Sun Exposure and the Incidence of Melanocytic Nevi in Young Australian Children

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Abstract

The number of melanocytic nevi (MN) is an important risk factor for cutaneous melanoma. The present study further investigated the relationship between sun exposure, the incidence of MN, and the prevalence of large acquired MN (≥5 mm). A cohort of 479 preschool children born in Townsville, Australia was examined for MN in 1991 and a year later. Sun exposure was assessed by questionnaire. The erythemally effective dose of solar UV radiation was estimated from questionnaire data combined with local UV biometry. Almost all (97.7%) children had acquired new MN (median, 12), with a median incidence rate of 11.0 per year (interquartile range, 7.0-16.5). Total number of hours of sun exposure during follow-up (P = 0.034) and tendency to burn (P = 0.028) were independent risk factors for MN incidence. Sunburn experience during follow-up failed to reach significance when adjusted for tendency to burn. Lifetime number of sunburns (P < 0.001) and the severity of sunburns experienced during follow-up (P < 0.001) were significantly related to the presence of large acquired MN at follow-up. Reducing the total number of hours of sun exposure is particularly relevant in sun-sensitive children and may restrain the development of MN, whereas avoiding sunburn in young children might prevent large MN, subsequently reducing the risk of melanoma. (Cancer Epidemiol Biomarkers Prev 2008;17(9):2318–24)

Introduction

Interest in melanocytic nevi (MN) stems from their clinical, histologic, and epidemiologic association with melanoma. The number of MN is a major risk factor for melanoma (1), whereas migrant data suggest that sun exposure during early childhood is related to subsequent melanoma risk (2, 3). There have been many risk factor studies of MN in school children (4-10), but few in younger children. However, previous studies have shown that the development of MN in most Caucasian children begins between the ages of 6 months and 2 years depending on the latitude of residence (11). Only three longitudinal studies of nevus development in infants and very young children have been published (11-13). Most studies involving this age group have only reported nevus prevalence (14-18).

Examination of MN in young children is simpler because they have fewer MN and freckles than older children; but propensity to sunburn is often not known by the parents of children under 2 years of age (19, 20).

Teenage twin studies conducted in Australia and the United Kingdom have suggested that up to 68% of variation in nevus densities can be explained by genetic factors (21, 22), and that ~25% of the variation can be attributed to environmental factors, specifically sun exposure (23). Genetic factors investigated included eye color, hair color, and skin type but the analysis also pointed to the likely existence of genes directly involved in the development of MN (22). These heritability analyses are consistent with the results of numerous studies showing that skin type (10, 12-15, 18, 24) and freckling, a phenotypic characteristic expressed after sun exposure (7, 9, 12-15, 17, 25), were related to increased numbers of MN in children.

Acute (12-15, 18, 23, 24) and chronic sun exposure (7, 9, 11, 13-15, 18, 26) were previously identified as risk factors for MN in children from temperate, subtropical, and tropical environments, although there is only one large study from a temperate environment which was able to link chronic sun exposure with prevalent (15) and incident MN (13).

Large (≥5 mm), clinically nondysplastic MN are thought to be an important risk factor for melanoma (27, 28) independent of the overall number of MN. However, only a few studies have investigated the growth of acquired MN (10, 29) with contradicting results concerning sun exposure.

The present study in very young children raised in an extreme UV radiation (UVR) environment further investigated the relationship between sun exposure, the incidence of MN, and the prevalence of large acquired MN.

Materials and Methods

The present longitudinal study was conducted in Townsville (19.16°S) in tropical Queensland, Australia.

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In 1991, a random sample of Caucasian children who were born in two Townsville maternity hospitals between 1985 and 1990, and who were still resident in the area in 1991, was recruited. In 1992, 479 (94.7%) of the original cohort of 506 1- to 6-year-old children reported by Harrison and coworkers (14) were re-examined for MN (all sizes) after 12 months of follow-up according to a standard international protocol (30). The first author (S.L. Harrison) examined all children at baseline and follow-up. For each subject, the body sites of all MN were marked individually on an anatomic chart and labeled according to size on a body map differentiating 30 body sites. In addition, photographs were taken from the back of all children. MN of all sizes were noted. The same examination methods were applied at baseline and at follow-up and charts and photographs were compared.

Skin reflectance was measured at the upper inner surface of the left arm and the dorsum of the left hand using a standard Colormet spectrocolorimeter. Skin reflectance for the upper inner arm was ranked using the cutpoints of Kelly et al. (7) to produce a categorical measure of relative natural skin reflectance (''olive'', 53-63%; ''medium'', 64-66%; and ''fair'', 67-87%).

After providing informed consent, parents were asked to complete self-administered questionnaires at baseline and follow-up. The baseline questionnaire included demographic questions, sun sensitivity, history of places lived and holidays taken, detailed sun exposure assessment for previous year, lifetime history of sunburn, and usual sun protection practices. The second questionnaire recorded the child's sun exposure during the follow-up period. The mean time between the initial and follow-up examination was 12.5 months (SD $\pm$ 0.8; range, 11-16 months).

The term ''incident MN'' refers to the total number of MN acquired between the initial examination in 1991 and follow-up in 1992. The number of incident MN was calculated by subtracting the total number of MN at baseline from the total number present in 1992. The rate of acquiring new MN per year of follow-up was the main outcome measure. Body surface area was estimated from height and weight using the formula by Du Bois and Du Bois (31). Density of incident MN was calculated as the number of incident MN divided by the surface area of the body (m^2) based on height and weight at follow-up.

A lifetime sunburn score similar to that used by Gallagher et al. (5) was calculated by assigning numerical values to the severity of sunburn (1, redness without peeling; 2, sunburn with peeling; 3, very painful burn with blistering) and multiplying each type of sunburn by the cumulative lifetime frequency of each type of burn using information from both questionnaires. A similar score was calculated for sunburns experienced during follow-up.

Total number of hours spent in the sun during 1 year of follow-up was calculated using information from the second questionnaire as described elsewhere (20). This variable was categorized into average hours per day during follow-up. The erythemally effective dose (EED) of UVR available during outdoor exposures in the year between examinations was estimated using a combination of questionnaire responses and local average daily EED measurements in minimal erythemal dose (MED) units and the mean fraction of diurnal ambient erythemally effective UVR per hour (20, 32). One MED equals 200 J/m^2 of erythemally effective UVR.

Ethical approval for the project was obtained from the Northern Regional Health Authority Ethics Committee and the institutional ethics committees of both the Queensland Institute of Medical Research and the James Cook University.

Statistical Methods. Numerical variables were described using mean and SD or median and interquartile range (IQR) as appropriate. Nonparametric Mann-Whitney-Wilcoxon tests, Kruskal-Wallis tests, and Spearman rank correlations (r_s) were used for bivariate analysis. The relationship between baseline number of MN and incident number of MN was assessed using Pearson's correlation coefficient (r) adjusted for regression towards the mean (33). Within-subject variance was based on blinded re-counts of MN done on 45 children randomly selected and reassessed 1 to 3 weeks after the initial examination by the same examiner. Concordance between counts and re-counts was high [concordance correlation coefficient, 0.99 (ref. 34); 95% confidence interval (95% CI), 0.98-0.99].

The outcome variable incidence rate of MN was slightly skewed and was square root–transformed to achieve approximate normality. Multiple linear regression analysis was done with the square root–transformed incident MN rate to assess the influence of age, gender, pigmentary characteristics, and sun exposure. The characteristic ''tendency to burn'' had 128 missing values. These 128 children were significantly younger than the children for whom parents were able to provide valid answers (38 versus 48 months; $P < 0.0001$). After a stable model was reached, remaining variables were considered for potential confounding (variation of estimate of coefficient by $\geq$5%). Possible two-way interactions were considered. Results of multiple linear regression analyses were presented as regression coefficients with 95% CI and P values. In addition, multiple logistic regression analysis was used to investigate the effect of sun exposure characteristics on the presence of large acquired MN ($\geq$5 mm). Results of logistic regression analysis were presented as odds ratios with 95% CI and P values.

Results

Description of Participating Children. At baseline, the 479 participating children (50.5% boys) were aged between 1 and 6 years (mean age 3.3 years; SD $\pm$ 1.7). At the follow-up examination in 1992, 51.8% of children had blue eyes, 60.3% had blonde or fair hair, and 3.1% had red hair whereas 82% had fair skin. Further details of the participants have been published elsewhere (14).

Incidence of MN, Prevalence of Large MN, and Bivariate Relationships. Ninety-nine percent of children had MN at the beginning of the study, and those who did not were exclusively 1-year-olds. The median prevalence of MN at baseline was 34 (range, 0-252; IQR, 13-59). All children had MN at follow-up (median, 47; IQR, 25-74; range, 3-268), and all but 11 (2.3%) children had incident MN. Of those 11 children without incident MN, 6 (1.3%) had fewer MN at follow-up than at the beginning of the study; one child had 6 and one had 7 fewer MN at

Table 1. Median count of incident MN, density of incident MN (MN/m^2 of body surface) and incident rate of MN per year at follow-up stratified by age at baseline

Baseline age (mo) [y]	Age at follow-up (mo)	Sample size	Median incident MN counts (IQR)	Median density of incident MN (MN/m^2; IQR)	Median incidence rate (MN/y of follow-up; IQR)
12-23 (1 y)	24-37	88	9 (6-14)	19.4 (12.3-27.6)	9.2 (6.0-13.5)
24-35 (2 y)	36-50	94	12 (7.8-18.3)	21.4 (13.4-33.6)	11.4 (7.4-17.8)
36-47 (3 y)	48-63	88	14 (8.3-20)	22.8 (14.5-32.8)	13.8 (8.1-19.5)
48-59 (4 y)	61-74	68	12.5 (9-18)	17.9 (12.8-28.4)	11.9 (8.1-17.4)
60-71 (5 y)	72-87	78	11 (6.8-14)	14.2 (8.4-19.2)	9.9 (6.6-13.4)
72-83 (6 y)	84-94	63	12 (6-17)	14.5 (8.0-22.1)	11.5 (6.2-16.5)
Total		479	12 (7-17)	18.4 (11.8-27.7)	11.0 (7.0-16.5)

NOTE: Results were based on 479 young Australian children followed-up between 1991 and 1992.

follow-up. The overall median count of incident MN was 12 and the overall incidence rate was 11 MN per year (Table 1). Median counts ($P = 0.866$), density ($P = 0.756$), and rates ($P = 0.742$) of incident MN did not vary by gender. Median counts ($P = 0.003$) and rates ($P = 0.007$) of incident MN varied significantly with age. There was a negative correlation between age and incidence density ($r_s = -0.2$; $P < 0.001$). Children aged between 1 and 3 years at baseline had a higher median incidence density than older children ($P < 0.001$; Table 1).

At baseline, there were 48 children with 62 nevi ≥5 mm in diameter (prevalence, 9.5%) that were not present at birth (i.e., large acquired MN); at follow-up, 94 children had 149 large acquired MN (prevalence, 19.6%). None of the large MN seen at follow-up were incident lesions.

Children with freckling developed significantly more new MN per year than children who did not have freckles ($P < 0.001$), whereas children with at least one parent with tertiary education developed significantly fewer new MN per year ($P = 0.018$; Table 2). Children with a high number of MN at baseline tended to develop more new MN during the follow-up period ($r = 0.36$; $P < 0.001$; adjusted for regression towards the mean; Fig. 1).

At baseline, 61.4% of children had experienced at least one sunburn during their lifetime. By the time of their second examination, 71.5% of children had experienced

Table 2. Bivariate relationships between constitutional factors of children and highest level of education of parents and incidence rate of MN (MN/y)

Predictors	Sample size	Median incidence rate (MN/y; IQR)	*P*
Gender			$P = 0.742$*
Male	242	11.6 (6.8-16.5)	
Female	237	10.6 (7.1-16.6)	
Eye color			$P = 0.135$†
Brown	105	10.1 (6.9-15.9)	
Hazel	126	10.5 (5.4-17.1)	
Blue	248	11.6 (7.3-17.1)	
Hair color			$P = 0.088$†
Dark	175	10.6 (6.9-16.5)	
Blonde/fair	289	11.6 (7.6-16.9)	
Red	15	8.5 (5.0-9.9)	
Skin reflectance at 685 nm (inner arm)			$P = 0.114$†
Olive	37	8.2 (4.7-14.2)	
Medium	49	10.1 (6.2-16.4)	
Fair	393	11.4 (7.3-16.8)	
Freckling			$P < 0.001$*
Absent	191	9.1 (5.9-13.1)	
Present	288	12.9 (7.9-19.1)	
Tendency to burn			$P = 0.070$*
No	46	10.4 (7.5-13.1)	
Yes	305	11.6 (7.0-17.1)	
Ability to tan			$P = 0.786$†
Deep tan	27	9.9 (5.9-15.9)	
Moderate tan	299	11.1 (7.1-16.8)	
Slight tan	70	10.8 (7.6-18.0)	
Unable to tan	77	11.7 (5.9-16.3)	
Parental education			$P = 0.018$†
Both ''some high school''	85	11.9 (7.6-17.3)	
At least one ''completed high school''	234	11.9 (7.7-17.4)	
At least one ''completed tertiary education''	160	9.7 (5.9-14.6)	

NOTE: Results were based on 479 young Australian children followed-up between 1991 and 1992.
*Wilcoxon Mann-Whitney *U* test.
† Kruskal Wallis test.

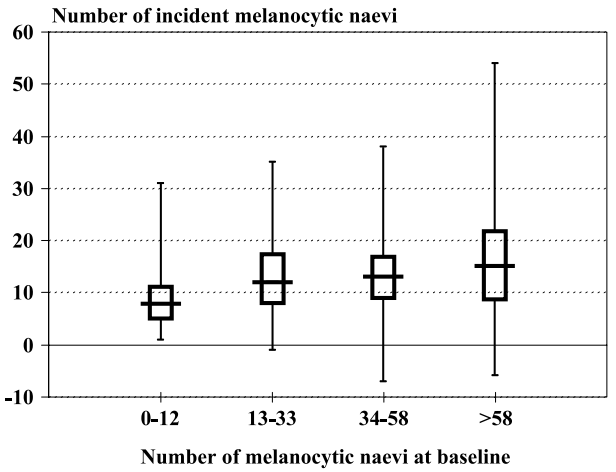

Figure 1. Box-and-whisker plots of the number of incident MN in quartile-defined categories of number of prevalent MN at baseline. *Boxes,* 25th and 75th percentiles; *bold lines,* median values; *whiskers,* minimum and maximum values of the distributions. Results were based on counts of MN found on 479 young Australian children followed-up between 1991 and 1992.

at least one episode of sunburn in their lifetime (range, 0-24; median, 2; IQR, 0-4) and the lifetime frequency-severity sunburn score ranged between 0 and 34 (median, 2; IQR, 0-4). In the year between examinations, 247 children (52.2%) experienced sunburns between one and eight times. Overall, the combined frequency-severity score for sunburns experienced during follow-up ranged between 0 and 16, with a median of 1 (IQR, 0-2). Number and severity of sunburns experienced during lifetime and during follow-up were significantly related with the incidence rate of MN during follow-up (Table 3).

In the year between examinations, the children were exposed to an average of 1,024.6 hours (IQR, 592.0-1,387.8) of sunshine, equivalent to a median EED of UVR of 1,889.9 hours MED (IQR, 966.7-2,836.7). Most children (66.2%) spent an average of ≥2 hours playing in the sun and/or swimming outdoors each day, with 22.1% of them averaging ≥4 hours in the sun per day (Table 3). Average hours of daily sun exposure and estimated total EED available while spent outdoors were significantly related with the incidence rate of MN during follow-up (Table 3).

Incidence of MN and Multivariate Results. Results of multiple linear regression analysis showed that tendency to burn (yes versus no; coefficient, 0.42; 95% CI, 0.05-0.79; $P = 0.028$) and total number of hours of sun exposure during 1 year of follow-up (coefficient, 0.00007; 95% CI, 0.000005-0.00009; $P = 0.034$) were independent predictors of the square root–transformed incidence rate of MN. This model was based on the information of 345 participants (tendency to burn was missing for 128 children) and was adjusted for the confounding effect of age. There were no significant two-way interactions. Sunburn experience failed to reach significance after adjustment for propensity to burn ($P = 0.114$). Stratified analysis revealed that tendency to burn was an effect modifier: the relationship between sunburn experience and incidence of MN was significant in children with no tendency to burn ($n = 46$, $P = 0.022$), but was not significant in children with a tendency to burn ($n = 305$; $P = 0.193$), and in the children with missing information on tendency to burn ($n = 128$; $P = 0.051$).

Large MN and Multivariate Results. Bivariate analysis showed that the presence of large acquired MN at follow-up was neither significantly related to the total hours of sun exposure received during 1 year of follow-up ($P = 0.541$) nor to EED during follow-up ($P = 0.573$). Lifetime number of sunburns ($P < 0.001$) and the severity of sunburns experienced during follow-up ($P < 0.001$) were significantly related to the presence of large acquired MN at follow-up. Multivariate logistic regression analyses, adjusted for age, showed that compared with 0 to 4 lifetime numbers of sunburns, children with 5 to 9 sunburns were 2.2 times more likely (95% CI, 1.1-4.2; $P = 0.022$), and children with 10 or more sunburns were 3.5 times more likely (95% CI, 1.9-6.3; $P < 0.001$) to have large acquired MN at follow-up.

Discussion

Townsville, north Queensland, is an example of a high-risk environment for skin cancer as its residents are of predominantly Anglo-Celtic descent living in a tropical environment with extreme ambient UVR (35). Our results indicate that the appearance of new MN in young Australian children raised in such an extreme UV environment is related to the total amount of time they spend in the sun, and the susceptibility of their skin to sun exposure. Sunburn experience, although significantly related with the incidence rate of MN bivariately, failed to reach significance after adjustment for propensity to burn. Sunburn experience remained significantly related to the incidence of MN only in the subgroup of children with no tendency to burn.

Of the five published longitudinal studies on nevus development in children and adolescents (9, 11-13, 25), only three examined the effect of individual sun exposure data on nevus development (9, 12, 13). The current study is the first which explores this issue in such young children raised in an extreme UV environment.

The present findings confirm the association between time spent in the sun in tropical Queensland and prevalent MN described in an earlier report from the same study (14). They also support the findings of a longitudinal study published by Luther and coworkers (12) who found that German children who experienced >3 weeks of intensive sun exposure per year developed more incident MN than children who experienced <3 weeks of intensive exposure per year (adjusted odds ratio, 1.6; 95% CI, 1.0-2.5). However, middle or northern Europeans only usually experience intense sun exposure during their holidays and the tropical location of Townsville is one of those potential holiday destinations.

Another large German study which followed-up 1,232 children in day-care centers found sun exposure received at home as well as vacation exposure and history and severity of sunburns to be independent predictors of incident MN (13). This finding implies that even

moderate levels of UVR may be sufficient to promote nevus development in young children. On the other hand, Darlington et al. who followed-up 111 adolescents living in a subtropical environment identified only habitual midday sun exposure as a predictor for MN development (9). There are many possible explanations for the inconsistencies between studies concerning the kind of sun exposure (i.e., habitual or acute) implied in the development of MN, including the statistical power of the study (inadequate sample size increases the likelihood of type II errors), the quality of the assessment of sun exposure, and differences in the UVR environments observed. In a tropical environment such as Townsville, nonerythemogenic doses of sun exposure, that is, strong UV exposure which does not result in discernable erythema, might blur the distinction between habitual and acute sun exposure.

The present analysis of large acquired MN (i.e., noncongenital MN ≥5 mm in diameter) focused on prevalence rather than incidence, because all of the large MN present at follow-up were already present at baseline (just smaller in size). The presence of large MN at follow-up (62 prevalent and 87 incident large MN) was related to sunburn history but not to habitual exposure. These results suggest that nevus growth in early childhood might be more closely related to intense UV exposure than to the total cumulative dose, and that the dose threshold for nevus growth may be higher than that required for the proliferation of melanocytes to form a nevus. This finding supports the work by Autier and coworkers who also concluded that nevus formation may only require low doses of UVR, whereas higher doses might stimulate the growth of existing MN, and hence, the development of larger nevi (10).

Gallagher et al. found a small, but significant, association between the severity of sunburns experienced and the number of prevalent MN (≥2 mm) in Canadian school children (5). However, unlike the present study, this relationship was linear (5). There are a number of contributing factors which may explain why in the

Table 3. Bivariate relationships between sun exposure and incidence rate of MN (MN/y)

	Sample size	Median incidence rate (MN/y) (IQR*)	P †
Lifetime number of sunburns experienced			$P = 0.004$
None	135	9.4 (5.6-13.6)	
One	89	10.7 (7.1-16.8)	
Two	67	10.8 (8.0-17.1)	
Three or four	82	13.2 (8.5-17.8)	
Five to nine	47	11.5 (6.8-18.8)	
Ten or more	53	12.6 (8.4-16.6)	
Number of sunburns experienced during follow-up			$P = 0.021$
None	226	10.1 (6.8-15.5)	
One	96	12.1 (8.1-18.2)	
Two	98	13.0 (7.1-18.0)	
Three or more	53	12.3 (7.3-17.8)	
Severity of the worst sunburn experienced during follow-up			$P = 0.019$
No sunburn	226	10.1 (6.8-15.5)	
Sunburn which only causes redness	209	12.6 (7.9-17.8)	
Sunburn causing redness and peeling	32	11.5 (7.3-22.1)	
Sunburn causing blistering	6	10.2 (6.9-16.6)	
Lifetime frequency-severity sunburn score			$P = 0.006$
No sunburn	134	9.4 (5.5-13.6)	
Score 1	74	10.6 (6.9-16.7)	
Score 2	55	10.7 (7.1-18.5)	
Score 3 or 4	70	13.0 (8.2-17.6)	
Score 5 to 9	48	12.8 (8.0-19.1)	
Score 10 or higher	59	12.6 (8.2-17.4)	
Frequency-severity sunburn score as experienced during follow-up			$P = 0.015$
No sunburn	226	10.1 (6.8-15.5)	
Score 1	92	11.8 (8.1-17.6)	
Score 2	89	13.4 (7.1-18.8)	
Score 3 or higher	66	12.1 (7.4-17.8)	
Average hours of daily sun exposure during follow-up (h/d)			$P = 0.012$
<1	80	8.3 (5.1-14.7)	
1-1.99	79	11.3 (7.2-16.9)	
2-2.99	102	10.7 (7.4-17.8)	
3-3.99	105	10.8 (6.7-16.0)	
≥4	104	13.0 (9.2-19.4)	
Total EED of UVR available in the time spent outdoors during follow-up			$P = 0.034$
≤555 MED	75	8.3 (5.6-15.2)	
556-1,114 MED	60	11.5 (7.1-18.2)	
1,115-1,763 MED	82	10.3 (6.8-15.1)	
1,764-2,582 MED	120	13.0 (8.6-19.1)	
≥2,583 MED	133	11.4 (6.9-16.2)	

NOTE: Results were based on 479 young Australian children followed up between 1991 and 1992.
*One MED equals 200 J/m^2 of erythemally effective UVR.
† Kruskal-Wallis test.

current study, the association between MN frequency and sunburn score was not monotonic: (*a*) the score does not account for differences in the surface area of the body sites affected by an episode of sunburn; (*b*) inability to account for episodes of intense nonerythemogenic exposure which may occur quite frequently in a tropical environment; (*c*) instability of estimates due to the smaller numbers of subjects generally found in the highest exposure categories; and/or (*d*) difficulties associated with accurately recalling the number of sunburns for children living in UVR-intense environments compared with the relative ease of recalling whether or not a child from a temperate climate has ever been sunburnt.

Site-specific sunburn data and data pertaining to the site-specific use of sun-protective strategies on body sites affected by sunburn in the year between examinations were not collected in this study, and would have been difficult to quantify accurately. In the context of sunburn, the influence of sun-protective behavior seems less relevant as sunburn is in itself an outcome. On the other hand, it is likely that the use of chemical sunscreens may have lengthened the duration of exposure necessary to cause the sunburn. This in turn may have some effect on nevus development, as discussed by Luther et al. (12) and others (36) who found that children who regularly used sunscreens stayed out in the sun longer and developed more MN than children who never used sunscreen.

In the present study, the median density of incident MN increased until ~4 years of age (i.e., baseline age of 3 years) and then began to decrease, implying that nevus development is most prolific in the very young age group. This finding is in contrast to the results presented from a large German study in which incidence steadily increased with age (13). The discrepancy could be explained by the previously noted observation that children raised in an UVR-intense environment develop more MN earlier in life (11). In a longitudinal comparison of Scottish and Australian children followed from birth, Australian children experienced a rapid increase in MN counts in their second year of life whereas children raised in the contrasting UVR environment of Scotland showed a delay of ~12 months (11). It is interesting to note that there is little difference in the MN counts of older Caucasians from diverse UV environments (7, 37, 38), despite the consistent differences in melanoma incidence (39, 40). These findings suggest that interventions in very young children are necessary to prevent the early onset of MN and melanoma later in life.

Propensity to sunburn was previously identified as a strong independent risk factor for the development of MN in children (12, 13) and was the only independent phenotypic characteristic identified by the present study to be related with incidence of MN. It was previously noted that accurate subjective assessment of propensity to sunburn is difficult for very young children who have had little sun exposure (19). The present study relied on the assessment of sun exposure of a child by its parents. In particular, parents were asked to estimate their children's propensity to sunburn at baseline when decisive answers were only available for 73.7% of the sample because the remaining parents, particularly those with 1-year-old children, were unable to determine how their child's skin would react to the sun because they had not been exposed to strong sunlight. In retrospect, it would have been better to repeat the question about tendency to burn in the follow-up questionnaire. Phototesting (determination of personal MED) may be the only way to obtain accurate and objective estimates of sun sensitivity in studies of MN development in young children, but poses considerable practical and ethical problems.

In conclusion, these results suggest that the development of MN in children raised in a UVR-intense environment is associated with the total amount of sun exposure received in early childhood. Incidence density was highest for children ages 1 to 3 years at baseline, indicating that very young children, especially those raised in intense UV environments, should be protected from excessive exposure to sunlight. In contrast, nevus growth in early childhood might be related to acute UV exposure rather than to the total cumulative dose.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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