Key messages

- Affluent people have a significantly higher risk of developing malignant melanoma than deprived individuals
- Paradoxically, five year disease free survival prospects are better for affluent people
- Variations in incidence could be explained by differences in sun exposure related to socioeconomic status
- Variations in nutrition and possibly immune function by socioeconomic status could explain survival differences
- In public education campaigns, deprived men should be targeted to encourage earlier diagnosis
- Primary prevention campaigns should be targeted to more affluent socioeconomic groups

in the affluent group, leading to earlier self referral and thus earlier diagnosis and treatment, does not wholly explain our results.

Recent results from the same geographic area also showed poorer survival for the less affluent patients with breast cancer.[9] We speculate that a common factor, such as poor nutrition leading to low levels of antioxidants, or immunological defects, could be responsible in both tumour types.

The pattern of higher incidence but better survival for the most affluent compared with the least affluent of both sexes is mirrored in the greater incidence of melanoma but better survival in women. The greatest risk of developing melanoma is seen in affluent women, and the poorest five year disease free survival prospects in deprived men. It is possible that behavioural differences with regard to sun exposure between the sexes and between affluent and deprived individuals may explain some of the differences in incidence, but this would not explain the differences in survival.

Table 2 shows clearly that over the three time periods studied the proportion of thin tumours has increased in all groups, and that this increase is significant in intermediate and deprived women and affluent and intermediate men. Over 50% of all tumours are now <1.5 mm thick, but among deprived men the proportion is only 39%, indicating that early detection activities need to be targeted particularly at less affluent men.

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Association between incidence of non-Hodgkin's lymphoma and solar ultraviolet radiation in England and Wales

Graham Bentham

Abstract

***Objectives*—To examine whether the incidence of non-Hodgkin's lymphoma in different areas of England and Wales is associated with levels of solar ultraviolet radiation.**

***Design*—Geographically based study examining the association between incidence of non-Hodgkin's lymphoma and estimated levels of solar ultraviolet radiation, controlling for social class and employment in agriculture.**

***Setting*—59 counties in England and Wales.**

***Subjects*—All registered cases of non-Hodgkin's lymphoma during the period 1968-85.**

***Main outcome measure*—Age and sex adjusted odds ratio for non-Hodgkin's lymphoma in each county.**

***Results*—Incidence of non-Hodgkin's lymphoma was significantly associated with solar ultraviolet radiation levels (P<0.001), even after social class and employment in agriculture were controlled for (P=0.004). In a comparison of counties in the highest and lowest quarters of solar ultraviolet radiation, the relative risk of non-Hodgkin's lymphoma was 1.27 (95% confidence interval 1.24 to 1.29), rising to 1.34 (1.32 to 1.37) after adjustment for social class and employment in agriculture.**

***Conclusions*—The incidence of non-Hodgkin's lymphoma in different areas of England and Wales is positively associated with levels of solar ultraviolet radiation. These results are consistent with the hypothesis that exposure to solar ultraviolet radiation increases the risk of non-Hodgkin's lymphoma.**

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Introduction

The incidence of non-Hodgkin's lymphoma has increased greatly in many countries,[1] including England and Wales.[2] An established risk factor is chronic immunosuppression[3 4]—as in individuals with congenital immunodeficiency syndromes,[5] patients treated with immunosuppressive drugs,[6] and those infected with HIV.[7] Particular types of non-Hodgkin's lymphoma are also associated with infection with the Epstein-Barr virus and with HTLV-I.[8] Risk is also raised in a number of occupations,[9 10] notably in agriculture, where exposure to pesticides may be a factor.[11] However, trends in known risk factors and in diagnostic practices can account for only a small part of the observed increase in non-Hodgkin's lymphoma.[12 13] Part of the rise may have been the result of increased population exposure to some other widespread risk factor.

It has been hypothesised that exposure to solar ultraviolet radiation may be a cause of non-Hodgkin's lymphoma.[14] This is an important cause of skin cancers,[15] which have been increasing even more rapidly than non-Hodgkin's lymphoma,[16] probably as a result of the adoption of lifestyles involving increased exposure to the sun.[15] Increased exposure to sunlight might also

have contributed to the increase in non-Hodgkin's lymphoma. Cartwright *et al* note that immunosuppression increases the risk of non-Hodgkin's lymphoma[14] and that ultraviolet B radiation has been shown to cause systemic immune suppression in mice and in humans.[17] Support for their hypothesis is provided by significant positive associations between the incidence, and change over time of incidence, of non-Hodgkin's lymphoma and non-melanoma skin cancers for a sample of cancer registries.[14] This has been strengthened by the results of a study showing that non-Hodgkin's lymphoma patients had an increased risk of subsequently developing squamous cell skin cancer and malignant melanoma. Similarly, there was a subsequent increase in non-Hodgkin's lymphoma among patients with squamous cell skin cancers and malignant melanoma.[18] In view of the importance of exposure to the sun for skin cancers, the authors take this to support the hypothesis of a role for ultraviolet radiation in the increasing incidence of non-Hodgkin's lymphoma.[18] However, it has been pointed out that this relation was examined only indirectly.[19] Also, the increased risk of skin cancer after non-Hodgkin's lymphoma could arise from immunodeficiency as a result of the disease itself or the drugs used to treat it,[20 21] although similar factors are unlikely to account for the excess of non-Hodgkin's lymphoma after skin cancers.[22] These doubts point to the need for further investigation using a different study design.

Ultraviolet radiation varies from place to place depending on factors such as latitude and cloud cover. Other things being equal, the doses received by the populations of different areas are likely to vary in a similar way.[23] The existence of geographical variations in ultraviolet radiation provides an opportunity to test the hypothesis that exposure to sunlight is a cause of non-Hodgkin's lymphoma. If the hypothesis is correct the geographical patterns of non-Hodgkin's lymphoma and ultraviolet radiation will be positively correlated. This study examines this question by using data on non-Hodgkin's lymphoma incidence and estimated solar ultraviolet radiation levels in different areas of England and Wales.

Methods

DATA

The *Atlas of Cancer Incidence in England and Wales* provides information on non-Hodgkin's lymphoma registrations for 59 counties for the period 1968-85.[24] In the atlas, age-standardised odds ratios were preferred to incidence rates because they were considered less likely to be affected by variations in the completeness of cancer registration. The odds ratios were obtained by considering the registration data as a series of case-control analyses, comparing risk of non-Hodgkin's lymphoma in a particular county with its risk in all other counties. Cases were the registrations for non-Hodgkin's lymphoma, and controls were a weighted sample of all other cancers.

The number of cases of non-Hodgkin's lymphoma and age-adjusted odds ratios for male and female patients for each county were taken from the atlas, and expected values for each sex were calculated by dividing the observed number of cases by the odds ratio. Data for males and females were combined and an age-sex adjusted odds ratio was calculated.

For the same 59 counties, given the lack of long runs of measurements, estimates of annual erythema producing ultraviolet radiation (in $10^5 J/m^2$) were calculated from a model that used data on latitude and cloud cover.[25] The latitude of the centre of each of 403 local authority districts was taken from official maps. Estimates of cloud cover at these locations for the period 1961-90 were derived from information on hours of bright sunshine.[26] District ultraviolet radiation values calculated from the model were aggregated to produce a population weighted estimate of ultraviolet radiation for each county. In recent years depletion of stratospheric ozone may have increased ultraviolet radiation,[27] but any such effect would be similar throughout England and Wales and would not affect the comparison between counties.

Table 1—*Regression analysis of relation between odds ratio for non-Hodgkin's lymphoma and estimated ultraviolet radiation, social class, and employment in agriculture*

Explanatory variable	Coefficient	SE	P value
Simple regressions:			
Constant	-0.022		
Estimated ultraviolet radiation*	0.372	0.082	<0.001
r^2 26.4%			
Constant	0.683		
Social class†	0.009	0.003	0.007
r^2 11.9%			
Constant	1.025		
Employment in agriculture‡	-0.003	0.003	0.365
r^2 1.4%			
Multiple regression:			
Constant	0.026		
Estimated ultraviolet radiation*	0.289	0.095	0.004
Social class†	0.006	0.004	0.107
Employment in agriculture‡	-0.004	-0.003	0.175
R^2 30.5%			

*Estimated annual erythemally weighted ultraviolet radiation (in $10^5 J/m^2$).
†% Of employed males in social classes I, II, and IIIN.
‡% Of employed people working in agriculture.

ANALYSIS

The possibility of an association between ultraviolet radiation levels and incidence of non-Hodgkin's lymphoma was examined by means of regression analysis of data for individual counties. The dependent variable was the age-sex adjusted odds ratio and the main explanatory variable of interest was the estimate of ultraviolet radiation. Information was also collected on two other explanatory variables which might confound the association. As the incidence of low grade non-Hodgkin's lymphoma in different areas of England and Wales is positively associated with socioeconomic status,[28] the percentage of employed men in social classes I, II, and IIIN (the non-manual social classes) was included as an explanatory variable. In view of evidence of an excess risk of non-Hodgkin's lymphoma for agricultural workers,[9 10] the percentage of employed people working in agriculture was also used. Both were based on data from the 1971 census.[29] Since the odds ratios for non-Hodgkin's lymphoma were based on substantial numbers of cases in each county (minimum 33), regression models were calculated using the ordinary least squares method.

The association was examined further by aggregating data for individual counties into four groups divided at the quartiles of ultraviolet radiation. Observed and expected numbers of non-Hodgkin's lymphoma cases were aggregated for each group and the ratios of observed to expected cases and their 95% confidence interval were calculated, with and without adjustment for social class and employment in agriculture.

Results

Incidence of non-Hodgkin's lymphoma was significantly positively associated with ultraviolet radiation and social class (table 1), but the association with employment in agriculture was negative and non-significant. The strongest association was with ultraviolet radiation (fig 1). The multiple regression analysis showed a highly significant positive association with ultraviolet radiation. The association with social class

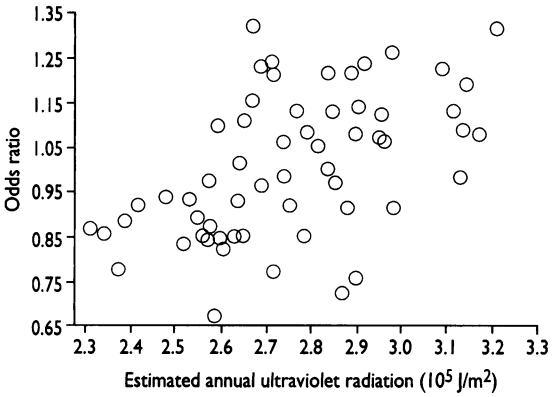

Fig 1—*Age and sex adjusted odds ratios for non-Hodgkin's lymphoma and estimated annual ultraviolet radiation (10^5J/m^2, erythemally weighted equivalent) in 59 counties of England and Wales, 1968-85*

remained positive but was not significant, and that with employment in agriculture was negative and non-significant.

Table 2 gives the ratios of observed to expected non-Hodgkin's lymphoma cases and their 95% confidence intervals for counties aggregated into ultraviolet radiation groups. It shows a clear tendency for the incidence of non-Hodgkin's lymphoma to increase with level of ultraviolet radiation. For the unadjusted data the relative risk of non-Hodgkin's lymphoma for the highest versus lowest ultraviolet radiation group was 1.27 (95% confidence interval 1.24 to 1.29). On adjustment for social class and employment in agriculture, using the coefficients for these variables from the multiple regression equation in table 1, this rose to 1.34 (1.32 to 1.37).

Discussion

This study shows that the incidence of non-Hodgkin's lymphoma in the counties of England and Wales was positively associated with levels of solar ultraviolet radiation and that this was not the result of confounding by social class or employment in agriculture. A study using data from the United States found a negative association between non-Hodgkin's lymphoma and ultraviolet radiation, but this was based on observations for only six areas over a five year period and no account was taken of other factors.[19] Though the present study uses cancer registrations over a longer period of time and for a larger number of areas, it has its own limitations.

LIMITATIONS

Being based on ecological correlation, the results of this study do not guarantee the same association for individuals. The overall explanatory power of the multiple regression model was not high, with the three explanatory variables accounting for only 31% of the variance in the dependent variable. Therefore, confounding of the association between ultraviolet radiation levels and incidence of non-Hodgkin's lymphoma by some other factor cannot be excluded.

Another problem is that the study is based on geographical variations in ultraviolet radiation levels rather than on the doses received by the population. Such doses will depend on variations in the patterns of behaviour of the population as well as on the ultraviolet radiation levels in different areas. Doses are likely to be greater for more affluent populations and where a high proportion of the population is involved in outdoor occupations such as farming.

EFFECT OF SOCIAL CLASS AND AGRICULTURAL WORK

The results of the multiple regression analysis showed that there was a significant positive association between incidence of non-Hodgkin's lymphoma and ultraviolet radiation levels after social class and employment in agriculture were taken into account.

The simple regression analysis showed a significant positive association between incidence of non-Hodgkin's lymphoma and social class, as in a previous study.[28] However, this became non-significant in the multiple regression model, in which ultraviolet radiation levels were the strongest explanatory variable, suggesting that some of the apparent association with social class may be the result of generally higher ultraviolet radiation levels in more affluent southern counties.

The negative association between incidence of non-Hodgkin's lymphoma and employment in agriculture is contrary to expectations based on several case-control studies that have shown an excess risk among farm workers.[9 10] However, the observed negative ecological correlation does not necessarily imply lower risk among individuals working in agriculture. It could be that other features of agricultural areas and their population are associated with a lower risk of non-Hodgkin's lymphoma.

IMPLICATIONS OF THE FINDINGS

In view of the contradictory findings for the United States[19] and the limitations of this and previous studies,[14 18 19] there is a need for further research before a firm conclusion is possible on whether or not solar ultraviolet radiation is a factor in the aetiology of non-Hodgkin's lymphoma. Nevertheless, the present study adds to the evidence from elsewhere[14 18] that supports such a possibility. An aetiological role for ultraviolet radiation could also explain some well established features of the epidemiology of non-Hodgkin's lymphoma. As is the case for malignant melanoma and other skin cancers,[15] some of the unexplained rise in the incidence of non-Hodgkin's lymphoma might be the result of increased population exposure to ultraviolet radiation. Higher exposure among more affluent groups might also contribute to the tendency for the incidence of non-Hodgkin's lymphoma to increase with social status.[28] This has been observed for malignant melanoma,[30 31] where the greater involvement of affluent social groups in outdoor leisure activities may increase risk.[32 33]

Table 2—*Ratio of observed to expected cases of non-Hodgkin's lymphoma 1968-85 by ultraviolet radiation group*

Group (quartile)	Mean annual ultraviolet radiation (10^5J/m^2)	No of cases observed*	Observed/expected cases (95% confidence interval)	
			Unadjusted	Adjusted for social class and employment in agriculture
1	2.48	16 737	0.880 (0.867 to 0.893)	0.859 (0.846 to 0.872)
2	2.66	8 764	0.998 (0.977 to 1.019)	0.972 (0.952 to 0.992)
3	2.85	8 096	1.002 (0.980 to 1.024)	1.002 (0.980 to 1.024)
4	2.98	22 221	1.115 (1.100 to 1.130)	1.155 (1.140 to 1.170)

*Some of the variation in the observed number of cases is the result of differences in the population size of the counties in each group.

Key messages

- There has been a large, unexplained increase in non-Hodgkin's lymphoma in recent decades
- It has been hypothesised that greater exposure of the population to sunlight, which can cause systemic immune suppression, may have contributed to the increase in non-Hodgkin's lymphoma
- The geographical pattern of non-Hodgkin's lymphoma in England and Wales tends to match that of solar ultraviolet radiation
- Exposure to sunlight may increase the risk of non-Hodgkin's lymphoma
- Risks might be reduced by adoption of a more cautious approach to sun exposure

Greater exposure to sunlight could also contribute to the excess risk of non-Hodgkin's lymphoma in several outdoor occupations such as farming, forestry, and construction,[9 10] although other factors, including chemical exposures, might also be important.[11] Enhanced exposure to ultraviolet radiation could also be a factor in the raised incidence of non-Hodgkin's lymphoma that has been observed in Vietnam War veterans in the United States. It has been hypothesised that this might be the result of exposure to the herbicide Agent Orange, but risk did not differ by level of exposure to the suspected chemicals, although it was associated with length of service in Vietnam.[34] Since the whole of Vietnam is within the tropics, service personnel based there could have been exposed to higher levels of ultraviolet radiation than if they had remained in the United States.

If exposure to solar ultraviolet radiation is a cause of non-Hodgkin's lymphoma it might be possible to reduce risk by encouraging people to limit their exposure to the sun. However, increases in the amount of ultraviolet B radiation reaching the surface as a result of stratospheric ozone depletion[27] could add to risk.

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Blood money: blood donors' attitudes to changes in the New Zealand blood transfusion service

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Blood is an unusual product in a market economy: donors give it freely to strangers. Titmuss concluded that if this gift was commercialised, donors would feel less inclined to donate blood without payment and would face incentives not to disclose diseases.[1] The opposing view is that the most efficient way of rationing a scarce product like blood is to put a price on it and let a market develop in which it can be traded.[2]

In 1993 a purchaser-provider split was introduced into the New Zealand health service. The Blood Transfusion Service was embedded in the new hospital organisations, crown health enterprises, which were required to be profit driven.[3] A National Blood Transfusion Trust was set up to preserve the gift relationship and to ensure that there is no profiteering in blood. Nevertheless, the costs associated with collecting, processing, and distributing blood products can be passed on to providers, who are later reimbursed. This study aimed to examine the motives of New Zealand blood donors and whether the changes in the blood transfusion service might affect their donations.

Method and results

After obtaining ethical committee approval we asked 345 consecutive blood donors attending the Wellington Transfusion Centre (and its mobile units) to fill in a questionnaire: 338 (98%) did so. Most were long term