Development of Melanocytic Nevins in the First Three Years of Life

Simone L. Harrison, Rona M. MacKie, Robert MacLennan

Interest in melanocytic nevi (moles) stems from their clinical, histologic, and epidemiologic association with melanoma. Few studies of nevi have been longitudinal (1,2), and all, apart from our own (3), have involved subjects 3 years old or older. Hence, little is known about the age at which nevi begin to develop.

We compared rates of development of nevi from birth to 3 years of age in two cohorts of Caucasian children of similar ethnicity from the contrasting climates of Townsville, Australia [19° S; high levels of ambient UV radiation (4)], and Glasgow, U.K. [55° N; low levels of ambient UV radiation (5)]. The Australian cohort was recruited by approaching postpartum women at three maternity hospitals in Townsville during September and October 1994; 96.7% of the eligible mothers participated, resulting in a cohort of 115 babies of European ancestry. Scottish neonates were recruited from October 1993 through August 1994 by inviting postpartum women at the Queen Mother’s Hospital, Glasgow, to participate in a randomized intervention trial focused on sun avoidance in infancy (consent rate for parents at Queen Mother’s Hospital, Glasgow = 97.4%). From the latter group, only control subjects (no intervention; n = 157) were included in this study.

The institutional review boards of the participating hospitals approved this study. The parents of all participants provided written, informed consent.

In both countries, a standard international protocol was used to define and to count nevi of all sizes (6). Full-body nevus counts were performed on the Australian infants by an experienced observer (S. L. Harrison) (3) who was previously trained by dermatologists to recognize nevi (7). Nevi on the Scottish infants were counted by one of two experienced research nurses, and their counts were checked by a dermatologist (R. M. MacKie). Prior to the study, S. L. Harrison and R. M. MacKie reviewed numerous pigmented lesions together to standardize their nevus counting.

Subjects were examined for nevi at birth (Australian cohort) or at 6 weeks of age (Scottish cohort) and within a month of their first, second, and third birthdays. Additional examinations of the Australian subjects were conducted at ages 6 and 18 months. Of the original 115 Australian infants, 88.7% and 77.4% were available for follow-up at ages 6 and 12 months, respectively. The retention rate for the Scottish cohort was higher, with 96.2% of the original cohort of 157 available for follow-up at 12 months of age. Retention for both cohorts is shown in Table 1. Only one of the 47 children lost from the Australian cohort over the 3-year period of follow-up withdrew by choice. The other 46 children were lost to follow-up because their families moved away. Of the 17 children lost from the Scottish cohort, 14 moved away or could not be contacted, one mother withdrew her consent, and follow-up of two subjects was not pursued for reasons unrelated to the study.

Nevus counts were positively skewed. Consequently, we have presented the data as median nevus counts and interquartile ranges (IQRs). The chi-square and Wilcoxon rank sum (WRS) tests were used as appropriate (8). All P values are two-tailed.

The proportion of Australian children with nevi increased rapidly in the first 2 years of life from 2.3% at birth to 65.2% (95% confidence interval [CI] = 54.3%–75.0%) at 12 months and 100% (95% CI = 95.3%–100.0%) at 24 months (Fig. 1). Corresponding proportions for the Scottish cohort were similar at age 6 weeks (3.2%; chi-square P for comparison with Australian children at birth = .781), but they were consider-
ably less at 12, 24, and 36 months of age, when 30.5% (95% CI = 23.2%–38.5%; chi-square \( P = .0001 \)), 61.7% (95% CI = 53.2%–69.8%; chi-square \( P = .0001 \)), and 83.6% (95% CI = 76.4%–89.3%; chi-square \( P = .0002 \)), respectively, of children presented with nevi. At 3 years of age, 77.9% (95% CI = 66.2%–87.1%) of Australian children had at least one nevus with a diameter of at least 2 mm compared with only 47.9% (95% CI = 39.4%–56.5%) of Scottish 3-year-old children (chi-square \( P = .0001 \)).

Median total nevus counts (Fig. 1) were consistently higher in Australian subjects than in Scottish subjects (WRS \( P = .0001 \)), but they did not differ in a statistically significant manner by sex in either cohort. Australian children who had noncongenital nevi by 12 months of age developed a larger number of additional nevi (median number = 13) between 12 and 36 months of age than did children who had not developed any noncongenital nevi by 12 months of age (median number of additional nevi = eight; WRS \( P = .0082 \)). For the Scottish cohort, no difference was evident by 3 years of age. The median number of new nevi was three, both for children who had noncongenital nevi at 12 months and for those who lacked them (WRS \( P = .35 \)).

The median incidence of nevi in Australian children was one (IQR = zero to two) in the first year, five (IQR = three to eight) in the second year, and six (IQR = four to 10) in the third year of life compared with zero (IQR = zero to one), zero (IQR = zero to two), and two (IQR = zero to four), respectively, for the Scottish children.

Although only 1%–2% of Caucasian neonates have nevi (9,10), our results show that the development of nevi is a continuous activity that begins between the ages of 6 and 12 months for most Caucasian infants raised in tropical Australia and before 2 years of age for most Caucasian children raised in Scotland’s temperate climate. The incidence of nevi was consistently higher in Australian than in Scottish children. Median nevus counts increased rapidly in the second year of life in Australian children and in the third year of life in Scottish children, and there was statistically significant evidence that onset of nevi in Australian children in the first 12 months of life was associated with higher nevus counts at subsequent ages up to 3 years. Because Scottish children begin to develop nevi later in life than Australian children, it will be necessary to follow up the Scottish children for a longer period to see if this association holds true for them as well. Differences in loss to follow-up are unlikely to explain these findings, which remained unchanged irrespective of whether analyses included all subjects or only those who remained at 3 years of age.

Comparisons of nevi in populations with contrasting melanoma rates and UV radiation levels suggest that the early onset of nevi may be a more important determinant of risk for melanoma than was previously thought. The incidence of melanoma in Australia is much higher than in the U.K. (11), and this study and other studies (12–15) have shown that nevi are more prevalent in young Australian subjects than in their British counterparts. However, there is little difference in nevus frequency between older Caucasian individuals from contrasting climates (15,16). In one study (7) that involved schoolchildren from Melbourne, Australia (38° S), Sydney, Australia (34° S), and Townsville (19° S), latitude of residence within Australia was shown to be inversely related to nevus frequency, but the difference diminished by age 15 years, despite the fact that incidences of melanoma in Sydney and Melbourne are approximately half the incidence reported for Townsville (11,17).

Some evidence suggests that high levels of cumulative sun exposure may expedite the natural maturation and
elimination of nevi (18). We propose that subjects from sunny climates who acquire nevi very early may, with continued high levels of exposure to solar UV radiation, have nevi that mature and regress earlier than those of subjects from environments with less ambient UV radiation. If correct, this hypothesis would explain the similarities in nevus frequency in adults from contrasting climates that exist in spite of striking differences during childhood. Since the incidence of melanoma appears to be highest in populations who develop nevi earlier in life (3,7,19,20), it is possible that the early acquisition of nevi is a risk factor for melanoma. This postulate is consistent with the finding that 44% of melanomas diagnosed in subjects under 30 years of age from Scotland develop on small, early-onset nevi (21).

To our knowledge, this study is the first population-based cohort study to document the development of melanocytic nevi in the first 3 years of life. These results suggest that interventions that aim to reduce the risk of developing melanoma in later life by preventing nevus development should begin before the age of 1 year in Australia and before the age of 2 years in Scotland.

REFERENCES


NOTES

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