Epidemiol. Infect. (2002), **129**, 593–597. © 2002 Cambridge University Press
DOI: 10.1017/S0950268802007793 Printed in the United Kingdom

The role of solar ultraviolet irradiation in zoster

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(*Accepted 10 August 2002*)

SUMMARY

Ultraviolet radiation (UVR) suppresses many aspects of cell-mediated immunity but it is uncertain whether solar UV exposure alters resistance to human infectious diseases. Varicella-zoster virus (VZV) causes varicella (chickenpox) and can reactivate from latency to cause zoster (shingles). The monthly incidence of chickenpox and zoster in a defined Polish population over 2 years was recorded and ground level solar UV was measured daily. There was a significant seasonality of UVR. Evidence of seasonal variation was found for all zoster cases and for zoster in males, with the lowest number of cases in the winter. The number of zoster cases with lesions occurring on exposed body sites (the face) demonstrated highly significant seasonality with a peak in July/August. Seasonal models for UVR and zoster cases showed similar temporal patterns. By contrast, for varicella, the maximum number of cases was found in March and the minimum in August/September, probably explained by the respiratory spread of VZV. It is tempting to speculate that the increase in solar UVR in the summer could induce suppression of cellular immunity, thus contributing to the corresponding rise in the incidence of zoster.

INTRODUCTION

Varicella-zoster virus (VZV) belongs to the subfamily alphaherpesvirinae, as does herpes simplex virus (HSV), and produces two clinical syndromes, varicella (chickenpox) and zoster (shingles) [1]. Varicella in northern countries is primarily a disease of childhood, with 90% of cases occurring before the age of 10 years and a seropositivity rate for young adults of 95% [2]. VZV is transmitted by inhalation of respiratory secretions or contact with skin lesions. During the primary infection, the virus becomes latent in the dorsal ganglia and zoster is due to reactivation from latency, a process which occurs most frequently in subjects over the age of 50 [3]. Each person with a history of varicella has approximately a 30% lifetime risk of at least one VZV reactivation [3]. Generally the lesions of zoster are unilateral and located at the site most severely affected by varicella, most commonly either the facial or the mid-thoracic to upper lumbar dermatomes. The circumstances surrounding the reactivation of VZV, resulting in the lesions of zoster, are not well described but are associated with a decline in virus-specific cell-mediated immunity, specifically a decreased T-cell proliferation in response to VZV antigens, because of a decrease in the VZV-specific responder cell frequency [4, 5].

It is recognized that exposure to ultraviolet radiation (UVR) can cause local and systemic cell-mediated

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immunosuppression [6]. Although several rodent models of infection have been developed in which the effect of UV on immune responses has been defined [7], comparatively little is known regarding solar UV exposure and altered resistance to infections in human subjects. One situation where sunlight play a role is in acting as a trigger for the reactivation from latency of HSV, possible through a temporary depression in local cutaneous immunity [8–10]. In the present study, the aim was to determine if there was a seasonal incidence of zoster cases in a defined population over a 2-year period and, if there was, to determine the relationship with solar UV radiance measured at the nearest monitoring station. The number of cases of varicella occurring monthly in the same population was also recorded for comparison with the number of zoster cases.

METHODS

Study population

The study of the patients with zoster took place during 1999 and 2000 in the biggest outpatient dermatology department (Medical University of Lodz) and hospital ward in Lodz, Poland, with a monthly average of 2000 outpatient visits and 100 hospital admissions for all illnesses. The subjects were seen by a consultant dermatologist at least twice and only cases who showed obvious clinical symptoms of zoster were included. Occupation, i.e. indoors or outdoors, was recorded but, as only 2·5% of the subjects worked outdoors, this parameter was disregarded in the statistical analysis. The distribution of the zoster lesions, i.e. whether they occurred on a sun-exposed site (the face) or an unexposed site, was noted where this information was given in the case history. It was available for all but 31 of the zoster cases. The varicella cases represent the numbers in the whole of the Lodz area and were obtained from medical records.

Solar UVR

The measurements of the solar UVR reaching the ground were made at the Central Geophysical Observatory in Belsk (52° 50′ N, 20° 47′ E), about 100 km north-east of Lodz, with the use of the Solar Light UV-Biometer Mod. 501A. The instrument was internally temperature stabilized to ensure measurement accuracy. The spectral response of the instrument sensor was close to the erythemal action spectrum [11], which represents the erythemal action spectrum of the average Caucasian skin. The output of the instrument could be converted into the dose rate; time integration of the value over the day gave the daily UV dose, expressed as effective erythemal joules per unit area where one unit is defined as 210 J/m². The UVR at Belsk has been measured since 1976 [12] and the data series has been re-evaluated in order to make the series homogeneous. In the present study the data for 1999 and 2000 were used.

Statistical analysis

Seasonal variation was assessed by 'cosina analysis' in which the first terms in the Fourier series (i.e. $\cos\theta$ and $\sin\theta$ where $\theta = 0$ in January 1999, 2Π in January 2000 and 4Π in January 2001) were fitted in a Poisson regression model for average daily number of cases of zoster and varicella, and a linear regression model for solar UV [specifically, the logarithmic transform, log(UV)]. This enables the statistical significance of the seasonal pattern to be assessed and, when it is significant, the peak month and predicted value at the peak can be derived from examination of the regression coefficients of $\sin\theta$ and $\cos\theta$. To test, directly, for associations with UV, inclusion of a term for log(UV) in the Poisson regression models for monthly zoster and varicella cases/day, both with and without inclusion of the terms sin and cos was evaluated. A similar procedure was applied with mean daily UV split into quintiles. Models were compared for statistical significance using the likelihood ratio test. Rank correlations between the solar UV and zoster and varicella cases per month were computed. Analyses used the software packages GLIM (linear modelling) and SPSS (rank correlations).

RESULTS

Solar UVR

Solar UVR, measured as effective erythemal joules each month during 1999 and 2000, is shown in Figure 1. The variability of the UVR over this period did not differ significantly from the long-term mean variability of the UVR. The monthly UV doses ranged from about 10 in December to about 400 units in June/July. As might be expected, analysis showed a distinct seasonal pattern of UVR with peak (acrophase) at the beginning of June and magnitude of the daily dose at a peak of 12·3 units.

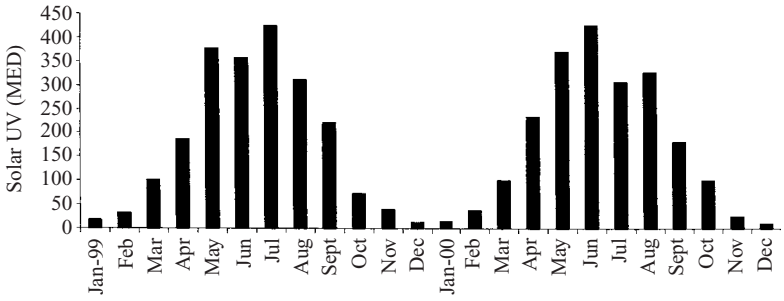

Fig. 1. Solar UV measured as effective erythemal joules in Belsk (Poland) each month during 1999 and 2000.

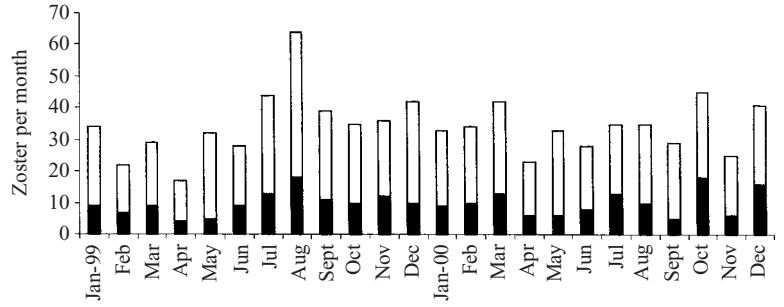

Fig. 2. Number of cases of zoster in total (white bars) and in males (black bars) in an area of Lodz (Poland) each month during 1999 and 2000.

Zoster

Figures for the number of cases of zoster were collected each month during 1999 and 2000 (Fig. 2): they totalled 585 (349 females and 236 males, range 13–46 per month). When Poisson regression modelling was applied to zoster cases, significant evidence of seasonal variation was found for total zoster cases ($P = 0{\cdot}04$) with a peak in July and magnitude at the peak of 0·15 cases/day (this magnitude gives a comparison with the overall mean). The same trend was seen for zoster in males ($P = 0{\cdot}02$) with a peak in June/July and magnitude at the peak of 0·25 cases/day (this magnitude gives a comparison with the overall mean). There was no statistically significant evidence of seasonality for zoster in females. Addition of log(UV) to the Poisson regression models containing sin and cos to models containing mean UV did not approach statistical significance. Conversely addition of sin and cos to models containing mean UV were statistically significant for total zoster cases and for zoster in males. Rank correlations of mean UV/day with zoster/day were all low and not statistically significant.

The number of cases of zoster lesions that occurred on body sites that are normally covered and normally exposed to sunlight were in the proportion 3:1 and are shown in Table 1. When seasonality was examined separately for zoster on the covered sites, Poisson regression showed no evidence of seasonality ($P = 0{\cdot}2$ for inclusion of sin and cos in the model). By contrast, the number of zoster cases with lesions occurring on exposed body sites showed highly significant seasonality ($P = 0{\cdot}0005$) with a peak in July/August. Logistic regression analysis of the proportion of cases in exposed sites also showed statistically significant seasonality. None of these analyses by body site gave any

Table 1. *Number of adult cases of zoster per month during 1999 and 2000 with lesions on covered body sites or on sites exposed to solar UVR (the face)*

	1999		2000	
	Covered	Exposed	Covered	Exposed
Jan.	17	8	16	4
Feb.	12	2	20	1
Mar.	13	2	22	4
Apr.	10	3	8	5
May	15	9	15	7
June	15	3	13	6
July	18	11	12	6
Aug.	28	12	14	7
Sept.	16	9	14	7
Oct.	21	2	17	8
Nov.	12	6	13	4
Dec.	25	6	18	2

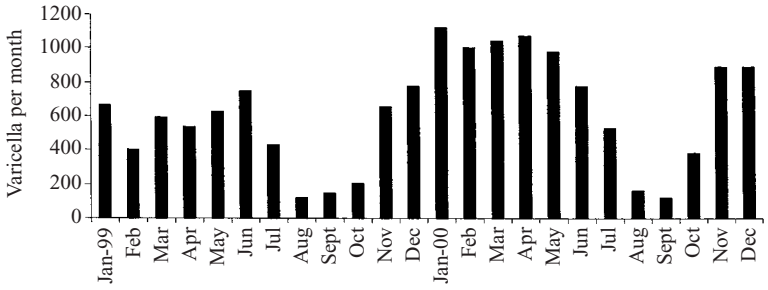

Fig. 3. Number of cases of varicella in Lodz (Poland) each month during 1999 and 2000.

indication of a direct association with solar UV irradiation (P values for addition of log(UV) to the models all exceeded 0·4).

Varicella

The total number of cases of varicella over the 2-year period of the study was 14 865 with a range of 120–1123 per month (Fig. 3). There was highly statistically significant evidence of seasonal variation for the number of cases of varicella: the maximum was in March and the minimum in August/September. Non-parametric correlations indicated quite large but non-significant negative correlations of solar UV/day and total zoster cases/day with total varicella cases/day.

DISCUSSION

The pattern of seasonality with respect to the incidence of varicella showed a peak of cases in the late winter months. This has been described previously for subjects living in temperate climates in the United States and elsewhere [2]. It is well recognized that many infections that are spread by the respiratory route, as is the case for varicella, tend to occur most frequently in the winter months when children spend more time indoors, resulting in an increased chance of transmission. In addition cold, wet weather may aid the survival of the virus outwith the host.

In considering the possible influence of seasons on the incidence of zoster, several studies have failed to demonstrate a correlation with any particular time of the year. For example, the number of cases of zoster in a general practice in England each month over the years 1947–62 was recorded and no perceptible seasonal effect was found out of a total of 192 cases, although it was noted that the highest figures occurred in July [13]. More results from a recent large-scale survey in Manitoba and the United Kingdom covering 1979–97 also indicate no seasonal pattern [3].

In contrast to these findings, Gallerani and Manfredini [14] reported a higher incidence of total zoster cases and zoster cases in males in the summer months (July to September) with significant acrophases in May–June in patients in Ferrara, north-east Italy, studied over the years 1992–8. They suggested that the increased exposure to solar UV in the summer months could lead to a suppression in the cellular immune response to VZV, thus allowing reactivation of the virus from latency in some individuals. Data giving local solar UVR over these years were not included, nor information regarding the seasonal incidence of any other infection.

Our results reported here support the hypothesis of Gallerani and Manfredini [14] as the peak incidence for all subjects and for males coincided with the months of highest solar UVR in the summer. This association was not found for females, considered alone. We do not know why this difference between men and women should occur but one possible explanation could be that older men tend to have more outside activities than women, such as gardening or walking, and thus more solar UV exposure. In addition to the increased incidence of zoster in the summer, there was a highly significant increase during the same period in cases where the lesions occurred on the face compared with body sites that are normally covered. This may indicate that the UVR has not only systemic immunomodulating effects but also acts locally, perhaps to alter cytokine expression in the irradiated skin. Such local immunosuppression has been described previously as being important in HSV recrudescences [15].

Further studies are required to assess the impact of solar UV exposure on other infectious diseases in human subjects, especially those caused by microorganisms which become persistent following the primary infection with the host, such as Epstein–Barr virus. In addition it should be established whether the resistance to infection induced by particular vaccines could be lowered significantly by sunlight exposure in the

summer months or following a sunshine holiday. This gap in our knowledge was noted in a report of the US Environmental Protection Agency in 1995 [16].

ACKNOWLEDGEMENTS

M.Z-P. and M.N. wish to thank the British Council for funding a British–Polish Joint Collaborative Programme. The work was also supported by the Medical University of Lodz, Poland Internal Grants 502-11-534-782 (25) (M.Z-P.).

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