

ORIGINAL ARTICLE

Season of birth and childhood food allergy in Australia

Raymond James Mullins^{1,2,3}, Sunday Clark⁴, Constance Katelaris⁵, Victoria Smith⁶, Graham Solley⁷ & Carlos A. Camargo, Jr⁸

¹Suite 1, John James Medical Centre, Deakin, ACT, Australia, ²Medical School, Australian National University, Canberra, ACT, Australia, ³Clinical Immunology, Faculty of Health, University of Canberra, Canberra, ACT, Australia, ⁴Division of General Internal Medicine, University of Pittsburgh, Pittsburgh, PA, USA, ⁵Professor, Department of Medicine, University of Western Sydney, Sydney, Australia, ⁶Rose Cottage Medical Centre, Launceston, Tasmania, Australia, ⁷Watkins Medical Centre, Brisbane, Queensland, Australia, ⁸Department of Emergency Medicine, and Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

To cite this article: Mullins RJ, Clark S, Katelaris C, Smith V, Solley G, Camargo CA, Jr. Season of birth and childhood food allergy in Australia. *Pediatric Allergy Immunology* 2011; Doi no: 10.1111/j.1399-3038.2011.01151.x.

Keywords

epidemiology; vitamin D; food allergy; birth season; sunlight

Correspondence

Raymond James Mullins, Consultant Physician, Clinical Immunology and Allergy, Suite 1, John James Medical Centre, 175 Strickland Crescent, Deakin ACT 2600, Australia
Tel.: +61-2-6282 2568
Fax: +61-2-6282 2526
E-mail: rmullins@allergycapital.com.au

Accepted for publication 22 January 2011

DOI:10.1111/j.1399-3038.2011.01151.x

IMS Australia is the actual name of a commercial company, and the letters used in the manuscript do not represent an abbreviation.

Abstract

Background: Recent studies suggest a possible role for low ultraviolet radiation exposure and low vitamin D status as a risk factor for food allergy. We hypothesized that children born in autumn/winter months (less sun exposure) might have higher food allergy rates than those born in spring/summer.

Methods: We compared IgE-mediated food allergy rates by season of birth in 835 children aged 0–4 yr assessed 1995–2009 in a specialist referral clinic, using population births as controls. To address potential concerns about generalizability, we also examined national prescriptions for adrenaline autoinjectors (2007) and infant hypoallergenic formula (2006–2007).

Results: Although live births in the general ACT population showed no seasonal pattern (50% autumn/winter vs. 50% spring/summer), autumn/winter births were more common than spring/summer births among food allergy patients (57% vs. 43%; $p < 0.001$). The same seasonal pattern was observed with peanut (60% vs. 40%; $p < 0.001$) and egg (58% vs. 42%; $p = 0.003$). Regional UVR intensity was correlated with relative rate of overall food allergy (β , -1.83 ; $p = 0.05$) and peanut allergy (β , -3.27 ; $p = 0.01$). National data showed that autumn/winter births also were more common among children prescribed EpiPens (54% vs. 46%; $p < 0.001$) and infant hypoallergenic formula (54% vs. 46%; $p < 0.001$).

Conclusions: The significantly higher rates of food allergy in children born autumn/winter (compared to spring/summer), the relationship between relative food allergy rates and monthly UVR, combined with national adrenaline autoinjector and infant hypoallergenic formula prescription data, suggest that ultraviolet light exposure/vitamin D status may be one of many potential factors contributing to childhood food allergy pathogenesis.

Despite evidence for rising food allergy (FA) prevalence (1), the pathogenesis of FA remains uncertain (reviewed in 2). A possible role for lesser exposure to ultraviolet light (UVR)/low vitamin D status has been proposed, based (in part) on observations of latitudinal variation in EpiPen prescription rates in the USA and Australia (3, 4), similar variations in infant hypoallergenic infant formula (IHf) prescriptions in Australia (5) and evidence that low vitamin D intake during pregnancy is associated with a higher rates of food sensitization in early life (6). The objective of the

present study was to examine the relationship between season of birth (SoB) and relative rates of childhood FA using data derived from a single centre providing half the regional ambulatory specialist allergy-related services in south-eastern Australia. On the basis of previous studies (3–7), we hypothesized that children born in autumn or winter months (with less sunlight exposure) might have higher rates of medically confirmed FA than those born in spring or summer, and that these seasonal differences would be reflected in two proxy measures of FA: national adrenaline

autoinjector and IHF prescription data for children the same age.

Patients and methods

Study population

The study was undertaken in the ACT, an inland urban city of 2358 km² within rural South-Eastern Australia, encompassing the city of Canberra and surrounding parkland (latitude 35.3°; ~324,000 inhabitants; 8). Birth origin [2006 Census data; 9 includes Australia (75%), Western Europe (7%), Asia (7%) and southern/eastern Europe (3%)]. ACT medical facilities service the local metropolitan population and surrounding regional areas. The characteristics of all ACT resident patients aged 0–4 yr referred to an ACT-based mixed adult/pediatric specialist allergy/immunology medical practice between January 1995 and August 2009 were analysed. The practice is the largest regional outpatient allergy practice, providing approximately half the local ambulatory specialist allergy services. The closest services outside the ACT are Sydney (300 km away) or Melbourne (800 km away). Referrals were received from general medical practitioners, accident and emergency departments and specialist paediatricians. Children aged 0–4 yr were studied because of the high incidence of FA in this group, a recent USA study suggesting a SoB pattern in this age group (10), and our ability to source national government-derived EpiPen and IHF data by birth month for the same age range. The Human Research and Ethics committee (Calvary Bruce/Calvary John James Private Hospitals) approved the study.

Patient evaluation and diagnostic criteria

The primary indication for undertaking SPT was a history of likely FA, with secondary indications for testing being another FA (where food had not yet been ingested or tolerated), or children with atopic eczema or siblings of a child with documented FA where parents were concerned about possible FA. Peanut, egg, milk, soy, prawn, fish, sesame seed and all available tree nut extracts were tested unless the patient regularly consumed and tolerated these foods. SPT was performed on the volar aspect of the forearm using metal lancets (Stallergenes, Antony, France) according to standard guidelines (11). Glycerinated allergen extracts (Hollister Stier, Spokane, WA, USA) and histamine 10 mg/ml positive control (Hollister Stier) were purchased from EBOS Australia (Sydney). A positive SPT was defined as a wheal size of at least 3 mm greater than a negative control (saline) at 15 min (11). IgE-mediated FA was diagnosed only if there was a history of acute systemic allergic reaction (one or more of urticaria, vomiting, bronchospasm or vascular collapse) within 2 h of known food exposure, combined with a SPT to the relevant food (i.e. not on the basis of history or testing alone). A diagnosis of anaphylaxis was assigned if either of the first two criteria of the 2005 National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network Symposium definition were fulfilled (12).

Calculation of relative rates of food allergy

The relative rate of FA by birth month was calculated using the number of ACT FA patients adjusted for the number of live ACT population births per year between 1997 and 2007. Specifically, relative rate FA for each birth month was calculated using the formula: actual/expected children with FA born that month $\times$ expected/actual children born the same month, where 'expected' data was the yearly figure divided by 12.

Ultraviolet radiation exposure

The intensity of monthly UVR data per month averaged 1990–2009 for the ACT (Canberra Airport) was obtained from the Australian Bureau of Meteorology (13).

Australian population and demographic data

The ACT Health Department (epidemiology branch) provided data on ACT births for 1997–2007 by calendar month (personal email communication, August 2009). The Australian Bureau of Statistics provided national birth data for 1997–2007 by calendar month (14) (Monthly births for 1995–1996 and 2008–2009 were unavailable for either ACT or Australia).

Government criteria for subsidized medication

Adrenaline autoinjectors are subsidized under the Australian Pharmaceutical Benefits Authority Scheme (PBAS) for the 'the anticipated emergency treatment of acute allergic reactions with anaphylaxis in a patient who: (i) has been assessed to be at significant risk of anaphylaxis by, or in consultation with, a clinical immunologist, allergist, paediatrician or respiratory physician. The name of the specialist consulted must be provided at the time of application for initial supply; or (ii) has been discharged from hospital or an emergency department after treatment with adrenaline (epinephrine) for acute allergic reaction with anaphylaxis'. The PBAS criteria for subsidized IHF limits subsidy to combined cows milk/soy protein intolerance in a child aged 0–2 yr in consultation with a paediatrician or allergy specialist, but neither for treatment of colic nor for FA prevention. Patients must first fail to respond to a hydrolysed formula. Importantly, direct-to-consumer promotion of prescription drugs (including adrenaline autoinjectors and IHF) is banned in Australia, penalties exist for doctors providing Authority prescriptions outside government guidelines (Vanna Mabbott, DOHA, personal communication, February 2009) and medical practitioner advertising is restricted to government-approved criteria. IMS Australia provided data on the proportion of medication subsidized under the PBAS.

Adrenaline autoinjector and infant hypoallergenic formula prescription data

Birth month data for number of individual children aged 0–4 yr prescribed adrenaline autoinjectors (calendar year

2007) and the number of children aged 0–2 yr prescribed IHF (2006–2007 calendar years) were obtained from the Federal Department of Health and Aging and Medicare Australia, Canberra (EpiPen was the only available adrenaline autoinjector in Australia during the study period). Importantly, data relate to the number of individuals given prescriptions by birth month, not the number of prescriptions (which could otherwise include refills).

Statistical analysis

All analyses were performed using STATA 10.0 (StataCorp, College Station, TX, USA). Data are presented as proportions. Seasons of birth (SoB) were defined as autumn (March–May), winter (June–August), Spring (September–November) and Summer (December–February). For statistical analysis, the year was also divided into 'dark' (autumn/winter) and 'light' months (spring/summer) which corresponds to the times of lesser and greater UVR intensity in the ACT, respectively. Comparisons across SoB were evaluated using chi-square tests. Linear regression was used to evaluate the association between UVR and relative rate of food and peanut allergy per birth month. All β coefficients are presented with 95% CIs. A two-sided p value < 0.05 was considered statistically significant.

Results

ACT demographic changes

The ACT population was relatively stable: 6% growth from 304,805 (1995) to an estimated 324,200 individuals (2007). There was a slight decline in the number of children aged 0–4 yr from 22,402 (1995) to 20,185 (2005), and a slight increase in live births to ACT resident mothers from 4415 to 4479 per year between 1995 and 2006. The net population loss from migration out of (compared to migration into) the ACT between 1995 and 2007 was 9079 individuals (15).

Patient characteristics

Between February 1995 and August 2009, 20,492 distinct patients were assessed by the first author (RJM). Among the 1961 patients aged 0–4 yr, 835 (58% male) had FA (as previously defined) and resided in the ACT; 341 (41%) of the 835 children with FA were allergic to peanut, with other triggers being hen's egg (365), cow's milk (223), tree nuts (145) and other foods (129).

Association between season of birth and food allergy

Live births in the general ACT population during 1997–2007 were evenly distributed across the year (e.g. 29,362 [50%] autumn/winter vs. 29,167 [50%] spring/summer; $p = 0.42$). By contrast, of 835 ACT patients with FA, 475 (57%) were born autumn/winter compared to 360 (43%) spring/summer ($p < 0.001$; Fig. 1). A statistically significant seasonal trend also was observed for allergy to peanut in

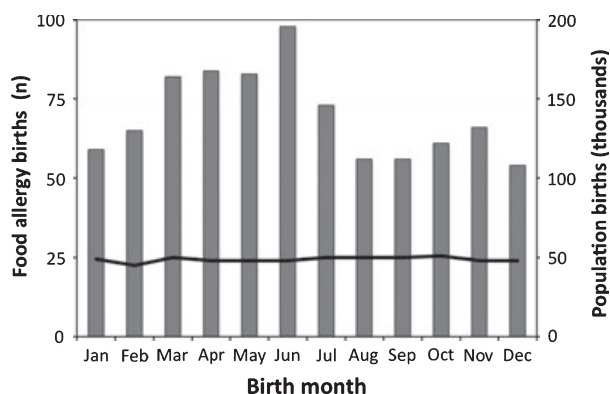


Figure 1 Distribution of children with food allergy by birth month. The birth month distribution of 835 children aged 0–4 yr, in the Australian Capital Territory, diagnosed with food allergy between 1995 and 2009 (grey bars) is compared with the distribution of live births between 1997 and 2007, by birth month (black line).

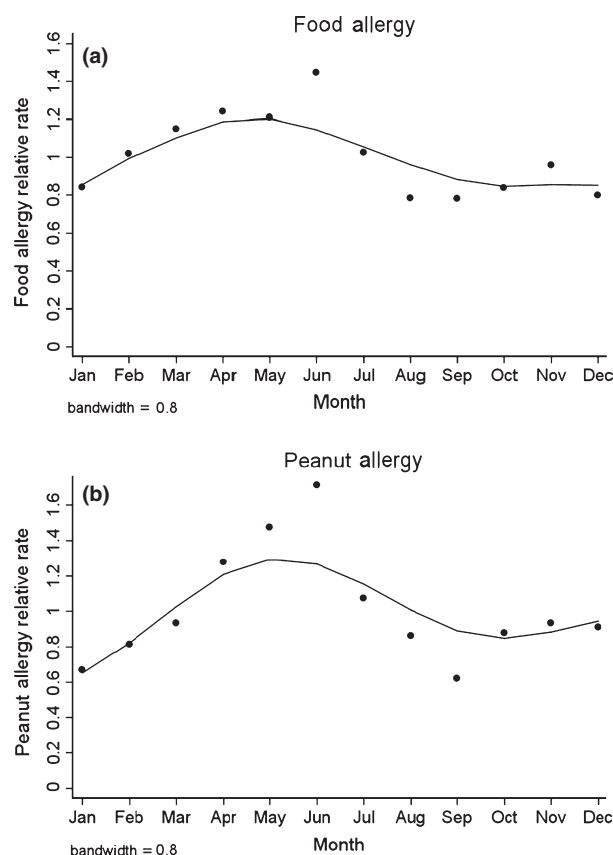


Figure 2 Relative rates of food allergy by birth month. The relative rates of food allergy (a) and peanut allergy (b) in children aged 0–4 yr, in the Australian Capital Territory, are presented by birth month. Rates were calculated by adjusting for corresponding birth rates/month for the region (see 'Methods' section for more details).

the overall 0–4 yr population (206 [60%] vs. 135 [40%]; $p < 0.001$; Fig. 2) and hen's egg (211 [58%] vs. 154 [42%]; $p = 0.003$). Although statistical power was limited, the

trends for cows milk (121 [54%] vs. 102 [46%]; $p = 0.23$) and tree nuts (79 [54%] vs. 66 [46%]; $p = 0.32$) were consistent with the primary results for FA. Likewise, a consistent but non-significant pattern was seen for children with a history of anaphylaxis (101 [56%] vs. 79 [44%]; $p = 0.12$). The same preponderance of autumn/winter births was observed for male and female children with FA aged 0–4 yr (data not shown). This SoB pattern was apparent within the first 12 months of life, with 94 children with FA born autumn/winter (59%) vs. 65 born spring/summer (41%; $p = 0.02$). While statistical power was limited, similar trends were also observed for peanut (16 vs. 9; $p = 0.16$) and egg (45 vs. 28; $p = 0.046$) but not cows milk (53 vs. 47; $p = 0.55$).

Association between UV radiation intensity and relative rate of food and peanut allergy

Given the seasonal fluctuation in FA births, we then examined whether there was a relationship between UVR intensity and relative FA rates. As shown in Fig. 3, there was an inverse association between UVR intensity and relative rate of FA by birth month such that there was a -1.83 change in the relative rate of FA for every 100 MJ/sqm increase in UVR intensity (β , -1.83 per $\uparrow 100$ MJ/sqm; 95% CI, -3.66 – 0.01 , $p = 0.05$). The association was stronger for peanut allergy (β , -3.27 ; 95% CI, -5.71 to -0.83 ; $p = 0.01$). Non-significant inverse associations were observed for tree nuts (β , -0.86 ; 95% CI -3.58 to 1.87 ; $p = 0.50$), egg (β , -1.92 ; 95% CI -4.75 to 0.90 ; $p = 0.16$) and cow's milk (β , -0.67 ; 95% CI -3.00 to 1.66 ; $p = 0.54$).

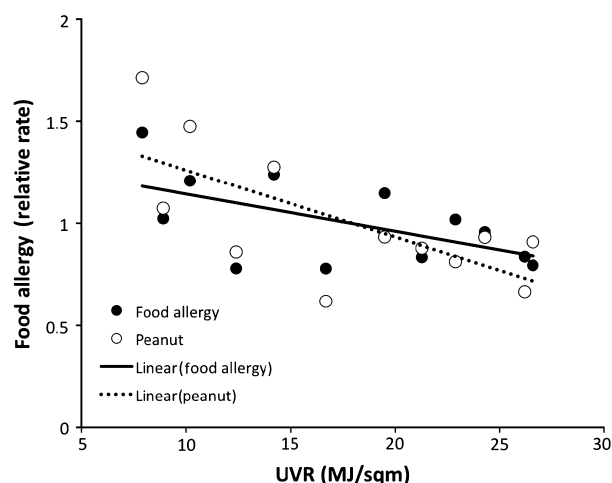


Figure 3 The relationship between average monthly ultraviolet radiation exposure and food and peanut allergy rates per month. The intensity of ultraviolet radiation was inversely associated with relative rates of food allergy (closed circles) and peanut allergy (open circles) in children, aged 0–4 yr, in the Australian Capital Territory. Trend lines for food allergy (unbroken line; solid circles) and peanut allergy (dotted line; open circles) are shown.

Association between season of birth and adrenaline autoinjector and IHF prescriptions

To determine whether local fluctuation in seasonal FA births in the ACT might be generalizable to the entire population and reflected in national data, we examined two proxy markers of childhood FA: adrenaline autoinjector (EpiPen) prescriptions for children aged 0–4 yr and IHF prescriptions for children aged 0–2 yr using government-derived data. During 2007, 9158 individual Australian children were prescribed an EpiPen under the PBAS, accounting for 87% of all devices sold in Australia (i.e. only 13% were purchased on private prescription or without prescription). In the years 2006–2007, 9861 individuals were prescribed IHF under with PBAS subsidy, accounting for 99% of all Australian sales (IMS Australia). Prescriptions were predominantly for those aged 0–2 yr (88% of all prescriptions). EpiPens were prescribed more commonly in children born in autumn/winter compared to those born in spring/summer (4964 [54%] vs. 4194 [46%]; $p < 0.001$). A similar pattern was observed for IHF prescriptions, with higher rates in children born in autumn/winter compared to those born in spring/summer (5276 [54%] vs. 4585 [46%]; $p < 0.0001$). These findings were not explained by monthly fluctuations in national birth rates between 1997 and 2007 (Fig. 4).

Discussion

We identified a significant relationship between SoB and the relative rate of medically confirmed FA in children aged 0–4 yr in the ACT. Consistent with our starting hypothesis, FA rates were higher among children with autumn/winter births as compared to spring/summer births, with a SoB pattern apparent within the first 12 months of life. When analysed by birth month, food and peanut allergy rates were up to two- to threefold higher in children born in mid-winter compared to mid-summer. These findings were not an artefact of

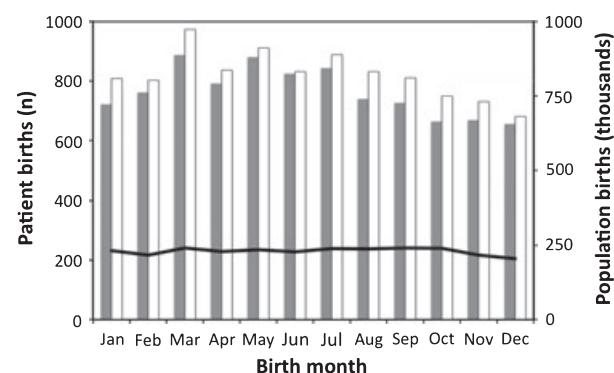


Figure 4 Distribution of Australian children prescribed EpiPen and infant hypoallergenic formula by birth month. The birth month distribution of children prescribed EpiPen during 2007 (aged 0–4 yr, grey bars) or infant hypoallergenic formula during 2009 (aged 0–2 yr, open bars) is compared with the national distribution of live births between 1997 and 2007 (black line).

month-to-month variation in birth rates. The generalizability of our findings is supported by an analysis of national EpiPen and IHF prescription data, in which a similar pattern was observed.

There are some caveats to be considered in interpreting our study. While we were only able to examine birth month pattern by location of residence (in the ACT) rather than location of pregnancy, birth or upbringing, the relative stability of the 0–4 yr population over the last decade and constant birth rates in the ACT together with national SoB trends for EpiPen and IHF formula prescriptions, argue against this being a significant confounder. The ecological study design precluded adjustment for other factors implicated in FA pathogenesis in our ecological study such as breast-feeding rates or timing of introduction of solids, as recently reviewed (2). Even if referral bias influenced the number of patients assessed (compared to other regional allergy/immunology services), it is unlikely to have operated in a systemic way to influence the SoB pattern observed. While it is also not possible to extrapolate the results to older FA patients based on our results, recent USA findings suggest SoB to be a more prominent FA risk factor in young children than adolescents and adults (10).

The relationship between SoB and later manifestations of allergic disease has fascinated authors for three decades (16), but so far, no unifying hypothesis has been presented to explain at times conflicting findings, as recently reviewed (17). SoB patterns have been variously attributed to greater intensity of allergen exposure during a vulnerable period of immune development, the adjuvant effects of intercurrent infection (18, 19) and more recently, even maternal exposure to pollen during pregnancy (20). Given evidence of recent increases in FA (peanut allergy in particular), and indirect evidence that UVR exposure might be a contributing factor (3–6), our specific interest was on the relationship between SoB, UVR and medically confirmed FA.

Our finding that autumn/winter birth was associated with higher rates of childhood FA is not unprecedented. Similar patterns have been described for IgE sensitization to egg and cows milk (7), childhood peanut allergy (21) and FA in an analysis of patients treated in Boston emergency departments (10). While the mechanisms by which autumn/winter birth is associated with higher FA rates is likely multifactorial, one potential mechanism is the strong relationship between eczema and FA in cohort studies (22). Eczema is more common in children born in winter (23). This has been attributed to relatively drier skin during winter, lack of the 'protective effect' of sun exposure, disruption of the skin barrier function, all potentially increasing the risk of percutaneous allergen sensitization, as demonstrated in animal models (24). Interactions between the adjuvant effects of wintertime infection and allergen exposure (19), and possible seasonal differences in gut microbiota or dietary factors in mother or child may also play a role in food as well as respiratory allergy. Autumn/winter birth may also indirectly reflect the timing of first exposure to solids 4–6 months later or more commonly 'allergenic' foods (e.g. peanut) 12–18 months later. While SoB is also a marker of season(s) of pregnancy, it is not

possible from our data to distinguish between pregnancy-related and early neonatal influences on the outcome assessed: FA by the age of 4 yr.

Our specific interest (and rationale for the study) was whether autumn/winter birth might also be a proxy for the effects of lesser sunlight exposure (and thus vitamin D status) on the developing immune system. This is relevant given the degree of vitamin D deficiency described in pregnant women in Australia (25), high rates of neonatal vitamin D deficiency in Australian and New Zealand neonates (26, 27) and seasonal fluctuations in vitamin D levels in mothers and neonates (26, 27). While the explanations for the SoB pattern for FA births are likely to be multifactorial, we propose that UVR/vitamin D status may offer a partial explanation for the SoB pattern noted in this and other studies, and as proposed for several non-allergic immune-mediated disorders (28). In part, this hypothesis is informed by growing evidence of the pleiotropic effects of vitamin D on the developing immune system (and allergic disease in particular), including suppression of allergen-specific IgE *in vitro* and *in vivo* by vitamin D receptor agonists (29) and immunomodulatory effects on dendritic cell maturation and on Th1, Th2 and regulatory T cell responses as recently reviewed (30). Specifically, recent studies have demonstrated associations between vitamin D receptor polymorphism and atopic disease, between genetic variants in the vitamin D activation enzyme, vitamin D levels and total IgE, between low vitamin D intake during pregnancy and low cord blood interleukin 10, as recently summarized (5). In the absence of significant dietary fortification with vitamin D in Australia or recommendations for routine pregnancy screening or supplementation in Australia (except high risk groups; 25), UVR/sunlight exposure and vitamin D status are likely to be essentially collinear, with some individual variability introduced by such factor as darker skin or obesity (30). Nonetheless, local ACT seasonal climatic factors (13) such as outdoor temperature (mean annual range 0.2–28.7°C), duration of sunlight hours (annual range 5.2–9.7 h), rainfall (97 days/yr) or lifestyle factors (e.g. occupation or recreational activities) may have influenced individual UVR exposure that cannot be accounted for by regional UVR measurements alone. It is conceivable that the SoB pattern observed in the ACT (temperate climate with a wide range of UVR exposure) may not be observed in regions where UVR is significantly lower (e.g. far south Australia) or higher (e.g. far north Australia). While confirmatory studies in other regions may help to clarify this possibility, the frequency of neonatal vitamin D deficiency in Queensland (far north Australia; 26) and national SoB pattern for EpiPen and IHF prescriptions make this less likely.

Even if UVR/vitamin D status plays a role in FA pathogenesis, the relationship between UVR/vitamin D status and FA risk may not be linear; excessive vitamin D levels might also be harmful, as recently reviewed (31). Further evidence of a possible role of UVR/vitamin D status in FA pathogenesis will require prospective cohort studies of neonatal or cord blood 25-hydroxyvitamin D levels and subsequent risk of FA. If a relationship were found, such studies could be followed by randomized trials to more formally test causality.

Regardless of the potential contribution by UVR/vitamin D status in FA pathogenesis, the frequency of vitamin D deficiency in Australia in pregnant women and their neonates is of some concern, and provides a rationale to screen and supplement individuals found to have very low vitamin D levels, and educate regarding 'safe sun' exposure (<http://www.cancer.org.au/cancersmartlifestyle/SunSmart/VitaminD.htm>).

Conflict of interest statement

Dr Mullins received unrestricted investigator-initiated grants from Commonwealth Serum Laboratories Australia and Alphapharm Australia (the past and current Australian distributors of EpiPen), Abbott Nutrition Australia and the Ilhan Food Allergy Foundation. Dr Camargo has received investigator-initiated research grants from, and consulted for, Dey (Basking Ridge, NJ, USA) and sanofi-aventis

(Bridgewater, NJ, USA). Study sponsors had no input into study design, data interpretation or the contents of this manuscript. The other authors report no conflict of interest.

Acknowledgments

We thank Vanna Mabbott (DOHA) for provision of additional EpiPen-related data and Louise Freebairn, Epidemiology Branch, ACT Health, for provision of ACT birth month data. Data purchase was funded with unrestricted investigator-initiated grants from Commonwealth Serum Laboratories Australia and Alphapharm Australia (the past and current Australian distributors of EpiPen), Abbott Nutrition Australia and the Ilhan Food Allergy Foundation. Study sponsors had no input into study design, data interpretation or the contents of this manuscript.

References

- Venter C, Pereira B, Voigt K, et al. Prevalence and cumulative incidence of food hypersensitivity in the first 3 years of life. *Allergy* 2008; **63**: 354–9.
- Lack G. Epidemiologic risks for food allergy. *J Allergy Clin Immunol* 2008; **121**: 1331–6.
- Camargo CA Jr, Clark S, Kaplan MS, Lieberman P, Wood RA. Regional differences in EpiPen prescriptions in the United States: the potential role of vitamin D. *J Allergy Clin Immunol* 2007; **120**: 131–6.
- Mullins RJ, Clark S, Camargo CA Jr. Regional variation in EpiPen prescriptions in Australia: more evidence for the vitamin D-anaphylaxis hypothesis. *Ann Allergy Asthma Immunol* 2009; **103**: 488–95.
- Mullins RJ, Clark S, Camargo CA Jr. Regional variation in infant hypoallergenic formula prescriptions in Australia. *Pediatr Allergy Immunol* 2010; **21**(2 Pt 2): e413–20. doi: 10.1111/j.1399-3038.2009.00962.x
- Nwaru BI, Ahonen S, Kaila M, et al. Maternal diet during pregnancy and allergic sensitization in the offspring by 5 yrs of age: a prospective cohort study. *Pediatr Allergy Immunol* 2010; **21**: 29–37.
- Nilsson L, Björkstén B, Hattveig G, Kjellman B, Sigurs N, Kjellman NI. Season of birth as predictor of atopic manifestations. *Arch Dis Child* 1997; **76**: 341–4.
- Population by Age and Sex, Australian States and Territories, Jun 2007. Australian Bureau of Statistics, Catalogue Number 3201.0 (<http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3201.0Main+Features1Jun%202007?OpenDocument>). Last accessed 1 July 2008.
- Australian Historical Population Statistics, 2006. Australian Bureau of Statistics, Catalogue Number 3105.0.065.001 (<http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3105.0.065.0012006?OpenDocument>). Last accessed 18 November 2008.
- Vassallo MF, Banerji AS, Rudders SA, Clark S, Mullins RJ, Camargo CA Jr. Season of birth is associated with food allergy in children. *Ann Allergy Asthma Immunol* 2010; **104**: 307–13.
- Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol* 2008; **100**: s1–148.
- Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report – Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006; **117**: 391–7.
- Climate Statistics for Australian locations. Monthly climate statistics. Australian Bureau of Meteorology (http://www.bom.gov.au/climate/averages/index.shtml?map_type=cdio&code=1). Last accessed 4 April 2009.
- Australian Births 1997–2007. Australian Bureau of Statistics, Catalogue Number 330.10 (<http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/330.102007?OpenDocument>). Last accessed 4 April 2009.
- Australian Historical Population Statistics 2008. Australian Bureau of Statistics, Catalogue Number 3105.0.65.001. (<http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3105.0.65.0012008?OpenDocument>). Last accessed 11 July 2010.
- Kemp AS. Relationship between the time of birth and the development of immediate hypersensitivity to grass-pollen antigens. *Med J Aust* 1979; **1**: 263–4.
- Wjst M, Dharmage S, André E, et al. Latitude, birth date, and allergy. *PLoS Med* 2005; **2**: e294.
- Aalberse RC, Nieuwenhuys EJ, Hey M, Stapel SO. 'Horoscope effect' not only for seasonal but also for non-seasonal allergens. *Clin Exp Allergy* 1992; **22**: 1003–6.
- 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.
- Pyrhönen K, Läärä E, Hiltunen L, Kaila M, Hugg T, Näyhä S. Season of the first trimester of pregnancy predicts sensitization to food allergens in childhood: a population-based cohort study from Finland. *J Epidemiol Community Health* 2010 (in press). doi:10.1136/jech.2009.105411.
- Sicherer SH, Furlong TJ, Muñoz-Furlong A, Burks AW, Sampson HA. A voluntary registry for peanut and tree nut allergy: characteristics of the first 5149 registrants. *J Allergy Clin Immunol* 2001; **108**: 128–32.
- Hill DJ, Hosking CS, de Benedictis FM, et al. Confirmation of the association between high levels of immunoglobulin E food sensitization and eczema in infancy: an international study. *Clin Exp Allergy* 2008; **38**: 161–8.
- Kusunoki T, Asai K, Harazaki M, Korematsu S, Hosoi S. Month of birth and prevalence of atopic dermatitis in schoolchildren: dry skin in early infancy as a possible etiologic factor. *J Allergy Clin Immunol* 1999; **103**: 1148–52.
- Strid J, Hourihane J, Kimber I, Callard R, Strobel S. Epicutaneous exposure to peanut protein prevents oral tolerance and enhances allergic sensitization. *Clin Exp Allergy* 2005; **35**: 757–66.

25. Teale GR, Cunningham CE. Vitamin D deficiency is common among pregnant women in rural Victoria. *Aust N Z J Obstet Gynaecol* 2010; **50**: 259–61.
26. Eyles D, Anderson C, Ko P, et al. A sensitive LC/MS/MS assay of 25OH vitamin D3 and 25OH vitamin D2 in dried blood spots. *Clin Chim Acta* 2009; **403**: 145–51.
27. Camargo CA, Ingham T, Wickens K, et al. The New Zealand Asthma and Allergy Cohort Study Group. Vitamin D status of newborns in New Zealand. *Br J Nutr* 2010; **50**: 259–61.
28. Staples JA, Ponsonby AL, Lim LL, McMichael AJ. Ecologic analysis of some immune-related disorders, including type 1 diabetes, in Australia: latitude, regional ultraviolet radiation, and disease prevalence. *Environ Health Perspect* 2003; **111**: 518–23.
29. Hartmann B, Heine G, Babina M, et al. Targeting the vitamin D receptor inhibits the B cell-dependent allergic immune response. *Allergy* 2010 (in press). doi: 10.1111/j.1398-9995.2010.02513.x
30. 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**: 217–222.
31. Hyppönen E, Berry DJ, Wjst M, Power C. Serum 25-hydroxyvitamin D and IgE – a significant but nonlinear relationship. *Allergy* 2009; **64**: 613–20.