

---

# Familial and cutaneous features of dysplastic nevi: A case-control study

Margaret A. Tucker, MD,<sup>a</sup> William A. Crutcher, MD,\* Patricia Hartge, ScD,<sup>a</sup> and Richard W. Sagebiel, MD<sup>b</sup> *Rockville, Maryland, and San Francisco, California*

**Background:** Although dysplastic nevi are an important risk factor for melanoma, little is understood about the epidemiology of these nevi. To further characterize some of the correlates of dysplastic nevi, we reexamined patients from one of the original prevalence reports and their first-degree relatives.

**Objective:** Our purpose was to characterize the prevalence and correlates of dysplastic nevi. **Methods:** We studied 25 persons originally diagnosed with dysplastic nevi in 1980 and 1981, 28 controls stratified by age, sex, race, and date of initial examination, and all willing first-degree relatives of both patients ( $n = 78$ ) and control subjects ( $n = 76$ ). Each study subject underwent a full skin examination and biopsy of nevi suspected of being dysplastic nevi, if willing.

**Results:** Eighty percent of the case kindreds were multiplex (2 members or more affected) for dysplastic nevi; the relative risk of having dysplastic nevi was 7.2 (95% confidence interval 2.1 to 24) if one or more relatives had dysplastic nevi. Three of the cases (12%) in multiplex families also had a first-degree relative with melanoma. Cases and relatives with dysplastic nevi of both patients and control subjects tended to have increased numbers of nevi. The risk of having dysplastic nevi rose 99-fold in persons with more than five nevi 4 mm or larger and/or scars on their back ( $p < 0.001$ ).

**Conclusion:** These data support the hypothesis that family members of unselected persons with dysplastic nevi are likely to have dysplastic nevi and may be at increased risk of melanoma.

(J AM ACAD DERMATOL 1993;28:558-64.)

Although dysplastic nevi (DN) are recognized as the major precursor lesion for both familial and sporadic cutaneous malignant melanoma (CMM),<sup>1-3</sup> little is known about the epidemiology of DN. Estimated prevalences of DN in nonmelanoma populations range widely from 1 in 50 persons to 1 in 6.<sup>1-6</sup> With different diagnostic criteria for DN, one group has estimated a prevalence of 1 in 2 persons.<sup>7</sup> Studies of the etiology of melanoma have been inconsistent in evaluating nevus counts and the presence of DN. The risk of melanoma is well established for a person with DN whose family is predisposed to melanoma<sup>2</sup>; for a DN-affected per-

son without a known family history of melanoma, risk estimates are much less certain.<sup>8</sup> Most studies of melanoma risk in relation to number of nevi have found a dose-response relationship,<sup>4, 5, 9-16</sup> but the relation between total number of nevi and presence of DN is unclear.<sup>5, 16, 17</sup>

Kraemer et al.<sup>18</sup> hypothesized that there are several forms of DN, both familial and nonfamilial, which they classified as kindred types A, B, C, D1, and D2. Type A is truly sporadic DN, without melanoma or dysplastic nevi in the family. Type B is familial DN without melanoma. Type C is DN and melanoma in one person. Type D1 is familial DN with one melanoma, and D2 is familial DN with at least two persons with melanoma. The frequencies of DN types A, B, C, and D have not been measured. Albert et al.<sup>19</sup> described typical case histories of patients with DN and concluded that examination of family members often revealed DN or melanoma.

To estimate how many patients with DN have a family history of DN or CMM and to examine the relation between total number of nevi and the pres-

From the Environmental Epidemiology Branch, National Cancer Institute, Rockville<sup>a</sup>; and the Department of Pathology, University of California, San Francisco.<sup>b</sup>

Accepted for publication Sept. 21, 1992.

Reprint requests: Margaret A. Tucker, MD, Environmental Epidemiology Branch, National Cancer Institute, 6130 Executive Blvd., Suite 439, Rockville, MD 20892.

\*Dr. Crutcher: P.O. Box 2099, Napa, CA 94558.

16/1/42831

ence of DN, we examined a randomly selected subgroup of patients with DN from one of the original prevalence reports.<sup>4</sup>

## METHODS

From October 1980 through March 1982, Crutcher and Sagebiel<sup>4</sup> studied 1109 consecutive new patients in a rural private general dermatology practice. They documented that 4.9% of these patients had clinical and histologically confirmed DN. These patients were evaluated for the presence of DN during a cutaneous examination for any presenting complaint other than melanoma or documented DN. At the time of the original identification of patients, the dermatologist examining the patients was establishing a new practice and was not known by the community to be interested in pigmented lesions. Therefore the presenting diagnoses of the patients were typical of a general dermatology practice. We chose a random sample of 25 of the 43 patients reported in 1984 as having histologically confirmed DN and a random sample of patients seen at the same time, stratified by age, sex, and race to match the case group. Study subjects who declined participation were replaced.

All potential study subjects were contacted by telephone and asked to participate in the study. Participation included full-body skin examination, biopsy of lesions suspected as being DN, completion of a brief self-administered questionnaire, permission to review medical records, and permission to contact parents, siblings, and children to ask them to participate also. Eighty-four percent of the cases contacted and 85% of the control subjects agreed to participate. Participants and nonparticipants were similar in age, sex, and race. All living parents, siblings, and children were contacted if possible. Relatives living within 100 miles of Napa, California, were asked to come to Napa for an examination. Relatives living outside that radius who were willing to participate were evaluated in Bethesda, Maryland ( $n = 16$ ). Fifty-eight percent of the identified case relatives and 51% of the control relatives were willing and able to participate. Informed consent was obtained, and full confidentiality maintained at all times. Similar percentages of cases' and controls' relatives refused to participate, had moved or were untraceable, or had other reasons for declining, but 14% of the control relatives versus 3% of the case relatives were too ill or incompetent to participate.

All study subjects underwent a full skin examination with a close, tangential, halogen incandescent examination lamp.<sup>20</sup> Data were recorded on a standardized form. Small nevi (2 to 4 mm), large nevi ( $\geq 4$  mm), DN (both large [ $\geq 4$  mm] and small [2 to 4 mm]), and excision scars were counted on the back from C7 to the posterior iliac crest, midaxillary line to midaxillary line. Nevi counts on other body areas were recorded as categorical variables. If a pigmented lesion was clinically characteristic of a

DN,<sup>20</sup> the study subject was offered excisional biopsy for histologic confirmation. Histologic criteria for DN were those previously published.<sup>21-23</sup> Clinical characteristics of excised nevi were also recorded in a standard fashion.

Attempts were made to obtain all previously excised nevi from all study subjects for histologic review by one of us (R. S.). None of the control subjects had had biopsies, but 26% of case relatives and 3% of control relatives had previous slides available for review. Persons were classified as affected with DN if they had clinical and histologic evidence of DN. Some cases had previously had clinically diagnosed DN that had been removed during the interval between original identification in 1983 and initiation of this follow-up study several years later.

This analysis included all examined cases with DN ( $n = 26$ ), their examined relatives ( $n = 78$ ), all examined control subjects ( $n = 28$ ), and their examined relatives ( $n = 76$ ). Analyses evaluating family history variables have only 25 cases because one participating person refused to identify family members. The measure of association used for evaluating the effects of a host or environmental factor is the relative risk (RR), the ratio of disease incidence in the exposed to the incidence in the unexposed. The effects of potentially confounding variables were evaluated by stratified contingency table analysis. We derived maximal likelihood estimates of rate ratios and 95% confidence intervals (95% CI), with Gart's method. For multiple levels of exposures, the  $p$  value of a linear trend was measured by the Mantel extension of the Mantel-Haenszel procedure. Correlations between nevus counts were measured by the Spearman correlation coefficient.

## RESULTS

Forty of the 78 case parents, siblings, and children had DN confirmed clinically and by excisional biopsy; 15 of 76 control relatives had DN confirmed clinically and histologically. Of the case kindreds, 20 (80%) had two or more family members affected with DN (multiplex families). The risk of having DN was increased if at least one relative also had DN (RR, 7.2; 95% CI, 2.1 to 24). At the time of reexamination of the initial cases and control subjects, six of the cases no longer had clinical DN, but all had numerous biopsies in the intervening years; and four of the six were older than 45 years of age. All of these six cases without clinical DN at the time of reexamination had family members with DN. Two of the control subjects had clinical DN that were confirmed by biopsy at the time of reexamination. Excluding the cases without clinical DN, the control subjects with DN, the family members of both of these, and any other person who had previously had

**Table I.** Relative risk (RR) of dysplastic nevus according to coloring of hair, eyes, skin, and distribution of cases' and controls' relatives

	Cases	Controls	RR	% Relatives	
				Cases (n = 78)	Controls (n = 76)
Hair color					
Brown or black	15	15	1.0	46 (36)*	64 (49)
Blonde or red	11	13	0.8	54 (42)	36 (27)
Eye color					
Brown	5	3	1.0	22 (17)	24 (18)
Blue	17	13	0.8	67 (52)	47 (35)
Green	4	12	0.2	12 (9)	28 (21)
Skin color (buttock)					
Medium or dark	13	15	1.0	43 (33)	47 (35)
Pale	13	12	1.3	57 (43)	53 (40)
Reaction to sun					
Always or usually burns	15	17	1.0	55 (42)	53 (40)
Always or usually tans	11	11	1.1	45 (35)	47 (36)

\*Data expressed as percentage with No. in parentheses.

**Table II.** Relative risk (RR) of dysplastic nevus according to skin conditions and distribution of cases' and controls' relatives

	Cases	Controls	RR	% Relatives	
				Cases (n = 78)	Controls (n = 76)
Solar damage on back of hands					
Mild	16	19	1.0	69 (53)*	64 (49)
Moderate	7	9	0.9	21 (16)	26 (20)
Severe	2	0	inf	10 (8)	9 (7)
Seborrheic keratoses					
None	6	10	1.0	35 (27)	39 (30)
Some	20	18	1.9	65 (51)	61 (46)
Actinic keratoses					
None	18	20	1.0	83 (65)	74 (56)
Some	8	8	1.1	17 (13)	26 (20)
Freckles					
Few	6	11	1.0	24 (19)	31 (23)
Many	20	17	2.4	76 (59)	69 (52)

inf, Infinity.

\*Data expressed as percentage with No. in parentheses.

DN, but currently did not, 19 case families and 26 control families remained. Sixty-eight percent (n = 13) of the case families were multiplex. The risk of DN was unchanged (RR, 7.2; 95% CI, 1.9-27). Three of the cases (all from multiplex-DN families) also had a first-degree relative with a history of melanoma. Two of the melanomas were diagnosed before the first examination of the index case, and one was diagnosed 2 years after the initial examination of the index case. One control without DN had a first-degree relative with a history of mel-

anoma, diagnosed before the original examination of the index control subject. One of the control subject's siblings had clinical DN, but declined biopsy.

The cases and their relatives differed little from the control subjects and their relatives with respect to hair color, eye color, skin color of unexposed skin, skin type, extent of solar damage, or other specific cutaneous conditions (Tables I and II). Cases were more likely than control subjects to have freckles (RR, 2.4; 95% CI, 0.7 to 8.1). The ages of the cases' and control relatives, as well as the cases and control

subjects themselves, were comparable (data not shown).

To compare the nevus distribution on different parts of the body in a group most representative of the general population, we used the control relatives group. Most of the persons who had many small nevi also had large nevi ( $r = 0.44 \pm 0.10$ ), but a few had several small nevi and no large nevi. The number of large nevi on the back correlated best with the number of nevi on the trunk ( $r = 0.60 \pm 0.08$ ). Successively less correlated with large nevi on the back were numbers of arm nevi ( $r = 0.51 \pm 0.09$ ), small nevi ( $r = 0.44 \pm 0.10$ ), leg nevi ( $r = 0.39 \pm 0.10$ ), head and neck nevi ( $r = 0.36 \pm 0.10$ ), and clinical DN ( $r = 0.35 \pm 0.11$ ). In general, those persons who had many nevi on other parts of their bodies, also had an increased number of large nevi on their backs. Of the 76 control relatives, 15 had clinical DN. Most of these (13 of 15) had one or more large nevi on their backs, and 60% had three or more large nevi on their backs, compared with 20% of those without clinical DN. The risk of DN among control relatives increased to 36-fold in those with 10 or more nevi on their backs. Heavily freckled persons tended to have more large nevi and scars on the back ( $r = 0.12 \pm 0.10$ ). Extent of solar damage on the backs of the shoulders correlated weakly with the number of large nevi on the back ( $r = 0.14 \pm 0.11$ ).

Nevi on the arm have been counted in several case-control studies as a surrogate measure of total body nevi. We compared arm nevus counts to the number of nevi larger than 4 mm on the backs of cases and control subjects (Table III). Although the RR of DN was highly associated with the number of arm nevi, it was even more strongly associated with number of back nevi and the combination of arm and back nevi. Arm nevus counts alone could lead to misclassification of persons with increased number of nevi. Arm nevi also do not appear to be a good surrogate for the presence of DN, although more than half the persons with DN have an increased number of arm nevi.

We compared several methods of counting nevi on the back. Small nevi, large nevi, large DN, and excision scars were counted. The number of large DN on the back was less useful than hypothesized for identifying persons with DN after they had been observed for at least 5 years with the diagnosis of DN (Table IV). Adding small nevi to the number of large nevi (all current nevi) did not improve the ability to identify persons with DN. Counting the scars as well as the large nevi or all current nevi was

**Table III.** Relative risk (RR) of dysplastic nevus according to numbers of nevi on the arm and back

	Cases	Controls	RR (95% CI)
Arm 0-4			
Back 0	2	6	1.0
Back 1-2	3	10	0.9 (0.1-5.9)
Back 3+	5	4	3.8 (0.5-26)
All	10	20	
Arm 5+			
Back 0	1	5	0.6 (0.1-6.5)
Back 1-2	4	2	6.0 (0.7-55)
Back 3+	11	1	33 (2.9-331)
All	16	8	
Arm (stratified by back)			
5+			4.0 (1.1-13.9)
Back (stratified by arm)			
1-2			2.5 (0.5-12)
3+			12 (2.3-58)
Trend			$p = 0.002$

more useful in this population that has been routinely observed with attention to pigmented lesions. All cases with DN had nevi or scars on their backs. The risk of DN was 99-fold increased in persons with 25 large nevi and scars and was more than 100-fold increased in persons with more than 20 large and small nevi and scars compared with persons with four or less nevi and scars on their backs. The persons with DN tended to have more large nevi and scars on their backs than those without DN (Fig. 1). The risks of DN in the cases were similar to the risks of DN among the control relatives.

The number of DN varied by age in this cross-sectional evaluation. Older persons tended to have fewer DN. Among cases younger than 40 years of age, 20% had none or one large DN, 60% had two to nine large DN, and 20% had more than 10. Among cases older than 60 years of age, half had none or one large DN, and half had two to nine. This difference could not be accounted for by the number of scars on their backs because the younger cases had more scars. The number of large nevi or scars or large nevi and scars did not vary as much.

## DISCUSSION

This small study of unselected persons with DN suggests that much of DN is familial. According to Kraemer's classification, in this small group, only 20% of the patients' families were type A kindreds (true sporadic DN), 68% were type B (familial DN), and 12% were type D (DN and melanoma). The

**Table IV.** Relative risk (RR) of dysplastic nevus according to different types of nevus counts on the back

	Cases	Controls	RR (95% CI)*	RR (95% CI)†	Trend
Large DN					
0	15	26	1.0	1.0	
1	5	2	4.3 (0.8-22)	9.5 (2.0-43)	
2+	6	0	21 (1.8-222)		$p = 0.001$
Large nevi					
0	3	11	1.0	1.0	
1-2	7	12	2.1 (0.5-9.5)	2.1 (0.5-9.5)	
3-9	9	5	6.6 (1.3-33)	12 (2.4-56)	
10+	7	0	51 (3.4-622)		$p < 0.001$
Large nevi + scars					
0	1	11	1.0	1.0	
1-4	7	15	5.1 (0.7-36)	5.1 (0.7-36)	
5-9	8	2	44 (4.0-430)	99 (9.5-928)	
10+	10	0	220 (9.7-3773)		$p < 0.0001$
All current nevi					
0	1	2	1.0		
1-4	1	16	0.1 (0.01-1.6)	1.0	
5-9	11	6	3.7 (0.4-33)	17 (3.0-85)	
10+	13	4	6.5 (0.6-63)	29 (5.0-165)	$p < 0.001$
All nevi and scars					
0	0	2	1.0		
1-4	1	16	0.3 (0.1-4.1)	1.0	
5-9	8	6	5.3 (0.4-69)	24 (3.0-173)	
10-19	8	3	11 (0.6-149)	48 (5.1-396)	
20+	9	1	36 (1.5-716)	162 (11-2362)	$p < 0.0001$

\*RR with zero cells adjusted to 0.5.

†RR with zero cells or small referent categories combined with next category.

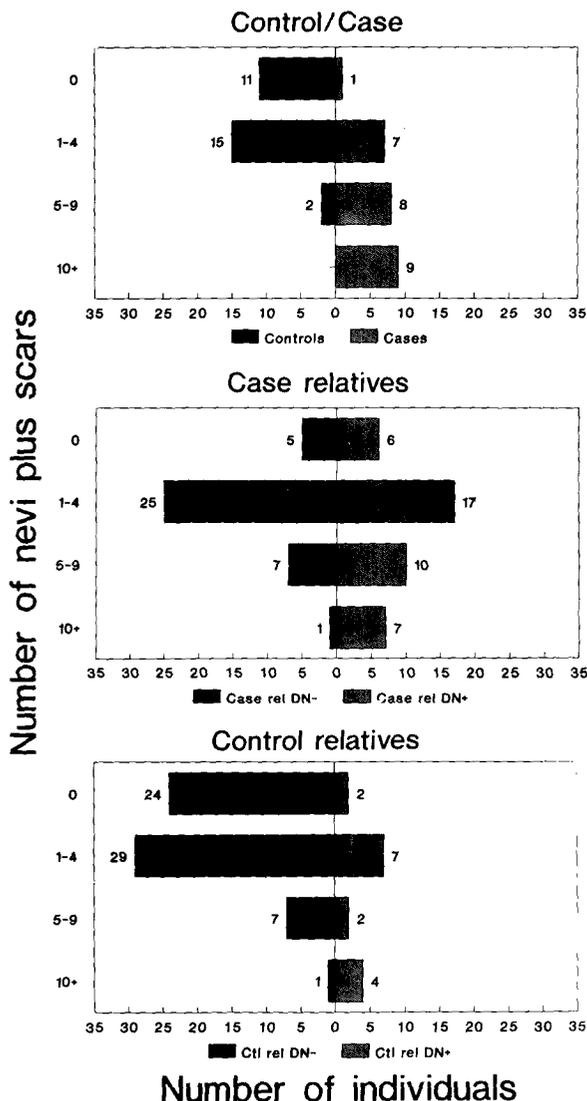
persons from the different kindred types did not differ with respect to the clinical characteristics of the DN, or the number, distribution, or size of nevi. The kindred type could not be predicted from the examination of the index case in the family.

The interpretation of these data is limited by the small number of families studied. There is also a potential bias in the participation of family members if relatives of cases were more likely to participate than relatives of control subjects. The equivalent response rates and comparability of the groups make this less likely. The proportions of families of the various types (A, B, C, and D) and the risk of melanoma in family members will have to be confirmed in larger studies. Despite these limitations, the data do support examination of family members of persons with DN for DN and melanoma.

The risk of melanoma among the original 26 cases could not be estimated because during the follow-up interval in none of the original 26 cases had melanoma developed (approximately 0.02 case would be expected from general population rates). However, one case had a borderline lesion (atypical melano-

cytic hyperplasia) removed during the follow-up period. The risk of melanoma among family members appeared to be increased but was not as high as among members of D2 families as previously estimated.<sup>3, 24</sup> The family members in whom melanoma developed all had DN, similar to the findings in D2 families, which have been reported extensively.<sup>3, 24, 25</sup>

Assessing the relation between number of nevi and the presence of DN was complicated because the cases with DN were observed for several years by a dermatologist knowledgeable about pigmented lesions. Therefore the cases had undergone multiple excisions of their most atypical lesions. Thus the number of DN at the time of this study did not reflect the original number, but the patients who had the highest number of nevi still were more likely to have DN. Only 7% of the control subjects but 69% of the cases had five or more large nevi and scars on their backs. The same phenomenon of missing nevi would apply to patients with melanoma who were under close surveillance because of their nevi before the diagnosis of melanoma. Previous studies that



**Fig. 1.** Number of large nevi and scars on backs of persons with and without DN. Top panel shows number of control subjects at left (solid bars) and cases at right (hatched bars) who have 0, 1-4, 5-9, or 10+ nevi and scars. Middle panel shows number of case relatives without DN at left (solid bars) and with DN at right (hatched bars) within each nevus category. Bottom panel shows number of control relatives without DN (solid bars) and with DN (hatched bars) within nevus categories.

counted nevi or DN as risk factors for melanoma may therefore be underestimating the association. In this study, the number of both large nevi and scars from excisions on the back was a strong risk factor for DN. The number of small nevi was correlated with the number of large nevi; counting all the nevi larger than 2 mm and scars did not add much discrimination over large nevi and scars.

The number of arm nevi correlated with the

number of back nevi, but arm nevus counts alone would lead to frequent misclassification of persons with large nevi or DN in this study. Thus risks of melanoma may have been underestimated in the case-control studies that used arm nevus counts. In these data, the body area with the highest yield was the back. Only one of the cases with DN had no large nevi or scars on his back. The relatively weak correlation between the number of nevi on other body sites may be due to the small number of study subjects; some other studies have found stronger correlations.<sup>17, 26</sup>

As expected,<sup>15, 17</sup> persons with many freckles tended to have more nevi and more DN, probably because sun exposure affects both freckle and nevus development. Although solar damage at the time of examination was not closely related to the number of nevi or presence of DN, most of the persons with little solar damage did not have large nevi. Other skin characteristics did not affect the risk of DN, although others have found that patients with DN are more likely to have sun-sensitive skin types.<sup>27</sup> As in other reports, the number of nevi, and number of DN decreased with age.<sup>17, 24-26, 28</sup> The decrease could not be accounted for by the number of surgical excisions of nevi because younger participants had more scars than older study participants.

These data indicate that nevus counts on persons who have been under medical care for pigmented lesions may not reflect the original number or even type of nevi, if the most atypical lesions have been removed. Thus studies evaluating number and type of nevi should incorporate information from previous nevus excisions. This may be an important consideration in the design of future studies evaluating the association of melanoma with number of nevi.

We thank Cynthia Lacey, Linda Mollet, Mary Fraser, and Beth Busching for their essential role of nursing, Kathy Moyne for technical assistance, Pat Lancey for her administration and oversight of the field work, and the study subjects and their families, without whom we could not have done this study.

**REFERENCES**

1. Precursors to malignant melanoma, Consensus Conference. JAMA 1984;251:1864-6.
2. Greene MH, Clark WH, Tucker MA, et al. High risk of malignant melanoma in melanoma-prone families with dysplastic nevi. Ann Intern Med 1985;102:458-65.
3. Rhodes AR, Sober AJ, Mihm MC, et al. Possible risk factors for primary cutaneous melanoma [Abstract]. Clin Res 1980;28:232A.

4. Crutcher WA, Sagebiel RW. Prevalence of dysplastic nevi in a community practice. *Lancet* 1984;1:729.
5. Holly EA, Kelly JW, Shpall SN, et al. Number of melanocytic nevi as a major risk factor for malignant melanoma. *J AM ACAD DERMATOL* 1987;17:459-68.
6. Cooke KR, Spears GFS, Elder DE, et al. Dysplastic naevi in a population-based survey. *Cancer* 1989;62:1240-4.
7. Piepkorn M, Meyer LJ, Goldgar D, et al. The dysplastic melanocytic nevus: a prevalent lesion that correlates poorly with clinical phenotype. *J AM ACAD DERMATOL* 1989;20:407-15.
8. Kraemer KH, Tucker MA, Tarone R, et al. Risk of cutaneous melanoma in dysplastic nevus syndrome types A and B. *N Engl J Med* 1986;315:1615-6.
9. Holman CDJ, Armstrong BK. Pigmentary traits, ethnic origin, benign nevi, and family history as risk factors for cutaneous malignant melanoma. *JNCI* 1984;72:257-66.
10. Green A, MacLennan R, Siskind V. Common acquired naevi and the risk of malignant melanoma. *Int J Cancer* 1985;35:297-300.
11. Nordlund JJ, Kirkwood J, Forget BM, et al. Demographic study of clinically atypical (dysplastic) nevi in patients with melanoma and comparison subjects. *Cancer Res* 1985;45:1855-61.
12. Swerdlow AJ, English J, MacKie RM, et al. Benign melanocytic naevi as a risk factor for malignant melanoma. *Br Med J* 1986;292:1555-9.
13. Elwood JM, Williamson C, Stapleton PJ. Malignant melanoma in relation to moles, pigmentation, and exposure to fluorescent and other lighting sources. *Br J Cancer* 1986;53:65-74.
14. Roush GC, Nordlund JJ, Forget B, et al. Independence of dysplastic nevi from total nevi in determining risk for non-familial melanoma. *Prev Med* 1988;17:273-9.
15. Osterlind A, Tucker MA, Hou-Jensen K, et al. The Danish case-control study of cutaneous malignant melanoma. I. Importance of host factors. *Int J Cancer* 1988;42:200-6.
16. Weinstock MA, Colditz GA, Willet WC, et al. Moles and site-specific risk of nonfamilial cutaneous malignant melanoma in women. *JNCI* 1989;81:948-52.
17. Kelly JW, Holly EA, Shpall SN, et al. The distribution of melanocytic naevi in melanoma patients and control subjects. *Australas J Dermatol* 1989;30:1-8.
18. Kraemer KH, Greene MH, Tarone R, et al. Dysplastic naevi and cutaneous melanoma risk. *Lancet* 1983;ii:1076-7.
19. Albert LS, Rhodes AR, Sober AJ. Dysplastic melanocytic nevi and cutaneous melanoma: markers of increased melanoma risk for affected persons and blood relatives. *J AM ACAD DERMATOL* 1990;22:69-75.
20. Kelly JW, Crutcher WA, Sagebiel RW. Clinical diagnosis of dysplastic nevi: a clinicopathologic correlation. *J AM ACAD DERMATOL* 1986;14:1044-52.
21. Sagebiel RW, Banda PW, Schneider JS, et al. Age distribution and histologic patterns of dysplastic nevi. *J AM ACAD DERMATOL* 1985;13:975-82.
22. Sagebiel RW. Histopathology of precursor melanocytic lesions. *Am J Surg Pathol* 1985;9(suppl):41-52.
23. Sagebiel RW. Diagnosis and management of premalignant melanocytic proliferations. *Pathology* 1985;17:285-90.
24. Tucker MA, Fraser MC, Goldstein AM, et al. The risk of melanoma and other cancers in melanoma-prone families. *J Invest Dermatol* (In press.)
25. Greene MH, Clark WH Jr, Tucker MA, et al. Acquired precursors of cutaneous malignant melanoma: the familial dysplastic nevus syndrome. *N Engl J Med* 1986;312:91-7.
26. English JSC, Swerdlow AJ, MacKie RM, et al. Site-specific melanocytic naevus counts as predictors of whole body naevi. *Br J Dermatol* 1988;118:641-4.
27. Kopf AW, Goldman RJ, Rivers JK, et al. Skin types in dysplastic nevus syndrome. *J Dermatol Surg Oncol* 1988;14:827-31.
28. Cooke KR, Spears GFS, Skegg DCG. Frequency of moles in a defined population in New Zealand. *J Epidemiol Community Health* 1985;38:48-52.