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INVESTIGATIVE REPORT

Frequency and Distribution Pattern of Melanocytic Naevi in Swedish 8–9-year-old Children

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The naevus profile was examined in a Swedish cohort of 8–9-year-old children; 524/545 individuals (96%) were examined (279 boys and 245 girls). There was a wide variation in the total number of naevi (0–79) and boys had more naevi than girls (median 9 and 7, respectively, $p < 0.01$). No dysplastic naevi were found. Overall, 15/524 (3%) had at least one lesion clinically diagnosed as a congenital melanocytic naevus. Boys had more naevi on the face (median 1) and trunk (median 5) than girls (median 0 and 3, respectively, $p < 0.001$). There was no difference in the number of naevi on the legs between the two sexes. The highest counts per unit surface area for both sexes were found on the back, chest and the lateral aspect of the arms, areas intermittently sun-exposed. Children with fair skin and light eye colours had significantly more naevi than those with darker colours but children with red hair had very few naevi. Children with one or more naevi on the buttocks (25%), dorsal surfaces of the feet (11%) or on the scalp (7%) had twice as many naevi in total compared with those without naevi in these regions. Children with naevi in all three regions (0.8%) had four times as many naevi in total. A relationship between total counts and counts on the back or lateral aspect of the arms was found ($r^2 = 0.59$). Either of these two areas might be suitable for predicting total naevus counts. ***Key words: melanocytic naevus; children.***

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Most melanocytic naevi are acquired (1) and ultraviolet (UV) radiation is an obvious environmental agent, inducing genetic damage as well as proliferation of melanocytes in the skin (2). Having a large number of naevi is related to sunburn during childhood (3–5), especially in those living in a sunny climate (3, 6) and with a tendency to burn rather than tan (4, 5).

While the incidence of cutaneous malignant melanoma is increasing in the adult Caucasian population, melanoma in the young has been shown to be extremely rare (7). One report from Australia, however, suggests that there is also an increasing incidence below the age of 15 (8). Over the 10-year period, 1973–1992, in Sweden we found a doubling of the mean annual melanoma incidence rate below the age of 20 from 0.2 to 0.5 per 100 000 (7). This increase is in the same order of magnitude as for the adult population during the corresponding time period. Superficial spreading melanoma is the most common (60%) but also the fastest increasing subtype in the young and 17% of those affected have a histologically associated precursor lesion (9). As with adults, the majority of melanomas were found on the trunk in boys and on the legs in girls.

Numerous case control studies in adults have shown that having many naevi is a major risk factor for developing malignant melanoma (10–15). There is also a site-specific risk relation, i.e. a high density of naevi in a specific anatomical region implies an increased risk of developing melanoma in that very region (2). Furthermore, an atypical distribution pattern of naevi and the existence of atypical/dysplastic moles have been shown to be useful variables for identifying adults at risk of developing melanoma (15, 16). Naevus numbers and distribution might be potential tools already in early age to select individuals at future risk for melanoma. This is the first descriptive report of the frequency and anatomical distribution of naevi and their relation to pigmentary phenotypes in a cohort of Swedish children.

MATERIALS AND METHODS

Subjects

This study was approved by the ethics committee at the Medical Faculty in Linköping. The original sample consisted of 788 children born in 1992. The parents of these children had earlier agreed to participate in a vaccination study. The sample corresponded to 46% of all children born in Linköping that year. Since then a number of families have moved from the community and for practical reasons we further limited our study to the 545 children still living within a 25 km distance from the city of Linköping, representing 69% of the original sample.

A letter was sent to the parents requesting permission for their child to participate in the study and offering a free skin examination by a dermatologist (I.S. or I.R.). Three parents were not willing to let their child participate in the study, 16 children were not at school on the day of the examination

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(illness, vacation), and two children did not co-operate and were therefore excluded. In all, 524/545 (96%) were examined (279 boys and 245 girls). The study was performed during the winter season (October – March) 2000 – 2001.

Skin examination

All children had a total body skin examination. All brown macular or raised lesions ≥ 2 mm considered to be melanocytic naevi were counted on all body sites including skin folds, palms, soles, scalp and genital skin areas. Lesions identified as congenital melanocytic naevi, dysplastic naevi and lentigines were registered separately. A naevus was considered as congenital if 10 mm or larger and the mole had been present since birth. A lentigo was defined as a brown macule, at least 5 mm in diameter that does not darken on sun exposure or disappear during the winter. A naevus was defined as dysplastic if larger than 5 mm with an irregular border and/or irregular pigmentation.

The regional distribution of naevi was registered using a schematic body chart divided into 16 areas (A – P) and the number of naevi was registered separately in each area (Fig. 1). The areas were outlined taking clothing habits and general UV exposure pattern into account. Areas A (face) and F (dorsal surfaces of the hands) were considered to be chronically UV-exposed and C (medial aspect of arms), H (lower abdomen and genitalia) and J (buttocks) rarely UV-exposed. With the exceptions of areas B, E and P (scalp, palms and soles), the remaining areas were considered intermittently exposed to UV light. These latter areas are usually covered by clothes in Sweden's cold climate, and are UV-exposed only intermittently in the short summer period or during holidays in sunnier climates.

The number of naevi per unit surface area was calculated using the estimates of body surface area described by Lund & Browder (17), modified for children (18). Four percent of the area of the arm was added to the trunk area in line with our specific subdivision of the body surface. Hence, the trunk area constituted 26% of the body surface and areas H and J were estimated to represent 10% of the total body surface.

Skin type was classified according to Melski et al. (19). Hair colour was classified as blonde, brown, black or red. Eye colour was registered as blue/grey, green or brown. The presence of freckles on the face was also registered.

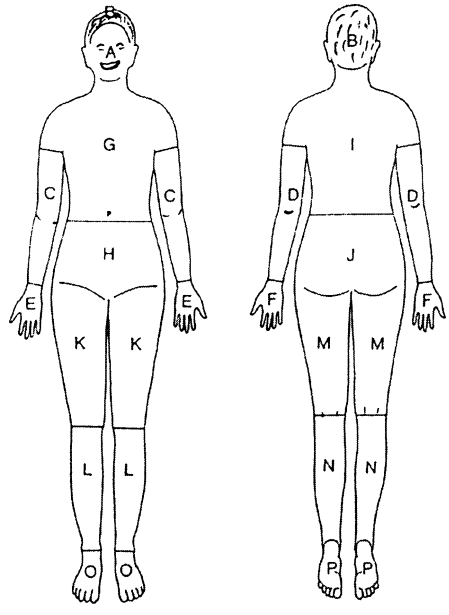

Fig. 1. Schematic figure illustrating the 16 areas (A – P) studied.

Statistical methods

For comparison between groups we used the Wilcoxon rank-sum test (Mann – Whitney) and the Kruskal Wallis test for comparison between more than two groups. To study correlation between variables, we used Spearman rank correlation. Regression analyses were performed using the robust method; this and all other statistical analyses were performed with Stata v 7.0 (Stata Corp., College Station, Texas, USA, 2001).

RESULTS

Total body naevus counts

In the 524 subjects we found a median total body naevus count of 8 and a wide range of 0 – 79 naevi (Fig. 2); 5% had no naevi at all and 15% had 20 naevi or more. Boys had a higher total naevus count than girls (median 9 and 7, respectively), $p < 0.01$ (Fig. 2). None of the children had any naevi fulfilling the clinical criteria for dysplastic naevi; 15/524 children (3%) had at least one lesion diagnosed as a congenital naevus; 6/524 children (1%) had at least one lesion clinically diagnosed as a lentigo. There was no significant correlation between presence of a congenital naevus or lentigo and a high total naevus count.

Regional naevus distribution

Boys had more naevi on the face compared with girls (median 1 and 0, respectively, $p < 0.001$). Boys also had more naevi on the chest (G) and back (I) than girls (median 2 and 1, and 3 and 2, respectively, $p < 0.001$) (Fig. 3). No significant difference between the sexes in number of naevi was found in the other skin areas

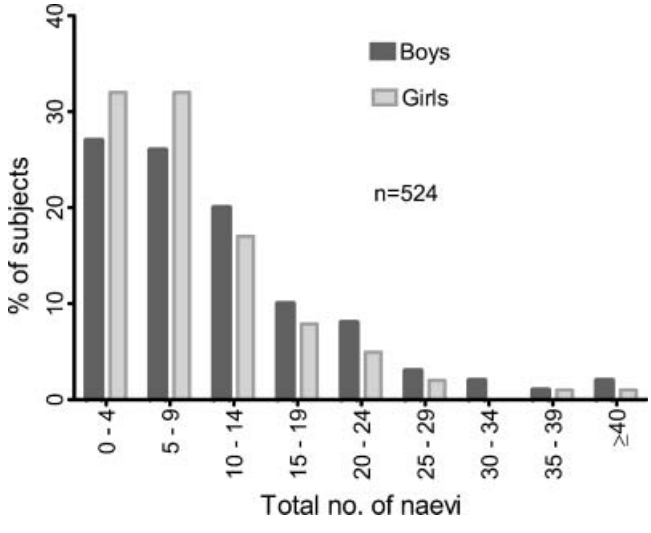

Fig. 2. Distribution of total naevus counts in 8 – 9-year-old Swedish children. Girls: $n = 245$, boys: $n = 279$.

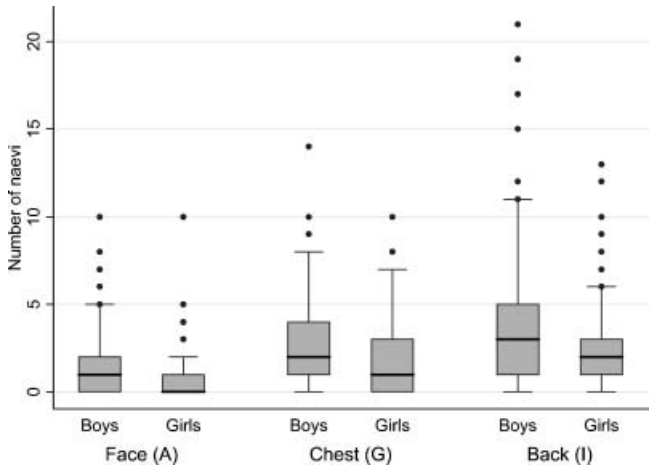

Fig. 3. Number of naevi on the face, chest and back in boys and girls. The thick lines indicate median values. Boxes indicate the 25th–75th percentiles and bars the 90th percentiles. Significant differences ($p<0.001$) in number of naevi were found between boys and girls in all three areas ($n=524$).

defined in Fig. 1. Of all subjects, 7% had naevi on the scalp (B), 2.5% had naevi on the palms (E) and 4% on the soles (P).

The number of naevi in each defined area (A–P) was compared with the expected number, assuming an even distribution of naevi over the body surface (Table I). Calculated as mean number of naevi/unit surface area, significantly more naevi than expected were found on the face, the lateral aspect of the arms and on the chest and back (Table I). Significantly lower naevus counts than expected were found on the scalp and legs.

In order to try to identify suitable skin regions for screening procedures, counts from several regions were tested for strength in predicting total naevus counts. Twenty-five per cent of the children had presence of naevi on the buttocks and these children had higher total naevus counts (median 12) compared with those lacking naevi on the buttock area (median 6), $p<0.001$. Eleven per cent of the children had naevi on the dorsal surfaces of the feet and their median total naevus counts was higher (22) than in those lacking naevi in this area (7), $p<0.001$. Similarly, those having naevi on the scalp had more naevi in total (median 14) than children without scalp naevi (median 8), $p<0.001$. Also, 4/524 children (0.8%) had naevi in all three areas, i.e. buttocks, feet and scalp and these children had a very high naevus count (median 39.5) compared with children lacking naevi in these areas (median 8), $p<0.01$. Furthermore, a relationship was found between total naevus counts and counts from the lateral aspect of the arms ($r^2=0.59$) and from the back ($r^2=0.59$) (Fig. 4). We investigated the sensitivity and specificity of classifying children with ≥ 6 on the lateral aspect of the arms in seven categories of total number of naevi by using a ROC analysis (Table II). The specificity was

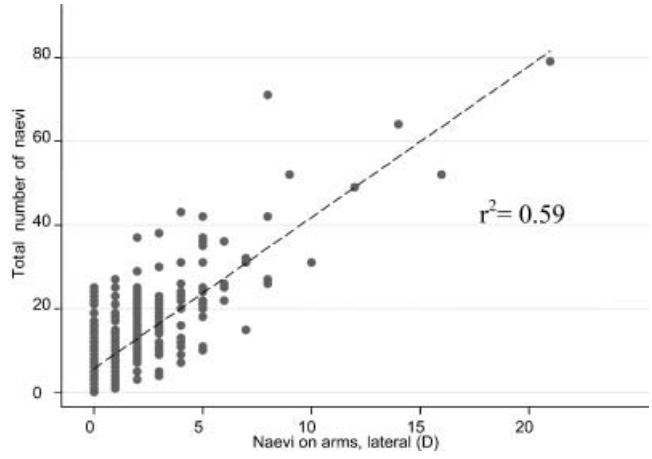

Fig. 4. Total number of naevi plotted against naevi on the lateral aspect of the arms for each individual. Dotted line represents a linear regression with $r^2=0.59$; $n=524$.

Table I. *Total number of naevi observed in areas A–P in 524 individuals**

Area (% of body surface area)	Observed	Ratio of observed to expected	*P* value
A. Face (6.5)	615	1.77	<0.001
B. Scalp (6.5)	45	0.13	<0.001
C. Arms: medial (6.0)	240	0.75	0.190
D. Arms: lateral (6.0)	680	2.12	<0.001
E. Palms (2.5)	18	0.13	0.550
F. Dorsum of hands (2.5)	93	0.70	0.620
G. Chest (12)	1097	1.71	<0.001
H. Lower abdomen (5.0)	40	0.15	0.220
I. Back (14)	1482	1.98	<0.001
J. Buttocks (5.0)	187	0.70	0.350
K+M. Thighs (16)	488	0.57	<0.001
L+N. Lower legs (11)	269	0.46	0.002
O. Dorsum of feet (3.5)	71	0.38	0.310
P. Soles (3.5)	22	0.12	0.430

*The observed total naevus count in a given area was compared with the expected number of naevi, assuming an even distribution of naevi on the body surface.

Table II. *Sensitivity and specificity of classifying the total number of naevi in seven categories in individuals with six or more naevi on the lateral aspects of the arms (n=524)*

Total no. of naevi	Sensitivity (%)	Specificity (%)	Correctly classified (%)
≥0	100	0	3
≥10	100	60	61
≥20	94	80	89
≥30	65	98	97
≥40	41	100	98
≥60	18	100	97
>80	0	100	97

>98% for having a total of 30 naevi or more, but the sensitivity was <65% for corresponding groups.

Distribution of naevi in relation to UV exposure

Very few naevi per unit surface were found in rarely exposed areas (C+H+J) compared with UV-exposed skin. When all areas considered as chronically (A+F) and intermittently UV-exposed (D+G+I+K+L+M+N+O) were pooled, no significant difference in mean number of naevi per unit surface area was found. Areas B, E and P were excluded from this analysis as it was not possible to classify these areas according to exposure pattern and because of the different nature of the skin in these anatomical regions.

Naevus counts in relation to pigmentary phenotype

Children with blue eyes had more naevi than brown-eyed children (median 9 and 6.5, respectively, $p<0.05$) (Table III).

Blonde children had more naevi (median 9) than children with red (median 3, $p<0.001$) and black hair (median 2.5, $p<0.001$). There was no significant difference in total naevus number between blonde and brown-haired children, but children with brown hair had significantly more naevi (median 8) than red-haired ($p<0.001$) and black-haired children ($p<0.05$).

Table III. *Median number of naevi in relation to pigmentary phenotype (n=524)*

Factor	Subjects (%)	Number of naevi
Eye colour		
Blue/grey	380 (72)	9
Green	46 (9)	8
Brown	98 (19)	6.5
Hair colour		
Blonde	394 (75)	9
Brown	85 (16)	8
Black	14 (3)	2.5
Red	31 (6)	3
Skin type		
I + II	477 (91.4)	9
III + IV	46 (8.4)	6.5
V	1 (0.2)	1
Freckles present on the face		
Yes	195 (37)	9
No	329 (63)	8

Children with skin types I–II ($n=477$) had a higher total naevus number (median 9) than those with skin types III–IV ($n=46$, median 6.5, $p<0.05$) (Table III). The median total naevus count in children with freckles was nine and in children without freckles eight ($p=0.056$). The majority of the children with freckles were blonde (71%) with blue eyes (79%) and had skin type I or II (97%).

DISCUSSION

This study describes the frequency and distribution of naevi in relation to pigmentation in 8–9-year-old Swedish children. Similar to our previous findings in adults (16, 20, 21), there was a wide variation in the total number of naevi in this young age group (0–79 naevi). The median total number of naevi was found to be 8 compared with 23 in the adult 18–50-year-old population, described earlier from the same geographical region (22). There are several reports of naevus density in children. Green et al. (3) found a mean total naevus count of 28 in 7–11-year-old school children in Brisbane, but in the UK (23) children aged 8–9 years had a median of only two naevi. Autier et al. (24) reported a median total number of six naevi in children aged 6–7 years from Central Europe. Comparisons between studies of naevus pattern are very complex, as moliness is influenced by genetic factors and sun exposure, the latter dependent on latitude and sun-related behaviour. Furthermore, various investigators have included different types and sizes of naevi in their counts, limited skin areas have been examined, and in most studies population-based samples have not been used. Nevertheless, it seems as if our naevus counts are relatively high in comparison with previous reports from Europe in this age group. This might be due to the phenotype and the sun exposure pattern in our population and the fact that we examined the total skin surface. In agreement with reports from Australia and Canada, we found that boys had more naevi than girls. This small but statistically significant difference seems to decrease with age, diminishing or disappearing during adolescence or adulthood (6, 17, 25, 26).

None of the children in the present study had any naevi that fulfilled the clinical criteria for a dysplastic naevus. The prevalence of dysplastic naevi in young children is not known, but the clinical characteristics of dysplastic naevi seem to appear first in adolescents (27, 28). We found a slightly higher prevalence of congenital naevi than that reported in newborns (29). In contrast to other authors (5, 30), we found no positive association

between the presence of a congenital naevus in an individual and high total naevus counts. Difficulties in diagnosing congenital naevi or other methodological differences may explain this discrepancy.

In agreement with previous observations in younger age groups (3, 6) we found children with light eye colours to have significantly more naevi than those with darker eye colours. In our earlier report (20, 21) of the naevus phenotype in adult Swedes, none of the pigmentary traits of eye and hair colour significantly affected the number of naevi. In contrast to that finding, the present study found children with skin types I–II to have significantly higher total naevus counts than subjects with skin types III–IV. It is conceivable that more pigmented subjects have a delayed debut of naevi. On the other hand, children with red hair had very few naevi.

The regional distribution of naevi and cutaneous malignant melanoma shows a marked conformity in adults. Men have most naevi and melanoma on the trunk while women have more naevi as well as melanoma on the legs (2, 31). Interestingly, a similar sex-related site distribution of melanoma has been found in subjects as early as age 12–15 years, with 50% of the melanoma on the trunk in boys and 50% on the legs in girls (7). The difference in melanoma site between the two sexes has been ascribed to the different clothing habits of men and women. However, additional explanations must be sought as young girls and boys dress in much the same way in our country, even when sunbathing. In agreement with data from previous studies of naevus distribution in children (26, 32) we found differences in naevus pattern of the trunk between the two sexes, with boys having more naevi than girls in this region. In the Vancouver Mole studies (26, 33) this difference was noted as early as in the 6–12-year-old age group, but became even more pronounced in the 13–18-year-old group (26). We found no significant gender-related difference in the number of naevi on the legs, which is in contrast to studies performed in adult Swedes (2, 15). We speculate that naevi on the legs in girls might develop later than naevi elsewhere on the body. This idea is supported by the finding by Gallagher et al. (26), who found no difference in naevus density on the legs before the age of 13–18 years. Growth and sex hormones affecting the sexes differently might be of importance for naevus development.

By grouping anatomical subsites according to sun exposure patterns, the naevogenic effect of UV exposure was studied separately in chronically, intermittently or rarely exposed areas. We found very few or no naevi at all in rarely exposed areas and no difference in naevus number between those areas defined as chronically and intermittently UV-exposed. In our previous study in adults (34), intermittently exposed areas had a high count of naevi, while chronically and rarely exposed areas had lower counts. We hypothesized that chronic exposure might be protective or in some way stimulates the maturation and/or the disappearance of naevi. Even if the present distribution in children was compatible with the idea that chronic exposure enhances the life cycle and disappearance of naevi it cannot be excluded that the difference between counts in adults in chronically and intermittently exposed regions is due to a later increase in naevus number only in intermittently exposed areas. From this perspective it is noteworthy that in children the highest naevus counts in both sexes were already found on the back, chest and the lateral aspect of the arms, three areas that are intermittently exposed.

Children with one or more naevi on the buttocks, scalp or dorsal surfaces of the feet had a total of twice as many naevi compared with children with no naevi in these areas. Less than 1% of the children had naevi in all three areas and they had four times as many naevi compared with those lacking naevi in these areas. The occurrence of naevi on the buttocks and scalp is probably genetically determined and not the result of UV exposure. Naevi in these areas might, therefore, be considered to be a marker identifying individuals with high naevus counts and a genetically determined increased risk of developing melanoma in the future. We found a strong dependence between counts on the lateral aspect of the arms or the back and the total number of naevi. Even if it is difficult to differentiate between naevi and freckles on the lateral aspect of the arms during the summer, this might be the most convenient area to use to predict total counts. It is possible that those with a high number of naevi in this area constitute a separate risk group from those with naevi on the scalp and buttocks, as naevi on the arms are considered mainly sun-induced.

For early preventive measures it is important to identify children with many naevi and an increased risk of developing melanoma in the future. From a population perspective, a change of naevus number in children might serve as an early marker for a change in melanoma incidence. This points towards the need for a prospective investigation of the naevus profile in children and a suitable screening procedure to identify children with high naevus number. We suggest the dorsal aspect of the arms as a suitable area for screening procedures to identify individuals with high total naevus counts and an increased future risk of developing malignant melanoma.

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