

Climate and prevalence of atopic eczema in 6- to 7-year-old school children in Spain. ISAAC PhASE III

**María Morales Suárez-Varela •
Luís García-Marcos Álvarez • Michael D. Kogan •
Agustín Llopis González • Antonio Martínez Gimeno •
Inés Aguinaga Ontoso • Carlos González Díaz •
Alberto Arnedo Pena •
Begoña Domínguez Aurrecoechea •
Rosa María Busquets Monge • Alfredo Blanco Quiros •
José Batlles Garrido • Iñiqui Miner Canflanca •
Ángel López-Silvarrey Varela**

Received: 13 December 2007 / Revised: 2 May 2008 / Accepted: 18 July 2008
© ISB 2008

Abstract Atopic eczema (AE) is a chronic skin disease. Recent reports indicate that the worldwide prevalence of AE is increasing and that various environmental factors are implicated in its aetiology. Climatic conditions have been related with AE prevalence, and Spain has varying climatic conditions. The aim of this study is to document the possible climatic influence on the prevalence of AE in schoolchildren aged 6–7 years in three different climatic regions in Spain. We conducted a cross-sectional population-based survey of 28,394 schoolchildren aged 6–7 years from 10 Spanish centres in three different climatic regions. The mean partici-

pation rate was 76.5%. AE prevalence was assessed using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire and the Spanish Academy of Dermatology criteria used in Spain to diagnose AE. The data, including annual temperature, precipitation, relative humidity and the annual number of sunny hours per climatic region, were obtained from the Spanish National Institute of Meteorology. Different AE prevalences were found in all three climatic regions studied: Atlantic, 32.9; Mediterranean 28.3; and Continental 31.2 per 100 children studied ($p < 0.005$). AE was positively associated with precipitation and

M. M. Suárez-Varela • A. L. González
Unit of Public Health, Hygiene, and Environmental care.
Department of Preventive Medicine, University of Valencia,
Valencia, Spain

M. M. Suárez-Varela • A. L. González
Research group CIBER CB06/02/0045,
CIBER actions - Epidemiology and Public Health,
Valencia, Spain

M. M. Suárez-Varela
Research Foundation. Hospital Universitario “Dr. Peset”,
Valencia, Spain

L. García-Marcos Álvarez
Unit of Clinical Research,
Cartagena and Department of Paediatrics, University of Murcia,
Murcia, Spain

M. D. Kogan
HRSA. Maternal and Child Health Bureau,
Rockville, USA

A. M. Gimeno
Section of Paediatric Pneumo-Allergy,
Hospital Infantil 12 de Octubre,
Madrid, Spain

I. A. Ontoso
Department of Health Sciences,
Public University of Navarre,
Navarre, Spain

C. G. Díaz
Department of Paediatrics, Hospital of Basurto,
Bilbao, Spain

A. A. Pena
Section of Epidemiology. Centre of Public Health,
Regional Ministry of Health, Castellón,
Castellón, Spain

B. D. Aurrecoechea
Health Centre of Otero – Oviedo,
Oviedo, Spain

humidity, and was negatively associated with temperature and the number of sunny hours. The results show that AE is significantly dependent on meteorological conditions.

Keywords Atopic eczema · Climate · Children · ISAAC phase III · Prevalence

Introduction

Atopic eczema (AE) is a chronic inflammatory skin disease characterised by itching, lesions and lichenification, especially at the flexure sites of the major joints of the upper and lower extremities (Maymí et al. 2007). The pain and itching associated with the disease may cause depressive symptoms, social isolation and reduced self-perception, thus negatively influencing the quality of life in both children and their caretakers (Fennessy et al. 2000).

AE affects between 5% and 20% of children aged up to 11 years at one time or another in different regions. Research suggests that AE prevalence is on the increase and that various environmental factors are implicated in its aetiology (Asher and Weiland 1998; Fennessy et al. 2000; Arruda et al. 2005). However, certain existing aetiopathogenic aspects remain unclear (Asher et al. 1995; Asher and Weiland 1998; Blanco et al. 2005).

An international study conducted by the International Study of Asthma and Allergies in Childhood (ISAAC) group (ISAAC Group 1998a, b) revealed substantial regional and seasonal variations in the frequency of AE and of other atopic diseases.

A potential role of climatic conditions in the aetiology of AE has long been suspected. Some studies on the effects of climate have investigated the association of variations in climate or meteorological conditions with the occurrence or severity of symptoms of atopic diseases (Charpin et al. 1988, 1991; Vocks et al. 2001; Weiland et al. 2004). Epidemiological studies suggest that climate influences the prevalence of the disease, and reports worldwide indicate that AE has been negatively associated with temperature (Vocks et al. 2001; Weiland et al. 2004) and positively associated with latitude (Weiland et al. 2004), whereas the effects of water vapour pressure, air pressure and hours of sunshine observed were less pronounced (Vocks et al. 2001). However, little is known about the effect of long-term climate conditions on AE prevalence because these results may be biased for different population types (genetic condition) or for different diagnostic AE criteria in the various regions studied.

Although most AE cases are minor (60% of all cases), they could be influenced by climate such as a certain range of hydrothermal atmospheric conditions (Vocks et al. 2001), and there is a tendency for relapses. The disease may become serious and generalised, and may cause a huge impact on the child's health and well-being (Lewis-Jones 2005). Furthermore, AE treatment and cures can involve a heavy financial burden ((Fennessy et al. 2000; Lewis-Jones 2005).

AE prevalence has continued to increase since the 1970s, particularly in Northern Europe (Aberg et al. 1995), with an incidence rate of 15% among children aged 0–7 years. Nonetheless, the reasons for this increase remain unclear (Aberg et al. 1995). In addition, a simultaneous increase in the case of atopic respiratory disorders, such as asthma and allergic rhinitis, was observed (Aberg et al. 1995).

However, whether these differences are real or attributable to measurement variations remains unknown. Two difficulties in studying AE prevalence are that most results may not be comparable due to the lack of standardised methods. Moreover, it is difficult to compare areas or countries with different populations, habits and lifestyles. Therefore, a standardised methodology is essential for comparing AE prevalences among different population groups (Haileamlak et al. 2005). In Spain, there are different climatic conditions and a homogeneous population.

The aim of this study was to investigate whether climate is related with the prevalence of AE in schoolchildren aged 6–7 years in the Spanish population across three climatic regions (Atlantic, Mediterranean and Continental).

Materials and methods

A cross-sectional population-based survey based on the ISAAC methodology was conducted to obtain epidemiological information on AE and other allergic diseases with standardised methods (Haileamlak et al. 2005).

R. M. B. Monge

Department of Paediatrics, Hospital del Mar,
Barcelona, Spain

A. B. Quiros

Department of Paediatrics, University of Valladolid,
Valladolid, Spain

J. B. Garrido

Department of Paediatrics, Hospital Torrecárdenas,
Almería, Spain

I. M. Canflanca

Department of Paediatrics, Hospital de Donostia,
San Sebastián, Spain

Á. L.-S. Varela

Foundation María José Jove,
A Coruña, Spain

M. M. Suárez-Varela (✉)

Unidad de Salud Pública, Higiene y Sanidad Ambiental,
Departamento de Medicina Preventiva y Salud Pública,
Avd. Vicente Andrés Estellés s/n,
46100 Burjassot (Valencia), Spain
e-mail: maria.m.morales@uv.es

The population groups were based on schoolchildren (6–7 years) with a sample size of 3,000 per centre (10 centres participated in Spain). Power calculations indicate that this represents a 90% statistical capacity rate for detecting 2% prevalence differences among schools at the 0.01 level of significance. Schools were chosen by cluster to participate in the study from a random school sample. Consents were obtained from school staff and parent associations. Questionnaires were answered by parents.

The mean response rate in Spain was 76.5%. Parents of 28,394 schoolchildren aged 6–7 years completed the ISAAC questionnaire. The Spanish schools participating were from Asturias, Barcelona, Bilbao, Cartagena (coordinating centre), Castellón, A Coruña, Madrid, Pamplona, San Sebastián and Valencia (Table 1).

A survey was conducted using the standardised and validated questionnaire of the ISAAC study in its phase III, which included questions on AE (Ellwood et al. 2005; Mata et al. 2005).

The questionnaire was used to assess AE prevalence, and questions were as follows: (1) has your child ever had an itchy rash which was coming and going for at least 6 months? (yes/no); (2) has your child had this itchy rash at any time in the last 12 months? (yes/no); (3) has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in the front of the ankles, under the buttocks, and around the neck, ears, or eyes? (yes/no); and (4) has your child ever been clinically diagnosed with eczema or atopic dermatitis by a specialist? (yes/no).

According to the ISAAC criteria questions (Haileamlak et al. 2005), affirmative responses to questions 1 to 3 were defined as having AE symptoms. Schoolchildren of parents who answered affirmatively to question 4 were defined as being diagnosed with AE by a medical specialist. In Spain, diagnosis is made according to the Spanish Academy of

Dermatology (SAD) criteria (based on the diagnostic criteria scale developed by Hanifin and Rajka in 1980). Diagnosed AE must present “an itchy skin condition” plus other signs and symptoms, such as: a personal history of asthma or hay fever (or history of atopic disease in the first degree in those under 4 years); a history of generally dry skin in the last year (xerosis); visible flexural dermatitis (or dermatitis involving the cheeks/forehead and outer area of the limbs in children under the age of 4); onset under the age of 2 (not used in less than 4 year olds); an acute sporadic itchiness or pruritus which generally worsens at night; this itchiness may become more irritable with scratching episodes; and/or particular sensitivity to external proteins, commonly known as atopens (Guerra 1997).

Data on environmental characteristics include mean annual temperature, mean annual precipitation, mean relative humidity, and the mean annual number of sunny hours in each geographic–climatic region. These environmental data were obtained from the Spanish National Institute of Meteorology, and the following climatic regions were determined: Atlantic (northern), Mediterranean (eastern) and Continental (central) (INE 2006a, b, c, d).

We also included different variables for the three regions: grade of atmospheric contamination, type of region (urban /rural), grade of industrialisation, socio-economic status, number of children per fertile women and smoking habit.

This study was approved by the Ethical Committee of the Hospital 12 de Octubre, Madrid (Spain), in accordance with the World Medical Association.

Data analysis

Prevalences were estimated as percentages of schoolchildren with symptoms, and were divided by the total number of participants from each centre. The χ^2 test was used to

Table 1 ISAAC III Centres in Spain, studied population of schoolchildren aged 6–7 years and percentage participation rate

Centres	Boys	Girls	Total participating schoolchildren	Participation rate (%)
Atlantic area				
Asturias	1,505	1,522	3,027	86.5
Bilbao	1,469	1,570	3,039	82.2
A Coruña	1,472	1,545	3,017	73.8
Pamplona	1,583	1,583	3,166	81.2
San Sebastián	465	432	897	62.0
Mediterranean area				
Barcelona	1,533	1,357	2,890	82.2
Cartagena	1,359	1,358	2,717	71.7
Castellón	2,038	1,879	3,917	88.1
Valencia	1,665	1,721	3,386	53.4
Continental area				
Madrid	1,162	1,176	2,338	89.0
Total	14,251	14,143	28,394	76.5

compare results. The association between climatic region and AE was expressed as Prevalence Ratio (PR). Confidence intervals of 95% were applied.

Results

The characteristics of each participating centre are shown in Table 1. The overall sample size comprised 28,394 schoolchildren. No statistically significant differences in participation were detected among the centres. All schoolchildren from selected schools were included. However, 1 school in A Coruña (1.7%), 18 in Valencia (18.4%), 23 in Barcelona (46.0%) and 18 in San Sebastián (50.0%) refused to participate. Response rates exceeded 70.0% in all centres except San Sebastián and Valencia where rates were 62.0% and 53.4%, respectively. Simple random sampling was conducted in Asturias, Madrid, San Sebastián and Valencia to obtain a school sample; the remaining centres included all the selected schools. The mean parental participation was 76.5%.

Table 2 shows the prevalence of rashes (based on questions 1–3) and diagnosed AE (based on question 4) by geographic area and gender. The prevalence of rashes was higher among boys in the Atlantic area, and a higher prevalence was also found in diagnosed AE. Such findings suggest a possible association between rashes and diagnosed AE. Therefore, early detection of rashes may prove very useful. In contrast, the higher prevalence of rashes in girls was detected in the Continental area, but the higher prevalence of diagnosed AE was noted in the Atlantic area.

Statistically significant differences were observed in rashes and diagnosed AE prevalence among three climatic regions (Table 2): boys: rashes ($p \leq 0.05$), diagnosed AE ($p < 0.001$); girls: rashes ($p \leq 0.05$); and diagnosed AE ($p < 0.001$).

Table 3 shows the prevalence of rashes per climatic region and age they were detected. There is a higher statistically significant prevalence in girls from the Continental area at an age of 2–4 years ($p \leq 0.05$) and >4 years ($p \leq 0.05$).

Table 4 shows the diagnosed AE prevalence, the climatic values and the rest of variables (grade of atmospheric contamination, type of area, grade of industrialization, social-economic status, number of children per fertile women and smoking habit) for each of the areas. The highest diagnosed AE prevalence (32.9%) was seen in the Atlantic area, whereas the lowest diagnosed AE prevalence (28.3%) was detected in the Mediterranean area. In the Continental area, the prevalence of diagnosed AE was 31.2% ($p < 0.001$). The Continental area had the highest prevalences of atmospheric contamination as well as smoking habit.

A higher prevalence for industrialisation and number of children per fertile women as well as the lowest social economic status was observed in the Mediterranean area.

Table 2 Prevalence of rashes and diagnosed AE in climatic areas arranged by gender in schoolchildren of 6–7 years

Climatic region	Boys ($n=14,251$)						Girls ($n=14,143$)						Total ($n=28,394$)					
	Rashes			Diagnosed atopic eczema			Rashes			Diagnosed atopic eczema			Rashes			Diagnosed atopic eczema		
	AF prevalence ^a (IC 95%)	PR (IC 95%)		AF prevalence ^a (IC 95%)	PR (IC 95%)		AF prevalence ^a (IC 95%)	PR (IC 95%)		AF prevalence ^a (IC 95%)	PR (IC 95%)		AF prevalence ^a (IC 95%)	PR (IC 95%)		AF prevalence ^a (IC 95%)	PR (IC 95%)	
Mediterranean	585 8.8 (8.2–9.5)	1		1,890 28.6 (27.5–29.7)	1		589 9.3 (8.6–10.0)	1		1,766 27.9 (26.8–29.0)	1		1,174 9.0 (8.6–9.5)	1		3,656 28.3 (27.5–29.1)	1	
Continental	113 9.7 (8.1–11.5)	1.1		356 30.6 (28.0–33.3)	1.1		140 11.9 (10.1–13.8)	1.4		375 31.8 (29.2–34.5)	1.2		253 10.8* (9.6–12.1)	1.2		731 31.2 (29.4–33.1)	1.2	
Atlantic	660 10.1 (9.4–10.9)	1.1		2,123 32.6 (31.5–33.8)	1.1		718 10.7 (10.0–11.5)	1.2		2,196 33.0 (31.8–34.1)	1.3		1,378 10.4 (9.9–11.0)	1.2		4,319 32.9 (32.0–33.6)	1.3	
Total	1,358 9.5 (9.0–10.0)	–		4,369 30.6 (29.9–31.4)	–		1,447 10.2 (9.7–10.7)	–		4,337 30.6 (29.9–31.4)	–		2,805 9.8 (9.5–10.2)	–		8,706 30.6 (30.1–31.1)	–	

^a Prevalence per 100 schoolchildren

AF Absolute frequency, CI confidence interval, PR prevalence ratio

* $p \leq 0.05$ comparison of climatic areas. Test of difference : Chi-square

Table 3 Prevalence of rashes per climatic region and age at which it was detected in schoolchildren of 6–7 years

	<2 years (<i>n</i> =1,090)			2–4 years (<i>n</i> =784)			>4 years (<i>n</i> =620)		
	<i>n</i>	PR	95% CI	<i>n</i>	PR	95% CI	<i>n</i>	PR	95% CI
Mediterranean									
Boys	197	2.9	2.5–3.4	183	2.7	2.3–3.1	126	1.9	1.6–2.2
Girls	206	3.2	2.8–3.7	146	2.3	1.9–2.7	134	2.1	1.7–2.5
Total	403	3.1	2.8–3.4	329	2.5	2.2–2.8	260	2.0	1.7–2.2
Continental									
Boys	49	4.2	3.1–5.4	19	1.6	1.0–2.4	28	2.4	1.6–3.4
Girls	45	3.8	2.8–5.0	42	3.5*	2.6–4.7	45	3.8*	2.8–5.0
Total	94	4.0	3.2–4.8	61	2.6	2.0–3.3	73	3.1	2.4–3.8
Atlantic									
Boys	295	4.5	4.0–5.0	175	2.6	2.3–3.1	128	1.9	1.6–2.3
Girls	298	4.4	4.0–4.9	219	3.2	2.8–3.7	159	2.3	2.0–2.7
Total	593	4.5	4.1–4.8	394	2.9	2.7–3.2	287	2.1	1.9–2.4
Boys	541	3.7	3.4–4.1	549	3.8	3.5–4.2	282	1.9	1.7–2.2
Girls	1,090	3.8	3.6–4.0	377	2.6	2.3–2.9	338	2.3*	2.1–2.6
Total	407	2.8	2.6–3.1	784	2.7	2.5–2.9	620	2.1	2.0–2.3

PR Prevalence rate, CI confidence interval

**p*<0.005 comparison boys and girls. Test of difference: Chi-square

Discussion

Spain is an interesting region to study the different AE prevalences among areas given its geographical characteristics. The fact that Spain is a large plateau, except for its coast, facilitates the geographical division of the ISAAC centres. One clear association with AE prevalence was found in our study: the prevalence of AE symptoms was positively correlated with precipitation and humidity, and a

negative correlation was noted for the mean annual temperatures and the mean annual number of sunny hours. Other studies detected that a variety of skin diseases, such as AE, tends to worsen during the dry winter season. This positive correlation with precipitation and humidity can be explained by the fact that humidity can irritate the skin (National Jewish Medical and Research Center www.njc.org). Results of other research suggest that a low environmental humidity increases mast cell number and

Table 4 Diagnosed AE prevalence, the climatic values and the remaining variables for each of the areas

	Mediterranean	Continental	Atlantic
Prevalence of clinically diagnosed atopic eczema (%) ^a	28.3	31.2	32.9
Climatic parameters ^b			
Mean annual temperature (°C)	16.8	14.1	13.5
Mean annual precipitation (mm)	469	386	1126
Mean relative humidity (%)	69	59	75
Mean annual number of sunny hours	2,593	2,658	1,830
Atmospheric contamination ^c	21.64	33.97	19.93
Type of area ^d	Urban	Urban	Urban
Grade of industrialisation (%) ^e	12.7	9.5	6.4
Social- economic status ^f	6.2	9.0	7.6
No. of children/ fertile women ^g	1.1	1.0	0.9
Smoking habit (%) ^h	32.6	38.1	36.7

^a=per 100 children

^b Data from Spanish National Institute of Meteorology (1971–2000)

^c % Days/ year that exceeded the limit level of air particulates (50ug/m³). Data from Ecologistas en Acción: www.ecologistasenaccion.es

^d Urban/rural. Data from Arnedo-Pena et al. 2005

^e Data from Anuario el País 2002

^f Index of provincial income. Data from Anuario el País 2002

^g Data from National Institute of Statistics www.ine.es

^h Data from the questionnaire Health of the Valencian Community, questionnaire Health of Navarra, questionnaire Health of Asturias, questionnaire Health of Catalunya, Report of State of Health of the Population of Madrid

dermal histamine content. In an experimental study, Ashida and Denda (2003) detected that histamine content in the dermal dermis of animals kept in a low environmental humidity (relative humidity < 10%) for 3 and 5 days was significantly higher than that of animals kept in a high environmental humidity (relative humidity > 80%) for the same period of time. They detected, too, that the number of mast cells in the dermis of the animals kept in a low environmental humidity was significantly higher than the animals kept in a high environmental humidity.

The negative correlation with temperature was found by other authors (Vocks et al. 2001; Weiland et al. 2004), but for the numbers of sunny hours it was less pronounced in other studies (Vocks et al. 2001). This negative correlation with the mean annual temperatures and the mean annual number of sunny hours is also bolstered by the observation that many skin pathologies worsen in colder climates (Huisson and Krishna 2008).

Similar to other research, significantly statistical differences between boys and girls in the prevalence of rashes and AE exist only in the Continental area (both prevalences are higher in girls) (Morales et al. 2007).

As in other studies (Blanco et al. 2005), a higher diagnosed AE prevalence was seen in northern Spain (near the Atlantic Ocean). In contrast, eastern Spain (near the Mediterranean Sea) presented the lowest AE prevalence. Madrid, located in central Spain with a Continental climate, indicated an intermediate prevalence rate.

We observed that, although statistical differences exist due to non-climatic variables among the three regions, a positive correlation between them and the prevalence of AE (the region with the highest prevalence of AE did not represent the highest level of atmospheric contamination, industrialisation, lower social-economic level nor a higher smoking habit) cannot be established.

This study shows that AE is common in Spanish schoolchildren with an overall estimated prevalence of 30.6%, as reported by parents (year 2003). However, this prevalence is different in each geographic-climatic study region.

Many difficulties arise when directly comparing findings among different studies as estimates were seen to be dependent upon disease definition and assessment methods, age groups, the year children were born, the time period the study was conducted in, and geographical areas (Marks et al. 1999; Yura and Shimizu 2001; Girolomoni et al. 2003; Bisgaard 2004).

To date, this is the largest and the most comprehensive study on physician-diagnosed AE prevalence in Spain. We believe our data are representative of the current clinically diagnosed AE prevalence among schoolchildren living in different Spanish urban areas given the sampling design of this study. However, we should indicate that AE prevalence may be overestimated given the response rate of 76.5%, as

parents of schoolchildren with skin problems may be more likely to participate in the study than those without them.

A couple of limitations should be borne in mind. In Spain, schools were not randomly selected in their area, rather their participation was voluntary, which limits inferences being made outside the study area. A further limitation is that all data from parental reports were not confirmed through medical records. However, this study also has its advantages: a large sample size, a high participation rate, similarity in ages and schooling, and standardised methodology. Other Spanish multi-centre studies with similar methodologies have led to reliable internal comparisons in schoolchildren (Martín et al. 2004; García-Marcos et al. 2005).

We found a higher prevalence of diagnosed AE in the three climatic regions studied (Atlantic 32.9%; Mediterranean 28.3%; Continental 31.2%) in comparison to earlier studies that determined a prevalence of 5–20% in children aged up to 11 years (Maymí et al. 2007). The high prevalence increase of AE makes Spain an important population to study. The variation in the prevalence of AE symptoms both within and among countries, inhabitants and similar ethnic groups, suggests that environmental factors may play a critical role in the disease expression (Williams et al. 1999). There is evidence that atopic disorders are increasing at the rate of 1% per year (Spergel and Paller 2003).

The ISAAC questionnaire proved to be an adequate, reproducible and reliable epidemiological tool for AE investigation in population settings (Fennessy et al. 2000). Parents reported AE lifetime prevalence, while dermatologists assessed AE period prevalence. Thus, the same phenomenon was measured on different time scales.

A more than 60-fold variation in the prevalence of AE symptoms among schools was seen in the ISAAC study (ISAAC Group 1998a, 1998b).

When self-reported symptoms of AE were taken into account, the highest prevalences were predominantly observed in English-speaking western countries, whereas decreasing prevalences were seen in north-western to south-eastern Europe.

Last but not least we would like to mention that it would be interesting to analyse how the different climatic factors interact between one another and with the child's environment, but more extensive data would be necessary.

Conclusions

The results show that AE is significantly dependent on meteorological conditions.

Acknowledgements We wish to thank the Spanish Ministry of Health and Consumption, the Institute of Health Carlos III, the Network of Centres (RCESP), the Oscar Rava Foundation 2001,

Barcelona, the Department of Health of the Regional Government of Navarre, the International Luis Vives Rotary Foundation 2002–2003, Valencia, the Department of Health of the Regional Government of Murcia, and AstraZeneca, Spain. Thank to all the parents who kindly participated and gave us some of their time. Finally, we thank the native translator who revised this article.

The members of the International Study of Asthma and Allergies in Childhood (ISAAC) in Spain are: L García-Marcos (coordinator), A Martínez Torres, JJ Guillén Pérez, V Pérez Fernández (Cartagena, coordinating centre); J Batlles Garrido, T Rubí Ruiz, A Bonillo Perales, MM Sánchez Gutiérrez, B Chamizo Moreno, J Momblan de Cabo, R Jiménez Liria, J Aguirre Rodríguez, A Losilla Maldonado, M Torres Daza (Almería); I Carvajal Urueña, C Díaz Vázquez, C Díez Fernández, A García Merino, B Domínguez Aurrecoechea, M Marcilla Escotet, MO Díez Fernández, I Huerta González (Asturias); RM Busquets Monge, O Vall Combelles (Barcelona); C González Díaz, A González Hermosa, N García Perez, M Ferrez Arriazu, M Villar Alvarez (Bilbao); A Amedo-Pena, A Artero, JB Bellido, JB Campos, M^a L Museros, M^a R Pac, J Puig (Castellón); A López-Silvarrey Varela (La Coruña); G García Hernández, A Marín Gimeno, C Luna Paredes, AL Moro Rodríguez, I González Gil (Madrid); F Guillén, I Aguinaga, B Marín, C Brun, J Hermoso, I Serrano, M Fernández, J de Irala, MA Martínez (Pamplona); EG Pérez-Yarza, P Gomez-Cabanillas, N García de Andoin, I Miner Canflanc (San Sebastián), MM Morales Suarez-Varela, A Llopis González, MC Jiménez López, M Gracia Antequera (Valencia); A Blanco Quirós, J Castrodeza Sanz, S Marín Urueña, E Burguenío Sánchez-Taiz (Valladolid).

References

- Aberg N, Hesselmar B, Aberg B, Erikson B (1995) Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991. *Clin Exp Allergy* 25:815–819 doi:10.1111/j.1365-2222.1995.tb00023.x
- Anuario el País (2002). Ed el País, pp 434
- Amedo-Pena A, García Marcos L, García G, Aguinaga I, González C, Morales M, Domínguez B, Busquets R, Blanco A, Batlles J (2005) Tendencia temporal y variaciones geográficas de la prevalencia de síntomas de rinitis alérgica en escolares de 6–7 años de ocho áreas españolas, según el ISAAC. *An Pediatr (Barc)* 62:229–236 doi:10.1157/13071837
- Arruda LK, Sole D, Baena-Cagnani CE, Nasipitz CK (2005) Risk factors for asthma and atopy. *Curr Opin Allergy Clin Immunol* 5:153–159
- Asher MI, Weiland SK (1998) The international study of asthma and allergies in childhood (ISAAC). ISAAC steering committee. *Clin Exp Allergy* 28:52–66 doi:10.1046/j.1365-2222.1998.028s5052.x
- Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martínez F, Mitchell EA, Pearce N, Sibbald B, Stewart AW (1995) International study of asthma and allergies in childhood-ISAAC: rationale and methods. *Eur Respir J* 8:483–491 doi:10.1183/09031936.95.08030483
- Ashida Y, Denda M (2003) Dry environment increases mast cell number and histamine content in dermis in hairless mice. *Br J Dermatol* 149:240–247 doi:10.1046/j.1365-2133.2003.05408.x
- Bisgaard H (2004) The copenhagen prospective study on asthma in childhood (COPSAC): Design, rationale, and baseline data from a longitudinal birth cohort study. *Ann Allergy Asthma Immunol* 93:381–389
- Blanco Quirós A, Díaz Castella JM, Balañá Vilanova M, Valveny Llobet N (2005) Risk factors for atopic dermatitis and familial prevalence in Spain (ELIHO study). *An Pediatr* 63:480–488
- Charpin D, Kleisbauer J, Lanteaume A (1988) Asthma and allergy to house dust mites in populations living in high altitudes. *Chest* 93:758–761 doi:10.1378/chest.93.4.758
- Charpin D, Birnbaum J, Haddi E (1991) Altitude and allergy to house dust mites. *Am Rev Respir Dis* 143:983–986
- Ellwood P, Asher MI, Beasley R, Clayton TO, Stewart AW (2005) The international study of asthma and allergies in childhood (ISAAC): phase three rationale and methods. *Int J Tuberc Lung Dis* 9:10–16
- Fennessy M, Coupland S, Popay J, Naysmith K (2000) The epidemiology and experience of atopic eczema during childhood: a discussion paper on the implications of current knowledge for health care, public health policy and research. *Epidemiol Community Health* 54:581–589 doi:10.1136/jech.54.8.581
- García-Marcos L, Suarez-Varela MM, Canflanca IM, Garrido JB, Quirós AB, López-Silvarrey Varela A, Hernández GG, Guillén Grima F, Díaz CG, González IH, Pena AA, Monge RB (2005) BCG immunization at birth and atopic diseases in a homogeneous population of Spanish schoolchildren. *Int Arch Allergy Immunol* 137:303–309 doi:10.1159/000086461
- Girolomoni G, Abeni D, Masini C, Sera F, Ayala F, Belloni-Fortina A, Bonifazi E, Fabbri P, Gelmetti C, Monfrecola G, Peserico A, Seidenari S, Giannetti A (2003) The epidemiology of atopic dermatitis in Italian schoolchildren. *Allergy* 58:420–425 doi:10.1034/j.1398-9995.2003.00112.x
- Guerra Tapia A (1997) Dermatitis atópica. In: Capdevila F (ed) *Dermatología pediátrica*. Grupo Aula Médica, Madrid, pp 83–13
- Haileamlak A, Lewis SA, Britton J, Venn AJ, Woldemariam D, Hubbard R, Williams HC (2005) Validation of the international study of asthma and allergies in childhood (ISAAC) and U.K. criteria for atopic eczema in Ethiopian children. *Brit J Dermatol* 152:735–741 doi:10.1111/j.1365-2133.2005.06511.x
- Huisson A, Krishna MT (2008) Images in clinical medicine. Cold-induced urticaria. *N Engl J Med* 21:358–359
- INE- Instituto Nacional de Estadística (2006a) Humedad media mensual en porcentaje por región, estación, años y meses. *Climatología*. Entorno físico y Medio Ambiente. In: *Anuario Estadístico de España 2006*. Madrid, pp 22
- INE- Instituto Nacional de Estadística (2006b) Número de horas de sol por región, estación, años y meses. *Climatología*. Entorno Físico y Medio Ambiente. In: *Anuario Estadístico de España 2006*. Madrid, pp 24
- INE- Instituto Nacional de Estadística (2006c) Temperaturas medias mensuales por región y estación, años y meses. *Climatología*. Entorno Físico y Medio Ambiente. In: *Anuario Estadístico de España 2006*. Madrid, pp 21
- INE- Instituto Nacional de Estadística (2006d) Precipitación total en milímetros por región, estación, años y meses. *Climatología*. Entorno Físico y Medio Ambiente. In: *Anuario Estadístico de España 2006*. Madrid, pp 23
- Informe del Estado de Salud de la Población de Madrid (www.madrid.org)
- ISAAC (1998a) The International Study of Asthma and Allergies in Childhood (ISAAC). Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 351:1225–1232 1998
- ISAAC (1998b) The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variations in prevalence of asthma symptoms: The International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 12:315–335
- Lewis-Jones S (2005) Measuring the burden of atopic eczema in young children and the family unit. *J Invest Dermatol* 125:1106–1111
- Marks R, Kilkenny M, Plunkett A, Merlin K (1999) The prevalence of common skin conditions in Australian school students: 2. Atopic dermatitis. *Br J Dermatol* 1999 140:468–473
- Martin Fernandez-Mayoralas D, Martin Caballero JM, García-Marcos Alvarez L (2004) Association between atopic dermatitis, allergic rhinitis and asthma in schoolchildren aged 13–14 years old. *An Pediatr (Barc)* 60:236–242
- Mata Fernandez C, Fernandez-Benitez M, Perez Miranda M, Guillen Grima F (2005) Validation of the Spanish version of the Phase III

- ISAAC questionnaire on asthma. *J Investig Allergol Clin Immunol* 15:201–210
- Maymí MA, Somolinos AL, Nazario CM, Sánchez JL (2007) The prevalence of atopic dermatitis in Puerto rican School children. *P R Health Sci* 26:127–133
- Morales MM, García-Marcos L, González C, Arnedo L, Domínguez B, Busquets RM, Blanco A, Batlles J, Miner I, López-Silvarrey A, Martínez A, Aguinaga I, Llopis A, Jiménez MC (2007) Prevalencia de dermatitis atópica y factores nutricionales en niños de 6–7 años. *Aten Primaria* 39:355–360
- Spergel JM, Paller AS (2003) Atopic dermatitis and the atopic march. *J Allergy Clin Immunol* 112:S118–127
- Vocks E, Busch R, Frohlich C, Borelli S, Mayer H, Ring J (2001) Influence of weather and climate on subjective symptom intensity in atopic eczema. *Int J Biometeorol* 45:27–33
- Weiland SK, Hüsing A, Strachan DP, Rzehak P, Pearce N (2004) Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. *Occup Environ Med* 61:609–615
- Williams H, Robertson C, Stewart A, Ait-Khaled N, Anabwani G, Anderson R, Asher I, Beasley R, Björkstén B, Burr M, Clayton T, Crane J, Ellwood P, Keil U, Lai C, Mallol J, Martínez F, Mitchell E, Montefort S, Pearce N, Shan J, Sibbald B, Strachan D, von Mutius E, Weiland SK (1999) Worldwide variations in prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 103:125–138
- Yura A, Shimizu T (2001) Trends in the prevalence of atopic dermatitis in school children: longitudinal study in Osaka Prefecture, Japan, from 1985 to 1997. *Br J Dermatol* 145:966–973