Site distribution of malignant melanoma

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In a continuous series of 300 patients with cutaneous malignant melanoma the site of the primary lesion was recorded, and incidence rates per unit area of skin were calculated. These rates were high for the face, back and upper arm and low for the abdomen, buttocks, forearm and hand for both sexes. Rates for the leg were high for the women but low for the men. Tumours on the back were evenly distributed among the men but occurred less frequently on the lower back among the women. In general, sites that were usually covered by clothing had lower rates than those usually exposed, with the exception of the forearms and hands. No relation was seen between tumour site and age, sex, depth of invasion or month of diagnosis. Superficial spreading and nodular melanomas did not differ in their site distribution. Incidence rates per unit area at different ages were estimated for sites grouped by their degree of usual exposure: while the rates for unexposed sites were low, those for usually or intermittently exposed sites were higher and similar to each other.

Chez une série de 300 patients souffrant de mélanome malin cutané on a enregistré le foyer de la lésion primaire et calculé les fréquences par unité de surface de peau. Chez les deux sexes ces fréquences étaient élevées pour le visage, le dos et la partie supérieure des bras; elles étaient basses pour l'abdomen, les fesses, les avant-bras et les mains. La fréquence pour les jambes était élevée chez les femmes mais basse chez les hommes. Les tumeurs localisées au dos étaient également distribuées chez les hommes, mais elles touchaient moins souvent le bas du dos chez les femmes. En général, les surfaces habituellement recouvertes de vêtement montraient des fréquences inférieures à celles des surfaces exposées, sauf pour les avant-bras et les mains. Aucun rapport n'a été établi entre la localisation de la tumeur et l'âge, le sexe, la profondeur d'envahissement ou le mois du diagnostic. Les mélanomes à extension superficielle ne différaient pas des mélanomes nodulaires par la distribution des foyers. Les fréquences par unité de surface à différents âges ont été appréciées pour des localisations regroupées selon leur degré d'exposition habituelle: alors que les fréquences des localisations cachées étaient faibles, celles des surfaces habituellement exposées ou exposées de façon intermittente étaient plus élevées et semblables entre-elles.

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The location of cutaneous melanoma is of interest for several reasons. First, the prognosis appears to vary by site, independent of sex and depth of invasion, with, for example, tumours on the trunk and foot having a worse prognosis.[1-4] Second, it is conceivable that melanomas in more observable sites will be diagnosed earlier and will not have invaded as deeply. Most importantly, however, study of the site distribution of melanoma should assist in understanding the causes of these tumours. Incidence and mortality rates for melanoma in many Caucasian populations have been increasing rapidly over recent decades, most markedly for tumours of the lower limb in women and the trunk in men.[5] The increase in melanoma incidence and mortality with decreasing latitude in North America and Australia suggests a positive relation to solar exposure.[6-8] This geographic distribution is not seen in Europe, perhaps because of differences in pigmentation characteristics in different countries.[9] However, the relation to solar exposure is clearly not as simple as it is with squamous cell carcinoma, as outdoor workers do not show a high incidence of melanoma, and, in contrast to squamous cell carcinoma, melanoma has a considerably higher incidence in the upper social classes.[10,11]

Information from cancer registries and mortality statistics[12] are based on broad groupings by site (e.g., trunk, upper limb, and head and neck). In this paper we present a detailed analysis, by site, of a large, continuous series of melanomas seen in one major centre, and we assess the relation of body site to incidence rates per unit area, depth of invasion and pathological subtype.

Methods

From Jan. 1, 1976 to Dec. 31, 1979, 300 adult patients with newly diagnosed cutaneous malignant melanoma were seen at the A. Maxwell Evans Clinic in Vancouver, which provides specialized cancer services for the province of British Columbia. A detailed history and results of examination at the first visit were recorded on standardized forms that included anatomic diagrams on which the site of the primary lesion was recorded. The pathological report on the tumour was reviewed in all cases, and the tumours were classified as lentigo maligna or as superficial spreading or nodular melanoma and by depth of invasion, according to the levels established by Clark and associates.[13] For this study the records were reviewed by one observer, and the tumour site was recorded by assigning coordinates on a grid matching the standard anatomic diagram. This allowed later computer plotting of the sites.

Previous studies have used a variety of schemes for documenting the surface area of paths of the body. However, some of these, such as the familiar "rule of nines"[14] and similar methods,[15] are gross approximations designed to aid memorization. Others are based on unverified geometric estimates.[16] Tables produced by Berkow[17] have been widely used. Lund and Browder[18] reviewed these earlier publications and presented figures for well defined body surface divisions that avoid the major errors of the Berkow estimates; thus, we used the Lund and Browder figures. Direct assessments of surface area based on measurements of an appropriate population sample do not appear to be available.

In assessing the significance of the ratio of observed to expected numbers of tumours at given sites, the conventional χ^2 statistic with continuity correction was used.

Table I—Site distribution of 281 cases of cutaneous melanoma (superficial spreading or nodular) and relative incidence per unit of surface area

Site	Surface area (%)	No. of cases		Ratio of observed to expected numbers*		
		Men	Women	Men	Women	Both
Face	3.5	8	14	1.9	2.5†	2.2
Scalp, neck	5.5	11	5	1.7	0.6	1.0
Chest	10.6§	15	7	1.2	0.4†	0.7
Back	10.6	43	25	3.4†	1.5	2.3
Abdomen, buttocks	10.8§	5	2	0.4‡	0.1†	0.2
Upper arm	8.0	13	24	1.4	1.8†	1.7
Forearm, hand	11.0	2	8	0.2†	0.5†	0.3
Hip, thigh	19.0	9	24	0.4†	0.8	0.6
Leg	14.0	6	46	0.4†	2.0†	1.3
Foot	7.0	6	8	0.7	0.7	0.7

*Statistically significant at †$p < 0.01$ and ‡$p < 0.05$.
§Areas given are for men; for women they are 11.6% and 9.8% respectively.

Results

The site distribution of all 300 melanomas in the series is shown in Figs. 1 and 2. For further analysis four tumours in the axilla and four subungual tumours were excluded because of the obvious difficulty in calculating the relevant area, seven cases of lentigo malignant melanoma were excluded because of the predilection of this type for exposed sites,[19] and four tumours were excluded because they could not be classified.

In Table I the distribution of the remaining 281 cases of superficial spreading or nodular melanoma is expressed more quantitatively: here the distribution of cases by site is compared with the distribution of surface area to yield a ratio; if the ratio is above 1, the occurrence rate per unit area at that site was greater than the average rate for the body as a whole.

The incidence per unit area of the face was higher than average for both sexes, while for the scalp and neck the rates were higher than average for the men and

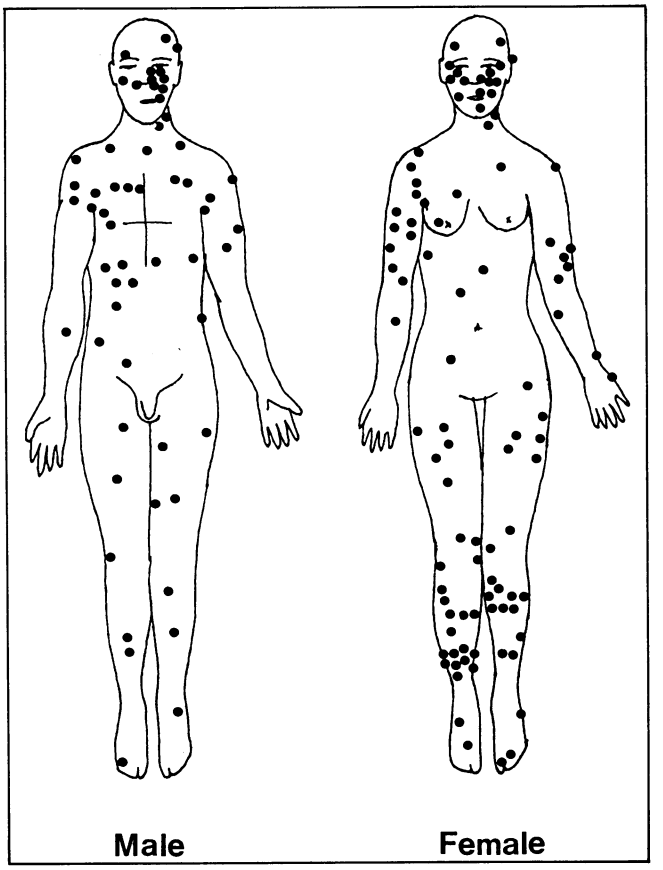

FIG. 1—Distribution of cutaneous malignant melanoma, anterior. (Four axillary tumours in men, three on right and one on left, not shown.)

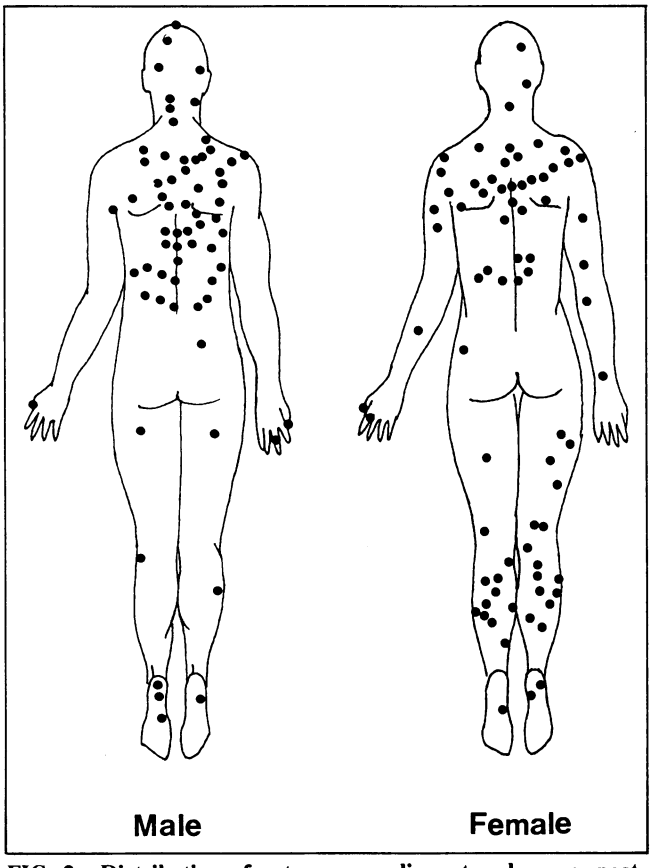

FIG. 2—Distribution of cutaneous malignant melanoma, posterior.

lower than average for the women, although the differences were not statistically significant. For the chest the incidence rate per unit area was significantly below average for the women but slightly above for the men. The frequency of tumours on the back was much higher than average for the men, while for the women it was somewhat above average, but Fig. 2 shows that the main difference between the sexes was in tumours of the back below the scalpulae; the frequency of tumours on the upper back and shoulders was similar in the two sexes. Few melanomas occurred on the abdomen or buttocks, where the rates per unit area were significantly below average for both sexes.

Melanoma appeared to be more common than average on the upper arms in both sexes, and significantly so in the women. Few tumours occurred on the forearm and hands, the rates per unit area being significantly below average for both sexes. Although a considerable number of tumours occurred on the hip and thigh, the rate per unit area was about average for the women and significantly below average for the men. On the leg the rate was also below average for the men, while it was significantly above average for the women. The incidence per unit area on the feet was about average for both sexes, although Fig. 1 suggests that while tumours on the soles of the feet had similar incidence rates in the two sexes those on the dorsum were more frequent in the women.

On the upper arm, thigh and leg, melanomas occurred more frequently on the anterior than on the posterior surface, the distribution being 73:41. This trend was seen for each sex and for each site. A lateral to medial comparison showed no marked difference.

There were no significant differences in the ratio of superficial spreading to nodular melanoma by site, sex or age. A total of 56 patients had nodular melanoma (24 men, 32 women) and 225 had superficial spreading tumours (94 men, 131 women).

The mean age at diagnosis was 44.9 years; 31% were under 35 years, 33% between 35 and 49 years and 36% 50 years or older. The age distributions did not differ appreciably by sex or by tumour type, but did vary by site, the mean age of patients with tumours of the face, scalp, neck and foot being 52 years, compared with 43 years for those with tumours of the trunk and 44 years for those with other limb tumours.

There was no significant variation in the depth of invasion of the tumour either by site or by sex. This was assessed separately for nodular and superficial spreading tumours, as the nodular tumours tended to be, as expected, more deeply invasive (Table II).

As a site-specific seasonal variation in melanoma incidence has been reported[20] we examined the month of diagnosis. Of the 281 melanomas 142 (51%) were diagnosed in the 6 months between October and March, and no variations by site, sex, age or tumour type were seen.

Seven patients with lentigo maligna melanoma were excluded from the main analysis. Four of these lesions (two in each sex) were on the face, and the other three (all in women) were on the shoulder, upper arm and calf. These patients were older than the others (mean age 58.1 years). The four unclassified melanomas were on the chest in a man and on the back, upper arm and leg in three women. We excluded four melanomas, two superficial spreading and two nodular, in the axilla (all in men). We also excluded four subungual tumours: three were superficial spreading lesions on the hand (two in men and one in a woman), and the fourth was a nodular tumour on the foot (in a woman).

To evaluate site differences at different ages we grouped the sites into those that are usually exposed (face, neck, scalp and hand), intermittently exposed (upper arm, back, thigh, leg, forearm and man's chest) and less frequently exposed (abdomen, foot and woman's chest). Such groupings are arbitrary and reflect only general patterns of dress. We then calculated incidence rates per unit area for site groupings at different ages. Table III shows that for each site group the incidence rates rise with age, that in each age group the rate for unexposed sites is lower than the rates for exposed or intermittently exposed sites, and that the last two rates are similar to each other.

Discussion

Malignant melanoma is justifiably receiving much attention because of its remarkably rapid increase in

Table II—Depth of invasion of nodular and superficial spreading melanoma

	No. (and %) of type of melanoma	
Level*	Nodular	Superficial spreading
I	0	1
II	1 (2)	58 (27)
III	13 (25)	58 (27)
IV	35 (66)	94 (43)
V	4 (8)	6 (3)
Unknown	3	8
Total	56	225

*Those established by Clark and associates.[13]

Table III—Estimated incidence rates per unit area by age and site

	Annual incidence rate* per 100 000 population per unit area of skin (and no. of patients) by age (yr)			
Site group	15–34	35–49	≥ 50	All ages†
Usually exposed‡	1.8 (10)	6.3 (11)	20.6 (20)	8.8
Intermittently exposed§	2.8 (69)	9.2 (73)	16.1 (70)	8.5
Less frequently exposed‖	0.9 (8)	3.1 (9)	6.9 (11)	3.3
Total	2.2 (87)	7.4 (93)	14.6 (101)	7.3

*When there are m melanomas in the series, of which s are at a given site constituting p% of the total skin area, the incidence rate = (s/mp) (population incidence rate), where the population incidence is derived from the British Columbia cancer registry.
†Age-standardized by direct method to British Columbia population in 1978.
‡Face, neck, scalp and hand.
§Upper arm, back, thigh, leg, forearm and man's chest.
‖Abdomen, foot and woman's chest.

incidence over the last few decades. In Canada mortality rates have doubled in about 15 years.[21] Incidence rates recorded in British Columbia since 1970 have shown an even greater rise,[22] although part of this rise is probably due to earlier diagnosis and the reporting of more borderline lesions. The increase in incidence and mortality has been demonstrated in every Caucasian population in which they have been studied.[5] While incidence and mortality rates have increased in all age groups, in Canada and in most other societies the greatest increase has been in people under the age of 50. The increase has been most marked for tumours of the lower limb in women and for tumours of the trunk in men. This was first shown with data from the Connecticut cancer registry covering a period from 1935 to 1970 and has since been demonstrated for several other societies.[5,23-26] The division into broad groupings (e.g., trunk and lower limb) was the only way in which such data could be analysed, as they were obtained from routine cancer registration or mortality registration systems using conventional coding schemes that did not allow any finer breakdown. In these studies cross-sectional data applicable to one recent period showed a very high female:male ratio for tumours of the lower limb and a high male:female ratio for tumours of the trunk.[11,12,27]

It seems possible that the recent rise in melanoma incidence, the excessively high incidence of melanoma in women, particularly younger women, and aspects of the site distribution might be explained by the more rapid recognition of early lesions, especially at exposed sites and in women. Thus, we could expect that lesions at exposed sites, lesions in women and perhaps lesions diagnosed in the summer would tend to be earlier and therefore smaller and less invasive; our data show that this is not the case.

Our data allow us to be much more specific about the male:female distribution of tumours. The high incidence of melanomas on the lower limb in women is most marked for melanomas of the leg but is clearly present for melanomas of the thigh and may be present for melanomas of the dorsum of the foot. The high incidence of melanomas of the trunk in men is most marked for tumours on the back below the scapulae and also for tumours of the chest. On the upper back from the scapulae to the neck there is an approximately equal sex distribution of melanoma, while there is a higher incidence of tumours of the upper arms and shoulders in women. Tumours of the face are common in terms of distribution per unit area in both sexes, while on the scalp and the neck there is a higher incidence in men.

These patterns of distribution are consistent with the areas left uncovered by clothing, especially the type of clothing worn by younger people today. The one exception to a general etiologic hypothesis of exposure to sunlight in the data presented here is the remarkable infrequency of melanomas on the forearms and hands, areas that are very frequently exposed. The large series of Davis and coworkers[28] showed a similar low proportion (4.3%) of melanomas on the forearms and hands.

In our series there were seven lentigo maligna melanoma tumours, four on the face; these tumours tended to occur at advanced ages. It is generally accepted that lentigo maligna melanoma, like squamous cell skin cancer, occurs on exposed sites at advanced ages and is probably related to long-term solar exposure. The possibility that nodular and superficial spreading melanoma have different causes has received little attention, but the lack of any difference in site distribution does not support this notion.

A more detailed study of the incidence rate of melanoma would not only take into account skin area and clothing habits but also epithelial thickness and perhaps melanocyte density. Estimates of melanocyte density per square millimetre for the skin of the head and neck, limbs and trunk are 2000, 1150 and 900 respectively.[29] In our study the age-standardized incidence rates per unit area of these sites were 12.5, 6.9 and 6.2 per 100 000 population per year, suggesting a positive correlation with melanocyte density.

However, this correlation between melanoma incidence and melanocyte density tells us little about the origins of melanoma. Melanocyte density can be increased by ultraviolet radiation.[30] Therefore, a positive association between ultraviolet radiation and melanoma incidence could result from ultraviolet radiation either increasing the probability of an individual melanocyte becoming cancerous or increasing melanocyte density alone, or from a combination of the two effects. In contrast to the positive correlation between melanocyte density and melanoma incidence suggested here, Sober and Fitzpatrick[31] found no correlation, but they compared melanocyte density with the proportion of melanomas occurring on that part of the body, taking no account of the percentage of surface area.

Earlier studies using less detailed data showed a lower mean age for women with tumours of the lower limb and for men with tumours of the trunk than for patients with other melanomas.[23,25] This distribution, taken with the increases seen over time, is consistent with a birth-cohort-related effect, suggesting that the cause is one to which younger people tend to be exposed. One hypothesis is that the increase in melanoma occurs because young people today expose themselves to sunlight more than earlier generations did at the same age. If melanoma occurrence were related directly to the total amount of solar exposure, as is the case for squamous cell carcinoma of the skin, the site-specific increase in melanoma could be explained by the argument that the exposure of those sites (the lower limbs in women and the back in men) has increased in recent years owing to changes in recreational and clothing habits, whereas the solar exposure of sites such as the face has presumably not changed. If this is so, then at any given age the incidence rates of melanoma at sites that are almost totally exposed, such as the face, should still be higher than the rates at sites that are only intermittently exposed, such as the chest and thighs. The data in Table III, however, suggest that the incidence rates per unit area for exposed sites, particularly at lower ages, are no higher than the rates for intermittently exposed sites.

How can the observation that the rates are similar for totally and intermittently exposed skin be explained? One explanation would be that the relation of melanoma incidence to total sunlight dose is not linear but becomes

less strong at higher doses, perhaps having an S-shaped curve; thus, intermittently exposed skin may be sufficiently exposed to achieve incidence rates nearly as high as totally exposed skin. An alternative explanation would be that intermittent acute exposure may be more harmful for a given dose of radiation than chronic exposure; thus, similar incidence rates can result from intermittent and continuous exposure. This hypothesis is consistent with the absence of a higher melanoma incidence in outdoor workers and with the markedly higher incidence in the upper social classes, which may be due to increased sun exposure during the recreational activities and vacations permitted by affluence.[10] It would also be consistent with the indication that melanoma patients tend to burn rather than to tan on exposure to the sun.[32] A third explanation would be to question whether the site distribution delineates sites in their degree of total solar exposure. The face, neck and scalp are not always exposed: the scalp and neck are protected by hair, particularly at lower ages, and the face may also be protected by hair on men or by hats. Light clothing still allows some exposure; a typical man's white shirt may transmit 20% of solar ultraviolet radiation, and open-weave clothing may transmit much more.[33]

Recording the precise site distribution of cutaneous melanoma has an important part to play in understanding the causes of the condition, and we urge colleagues in other centres to employ precise recording of site. Moreover, because the site distribution of melanoma has been changing over time and may differ from one centre to another because of differences in site-specific incidence or differences in referral patterns, recording of site is important, as the prognosis of melanoma varies by site, independently of sex and depth of invasion. This has to be kept in mind when comparing treatment results from different centres, and in designing and interpreting clinical trials.

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References

1. ELDH J, BOERYD B, PETERSON LE: Prognostic factors in cutaneous malignant melanoma in stage I. A clinical, morphological and multivariate analysis. *Scand J Plast Reconstr Surg* 1978; 12: 243–255
2. PETERSEN NC, BODENHAM DC, LLOYD OC: Malignant melanomas of the skin. A study of the origin, development, aetiology, spread, treatment, and prognosis. II. *Br J Plast Surg* 1962; 15: 97–116
3. MCLEOD GR: Factors influencing prognosis in malignant melanoma. *Prog Clin Cancer* 1975; 6: 177–182
4. LARSEN TE, GRUDE TH: A retrospective histological study of 669 cases of primary cutaneous malignant melanoma in clinical stage I. 7. The relative prognostic value of various clinical and histological features. The result of a stepwise multiple regression analysis of 553 of these cases. *Acta Pathol Microbiol Scand [A]* 1979; 87: 469–477
5. ELWOOD JM, LEE JAH: Recent data on the epidemiology of malignant melanoma. *Semin Oncol* 1975; 2: 149–154
6. LANCASTER HO: Some geographical aspects of the mortality from melanoma in Europeans. *Med J Aust* 1956; 1: 1082–1087
7. ELWOOD JM, LEE JAH, WALTER SD, MO T, GREEN AE: Relationship of melanoma and other skin cancer mortality to latitude and ultraviolet radiation in the United States and Canada. *Int J Epidemiol* 1974; 3: 325–332
8. FEARS TR, SCOTTO J, SCHEIDERMAN MA: Skin cancer, melanoma and sunlight. *Am J Public Health* 1976; 66: 461–464
9. LEE JAH, ISSENBERG HJ: A comparison between England and Wales and Sweden in the incidence and mortality of malignant skin tumours. *Br J Cancer* 1972; 26: 59–66
10. LEE JAH, STRICKLAND D: Malignant melanoma: social status and outdoor work. *Br J Cancer* 1980; 41: 757–763
11. HOLMAN CDJ, MULRONEY CD, ARMSTRONG BK: Epidemiology of pre-invasive and invasive malignant melanoma in Western Australia. *Int J Cancer* 1980; 25: 317–323
12. CROMBIE IK: Distribution of malignant melanoma on the body surface. *Br J Cancer* 1981; 43: 842–849
13. CLARK WH JR, FROM L, BERNARDINO EA, MIHM MC JR: The histogenesis and biologic behaviour of primary human malignant melanomas of the skin. *Cancer Res* 1969; 29: 705–727
14. WALLACE AB: The exposure treatment of burns. *Lancet* 1951; 1: 501–504
15. RUDOWSKI W, NASILOWSKI W, ZEITKIEWICZ W, ZIENKIEWICZ K: Estimating the extent of burns. In RUDOWSKI W, NASILOWSKI W (eds): *Burn Therapy and Research*, Johns Hopkins U Pr, Baltimore, 1977: 5–11
16. SKERLJ B, KULCAR Z: Surface areas of body parts and their possible implications in treating burns. *Br J Plast Surg* 1956; 9: 165–167
17. BERKOW SG: A method of estimating the extensiveness of lesions (burns and scalds) based on surface area proportions. *Arch Surg* 1924; 8: 138–148
18. LUND CC, BROWDER NC: The estimation of areas of burns. *Surg Gynecol Obstet* 1944; 79: 325–358
19. CLARK WH JR, MIHM MC JR: Lentigo maligna and lentigo-maligna melanoma. *Am J Pathol* 1969; 55: 39–67
20. SCOTTO J, NAM JN: Skin melanoma and seasonal patterns. *Am J Epidemiol* 1980; 111: 309–314
21. ELWOOD JM, LEE JAH: Trends in mortality from primary tumours of skin in Canada. *Can Med Assoc J* 1974; 110: 913–915
22. Cancer Control Agency of British Columbia and division of vital statistics, BC Ministry of Health: *Cancer in B.C.*, Victoria, 1978
23. MAGNUS K: Incidence of malignant melanoma of the skin in the five Nordic countries: significance of solar radiation. *Int J Cancer* 1977; 20: 477–485
24. Idem: Habits of sun exposure and risk of malignant melanoma: an analysis of incidence rates in Norway 1955–57 by cohort, sex, age, and primary tumor site. *Cancer* 1981; 48: 2329–2335
25. MALEC E, EKLUND G: The changing incidence of malignant melanoma of the skin in Sweden, 1959–1968. *Scand J Plast Reconstr Surg* 1978; 12: 19–27
26. TEPPO L, PAKKANEN M, HAKULINSEN T: Sunlight as a risk factor of malignant melanoma of the skin. *Cancer* 1978; 41: 2018–2027
27. LEE JAH, YONGCHAIYUDHA S: Incidence of and mortality from malignant melanoma by anatomical site. *J Natl Cancer Inst* 1971; 47: 253–263
28. DAVIS NC, HERRON JJ, MCLEOD GR: Malignant melanoma in Queensland. Analysis of 400 skin lesions. *Lancet* 1966; 2: 407–410
29. FITZPATRICK TB, SZABO G: The melanocyte: cytology and cytochemistry. *J Invest Dermatol* 1959; 32: 197–209
30. QUEVEDO WC, FITZPATRICK TB, PATHAK MA, JIMBOW K: Light and skin color. In PATHAK MA, HARBER LC, SEIJI M, KUKITA A, FITZPATRICK TB (eds): *Sunlight and Man: Normal and Abnormal Photobiologic Responses*, U of Tokyo Pr, Tokyo, 1974: 165–194
31. SOBER AJ, FITZPATRICK TB: The melanin pigmentary system in man. In CLARK WH, GOLDMAN LI, MASTRANGELO MJ (eds): *Human Malignant Melanoma* (Clinical Oncology Monogr, vol 3), Grune, New York, 1979
32. KLEPP O, MAGNUS K: Some environmental and bodily characteristics of melanoma patients. A case–control study. *Int J Cancer* 1979; 23: 482–486
33. ROBERTSON DF: The prophylaxis of ultraviolet radiation damage: a physicist's approach. In MCCARTHY WH (ed): *Melanoma and Skin Cancer*, New South Wales Government Printer, Sydney, 1972: 273–291