Acta Derm Venereol (Stockh) 1992; 72: 123–127

Regional Distribution of Melanocytic Naevi in Relation to Sun Exposure, and Site-specific Counts Predicting Total Number of Naevi

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The role of exposure to ultraviolet light in the formation of melanocytic naevi was analysed by investigating the regional naevus distribution in 310 subjects (30–50 years) from a Swedish census file. The lateral aspect of the arms and the back had the largest concentration of naevi. The mean naevus count per unit surface area was higher in intermittently exposed than in rarely exposed skin ($p < 0.001$), while the lowest mean count was found in chronically exposed skin. These results support the idea that intermittent exposure to ultraviolet light has a "naevogenic" effect while chronic exposure might be protective. Dysplastic naevi had a distribution pattern quite different from common naevi. Considering the distribution pattern solely, dysplastic naevi seem to develop independently of exposure to ultraviolet light. The numbers of naevi in different skin areas were tested for their power in predicting the total body naevus count. The strongest correlations were found between total counts and counts on the anterior surface of the thighs and the lateral aspect of the arms. Counts from any of these areas will provide a practical and satisfactory estimate of the total number of naevi. ***Key words: Regional naevus distribution; Common naevus; Dysplastic naevus.***

(Accepted August 13, 1991.)

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In recent years, it has been found that a large number of melanocytic naevi is a major risk factor for developing cutaneous malignant melanoma (CMM) (1,2). This might be explained by both tumours sharing (a) common etiological factor (s). Ultraviolet (UV) light is the most obvious environmental stimulus inducing proliferation of melanocytes in the skin (3). Several studies have shown that UV-light plays an important role in the development of melanoma (4,5). It has also recently been demonstrated that UV-light promotes the formation of melanocytic naevi (6,7).

In a previous population study, we found that Swedes have extremely high total body naevus counts compared with what has been described from Caucasian populations (8). Furthermore, we found a fourfold increase in naevus counts in a defined sun-exposed area on the back compared with counts in an adjacent sun-protected area, demonstrating that UV-light is an important naevus inducer (7). Altogether, these results are of interest in view of the Scandinavian sunbathing habits, with intense but short UV-exposure periods with long intervals.

To further analyse the potency of chronic and intermittent UV-exposure on naevus formation, we have now studied the regional distribution of common and dysplastic naevi (CN and DN). In addition, counts from different skin areas were tested for their power in predicting the total body naevus count.

METHODS

Subjects

Five hundred Caucasian subjects, 30–50 years of age, were randomly selected from the census file in Göteborg, Sweden. The participation rate was 82%. For details regarding exclusions and drop-outs see ref. 8. This part of the investigation started when 69 subjects were already examined. Thus, 310 consecutive subjects (152 men, 158 women, mean age 41.4 years) were included in the study which was performed during the winter season.

Questionnaire

At the time of the examination, the doctor and the patient together filled in a form. Age, sex and skin type (I-IV) (9) were registered. Occupation was recorded as mainly indoor, indoor+outdoor or predominantly outdoor. An estimate of the amount of exposure to sunlight during spare time (based on life style and leisure activities) was made and rated according to a three-point scale as minimal, moderate or excessive. The number of weeks in southern countries was noted. The number of burns, defined as painful blistering for more than 48 h, was scored as none, one to three or more than three. The age at the first burn was registered and the use of UVA sunbeds was recorded.

Naevus counts

All subjects had a general skin examination by one trained dermatologist (A.A.). In 20 randomly selected individuals, independent naevus counts were performed by another dermatologist (I.R.). 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 area. Precautions were taken not to misdiagnose other pigmented lesions as naevi. If in doubt, the lesion was not counted.

Dysplastic naevi were registered separately. The diagnosis DN was based on clinical characteristics only. The major clinical criterion for a dysplastic naevus was a diameter ≥ 5 mm. In addition, at least two of the following criteria were required: an ill-defined or irregular border, speckled pigmentation, erythema or a pebbled surface (10). All DN were photographed and re-evaluated by the other two clinicians.

The exact location of each CN and DN was plotted on schematic figures. To compare naevus counts between different body sites, the figures were later divided into 16 separate areas (A-P) (Fig. 1). The areas were defined taking clothing habits and amount of UV-exposure into account. Areas A and F were considered chronically and C, H and J rarely UV-exposed. With the exception of areas B, E and P (scalp, palms, and soles), the remaining areas were considered intermittently exposed to UV-light.

The number of naevi per unit surface area was calculated using the estimates of body surface area by Lund & Browder (11) with minor adjustments. Four per cent was subtracted from their calculated area of the arms and was added to the trunk area, due to our different sub-divisions, as indicated on the schematic figure. Thus, the trunk area constituted 38% of the body surface. We subdivided the trunk and estimated areas H and J to represent 14% of the total body surface.

Statistical methods

Spearman's rank test was used for the correlation analyses. For comparisons between groups, we used Wilcoxon's two-sample test. For comparisons of proportions between groups, Fisher's exact test was used. Trends in contingency tables were analysed using the Mantel-Haenszel chi square test (12). To study the correlation between the

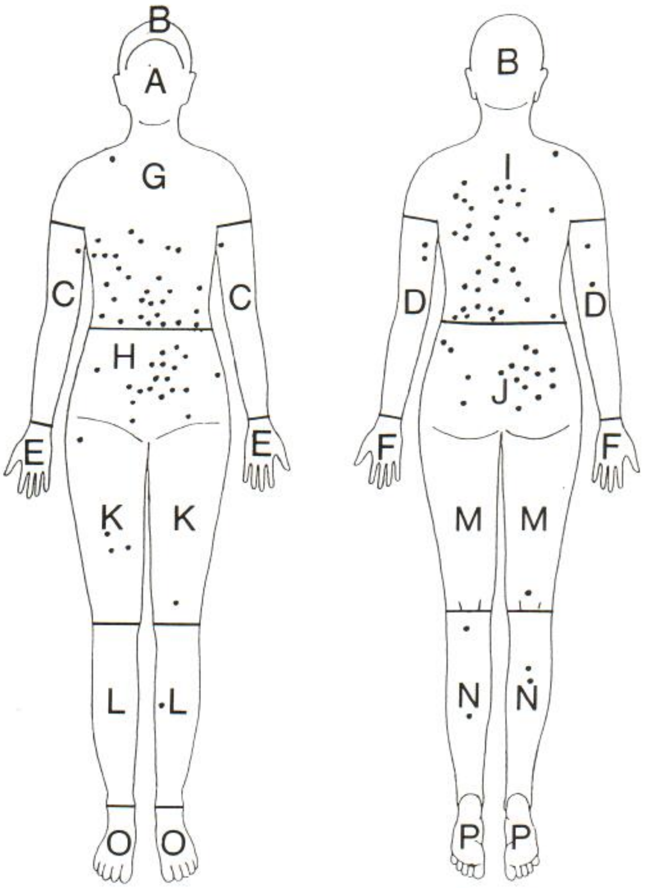

Fig. 1. Schematic figure illustrating the 16 areas (A-P) studied, and the regional distribution of clinical dysplastic naevi (n = 117) in 59 subjects. Each dot represents one naevus.

number of naevi in each defined area (A-P) and the total body naevus count, Pearsson's correlation test and a standard regression analysis were used. When the number of naevi per unit surface area was compared between areas of different UV-exposure categories, Wilcoxon's test for paired observations was used. Two-sided tests were used.

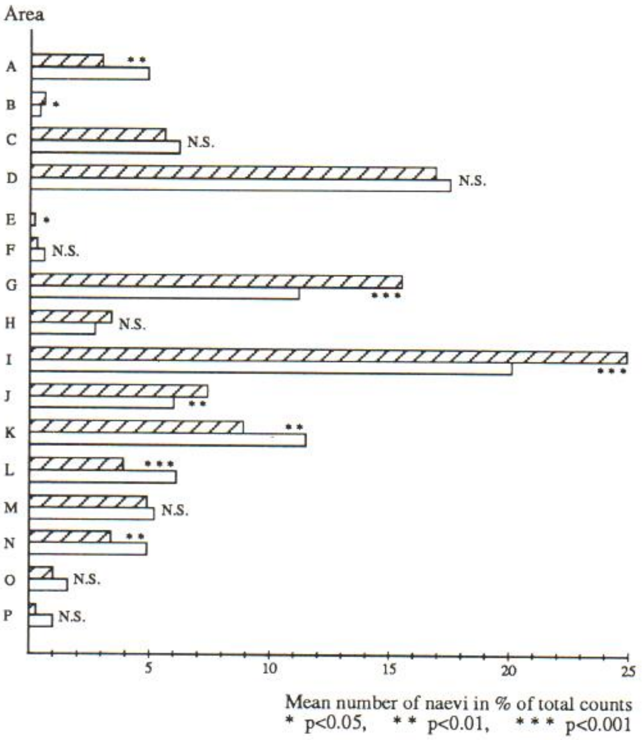

Fig. 2. Mean number of naevi per area adjusted for the total body naevus count in each individual. Men ▨ Women ☐.

RESULTS

Total body naevus counts and regional naevus distribution in men and women

The mean total body naevus count in the 310 subjects was 66 (median 53) (8). There was no significant difference in the mean total number of naevi between men (69.0) and women (62.7). The number of naevi in each defined area (A-P) was registered. In both sexes, there was a wide variation in naevus concentration between the different areas. The observed mean naevus count in a given area was compared with the expected

Table I. *Mean number of naevi/unit surface area in men and women*

Area	Surface area %	Observed		Ratio of observed to expected	
		Men	Women	Men	Women
(A) FACE	3.5	0.5	0.7	0.8	1.1
(B) SCALP	3.5	0.1	0.1	0.2	0.1
(C) ARMS (medial)	5.0	0.8	0.7	1.1	1.1
(D) ARMS (lateral)	5.0	2.3	2.2	3.4	3.6
(E) PALMS	2.5	<0.1	<0.1	<0.1	<0.1
(F) DORSUM OF HANDS	2.5	0.1	0.1	0.1	0.2
(G) CHEST	12.0	0.8	0.6	1.2	0.9
(H) LOWER ABDOMEN	6.0	0.4	0.3	0.6	0.5
(I) BACK	12.0	1.3	1.0	1.9	1.5
(J) BUTTOCKS	8.0	0.6	0.5	0.9	0.8
(K) THIGHS (anterior)	10.0	0.7	0.8	1.0	1.2
(L) LOWER LEGS (anterior)	7.0	0.5	0.7	0.7	1.0
(M) THIGHS (posterior)	9.0	0.4	0.4	0.6	0.7
(N) LOWER LEGS (posterior)	7.0	0.4	0.5	0.6	0.8
(O) DORSUM OF FEET	3.5	0.2	0.3	0.3	0.5
(P) SOLES	3.5	0.1	0.1	0.1	0.1

Table II. *Mean number of naevi/unit surface area in relation to UV-exposure in subjects with and without dysplastic naevi (DN)*

Categories of UV-exposure	All (n=310)	Subjects with DN (n=59)	Subjects without DN (n=251)
Intermittent	0.81	1.25	0.70
	I	I	I
	(***)	(***)	(***)
	I	I	I
Rare	0.53	0.89	0.45
	I	I	I
	(***)	(***)	(**)
	I	I	I
Chronic	0.41	0.53	0.38

*** $p<0.001$, ** $p<0.01$

number assuming an even distribution of naevi over the body surface (Table I). More than three times as many naevi as expected were found on the lateral aspect of the arm and almost twice as many on the back. Low ratios were seen for the scalp, the hands and the soles. Two per cent of the men and 8% of the women had naevi on the palms. The corresponding figures for the soles were 13% and 17% respectively.

After adjustment for the individual total naevus count, the mean number of naevi in each of the areas A to P was compared between the two sexes (Fig. 2). Men had significantly more naevi than women on the chest, the back and the buttocks, while women had more naevi than men on the face, the anterior surface of the thighs and the lower limbs.

Regional naevus distribution in relation to UV-exposure

The mean number of naevi per unit surface area was significantly larger in the UV-exposed skin (0.78) than in skin areas rarely exposed (0.53), $p< 0.001$, supporting the idea that UV-light promotes naevus development. To study the "naevogenic" effect of different types of UV-exposure, intermittently and chronically exposed areas were studied separately. Intermittently exposed skin had a high mean count of naevi per unit surface area (0.81), while chronically exposed areas had a mean count comparable with that of rarely exposed areas (0.41) (Table II). Areas B, E and P were excluded from the analysis due to the different nature of the skin in these anatomical areas.

Naevus counts in relation to skin type and habits of UV-exposure

We found no correlation between the total body naevus count and skin type (I-IV). Furthermore, there was no significant difference in the regional distribution of naevi between subjects with skin type I + II (n = 23) and subjects with skin type III + IV (n = 287), when testing each area separately.

A significant inverse correlation was found between the total body naevus count and the amount of occupational sun exposure. That is, subjects with predominantly indoor work had higher mole counts than outdoor workers, $p< 0.05$ (Table III). We found no significant correlation between the total number of naevi and any of the other anamnestic parameters grading the life-time amount of UV-exposure. Nor was there any correlation between the total naevus count and age at the first burn. Subjects reporting more than three burns had, however, a higher mean count (82.7) than the rest of the sample (64.6), $p< 0.05$. Eighty per cent of the population reported at least one visit to southern countries. The number of weeks in sunny climates varied from 1 to 156 (mean 14). Although these visits did not always include intense sunbathing, we were quite surprised not to find any correlation between the total naevus counts and the number of weeks in southern countries.

Dysplastic naevi

One or more clinical DN were found in 19% of the subjects, (59/310). When the diagnosis DN was re-evaluated from photographs there was good agreement between the three clinicians. The minor difference did not change the prevalence figure. The presence of DN was not influenced by age or sex. Altogether, 117 DN were registered and the location of each DN was plotted on a separate figure (Fig. 1). The distribution of DN was similar to what has been described for DN in the hereditary form of dysplastic naevus syndrome, i.e. a predominance on the trunk. Few DN were found on the extremities, and virtually no DN on the face and the upper chest.

Subjects with DN had a larger mean total number of naevi, 102 (median 95), than those without DN, 57 (median 45), $p< 0.001$ (8). The regional distribution pattern was similar in the two groups. The mean naevus count per unit surface area was higher in intermittently UV-exposed than in rarely exposed areas in both subjects with (1.25 versus 0.89) and without DN (0.70 versus 0.45), $p< 0.001$ (Table II). The difference in counts between intermittently and rarely exposed skin was, however, larger in subjects with than in those without DN. Subjects with DN had a more sun-sensitive skin type than those without DN but there were no differences in the UV-related behavioural parameters studied between the two groups (data not shown).

Table III. *Mean total body naevus counts in relation to estimates of life-time UV-exposure*

	Number of subjects	Mean (median) number of melanocytic naevi	
Occupation			
Indoor	235	69.5 (57)	*
Indoor+outdoor	46	57.0 (49)	
Outdoor	29	49.9 (36)	
Spare-time exposure			
Minimal	8	49.3 (46)	N.S.
Moderate	221	67.2 (56)	
Excessive	81	63.6 (49)	
Number of burns[§]			
0	174	64.9 (52)	N.S.
1–3	113	64.2 (49)	
>3	22	82.7 (78)	
Use of sunbeds			
No	268	66.0 (54)	N.S.
Yes	42	64.9 (50)	

[§] Missing data one subject, * $p<0.05$

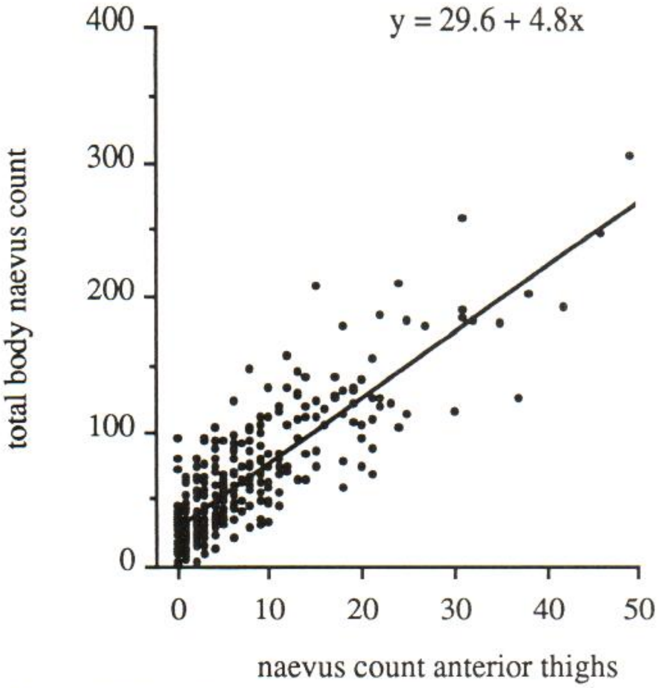

Fig. 3. Correlation between individual total body naevus count and counts on the anterior surface of the thighs.

Site-specific naevus counts predicting total body count

The number of naevi in each area (A-P) was tested for its power in predicting the total body naevus count. In both sexes, there were strong, highly significant correlations between total counts and counts on the anterior surface of the thighs, the lateral aspect of the arms and the back, $p < 0.001$ (corr. coeff. 0.82 –0.88). The anterior surface of the thighs seem to be the most suitable for screening procedures since naevi are easy to count in this area. The anterior surface of the thigh was defined by the proximal edge of the patella, the groins and a demarcation in the middle of the medial and lateral aspects of the thigh. The excellent correspondence between counts on the anterior surface of the thighs and the total body count ($r^2 = 0.72$) is shown by a regression plot (Fig. 3). An even better correspondence was obtained if counts from the anterior surface of the thighs and the lateral aspect of the arms were summed ($y = 12.7 + 2.8x$ # $r^2 = 0.87$).

DISCUSSION

In this study, the role of UV-exposure in the formation of melanocytic naevi has been analysed by investigating the regional naevus distribution.

The classification of the areas (A-P) into different exposure categories was based on clothing habits and general behaviour in the sun. Since some of the analyses were performed on naevus counts per unit surface area, the estimates of area sizes are crucial. The areas H and J on the lower trunk are the most difficult ones to estimate. Therefore, we tested the validity of our conclusions based on data from these two areas. Most important for our conclusions was that the areas H and J were not overestimated. We therefore tested our counts for the possibility that the areas instead of 14% equalled 10% of the body surface. It was reassuring to find that this intentional underestimation did not change our conclusions.

In accordance with others (13,14), we found large concentrations of naevi on the lateral aspect of the arms and on the back. To avoid interference of freckles and solar lentigines, this study was performed during the winter season and all subjects were examined by the same trained dermatologist. In 20 randomly selected subjects, independent naevus counts were performed by another dermatologist. There were no systematic differences in the counts between the two observers and the overall deviation was less than 10%. If it was difficult to differentiate between freckles and naevi, the lesion was not counted. With these precautions, we are convinced that the high counts are close to the true number of naevi in these two areas.

We found that intermittently UV-exposed skin areas had a higher mean naevus count per unit surface area than rarely exposed areas. The lowest mean count was found in chronically exposed skin. Furthermore, subjects reporting more than 3 burns had a higher mean total naevus count than the rest of the sample. Altogether, these findings demonstrate that intermittent UV-exposure has a potent "naevogenic" effect, while chronic exposure seems to be protective. The finding that outdoor workers more regularly exposed to sunlight had lower naevus counts than indoor workers lends further support to the idea that chronic UV-exposure has a protective effect against naevus formation. It might also be possible that chronic exposure in some way stimulates the maturation and/or the disappearance of naevi (6). The rationale for UV-light having both a stimulating and a protective effect on naevus development might be that a slight tan in chronically exposed skin protects from the immediate UV-insults, while the intermittently exposed skin is unprepared. This is interesting in view of the fact that several studies have favoured an association between intense and intermittent UV-exposure and an increased melanoma risk (15,16) while long-term, low-dose UV-exposure seems to be protective (16,17).

No relationship was found between the number of naevi and other anamnestic parameters grading the life-time amount of UV-exposure. It is obvious that data acquired by asking the subject to try to recall the amount of UV-exposure since childhood are unreliable and that comparisons between individual estimates are difficult to evaluate. Information on occupation and several burns is probably the most authentic data. In consistency with data from previous studies on Caucasians, we found differences in naevus patterns between the two sexes (13,14,18). Naevus counts on the trunk were higher in men than in women, while women had more naevi on the face and the lower limbs. This might reflect different clothing habits and/or different behaviour in the sun. The sex difference in naevus distribution is interesting in view of the fact that men have more melanoma on the back than women, while women have more melanoma on the lower legs (13,19).

The regional distribution of dysplastic naevi has previously been described only in subjects with the hereditary form of the dysplastic naevus syndrome (20). In those families, the dysplastic naevi were located predominantly on the trunk. A similar distribution pattern of DN was found in our population sample, where most DN were of the sporadic form. Our finding of few DN on the UV-exposed face and upper chest and many DN in protected areas, such as the buttocks and abdomen, speaks against UV-light as a major etiological factor for DN.

Subjects with DN had, however, a more sun-sensitive skin type and more naevi than subjects without DN. We have recently reported that they also have a larger difference between naevus counts in a sun-exposed area on the back and a sun-protected area on the buttocks (7). Similarly, in this study subjects with DN had a larger difference in naevus counts between intermittently and rarely exposed skin than subjects without DN. This difference was, however, not as pronounced as in the "extreme" areas on the back and buttocks. These findings indicate that subjects with DN are more prone to form CN after UV-exposure, whereas the dysplastic naevi as such seem to develop independent of UV-light.

A large number of naevi is a strong risk factor for developing malignant melanoma. So far, there are few comparable studies on naevus counts from the total body (13,14,18,21). This might partly be due to the fact that total body counts are time-consuming and impracticable to perform. For population studies, it would therefore be of great value to find smaller, well-defined areas predicting total body naevus counts. Such a simplified counting procedure would also be useful for screening purposes, to identify individuals at risk for developing malignant melanoma. English et al demonstrated strong correlations between total number of naevi and counts on each of the upper limbs, the lower limbs and the trunk (21). We studied even smaller areas and found strong correlations between total counts and counts on the anterior surface of the thighs, the lateral aspect of the arms and the back. Unfortunately, it is difficult for non-professionals to differentiate between naevi, freckles and lentigines common on the lateral aspect of the arms. For non-professionals the anterior surface of the thighs therefore seem to be the most suitable area to count. For investigations conducted by medically trained observers we suggest that naevi be counted on the anterior surface of the thighs together with the lateral aspect of the arms to reach even better predictive values of the total body count.

The lack of animal models makes it difficult to get more direct and detailed evidence of the relationship between UV-light and naevus evolution. To obtain further knowledge on the influence of UV-light on the natural history of naevi it will be necessary to perform prospective cohort-studies of naevus distribution in children.

ACKNOWLEDGEMENTS

This investigation was supported by the King Gustaf V Jubilee Clinic Cancer Research Foundation, the Medical Society in Göteborg and the Finsen and Edvard Welander Foundations.

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