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Melanoma is not caused by sunlight

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Abstract

When comparisons are made of cutaneous melanoma with cutaneous squamous cell cancer (SCC) and basal cell cancer (BCC) of the skin with respect to age dependence, sex ratio, distribution on the body, association with sun exposure, and variation with latitude, it is clear that SCC is due almost entirely to sun exposure, that BCC is partly due to sun exposure, and that melanoma is not due to sun exposure. For melanoma, it is only latitudinal variation that favours the hypothesis of exposure causation. However, an examination of the latitudinal variation of SCC incidence reveals that this is several greater than can be accounted for by variation of exposure to UV-B. The other factor operating appears to be skin temperature. For melanoma, it is postulated that the latter factor by itself may suffice to account for the observed variation with latitude. The higher incidence of melanoma in the higher social classes and its increasing incidence with age may be readily explained by the hypothesis that melanoma incidence increases with increase in skin temperature.

Keywords: Cutaneous melanoma; Body distribution; Sunlight; Latitude; Skin temperature

1. Introduction

Arguments against sunlight being a cause of melanoma (other than lentigo maligna melanoma and acral lentiginous melanoma) will be made under the following headings: age dependence; sex ratio; distribution on the body; association with sun exposure; variation with latitude. Arguments for another cause of melanoma will be advanced under two headings: social class; increasing incidence with time.

When comparison is made of the three skin cancers—squamous cell cancer (SCC), basal cell cancer (BCC), and melanoma, it will be seen that SCC is a tumour with features typical of those expected of one largely due to accumulated exposure to the sun, that BCC is not so typical but nevertheless at least in part caused by sun exposure, and that only latitudinal change in incidence favours this hypothesis insofar as melanoma is concerned.

2. Age dependence

When incidence of SCC is plotted against age, the outcome is a roughly exponential curve which shows a large increase in incidence of approximately 450-fold from 25 to 75 years of age [1]. By comparison, the increase over the same period for BCC is 24-fold [1], whereas for melanoma it is only 5-fold [2]. Many commentators have pointed out that these findings are a stumbling block for the hypothesis that sunlight is a major cause of melanoma. They do however

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indicate that sunlight exposure may be important as a cause of BCC, but a less important cause than it is for SCC.

3. Sex ratio

If sunlight is a cause of a skin tumour, then one would expect that tumour type to be more common in men than women: this is the case for both SCC and BCC, but not for melanoma.

The male-to-female ratio for SCC is 2.8 [3] and for BCC, the ratio is about 1.6 [3]. For melanoma this ratio is close to unity [4], in some countries being slightly more than one and in others slightly less than one. A study in the US has estimated that the total sun exposure is a factor of 1.6 or so greater in males than in females [5]. Other commentators have also concluded that the finding of a rough equality of incidence between the sexes in the face of a clearly greater sun exposure in males is a stumbling block for the hypothesis of sunlight being a cause of melanoma.

4. Distribution on the body surface

If a skin cancer is due to sunlight, then its site density on the areas of the body more exposed to sunlight should be greater than its site density on the less exposed areas of the body, and the difference should roughly reflect the difference in accumulated sun exposure of these areas. The more exposed areas of the body are the neck, head, ears, and the backs of the hands, and these areas constitute about 0.062 of the total skin area of the body; the less exposed areas are the rest of the body and constitute about 0.94 of the total area [3].

From data provided by Scotto and Fraumeni [3], it may be calculated that for SCC, 0.87 of all cancers are found in the more exposed areas and 0.13 in the less exposed areas. The site density for the more exposed areas is 14; for the less exposed areas it is 0.14. Thus the relative site density is about 100.

From data provided from the same source, it may be calculated that, for BCC, 0.825 of all cancers occur on the more exposed areas, and 0.175 on the less exposed areas, giving a site density for the former areas of 13.3 and a site density for the latter areas of 1.86. The relative site density of the two areas is 7.2.

From data provided by Lee [6], it may be calculated that, for melanoma, 0.22 of all cancers occur on the more exposed areas, and 0.78 on the less exposed areas, giving a site density for the former areas of 3.5 and a site density of the latter areas of 0.83. The relative site density of the two areas is 4.2.

The relative site densities for SCC, BCC, and melanoma are, therefore, respectively: 100, 7.2, and 4.2. The fact that for melanoma the relative site density is clearly greater than one has been used by some reviewers as an argument that melanoma is caused by sunlight. However when it is considered that the relative site density for SCC is about 25 times greater than that for melanoma, this argument is seen to be a weak one.

5. Sun exposure

The exposure of the relevant cells to UV-B depends not only upon the radiation falling on the skin surface, but also on the protection offered by the skin pigment. Hence the almost complete absence of SCC in people with dark skin. The fact that melanoma is also rare in such people similarly suggests that this tumour is due to UV-B exposure. This is, however, not necessarily so. Testicular tumours are rare in people with dark skin [7]; but this has nothing to do with protection from UV-B. It is due to hereditary factors by which immunity to testicular tumour is linked to hereditary factors conferring dark skin colour.

The question of whether immunity to the tumour is due to the protection offered by the dark skin is resolved by epidemiological studies which examine association between sun exposure and tumour. In such studies, like must be compared with like. This means that both the cases and the controls must be similar in respect to skin colour and to the reaction of the skin to sun exposure. Comparison should therefore be made using subjects all of whom have light skin and who do not react to sun exposure by tanning. Within this population, subjects who have the least sun exposure should be compared with those that have had the most. Such a study has been

carried out by Vitaliano and Urbach [8]. For both SCC and BBC, they made a comparison of those having total sun exposures of 30,000 h or more with those having less than 10,000 h exposure. They found that for SCC, the increase in risk for those having the greatest exposure compared to those having the least exposure with was 23; for BCC, it was much less: 3.2.

It will be shown that, in contrast to SCC and BCC, for melanoma there is no more risk for those most exposed to the sun as compared with those exposed least. This is important because if it is true it means that sunlight cannot be a cause of melanoma. The answer to this question is to be found in an examination of the findings of the numerous case-control studies that have examined the relationship between melanoma and accumulated sun exposure.

From 1969 to 1990, there have been 14 case-control studies which have examined the relationship between melanoma incidence and total accumulated sun exposure as measured by personal questionnaires. In seven of these, there was found to be no statistically significant association between melanoma incidence and sun exposure [9–15]. In five of these, there was a statistically significant negative association between melanoma incidence and sun exposure [5,16–19]. Only two studies found a statistically significant positive association between the two [20,21].

The conclusion that can be drawn from looking at these studies as a whole is that melanoma is not due to sun exposure. Indeed the conclusion is so clear that it is difficult to understand why scientific consensus still clings to the idea that sunlight is a cause of melanoma.

6. Albinos in black races—nature's epidemiological study

Albinos in black races present a unique opportunity to study the effect of removing the pigment protection without disturbing the hereditary protective influences. Skin cancers in albinos among the black populations in Johannesburg were investigated by Kromberg's group [22]. Among 17 cases with skin cancer who were biopsied, they found 15 cases of SCC, 2 cases of BCC, and none of melanoma. In a similar study, Lookingbill et al. [23] found that among a total of 164 albinos in Tanzanian black populations there were seven cases of SCC, three cases of BCC, and no cases of melanoma. The statistical significance of these findings is not high with respect to melanoma, but further evidence relating to the experience of albinos is awaited with interest.

7. Latitude

The change in the incidence of melanoma with latitude was noticed early and a classic study by Elwood et al. [24] put this question beyond doubt. They plotted the age-standardized male mortality from melanoma for each US state and Canadian province against the latitude of the largest city in each. There was a roughly linear relationship which showed that melanoma mortality doubled in going from latitude 47°N to 28°N. A few years later, Fears et al. [25] plotted the variation in UV-B exposure over the same latitude differential, and found a linear relationship for UV-B exposure (which also almost doubled with the relevant decrease in latitude). The similarity of the gradient of change in these two graphs was taken as strong support for the view that melanoma is due to UV-B exposure.

However, further investigations have raised difficulties with this explanation. Comparisons of incidence rates for the three key skin cancers (SCC, BCC and melanoma) between low latitude (> 29°S) areas and high latitude (> 37°S) areas on the continent of Australia have shown large differences for these three cancers. Thus the incidence of SCC was found to be 9.0 times higher in the low latitudes than in the high latitudes, while for BCC it was 4.2 times higher [1]; interestingly and importantly, the incidence of melanoma increased only 2-fold in going from the higher latitudes to the lower latitudes [26]. Exposure to UV-B also appeared to double with this change of latitude [27]. These findings support the previous findings of Elwood et al. for the north American continent, and has served to confirm many researchers in the view that melanoma is caused by sun exposure.

However, this conclusion must be questioned when one takes into account the effect of the 18°

latitudinal change on SCC incidence in Australia. The incidence rate of this tumour increases 9-fold towards the north, which is of course far more than can be accounted for by the observed change in UV-B exposure alone. This finding forces the conclusion that there must be some factor, almost certainly climatic, that operates on SCC incidence in addition to UV-B exposure.

I suggest that this factor is none other than temperature, almost certainly as primarily manifest in skin temperature. Acceptance of this postulate solves several problems. It allows us to explain the huge increase in latitudinal change of SCC incidence by a combination of UV-B exposure and temperature, and it allows the explanation of latitudinal change of melanoma incidence by temperature alone. On this schema, SCC is strongly influenced by the climatic effects of both UV-B and temperature; BCC is less strongly influenced by the same climatic factors; and melanoma is influenced by temperature alone.

8. Temperature

For most cancers, internal in origin as they are, the question of temperature being an important factor in their aetiology hardly arises as homeostasis allows little change in this factor. It can, however, be important as a factor in two organs whose temperature varies with the environment. These organs are the testes and the skin. Of all organs, the skin bears the greatest brunt of temperature change; the testes are less affected as they have the protection of their own small temperature regulating device. Strangely, the possibility that temperature is a factor in testicular cancer has been canvassed, but on detailed investigation found wanting. The possibility does not even seem to have been raised in the context of skin cancer, however.

9. Social class

There are two features of melanoma which support the hypothesis of temperature being a factor in its causation: one of these concerns the higher incidence of melanoma in people of higher social class. Whenever it has been examined, social class has emerged as an important risk factor for melanoma [6]. The higher the social class, the higher is the risk of this cancer. A ready explanation in terms of temperature is obvious. Those in the highest social class tend to live in a house that is heated in cold weather; they are more likely to travel to work in a heated car; and they may well work in a heated office.

10. Increase in incidence of melanoma with time

For many decades, the incidence of melanoma has been increasing although the rate of increase appears to be declining at the present time [6]. The steady increase over recent decades has a ready explanation in terms of temperature. As society has become more affluent over the past decades, people in the colder climates have been able to keep themselves warmer.

11. Conclusion

The fact that melanoma has little or nothing to do with sun exposure becomes obvious when comparisons are made of the three main skin tumours (SCC, BCC, and melanoma). This approach to the data makes it clear that sun exposure is the predominant factor in the aetiology of SCC, is a somewhat less significant factor in BCC, and has little or no involvement in melanoma.

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