

The Evaluation of Possible Melanoma Risk Groups of Patients in a Series of Pigmented Naevi

Clinical and Histological Intercorrelations

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The trends of the clinical/histological intercorrelations in two series of pigmented naevi have been compared. One series of naevi represents patients who are habitual sunbathers and/or who have travelled to Southern sunny climates. The other series includes naevi from easily sunburned patients. The sunburner-group is correlated to histological features such as mitoses, atypia and fibrosis of the tumour as well as to an irregular/atypical tumour type. Such trends are not found in the other target group. The sunburners have a poor ability to suntan, while the sunbather group includes good suntanners. This indicates the importance of the melanin UV-filter effect of the skin as a protection against the promotion of potential MM-precursors, such as irregular/atypical naevi. (Received July 3, 1987.)

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In an earlier paper a series of 577 patients presenting with an equal number of pigmented naevi was discussed (1). The blind histological classification of regular, irregular and atypical naevi as well as the correlations between histological and clinical variables were described in detail, while a later paper discussed seasonal variations (2). Travelling to sunny regions has been found to be related to the risk of developing malignant melanoma (MM) (3, 4) as have previous episodes of sunburn (5, 6). The present study proposes a more detailed examination of those patients considered at risk, either because of previous exposure to large doses of natural UV light, or a propensity to sunburn easily.

MATERIAL AND METHODS

Selection of the series

The present paper deals with two groups of patients from the original series: The 'sunbather/traveller-group' includes patients who claimed to be habitual sunbathers and/or have travelled to Southern Europe, the Middle East, Africa or other sunny areas on a 'sun vacation' since September 1st, 1983. The 'sunburn-group' includes patients who claimed to have a high tendency to sunburn. Patients who have used a solarium since September 1st, 1983, were excluded from both these target groups. In addition, patients who have claimed to 'always' use a sun-cream are excluded from the sunbather/traveller-group, while patients who have been on a 'sun vacation' are excluded from the 'sunburn-group'. These exclusions reduced the total original series from 577 to 163 patients.

Clinical information

This was obtained by sending a questionnaire to the patients, of whom 84% responded. The following clinical features were recorded: sex, age, hair and eye colour, freckles, suntan ability, tendency to sunburn, habitual sunbathing, use of sun filter creams, tumour duration and localization and reason for tumour excision including warning signals such as tumour growth, change of colour and itching.

Many sunbathers use different sun-creams containing varying combinations of UV-filter substances during the summer season. No detailed specification of the contents of these substances used by the

patients of the present series, was requested. The assessment of the effect of the use of sunscreens is limited by the inability of some patients to recall, months later, the frequency of use and the type of sunscreen used. Therefore, the results as regards use of sun creams are of a limited value in this study.

Histological evaluation

This was made without access to any clinical information. The following histological variables were recorded: Tumour type (regular, irregular and atypical), growth pattern (intra-epidermal and compound), lentiginous melanocytic growth at the epidermal basal layer, number of involved epidermal rete ridges, tumour diameter, upward intra-epidermal melanocytic progression, hypertrophic melanocytes at the epidermal basal layer, nuclear atypia, mitoses, epidermal pigmentation, dermal melanophages, subepidermal fibrosis, lymphocyte reaction, tumour cells in the dermal papillae, tumour regression, 'shoulder' phenomenon and surface protrusion. Definitions of terms and grading have been described elsewhere (1).

Statistical methods

The association of both target groups with the clinical and histological variables has been assessed by χ^2 -tests. In these tests the *sunbather/traveller group* is compared with a control group of the remaining patients from the original series with the same exclusions as concerns this target group. The *sunburn group* is compared with those remaining cases of the original series who have a low tendency to sunburn with in addition the same exclusions as concerns this target group. Only the significant correlations will be discussed. The terms 'correlated' and 'correlation' indicate a significant relationship in this paper. The terms 'slightly', 'moderately' and 'strongly' correlated indicate the following *p*-values: <0.05 , ≤ 0.01 and <0.001 . The procedure of testing a vast number of hypotheses has not been subjected to any kind of adjustment for multiple comparisons. The analysis is thus of an explorative nature and the *p*-values should be interpreted with care.

The series

The sunbather/traveller group included 130 patients, of whom 88 (68.2%) are habitual sunbathers, and 66 (50.8%) have been on a sun vacation (18 of whom on several occasions), while 24 (18.5%) fulfil both criteria. In summary, 27.3% of the habitual sunbathers are also travellers, and 36.4% of the travellers are also habitual sunbathers. The respective control group included 266 cases. The sunburn group included 37 patients all of whom are non-travellers. The remaining control group included 120 cases. Four patients fulfilled the criteria for inclusion in both target groups being habitual sunbathers as well as having a strong tendency to sunburn.

RESULTS

The sunbather/traveller-group

This target group included 130 patients of whom 93 (71.5%) are women and 37 (28.5%) are men. This is (almost significantly) more women than in the control group ($p=0.051$). The age distribution of the patients and the localization of the tumours are shown in Tables I and II. These findings do not differ significantly from the findings in the control group. A good suntanning ability was found in 45.5% of the 88 habitual sunbathers and in 37.9% of the 66 travellers. Only 7 (5.4%) of all 130 patients are poor suntanners and 4 of these have a tendency to sunburn. This is significantly fewer cases than what is found in the control

Table I. Age distribution

	Age	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	Total
Sunbather/ trav. group	<i>n</i>	2	25	50	27	11	10	4	1	130
	%	1.5	19.2	38.5	20.8	8.5	7.7	3.1	0.8	100.0
Sunburn group	<i>n</i>	2	7	9	11	2	3	3	0	37
	%	5.4	18.9	24.3	29.8	5.4	8.1	8.1	0	100.0

group (Table IV). Sun-creams have been used intermittently by 83.3% of the 130 patients. Among the histological variables there are 12 (9.2%) intra-epidermal and 118 (90.8%) compound naevi in this target group. Neither this prevalence nor the tumour type differed significantly from the control group (Table III). The only significant findings involve the correlations of the target group with the presence of hypertrophic melanocytes and of few necrotic cells in the basal layer (Table IV).

The intercorrelations of the clinical and histological features within this target group

Table II. Localization

Region		Head/ neck	Upper extr.	Lower extr.	Back	Rest of trunk	Total
Sunbather/ trav. group	<i>n</i>	22	8	15	52	33	130
	%	16.9	6.2	11.5	40.0	25.4	100.0
Sunburn group	<i>n</i>	2	3	6	17	8	36 ^a
	%	5.6	8.3	16.7	47.2	22.2	100.0

^a Localization is unknown in 1 case.

Table III. Tumour type

Tumour type		Regular	Irregular	Atypical	Total
Sunbather/ trav. group	<i>n</i>	88	38	4	130
	%	67.7	29.2	3.1	100.0
Sunburn group	<i>n</i>	18	16	3	37
	%	48.7	43.2	8.1	100.0

Table IV. The trends of the two target groups as compared with the respective control group by χ^2 -tests

The significant *p*-values are shown

Variable	Sunbath./trav. group		Sunburn group	
	Trend	<i>p</i> -value	Trend	<i>p</i> -value
Habitual sunbathing	Yes	<0.001	No	0.005
Sun vacation	Yes	<0.001	(excluded)	
Ability to suntan	Good	<0.001	Poor	<0.001
Tendency to sunburn	Low	<0.001	High (all)	<0.001
Freckles	X ^a		Yes	<0.001
Hair colour	X		Red/fair	<0.001
Eye colour	X		Blue/grey	0.044
Tumour type	X		Irreg./atyp.	0.030
Atypia	X		Present	0.025
Mitoses	X		Present	0.023
Fibrosis	X		Present	0.024
Hypertrophic melanocytes	Present	0.001		X
Necrotic cells in BL	Present	0.043		X

^a No significant trend.

have been studied by χ^2 -tests. Most of the findings are similar to those of the previous study (1). Some new trends are noted (for p -values, see Table V): A good suntanning ability is correlated to habitual sunbathing and to non-use of sun-creams. Furthermore, the latency time from a sun vacation to tumour excision is shorter among the travellers who are not habitual sunbathers, compared with those who are (latency time of <3 months and 4–6 months, respectively). Warning signals are correlated slightly to tumour excision during the late summer and early autumn months of July–September, while the travellers are correlated to tumour excision during the months of July–December. Finally, with regard to the histological variables, those patients who are not habitual sunbathers (but travellers) are correlated to all grades of lymphocyte reaction, while the sunbathers are correlated to a moderate heavy pigmentation of intraepidermal cells (epithelial and neoplastic).

The sunburn group

This target group includes 21 (56.8%) women and 16 (43.2%) men. The sex and age distribution and the tumour localization in this group are not significantly different from those in the control group (Tables I and II). The sunburners include 21 (56.8%) patients with a poor suntanning ability and, surprisingly, 1 patient who suntans easily. The number of poor suntanners is significantly higher than in the control group, as is the number of patients with freckled skin, red or fair hair and blue or grey eyes (Table IV). As mentioned previously, only 4 patients are habitual sunbathers, which is significantly fewer than that found in the control group (Table IV). Sun creams have been used intermittently by 25 patients and regularly by 8 patients. Finally, as regards the histological variables this target group includes 4 (10.8%) intra-epidermal and 33 (89.2%) compound naevi. This prevalence is almost identical with that in the control group. There are, however, significantly more irregular and atypical naevi among the sunburners than in the control group (Tables III, IV). This is explained by the correlation of mitoses, cellular atypia and stromal fibrosis to the sunburn group (Table IV). This target group is considered to be too small for the study of any intercorrelations between the variables within the group.

DISCUSSION

The sunbather/traveller group represents patients, who are assumed to have been exposed to large doses of UV light. The habitual sunbathers appear to possess the ability to achieve the desired suntan easily without getting sunburned (Table V). Relatively many of these

Table V. *The correlations of the clinical and the histological variables within the sunbather/traveller group*

The significant p -values are shown

Pair of variables	p -values
Habitual sunbathing/suntanning ability	0.029
Habitual sunbathing/use of suncreams	0.029
Habitual sunbathing/tendency to sunburn	0.021
Habitual sunbathing/time from a vacation to tum. excis.	0.025
Habitual sunbathing/lymphocyte reaction	0.043
Habitual sunbathing/intraepidermal pigmentation	0.017
Warning signals/season for excision	0.026
Sun vacation/season for excision	0.008

patients do not use any sun-creams, probably because they do not feel a need for protection against sunburning (Table V). The travellers in the group seem to have a more varied skin type than the sunbathers. Only 36.4% of the travellers claim the habit of regular sunbathing. It is interesting that the ability to produce melanin among the sunbathers is demonstrated by a relatively high grade of intra-epidermal pigmentation at the tumour site (Table V). As this pigmentation includes the tumour cells, this trend may indicate that habitual sunbathing leads to a pigmentary darkening of the naevi, as described elsewhere (1).

Even though the sunbather/traveller-group represents a group of highgrade UV-exposed patients, the correlations to histological variables are unremarkable and do not include tumour type or any variables correlated to this (1). Nevertheless, the significant finding of scattered hypertrophic melanocytes along the basal layer in these patients may indicate some photoactivation (Table IV). The exposure of the skin to large doses of UV light is likely to be correlated to a short latency period as regards tumour promotion. This contention, which is discussed in another paper (2) is further supported by the present trend of a latency time of <3 months to 6 months from a sun vacation to subsequent tumour excision among the habitual sunbathers. The fact that tumour excision in the travellers group occurred during the months of July–December corresponds well to the habit of some Norwegians who travel to sunny areas during the winter, the spring and the summer seasons.

The sunburn group includes patients who are not habitual sunbathers and have not travelled to especially sunny areas. The low number of sunbathers in the group is probably explained by the easily sunburned and poorly suntanned skin type of these patients (Table IV). The correlations to the histological variables of cellular atypia, mitoses, fibrosis and tumour type (Tables III, IV) indicate that sunburners are especially susceptible to development of irregular/atypical naevi, which may be suspected to be potential MM precursors (1, 7, 8). These trends underline the protective value of a natural melanin UV-filter in the epidermis and corresponds well to the finding of a low incidence of MM among individuals with a pigmented skin type (9). It is, however, still a point of contention as to whether it is the reduced UV-filter effect due to a deficiency of melanin or the actual episodes of sunburn which predispose to the development of MM. Episodes of sunburn are correlated with the risk of developing MM in some studies (5, 6). One study has, however, using regression analysis, shown that fair/red hair and blue eye colour as well as a poor tanning ability, i.e. genetically related features, are more important predisposing features than episodes of sunburn in the development/activation of naevi (10).

In the present study of sunburners, information regarding the occurrence of the last episode of sunburn prior to tumour excision is not available. Therefore, this study cannot fully evaluate the question about the importance of sunburn and the need of a prospective study with personal interviews with the patients is obvious. Furthermore, the sunburn group includes 8 patients who claim to have used sun-creams regularly. Among these, 4 irregular naevi were found. As indicated early in this paper, the value of this information is, however, limited. The question about the efficacy of UV-filter creams as a protection against the induction of MM-precursor lesions ought to be studied prospectively.

CONCLUSION

A comparison of the trends in the two target groups in this study (Table IV) indicates that 'sunburners' associated with a non-habitual exposure to UV-light are more likely to develop irregular/atypical naevi, than are habitual sunbathers and 'travellers' exposed to relatively larger UV doses. In the present study the importance of sunburn episodes for

this trend is unknown. The latter would appear to be related to the different skin types of these patients, as the sunburners, unlike the sunbathers, are poor suntanners. The travelers in this respect show no correlation to any special skin type in this study.

The correlation of the irregular/atypical naevi to the group of sunburners illustrates the importance of a sufficient cutaneous UV-filter and supports the theory that these naevi are potential MM-precursor lesions. Most of them will probably not proceed to the stage of malignancy (8). However, the incidence of MM is still increasing (11). Patient orientation is therefore important, and caution is advised for those individuals with UV-sensitive skin. UV-filter creams are recommended, especially for the poor suntanners. The manner in which these creams are used as well as their actual value as a protection against the development of MM-precursor lesions requires further investigation, however.

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