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STATE OF THE ART

I. Sun Exposure, UVA Lamps and Risk of Skin Cancer: Epidemiological Studies

S. Rosso, R. MacKie, R. Zanetti

AWARENESS OF the complex association between skin cancer and solar exposure has significantly increased over the last few decades in the international epidemiological community. This is due to the steep upward slope of incidence trend, particularly in the case of malignant melanoma of the skin [1–4].

Although sharing the same site of origin, histological types of skin cancer differ in both epidemiological and clinical characteristics, and in their relationship with aetiological determinants. There is general agreement that basal cutaneous carcinoma (BCC) and squamous cutaneous carcinoma (SCC) have different characteristics. They both differ substantially from cutaneous malignant melanoma (CMM). Lentigo malignant melanoma (LMM) should be considered separately since it has a clearer association with sun exposure than other cutaneous melanomas.

Unfortunately, comparing epidemiological findings from routine data is not always straightforward. Some authors showed that even incidence data from cancer registries were under estimated because of under reporting [5]. The under reporting of non-melanoma skin cancer has been more than a problem for epidemiological studies. This is because there is a continuing tendency to diagnose a proportion of these lesions clinically, and to then treat them with non-excisional techniques such as liquid nitrogen, diathermy interferon or 5-fluorouracil. As a consequence, *ad hoc* studies have been carried out in the U.S.A. and Australia, involving additional reporting from general practitioners, out-patient clinics and specific population surveys [6–10].

Under reporting may also be related to the location of the tumour on the body. This could affect the findings from studies which reported that BCC, SCC and LMM occur more frequently on exposed body parts like the head, the face and the limbs, while CMM occurs mainly on the trunk and the extremities [11]. Indeed, the Australian survey in Geraldton showed a striking difference between prevalence and incidence data. The majority of prevalent BCC were on the trunk, whereas the majority of incident BCC were on the face, the neck and the upper limbs. This suggests that there is a significant amount of BCC on the trunk that does not come to medical attention.

Considering those studies with multiple data sources, some patterns clearly emerge.

Non-melanoma skin cancers

It is general knowledge that both BCC and SCC incidence rates are higher in males than females, vary with latitude and are low in non-Caucasians. Observations of Australian immigrants indicated that BCC and SCC incidence rates are higher for immigrants with northern European origins than those from the south [12]. Other studies revealed that people holding outdoor occupations such as fishing and farming showed high incidence rates compared to those with indoor occupations [13]. Animal models suggest that cumulative life-time exposure to ultraviolet radiation is the major risk factor for squamous cell carcinoma, and that this can be accelerated by therapeutic immunosuppression.

For elucidating the role of solar exposure and its interaction with skin pigmentation, it was necessary to rely on the limited number of published studies available up to now [14–18]. These publications revealed the following: principal host risk factors are skin reaction to sun exposure (tendency to sunburn), pigmentary traits (fair complexion, light hair colours), and ethnic origin (northern Europe). Controlling for the effect of host factors, cumulative solar exposure, as measured as time spent in outdoor activities, had a limited association to BCC and SCC. Even for individuals working outdoors, the relative risks (RR) ranged between 1.5 and 1.6. A recent report from a case–control study indicated that intermittent sun exposure, mainly associated with outdoor sports, also increased significantly the risk for SCC and BCC (RR 1.5) [19].

Results from the Australian case–control study suggested a direct association between skin cancer and sun exposure. Their findings were based on subjects with keratoses and elastoses.

These subjects had relative risks for BCC ranging between 5.3 and 10.4, and for SCC ranging between 7.2 and 34.3 for more than 15 keratoses [16]. The same results were also reported in a data collection from several Australian surveys [20].

Keratoses and elastoses are not only a measure of exposure but also a measure of direct solar skin damage. They share the same risk factors as BCC and SCC: age, ethnic origin, ability to tan, outdoor activities and latitude of residence [20]. Keratoses and elastoses are thus an intermediate step linking sun exposure habits to skin cancer. Indeed, with the available information, BCC and SCC risk factors cannot be addressed independently for individuals with keratoses and elastoses.

Sunscreens could give marginal protection against risk associated to sun exposure. A cohort study on BCC showed that individuals who spend 8 h or more weekly outdoors in the summer without using sunscreens have a relative risk of 1.42 (adjusted for host factors) compared to those who used sunscreens [17]. The relative risk for individuals who used sunscreens and stayed outdoors (for the same period) compared to those who stayed indoors was 1.6. Nevertheless, it is not clear if sunscreen use favours prolonged exposure to the sun and then chronic damage, since it prevents sunburns.

Ultraviolet A (UVA) radiation from artificial sources is a newer hazard with regard to risk of developing any type of cutaneous malignancy. Tubes emitting relatively pure UVA or long wave ultraviolet radiation (320–360 nm) have only been available for approximately the last 15 years. Initially they were introduced for the therapeutic management of certain severe dermatological disorders such as psoriasis and cutaneous lymphoma. Long wave UVA tubes are used in conjunction with an oral photosensitising agent or psoralen. An off-shot of these medically recommended UVA cabinets, however, has been the widespread availability of the long tube UVA sunbeds, available for home purchase and for use in beauticians and hairdressers salons.

The exact relationship between UVA and skin cancer is not yet totally quantitated. Long-term follow-up studies of patients on photochemotherapy (PUVA) have clearly demonstrated an increasing incidence of SCC in patients who have received over 1000 joules of UVA in combination with oral psoralens [21]. The relationship between non-melanoma skin cancer and exposure to non-medical sunlamps was addressed in only one study. It showed a significant RR of 13.4 (adjusted for host factors) for long tube UVA sunlamps use [15].

Cutaneous melanoma

The role of solar exposure in inducing LMM (which occurs in old people on exposed body parts) is clearer than its role in inducing CMM. For this reason, many studies exclude LMM from their analysis or treat it separately.

Descriptive data from registries and surveys indicate a steadily increasing trend in incidence and mortality in cutaneous melanoma [22], even though the mortality rate of this tumour is not as high as in other solid tumours: approximately 50% of patients survive after 5 years. A doubling of incidence was documented between 1973 and 1987 in British Columbia, Canada, even though there were improvements in diagnostic techniques for the tumour [3]. The increase in melanoma incidence can be even more dramatic if we consider that under reporting has also increased over the last decades due to an easier referral of patients to physicians' offices outside the hospital setting [23].

CMM occurs mainly in individuals aged 40 to 50 years. Occurence prevails on the trunks of males, and the lower limbs of females. This anatomical distribution may suggest an association between exposed body surfaces and melanomas. However, considering that other parts of the body (face and arms) are normally more exposed to the sun than the trunks and legs, a more complex aetiological mechanism is indicated. Studies on American and Australian immigrants showed an increased risk associated with young age at the time of arrival rather than length of stay [12, 24]. In addition, some descriptive studies [24–27] indicated that outdoor occupations seem to provide a slight protective effect against CMM. These results addressed both intermittent and continuous sun exposure.

Several case–control studies investigated this hypothesis. The most common finding was that the risk factor was significantly increased for people who were exposed to the sun during summer holidays either at beaches or while engaged in sports activities with intense sun exposure such as bathing and sailing [16, 28–32]. Nevertheless, another recent study failed to link exposed body surfaces to the site of the melanoma [33]. The same study also pointed out that while the risk factor for solar exposure increased significantly amongst "sun-sensitive" women in swimsuits, it did provide a protective effect for "sun-resistant" women [33]. Host factors, or sun sensitivity seemed to be identical to host factors of BCC and SCC: reaction to sun exposure, complexion and ethnic origin [16].

Naevi on the body are a good indicator for the risk factor of a melanoma. The number of naevi is directly proportional to the risk factor. Moreover, the number of acquired naevi on the body increases with solar exposure [34]. It is, therefore, unclear if naevi can be considered as an expression of skin reaction to sun exposure or rather as an independent risk factor. Finally, most naevi develop during childhood and most of the increase in incidence is before the age of 50. If parallels are to be drawn between naevi and melanoma, it would be a leading risk factor for melanoma [35].

In fact this was confirmed by several case–control studies which showed a 2- to 3-fold increase in the risk for sunburns during childhood [16, 31, 33, 36–39]. This increase was not present when the same exposure occurred at later periods in life. Thus, it can be assumed that childhood sun exposure acts as an initiating factor, and that other factors, possibly further UV exposure, are promoting factors in the stepwise progression to malignancy.

The use of sunlamps/sunbeds has been addressed in seven case–control studies [30, 31, 40–44]. Four of them showed little or no association with melanoma. However, the rate of usage among sampled subjects was quite low in these studies [30, 31, 40, 41]. Three other studies reported in more detail and found an overall positive association (2-fold elevation of risk) with increasing duration of use [42–44]. Also, a significant increase of risk was shown for persons first exposed before 30 years of age in one study [44]. However, we must consider the changing pattern of ultraviolet emissions of sunlamps and sunbed devices over time.

In conclusion, scientific evidence confirms an association between solar exposure and both carcinoma and melanoma. This relationship must be further clarified in order to understand its mechanism. In particular, for melanoma, there is a need to improve measurement techniques for examining intermittent sun exposure at different ages. More data are needed in assessing the risk for sunlamps, and it is essential that the exact characteristics of the UV tubes used are reported in subsequent studies. Public health recommendations based on findings from epidemi-

ological studies should focus on high risk groups avoiding intense exposure to sunlight especially at early ages.

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