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INVESTIGATIVE REPORT

Prevalence of Pigmented Naevi in a Swedish Population Living Close to the Arctic Circle

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The prevalence of common naevi and dysplastic naevi was investigated in a Swedish population with a low incidence of melanoma. A total of 201 subjects aged 30–50 years living in northern Sweden participated. The median number of common naevi per individual was 15, and 11% had dysplastic naevi. Higher numbers of common naevi were found in individuals with dysplastic naevi (median 68) and in those who had spent their childhood in southern Sweden (median 44). The prevalence of common naevi and dysplastic naevi was significantly lower than reported from a previously studied population in southern Sweden, with a melanoma incidence 4 times higher than in the north. The strong variability in naevus phenotype, and in melanoma incidence, between different regions of Sweden seems to be due to different levels of sun exposure rather than to differences in constitutional factors. ***Key words: northern Swedish population; regional variation; sun exposure; systemic effects.***

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Case-control studies from several parts of the world have shown dysplastic naevi (DN) and large numbers of common naevi (CN) to be strong risk factors for malignant melanoma (1–5). In a previous population-based study, the prevalence of CN and DN was investigated in adults aged 30–50 years in Sweden (6). The study was performed in Gothenburg, a city situated on the west coast in southern Sweden (latitude 58° N). The incidence of melanoma in Gothenburg is one of the highest in the country, with a relative risk of 1.3 compared with Sweden in general (7). The median number of CN per individual was 53 (mean 67), and 19% of the individuals had at least one clinically diagnosed DN. This prevalence of CN and DN was surprisingly high, comparable to naevus counts seen in Australia (5), which has a melanoma incidence much higher than in Gothenburg.

In a multinational study (8), the naevus phenotype was investigated in the city of Linköping, at the same latitude as Gothenburg, but in inland Sweden. The relative melanoma risk in Linköping was 1.0 (7). Much lower naevus counts were found in Linköping than in Gothenburg, a median of 23 CN per individual, while the prevalence of DN was the same as in Gothenburg (9). The aim of the present study was to elucidate further the variation in naevus profile in regions with different levels and patterns of sun exposure and different melanoma incidence. The naevus phenotype in the community of Storuman in the northern part of Sweden was investigated and compared with that seen in Gothenburg. Storuman is situated in an area with a short and cold summer, and with a relative melanoma risk of 0.3 compared with the country in general (7).

MATERIAL AND METHODS

Geography and climate

Storuman is situated inland in northern Sweden (latitude 65° N), not far from the Arctic Circle. Its population is 4,000. The summer season, when the mean temperature is at least 10°C, is only 86 days in Storuman compared with 154 days in Gothenburg. The maximum mean temperature in July is 18°C in Storuman compared with 21°C in Gothenburg (10). In northern Sweden, the intensity of ultraviolet (UV) radiation has been estimated at 35–50%, lower than in southern parts (11).

Study base

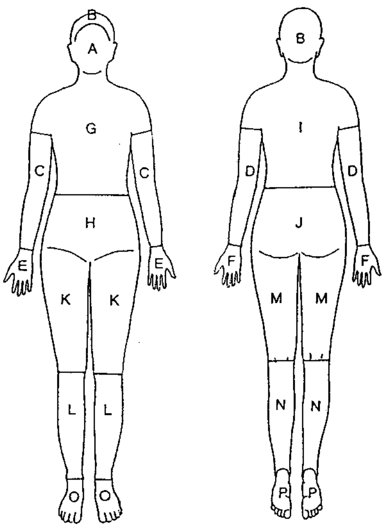
The study design was made as similar to the previous Gothenburg study as possible. Approval was obtained from the local Ethics Committee. In total, 282 inhabitants of the municipality of Storuman aged 30–50 years were randomly selected from the census file. Subjects were invited to participate by letter and one reminding letter was sent to non-responders. A total of 191 (68%) accepted to be examined. Women were more interested in participating than men were, with participating rates of 73% (96/132) and 63% (95/150), respectively. Another 10 subjects were randomly selected from the general practice where the examinations took place. These were local staff and occasional patients sitting in the waiting room and not consulting for skin tumours. Staff or patients who specifically requested to be examined were excluded, in order to avoid any eventual bias. In total, 201 individuals were included, 95 men and 106 women. The mean age at examination was 39.8 years.

Some of the 91 persons who declined examination gave a reason for not participating in the answering letter or by telephone: 17 gave lack of time as a reason, 5 had moved from the area and 6 thought that they had too few naevi.

Counting procedure and questionnaire

All subjects had a full body examination, excluding the genital area. All CN measuring at least 2 mm in diameter were counted. Dysplastic naevi were defined as naevi measuring at least 5 mm in diameter, with a diffuse or irregular border and a mottled or irregular pigmentation (6). The body surface was divided into 16 body sites in the same way as in the Gothenburg study, and the number of CN and DN in each body site was recorded (see Table I) (12). The lower abdomen (area H) and buttocks (J), which are usually covered even when sunbathing, were, together with the medial aspects of the arms (C), considered as rarely UV-exposed. The face (A) and dorsal aspects of the hands (F) were considered as chronically UV-exposed. With the exception of the

Table I. *Median number of common naevi (CN) per individual and body area (body areas from Ref. 12)*



Area		Median number of CN
A	Face	1
B	Scalp	0
C	Arms, medial	0
D	Arms, lateral	2
E	Palms	0
F	Dorsum of hands	0
G	Chest	3
H	Lower abdomen	0
I	Back	5
J	Buttocks	0
K	Thighs, anterior	1
L	Lower legs, anterior	0
M	Thighs, posterior	0
N	Lower legs, posterior	0
O	Dorsum of feet	0
P	Soles	0

scalp (B), palms (E) and soles (P), the rest of the body was considered as intermittently UV-exposed. Such body areas are usually covered by clothes in Sweden's cold climate, and are UV-exposed only intermittently, in the short summer period or on holidays in sunnier climates. The size of each area, expressed as a percentage of the total body surface, was calculated according to Lund & Browder (13) with the same minor modifications as in the previous study (12). The subject's skin type according to Melski et al. (14), hair and eye colours were registered. In connection with the examination, the participants answered a short questionnaire on heredity of melanoma, ethnicity, and occupational and spare-time sun exposure. The subjects were also asked where in Sweden they had spent their childhood. The examinations were conducted in the spring, in the beginning of June 1997 and in April 1998.

One observer (PK) examined all the subjects. One of the authors (IR) had participated in the Gothenburg study. In order to validate the counting technique, IR independently examined 48 of the subjects.

Statistical analysis

The Mann–Whitney *U*-test was used to compare 2 variables and the number of CN per individual. The Kruskal–Wallis test was used to compare 3 variables. Fisher's exact *p*-test was used to compare proportions of individuals with and without DN, and subjects with 100 CN or less. The χ^2-test was used when the proportions of more than 2 categories were compared. Unless otherwise specified, 95% significance levels ($p<0.05$) were used. The numbers of CN in Storuman and Gothenburg were compared using the χ^2-test, with categories of 0–24, 25–49, 50–74, 75–99 and $\geq$100 CN per individual. Agreement between the 2 observers was estimated using the kappa statistic, with the same categories as above.

RESULTS

Total number of common naevi and presence of dysplastic naevi

The median number of CN was 15 naevi per individual (range 0–332) (Fig. 1); 30% had fewer than 10 CN per individual and 6% had 100 or more. One or more DN was present in 11% (23/201) of the subjects. The subjects with at least 1 DN had a higher median number of CN (68 naevi per individual) than those without DN ($p<0.01$). No significant differences in numbers of CN or prevalence of DN were found between men and women or between younger and older subjects when compared in 5 year age groups.

There was a strong agreement between the 2 observers, the kappa value being 0.79 (95% confidence interval 0.59–0.99). The median values of the total body counts of the 48 doubly examined subjects varied slightly, 11 and 12.5. The percentage of individuals with at least 1 DN was assessed as 8% and 10%.

Body distribution of common and dysplastic naevi

Most of the naevi were situated on the trunk (Table I). Men had a significantly higher proportion of their total number of naevi on the back than women (median 35% and 22%, respectively), while women had a higher proportion of their naevi on the legs than men (median 14% and 8%, respectively). The highest concentration of CN for the total

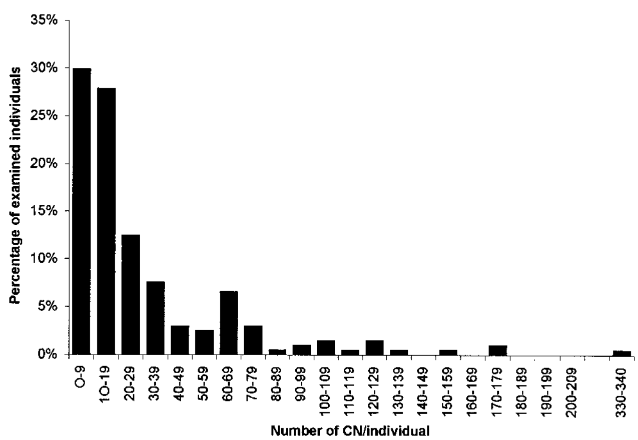


Fig. 1. Distribution of total body naevus counts in the population of Storuman (n= 201). CN: common naevi.

population, calculated as median number of CN/percentage of body surface, was found on the back (0.42), the lateral aspects of the arms (0.40), the face (0.29) and the chest (0.25).

A comparison of the median number of CN/percentage of body surface was also made between body areas in the Gothenburg study defined as intermittently, rarely and chronically UV-exposed (12). In Storuman chronically and intermittently exposed areas had around the same concentration of CN (median 0.17 and 0.20, respectively). The lowest concentration of naevi was found on rarely exposed sites (median 0.05). This was significantly lower than the concentration in intermittently exposed areas, but statistical significance was not reached when compared with chronically exposed areas. In total, 38 DN were found in the study population. These were mainly situated on the back and chest (33/38), and some were found on the lower abdomen and buttocks (4/38).

Pigmentary traits

All participants were Caucasians. One-third had skin type I or II (61/201) and the rest had skin type III or IV. Almost every second individual had dark brown or black hair (91/201) and the majority had blue or grey eyes (156/201). No significant differences in number of CN or prevalence of DN was found with regard to skin type, or hair or eye colour.

Sun exposure

Indoor work was more common than outdoor work (129/201 and 52/201, respectively) while leisure time was mainly spent outdoors (133/201). Common activities were hunting, fishing, snow scooter riding, gardening and open-air life. No significant differences in numbers of CN or prevalence of DN were found between indoor and outdoor workers, but individuals who mainly spent their spare time outdoors had more CN than those who preferred indoor activities (median 18 and 9, respectively; $p<0.05$).

Sixty-two per cent (124/201) of the subjects in Storuman had spent at least 1 week in a sunnier climate, e.g. in the Mediterranean area. Almost half of the population (90/201) had been burnt in the sun with persisting pain for at least 48 h. Only 11 subjects used sunbeds regularly. No significant differences in the prevalence of CN or DN were found with regard to holidays, burns or the use of sunbeds.

Thirteen subjects had spent their childhood in southern Sweden and had moved to Storuman as adults. In this small subgroup there was a clear tendency towards higher numbers of CN per individual than in subjects who were born in northern Sweden (median 44 and 15, respectively; $p=0.08$). This subgroup also had a significantly higher prevalence of DN (31%, 4/13) than the rest of the population ($p<0.05$).

Seven subjects, 6 as adults, had spent at least a year abroad in sunnier countries. No significant differences in the prevalence of CN or DN could be found when this small group of individuals was compared with the rest of the study population.

Ethnicity and heredity of melanoma

Only 3% (5/201) had at least one non-Scandinavian parent. Eight per cent (17/201) reported at least one relative of Saami origin, of whom 4 subjects reported Saami relatives of the first degree. Seven subjects, of whom 4 originated from southern Sweden, reported heredity for malignant melanoma. No significant differences in the prevalence of CN or DN were found with regard to ethnicity or melanoma heredity.

Individuals with 100 or more common naevi

Above, individuals with a specific trait (e.g. heredity of melanoma) were compared with those without this trait (no melanoma heredity) with regard to numbers of CN and presence of DN. In order to study whether there were any specific features that discerned individuals with many CN, the 12 subjects with at least 100 CN were also compared with those with fewer than 100 CN. The subjects with 100 CN or more had a significantly higher prevalence of DN (67%, $p<0.01$) than those with fewer than 100 CN. At a 90% significance level, more had spent a year abroad in a sunnier climate ($p=0.06$) and they had a higher prevalence of dark blond/light brown than dark brown/black hair ($p=0.08$).

DISCUSSION

In Storuman a different naevus phenotype was found to that seen in Gothenburg (6). The population in Storuman had significantly fewer CN per individual than in Gothenburg (median 15 and 53, respectively; $p<0.0001$) (Fig. 2) and the proportion of individuals with DN was smaller (11% compared with 19%; $p=0.05$). These differences are unlikely to be explained by a systematic interobserver bias, as there was a close correlation between the naevus counts of the 2 examiners. In Storuman the examination was for practical reasons limited to a couple of weeks. This was probably the main reason for the participation rate being lower in Storuman than in Gothenburg (68% and 82%, respectively). If this difference systematically affected the results it is more likely that the difference between the 2 populations would have been even larger, as having few or no naevi was a reason for not participating.

Both genetic and environmental factors might be of importance for this difference in phenotype. The ethnic minority of Saami lives in the northern parts of Sweden. The Saamish influence in the region of Storuman has been

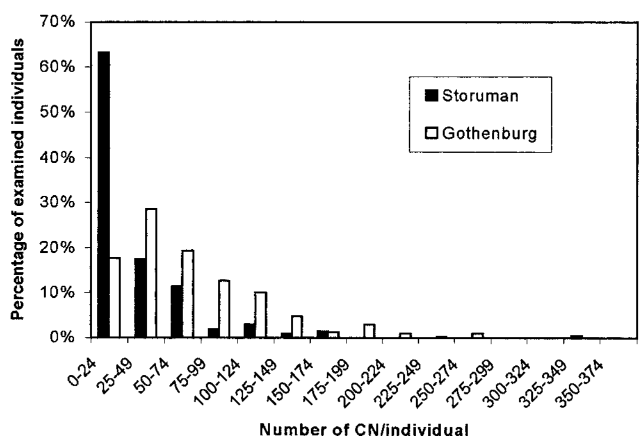


Fig. 2. Distribution of total body naevus counts in the populations of Storuman (n= 201) and Gothenburg (n= 378) (6).

estimated to be 7% by means of genetic markers in blood sample analyses (15). This is in line with the result in the present study, where 8% of the subjects stated that they had Saami relatives. In Gothenburg, in contrast, there was a higher percentage of individuals with non-Scandinavian parents, 8% compared with 3% in Storuman (6). However, neither Saami ethnicity nor non-Scandinavian parentage was associated with any significant difference in naevus counts or presence of DN, and these subgroups were quite small in the studied population. The eye colour was similar in the 2 populations (Storuman 13% green, 65% grey/blue, 21% brown/mixed eye colour; and Gothenburg 15%, 65%, 20%, respectively), as was the proportion of subjects with red or blond hair (Storuman 16%, Gothenburg 22%). Skin types I or II were more common in Storuman than in Gothenburg (30% and 8%, respectively), as was dark brown or black hair (45% and 16%, respectively). None of these pigmentary traits significantly affected the presence of CN or DN in the 2 studies. Based on these findings it was concluded that the differences in genetic pigmentary traits between the 2 populations were not the main reason for the difference in naevus phenotype found.

The UV radiation in Gothenburg in southern Sweden is more intense and the summers are longer than in Storuman. Sailing, swimming and other activities with the body exposed to the sun are more common in Gothenburg than in Storuman, where the body usually is also covered by clothes in leisure time. Furthermore, people in Gothenburg went on holidays to sunnier countries more frequently than people did in Storuman. In Storuman 62% had at least spent 1 weak in a sunnier climate compared with 89% in Gothenburg. Regular use of sunbeds was more common in Gothenburg than in Storuman (14% and 5%, respectively). In the Gothenburg study there was also a higher proportion of individuals with predominantly indoor work (76% and 64%, respectively). In Gothenburg these individuals had higher numbers of CN than outdoor workers (6), a difference which was not noted in Storuman. This difference in UV exposure is probably of major importance for the differences in naevus phenotype found between the 2 populations in Gothenburg and Storuman.

Interestingly, a small subgroup of individuals in Storuman who had spent their childhood in southern Sweden had a naevus profile similar to the Gothenburg population, with high naevus counts and a high prevalence of DN. This would support the findings in other studies that sun exposure in childhood is of major importance for naevus formation (16). In the 12 subjects with more than 100 CN the proportion of subjects who had lived abroad in a sunnier climate was higher than expected. This lends further support to the concept that UV exposure leads to the development of CN. It might seem confounding that no significant difference was found in numbers of CN when the subgroup of individuals who had spent a year abroad was compared as a whole with those who had not. This could be explained by the large interindividual variation in numbers of naevi, and by the subgroup studied constituting too small a sample size (β-error) to reveal a significant difference.

Chronically UV-exposed areas had fairly the same concentrations of naevi in both populations (Storuman median 0.17 CN/percentage of body surface; Gothenburg men 0.17, women 0.33, unpublished data). In contrast to the findings in Gothenburg, where intermittently exposed areas had the highest concentration of CN (men 0.64, women 0.61), chronically and intermittently UV-exposed areas had around the same low concentration of CN in Storuman (0.17 and 0.20, respectively). A probable explanation for this is that most subjects in Storuman were simply not intermittently exposed enough in these areas due to the cold climate and short summer. If so, their low numbers of CN and their distribution over the body surface would represent a more basic naevus phenotype than in the Gothenburg population.

In Gothenburg the subjects had higher concentrations of CN in rarely exposed areas than in Storuman (0.42 and 0.05, respectively). CN in unexposed areas has been considered to be genetically determined. However, it may be hypothesized that UV radiation can also influence the number of CN in covered body sites. It is speculated that intensive UV radiation can systemically promote naevus development. Previous studies have demonstrated that UV radiation induces melanocyte proliferation not only in irradiated areas but also in covered skin areas (17). Therefore, it is conceivable that naevus formation can be stimulated not only by direct local UV insults, but also through more indirect mechanisms. Immunosuppression has been shown to induce the development of CN (18, 19) and UV radiation has not only local, but also systemic immunosuppressive effects (20).

In Linköping, the number of CN per individual (median 23) was closer to that in Storuman, while the prevalence of DN (18%) was as high as in Gothenburg (9). In the multinational study, the subjects were randomly selected from a general practice. However, the different study design is unlikely to have affected the results to any higher degree. If a linear relation existed between numbers of naevi, prevalence of DN and melanoma incidence, one would expect a higher median number of CN and a lower prevalence of DN in Linköping as the melanoma incidence in Linköping was higher than in Storuman but lower than in Gothenburg. However, the relationship of naevus prevalence to melanoma incidence in a population seems to be more complex than that.

In conclusion, there is a strong variability in naevus phenotype in different regions of Sweden. In northern Sweden, where the UV exposure and melanoma incidence are low, the population has few CN and DN compared with the population in southern Sweden, where the UV exposure and melanoma incidence are higher. These results are consistent with the hypothesis that UV exposure is a common aetiological factor for both naevus formation and melanoma development. Fewer naevi occurring in unexposed skin areas in the northern population is in keeping with the idea that UV exposure also promotes naevus formation systemically.

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