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SITE DISTRIBUTION OF CUTANEOUS MELANOMA IN QUEENSLAND

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The age-adjusted incidence rates of cutaneous melanoma in Queensland in 1987 have been analysed for 16 anatomic sites, taking into account their surface areas. In men, the incidence of invasive melanoma on the ears, a chronically sun-exposed site, was extraordinarily high with annual rates of over 200 per 10^5 units of surface area in the Queensland population. Next highest rates of over 100 melanomas per 10^5 units were found on the face, neck, shoulders and back in men and the face and shoulders in women. Comparison with site-specific incidence rates in the same population 7½ years previously showed that incidence of invasive disease had significantly increased for all these sites, though the largest relative increase in this period occurred on the forearm in both men and women. Melanoma was very rare on the buttocks of both sexes and on the scalp in women, sites which receive the least sun exposure. These findings are consistent with the theory that excessive total sun exposure plays a major role in the aetiology of cutaneous melanoma.

While there is general agreement that exposure to UV radiation is the chief environmental cause of skin cancer in White populations, the nature of the role of sun exposure in the aetiology of melanoma is frequently questioned on the basis of its site distribution (Vagero *et al.,* 1986; Koh *et al.,* 1990). Squamous-cell carcinoma (SCC) and, to a lesser extent, basal-cell carcinoma (BCC), are most numerous on heavily-exposed sites, namely the face and neck, the backs of the hands and the forearms (Pearl and Scott, 1986), and thus the causal role of sun exposure is accepted without question for these cancers. On the other hand, it is widely reported that cutaneous melanoma occurs most commonly on less sun-exposed sites such as the back and the lower limbs of women (Koh *et al.,* 1990).

One difficulty has been that much of the published information regarding melanoma site distribution has been open to various interpretations, allowing the data to be presented as evidence both for and against a dose-response relationship between sunlight and the development of melanoma. In an analysis of body site of melanoma occurring in the 1960's which took account of surface area (Elwood and Lee, 1975), sites with significant excesses of melanomas were, in general, exposed areas. Magnus (1981) analysed incidence rates of melanoma per unit area (1%) for 3 broad site-groups: face and neck combined, trunk, and lower limb, based on reports to the Cancer Registry of Norway between 1955 and 1977. He found that generations born between 1930 and 1949 had a higher incidence of melanoma on the trunk in males and on the lower limbs in females, than on the face and neck. Later Crombie (1981) examined the distribution of melanoma among 4 major sites, head, upper limbs, lower limbs and remainder (trunk and unspecified sites combined) based on registry data for 37 White populations. Compared with the proportion of melanocytes at each of these sites, small excesses of melanoma were found on the head and trunk among men and on the head in women, and a large excess on the lower limbs in females. Crombie (1981) concluded that the solar hypothesis could explain neither the excesses on "little-exposed" sites, nor the sex differences. Pearl and Scott (1986) later used Relative Tumour Densities (RTD) to compare the anatomic distribution of skin cancers between populations around the world, based on a variety of data sources. RTD was calculated as the proportion of tumours at a particular site divided by the proportion of skin-surface area at that site. The authors observed an extreme excess of SCC and BCC on exposed areas of the face such as the nose, but a more even spread of melanomas over the body, which they suggested might be explained by "intense recreational exposure with little clothing" (Pearl and Scott, 1986). In a study of the detailed anatomic distribution of melanomas in Denmark, 1978–1982, standardized incidence rates per unit surface area were calculated, although lentigo maligna melanomas were excluded (Osterlind *et al.,* 1988). Highest rates were observed, in men, for the back, followed by the chest, face, and scalp and neck. In women, highest rates were for the leg, followed by the back and face.

Because incidence rates of melanoma continue to climb (MacKie *et al.,* 1992; MacLennan *et al.,* 1992), accurate and current data regarding the sites of predilection of melanoma are needed, being fundamental to a consideration of the causal role of site-specific sun exposure. We have therefore examined in detail the site-specific incidence rates of melanoma in a single high-risk population, namely that of Queensland, Australia.

METHODS

Case ascertainment

Pathology reports for all primary cutaneous melanomas (ICD 9th revision site codes 172.0–172.9 and 232.0–232.9) diagnosed in Queensland were gathered for 2 separate 12-month periods, 7½ years apart. In the first study year, reports on all first primary melanomas of the skin diagnosed between 1 July 1979 and 30 June 1980 were gathered from 24 government, hospital and private pathology laboratories throughout Queensland, largely during personal visits by A.G. to each laboratory (Green, 1982). This was prior to the establishment of the Queensland Cancer Registry (QCR) in 1982, which was the principal data source for the 1987 cases. Although notification of reportable neoplasms, including pre-invasive and invasive melanoma, is legally required from all hospitals, nursing homes and pathology laboratories, our quality control procedures included verification of QCR listings against pathology laboratory indexes and the written histological reports of all melanomas diagnosed in 1987. During the period 1979 to 1987, there were no known systematic alterations in methods of diagnosis and treatment of melanomas in Queensland to explain the observed trends.

Sites of melanoma

Site was recoded from pathology reports for 1987 using the same classification as used in 1979/80. For approximately one-third of cases involving the upper and lower limbs in 1987, there was a lack of precision as to exact subsite and the case was coded as "unknown" upper or "unknown" lower limb. In analysis, these cases were assigned to specific sites within the upper limb (shoulder, arm, forearm, back of hand) and lower limb (thigh, leg, dorsum of foot, sole of foot) in the same proportion as the specified subsites according to level (pre-invasive; invasive), sex and 10-year age group. Similarly, subsite was proportionately assigned for melanomas on the head and neck (2% of cases) and trunk (2%) when it had not

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been specified. For 8% of all cases no site information had been reported, and unknown sites were likewise assigned to all body sites within sex- and age-specific groups, in proportion to the numbers with site information available. There were 44 persons (34 male and 10 female) who presented as incident cases with metastases from an unknown primary, and these cases were excluded from the analysis.

Pathology for 1979/80 was coded according to McGovern (1970) and, in 1987, by QCR according to the first edition of the International Classification of Disease for Oncology (ICD-O) (1976). Thus, the code 8742/2 was used for lentigo maligna (Hutchinson's melanotic freckle) whether or not melanoma was also diagnosed, and both are included in our pre-invasive category. There is likely to be some under-reporting of lentigo maligna since some pathologists do not regard it as a cancer. A large number of lesions in 1987 coded to "melanoma not otherwise specified" ICD-O group 8720/3 would have been distributed among other McGovern (1970) categories in 1979/80.

Data analysis

Only persons resident in Queensland were included. Population denominators were from the Australian Bureau of Statistics for June 1980 and June 1986 (Census Year). Site-specific, age-standardized rates were calculated per 10^5 units, where the unit is the equivalent of the total surface area of the skin of a person. In the calculation of rates for a site per unit surface area, each sex- and 10-year age-group population denominator was multiplied by the proportion of the total surface area of the body occupied by that site (Lund and Browder, 1944). For example, in calculating rates for the back, each population denominator was multiplied by 0.1 prior to the calculation of age-specific rates and direct standardization, because the back is estimated as 10% of the total body surface area; thus, the denominator for the surface area of the backs of 91,000 males aged 30–39 years became 9,100. Rates and their confidence limits were calculated as described by Boyle and Parkin (1991)—the Poisson approximation method was used to calculate the standard errors of directly age-standardized rates. Incidence rates for 1979/80 and 1987 were age-standardized to the standard world population (Boyle and Parkin, 1991). Standardized rate ratios and their confidence intervals were calculated according to the approximation of Smith (1987).

RESULTS

General incidence

The incidence of melanoma, pre-invasive and invasive, in Queensland in 1987 was 66.6 per 10^5 among men and 56.4 among women, age-standardized to the world population (MacLennan *et al.*, 1992). The incidence rates of invasive melanoma alone were 48.9 and 39.7 per 10^5 among men and women, respectively. Based on these data, it is estimated that 1 in 14 men and 1 in 17 women in Queensland will develop melanoma in their lifetime (MacLennan *et al.*, 1992).

Site-specific incidence of melanoma in 1987

For ease of descriptive ranking, site-specific incidence rates have been arbitrarily classified into 6 groups: extremely high (300+ per 10^5 units of surface area); very high (100–299 per 10^5 units); high (50–99 per 10^5 units); moderately low (30–49 per 10^5 units); low (5–29 per 10^5 units); and extremely low (<5 per 10^5 units). (Low categories in Queensland may be considered high in many other populations of similar phenotype.)

Site-specific incidence of pre-invasive melanoma

For pre-invasive melanoma only, the highest rates per unit area of skin among men in 1987 occurred on the face (208.8 per 10^5) and ears (138.8 per 10^5) (Table I). On the neck, shoulders, back and forearms, rates were moderate, while on the chest, dorsum of hands, legs and upper arms they were low. Among women the only site with a high rate of pre-invasive melanoma was the face (192.5 per 10^5 units); rates for all other sites were low or extremely low (Table I).

Site-specific incidence of invasive melanoma

For invasive melanoma, the highest incidence of all was seen in men on the ear (209.9 per 10^5 units) and shoulder (161.9); the back, face and neck also showed very high incidence rates (Table II). Rates of disease were high for the chest; moderate for the upper limbs and legs; and low or extremely low for the remainder of the body (Table II). No melanomas were diagnosed on the buttocks or the soles of the feet in men in 1987.

Among women, very high rates of invasive melanoma were seen only on the face (115.1 per 10^5 units) and shoulders (103.8), though high rates were observed on the upper arms, back, forearms, legs and ears (Table II). There were moderate rates of invasive melanoma for the neck and thighs in women,

TABLE I – AGE-STANDARDIZED INCIDENCE RATES PER UNIT SURFACE AREA × 10^5 IN QUEENSLAND IN 1987 BY ANATOMIC SITE AMONG MEN AND WOMEN, AND COMPARISON WITH 1979/80 RATES: PRE-INVASIVE MELANOMA

Site	Men					Women				
	1979/80		1987		Ratio (95% CL)[1]	1979/80		1987		Ratio (95% CL)[1]
	Number of cases	Rate	Number of cases	Rate		Number of cases	Rate	Number of cases	Rate	
Scalp	1	2.1	4	6.9	3.2 (2.2, 4.7)	0	—	0	—	—
Face	48	158.8	74	208.8	1.3 (1.2, 1.4)	45	155.91	75	192.5	1.2 (1.2, 1.3)
Ears	6	93.6	11	138.8	1.5 (1.4, 1.6)	0	—	1	8.4	—
Neck	10	30.0	21	58.8	2.0 (1.7, 2.2)	10	35.3	12	32.7	0.9 (0.8, 1.1)
Shoulders	11	29.1	19	41.8	1.4 (1.3, 1.6)	5	12.2	5	12.0	1.0 (0.8, 1.2)
Chest	7	9.7	16	17.8	1.8 (1.5, 2.3)	4	5.4	12	12.8	2.4 (1.8, 3.1)
Abdomen	4	4.9	3	3.1	0.6 (0.4, 0.9)	4	5.0	3	2.7	0.5 (0.4, 0.8)
Back	25	21.8	55	38.0	1.4 (1.5, 2.0)	12	10.8	26	18.9	1.7 (1.4, 2.2)
Buttocks	0	—	0	—	—	1	1.9	0	—	—
Upper arms	6	5.8	7	5.1	0.9 (0.6, 1.2)	19	20.4	32	25.6	1.3 (1.1, 1.5)
Forearms	4	6.0	26	30.1	5.0 (4.1, 6.2)	7	10.5	26	29.3	2.8 (2.3, 3.3)
Dorsum of hands	1	2.7	5	10.6	3.8 (2.9, 5.2)	1	4.4	1	1.7	0.4 (0.2, 0.6)
Thighs	5	2.5	8	3.0	1.2 (0.7, 1.9)	4	1.8	21	8.4	4.7 (3.1, 7.2)
Legs	6	3.3	15	7.3	2.2 (1.6, 3.1)	22	13.7	41	18.5	1.3 (1.1, 1.6)
Dorsum of feet	0	—	2	4.4	—	0	—	2	3.4	—
Soles	0	—	0	—	—	0	—	1	1.7	—

[1]95% confidence limits.

TABLE II – AGE-STANDARDIZED INCIDENCE RATES PER UNIT SURFACE AREA × 10^5 IN QUEENSLAND IN 1987 BY ANATOMIC SITE AMONG MEN AND WOMEN, AND COMPARISON WITH 1979/80 RATES: INVASIVE MELANOMA

Site	Men					Women				
	1979/80		1987		Ratio (95% CL)[1]	1979/80		1987		Ratio (95% CL)[1]
	Number of cases	Rate	Number of cases	Rate		Number of cases	Rate	Number of cases	Rate	
Scalp	7	14.4	11	20.3	1.4 (1.2, 1.7)	1	2.0	1	0.83	0.4 (0.2, 0.8)
Face	24	81.1	53	143.3	1.8 (1.7, 1.9)	29	85.8	47	115.1	1.3 (1.2, 1.4)
Ears	6	96.4	16	209.9	2.2 (2.0, 2.3)	2	32.5	4	50.1	1.5 (1.4, 1.7)
Neck	15	55.1	44	123.1	2.2 (2.1, 2.4)	12	40.8	13	31.2	0.8 (0.7, 0.9)
Shoulders	25	66.7	71	161.9	2.4 (2.3,2.6)	17	49.7	45	103.8	2.1 (1.9, 2.3)
Chest	23	30.2	53	54.8	1.8 (1.6,2.0)	16	22.7	25	27.3	1.2 (1.0, 1.4)
Abdomen	7	9.2	19	20.1	2.2 (1.8, 2.7)	4	5.2	10	10.2	2.0 (1.5, 2.6)
Back	91	78.1	214	145.6	1.9 (1.7, 2.0)	55	46.1	89	61.6	1.3 (1.2, 1.5)
Buttocks	1	1.1	0	—	—	0	—	3	3.3	—
Upper arms	18	18.6	51	44.0	2.4 (2.0, 2.9)	50	51.7	87	74.7	1.4 (1.3, 1.6)
Forearms	6	8.4	38	43.6	5.2 (4.4, 6.6)	9	12.4	52	56.5	4.6 (3.9, 5.3)
Dorsum of hands	2	5.1	4	10.3	2.0 (1.6, 2.7)	1	3.5	2	5.3	1.5 (1.1, 2.2)
Thighs	12	5.7	41	14.4	2.5 (2.0, 3.3)	25	11.4	80	30.0	2.6 (2.2, 3.2)
Legs	25	14.7	72	35.7	2.4 (2.1, 2.8)	86	52.0	106	50.7	1.0 (0.9, 1.1)
Dorsum of feet	3	7.8	3	5.6	0.7 (0.5, 1.0)	0	—	12	24.6	—
Soles	3	7.4	0	—	—	1	2.1	6	9.8	4.6 (3.2, 6.6)

[1]95% confidence limits.

while the incidence rates for remaining body sites were low or extremely low.

The age distribution for melanomas on the sites with very high to extremely high rates varied according to site, though not by sex. About 90% of lesions on the face, ears and neck occurred over the age of 40 years, in contrast to lesions on the shoulders and back, at least 25% of which occurred before 40.

In order to compare rates of melanoma at different anatomic sites, age-standardized incidence rates of invasive melanoma per 10^5 units by body site, relative to incidence rates for the whole body (set to 1) were calculated separately for each sex. The incidence rate for the ears in men was over 4 times the rate for the body as a whole and the rates for the face, shoulders and back in men were over 3 times the whole-body incidence (Fig. 1). On the face and shoulders in women and on the neck in men the relative incidence was over twice the age-standardized whole-body incidence of invasive melanoma. In contrast, the relative incidence rate of melanoma was extremely low for the scalp in women and for the buttocks in both sexes compared to whole-body incidence rates, and on the dorsal surfaces of feet in men and of hands in women (Fig. 1).

Recent trends in site-specific incidence

In men and women, overall incidence rates of pre-invasive melanoma were 11.1 and 11.5 per 10^5 in 1979–80, and these rates rose similarly and significantly ($p < 0.05$) to 17.6 and 16.6 per 10^5 in men and women respectively over the period up to 1987 (MacLennan *et al.*, 1992). In men, pre-invasive disease increased for all sites except the abdomen and upper arms which showed decreases (Table I). While there was a 30 to 50% rise in pre-invasive melanoma on the face and ears, the greatest relative increases occurred on the low-incidence sites of scalp, forearms and backs of hands. In women, pre-invasive melanoma increased by 20% on the face and by more than 200% on the less common sites of the thighs, chest and forearms, while the neck showed a decrease in pre-invasive disease between 1979 and 1987 (Table I). However, since ascertainment of pre-invasive melanomas would have varied in completeness with time and perhaps by site, the data for pre-invasive disease, and the statistical significance of the apparent trends, should be interpreted with caution.

Invasive melanoma for all sites combined increased by more than 100% in men to 49 per 10^5, due almost entirely to a steep increase in rates among men aged over 50 years, and by 50% in women to 40 per 10^5 (MacLennan *et al.*, 1992). Regarding site-specific changes among men between 1979 and 1987, there was a significant increase in incidence of invasive melanoma diagnosed on every site except the foot (Table II). On the forearms, the rates increased 5-fold, with a significant doubling of rates for all other sites except the scalp and dorsum of foot. The ear, in first place in 1987, was also ranked first in 1979/80. The shoulder, second place in 1987, was ranked fourth in 1979/80 (Table II).

On the other hand, women did not show uniformly increasing trends in invasive melanoma at all sites, though significant rises were seen at some sites. The site which showed the greatest relative increase in rates was the same as in men, namely the forearms. (In addition, the sole of the foot showed a large increase, but this was based on a rise of only 5 cases.) Significant doubling of rates over the 7½-year study period occurred for the thighs, shoulders and abdomen; the neck showed a significant decrease (Table II). A notable rise occurred in rates of invasive melanoma on the dorsal surface of the feet in women in the study period: no melanomas were diagnosed at this site in 1979/80, compared with 12 cases in 1987. As in men, the ranking of sites by incidence changed between 1979/80 and 1987. In 1979/80 the top 4 sites were the face followed by the leg, upper arm and shoulder which had similar rates; in 1987 the ranking was face, shoulder, upper arm and back (Table II).

In both sexes, the lowest rates of invasive melanoma per unit area of skin were recorded on the buttocks and the soles of the feet; in men, on the dorsum of the foot, and in women, on the scalp. No melanomas occurred on the palms of the hand in the Queensland population during the 2 study years.

DISCUSSION

The most salient feature of these descriptive data is the match between the anatomic sites that have the extremes of incidence of melanoma and the extremes of sun exposure. The peak incidence of melanoma overall occurs on the face in both sexes and the ears in men where maximum sun exposure is received, while melanomas rarely occurred on the buttocks or scalp in women, the sites which have the least sun exposure. The predominance of melanomas on the face overall did not simply result from the effects of early diagnosis and removal of pre-invasive lesions, as shown by the very high absolute rates of invasive melanomas on the face in men and women, and the approximately 3-fold higher incidence on the face compared to

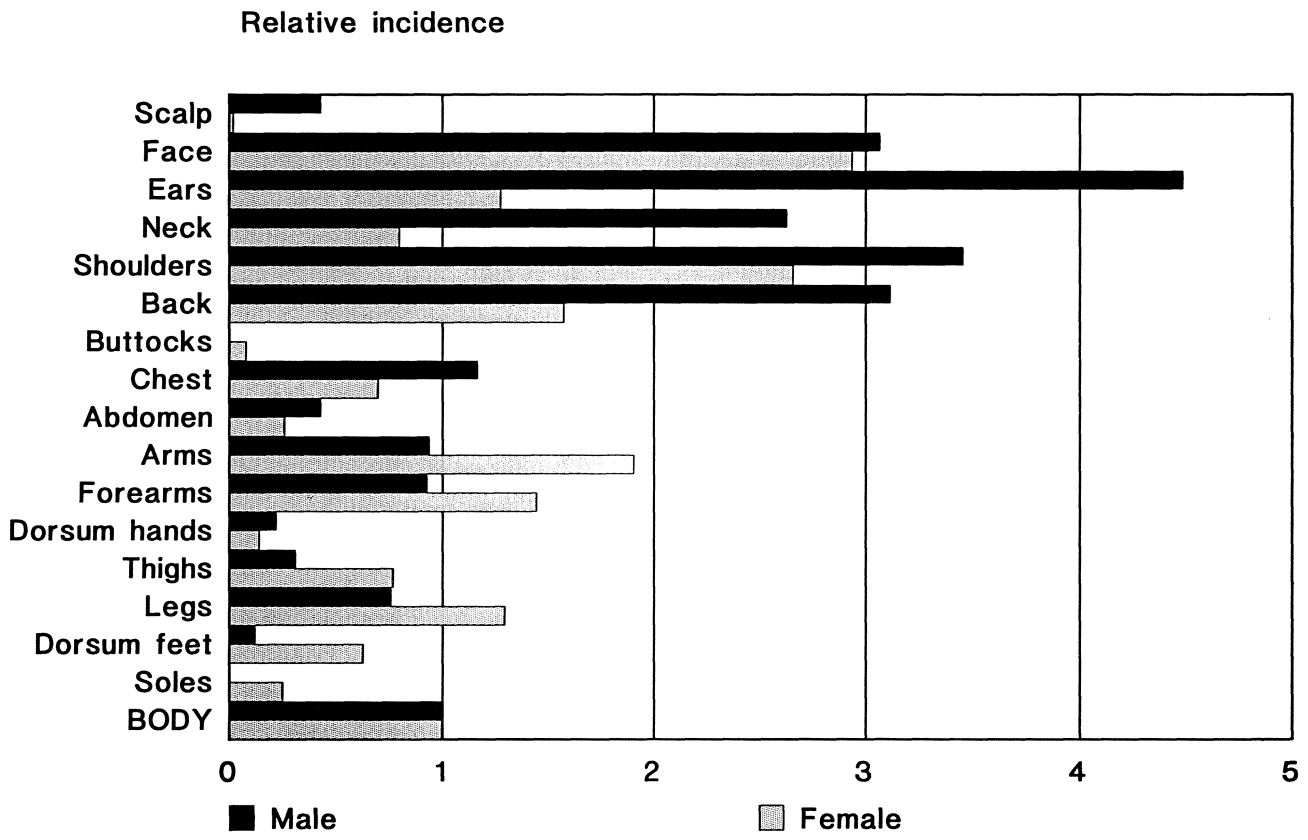

FIGURE 1 – Incidence rates of invasive melanoma by body site relative to those for the whole body, by sex. (Site-specific rates are age-adjusted per 10^5 units, and those for the whole body are adjusted and set to 1 for each sex.) ■, Male; □ , female.

the rates for the whole body. Moreover, the majority of invasive melanomas on the face and male ear were not lentigo maligna melanoma. This histological subtype, which is classically linked to chronic sun exposure, accounted for only 20% of melanomas on the male ear and 31% and 26% of melanomas on the face in men and women respectively. Similar findings have been reported in a study of anatomic distribution of melanomas in Denmark where high incidence rates per unit surface area were observed for the face, scalp and neck in men and for the face in women after all lentigo maligna melanomas had been excluded (Osterlind *et al.*, 1988). The higher incidence for the ears of men compared to the face, might be due to a tendency for the ears to be less commonly shaded, or perhaps to some protection being afforded by men's facial hair (though there are no data available to support this). Again, the lower rates for women's faces might be consistent with social customs of protection and adornment. Furthermore, the scalp is a site which can be chronically exposed after middle age only in men, and indeed melanoma of the scalp occurred with consistently moderate to low frequency in men, but to a negligible extent in women.

To check that the redistributions of cases of melanoma at unknown sites did not distort these results, an analysis was carried out for the subsites for which ICD-O coding was available (face, ears, scalp and neck combined) after excluding the 8% of cases with missing site data. Results were virtually identical to those obtained in the analyses presented. While the precision of the estimated incidence was lower for other subsites such as forearm or thigh (which were only included in the overall location "upper" or "lower limbs"), their ranking in the final analysis strictly reflected the ranking of limb melanomas at specified subsites.

Interpretation of the present population-based incidence data for body sites which do not have definite and general extremes of exposure is, of course, very difficult because of the variability of behaviour modifying exposure of these sites. However, the relative magnitude of rates for specific sites, and the rapidity of change in site-specific incidence rates, may be plausibly related to patterns of sun exposure in the community. The body site which is striking because of its rapid emergence as one of the major sites of melanoma, in less than 8 years to 1987, is the shoulder. Among women in Queensland, the shoulder had very high rates of invasive melanoma—second only to the face, whereas in men, the shoulder was in second place after the ear. In both sexes the incidence rate of melanoma on the shoulder more than doubled in 7½ years, though the arbitrary definition of what constitutes "shoulder" will have varied greatly among the doctors completing requests for pathological reports, and thus interpretation of calculated incidence rates and trends for melanoma of the shoulder finally remains tentative. However, the broad definition of "shoulder" as the uppermost surface of the trunk will not have varied. As such, it is a site that would receive maximum sun exposure when uncovered, as is commonly the case in subtropical and tropical Queensland. (Comparison with reported rates in other populations is not possible because to date, melanomas on the shoulder have mostly been combined with melanomas on the back or upper limb.) The combination of the extraordinarily high rates of invasive melanoma in men in 1987 on the region of the body comprising the head, neck, shoulders and back, with the overall doubling of incidence at all sites in this region in less than 8 years, is consistent with sun exposure without the protection of a shirt, for example, possibly in an

occupational setting, for some years preceding the study period.

The other individual site which stands out because it showed the highest increases in melanoma between 1979/80 and 1987 is the forearm. Both men and women experienced approximately 4- to 5-fold rises in invasive melanoma incidence at this site, which would be consistent with decreases in external protection due to modern sleeveless garments, for example. In the US state of Connecticut, marked increases in incidence of melanoma on the forearm—16-fold in men and 14-fold in women—between 1935 and 1984 have also been reported (Dubrow *et al.,* 1991). The much lower increases in incidence observed on the dorsal surface of the hand over the same period in the Connecticut population were also observed in Queensland and, together with the low rates seen overall in this highly sun-exposed area, would suggest some protective factor or a difference in susceptibility according to site (Green, 1992).

The substantially higher rates in men, and the variation in the patterns of melanoma between men and women in less than a decade, also reflect some sex-specific difference in environmental exposure. In men, the significant increase in disease on chronically and irregularly exposed sites alike would be consistent with a rise in their overall sun exposure and a concomitant decrease in clothing protection. This uniform rise was not observed in women, which suggests that neither their general exposure nor their exposure of traditionally covered sites changed as greatly or quickly as in men. Because the largest increases were in men aged over 50 years, these trends would seem to reflect environmental changes which may have taken place in men born before 1940, who were children or young adults in the 'thirties or 'forties and the post-war period. Comparison of site-specific sun-exposure histories between these men, and those of women of the same cohort or those of men from earlier generations, would be needed to confirm such secular changes in patterns of sun exposure among men now aged over 50 years.

Despite the limitations in interpretation of melanoma rates for variably exposed sites such as the shoulder or the leg, these descriptive data about the occurrence of melanoma on sites which universally receive extremes of sun exposure can powerfully inform the debate about the causal role of cumulative sun exposure.

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