ORIGINAL ARTICLE

The influence of sun exposure in childhood and adolescence on atopic disease at adolescence

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Abstract

Background: It has been postulated that ultraviolet ray exposure in childhood might influence the development of allergic disease. We examined whether reported sun exposure during childhood or in adolescence is related to the occurrence of atopy or allergic disease.

Methods: Population-based longitudinal cohort study with sixteen-year follow-up (N = 415). Subjects were recruited at birth as part of an infant health study. The reported daily duration of sun exposure in the summer months was recorded at 8 and 16 yrs of age. Allergen sensitization and the presence of eczema, asthma, and rye grass positive rhinitis were recorded at age 16.

Results: Reported sun exposures of more than 4 h per day during summer holidays in adolescence were associated with reduced eczema and rhinitis but not inhalant allergen sensitization or asthma risk. Thus, higher sun exposure during summer holidays and summer weekends in adolescence was associated with significantly reduced eczema (test of trend p-value = 0.001 summer holidays; test of trend p-value = 0.003 summer weekends) and rye grass positive rhinitis (test of trend p-value = 0.03 summer holidays; test of trend p-value = 0.02 summer weekends). Sun exposure at adolescence or age 8 was not related to inhalant allergen sensitization. There was no association between serum 25(OH)D levels at adolescence with either inhalant allergen sensitization or allergic disease and adjustment for serum 25(OH)D levels did not alter these findings.

Conclusions: Increased sun exposure during summer holidays in adolescence was associated with reduced eczema and rhinitis risk, independently of measured vitamin D levels but no difference in inhalant allergen sensitization or asthma. The beneficial effects of sun exposure on allergic disease may operate independently from vitamin D or an effect on allergen sensitization.

There is currently much interest in the possible effects of ultraviolet (UV) exposure and its derivative vitamin D on the development of allergic disease (1). Ultraviolet exposure can suppress allergic immune responses and has been observed to improve atopic dermatitis (2). It is possible that the effect is a direct one on the inflammatory response in the skin. However, UV exposure induces active forms of vitamin D, and these exhibit important regulatory activities on the immune responses leading to allergic disease (3). It is also possible that the mechanism for the influence of sun exposure is related to vitamin D metabolism, reviewed in Mullins et al. (4).

Some investigators have observed correlations between allergic and autoimmune diseases and latitude. Thus, Hughes et al. (5) found an inverse latitude gradient for asthma (a 9% decrease per increasing degree of latitude); however, this pattern did not persist after adjusting for average daily temperature. In both, the USA and Australia, Krstic found an increased incidence of asthma with increasing latitude (6). Fsadni found that latitude correlated negatively with type 1 diabetes and positively with rhinitis and rhinoconjunctivitis; however, there was no significant correlation with wheeze or eczema (7). In contrast in an adult study by Wjst, allergic rhinitis decreased with geographical latitude (8). Childhood eczema and food allergy were also correlated with increasing latitude in Australia (9).

Possible explanations for an effect of latitude on immunological diseases are immunomodulation mediated by a direct effect of UV irradiation or an indirect effect mediated by

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vitamin D. Rarely, studies have attempted to document sun exposure. Hughes et al. (5) found there was no association between any of the UVR- or vitamin D-related measures and childhood asthma; however, greater time in the sun in winter between the ages 6 and 15 yrs was associated with an increase in the odds of having hay fever.

Concerning vitamin D, most, but not all, studies have shown that low vitamin D levels increase the risk of asthma and allergies, but a few suggest an increased risk with high D levels (10); however, the mechanism is unclear and the role of UV exposure is uncertain. Serum vitamin D was negatively associated with asthma and allergic phenotypes in Western Australia (11), and vitamin D deficiency is associated with higher levels of IgE sensitization in children and adolescents (12). Thus, both sensitization and atopic disease have been associated with reduced vitamin D. However, there is a need for further prospective information on the possible roles of both sun exposure and vitamin D levels on the development of allergic disease.

In this study, we have examined whether there is an association between sun exposure and the development of atopic disease or sensitization. The Tasmanian Infant Health Cohort (13) is a population-based longitudinal cohort study with sixteen-year follow-up. Longitudinal information has been collected on sun exposure and on the development of atopic disease. In a previous study, we demonstrated there was some agreement comparing sun exposure at summer weekends and summer holidays by questionnaire and objective measure (14). This cohort provides the opportunity to examine the influence of reported sun exposure at 8 and 16 yrs of age on the development of atopic disease and allergic sensitization.

Methods

In 1988 and 1989, there were 13,592 live births in Tasmania. A scoring system selected newborn infants at higher risk of sudden infant death syndrome (SIDS) for possible participation in a Tasmanian Infant Health Study (TIHS) (15). The scoring system weighted infants according to their birth weight, season of birth, gender, mother's age, duration of second stage labor, and intention to breastfeed. All multiple births were included. In Southern Tasmania in 1988 and 1989, 1500 infants were born who were eligible to join the study. Of the original birth cohort of 1433 infants whose mothers agreed to an in-hospital interview 415 were followed up at 16 yrs. At age 8 TIHS cohort children residing in Southern Tasmania were followed up for studies on bone density and blood pressure in 1996, and health and development and vitamin D in 1997 (16). Using school lists, 1156 of these subjects were identified (or 81% which is in close agreement to the Australian Bureau of Statistics data on annual outward migration rates from Tasmania of 2.5%). A total of 888 took part. In 2004/5 a total of 730 were traced and approached to participate in a follow-up study of bone health and allergy at age 16 (17). Of these, 139 failed to respond to the first or subsequent contacts, 129 responded but declined, 38 failed to attend for assessment, and 9 were not included for other reasons. Thus, 415 participated in the 15-year follow-up.

Allergic disease

We utilized the following questions from the ISAAC study to determine the presence of current (in the past 12 months) allergic disease at ages 8 and 16 (18, 19).

Asthma: Have you had wheezing or whistling in the chest in the past 12 months?

Rhinitis: In the past 12 months have you had a problem with sneezing, or a runny, or blocked nose when you did not have a cold or the flu? We examined rye grass positive rhinitis defined as a positive answer to the ISAAC question and a positive ImmunoCAP® (Pharmacia Diagnostics AB, Uppsala, Sweden) test to rye grass at age 16.

Eczema: Have you ever had an itchy rash which was coming and going for at least 6 months? Have you had this itchy rash at any time in the past 12 months?

A family history of asthma was defined as any of the participant's siblings, parents, or grandparents having any history of asthma at the time of the participant's birth.

Allergen sensitization

Of the 415 participants of the 16-year follow-up, we obtained sufficient sera for allergen testing at age 16 in 373, 89.9% (20). Allergen sensitization was determined by the ImmunoCAP® (Pharmacia Diagnostics AB). Tests were conducted for specific IgE to ryegrass, Alternaria, D. pteronyssinus (Der p 1), D. farinae (Der f 1), cat, dog, cow's milk, egg, and peanut allergens. A test result ≥ 0.35 kU_A/l of allergen specific IgE was regarded as positive.

Vitamin D measurement

Serum 25(OH) D was measured at age 16 using a radioimmunoassay kit (DiaSorin, Stillwater, MN, USA) and expressed as nmol/L. The intraassay and interassay precisions of these assays are 6% and 15%, respectively. (21)

Sun exposure

Parents were asked about the amount of time their child would normally have spent in the sun during weekends and holidays in summer at age 8 (childhood) and age 16 (adolescence). It has previously been demonstrated that these questions related to sun exposure in summer weekend or holidays are a useful proxy for the direct measurement of sun exposure (22).

The infant's sun exposure was determined from a 24 h grid which parents completed when the child was approximately one-month old. This grid indicates where the baby typically was for each hour of the day. Baby being 'Outside' was taken to indicate sun exposed. In infancy sun exposure was stratified as outside exposure of less than or more than 1 h. Childhood or adolescent sun exposures were also stratified by the duration of sun exposure in summer holidays and summer weekends into more than 4, 3–4, 2–3, and <2 h. We examined the association of reported sun exposure in infancy, childhood, and adolescence with the

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presence of allergic disease (asthma, eczema, rye grass positive rhinitis), and inhalant allergen sensitization in adolescence.

Melanin density was calculated from readings obtained from a Minolta Spectrophotometer (Minolta 2500d, Tokyo, Japan) at 400 and 420 nm wavelengths (23).

Other factors

We obtained data on other potential confounders that might influence the development of allergen sensitization or atopic disease: maternal antenatal smoking, maternal postnatal smoking, any breastfeeding at 1 month, early introduction of solids, cat as pet at 1 month, dog as pet at 1 month, male, premature birth, and low birth weight.

Statistical analysis

Odds ratios for various sun exposure measures and atopic disease or sensitization were calculated. Logistic regression was used with exposure terms for the amount of time spent in the sun during summer weekends or holidays in childhood or adolescence and >1 h outside at 1 month of age, and the outcome of current eczema, current rhinitis, current asthma, and any inhalant sensitization at adolescence. Variables for potential confounders were added as covariates to the model. To examine whether any putative association between sun exposure and allergic disease was mediated by vitamin D we included vitamin D as a covariate and examined the residual apparent influence of sun exposure. The fewer numbers in tables than the 415 followed up reflects the occasional questionnaire with incomplete data. The minimum level of association (OR) between past sun exposure or vitamin D level given an exposure prevalence of 50% is 1.88 for which this study will have at least 80% power at $p < 0.05$, for $n = 373$.

Ethics approval was obtained from the University of Tasmania Human Research Ethics Committee and the Southern Tasmania Health and Medical Human Research Ethics Committee, Australia.

Results

The prevalence of current asthma eczema and hay fever at 16 yrs of age was 25%, 13%, and 33%, respectively. We therefore examined the reported sun exposures at ages 8 and 16 yrs. 76.3% (305/400) of children and 56.6% (235/415) of adolescents reported >4 h sun exposure per day at summer weekends and 82.7% (329/398) of children and 65.3% (271/415) of adolescents reported >4 h sun exposure per day in summer holidays.

We examined the longitudinal associations for sun exposure behaviors over time. After accounting for month of birth, a higher number of hours spent regularly outdoors at 1 month of age was positively associated with higher categories of sun exposure for summer weekends or holidays in childhood ($p = 0.046$, $p = 0.048$, respectively) but not adolescence ($p = 0.70$, $p = 0.73$, respectively). After accounting for month of child interview, child and adolescent measures were in strong agreement for higher sun exposure on summer weekends and holidays ($p = <0.001$, $p = 0.003$, respectively). Thus, sun behaviors appeared to track over time.

We examined the relation between sun exposure at 1 month of age, at age 8 and at age 16, and the occurrence of allergic disease or inhalant allergen sensitization at age 16 (Tables 1 and 2). Higher sun exposure during summer holidays and summer weekends in adolescence was associated with significantly reduced risk of eczema and rye grass positive rhinitis (Table 1). Sun exposure at adolescence was not related to asthma or inhalant allergen sensitization.

In addition to the ISAAC questions, we examined asthma by the categories of doctor diagnosed asthma and use of asthma medications. In both, these categories asthma was not related to sun exposure at summer weekends or holidays (doctor diagnosed asthma—summer weekend, $p = 0.1$, summer holidays, $p = 0.92$; recent asthma medications – summer weekends, $p = 0.55$, summer holidays, $p = 0.76$).

There was no significant association between sun exposure in infancy and allergic disease or allergen sensitization at age 16 (Table 2). There was no significant association of sun exposure in childhood and occurrence of eczema, rhinitis, asthma, or inhalant allergen sensitization at 16 (Table 2).

We also examined winter sun exposure in childhood and adolescence. Winter sun exposure in adolescence but not at age 8 was associated with current eczema but not with rye positive rhinitis or ImmunoCAP® sensitivity to any inhalant. There was also a suggestion of an effect on asthma on winter weekend sun exposure at age 8 (Table 3).

One possible mechanism for the effect of sun exposure on eczema and rhinitis is by influencing the immunoregulatory activity of vitamin D. We examined the association between vitamin D levels and allergic disease or inhalant allergen sensitization. Indeed, there was no significant association with blood vitamin D levels (Table 4). After accounting for the month of collection, participants with higher reported sun exposure had higher 25(OH) D levels. Thus, comparing the highest and lowest categories of sun exposure (more than 4 and <2 h), the mean differences were −12.6 nmol/L (−3.6, −21.6 nmol/L, $p = 0.006$) for summer weekend sun exposure and −12.6 nmol/L (−2.1, −23.1 nmol/L, $p = 0.02$) for summer holiday sun exposure. However, vitamin D levels were not associated with allergic disease, and the association between higher sun exposure and reduced eczema and rhinitis in adolescence persisted after accounting for vitamin D levels (AOR = 0.63 and AOR = 0.78, respectively, for test of trend over the time in sun categories during summer holidays).

As exercise and obesity might be factors affecting sun exposure, we examined their association with eczema. There was no association with strenuous or light exercise or obesity (strenuous exercise, eczema; $p = 0.64$, light exercise, eczema; $p = 0.13$, obesity, eczema; $p = 0.48$. There was also no association between strenuous ($p = 0.15$) or light exercise ($p = 0.79$) or obesity ($p = 0.83$) and a positive ImmunoCAP® to any inhalant allergen.

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Table 1 Sun exposure in adolescence and reported atopy and ImmunoCAP® sensitivity

Sun exposure (h/day)	More than 4 h	3–4 h	2–3 h	<2 h	Test of trend p-value
Current eczema/Summer weekends in adolescence					
% (n/N) with outcome	44.23 (23/52)	23.08 (12/52)	21.15 (11/52)	11.54 (6/52)	0.003
% (n/N) without outcome	58.29 (211/362)	23.76 (86/362)	13.54 (49/362)	4.42 (16/362)	
AOR* (95% CI)	Ref	1.51 (0.70, 3.20)	2.41 (1.07, 5.44)	4.13 (1.40, 12.18)	
p-value	–	0.29	0.03	0.01	
Current eczema/Summer holidays in adolescence					
% (n/N) with outcome	51.92 (27/52)	17.31 (9/52)	25.00 (13/52)	5.77 (3/52)	0.001
% (n/N) without outcome	67.13 (243/362)	20.72 (75/362)	8.56 (31/362)	3.59 (13/362)	
AOR* (95% CI)	Ref	1.23 (0.53, 2.65)	4.84 (2.11, 10.38)	3.05 (0.65, 9.68)	
p-value	–	0.62	<0.001	0.11	
Current rye positive rhinitis/Summer weekends in adolescence					
% (n/N) with outcome	48.00 (36/75)	22.67 (17/75)	24.00 (36/75)	5.33 (4/75)	0.02
% (n/N) without outcome	61.74 (124/298)	21.45 (64/298)	11.74 (35/298)	5.03 (15/298)	
AOR* (95% CI)	Ref	1.39 (0.71, 2.71)	2.85 (1.42, 5.71)	1.36 (0.42, 4.40)	
p-value	–	0.34	0.003	0.61	
Current rye positive rhinitis/Summer holidays in adolescence					
% (n/N) with outcome	52.00 (39/75)	30.67 (23/75)	8.76 (12/137)	7.30 (10/137)	0.03
% (n/N) without outcome	68.79 (205/298)	18.79 (56/298)	11.51 (32/278)	2.16 (6/278)	
AOR* (95% CI)	Ref	2.26 (1.23, 4.18)	1.96 (0.84, 4.60)	1.93 (0.55, 6.73)	
p-value	–	0.01	0.12	0.31	
Current asthma/Summer weekends in adolescence					
% (n/N) with outcome	56.73 (59/104)	17.31 (18/104)	19.23 (20/104)	6.73 (7/104)	0.34
% (n/N) without outcome	56.35 (173/307)	26.06 (80/307)	13.03 (40/307)	4.56 (14/307)	
AOR* (95% CI)	Ref	0.65 (0.35, 1.21)	1.42 (0.75, 2.67)	1.53 (0.57, 4.08)	
p-value	–	0.18	0.28	0.40	
Current asthma/Summer holidays in adolescence					
% (n/N) with outcome	62.50 (65/104)	20.19 (21/104)	12.50 (13/104)	4.81 (5/104)	0.41
% (n/N) without outcome	66.45 (204/307)	20.20 (62/307)	9.77 (30/307)	3.58 (11/307)	
AOR* (95% CI)	Ref	1.09 (0.60, 1.95)	1.36 (0.66, 2.82)	1.26 (0.41, 3.92)	
p-value	–	0.79	0.41	0.69	
Positive ImmunoCAP® to any inhalant/Summer weekends in adolescence					
% (n/N) with outcome	55.72 (112/201)	23.88 (48/201)	15.92 (32/201)	4.48 (9/201)	0.37
% (n/N) without outcome	62.79 (108/172)	19.19 (33/172)	12.21 (21/172)	5.81 (10/172)	
AOR* (95% CI)	Ref	1.44 (0.84, 2.45)	1.58 (0.84, 2.98)	0.82 (0.32, 2.13)	
p-value	–	0.18	0.16	0.69	
Positive ImmunoCAP® to any inhalant/Summer holidays in adolescence					
% (n/N) with outcome	65.17 (131/201)	22.39 (45/201)	9.45 (19/201)	2.99 (6/201)	0.68
% (n/N) without outcome	65.70 (113/172)	19.77 (34/172)	9.88 (17/172)	4.65 (8/172)	
AOR* (95% CI)	Ref	1.08 (0.64, 1.83)	1.05 (0.51, 2.17)	0.58 (0.19, 1.76)	
p-value	–	0.77	0.89	0.33	

*Adjusted for age at adolescent questionnaire completion, sex, family history of asthma, perinatal score and upper arm melanin density

Attrition bias

As a sensitivity analysis, we fitted population weighted models to determine whether the results were influenced by differences in demographic characteristics between the 415 participants analyzed in this study and the remaining participants from the original TIHS cohort. We used weights that adjust the analyzed sample to be representative of the full TIHS cohort with respect to sex, birth weight, mother's age at child's birth, and scoring system. The weights were the inverse of the probability of being analyzed in this study, and we calculated them using the probabilities obtained after we fitted a logistic regression of whether analyzed in this study (0 = not analyzed; 1 = analyzed) on sex, birth weight, mother's age at child's birth, and scoring system, using the full TIHS cohort. When we weighted the regression analyses to allow for potential loss to follow-up, taking account of the composition of the entire group of TIHS participants, the results were similar to those of the main analysis (data not shown). This suggests that no loss to follow-up bias exists related to lack of representativeness on the variables used to calculate the weights.

The issue of rural versus city living has been examined by use of a Remoteness index (24). There was no association between adolescents currently living in Outer Regional Australia or

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Table 2 Reported atopy and ImmunoCAP® sensitivity to any inhalant at adolescence and sun exposure in infancy and childhood

Infancy: Baby outside at 1 month*,†	p-value
Current eczema	0.26
Current rye positive rhinitis	0.43
Current asthma	0.17
Positive ImmunoCAP® to any inhalant	0.15
Childhood: Hours of sun exposure per day ‡,§	**p-value (test of trend)**
Current eczema/Summer weekends in childhood	0.64
Current eczema/Summer holidays in childhood	0.53
Current rye positive rhinitis/Summer weekends in childhood	0.11
Current rye positive rhinitis/Summer holidays in childhood	0.14
Current asthma/Summer weekends in childhood	0.99
Current asthma/Summer holidays in childhood	0.60
Positive ImmunoCAP® to any inhalant/Summer weekends in childhood	0.93
Positive ImmunoCAP® to any inhalant/Summer holidays in childhood	0.45

*Adjusted for post-conceptual age at home visit, age at adolescent questionnaire completion, sex, family history of asthma, perinatal score, and upper arm melanin density.
†Sun exposure stratified for baby outside at 1 month – under 1 h per day (reference) and greater that 1 h per day.
‡Adjusted for age at childhood and adolescent questionnaire completion, sex, family history of asthma, perinatal score, and upper arm melanin density.
§p-value test for trend, sun exposure stratified by more than 4 (reference), 3–4, 2–3 and <2 h.

Remote Australia compared with adolescents living in Inner Regional Australia with regard to current eczema, rhinitis, asthma, or positive RAST to any inhalant.

Discussion

We have examined the influence of sun exposure during childhood and adolescence and vitamin D levels at adolescence on the development of atopic disease and allergic sensitization. Higher sun exposure using these questions has also been previously shown to be associated with higher vitamin D levels (22) and other objective markers of sun exposure (14).

Here, higher reported sun exposures during summer holidays in adolescence were associated with protection against eczema and rhinitis, but not asthma or inhalant allergen sensitization. In addition, winter sun exposure was also protective for eczema. It is possible that the apparent protective effects of winter sun exposure reflects higher non-winter exposures as well. These findings were independent of the measured vitamin D levels. Previous studies have examined the relationship between vitamin D levels and atopic disease and suggested that lower levels of vitamin D during childhood or adolescence may be associated with increased asthma or allergen sensitization (11, 12). The National Health and Nutrition Examination Survey of over 3000 children and adolescents found an association between low levels of 25 (OH) D and asthma in adolescence; however, there was no association with eczema or hay fever (12).

Table 3 Reported atopy and ImmunoCAP® sensitivity to any inhalant at adolescence and winter sun exposure in childhood and adolescence

Atopic disease/Time of sun exposure*	Child †,‡	Adolescence‡
Current eczema/Winter weekends	0.879	0.003
Current eczema/Winter holidays	0.435	0.001
Current rye positive rhinitis/Winter weekends	0.761	0.51
Current rye positive rhinitis/Winter holidays	0.852	0.41
Current asthma/Winter weekends	0.032	0.733
Current asthma/Winter holidays	0.051	0.375
Positive ImmunoCAP® to any inhalant/Winter weekends	0.569	0.834
Positive ImmunoCAP® to any inhalant/Winter holidays	0.832	0.648

*Adjusted for age at childhood and adolescent questionnaire completion, sex, family history of asthma, perinatal score, and upper arm melanin density.
†Age at adolescent questionnaire completion, sex, family history of asthma, perinatal score, and upper arm melanin density.
‡p-value test for trend, sun exposure stratified by more than 4 (reference), 3–4, 2–3 and <2 h.

A number of studies have found a relationship between latitude and the occurrence of immunological or allergic disease and suggested this may be mediated by UV irradiation effects on vitamin D (25). An important feature of the present study is that we have examined both vitamin D levels and reported sun exposures. Our findings suggest that the influence of sun exposure may operate independently of vitamin D. The findings of this study do not conclusively demonstrate that higher sun exposure will prevent allergic disease. The effect of the sun exposure on atopic dermatitis and rhinitis observed in the present study was not long term in nature with the exception of winter weekend sun exposure at age 8. Otherwise there was no association with sun exposure at 8 yrs and subsequent atopic disease at 16 yrs. Thus, we did not demonstrate that childhood UV exposure influences subsequent atopy as has been postulated by others (25).

Strengths of the present study include follow-up over 16 yrs, and the use of previously validated questions on past sun exposure (14, 22). As recruitment was as part of a community-based study relating to SIDS and bone health and not one directed to subjects at high risk of atopic disease, the potential for selection bias for those interested in or affected by atopic disease is likely to be minimal. Further, we demonstrated that loss of follow-up did not affect study findings.

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Table 4 Reported atopy and ImmunoCAP® sensitivity to any inhalant and vitamin D levels in adolescence in quartiles

Vitamin D (nmol/L)	68–167	54–67	44–53	13–43	Test of trend p-value
Current eczema/Vitamin D in adolescence					
% (n/N) with outcome	24.44 (11/45)	20.00 (9/45)	28.89 (13/45)	26.67 (12/45)	0.74
% (n/N) without outcome	24.09 (79/328)	25.91 (85/328)	25.00 (82/328)	25.00 (82/328)	
AOR* (95% CI)	Ref	0.80 (0.30, 2.12)	1.04 (0.42, 2.53)	1.08 (0.42, 2.76)	
p-value	–	0.65	0.94	0.88	
Current rye positive rhinitis/Vitamin D in adolescence					
% (n/N) with outcome	14.67 (11/75)	25.33 (19/75)	33.33 (25/75)	26.67 (20/75)	0.11
% (n/N) without outcome	26.51 (79/298)	25.17 (75/298)	23.49 (70/298)	24.83 (74/298)	
AOR* (95% CI)	Ref	1.78 (0.79, 4.09)	2.36 (1.07, 5.21)	1.90 (0.84, 4.30)	
p-value	–	0.16	0.03	0.13	
Current asthma/Vitamin D in adolescence					
% (n/N) with outcome	20.41 (20/98)	25.51 (25/98)	30.61 (30/98)	23.47 (23/98)	0.62
% (n/N) without outcome	25.37 (69/272)	25.37 (69/272)	23.90 (65/272)	25.37 (69/272)	
AOR* (95% CI)	Ref	1.12 (0.55, 2.29)	1.52 (0.75, 3.05)	1.09 (0.52, 2.29)	
p-value	–	0.76	0.24	0.83	
Positive RAST to any inhalant/Vitamin D in adolescence					
% (n/N) with outcome	21.89 (44/201)	25.37 (51/201)	31.84 (64/201)	20.90 (42/201)	0.94
% (n/N) without outcome	26.74 (46/172)	25.00 (43/172)	18.02 (31/172)	30.23 (52/172)	
AOR* (95% CI)	Ref	1.22 (0.66, 2.25)	2.17 (1.17, 4.04)	0.80 (0.42, 1.50)	
p-value	–	0.53	0.01	0.48	

*Adjusted for age at adolescent questionnaire completion, sex, family history of asthma, perinatal score, and month of blood collection for vitamin D.

Potential limitations of the study include the absence of vitamin D levels over the life course, and the fact that the incidence of allergic disease has been assessed by questionnaire. However, such assessment by questions from the ISAAC study has been widely utilized in epidemiological studies. Furthermore, the long follow-up time from birth to 16 yrs of age and the prospective collection of information concerning sun exposure in childhood provide a unique data set from which to examine the influence of sun exposure on the occurrence of atopic disease.

Sun exposure and UV irradiation have been reported to improve atopic dermatitis with the beneficial effects lasting for several months (2, 26). This could be an explanation for the association of the higher reported duration of sun exposure and the reduced eczema we have observed. However, such an explanation does not readily explain the effect of sun exposure on allergic rhinitis. In view of the immunomodulatory effects of UV irradiation, it could be postulated that exposure to sun might influence the development of allergic sensitization; however, there was not a significant association between inhalant sensitization and sun exposure. This suggests that beneficial effects of UV exposure may be exerted by mechanisms other than reducing allergen sensitization.

A number of studies have shown that UV exposure can suppress the immune system (reviewed in reference 27). Schwarz postulated that immunosuppression by physiological UVR doses might be beneficial in taming overshooting immune reactions and that UV exposure may modulate inflammation via suppression of dermal cytokine and inflammatory cell activities (27). However, such a consideration does not readily explain the effect on allergic rhinitis where the site of inflammation is not directly exposed to UV radiation. It is possible that cells modulated by UV, following migration from the skin to other organs, might produce effects elsewhere. It has also been suggested sun exposure by inducing antimicrobial peptides may enhance antibacterial defences (27). This could benefit diseases such as eczema where bacterial colonization of the skin is considered to play a significant role. However, the extent to which the immunomodulatory effects of dermal sun exposure is a mechanism that influences atopic disease remains to be determined (27).

Other possibilities require consideration. It might be postulated that children with eczema avoided the sun as heat could exacerbate the discomfort associated with the dermatitis. This was not substantiated by other parameters as there was no difference in strenuous exercise levels in those with dermatitis. Another possibility is that the increased use of sunscreens by those with greater outdoor exposure might benefit eczema by virtue of its moisturizing effect. We do not have data on sunscreen usage; however, the beneficial effect of sun exposure was demonstrated in winter at a time when sunscreen usage is reduced. It could also be suggested that children with allergic rhinitis would avoid outdoor activities to reduce grass pollen exposure in summer months. In Southern Australia, the predominant grass pollen antigen is rye grass, and the season for pollination is the early summer months (28, 29). As exercise activity or obesity might be significant factors affecting sun exposure, we examined the association of these factors with eczema and rhinitis. However, we found no association with exercise levels which may be considered as a proxy for outdoor

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activities. Similarly, there was no association with the presence or absence of rye grass pollen sensitization. Furthermore, there was no association with obesity which is well recognized to be associated with reduced outdoor activities (30).

Ultraviolet exposure is well documented to reduce immune responses in the skin and also has systemic immune effects (31) which are unrelated to activation of vitamin D (32). In Australia, the estimated daily times of sun exposure to produce current recommended levels of vitamin D are of the order of 2–6 min in summer and 4–17 min in winter (33). The exposure reported by participants was in hours per day well in excess of these times. However, there is uncertainty about the levels of vitamin D required for immune modulation, and it might be that these differ from those optimal for bone health.

In summary, we demonstrate an association between higher sun exposure and the occurrence of eczema and rhinitis but not asthma in adolescence. There was not a significant association with vitamin D levels. We did not demonstrate that sun exposure in earlier life was related to current disease. There are currently issues relating to guidelines for childhood sun exposure, and suggestions that these might be modified to counteract the rising incidence of atopic disease (34). The findings from this long-term cohort indicate that further studies are required before recommending sun exposure to reduce the incidence of allergic disease. Such studies should consider both UVR exposure and vitamin D.

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References

1. Gorman S, McGlade JP, Lambert MJ, et al. UV exposure and protection against allergic airways disease. *Photochem Photobiol Sci* 2010: **9**: 571–7.
2. Vahavihu K, Ylianttila L, Salmelin R, et al. Heliotherapy improves vitamin D balance and atopic dermatitis. *Br J Dermatol* 2008: **158**: 1323–8.
3. Searing DA, Leung DY. Vitamin D in atopic dermatitis, asthma and allergic diseases. *Immunol Allergy Clin North Am* 2010: **30**: 397–409.
4. Mullins RJ, Camargo CA. Latitude, sunlight, vitamin D, and childhood food allergy/anaphylaxis. *Curr Allergy Asthma Rep* 2012: **12**: 64–71.
5. Hughes AM, Lucas RM, Ponsonby AL, et al. The role of latitude, ultraviolet radiation exposure and vitamin D in childhood asthma and hay fever: an Australian multicenter study. *Pediatr Allergy Immunol* 2011: **22**: 327–33.
6. Krstic G. Asthma prevalence associated with geographical latitude and regional insolation in the United States of America and Australia. *PLoS ONE* 2011: **6**: e18492.
7. Fsadni P, Fsadni C, Fava S, et al. Correlation of worldwide incidence of type 1 diabetes (DiaMond) with prevalence of asthma and atopic eczema (ISAAC). *Clin Respir J* 2012: **6**: 18–25.
8. Wjst M, Dharmage S, Andre E, et al. Latitude, birth date, and allergy. *PLoS Med* 2005: **2**: e294.
9. Osborne NJ, Ukoumunne OC, Wake M, et al. Prevalence of eczema and food allergy is associated with latitude in Australia. *J Allergy Clin Immunol* 2012: **129**: 865–7.
10. Litonjua AA, Vitamin D. Deficiency as a risk factor for childhood allergic disease and asthma. *Curr Opin Allergy Clin Immunol* 2012: **12**: 179–85.
11. Hollams EM, Hart PH, Holt BJ, et al. Vitamin D and atopy and asthma phenotypes in children: a longitudinal cohort study. *Eur Respir J* 2011: **38**: 1320–7.
12. Sharief S, Jariwala S, Kumar J, et al. Vitamin D levels and food and environmental allergies in the United States: results from the National Health and Nutrition Examination Survey 2005–2006. *J Allergy Clin Immunol* 2011: **127**: 1195–202.
13. Dwyer T, Ponsonby AL, Newman NM, et al. Prospective cohort study of prone sleeping position and sudden infant death syndrome. *Lancet* 1991: **337**: 1244–7.
14. Dwyer T, Blizzard L, Gies PH, et al. Assessment of habitual sun exposure in adolescents via questionnaire–a comparison with objective measurement using polysulphone badges. *Melanoma Res* 1996: **6**: 231–9.
15. d'Espaignet ET, Dwyer T, Newman NM, et al. The development of a model for predicting infants at high risk of sudden infant death syndrome in Tasmania. *Paediatr Perinat Epidemiol* 1990: **4**: 422–35.
16. Jones G, Dwyer T. Bone mass in prepubertal children: gender differences and the role of physical activity and sunlight exposure. *J Clin Endocrinol Metab* 1998: **83**: 4274–9.
17. Yin J, Dwyer T, Riley M, et al. The association between maternal diet during pregnancy and bone mass of the children at age 16. *Eur J Clin Nutr* 2010: **64**: 131–7.
18. Worldwide variation in prevalence of symptoms of asthma, allergic

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rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998: **351**: 1225–32.
19. Asher MI, Keil U, Anderson HR, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995: **8**: 483–91.
20. Kemp AS, Ponsonby AL, Dwyer T, et al. Maternal antenatal peanut consumption and peanut and rye sensitization in the offspring at adolescence. *Clin Exp Allergy* 2011: **41**: 224–31.
21. van der Mei IA, Ponsonby AL, Engelsen O, et al. The high prevalence of vitamin D insufficiency across Australian populations is only partly explained by season and latitude. *Environ Health Perspect* 2007: **115**: 1132–9.
22. van der Mei IA, Blizzard L, Ponsonby AL, et al. Validity and reliability of adult recall of past sun exposure in a case-control study of multiple sclerosis. *Cancer Epidemiol Biomarkers Prev* 2006: **15**: 1538–44.
23. Dwyer T, Muller HK, Blizzard L, et al. The use of spectrophotometry to estimate melanin density in Caucasians. *Cancer Epidemiol Biomarkers Prev* 1998: **7**: 203–6.
24. Australian Bureau of Statistics. *Statistical Geography, Volume 1: Australian Standard Geographical Classification (ASGC)*. Catalogue 1260, Australian Bureau of Statistics, Canberra, 2001.
25. Vassallo MF, Camargo CA Jr. Potential mechanisms for the hypothesized link between sunshine, vitamin D, and food allergy in children. *J Allergy Clin Immunol* 2010: **126**: 217–22.
26. Reynolds NJ, Franklin V, Gray JC, et al. Narrow-band ultraviolet B and broad-band ultraviolet A phototherapy in adult atopic eczema: a randomised controlled trial. *Lancet* 2001: **357**: 2012–6.
27. Schwarz T. The dark and the sunny sides of UVR-induced immunosuppression: photoimmunology revisited. *J Invest Dermatol* 2010: **130**: 49–54.
28. Kemp A, Ponsonby AL, Dwyer T, et al. The interaction between early life upper respiratory tract infection and birth during the pollen season on rye-sensitized hay fever and ryegrass sensitization–a birth cohort study. *Pediatr Allergy Immunol* 2009: **20**: 536–44.
29. Ong EK, Singh MB, Knox BR. Grass pollen in the atmosphere of Melbourne: seasonal distribution over nine years. *Grana* 1995: **34**: 58–63.
30. Xi B, Wang C, Wu L, et al. Influence of physical inactivity on associations between single nucleotide polymorphisms and genetic predisposition to childhood obesity. *Am J Epidemiol* 2011: **173**: 1256–62.
31. Kelly DA, Walker SL, McGregor JM, et al. A single exposure of solar simulated radiation suppresses contact hypersensitivity responses both locally and systemically in humans: quantitative studies with high-frequency ultrasound. *J Photochem Photobiol, B* 1998: **44**: 130–42.
32. Hart PH, Gorman S, Finlay-Jones JJ. Modulation of the immune system by UV radiation: more than just the effects of vitamin D? *Nat Rev Immunol* 2011: **11**: 584–96.
33. Samanek AJ, Croager EJ, Gies P, et al. Estimates of beneficial and harmful sun exposure times during the year for major Australian population centres. *Med J Aust* 2006: **184**: 338–41.
34. Youl PH, Janda M, Kimlin M. Vitamin D and sun protection: the impact of mixed public health messages in Australia. *Int J Cancer* 2009: **124**: 1963–70.

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