Demographic Study of Clinically Atypical (Dysplastic) Nevi in Patients with Melanoma and Comparison Subjects


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ABSTRACT

We examined 296 patients with a history of melanoma and 145 controls for the presence of atypical (dysplastic) nevi. We found that 34% of patients with melanoma and 7% of controls had clinically atypical (dysplastic) nevi. Patients and controls with atypical (dysplastic) nevi had more nevi than the subjects without. The number of nevi varies negatively and significantly with age ($r = -0.37, P < 0.001$). Ten % of patients and controls had hypopigmented halos around one or more nevi. Both patients and comparison subjects with atypical (dysplastic) nevi tended to have this subtle variant of halo nevi more often than those without ($r = 0.17, P < 0.01$). The number of nevi on the irides of melanoma patients was greater than that in the comparison group. The results of this study suggest that patients with a melanoma exhibit more commonly cutaneous and ocular pigmented lesions than comparison subjects without a melanoma.

INTRODUCTION

It is accepted that a nevocellular nevus may undergo transformation into a melanoma. In the last 5 years, Clark et al. (1–3) have described several kinships in which family members had large numbers of clinically atypical moles associated with multiple primary melanomas, the so-called BK mole syndrome. Similar unusual nevi associated with melanomas have been observed by other investigators in patients with (4, 5) or without (6) a familial history of similar cancers. More recently, the term dysplastic nevus syndrome has been proposed to describe both the familial and nonfamilial variant of these atypical nevi associated with melanoma (7).

Less is known about the frequency of atypical (dysplastic) nevocellular nevi in patients with nonfamilial melanomas, the frequency of these lesions in the general population, the effects of age and sex on the number of atypical (dysplastic) nevi visible on the integument, and the association of nevi with other pigmented lesions like halo nevi or nevi on the irides. To gather this information, we have examined the skin and eyes of 296 patients with documented melanoma and 145 controls. Biopsies of 81 clinically atypical nevi were obtained from 48 patients. This report described results of the clinical and demographic studies.

MATERIALS AND METHODS

Terminology

The nevi first described by Clark in the BK mole syndrome (1–3) currently are labeled dysplastic nevi (1–3). Dysplastic is a pathological term. This study was a clinical evaluation of pigmented lesions on skin of patients with melanomas. In this paper, we label the unusual nevi as atypical rather than dysplastic. We briefly report the dysplastic features observed microscopically in 81 biopsies from 48 patients. In a separate report, the histological features of these lesions will be reported in greater detail.3

Patients

Two hundred ninety-six patients from the Melanoma Unit of the Sydney Hospital, Sydney, Australia, most of whom were of English, Welsh, or Irish descent, were invited to participate in this project. Patients were questioned about their ethnic ancestry. Patients were selected because they lived within several hours’ driving time to the hospital. Each patient’s entire integument was examined by a dermatologist, an oncologist, and a clinical nurse specialist. Nevis counts were made by any one of the team. A difficult lesion was evaluated by all three investigators, and a consensus was reached about the clinical diagnosis. Each patient had a complete ocular examination by an ophthalmologist. The ophthalmological examination included measurement of the visual acuity, slit lamp examination, an external count of the nevi on the irides, and direct and indirect ophthalmoscopic examination through dilated pupils with recording of choroidal nevi.

Nonmelanoma Subjects

One hundred forty-five subjects served as a comparative control group. The single criterion for exclusion from the control group was past or present diagnosis of melanoma. One hundred patients hospitalized at Sydney Hospital on the medical and surgical wards participated. No patients on any ward refused participation. These patients had been admitted for a variety of injuries and illnesses. Prisoners incarcerated in a local prison were asked by prison officials to volunteer to have their skin and eyes examined. No inducements were offered. Forty-five individuals volunteered. Prison officials were entirely responsible for recruiting the volunteers. They arranged for the examination by the investigators on a preset day within the hospital prison. Most control subjects were of English, Welsh, or Irish ancestry.

The nonmelanoma group in the hospital and prison were selected for their convenient location accessible to the examining team. The study was designed to compare the frequency of pigmented abnormalities in the skin and eyes of patients with melanoma to the frequency of these lesions in subjects without melanoma. Therefore, the data from the 2 comparison groups were compiled together.

3 J. Nordlund et al., manuscript in preparation.
DEMEOGRAPHIC STUDY OF CLINICALLY ATYPICAL NEVI

Nevi

Typical Nevi. Normal or typical nevi were defined as pigmented macules or papules which were round or oval. The margins were regular. The colors ranged from dark brown, most commonly observed in macular Nevii macules or papules which were round or oval. The margins were regular. The distribution of color patterns was not haphazard. Depigmented areas or outer edges may have been lighter or darker than the center, but the were arbitrarily considered to be normal. Size has been one criterion of atypicality (1–8).

The number of typical or atypical nevocellular nevi on the integument of each patient was determined by counting pigmented nevii visible by inspection of the patient lying in bed. Pigmented lesions of nonmelanocytic origin, like seborrheic or actinic keratoses, were not included.

Atypical Nevi. Clinically atypical nevi all had one of the following 3 characteristics: one diameter greater than 5 mm; irregular borders; and haphazard coloration (1–8). Atypical nevi in this study exhibited a variety of shades of black, brown, and reddish-brown. Often, there was an erythematous margin or border around all or part of the lesion. The erythema blanched on diascopy in some but not all lesions. The topography of lesions was variable, i.e., flat, minimally raised, or elevated. Patients with large atypical nevocellular nevi usually also had nevi with diameters less than 5 mm. Many of these smaller nevi also had irregular outlines and colorations. Because of their size, they were considered clinically to be normal.

Statistical Analysis

Data on age and sex of patients, stage and thickness of the melanomas, the numbers of normal or atypical nevocellular nevi, and halo nevi and iris nevi were recorded on standardized forms. Data were coded for computer analysis. The mean, median, standard deviation, standard errors of the mean, and other descriptive data were determined for each variable. Data from patients were compared to those from controls, and the significance of difference was determined by Pearson correlations, χ², and Student’s t- and z-tests.

The age of the individuals seems to have a significant influence on the presence or absence of pigmentedary lesions. Therefore, the data from 145 nonmelanoma subjects was compared to 145 randomly selected age-matched melanoma patients. In a separate analysis, the 145 patients in the comparison group was compared to 145 sex-matched patients of identical or similar ages. The results of these analyses are reported in the text.

RESULTS

General Characteristics of Patient and Control Subjects

The age range for patients with melanoma was 13 to 86 years. The mean and median ages of this group were 49 and 50 years, respectively. The age range of the control subjects was 18 to 88 years, and the mean and median ages were 46 and 47 years, respectively. The difference between the ages of the patients and controls was not statistically significant. There were 92 (66%) males in the control group compared to 151 (51%) in the patient population. This difference is significant (χ² = 8.42; P < 0.01). It should be noted that 7% of the patients had a history of one or more first-degree family members with a melanoma.

Prevalence of Clinically Normal or Atypical Nevocellular Nevi

The entire integument of 296 patients with a documented melanoma and 145 comparative subjects was examined for the presence of clinically normal or atypical nevi. For a nevus to be considered clinically atypical, it had to exhibit all of the following features: a diameter greater than 5 mm; an irregular border; and haphazard pigmentation. Smaller nevocellular nevi or those with a regular border or a homogenous color were considered clinically normal. Patients and comparison subjects were grouped into arbitrarily selected categories according to the number of atypical nevi: none; 1 to 3; 4 to 6; 7 to 10; 11 to 20; or more than 20.

The total number of nevocellular nevi (normal plus atypical) was also assessed. Subjects also were grouped into arbitrarily designated groups by the total number of their nevi: 0 to 15; 16 to 30; 31 to 45; or more than 45 nevi. Ninety-three (34%) of the 268 patients with a melanoma had one or more clinically atypical nevi (Table 1). Ten (7%) of 140 controls had similar lesions. This difference in the prevalence of clinically atypical nevi between the patient and comparison groups was significant (P < 0.001; χ² = 34.74). The prevalence of atypical nevi in 145 melanoma and age-matched comparison subjects was determined. Thirty-seven percent of melanoma patients and 7% of the age-matched comparison subjects had atypical nevi (P < 0.001; χ² = 35.58). Thirty-six percent of melanoma patients and 7% of the sex-age-matched comparison subjects had atypical nevi (P < 0.001; χ² = 34.16).

The average number of clinically atypical nevi per individual was determined. The 90 melanoma and 10 comparison subjects each had a mean of nine clinically atypical nevi (Table 2). Some subjects in both patient and control groups exhibited a single lesion, while others had dozens of atypical nevi. Thirty-four of the 90 patients with both a melanoma and atypical nevi had between one and 3 atypical nevi, compared to one of the 10 comparison subjects. It appears that the number of atypical nevi per individual was similar for both the melanoma and comparison patients.

### Table 1

Number and percentage of subjects with clinically atypical nevi

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<tr>
<th>Atypical nevi</th>
<th>Present</th>
<th>Absent</th>
<th>Subtotal</th>
<th>Data missing</th>
<th>Total</th>
<th>% of subjects with atypical nevi</th>
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<td>178</td>
<td>268</td>
<td>28</td>
<td>296</td>
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<td>Controls</td>
<td>10</td>
<td>130</td>
<td>140</td>
<td>5</td>
<td>145</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>308</td>
<td>408</td>
<td>33</td>
<td>441</td>
<td>100</td>
</tr>
</tbody>
</table>

### Table 2

Number of atypical nevi observed in patients and control subjects

<table>
<thead>
<tr>
<th>Atypical nevi</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
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</thead>
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<td>0</td>
<td>178</td>
<td>66</td>
<td>130</td>
<td>93</td>
</tr>
<tr>
<td>1–3</td>
<td>34</td>
<td>13</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4–6</td>
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<td>11–20</td>
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<td>1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>296</td>
<td>145</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean no. of atypical nevi on affected subjects</td>
<td>9</td>
<td>9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DEMOGRAPHIC STUDY OF CLINICALLY ATYPICAL NEVI

...the total number of nevocellular nevi clinically normal plus atypical was determined for each patient and for each comparison subject. Patients and comparison subjects were divided into arbitrary groups with 0, 1 to 6, or more than 6 atypical nevi. The number of atypical nevi was compared to the total of nevi for each individual (Table 4). Patients and comparison subjects without atypical nevi tended to have fewer total nevi. However, patients with atypical nevi appeared to have a greater total number of nevi than did controls (P < 0.001). Similar results and a statistical significance was obtained comparing the 145 age-matched melanoma and control subjects with and age-sex-matched groups.

Table 3

| Patients versus controls: χ² = 8.78; P < 0.05. |
|-----------------|-----------------|
|                | Patients        | Controls        |
| Total nevi     | No.  | %    | No.  | %    |
| 0-15           | 121  | 42   | 77   | 54   |
| 16-30          | 52   | 18   | 23   | 16   |
| 31-45          | 48   | 17   | 11   | 8    |
| >45            | 67   | 23   | 32   | 22   |
| Subtotal       | 286  | 100  | 143  | 100  |
| Data missing   | 8    | 2    | 2    | 2    |
| Total          | 296  | 100  | 145  | 100  |

Table 4

| Patients versus controls: atypical nevi (0, 1 to 6, >6) versus total nevi (0 to 30): χ² = 16.03; P < 0.001; atypical nevi (0, 1 to 6, >6) versus total nevi (more than 30): χ² = 17.77; P < 0.001. Patients: total nevi (0 to 30 versus >30): χ² = 54.56; P < 0.001. Controls: total nevi (0 to 30 versus >30): χ² = 15.31; P < 0.001. |
|-----------------|-----------------|
| Total nevi      | No.  | %    | No.  | %    |
| 0-30            | 134  | 61   | 76   | 39   |
| >30             | 42   | 26   | 18   | 11   |
| Total           | 176  | 100  | 94   | 100  |
| Patients        | No.  | %    | No.  | %    |
| 0-30            | 97   | 88   | 44   | 45   |
| >30             | 33   | 27   | 17   | 15   |
| Total           | 130  | 100  | 61   | 100  |
| Patients        | No.  | %    | No.  | %    |
| 0-30            | 38   | 34   | 19   | 18   |
| >30             | 6    | 6    | 3    | 3    |
| Total           | 44   | 100  | 22   | 100  |
| Patients        | No.  | %    | No.  | %    |
| 0-30            | 99   | 99   | 41   | 41   |
| >30             | 10   | 10   | 5    | 5    |
| Total           | 109  | 100  | 46   | 100  |
| Patients        | No.  | %    | No.  | %    |
| 0-30            | 286  | 100  | 145  | 100  |
| >30             | 22   | 8    | 10   | 4    |
| Total           | 308  | 100  | 155  | 100  |

Table 5

| Effect of age on the total number of nevi per subject clinically normal plus atypical |
|------------------------------------------|-----------------|
| Patients versus controls over 49: χ² = 12.98; P < 0.01. Controls: χ² = 0.06; not significant. |
|------------------------------------------|-----------------|
| Patients                                | Controls        |
| Total no. of nevi <50 yr (no./%)         | >49 yr (no./%)  |
| 0                                        | 77/57           | 101/75          |
| 1-6                                      | 28/21           | 23/17           |
| >6                                       | 29/22           | 10/8            |
| Subtotal                                 | 134/100         | 134/100         |
| Missing                                  | 28              | 7               |
| Total                                    | 296             | 145             |

Table 6

| Effect of age on the total number of nevi per subject clinically normal plus atypical |
|------------------------------------------|-----------------|
| Patients versus controls over 49: χ² = 4.57; P < 0.05. Controls: χ² = 0.06; not significant. |
|------------------------------------------|-----------------|
| Patients                                | Controls        |
| Total no. of nevi <50 yr (no./%)         | >49 yr (no./%)  |
| 0                                        | 66/46           | 107/74          |
| >30                                      | 77/54           | 38/26           |
| Subtotal                                 | 143/100         | 145/100         |
| Missing                                  | 8               | 4               |
| Total                                    | 296             | 145             |
had 15 or fewer nevi (Chart 1). The percentage of patients and controls with 16 to 44 nevi remain relatively constant for all age groups.

The controls also were divided into two groups: those 50 years and older and those 49 years and younger. The comparison subjects in the younger group had more total nevi than the older subjects \( P < 0.05; \chi^2 = 4.57 \). The relationship of age and frequency of atypical nevi in the comparison group could not be analyzed because of the paucity of comparison subjects with such lesions.

Histopathology

A biopsy from 94 lesions from 51 patients was obtained and sent for histopathological examination. Six of these were considered to be a melanoma and were not included in our analysis of histopathological features of clinically atypical nevi. Seven other lesions clinically were thought to be blue nevi, solar lentigines, or seborrheic keratoses. Biopsies were taken to confirm the diagnosis and to reassure the patients that they had neither a second primary tumor nor metastases.

The histological features of 81 clinically atypical lesions were determined. Seventy-five (93%) exhibited lentiginous hyperplasia of the epidermis. Sixty-seven (83%) had moderate to marked increased numbers of atypical nevus cells within the epidermal basal layer. Thèques of nevus cells were considered irregular in morphology in 47 (60%). Seventy-three (90%) had a lymphohistiocytic infiltrate and pigment incontinence. Although all 81 biopsies were taken from clinically atypical nevi, 6 (7%) lesions did not exhibit histological features that were sufficiently abnormal to distinguish them from a normal nevus.

Melanoma Patients
Control Subjects

Nevi with Hypopigmented Halos

Each patient was first examined with fluorescent/incandescent lighting and then with a Wood’s lamp. A few patients had classical halo nevi easily visible by simple inspection. However, under Wood’s lamp, 10% of patients with melanomas and 10% of the control subjects were observed to have hypopigmented halos around one or more nevi. The Wood’s lamp accentuated the hypopigmentation. The number of nevi with hypopigmented halos per patient or comparison subject was similar. No comparison subject had more than 12 such lesions. One melanoma patient had 15, another had 37, and a third had 46 such halo nevi. None of these lesions was excised for histopathological examination.

The relationship of hypopigmented halos around nevi and other pigmented lesions was analyzed statistically. Patients with atypical nevi tended to have halos around nevi more often than did patients without atypical nevi \( P < 0.001; \chi^2 = 11.34 \). The more atypical nevi a subject had, the more likely he was to have one or more halo nevi \( P < 0.001; \chi^2 = 11.51 \) (Table 7). Comparison subjects with atypical nevi were more likely to have halos than were the other nonmelanoma controls \( P < 0.01; \chi^2 = 11.88 \). This analysis was repeated with the age-matched and age-sex-matched melanoma and control populations. The results also indicate that halos around nevi are more prevalent in patients with atypical nevi (age-matched, \( P < 0.05; \chi^2 = 4.79 \); age-sex-matched, \( P < 0.05, \chi^2 = 7.83 \)). Nevi on the iris, as well as nevi on the choroid and conjunctiva, did not exhibit a statistical correlation with the presence of halo around nevi on the skin.

Ocular Pigmentary Abnormalities

Iris Nevi. The number of nevi on the irides was counted by inspection of the eyes of 239 patients and 144 controls without the aid of a slit lamp. Iris nevi were defined as tan or brown minimally raised spots. Their shapes were oval or irregular. Melanoma patients had light-colored irides. The total number of iris nevi was significantly greater in melanoma patients than in controls \( P < 0.01; \chi^2 = 19.90 \) (Table 8). The mere presence or absence of nevi on the irides was similar for 145 age-matched and age-sex-matched melanoma and comparison subjects \( P < 0.70; \chi^2 = 0.22 \). The number of nevi on the irides was also

<table>
<thead>
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<th>Age of Patients (years)</th>
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<td>70</td>
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<td>&gt;70</td>
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<table>
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<tr>
<td>&gt;70</td>
<td>2/12</td>
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</table>

Table 7

Relationship between atypical nevi and nevi with hypopigmented halos

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<th>Nevi Count</th>
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<td>1-45</td>
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<td>&gt;45</td>
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<td>Total</td>
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CANCER RESEARCH VOL. 45 APRIL 1985
1858

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Table 8

<table>
<thead>
<tr>
<th>Nevi in the Irides</th>
<th>Patients</th>
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</thead>
<tbody>
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</table>

Patients versus controls (5 by 2): \( x^2 = 19.90; P < 0.01 \). Patients versus controls (2 by 2): \( x^2 = 4.98; P < 0.05 \).

Atypical Nevi and Melanoma-related Variables

Patients with atypical nevi may have melanomas which exhibit a different behavior than patients without such nevi (4, 5). The following variables relating to the primary melanoma in patients with atypical nevi were compared to those in melanoma patients without atypical nevi: the site of primary, the occurrence of an occult primary, interval to diagnosis, the presence of a lymphocytic infiltrate within the melanoma, evidence of tumor regression, Clark level, Breslow depth of invasion, frequency of metastases, and clinical stage and diagnosis. No significant differences were found between the melanomas in patients with or without atypical nevi.

DISCUSSION

We have used the term atypical nevi throughout this report (8). We presume the patient sample in this report had the sporadic form of atypical nevi. Few if any patients could give accurate assessment of the number or the appearance of nevi in other family members. Kinships were not examined, because the purpose of the study was to identify and correlate melanomas with other pigmentary abnormalities on the skin or in the eyes. We have used the term atypical nevus because we are reporting clinical observations. However, those lesions confirmed to be abnormal histologically are more commonly labeled dysplastic.

We have attempted to determine the prevalence of clinically atypical nevocellular nevi in a large sample of patients with melanomas and in a comparable comparison group. We have used three features to distinguish an atypical nevus from a normal one; large size, i.e., one diameter greater than 5 mm; irregular outline; and haphazard array of colors, i.e., a variety of hues of brown, black, red, and tan. These are the criteria established by others for the clinical identification of atypical nevi (1–8). Patients with large atypical nevi greater than 5 mm in diameter also have many smaller lesions similar in morphology. In this study, these smaller lesions were arbitrarily considered to be normal. Ninety-four of the larger atypical nevi were excised for histopathological examination. More detailed results of these histological studies will be presented in a separate report.

The most striking observation is that 34% of patients with sporadic melanomas had atypical nevi, but only 7% of the control population had similar lesions. In a recent report, others noted that 4.9% of 881 random patients had atypical nevi (10). By statistical analysis, the difference between the 34 and 7% observed in our study is a highly significant difference \( (P < 0.001; x^2 = 37.74) \). In a similar study published previously, only 8% of patients with melanoma were found to have atypical nevi (11). The latter author inspected photographs to obtain the data (6). Thus, the lower prevalence of 8% would be a minimal estimate.

It should be noted that the study recorded here was conducted in Sydney, Australia and that nearly every patient was of Celtic ancestry and had fair skin. No patients with known aboriginal ancestry were part of this study. It has been noted before that patients with the familial variant of atypical nevi tended to have very fair skin (8). Mackie’s study was conducted in Scotland. In our study and that of Mackie, the patient’s Celtic ancestry and skin color were representative of the Caucasian population living in the vicinity.

Patients with melanomas had, on the average, 31 nevi; controls had a mean of 27 nevi. The mean age of our patients was 49 years. Stegmaier reported that younger adults, ages 20 to 25, had an average of 41 nevi (range, 14 to 80) (12). In a different study, Stegmaier noted that patients 50 years or older had many fewer nevi (mean, of 3 to 4 per person) (13). Mackie’s patients were in the fourth decade of life and had 15 to 25 nevi per subject (8). Her patients had atypical nevi as well as melanomas. It has been noted that even nevi in the oral cavity seem to increase in number from childhood, reaching a maximum number around the mid-30s (14, 15). This variation of nevi with age has been observed in this study (Chart 1). The frequency of atypical and the total number of nevi in patients with melanoma also seems to vary with age (Tables 5 and 6). Clearly, after the age of 50 years, the frequency of atypical nevi and total nevi decreases in patients with melanoma. In what decade of life atypical nevi are most prevalent and/or most numerous has not been defined precisely. That atypical nevi disappear like normal nevi, however, indicates that the cells are still responsive to some of the factors which regulate the behavior of normal nevi.

Sunlight has been implicated in the expression of nevi. The Celtic patients in our study had been exposed to the very bright sun of the Australian environment. The observation that the prevalence of oral nevi increases in number similar to that of cutaneous nevi suggests that sunlight may have a lesser role in...
the induction of these spots than was believed previously. On
the other hand, sunlight may cause release of a "solar circulating
factor" that stimulates nevus and pigment cell growth (16).
Rosdahl found evidence for such a circulating factor in
her experiments on mice (17). Why nevi tend to involute in the second
half of life is not clear (Chart 1) (Tables 5 and 6).

Patients with atypical nevi and melanoma had more nevi than
those without. This difference has been reported recently by
others (18). This observation suggests that at least some pa-
tients with melanoma may have a generalized abnormality of
pigment cells. The number of iris nevi also was greater in all
patients with melanomas. Patients with atypical nevi, however,
did not have more iris nevi. It has been noted that ocular
melanomas have been linked to the atypical mole syndrome (4,
19).

The sex of an individual seems to have no effect on the
presence or absence of atypical nevi, although hormonal influ-
ences have been implicated in the causation of melanoma (4).
Male control subjects did have more nevi than did the female
controls, but this difference is probably due to the much higher
percentage of younger males in the control group. Many of the
control subjects were males under 45 years of age who had
been incarcerated in a prison. Age correlated significantly (P <
0.01) with a total number of normal and/or atypical nevi. Younger
patients (those under 50 years of age with or without atypical
nev) tended to have more nevocellular nevi than did those
subjects over 50 years of age. The effect of age on atypical nevi
in comparison group was difficult to assess, because the fre-
quency of subjects with atypical nevi was low.

Hypopigmented halos around nevi were observed frequently
in both the patient and control groups. Ten % of both populations
exhibited nevi surrounded by halos. The halos generally were
not the striking depigmented rings described by Sutton. The
hypopigmented halos typically were hard to visualize by visible
light and were accentuated by examination with a Wood's lamp.
That nevi frequently have faint halos had been observed by
others (20). Eight patients with a melanoma (21) and four controls
had vitiligo. Although the patients with vitiligo did have nevi, none
had either a classic Sutton's nevus or nevi with subtle hypopig-
menced rings.

Halos around nevi in the melanoma group strongly correlated
with the presence of atypical nevi (P < 0.01) (Table 7). In the
accompanying report, we have noted that one histological char-
acteristic of atypical nevi is a mild to moderate lymphocytic
infiltrate and the presence of pigment incontinence within the
dermis. These histological features are similar to those found in
a classic Sutton's nevus. It may be a similar but less aggressive
mechanism for the destruction of normal pigment cells that
causes halos in the Sutton's lesion is operative in these more
subtle forms of halo nevi. Preliminary studies indicate that pa-
tients with subtle halos around nevi do not have in their sera
antibodies against melanoma cells or normal melanocytes (22).

It has been suggested that melanomas arising in familial
form of atypical nevus syndrome may be less aggressive than those
arising de novo or from a typical nevocellular nevus (4). Analy-
zes of the depth of the primary lesion either by the Clark or
Breslow method, of the clinical stage, and of the rates of recurrence
of melanomas in patients with atypical nevi did not indicate a
significant difference from those melanomas removed from pa-
ients without atypical nevi. It may be that melanomas in patients
with the sporadic atypical nevi are not biologically different from
those in patients without such nevi. We examined a group of
patients whose melanoma exhibited a variety of types and stages
of diagnoses. Some patients, when examined, had advanced
disease. Many had had their melanomas removed within a few
years of this study and had no evidence of recurrence. It seems
unlikely that we selected a sample of patients with atypical
melanoma that survived for an unusually prolonged period of
time. However, we cannot determine whether the melanomas in
these patients actually arose from an atypical nevus, from a
normal nevus, or from a single pigment cell. Thus, we cannot
conclude that melanomas arising from an atypical nevus will
exhibit behavior similar or different from melanomas arising de
novo or from a normal nevus.

Patients with multiple melanomas often have atypical nevi (23).
This observation suggests the sporadic form of atypical nevi, like
familiar variant, may predispose to melanoma. Other data are
consistent with this idea, i.e., the higher prevalence of atypical
nev in patients with melanomas and the larger number of iris
nev in this same population. However, the data are not conclu-
sive to prove this point. We observed that 7% of the control
group had atypical nevi. Because many patients with melanomas
are cared for in special pigmented lesion-melanoma clinics, many
patients with atypical nevi and melanoma may have been gath-
ered into selected study groups. That several members of kin-
ships with the familial variant of atypical mole syndrome have
developed melanomas suggests that all patients with atypical
nev should be observed carefully. They should be cautioned
about excessive sun exposure. Any atypical nevus undergoing
change should be excised and carefully examined by a dermato-
pathologist. However, only a prospective study in which
hundreds of patients with and without atypical nevi are observed
for long periods of time will definitively answer whether such
patients have a higher risk for melanomas.

One important point which also remains unanswered is
whether small nevi with irregular coloration and outlines are
atypical. The answer to this question will require another study
in which small lesions are excised and examined histologically.
In a subsequent paper, we present the histological features we
observed in the 94 biopsies from the larger atypical nevi. Detailed
information about normal and atypical nevi may provide clues to
the origin of melanoma.

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CANCER RESEARCH VOL. 45 APRIL 1985
1860

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DEMOGRAPHIC STUDY OF CLINICALLY ATYPICAL NEVI

Demographic Study of Clinically Atypical (Dysplastic) Nevi in Patients with Melanoma and Comparison Subjects


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