Acral Melanocytic Nevi

Prevalence and Distribution of Gross Morphologic Features in White and Black Adults

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Objective: To determine prevalence and morphologic features of acral melanocytic nevi in white and black adults.

Design: Point prevalence survey.

Setting: Outpatient dermatology clinic.

Patients: Convenience sample of subjects 18 years or older.

Main Outcome Measures: Prevalence and morphologic features based on ethnicity, sex, and age.

Results: Palmar or plantar nevi were detected in 42.0% of blacks (50 of 119) vs 23.0% of whites (79 of 343) (P < .001). Palmar or plantar nevi of 6-mm diameter or larger were detected in 3.4% of blacks (4 of 119) vs 0.6% of whites (2 of 343) (P = .04). Diffusely black acral nevi were uncommon in whites (0 of 343) and blacks (1 of 119). The prevalence of palmar or plantar nevi increased directly with degree of skin pigmentation (P < .001). In whites, this prevalence was greater in women (27.1%, 51 of 188) than in men (18.1%, 28 of 155) (P = .047); in subjects younger than 50 years (30.8%, 57 of 185) than in those 50 years or older (13.9%, 22 of 158) (P < .001); in subjects with a history of atypical nevus removal than in those without (odds ratio [OR], 3.6; 95% confidence interval [CI], 1.9-6.9); in those with at least 1 extant atypical nevus than in those without (OR, 3.2; 95% CI, 1.7-6.0); and in those with at least 20 nevi of 2-mm diameter or larger than in those without (OR, 3.0; 95% CI, 1.6-5.6).

Conclusions: Acral nevi appear to be associated with ethnicity, pigmentation, age, and cutaneous melanoma (CM) risk factors. While relatively large and/or very darkly pigmented acral nevi appear to be more common in blacks than in whites, diffusely black acral nevi are uncommon in both groups. These findings are relevant to the assessment of pigmented lesions in the differential diagnosis of acral CM.

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According to Surveillance, Epidemiology, and End Results (SEER) data reported for 1975 to 2007, the age-adjusted incidence rate of cutaneous melanoma (CM) in the United States was 25.3/100,000/y for whites vs 1.1/100,000/y for blacks. This difference may relate to constitutive pigmentation and/or genetic factors associated with pigmentation and melanocytic neoplasms. While the incidence of CM is significantly greater in whites than in blacks, the incidence of CM on acral surfaces is similar: 1.7/million/y for blacks vs 2.0/million/y for whites. Acral CM as a percentage of all CM cases has been reported to be 60% to 75% in blacks, 43% to 49% in Asians, and 5% to 7% in whites. The 5-year CM-related survival is significantly worse in blacks than in whites. When stratified by stage, blacks have a prognosis similar to that of whites, suggesting that CM in blacks tends to be diagnosed at a later stage of tumor progression.

While acral CM is uncommon, acral melanocytic nevi are relatively common. Thus, acral nevi are a source of confusion that challenges physicians and the lay public in the differentiation of typical vs atypical acral nevus and acral CM. There are limited published data relevant to the prevalence and morphologic features of common and uncommon acral nevi as a function of ethnicity. Given the paucity of quantitative information, we attempted to determine the prevalence and morphologic features of unselected acral nevi (those not selected for excision) in white and black adults. Our goal was to provide additional information related to the

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prevalence of common (typical) and uncommon (atypical) acral nevi according to ethnicity.

METHODS

STUDY POPULATION

Between June 27 and August 25, 2005, 528 adults visiting the outpatient Dermatology Service at Rush University Medical Center for routine care were recruited for this study and had their acral surfaces examined. Consent to participate was verbal for this convenience sample. The study protocol and consent procedures were approved by the institutional review board on human studies at Rush University Medical Center.

Subjects 18 years or older were included regardless of ethnicity, sex, or pregnancy status. Subjects were excluded if the encounter concern included an acral pigmented lesion or surgical procedure or if unrelated exigencies precluded examination or data collection.

Ethnicity of subjects was assessed by observation, with clarification by subjects as needed. The term white was used to describe people of European origin. The term black was used to describe people of African origin. Results of subjects whose ethnicity was other than white or black were excluded from analysis owing to small sample size (n = 51).

DATA COLLECTION

Subject information included personal and family history of CM and previous removal of nevi. If available from the current or prior medical encounters, the following information was recorded based on a total mucocutaneous examination by one of us (A.R.R.): number of melanocytic nevi with a greatest diameter of at least 2 mm and at least 5 mm and presence of any atypical melanocytic nevi. Atypical melanocytic nevi were defined as melanocytic nevi having a diameter of 5 mm or larger plus 1 or more of the following: variegation of pigmentation, fried-egg pattern, irregular and/or ill-defined margin, and/or black pigmentation in toto. The designation benign nevus pattern was defined as (1) fewer than 20 nevi at least 2-mm diameter; (2) fewer than 5 nevi of at least 5-mm diameter; and (3) no extant atypical nevi. Subjects not meeting all criteria of benign nevus pattern were designated as having an atypical nevus pattern. Reasons for medical encounter were recorded, with the most urgent reason given priority when there were multiple issues. Palmar and plantar surfaces were examined, including volar fingers and toes and nail apparatus of hands and feet. Results of nail findings are not reported herein.

According to the histopathologic studies by Van Scott et al, common or typical discrete pigmented lesions on acral surfaces may be lentigo simplex, junctional melanocytic nevus, compound melanocytic nevus, intradermal nevus, and occasionally epidermal basal layer hyperpigmentation without other features. Thus, any discrete pigmented lesion detected by naked-eye examination in our study was presumed to be a melanocytic nevus, and the following information was collected: anatomic location; longest diameter and perpendicular greatest diameter; topography; maximum estimated height; lesion color; degree of pigmentation variegation; degree of border irregularity and demarcation; presence of halo depigmentation without the use of a Wood’s light; scaling; erosion; and ulceration. Topography was graded as flat to tangential lighting (TL); slightly raised to TL only (not palpable); slightly raised to visual inspection without TL or palpation; or markedly raised to visual inspection and palpation. Pigmentation variegation was graded as none (1 shade or hue); 2 shades or hues; 3 shades or hues; or more than 3 shades or hues. Border irregularity was graded as none, slight, moderate, or marked. Border demarcation was graded as well defined, slightly ill defined, moderately ill defined, or markedly ill defined.

Constitutive skin color was assessed on the medial upper arm using a universal color scheme (Pantone Color Overlay Selector; Letraset USA, Paramus, New Jersey). Color was related to common objects and included white (absence of color); very light brown (Pantone 466-A, walnut shell); light brown (Pantone 465-A superimposed on 473-A, skin of lightly toasted almond); medium brown (Pantone 464-A, Brazil nut shell); dark brown (Pantone 469-A, milk chocolate); very dark brown (Pantone 497-A, bittersweet chocolate); and black (Pantone opaque black-A, charcoal). Examination of acral surfaces was performed jointly by both of us for 89% of the subjects (455 of 513) and by 1 of us alone (G.A.P.) for 11% (58 of 513).

STATISTICAL ANALYSIS

Analysis was performed using SPSS 14.0 for Windows (SPSS Inc, Chicago, Illinois). A Pearson χ2 test was used for comparison of proportions between groups when every table cell value was 5 or greater. The Fisher exact test was used for comparison of proportions between groups when at least 1 cell value was less than 5. A Pearson χ2 test was used for comparison of proportions between subjects grouped by skin pigmentation (3 groups) if the following conditions were met: no more than 20% of table cell values were less than 5, and all table cell values were at least 1. A McNemar test was used for comparison of proportions between anatomic sites. All reported P values are 2 sided. When analyzing association of acral nevi with CM risk factors in whites, we excluded subjects with unknown or missing parameters (85 subjects). Reasons for exclusion in this analysis were the following: subjects did not know if an atypical nevus had been removed; or numbers and size of nevi or presence of atypical nevus based on a total mucocutaneous examination were not available. Patients determined to have pigmented lesions that were regarded as atypical were counseled about need for excision or close periodic surveillance, according to current standards of care.

RESULTS

Of the 528 adults asked to participate, 3 declined and 12 were excluded for other reasons: (1) they were under observation for atypical acral nevus; (2) they had acral surfaces obscured by bandages and/or other lesions; or (3) they resisted participation. Of the remaining 513 participants, 343 were white, 119 black, and 51 were other ethnicities. Our analysis excluded the 51 adults of ethnicities other than white or black. The final study population included 187 men and 275 women, ranging in age from 18 to 89 years (median age, 47 years; mean [SD] age, 47 [17] years), and consisting of 343 whites (median age, 48 years; mean [SD] age, 48 [17] years); and 119 blacks (median age 46 years; mean [SD] age, 46 [16] years).

The dominant reasons for medical encounter for the 462 subjects included (1) concern or screening for skin cancer, 26.2% (121 of 462); (2) CM surveillance because of perceived high risk based on prior medical encounter, 12.8% (59 of 462); and (3) other reasons, 61.0% (282 of 462).

Constitutive skin color for white subjects was white (98.3%, 337 of 343), very light brown (1.5%, 5 of 343), and light brown (0.3%, 1 of 343). Constitutive skin color for black subjects was white (0.8%, 1 of 119), very light brown (0.9%, 1 of 119), and dark brown (87.8%, 103 of 119).
brown (9.2%, 11 of 119), light brown (71.4%, 85 of 119), medium brown (15.1%, 18 of 119), and dark brown (3.4%, 4 of 119).

In whites, the prevalence of palmar or plantar nevi was 23.0% (79 of 343): 13.7% had at least 1 palmar nevus (47 of 343), and 12.0% had at least 1 plantar nevus (41 of 343) (Table 1). In blacks, the prevalence of palmar or plantar nevi was 42.0% (50 of 119): 29.4% had at least 1 palmar nevus (35 of 119), and 20.2% had at least 1 plantar nevus (24 of 119). The prevalence of palmar, plantar, and palmar or plantar nevi was each significantly greater in blacks than in whites (P < .001, P = .03, and P < .001, respectively). The prevalence of palmar vs plantar nevi within a given ethnic group did not differ significantly for blacks (29.4% vs 20.2%) (P = .12) or whites (13.7% vs 12.0%) (P = .55). Examples of acral pigmented lesions designated as melanocytic nevi are illustrated in Figures 1, 2, and 3.

The prevalence of palmar or plantar nevi in white women (27.1%, 51 of 188) was greater than that in white men (18.1%, 28 of 155) (P = .047). Our sample population of blacks was not large enough to assess a difference between women and men for prevalence of palmar or plantar nevi. The prevalence of palmar or plantar nevi increased directly with degree of constitutive skin pigmentation (P < .001) (Table 1).

For subjects with any palmar nevi, 72.3% of whites (34 of 47) and 71.4% of blacks (25 of 35) had only 1 palmar nevus; 17.0% of whites (8 of 47) and 17.1% of blacks (6 of 35) had only 2 palmar nevi. Similarly, for subjects with any plantar nevi, 80.5% of whites (33 of 41) and 83.3% of blacks (20 of 24) had only 1 plantar nevus.

In whites, the greatest diameter of palmar nevi ranged from 0.5 to 3.0 mm, and for plantar nevi, 0.8 to 7.0 mm (Table 2). For the largest palmar or plantar nevi smaller than 1 mm in diameter in 3 subjects, lesion diameter ranged from 0.5 to 0.8 mm. In blacks, the greatest diameter of palmar nevi ranged from 0.5 to 8.0 mm; and for plantar nevi, 1.0 to 10.0 mm. For the 1 subject whose largest nevus was smaller than 1 mm in diameter, lesion diameter measured 0.5 mm. The prevalence of palmar or plantar nevi of at least 4 mm in diameter was 4.5 times greater in blacks (11.8%, 14 of 119) than in whites (2.6%, 9 of 343) (P < .001). The prevalence of palmar or plantar nevi of at least 6 mm in diameter was 5.8 times greater in blacks (3.4%, 4 of 119) than in whites (0.6%, 2 of 343) (P = .04). The prevalence of palmar or plantar nevi larger than 6 mm in diameter was 2.5% in blacks (3 of 119) vs 0.3% in whites (1 of 343) (P = .054). Palmar or plantar melanocytic nevi larger than 7 mm in diameter were detected in 0.3% of white subjects (1 of 343) vs 2.5% of black subjects (3 of 119) (P = .054).

### Table 1. Prevalence of Acral Nevi According to Ethnicity, Sex, Skin Pigmentation, and Anatomic Location

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects Examined, No.</th>
<th>Palmar</th>
<th>Plantar</th>
<th>Palmar and Plantar</th>
<th>Palmar or Plantar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites</td>
<td>343</td>
<td>47 (13.7)</td>
<td>41 (12.0)</td>
<td>9 (2.6)</td>
<td>79 (23.0)</td>
</tr>
<tr>
<td>Women</td>
<td>188</td>
<td>28 (14.9)</td>
<td>28 (14.9)</td>
<td>5 (2.7)</td>
<td>51 (27.1)</td>
</tr>
<tr>
<td>Men</td>
<td>155</td>
<td>19 (12.3)</td>
<td>13 (8.4)</td>
<td>4 (2.6)</td>
<td>28 (18.1)</td>
</tr>
<tr>
<td>Blacks</td>
<td>119</td>
<td>35 (29.4)</td>
<td>24 (20.2)</td>
<td>9 (7.6)</td>
<td>50 (42.0)</td>
</tr>
<tr>
<td>Women</td>
<td>87</td>
<td>27 (31)</td>
<td>19 (22)</td>
<td>7 (8)</td>
<td>39 (45)</td>
</tr>
<tr>
<td>Men</td>
<td>32</td>
<td>8 (25)</td>
<td>5 (16)</td>
<td>2 (6)</td>
<td>11 (34)</td>
</tr>
<tr>
<td>Skin pigmentationa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White or very light brown</td>
<td>354</td>
<td>47 (13.3)</td>
<td>42 (11.9)</td>
<td>9 (2.5)</td>
<td>80 (22.6)</td>
</tr>
<tr>
<td>Light brown</td>
<td>86</td>
<td>28 (33)</td>
<td>18 (21)</td>
<td>8 (9)</td>
<td>38 (44)</td>
</tr>
<tr>
<td>Medium or dark brown</td>
<td>22</td>
<td>7 (32)</td>
<td>5 (23)</td>
<td>1 (5)</td>
<td>11 (34)</td>
</tr>
</tbody>
</table>

*Skin pigmentation determined by visual inspection of subject’s medial upper arm.*

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Figure 1. Typical-appearing medium brown common melanocytic nevus measuring 2 mm at its greatest diameter on the palmar hand of a 41-year-old white man. Note the medium brown furrow lines in a light brown macular background. Each line on the centimeter scale represents 1 mm.

Figure 2. Typical-appearing medium brown common melanocytic nevus measuring 3 mm at its greatest diameter on the plantar foot of a 65-year-old white man. Each line on the centimeter scale represents 1 mm.

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In whites, the prevalence of palmar or plantar nevi in subjects younger than 50 years (30.8%, 57 of 185) was 2.2-fold greater than in older subjects (13.9%, 22 of 158) \( (P < .001) \). Our sample population of blacks was not large enough to assess a significant difference between subjects younger than 50 years (n=68) and those 50 years or older (n=51) for prevalence of palmar or plantar nevi.

The following gross morphologic features were uncommon in palmar or plantar nevi in whites: raised topography (3.8%, 3 of 79); darkest pigmentation of dark brown or darker (3.8%, 3 of 79); 3 or more shades or hues (0 of 79); border irregularity was moderate or marked (1.3%, 1 of 79); lesion border was moderately or markedly ill defined (7.6%, 6 of 79); scaling (0 of 79); erosion or ulceration (0 of 79); or associated halo of depigmentation (0 of 79) \( (\text{Table 3}) \). The following characteristics were uncommon in palmar or plantar nevi in blacks: raised topography (0 of 50); darkest pigmentation of very light brown (2.0%, 1 of 50) or black (2.0%, 1 of 50); 3 or more shades or hues (8.0%, 4 of 50); border irregularity graded as moderately or marked (4.0%, 2 of 50); border demarcation graded as moderately or markedly ill defined (4.0%, 2 of 50); scaling (0 of 50); erosion or ulceration (0 of 50); or depigmented halo (0 of 50) \( (\text{Table 4}) \).

For the largest nevus per black subject, the following features were significantly more common in acral nevi of at least 5 mm in diameter than in smaller acral nevi: coloration of dark brown or darker (90.0%, 9 of 10, vs 50.0%, 20 of 40) \( (P = .03) \); and 3 or more shades or hues (30.0%, 3 of 10 vs 2.5%, 1 of 40) \( (P = .02) \). For the largest nevus per black subject, the following features were not significantly different in acral nevi that were at least 5 mm in diameter vs smaller ones: raised topography (0 of 10 vs 0 of 40); border irregularity was moderate or marked (10.0%, 1 of 10, vs 2.5%, 1 of 40) \( (P = .36) \); or border was moderately or markedly ill-defined (10.0%, 1 of 10, vs 2.5%, 1 of 40) \( (P = .36) \).

Presence of at least 1 palmar or plantar nevus in whites was significantly associated with a history of atypical nevus removal (odds ratio [OR], 3.6; 95% confidence interval [CI], 1.9-6.9) and the following examination findings: at least 1 extant atypical nevus (OR, 3.2; 95% CI, 1.4-6.9); an atypical nevus pattern (OR, 2.6; 95% CI, 1.7-6.0); at least 20 nevi of 2-mm diameter or larger (OR, 2.2; 95% CI, 1.2-4.2) \( (\text{Table 5}) \). Presence of at least 1 palmar or plantar nevus in whites was not significantly associated with having a first-degree blood relative with CM (OR, 1.3; 95% CI, 0.4-3.7) or a personal history of CM (OR, 1.0; 95% CI, 0.3-3.6), but numbers were small. Presence of at least 1 palmar or plantar nevus in whites was significantly associated with having any CM risk factor listed in Table 5 (OR, 2.2; 95% CI, 1.2-4.0). Of the 258 white subjects included in this analysis, 14 had a personal history of CM, and 19 had a family history of CM in a first-degree relative. Of the 14 white subjects, 3 had a personal history of melanoma, 29% had a family history of CM in a first-degree relative (4 of 14).
Size, pigmentation characteristics, and ethnicity-related prevalence of acral melanocytic nevi are relevant to the differential diagnosis of CM on acral surfaces. For any pigmented lesion, the usefulness of any diagnostic test for CM, including gross morphologic features, is a function of sensitivity and specificity of the morphologic feature(s) in question as well as the prevalence of CM in the population being tested. The distribution of morphologic features of unselected acral nevi is relevant to the population being tested. The distribution of sensitivity and specificity of the morphologic features used for the differential diagnosis of CM on acral surfaces. For any pigmented lesion, the usefulness of any diagnostic test for CM, including gross morphologic features, is a function of sensitivity and specificity of the morphologic feature(s) in question as well as the prevalence of CM in the population being tested. The distribution of morphologic features of unselected acral nevi is relevant to the population being tested. The distribution of sensitivity and specificity of the morphologic features used for the differential diagnosis of CM.

**PREVALENCE ACCORDING TO ETHNICITY**

Prior studies have reported the prevalence of palmar or plantar nevi to be lower in whites (Table 6) than in blacks (Table 7).20 Herein, we have reported similar numbers of acral nevi in whites and blacks for subjects who had any acral nevus. Among Colombian children with at least 1 palmar or plantar nevus, 71% had 1 palmar or plantar nevus, and 23% had 2 palmar or plantar nevi.21 These values are similar to ours, which suggests that numbers of palmar or plantar nevi may not vary according to ethnicity for people who have acral nevi. These findings need corroboration.

**PREVALENCE ACCORDING TO AGE**

Our findings suggest that the prevalence of palmar or plantar nevi in white subjects younger than 50 years may be greater than that of older subjects, similar to findings of other studies.11,13,15,22 Lund and Stobbe23 reported a scarcity of nevi on the hands and feet of patients older than 50 years. These observations for nevi on acral surfaces are similar to the age-related reduction of melanocytic nevi noted for the entire skin surface.15,24-26 Explanations for the age-related difference in prevalence of melanocytic nevi may be secondary to true disappearance or loss of surface pigmentation that would suggest disappearance.
PREVALENCE ACCORDING TO SEX

In our study, the prevalence rate of palmar or plantar nevi in white women was significantly greater than that in white men, similar to results reported by Wilson and Anderson.13 In contrast, Van Scott et al11 found similar prevalence rates of palmar and plantar nevi for white men and white women. Our sample size of white women was slightly greater than that for white men (188 vs 155), possibly related to a greater tendency of women to visit a dermatologist and thus resulting in self-selection bias that contributed to the observed sex difference. Our sample size of black subjects was not large enough to assess sex-related differences in the prevalence of palmar or plantar nevi.

PREVALENCE ACCORDING TO CONSTITUTIVE PIGMENTATION

Our results suggest that the prevalence of palmar or plantar nevi increases with degree of constitutive skin pigmentation. Similarly, Coleman et al20 reported that among African blacks living in New Orleans, Louisiana, darker subjects had a higher prevalence of palmar or plantar nevi than lighter subjects. In Colombian school children, the frequency of melanocytic nevi in general appeared to increase linearly with darkness of skin color.21 In contrast, Lewis and Johnson27 reported no difference in prevalence of plantar nevi among Ugandan African tribes according to degree of skin pigmentation.

SIZE OF ACRAL MELANOCYTIC NEVI ACCORDING TO ETHNICITY

Among whites in our study, the greatest diameter of palmar and plantar nevi ranged from 0.5 to 3.0 mm and 0.8 to 7.0 mm, respectively. In blacks, the greatest diameter of palmar and plantar nevi ranged from 0.5 to 8.0 mm and 1.0 to 10.0 mm, respectively. These values are within the range of 0.5 to 12.0 mm reported by Van Scott et al11 for palmar and plantar nevi of a mixed population of white and black adults and within the range of 1.0 to 11.0 mm reported by Jaramillo-Ayerbe and Vallejo-Contreras21 in Colombian children.

We found that the prevalence of palmar or plantar nevi at least 4 mm in diameter was 4.5 times greater in blacks (11.8%) than in whites (2.6%) (P < .001); and the prevalence of palmar or plantar nevi of at least 6 mm in greatest diameter was 5.8 times greater in blacks (3.4%) than in whites (0.6%) (P = .04). Palmar or plantar nevi of at

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Table 5. Melanoma Risk Factors Associated With Acral Nevi in 258 White Adults

<table>
<thead>
<tr>
<th>Melanoma Risk Factor</th>
<th>Presence of Palmar or Plantar Nevi, No. of Patients</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical nevus removed</td>
<td>Yes: 22, No: 30</td>
<td>3.6 (1.9-6.9)</td>
</tr>
<tr>
<td>At least 1 extant atypical nevus</td>
<td>Yes: 27, No: 44</td>
<td>3.2 (1.7-6.0)</td>
</tr>
<tr>
<td>At least 20 nevi ≥2 mm in diameter</td>
<td>Yes: 27, No: 46</td>
<td>3.0 (1.6-5.6)</td>
</tr>
<tr>
<td>Melanoma in first-degree relative</td>
<td>Yes: 5, No: 14</td>
<td>1.3 (0.4-3.7)</td>
</tr>
<tr>
<td>Personal history of melanoma</td>
<td>Yes: 3, No: 11</td>
<td>1.0 (0.3-3.6)</td>
</tr>
<tr>
<td>Any melanoma risk factor</td>
<td>Yes: 32, No: 74</td>
<td>2.2 (1.2-4.0)</td>
</tr>
<tr>
<td>Melanoma in first-degree relative</td>
<td>Yes: 5, No: 14</td>
<td>1.3 (0.4-3.7)</td>
</tr>
<tr>
<td>Personal history of melanoma</td>
<td>Yes: 3, No: 11</td>
<td>1.0 (0.3-3.6)</td>
</tr>
<tr>
<td>Any melanoma risk factor</td>
<td>Yes: 32, No: 74</td>
<td>2.2 (1.2-4.0)</td>
</tr>
</tbody>
</table>

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Table 6. Prevalence of Acral Nevi in Whites Found in Selected Studies

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Location</th>
<th>Subjects, No.</th>
<th>Age Range, y</th>
<th>Lesion Diameter, mm</th>
<th>Prevalence of Acral Nevi, % of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pack et al.12 1952</td>
<td>New York, New York</td>
<td>1000</td>
<td>Adults</td>
<td>Any size</td>
<td>0.0 &lt;1</td>
</tr>
<tr>
<td>Van Scott et al.11 1957</td>
<td>Maryland and Washington, DC</td>
<td>494</td>
<td>All ages</td>
<td>≥0.5</td>
<td>10.5</td>
</tr>
<tr>
<td>Wilson and Anderson,13 1961</td>
<td>Washington, DC</td>
<td>1100</td>
<td>20-60</td>
<td>≥0.6</td>
<td>5.5</td>
</tr>
<tr>
<td>Cullen,14 1962</td>
<td>San Antonio, Texas</td>
<td>5332</td>
<td>17-25</td>
<td>Any size</td>
<td>5.35</td>
</tr>
<tr>
<td>Allyn et al.15 1963</td>
<td>New York, New York</td>
<td>632</td>
<td>All ages</td>
<td>≥0.5</td>
<td>6.5</td>
</tr>
<tr>
<td>MacKie et al.16 1985</td>
<td>United Kingdom</td>
<td>432</td>
<td>4-96</td>
<td>≥3</td>
<td>0.9</td>
</tr>
<tr>
<td>Present study</td>
<td>Chicago, Illinois</td>
<td>343</td>
<td>18-89</td>
<td>Any size</td>
<td>13.7</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

a Male patients only; fingers excluded for palmar sites.

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least 7 mm in diameter were uncommon in blacks (2.5%, 3 of 119) and whites (0.3%, 1 of 343) (P = .054). We were unable to find published studies that quantify such comparisons.

GROSS MORPHOLOGIC FEATURES OF ACRAL NEVI ACCORDING TO ETHNICITY

In our subjects, all of the palmar nevi detected were flat. In a heterogeneous population, Allyn et al15 reported that only 3% of palmar nevi were raised. We found that in whites, only 4.9% of plantar nevi were slightly raised, and 2.4% were obviously raised and palpable. Our results in blacks demonstrated that all plantar nevi were flat. In a heterogeneous population, Allyn et al15 found that 12% of plantar nevi were slightly raised and 6% were more elevated. Differences in results may relate to degree of care in assessing surface distortion of acral nevi.

In whites, we found that the most common color was light brown in palmar (55.3%) and plantar (48.8%) nevi. In blacks, very dark brown was the most common color in palmar (28.6%) and plantar (37.5%) nevi. In a heterogeneous population, Allyn et al15 found that the color of palmar nevi was found brown in 52%, medium brown in 42%, and dark brown in 6%; the color of plantar nevi was found brown in 37%, medium brown in 49%, and dark brown in 14%. According to our studies, the following atypical features were uncommon in acral nevi in both whites and blacks: black coloration, 3 or more hues or shades, raised topography, moderate or marked border irregularity, and moderately or markedly ill-defined border. In our study, for subjects who had any acral nevi, dark brown or darker coloration in the largest nevus per subject was less common in whites (3.8%, 3 of 79) than in blacks (58.0%, 29 of 50) (P < .001). In our white subjects, dark brown acral nevi were noted in only 0.9% (3 of 343), and none of the acral nevi were darker. Of our black subjects, 13.4% had at least 1 very dark brown acral nevus (16 of 119), and only 1 of 119 had a black acral nevus (0.8%). Additional studies of gross morphologic features of unselected acral nevi according to ethnicity and skin color are required to confirm these findings.

According to our study of blacks for the largest nevus per subject, the following features were significantly more common in lesions at least 5 mm in diameter than in smaller ones: dark brown or darker coloration (90.0%, 9 of 10 vs 50.0%, 20 of 40) (P = .03) and 3 or more shades or hues (30.0%, 3 of 10 vs 2.5%, 1 of 40) (P = .02). Our sample size in whites was too small to assess morphologic features of nevi at least 5 mm in diameter vs smaller ones. We were unable to find published studies with which to compare these findings.

MELANOMA RISK FACTORS

Rokuhara et al26 have suggested that the relation between acral CM and acral nevi does not appear to be significant. Kogushi-Nishi et al28 reported that the prevalence of plantar nevi was not significantly higher in subjects who had plantar CM than it was in a control group. In contrast, Green et al29 reported that CM of acral surfaces was strongly associated with high total body nevus counts and presence of plantar nevi. Available studies7,30,31 report a 10% to 27% in-contiguity association between ALM and melanocytic nevi, both junctional and dermal varieties.32,33 Biologically advanced tumors are likely to destroy associated melanocytic nevi, so any reported histopathologic in-contiguity association between CM and melanocytic nevi is likely to be biased downward.34 Difficulty of self-examination adds to the unreliability of patient recall about preexisting nevi at the site of plantar CM as well as to delayed recognition and tumor progression. Further study is needed to clarify the relation between acral nevi and CM risk.

HISTOPATHOLOGIC FEATURES OF ACRAL NEVI

Our study designated discrete pigmented lesions, flat or raised, as melanocytic nevi based on the clinical-histopathologic studies by Van Scott et al.31 Numerous reports describe atypical histopathologic features of se-
lected acral melanocytic nevi requiring excision.\textsuperscript{35-37} Acral nevi selected for excision are more likely to demonstrate atypical histopathologic features than are common (unselected) acral nevi. Cellular atypia of melanocytes was not reported by Van Scott\textsuperscript{11} in their studies of acral pigmented lesions. We cannot exclude misclassification bias for the acral pigmented lesions designated melanocytic or nevomelanocytic in our study.

**CLINICAL RELEVANCE**

There is a pressing need for clinical-histopathologic correlation studies of common acral nevi to determine the sensitivity and specificity of gross morphologic features in predicting histopathologic melanocytic dysplasia or acral CM. The prevalence rates of lentigo simplex, typical nevomelanocytic nevi, and dysplastic melanocytic nevi on acral surfaces have not been determined in whites or blacks. Our own studies suggest that while markedly atypical-appearing acral melanocytic nevi were relatively uncommon in whites and blacks, there was a notable higher rate of relatively large acral nevi in blacks than in whites, and a higher rate of relatively atypical features (ie, dark brown or darker coloration and 3 or more shades or hues) in acral nevi of at least 5-mm diameter in blacks.

Notwithstanding the ABCD mnemonic for suspecting CM in a given skin lesion (asymmetry, border irregularity, color variegation, and diameter \(>6\) mm),\textsuperscript{38,39} multiple studies\textsuperscript{40-48} have reported that 2.6% to 38.2% of CM cases have a greatest diameter of 6 mm or less. Thomas et al\textsuperscript{49} reported that experienced dermatologists assessing a pigmented lesion using the D criterion of at least 6 mm alone had a sensitivity of 90% and a specificity of 63% for predicting CM, and using 3 or more of the ABCDE criteria (ABCD plus nevus evolution) had a sensitivity of 65.5% for predicting CM. The E criterion, defined as enlargement according to studies by Thomas et al,\textsuperscript{49} appeared to be extremely sensitive and specific in predicting a diagnosis of CM. The ABCD features are of limited value in distinguishing atypical or dysplastic nevi from CM.

Saida et al\textsuperscript{50} proposed that plantar nevi larger than 7 mm in diameter need to be resected because few benign plantar nevi exceed 7 mm in maximum diameter, while most plantar CMs have a diameter of 9 mm or more. According to our results, plantar nevi greater than 7 mm in diameter were detected in none of our white subjects and in 1.7% of our black subjects. Thus, we agree that any lesion attaining a diameter of 7 mm should be viewed with suspicion, regardless of ethnicity, because of the obvious deviation from normal. Ishihara et al\textsuperscript{51} described acral in situ CM lesions that were 7 mm in diameter or smaller in 2 of 20 clinically and histopathologically subtle cases. Other authors have reported the greatest diameter of palmar and plantar CM lesions to range from 2 to 80 mm.\textsuperscript{20,31,50,52} We suggest that diameter alone may not be sufficient to require biopsy to exclude acral CM or to obviate the need for biopsy for a clinically atypical or unstable lesion smaller than 7 mm in diameter. It is possible that there are unique varieties of acral nevi that represent risk factors and/or potential precursors of acral CM. Preliminary data suggest that BRAF, NRAS, and KIT mutation profiles may vary according to anatomic location of CM,\textsuperscript{35-37} supporting the concept of a heterogeneous origin of CM.

**LIMITATIONS**

At first glance, our study can be criticized for 2 reasons: (1) a potentially biased population including a substantial proportion of patients being seen for CM and/or non-CM skin cancer screening or surveillance; and (2) lack of histopathologic confirmation of acral pigmented lesions as melanocytic nevi. If acral nevi are significantly associated with CM risk factors, then the prevalence rate of acral nevi in our subgroup of white subjects may be biased upward. However, mixed groups of patients coming from the same population, at least a third at high risk and the rest not at high risk for CM, are ideal for study of the association between acral nevi and CM risk factors. Based on our observations, patients who have acral nevi are significantly more likely to have objective CM risk factors. This finding was not anticipated during the design of our study, and the association requires further study, as does the histopathologic evaluation of a large number of unselected acral pigmented lesions to confirm that the vast majority are melanocytic.

Additional limitations of our study include absence of surface microscopic evaluation and photographic documentation of morphologic features; possible misclassification of ethnicity based on visual designation; and lack of evaluation of interobserver reliability and accuracy of assessment of gross morphologic features of acral nevi. It is true that surface microscopy was not conducted routinely on the discrete pigmented lesions in this survey. However, published prospective studies are lacking that compare surface microscopic features of unselected discrete pigmented lesions on acral surfaces with their histopathologic characteristics to differentiate among the categories of common, atypical, and malignant melanocytic neoplasms. Moreover, the methods we used in the gross morphologic evaluation of acral nevi attempted to duplicate day-to-day clinical practice. Physicians cannot be expected to conduct surface microscopy on each and every discrete acral pigmented lesion. Even specialists scan lesions for size and color to determine if further detailed surface microscopic evaluation is warranted.

Further investigations with larger numbers of whites, blacks, nonwhite Hispanics, Asians, and East Indians are needed to supplement available clinical-histopathologic studies on acral nevi according to ethnicity.\textsuperscript{21,56} In conclusion, our study demonstrated significant differences in prevalence of acral nevi according to ethnicity, age, degree of constitutive pigmentation, and sex and significant differences in size of acral nevi according to ethnicity. We also showed that relatively large and atypical-appearing acral nevi are relatively uncommon and that the presence of at least 1 acral nevus in whites is positively associated with several objective CM risk factors. The size cutoff clinicians use for an acral nevus to be suspect for CM may be a moving target as greater numbers
of relatively small-diameter CM cases (<7 mm) are diagnosed. A clinical-histopathologic correlation study of large numbers of unselected acral melanocytic nevi is needed to assess the predictive value of gross morphologic criteria in the diagnosis of melanocytic dysplasia and CM on acral surfaces. Such a study must use all available methods of in vivo imaging to record and quantitatively assess clinical characteristics, and melanocyte density to supplement microscopic analysis, as used in the differentiation of subungual lentigo from subungual melanoma.

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Study concept and design: Palicka and Rhodes. Acquisition of data: Palicka and Rhodes. Analysis and interpretation of data: Palicka and Rhodes. Drafting of the manuscript: Palicka and Rhodes. Critical revision of the manuscript for important intellectual content: Palicka and Rhodes. Statistical analysis: Palicka and Rhodes. Administrative, technical, and material support: Rhodes. Study supervision: Rhodes.

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References:


Articles of Faith

Variant Gone Today, Hair Tomorrow

Originally, all I wanted was to illustrate various folk remedies to prevent or reverse hair loss. Once I started researching the subject, I was impressed by how many herbal substances have been used for baldness. While I was mulling over how best to incorporate all these items into an artwork, I was fortunate enough to discover a Venetian mask maker, Antonia Sautter, who uses the same technique that was made famous by the 16th-century Italian painter Giuseppe Arcimboldo. Both artists create their phantasmagorical portraits using natural objects to construct the semblance of a human face. For example, red apples become rosy cheeks and a cucumber serves duty as a nose. I could no more resist adding these masks to my collection than I could creating my own homage to Arcimboldo (Figure).

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