Ecologic Analysis of Some Immune-Related Disorders, Including Type 1 Diabetes, in Australia: Latitude, Regional Ultraviolet Radiation, and Disease Prevalence

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The apparent immune-suppressive effect of ultraviolet radiation (UVR) has suggested that this environmental exposure may influence the development of immune-related disorders. Self-reported prevalence rates of type 1 diabetes mellitus, rheumatoid arthritis (RA), eczema/dermatitis, and asthma, from the 1995 Australian National Health Survey, were therefore examined by latitude and ambient level of UVR. A positive association of type 1 diabetes mellitus prevalence was found with both increasing southern latitude of residence ($r = 0.77$; $p = 0.026$) and decreasing regional annual ambient UVR ($r = –0.80$; $p = 0.018$); a 3-fold increase in prevalence from the northernmost region to the southernmost region was evident. In contrast, asthma correlated negatively with latitude ($r = –0.72$; $p = 0.046$), although the change in asthma prevalence from the north to the south of Australia was only 0.7-fold. For both RA and eczema/dermatitis, there were no statistically significant associations between latitude/UVR and disease prevalence. These ecologic data provide some support for a previously proposed beneficial effect of UVR on T-helper 1–mediated autoimmune disorders such as type 1 diabetes. The inverse association of type 1 diabetes prevalence with UVR is consistent with that previously reported for another autoimmune disease, multiple sclerosis, in Australia, and also with type 1 diabetes latitudinal gradients in the Northern Hemisphere. The finding also accords with photoimmunologic evidence of UVR-induced immunosuppression and may suggest a beneficial effect of UVR in reducing the incidence of such autoimmune conditions. In light of this study, analytic epidemiologic studies investigating risk of immune disorders in relation to personal UVR exposure in humans are required. *Key words:* **asthma, Australia, autoimmune disease, ecologic analysis, eczema/dermatitis, immune disorders, latitude, rheumatoid arthritis, type 1 diabetes, ultraviolet radiation.** *Environ Health Perspect* **111:518–523 (2003). doi:10.1289/ehp.5941 available via *http://dx.doi.org/* [Online 19 December 2002]**

Autoimmune diseases such as type 1 diabetes mellitus, multiple sclerosis (MS), and rheumatoid arthritis (RA) are immune system disorders that share common features of self-reactive T cells and the presence of autoantibodies; as a group they affect some 5% of the population (Davidson and Diamond 2001). Although their precise etiologies are unknown, these autoimmune disorders are generally agreed to reflect interactions of polygenic traits with various ill-defined environmental factors (Cantorna 2000; Dahlquist 1998; Hayes et al. 1997; Karges et al. 1995; Weinshenker 1996). Descriptive epidemiology may further elucidate the role of environmental factors in the etiology of the autoimmune diseases MS, type 1 diabetes, and RA, as well as other immune-related disturbances such as asthma and eczema/dermatitis.

MS, type 1 diabetes, and, to a lesser extent, RA in the Northern Hemisphere, particularly in Western Europe and North America, display a latitudinal gradient in disease frequency, with the prevalence of these disorders increasing at higher latitudes (Cantorna 2000; DERIG 1988; Hayes et al. 1997; Karvonen et al. 1993). MS exhibits a similar prevalence gradient in the Southern Hemisphere, in Australia and New Zealand (Hammond et al. 2000; Miller et al. 1990). In Australia, however, where the opportunity exists to study gradients in rates across a large-area population that is less ethnically and genetically diverse than across Europe, analyses for other immune-related disorders have not been done previously.

Ultraviolet radiation (UVR) reaching the earth's surface varies inversely with latitude; UVR is thus a prominent latitude-related environmental factor. Recent photoimmunologic work shows that UVR downregulates cellular immunity (Damian et al. 1998; Kelly et al. 1998), attenuating T-helper (Th)1 T-cell–mediated immune responses (Clydesdale et al. 2001). These responses are thought to be significantly involved in some autoimmune disorders such as MS, type 1 diabetes, and RA (Mackay 2000). UVR might therefore be expected to be beneficial for these disorders. Few autoimmune or other immune-related disorders, however, have been assessed ecologically with respect to UVR. A notable exception for the Southern Hemisphere is a recent analysis of MS in Australia, where the regional variation in MS prevalence was strongly inversely associated with ambient UVR levels ($r = –0.91$; $p = 0.01$) (van der Mei et al. 2001). This finding supports the possibility of UVR being a protective modulator of immune and autoimmune processes involved in the etiology of such immune disorders (McMichael and Hall 1997). Type 1 diabetes and RA were therefore chosen for ecologic analysis to determine whether these disorders showed environmental gradients similar to those observed for MS in Australia.

By downregulating Th1-mediated immunity, UVR has been thought to effect a shift from Th1- to Th2-mediated processes (Clydesdale et al. 2001). Th2 cells are responsible for immediate-type hypersensitivity to allergens such as dust mites; UVR may thus have the potential to exacerbate allergic disease (Selgrade et al. 1997). However, recent work has cast doubt on the mutual antagonism of Th1 and Th2 cytokine expression, particularly in humans (Davidson and Diamond 2001; Mackay 2000; Platts-Mills 2002; Platts-Mills et al. 2001). Ultraviolet B, particularly through interleukin 10, can inhibit both Th1- and Th2-mediated immune responses in mice (Garssen et al. 1999). In children, asthma can coexist with Th1-type disorders such as type 1 diabetes, RA, and celiac disease, suggesting a common environmental influence (Kero et al. 2001). A recent randomized controlled trial in the United Kingdom on adult atopic eczema has shown UVR, particularly narrow-band ultraviolet B, to also have a beneficial effect (Reynolds et al. 2001). Eczema/dermatitis, together with asthma, were therefore chosen to be similarly analyzed for regional prevalence gradients to compare with any associations evident for type 1 diabetes and RA.

We have examined the association between latitude and prevalence of the immune-related disorders type 1 diabetes mellitis, RA, eczema/dermatitis, and asthma in Australia, a country with a relatively genetically homogeneous population. We further considered

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regional differences in ambient UVR to examine possible associations between regional and seasonal UVR levels and the prevalence of these immune disorders in Australia.

Methods

Prevalence data source. The 1995 Australian National Health Survey (NHS) was conducted by the Australian Bureau of Statistics (ABS) during the 12-month period from January 1995 to January 1996. Approximately 54,000 people from all states and territories and across all age groups provided information about their own health status. Residents of a stratified, multistage area, random sample of 23,800 private households and households in nonprivate dwellings were interviewed in person by ABS interviewers; persons within each state/territory had a known, and in the main equal, chance of selection. Residents of hospitals and other institutions were excluded, however, and the Northern Territory (NT) sample was predominantly urban. Responses were received from 91.5% of households and 97% of people from these households fully completed questionnaires. Quarterly population estimates were used by ABS for standardization, and prevalence rate estimates were adjusted for household size (ABS 1995a).

The survey interviewers recorded information on recent illness and/or long-term conditions, as reported by respondents. Specific questioning about conditions, including diabetes, arthritis, and asthma, was followed by action-based questions on recent visits to hospitals or health professionals. Information on medication usage, including insulin and medications for asthma, arthritis, and allergies, was also elicited (ABS 1995b). Disease conditions were classified by the *International Classification of Diseases, 9th Revision* (cited by ABS 1995a), categories. Information recorded in the survey was not medically verified, however.

For this study we used summary-data prevalence estimates for four immune-related disorders from the published survey results (ABS 1995c). We compared the age- and sex-standardized prevalence rates of type 1 diabetes, RA, eczema/dermatitis, and asthma, per 1,000 population, over the eight major state and territory regions of Australia, as listed in Table 1.

Latitude and ultraviolet radiation. The latitude of the regional capital city (decimal degrees south; Geoscience Australia mapping agency) was used for each region (Table 1). Three UVR measures were examined, each relating to the Australian UV index (Lemus-Deschamps et al. 1999) and expressed in milliwatts per square meter (where 1 UV index unit = 25 mW/m^2). The measures were, for each regional capital, an arithmetic mean of 12 monthly UV index averages, each monthly average calculated from single, daily (at local solar noon), erythemally weighted clear-sky UV index values derived from ozone data over the period 1979–1993 (Lemus-Deschamps L. Personal communication), a midwinter minimum (June) solar-noon UVR value, and a midsummer maximum (January) solar-noon UVR value (Table 1).

Statistical analysis. To account for the NHS sampling variability between regions, we calculated approximate standard errors (SEs) for each regional prevalence estimate, as outlined in Appendix H and "Technical Note: Sampling Variability" in the respective ABS publications (ABS 1995a, 1995c). The approximate SEs were calculated from SEs for the corresponding numerator estimates shown in Table 2, as listed by ABS for each region (ABS 1995a, 1995c). Age-standardization factors for the different regions were also applied, as recommended in the same Technical Note, and the final SEs for the prevalence rates calculated (Table 2). The reciprocal of the variance of each prevalence rate was then used to weight the relationships to account for differing sample sizes in the regions.

Associations between the environmental variables and the immune disorder prevalence rates were examined by variance-weighted least-squares regression of the prevalence rate estimates versus, first, the latitude values of the regional capital cities, and second, the three UVR measures for each of the regional capitals. The magnitude of change in disease prevalence rates over the north-south range was compared by substituting latitude values for Darwin and Hobart into the regression equations. The statistical program Stata 7.0 (Stata Corporation, College Station, Texas, USA) was used for regression analyses.

Table 1. Australian state and territory regions and approximate latitude ranges; regional capitals and their latitudes (decimal degrees south) shown together with midsummer (January) and midwinter (June) solar-noon UVR[a] for each regional capital.

State/territory region	Latitude range for region (degrees)	Regional capital	Latitude of capital (degrees)	Midsummer UVR (mW/m^2)	Midwinter UVR (mW/m^2)
Northern Territory	11–26	Darwin	12.45	339.5	205.9
Queensland	10–29	Brisbane	27.47	332.4	103.9
Western Australia	14–35	Perth	31.95	326.1	82.9
New South Wales	28–37	Sydney	33.87	306.1	66.5
South Australia	26–38	Adelaide	34.93	303.4	60.7
Australian Capital Territory	35–35.5	Canberra	35.30	302.7	55.7
Victoria	34–39	Melbourne	37.82	287.6	48.6
Tasmania	41–43.5	Hobart	42.88	256.7	31.4

[a]UVR data are monthly averages calculated from daily (at local solar noon) erythemally weighted clear-sky UV Index values derived from ozone data over the period 1979–1993 (courtesy of L. Lemus-Deschamps, Bureau of Meteorology Research Center, Australia) and expressed as mW/m^2.

Table 2. Regional immune disorder (excluding MS) prevalence rates[a] (shaded lines with SE[b] in parentheses) together with numerator data on which SE estimates were based.

State/territory	Type 1 diabetes	Rheumatoid arthritis	Eczema/dermatitis	Asthma	Regional population
Northern Territory					
No. cases	200	1,500	2,900	17,200	145,300
Prevalence	2.9 (1.80)	18.2 (5.56)	19.2 (4.43)	127.2 (13.11)	
Queensland					
No. cases	10,500	82,100	96,900	438,000	3,277,800
Prevalence	3.2 (0.62)	25.7 (1.34)	29.5 (1.40)	132.6 (2.51)	
Western Australia					
No. cases	6,900	49,000	82,400	201,500	1,732,400
Prevalence	4.2 (0.79)	29.8 (1.66)	47.1 (1.90)	115.2 (2.76)	
New South Wales					
No. cases	26,300	170,700	181,900	633,700	6,120,500
Prevalence	4.2 (0.56)	27.3 (1.24)	29.8 (1.30)	103.9 (2.10)	
South Australia					
No. cases	8,300	41,900	73,000	163,500	1,474,800
Prevalence	5.4 (0.63)	26.8 (1.15)	50.3 (1.55)	112.4 (2.16)	
Australian Capital Territory					
No. cases	1,100	5,600	14,400	35,500	304,900
Prevalence	4.6 (0.99)	21.4 (1.65)	45.5 (3.98)	111.9 (2.65)	
Victoria					
No. cases	23,800	106,400	171,500	501,500	4,503,100
Prevalence	5.2 (0.50)	23.2 (0.88)	38.2 (1.07)	111.8 (1.63)	
Tasmania					
No. cases	2,100	19,100	20,700	48,800	473,600
Prevalence	4.5 (1.14)	39.5 (2.38)	44.0 (2.53)	102.1 (3.48)	

[a]Rate per 1,000, age- and sex-standardized to the 1995/1996 Australian population. Data from ABS (1995c). [b]Approximate SE calculated from ABS-provided SE for numerator (ABS 1995a, 1995c).

Because the use of capital city latitudes may not have been representative of the regional population distribution, particularly for larger regions with the capital at either a northern or southern extreme of the region rather than medially placed, a sensitivity analysis was carried out to test the effect of using an alternative latitude value midway between the two main population centers in these regions. Results were then compared with those obtained from the regional capitals.

Results

Latitude and immune disorders. The relationships between latitude of the regional capitals and immune disorder prevalence are shown in Figure 1 as regression lines fitted to the prevalence estimates; 95% confidence intervals (CIs) are also shown, and these indicate, reciprocally, the relative weighting applied to each estimate in the regression analysis.

Prevalence of type 1 diabetes was positively correlated with latitude (Pearson $r = 0.77$; $p = 0.026$), with the prevalence increasing 2.97-fold over the north-south latitude gradient. Asthma prevalence, on the other hand, was inversely correlated with latitude (Pearson $r = -0.72$; $p = 0.046$), with the prevalence rate decreasing 0.7-fold, i.e., by approximately one-third, over the same latitude range. Although both eczema/dermatitis and, to a much lesser extent, RA showed trends of increasing prevalence with increasing latitude, these were not statistically significant (Figure 1).

Sensitivity analysis. In four of the eight regions, Western Australia (WA), South Australia (SA), Victoria (VIC), and Australian Capital Territory (ACT), at least 70% of the state or territory populations resided in the capital metropolitan area (ABS census data 1991/1996, not shown). Among the remaining regions in which the population was more dispersed outside of the capital, only NT and Queensland (QLD) were also both of wide latitudinal range and had capitals located noncentrally in terms of the regional latitude range, thus potentially biasing the associations markedly.

The effect on the initial associations of using alternative latitude values midway between the two main population centers, Darwin and Alice Springs, for NT (i.e., latitude 18.08 degrees south), and Brisbane and Townsville for QLD (i.e., latitude 23.36 degrees south), was to strengthen the statistical significance of the associations for type 1 diabetes, asthma, and eczema/dermatitis when one or both midway latitudes were substituted. For example, for type 1 diabetes and asthma, the statistical significance of the associations was raised maximally [from $p = 0.026$ to $p = 0.010$ for diabetes ($r = 0.77$ to 0.84), and from $p = 0.046$ to $p = 0.013$ ($r = -0.72$ to -0.82) for asthma] when midway latitudes were used for both regions. Both approaches unavoidably entail some exposure misclassification for dispersed regional populations. Whereas the latter (midway latitude) approach may lead to better estimation of the correlation, by using the capital latitude values for type 1 diabetes and asthma as we have done (Table 1), the estimate was somewhat biased toward the null hypothesis of no association and thus toward underestimation of r. Similarly, for eczema/dermatitis the statistical significance was raised maximally [from $p = 0.206$ to $p = 0.174$ ($r = 0.50$ to 0.54)] when only the QLD latitude was altered, but this was still nonsignificant at the 5% level. For RA, on the other hand, using both midway latitudes gave maximal change, but the statistical significance of the observed trend was lowered [from $p = 0.727$ to $p = 0.795$ ($r = 0.15$ to 0.11)]. In summary, the use of the regional-capital latitude values rather than latitude values of the midway points did not alter the overall conclusions of whether the observed associations were statistically significant at the 5% level.

Ultraviolet radiation and immune disorders. In light of the sensitivity analysis, UVR values for the regional capitals were used. A solar-noon, clear-sky measure of ambient UVR was chosen because midday, or noontime, exposure to the maximal UVR level in sunlight in Australia suppresses the systemic immune response in humans (Hersey et al. 1983). Type 1 diabetes prevalence was inversely correlated with regional average solar-noon UVR (Pearson $r = -0.80$; $p = 0.018$), whereas asthma prevalence was positively correlated with regional average solar-noon UVR (Pearson $r = 0.73$; $p = 0.040$) (Figure 2). Eczema/dermatitis and RA prevalence showed inverse trends with average solar-noon UVR, but these were not significant (Table 3). The prevalence of asthma was positively correlated with either average or midwinter solar-noon UVR but not midsummer UVR. Although type 1 diabetes prevalence was inversely correlated with all three ambient UVR measures, it was more closely correlated with average or midwinter solar-noon UVR than with midsummer UVR (Table 3).

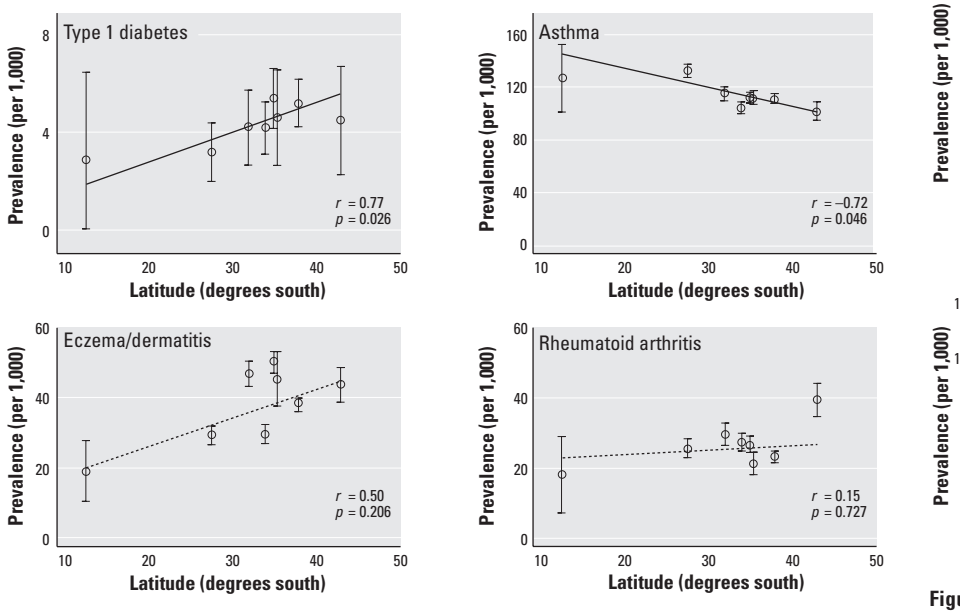

Figure 1. Associations between latitude and prevalence per 1,000 (open circle) of type 1 diabetes, asthma, eczema/dermatitis, and RA. 95% CIs of prevalence estimates shown as error bars; solid lines denote statistically significant association, $p < 0.05$; dotted lines denote nonsignificant trend.

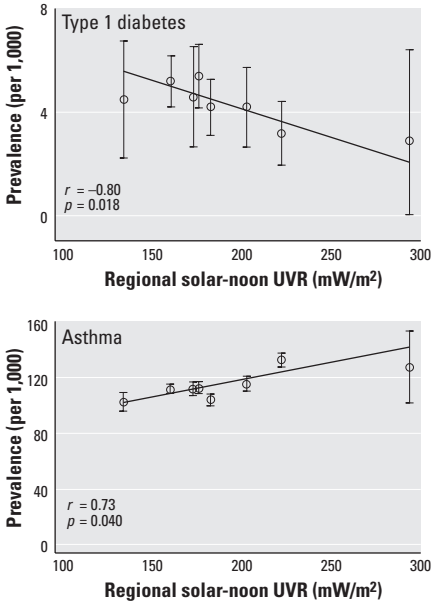

Figure 2. Associations between regional average ambient solar-noon UVR and prevalence per 1,000 (open circle) of type 1 diabetes and asthma. 95% CIs of prevalence estimates shown as error bars.

Discussion. Using summary age- and sex-standardized data on self-reported prevalence of immune disorders from the ABS 1995 NHS, strong gradients in type 1 diabetes prevalence with latitude and also, inversely, with UVR were observed. The magnitude of change for type 1 diabetes in Australia was an approximately 3-fold increase in prevalence from the northernmost region, NT, to the southernmost region, Tasmania (TAS). These ecologic data provide support for a previously proposed beneficial effect of UVR on autoimmune disorders such as type 1 diabetes (McMichael and Hall 1997). In contrast to type 1 diabetes, asthma correlated negatively with latitude and positively with regional annual or midwinter UVR, but the magnitude of change for asthma prevalence from the north to south of Australia was only 0.7-fold. For both RA and eczema/dermatitis, there were no statistically significant associations between latitude/UVR and disease prevalence.

A strength of this ecologic analysis derives from the relative genetic homogeneity of the Australian population (McLeod et al. 1994) and relative uniformity also in the standard of national health care. A further advantage is the wide latitude range and the resulting wide range of ambient UVR levels over the Australian continent. A high total response rate to the survey was achieved by the ABS over all regions.

One potential source of (probably random) error, however, lies in the self-reported, nonverified nature of the data, which could have resulted in some misclassification of disease conditions. This is particularly so for eczema/dermatitis, the classification of which appears to have been based largely on medication usage; there were no direct disease-specific questions on eczema (ABS 1995b). The classification eczema is often used as an umbrella term encompassing various dry, itchy skin conditions (McNally et al. 2000); dermatitis similarly can include contact dermatitis. Also the eczema/dermatitis category in the NHS included heat eczema and sunburn (ABS 1995a), leading to possible regional differences in prevalence. In addition, although arthritis was allocated four specific questions, misclassification between rheumatoid arthritis, osteoarthritis, and general arthritic or rheumatism conditions could have occurred. Type 1 diabetes, on the other hand, was classified on the basis of 24 direct questions for diabetes and insulin usage, including duration of use, both past and future expected use, and age at first use (ABS 1995b). The relative validity of classification of type 1 diabetes, a serious disease requiring specific treatment, should therefore have been more regionally consistent.

Exposure misclassification at the ecologic (i.e., state or territory) level compared with the individual level could have occurred because actual personal UVR exposure depends on both behavior in relation to the sun (i.e., whether sun avoidant or taking sun protection measures) and on regional ambient UVR. For example, regional UVR would not have been a good measure of personal sun exposure among sun-avoidant people, and if the proportion of such people in each local population varied markedly, then population-level exposure assessment would be biased. In fact, the proportion was small and did not vary substantially by region [percentage recording "don't go out in sun" was 3.4% for NT, 2.0% for QLD, and 2.3% for TAS (ABS 1995c)]. For most individuals, however, personal UVR exposure varies between 5 and 15% of daily total ambient UVR (Gies et al. 1999). Ambient UVR levels thus may provide a reasonable measure of average personal sun exposure at the population level.

Another possible source of measurement error—using capital city latitudes and UVR values as representative of each region—was shown by sensitivity analysis not to significantly bias the results even for the two regions having the most noncentral capitals and the widest latitude range, QLD and NT. However, we considered only current residence and could not take into account the contribution of prior residence areas, or the timing of the critical UVR exposure, which may have occurred earlier in life, or even possible migration after disease initiation, as prevalence rather than incidence data were used. In addition, we could not control for latitude when examining the relationships between the immune disorders and UVR because of collinearity between UVR and latitude.

Potential ecologic confounders include other possible causal factors for immune-related disorders that vary with latitude or UVR; for example, regional infection patterns that may be associated with climatic differences. Infectious agents have been linked to the etiology of immune disorders, including diabetes (Dahlquist 1998; EURODIAB 2000; Kamradt and Mitchison 2001; Notkins and Lernmark 2001), RA (Albert and Inman 1999; Ebringer and Wilson 2000; Wilson et al. 2000), and asthma (Blasi et al. 2001). A lack of infections in early life may also adversely affect immune development—the so-called hygiene hypothesis (Bach 2002). A second important ecologic factor to consider for asthma is that there are marked regional differences in allergen levels. For example, an 11-fold higher level of mean house dust mite allergen (Der p1) concentration in homes in Sydney, New South Wales (low latitude, warm and more humid) compared with TAS (higher latitude, cool and dry) (Couper et al. 1998) may contribute to the inverse latitude gradient for asthma. Other confounding factors could include environmental temperature and dietary differences (Dahlquist 1998). These potential confounders warrant more detailed consideration in future research. There may also be interaction between some of these environmental exposures, for example, infection and nutritional factors (Haverkos 1997). However, it is not possible to determine such interactions in ecologic analyses, as there is a lack of data on joint environmental exposures at the individual level (Ponsonby et al. 2002).

UVR has an inverse, or lack of, association with the immune-related disorders analyzed except for asthma, which showed a positive association between prevalence and UVR. We are uncertain of the significance of this finding, particularly as the prevalence increase over the UVR range was only low. UVR-induced Th2 upregulation is one possibility, but UVR can also suppress Th2 responses (Garssen et al. 1999). In addition, the contribution of regional allergen levels to asthma prevalence could be important. Furthermore, much of asthma at the population level may be nonallergic (Pearce et al. 1999), with Th2 mechanisms not involved.

The stronger association found between latitude and type 1 diabetes prevalence in Australia is consistent with similar incidence gradients found in Western Europe and North America (DERIG 1988; Karges et al. 1995; Karvonen et al. 1993) and also within China (Yang et al. 1998). The corresponding inverse association between UVR levels in Australia and type 1 diabetes prevalence is also consistent with previous photoimmunologic work showing that ultraviolet B irradiation has systemic as well as local

Table 3. Correlations between immune disorder prevalence and regional UVR levels in the 1995 NHS.[a,b]

Prevalence of disorder	Regional solar-noon UVR		
	Average	Midwinter	Midsummer
Type 1 diabetes	–0.80 (0.018)*	–0.77 (0.024)*	–0.72 (0.045)*
Eczema/dermatitis	–0.47 (0.243)	–0.49 (0.215)	–0.34 (0.412)
RA	–0.08 (0.845)	–0.06 (0.880)	–0.12 (0.774)
Asthma	0.73 (0.040)*	0.72 (0.044)*	0.68 (0.060)

[a]Pearson correlation coefficients (correlations based on the eight Australian state/territory regions) between immune disorder prevalence and solar-noon UVR, for each type of immune disorder and three different measures of UV Index values—average over year, midwinter minimum, and midsummer maximum. [b]*p*-Values in parentheses. Strength of association examined by variance-weighted least-squares regression. *Statistically significant association, $p < 0.05$.

immunosuppressive effects in humans and animals (Clydesdale et al. 2001; Duthie et al. 1999; Garssen et al. 1999; Sleijffers et al. 2001), as does also ultraviolet A irradiation (Nghiem et al. 2001). UVR exposure may be protective against Th1-mediated disorders such as type 1 diabetes by downregulating Th1 autoimmune responses by several different immunoregulatory mechanisms (Clydesdale et al. 2001; Duthie et al. 1999; Ponsonby et al. 2002).

One of these possible mechanisms for downregulation involves UVR-induced vitamin D. Thus, the proposed protective role of UVR for autoimmune type 1 diabetes may act through its important role in vitamin D synthesis in the skin. Some 90% of plasma vitamin D in humans is produced endogenously via skin exposure to UVR in sunshine (Norris 2001) and particularly so in Australia where foods are not generally fortified with vitamin D (Mason and Diamond 2001; Pasco et al. 2001). There are also recent reports of vitamin D deficiency in some Australian populations (Grover and Morley 2001), particularly in winter (McGrath et al. 2001; Pasco et al. 2001). For type 1 diabetes, this possible mechanism is consistent with recent reports of decreased risk of this disorder in offspring of mothers supplemented with cod liver oil in pregnancy (Stene et al. 2000), and decreased incidence of type 1 diabetes in children supplemented with vitamin D in infancy (EURODIAB 1999; Hypponen et al. 2001). The Finnish birth cohort study reported a rate ratio of 0.12 (95% CI, 0.03–0.51) for diagnosis of type 1 diabetes by adulthood comparing regular versus no vitamin D supplementation in the first year of life (Hypponen et al. 2001). These studies suggest that vitamin D may prevent initiation of type 1 diabetes, and thus accord with the vitamin D–protective hypothesis proposed for this and other autoimmune disorders such as MS (Cantorna 2000; Hayes et al. 1997). For MS this hypothesis is consistent with the recent finding of a strong inverse gradient between ambient UVR levels and MS prevalence in another Australian ecologic study (van der Mei et al. 2001). Our analogous finding for ambient UVR and type 1 diabetes in Australia supports the specific prediction that autoimmune diseases other than MS, such as type 1 diabetes, should show latitude and/or UVR gradients similar to those seen for MS if these immune disorders are influenced by UVR exposure (McMichael and Hall 1997).

In conclusion, our ecologic analysis of data from the 1995 NHS has demonstrated a regional gradient of type 1 diabetes prevalence within Australia that is inversely associated with regional UVR levels measured at local solar noon. The inverse association with UVR is consistent with that found for another autoimmune disease, MS, in Australia and consistent with type 1 diabetes latitudinal gradients seen in the Northern Hemisphere. The finding is also consistent with photoimmunologic evidence of UVR-induced immunosuppression and suggests a beneficial effect of UVR in preventing both these autoimmune conditions. Analytic epidemiology studies investigating risks of type 1 diabetes and other immune disorders in relation to personal UVR exposure in humans are now required (McMichael and Hall 2001).

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