Sun exposure and melanocytic naevi in young Australian children

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Summary

Queensland, Australia, has the highest rates of melanoma in the world and Queensland children have the greatest numbers of melanocytic naevi, the strongest risk factor for melanoma. Although both melanoma and naevi are broadly related to sun exposure in childhood, the relation to individual exposure early in life is difficult to study retrospectively in adults.

We surveyed 506 children aged 1–6 years who had been born in Townsville, North Queensland. Sun exposure was assessed by questionnaire and melanocytic naevi were counted using a standard international protocol. Very high counts (upper quarter) of melanocytic naevi were significantly associated with sun exposure of more than 4 hours per day (adjusted relative risk ratio 3·29; 95% CI 1·12–9·69), and with a history of sunburn (1·89; 1·11–3·21). Melanocytic naevus counts increased with age, light skin reflectance, and freckling.

With exposure to intense ultraviolet light in Townsville, children develop melanocytic naevi early in life and in large numbers. We found that both acute and chronic exposure to sun are associated with their development.

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Introduction

Malignant melanoma is a major cause of death from cancer among adults under 45 years in Australia and incidence rates increased substantially in the 1980s.[1] Although the most important risk factor for development of melanoma is an increased number of melanocytic naevi,[2-7] their relation to different aspects of sun exposure is uncertain.

Increased numbers of melanocytic naevi have been shown to be related to sunburn during childhood,[8-10] a tendency to burn rather than tan,[9,10] a lifestyle involving increased sun exposure,[10] proximity to the equator,[11] and holidays spent in a hot climate;[10,12] factors that suggest sun exposure is the cause. This notion is further substantiated by the concentration of naevi on skin surfaces that are exposed to the sun[13-18] and by studies showing that naevi are less common among migrants to sunnier climates than among native-born residents.[19,20] Despite this evidence, some studies have found no correlation between sun exposure and melanocytic naevi.[21]

Accurate documentation of lifetime sun exposure in adults is difficult because most methods rely on long-term recall. Studies of young children raised in sunny environments where naevus acquisition is rapid[8,11] are more likely to provide information.

Subjects and methods

Townsville (latitude 19·16°S), an urban coastal community in tropical Queensland, Australia, has a dry tropical climate and high levels of solar radiation throughout the year.[22] Demographic details were extracted from labour ward records of Townsville's 2 main maternity hospitals for all white mothers resident in west Townsville. Older children from this area had been surveyed previously.[11] Mothers thought still to be resident in the study area were sent a letter inviting them to participate and a questionnaire requesting information about their child. Of the 707 children selected, 118 had moved away; 516 (87·6%) participated: 56 refused, 16 did not respond, and 1 child did not allow completion of skin examination. Children with two or more non-European grandparents were excluded from analysis (n = 10).

Height and weight were measured to estimate body surface area.[23] A standard Colormet spectrocolorimeter (Colormet 3·1, Newfoundland, Canada) was used to measure skin reflectance at 680 nm for the left inner upper arm. For analysis, skin reflectance, hair colour, and eye colour were categorised as in Kelly et al.[11] Distribution of freckling on the face, arms, and shoulders was estimated,[11] with total freckling as the sum of the distribution recorded at these 3 sites.

A standard protocol[24] was used to define and count melanocytic naevi: brown to black pigmented macules or papules of any size, darker in colour than the surrounding skin, excluding lesions with the clinical characteristics of freckles, solar lentigines, or café-au-lait spots. No attempt was made to differentiate lentigo simplex from junctional melanocytic naevi. Skin-coloured palpable lesions with the morphological features of compound or intradermal melanocytic naevi, halo naevi, naevi spili, congenital naevus-like-naevi, and blue naevi were counted separately and included in the total count of melanocytic naevi. The number of café-au-lait spots and distribution of freckling were recorded separately.

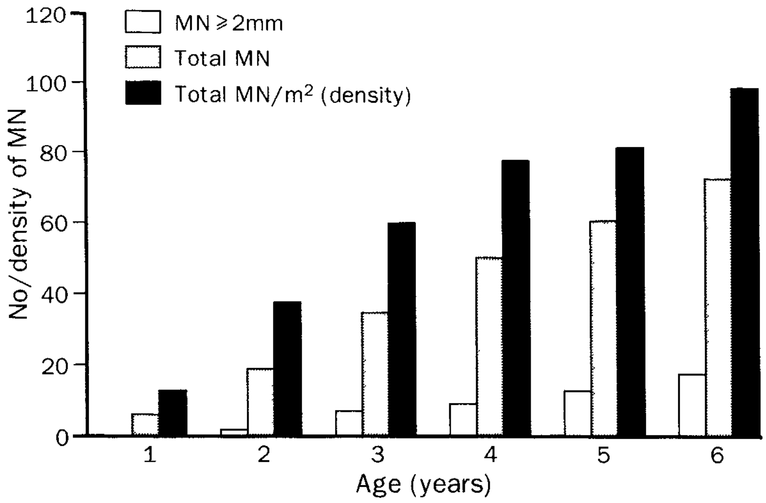

Figure 1: **Melanocytic naevi by age for children born and raised in Townsville, Queensland**

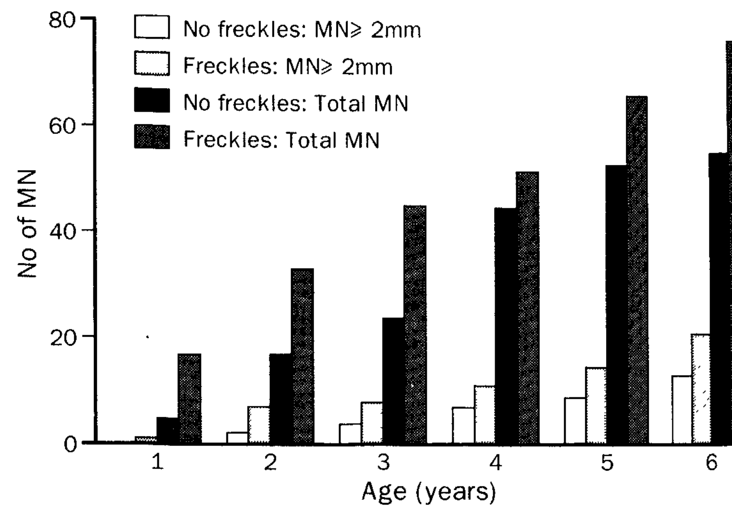

Figure 2: **Melanocytic naevi by age and freckling in Townsville-born children aged 1–6 years**

The body surface was divided into 30 body sites[24] (excluding scalp, buttocks, and genitalia) which were assessed in the same sequence. Melanocytic naevi were measured with a clear plastic film imprinted with circles of 2, 3,4, and 5 mm diameter attached to an illuminated (× 3) magnifying glass. Lesions were measured with the skin unstretched and judged to be of a specified size if the greatest diameter of the lesion touched both sides of the circle. Locations were marked on an anatomical chart and a colour photograph of the back was taken. The same observer (SLH), trained in the recognition of melanocytic naevi by dermatologists during a previous prevalence survey,[11] examined all participants and obtained similar counts when re-examining a sample of children. Replicate counts on 9% of subjects showed 93% intra-observer reliability.

Melanocytic naevi counts were obtained by summing the counts for each body site. Body surface area was reduced by 9·7% because of the areas not examined.[25]

Because the distribution of melanocytic naevi was found to be positively skewed, medians are given unless otherwise stated. Kruskal-Wallis test was used to assess differences between medians. For multivariate analysis, counts were in 25, 50, and 75 percentiles within each age group and logistic regression produced relative risk ratios and 95% CIs for each phenotypic characteristic in relation to melanocytic naevus category. A similar analysis was done to assess the effect of acute and chronic sun exposure, after controlling for age and significant phenotypic characteristics which were not significantly co-linear.

Results

500 of the 506 children (99%) had at least 1 melanocytic naevus. 85% had at least 1 lesion of 2 mm or more and 13% had at least 1 of 5 mm or more. The median number per child was 34 for lesions of all sizes (mean 41·0), 5 for lesions 2 mm or more (mean 9·1) and 0 for lesions 5 mm or more (mean 0·2). The highest number recorded for an individual was 252 in a 6-year-old girl. 27 congenital naevi were found in 24 children (4·7%), and did not vary with age or sex.

Melanocytic naevi increased progressively with age for both total lesions (p=0·0001) and those 2 mm or more (p=0·0001) (figure 1), an increase not explained by increasing body size since there was a similar increase in the the number per square metre of body surface area examined with age (p=0·0001) (figure 1). Melanocytic naevi did not differ significantly in counts or density by sex, irrespective of size (37 in boys *vs* 32 in girls; p=0·5388; density 59·3/m² in boys *vs* 52·6/m² in girls; p=0·6361).

Constitutional variables	No*	Moderate naevi			High naevi			Very high naevi		
		RRR†	95% CI	p	RRR†	95% CI	p	RRR†	95% CI	p
Sex										
Male	190	1 00			1 00			1 00		
Female	179	0 96	0 51–1 80	0 885	0 80	0 43–1 50	0 486	0 78	0 41–1 49	0 454
Skin reflectance										
Dark	30	1 00			1 00			1 00		
Medium	39	0 95	0 27–3 38	0 935	1 17	0 31–4 50	0 819	2 87	0 45–18 27	0 264
Light	300	1 29	0 49–3 43	0 609	1 86	0 65–5 27	0 247	5 09	1 01–25 67	0 049†
Eye colour										
Brown	91	1 00			1 00			1 00		
Hazel	84	0 88	0 35–2 22	0 790	0 33	0 14–0 81	0 015	0 48	0 19–1 23	0 125
Blue	194	1 91	0 79–4 60	0 148	0 79	0 35–1 78	0 572	1 09	0 45–2 61	0 851
Hair colour										
Dark	116	1 00			1 00			1 00		
Fair	242	1 12	0 53–2 36	0 768	1 14	0 55–2 40	0 721	0 92	0 43–1 94	0 817
Red	11	0 13	0 01–1 22	0 074	0 19	0 03–1 07	0 060	0	ins	ins
Freckles										
Absent	157	1 00			1 00			1 00		
Present	212	1 74	0 90–3 36	0 100	1 73	0 90–3 32	0 100	3 73	1 87–7 44	0 0005
Depth of tan										
Dark	43	1 00			1 00			1 00		
Moderate	233	0 78	0 32–1 88	0 578	0 95	0 37–2 43	0 914	9 94	1 20–82 53	0 034
Slight	43	0 71	0 16–3 20	0 658	1 61	0 39–6 60	0 509	17 72	1 70–184 39	0 016
No tan	50	0 45	0 12–1 67	0 233	0 56	0 15–2 13	0 398	13 19	1 39–125 62	0 025
Burn 1st exposure										
No	47	1 00			1 00			1 00		
Yes	322	1 05	0 46–2 40	0 916	2 64	1 03–6 79	0 044	8 10	1 70–38 63	0 009

*Subjects with data missing for any variable were excluded from this analysis. †Relative risk ratio using the lowest quarter of the distribution of naevi (mild naevi) and the first level of each constitutional variable as referent levels (set to 1 00). ins=insufficient data.

Table 1: **Association of constitutional factors and melanocytic naevus counts for Townsville-born children aged 1–6 years**

Sun exposure variables*	No	Moderate naevi			High naevi			Very high naevi		
		RRR†	95% CI	p	RRR†	95% CI	p	RRR†	95% CI	p
History of sunburn‡										
No	190	1 00			1 00			1 00		
Yes	308	1 00	0 59–1 68	0 993	1 62	0 95–2 75	0 074	1 89	1 11–3 21	0 019
Annual sun exposure§										
0–365 h/yr (0–1 h/day)	45	1 00			1 00			1 00		
366–730 h/yr (>1–2 h/day)	60	1 59	0 49–5 18	0 439	1 74	0 59–5 16	0 318	3 00	0 89–10 17	0 077
731–1095 h/yr (>2–3 h/day)	77	1 03	0 37–2 87	0 953	0 40	0 14–1 14	0 086	1 24	0 41–3 74	0 701
1096–1460 h/yr (>3–4 h/day)	68	1 01	0 34–2 99	0 987	0 79	0 29–2 18	0 647	1 62	0 52–5 03	0 408
>1460 h/yr (> h/day)	107	1 48	0 52–4 19	0 460	1 22	0 46–3 22	0 689	3 29	1 12–9 69	0 030

*Each factor is adjusted in multivariate analysis for constitutional factors significantly related to MN numbers in table 1 that are not significantly co-linear.
†Relative risk ratio using the lowest quarter of the distribution of naevi (mild naevi) and the first level of each constitutional variable as referent levels (set to 1 00).
‡Subjects with data missing for the sunburn history analysis were excluded from this analysis.
§Subjects with data missing for the annual sun exposure analysis were excluded from this analysis.

Table 2: **Association of sun exposure variables to melanocytic naevus counts**

Significantly more melanocytic naevi were associated with light natural skin colour compared with other skin types—36·5 for light skin, 25·0 for medium skin, and 13 for dark skin (p = 0·0024)—and with darker hair colour—28 for red/auburn hair, 30·5 for blonde/fair hair, and 43 for dark hair (p = 0·0001). There was the same trend for density (p = 0·0003) and counts of 2 mm or more (p = 0·0125) in relation to hair colour. Counts (total and ≥2 mm) and densities were not significantly related to eye colour. Freckling was significantly associated with counts (p = 0·0001) (figure 2). When freckling was ranked and divided into categories, the median number of melanocytic naevi increased with the extent of freckling from 16 for children without freckles, to 43·5 for mild freckling, 66 for moderate freckling, and 70 for heavily freckled children.

Polytomous logistic regression analysis of melanocytic naevi in relation to phenotype (table 1), showed the difference between the sexes was not significant after adjustment for constitutional factors. Depth of tan after exposure to sunlight was significantly related to total number—children with a moderate tan, a slight tan or no tan were 10, 18 and 13 times (respectively) more likely than dark tanners to have very high numbers of melanocytic naevi. Children who were unable to tan spent significantly less time in the sun than children in the other three tanning groups: mean annual exposure of 1171 h/year for deep tanners, 1122 h/year for moderate tanners, 1197 h/year for slight tanners, and 794 h/year for those who could not tan (p = 0·001). Children with a tendency to burn were 8 times more likely to be in the highest category of melanocytic naevi, than children of the same age who tend not to burn. Use of summer sunscreen significantly reduced the number of sunburns (p = 0·022) but was not associated with annual sun exposure or with naevus number or density.

Children who had had at least one episode of sunburn had more than twice as many melanocytic naevi overall (43, 8 ≥2 mm) compared with children who had never been sunburnt (18, 2 ≥2 mm; p = 0·0001). Melanocytic naevi also increased with the total number of hours spent in the sun in the year before examination; 19 for 0-365 h, and 44 for ≥1461 h (p = 0·0002). This trend persisted for the density of naevi and for lesions which were 2 mm or more.

The effect of type of sun exposure was considered after adjustment for age and all of the significant constitutional factors that were not significantly correlated by polytomous logistic regression analysis. Significant correlations existed for sunburn (r = 0·32; p = 0·001), and freckling (r = 0·36; p = 0·001) in relation to sunburn history.

A history of sunburn was associated with the highest category of melanocytic naevus counts after controlling for age and phenotype. Children who had been sunburnt were twice as likely as children who had never been sunburnt to have very high numbers of melanocytic naevi (table 2), an association that remained significant even after addition of annual sun exposure to the model (relative risk ratio = 1·79; p = 0·039), and increased in strength when very high density (3·17; p < 0·0005) and very high numbers of naevi ≥2 mm (2·91; p < 0·0005) were considered.

Children who averaged more than 4 hours per day in the sun were three times as likely to have very high numbers of melanocytic naevi than were children who spent 1 hour or less per day, after adjustment for constitutional factors (table 2). The relative risk associated with the second lowest category of exposure (> 1–2 h/day) was raised, although not significantly, after controlling for constitutional factors whereas the relative risk ratios associated with the intermediate categories of sun exposure were only slightly affected. Even higher relative risk ratios were produced for the highest category of naevus density (3·86; p = 0·016) and the highest category of naevi 2 mm or more (3·37; p = 0·023).

Discussion

Our data support a contribution of acute and chronic sun exposure to the development of melanocytic naevi. The association between sun exposure and naevi is unlikely to be due to biased response because the participation rate (87·6%) was high. Selective recall cannot be excluded with certainty; however, sun-exposure histories were taken before naevus counts were done and almost all participants expressed surprise when high counts of naevi were found. Further support for the part played by exposure to sun comes from the site distribution of melanocytic naevi—higher counts were found on sun-exposed surfaces such as the outer arms.

Studies of naevus prevalence have produced circumstantial evidence implicating exposure to sun[9-11,13-20] and others have found evidence for a relationship with sunburn,[9,10] as have we. However, no other study has shown a significant relation between chronic solar exposure in childhood and melanocytic naevi. It seems that living in Townsville is, in itself, sufficient for children to acquire large numbers of melanocytic naevi early in life; only 6 children (1%) had none and even children with minimal exposure to sun acquired relatively large numbers. 193 children who had never been sunburnt had a median of 18 naevi and a similar number (19) was found for children with a low annual exposure to sun. The median number of naevi measuring 2 mm or more for 6-year-old Townsville children was 17·5—almost as high as that reported by Green et al[8] for older chidren (7–12 years) living in southern

Queensland. These findings support those of Kelly et al,[11] who showed that the acquisition of melanocytic naevi to age 12 in Australia is greater with increasing proximity to the equator.

As anticipated, melanocytic naevi (total and 2 or more mm) increased with age[10-12,14,16,18,26] but did not vary significantly with sex. Age may act as a proxy for cumulative lifetime sun exposure: the increase was not explained by increasing body size. This association shows the need to control for age when comparing naevus counts,[10] particularly in children.

We found that melanocytic naevi were related to previously identified phenotypic risk factors for melanoma, including propensity to sunburn,[2,3,6,27,28] depth of tan,[6] and freckling.[27-29] Melanocytic naevi were inversely related to depth of tan for all children except those who could not tan. Our results suggest that this may be explained by sun avoidance in the most sun-sensitive group.

Studies of naevi in older children have reported comparable findings with respect to the tendency to sunburn,[9-11] and the presence of freckling.[9-11,16,30] Others[10,16] report a similar trend to that described here in relation to depth of tan and Gallagher[9] showed an inverse relationship with tanning score which was similar except that there was no downturn in naevus frequency for children who were least able to tan.

Natural protection from ultraviolet radiation as indicated by melanin in the unexposed skin of the inner upper arm was related to counts of melanocytic naevi similar to the findings of others.[8,11,30] Our finding of a low count of melanocytic naevi in redheads is unlikely to be due to small sample size, since it has also been reported in two recent studies[11,16] Paradoxically, naevi were generally more prevalent on sun-protected than sun-exposed skin in red heads.

We found no association between eye colour and melanocytic naevi. This is contrary to recent observations in schoolchildren which showed lighter eye colour to be associated with higher geometric mean numbers of naevi.[11] This lack of association may be explained by the instability of eye colour in early childhood, especially among blue-eyed individuals whose eyes often darken as they grow older. In our sample, 69% of children aged 1 year had blue eyes whereas only 51% of Townsville school children aged 6–15 years had blue eyes.[11]

Sun exposure plays a role in the development of melanocytic naevi in childhood. If the relation between melanocytic naevi frequency and melanoma risk is the same for children as for adults, then the pattern of risk seems to be established very early in life in Queensland children in the tropics.

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