on the observation that the intensity of UV radiation is greatest in the middle of the day. For example, in Perth in January, the (clear sky) UV index is 12 at noon, 7 at 3 p.m., and 4 at 4 p.m.[4] Comparisons of melanoma incidence and of nevus numbers by place of residence show the importance of intensity of UV radiation. Australia, with generally high UV radiation, has much higher incidence of melanoma than the United Kingdom, with generally low levels, and children in Australia have more nevi than children in the United Kingdom (14-16).

Two European studies found that wearing clothing during vacations was associated with fewer nevi (7, 12), whereas a third found no association (13). In a study of 6- to 7-year-old children, exposure was measured during vacations away from home (12). Children who wore clothes ''often'' had 40% fewer nevi on the trunk than those who ''never'' wore clothes covering the trunk. A weaker association was seen for nevi on the head and neck. Bauer et al. found that German children who wore the most number of clothes at the beach or pool had whole-body nevus counts 24% lower than those who wore the fewest clothes (7). In contrast, a third study of twins in the United Kingdom found no association between nevi on the trunk and wearing shirts while on the beach during a ''hot holiday'' (13).

The role of sunscreen in the prevention of nevi is uncertain. The only randomized trial found evidence of benefit (2), whereas several observational studies have found positive (i.e., ''harmful'') associations between sunscreen use and nevi (12, 13, 17-21). This may be due to confounding by skin type or because those wearing sunscreen may stay outdoors longer (22). Another possible explanation is measurement error due to imprecise questions on sunscreen use; for example, had we classified children whose backs were always covered as nonusers of sunscreen, we would have observed a positive association between use of sunscreen and nevi. In at least one study that reported a positive association, the questions on sunscreen use did not seem site specific or to take account of clothing cover (12).

Our results indicate that avoiding exposure in the middle of the day during summer and wearing clothing while outdoors have potential to reduce the number of nevi in children. The majority of participants in Kidskin wore protective swimwear that covers the trunk (23), indicating that sun protection can be achieved without compromising recreational activity. Importantly, for other health promotion goals, such as increasing children's physical activity, our results indicate that nevi may be prevented by reducing the time that children spend outdoors in the middle of the day without reducing their total time outdoors.

[4] John Javorniczky, Australian Radiation Protection and Nuclear Safety Agency, 15 April 2005, personal communication.

Table 3. Association between nevi on the back at 12 years of age and average sun protection measures during the previous summer and the summer 2.5 years before

	n (total = 921)	Ratio (95% confidence interval)*	*P*	Adjusted mean†
Time spent outdoors between 11 a.m. and 2 p.m.				
Actual time ‡	917	1.09 (1.05-1.12)	<0.001	
Proportion of total ‡,§	907	1.10 (1.05-1.14)	<0.001	
Percentage of time back covered with clothing				
<70%	224 (24%)	1.53 (1.34-1.75)	<0.001∥	12.0
70-84%	204 (22%)	1.34 (1.17-1.53)		10.5
85-99%	288 (31%)	1.29 (1.14-1.45)		10.1
100%	205 (22%)	1.00		7.9

*Ratio of geometric means. Adjusted for sex, southern European ethnicity, parental education, propensity to burn, hair color, inner arm skin reflectance, and study group. Time spent outdoors and back cover were adjusted for each other.

†Adjusted geometric mean of ''nevi + 1,'' with values of covariates set to the distribution of the subjects included in the analysis.

‡Estimate corresponds to a doubling of the time outdoors.

§Proportion of the total time spent outdoors between 8 a.m. and 5 p.m.

∥*P* for trend.

Our results do not support the use of sunscreen as an effective means of preventing nevi, although given the results of the only published randomized trial, we recommend that sunscreen be used on body sites not easily covered by clothing. More definitive evidence on whether sunscreen can prevent nevi (and skin cancer) should come from randomized trials and not from observational studies (24).

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