ORIGINAL ARTICLE

Diet and Prevalence of Atopic Eczema in 6 to 7-Year-Old Schoolchildren in Spain: ISAAC Phase III

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Abstract

Background: The prevalence of atopic dermatitis (AD), a chronic skin disease, has increased substantially in recent decades, and different factors have been implicated in its etiology. Although dietary habits are being investigated, few conclusive findings have been reported. Nevertheless, increased consumption of polyunsaturated fatty acids (PUFA) and a diet poor in antioxidants have been related to AD.
Objectives: The objectives of this study were to investigate the association between AD, the intake of different foods, and the effect of a Mediterranean diet among Spanish schoolchildren aged 6 to 7.
Methods: We performed a cross-sectional study with 20 106 schoolchildren aged 6-7 years from 10 different areas of Spain. The participation rate was 76.50%. The prevalence of AD was assessed using the International Study of Asthma and Allergies in Childhood questionnaire and the criteria of the Spanish Academy of Dermatology. To calculate the Mediterranean diet score, we classified food into 2 groups: Mediterranean food, including fruit, seafood, vegetables, pulses, cereals, pasta, rice, and potatoes; and non-Mediterranean food, including meat, milk, and fast food.
Results: Milk was negatively associated with AD. Butter and nuts also were negatively associated, although statistical significance was only reached when these foods were consumed 3 or more times a week.
Conclusions: We found no association between the Mediterranean diet score and AD and a positive association between AD and obesity.

Key words: Atopic dermatitis. Children. ISAAC phase III. Mediterranean diet.

■ **Resumen**

Antecedentes: Recientes estudios han observado que la prevalencia de dermatitis atópica (DA), una enfermedad cutánea crónica, ha aumentado sustancialmente en estas últimas décadas y que diferentes factores están implicados en su etiología. A la luz de estos resultados, los hábitos dietéticos están siendo investigados, aunque se han obtenido escasos resultados concluyentes. Sin embargo, el aumento del consumo de ácidos grasos poliinsaturados (PUFA) y una dieta pobre en antioxidantes se han relacionado con la DA.
Objetivos: Investigar la asociación entre la DA y la ingesta de diferentes alimentos, y el efecto de la dieta mediterránea entre escolaes españoles de 6-7 años.
Métodos: Realizamos un estudio trasversal con 20106 escolares de 6-7 años de edad procedentes de 10 centros geográficos españoles. Se obtuvo una participación media del 76.50%. La prevalencia de DA fue evaluada utilizando el cuestionario del proyecto International Study of Asthma and Allergies in Childhood (ISAAC) y los criterios establecidos por La Academia Española de Dermatología. Para calcular 'Mediterranean diet score', la fruta, marisco, vegetales, legumbres, cereales, pasta, arroz y patatas se consideraron comida 'pro-Mediterranea', mientras que la carne, leche y comida rápida se consideraron comida 'no Mediterranea'.
Resultados: Se obtuvo una asociación negativa entre la leche y la DA. La mantequilla y los cacahuetes se asociaron también negativamente, pero sólo cuando se consumen tres o más veces a la semana fue estadísticamente significativa.
Conclusiones: No se observa una asociación entre 'Mediterranean diet score' y la DA, y una asociación positiva entre la DA y la obesidad.

Palabras clave: Dermatitis atópica, niños, ISAAC fase III, Dieta Mediterránea.

Introduction

Atopic dermatitis (AD), or atopic eczema, is an inflammatory skin manifestation associated with atopy, which is a genetic predisposition to mounting immunoglobulin (Ig) E–mediated hypersensitivity responses to some antigens [1,2]. AD often occurs in patients with a family or personal history of atopy. It is more frequent among infants, and its prevalence and severity usually lessen with age [3].

In recent decades, the prevalence of atopic diseases has increased substantially [4,5], especially among children in Western countries [6]. Dietary habits have often been investigated to determine the reasons for this increase.

One hypothesis for the increased prevalence of atopic diseases is the growing consumption of polyunsaturated fatty acids (PUFAs), specifically a high intake of ω-6 in relation to ω-3. The presence of PUFAs could intensify the production of IgE through the formation of arachidonic acid–derived eicosanoids, which could in turn favor the development of allergic diseases [7,8]. A diet rich in antioxidants, on the other hand, could have a protective effect against atopic diseases [9].

Although many studies have been conducted to establish the link between diet and atopy, findings are often conflicting, inconsistent, and inconclusive [10]. The present study investigated the association between AD, the intake of different foods, and the effect of a Mediterranean diet on children aged 6 to 7 years attending Spanish schools.

Methods

Design

We conducted a cross-sectional study using data from the International Study of Asthma and Allergies in Childhood (ISAAC), Phase 3. Parents of children aged 6 to 7 years who attended schools in 10 Spanish centers (Cartagena, Barcelona, Bilbao, Castellón, Pamplona, Valencia, Madrid, Asturias, San Sebastián, and La Coruña) were surveyed. Each center included all the schools or a random sample of schools within the city district with schoolchildren of the target age group.

Questionnaires were translated into Spanish and back-translated into English, according to the ISAAC protocol, and were subsequently validated [11]. They were handed out to the schoolchildren by their teachers and were filled in by parents at home and returned to the school within 1 week. The response rate was 76.50%.

The initial sample comprised 20 106 children. However, our study only included children whose parents answered all the questions of interest correctly. We excluded those children whose parents provided incomplete information on body mass index (BMI) (n=2961), Mediterranean diet score (n=1164), and diet (n=2828) to obtain a final sample size of 13 153 children from the 10 centers.

AD was determined when parents responded in the affirmative to 2 specific questions: 1) Has your child ever had an itchy rash in the past 12 months? 2) Has this itchy rash affected any of the following places at any time: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?

The questionnaire asked about the frequency of consumption of 16 foods or groups of foods: meat, seafood and fish, fruit, vegetables, pulses (peas, beans, and lentils), cereal, pasta, rice, butter, margarine, nuts, potatoes, milk, eggs, fast food, and yoghurt. Parents could respond using the following categories: never or occasionally, 1 to 2 times/wk, and 3 or more times/wk. Information was also recorded on the mother and father's current smoking habits (yes or no) and the past smoking habits of the child's mother or female guardian during the first year of life (yes or no). Parents reported the weight and height of their children, and this information was used to calculate the BMI in kg/m^2. Obesity was defined according to the international BMI

cutoff points reported by Cole et al [12] for each age group and for gender.

We calculated a Mediterranean diet score based on the work of García-Marcos et al [13]. Fruit, seafood, vegetables, pulses, cereals, pasta, rice, and potatoes were considered Mediterranean foods and scored 0, 1, or 2 points, ranging from the least frequent to the most frequent intake: never or occasionally (0), 1 to 2 times/wk (1), and 3 or more times/wk (2). Meat, milk, and fast food were considered non-Mediterranean foods and scored 0, 1, or 2 points, ranging from the most frequent to the least frequent consumption: never or occasionally (0), 1 to 2 times/wk (1), and 3 or more times/wk (2). In all the analyses, the Mediterranean diet score was the sum of the points of each food, ranging from 0 to 22; the higher the score, the greater the adherence to the Mediterranean diet.

Statistical Procedures

We assessed the relationship between AD, consumption of each food type (1 to 2 times/wk or 3 or more times/wk compared with never or occasionally), gender, the Mediterranean diet score, obesity, and exercise by logistic regression adjusted for gender, obesity, exposure to tobacco smoke in the first year of life, younger and older siblings, and exercise. The Mediterranean diet score was introduced as a continuous variable in the regression. All the analyses were performed with Stata 10.0 software (College Station, Texas, USA) and SPSS 15.0 (Copyright, SPSS, Inc, 1986-2006. Chicago, Illinois, USA).

Table 1. Characteristics of the Study Population

		No. (%)
Sex	Male	6621 (50.41)
	Female	6512 (49.59)
Atopic dermatitis		
	Yes	779 (5.92)
	No	12 374 (94.08)
Mean (SD) Mediterranean diet score		13.26 (1.90)
Obesity		
	Yes	1238 (9.43)
	No	11 893 (90.57)
Parents smoked during child's first year of life		
	Yes	4272 (32.79)
	No	8757 (67.21)
Younger siblings		
	0	8156 (63.49)
	1	4235 (32.97)
	>1	455 (3.54)
Older siblings		
	0	7022 (54.04)
	1	4853 (37.35)
	>1	1119 (8.61)
Exercise		
	Never	1855 (14.27)
	At least once a week	11 144 (85.73)

Results

Table 1 shows the characteristics of the study population. The prevalence of AD was 5.92%, only 9.43% of the study

Table 2. Intake Frequencies of Different Foods Among Children Aged 6 to 7 Years

Food	Never or Occasionally		Once or Twice a Week		Three or More Times a Week	
	N	%	N	%	N	%
Meat	83	0.63	2975	22.62	10 095	76.75
Seafood/fish	798	6.07	8800	66.90	3555	27.03
Fruit	757	5.76	2259	17.17	10 137	77.07
Vegetables	1399	10.64	6533	49.66	5221	39.70
Pulses	495	3.77	8536	64.89	4122	31.34
Cereal	232	1.77	1159	8.81	11 762	89.42
Pasta	266	2.02	9783	74.37	3104	23.61
Rice	537	4.09	10 942	83.17	1674	12.74
Butter	9708	73.81	2528	19.21	917	6.98
Margarine	9763	74.23	2391	18.17	999	7.60
Nuts	7899	60.06	4542	34.52	712	5.42
Potatoes	360	2.75	5995	45.57	6798	51.68
Milk	250	1.90	365	2.78	12 538	95.32
Eggs	675	5.13	10 166	77.28	2312	17.59
Fast food	10 618	80.73	2412	18.33	123	0.94
Yogurt	599	4.56	2317	17.61	10 237	77.83

Table 3. Adjusted Odds Ratios and 95% Confidence Intervals for the Association Between Atopic Dermatitis and the Frequency of Intake of Each Food, Compared With Never/Occasionaly

	Once or Twice a Week			Three or More Times a Week		
	aOR[a]	(95% CI)	*P* Value[b]	aOR[a]	(95% CI)	*P* Value[b]
Meat	0.84	0.33-2.11	0.710	0.86	0.35-2.16	.750
Seafood and fish	1.22	0.87-1.71	0.250	1.27	0.89-1.81	.190
Fruit	1.05	0.81-1.36	0.700	1.14	0.88-1.49	.320
Vegetables	0.78	0.55-1.12	0.180	0.89	0.66-1.21	.470
Pulses	1.22	0.79-1.87	0.370	1.30	0.84-1.02	.240
Cereal	1.12	0.59-2.12	0.720	1.13	0.63-2.04	.670
Pasta	1.20	0.68-2.12	0.520	1.24	0.69-2.21	.460
Rice	1.55	0.98-2.43	0.060	1.51	0.92-2.47	.100
Butter	0.82	0.67-1.01	0.060	0.70	0.50-0.97	.040
Margarine	1.01	0.83-1.23	0.900	0.97	0.72-1.29	.820
Nuts	0.89	0.76-1.05	0.170	0.51	0.33-0.80	.003
Potatoes	1.14	0.70-1.85	0.610	1.13	0.70-1.84	.620
Milk	0.42	0.22-0.79	0.007	0.50	0.33-0.75	.001
Eggs	0.86	0.62-1.19	0.360	1.01	0.71-1.45	.940
Fast food	1.10	0.91-1.33	0.320	0.83	0.36-1.90	.670
Yogurt	1.16	0.79-1.74	0.460	1.11	0.76-1.61	.590

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.
[a]Adjusted for gender, obesity, exposure to tobacco smoke in the first year of life, younger and older siblings, and exercise.
[b]χ^2 test.

Table 4. Adjusted Odds Ratios and 95% Confidence Interval for the Association Between Atopic Dermatitis and Male Sex, Mediterranean Diet Score, Obesity, and Exercise

Variables	aOR[a]	(95% CI)	*P* Value[b]
Male sex	0.86	0.74-1.00	.053
Mediterranean diet score	1.03	0.99-1.08	.071
Obesity	1.38	1.10-1.74	.006
Exercise	0.72	0.59-0.88	.001

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.
[a]Adjusted for gender, Mediterranean diet score, obesity, exposure to tobacco smoke in the first year of life, younger and older siblings, and exercise.
[b]χ^2 test.

population was considered obese, and the mean Mediterranean diet score was 13.26.

The intake frequency of the foods studied is summarized in Table 2.

Table 3 presents the odds ratios (OR) for AD per individual food item adjusted for gender, obesity, exposure to tobacco in the first year of life, younger and older siblings, and exercise. The results reveal a negative association between the consumption of milk and AD. Butter and nuts were also negatively associated with AD, but statistical significance was only reached when these foods were consumed 3 or more times a week.

Table 4 shows the results of the logistic regression analysis using the following factors: gender, the Mediterranean diet score, obesity, exposure to tobacco smoke in the first year of life, younger and older siblings, and exercise. We found no association between the Mediterranean diet score and AD, although we did note an association between obesity and AD.

Discussion

This study examined the relationship between diet and AD in 2 different ways: firstly, by investigating the consumption of foods or groups of foods; and secondly, by grouping the individual categories and computing the Mediterranean diet score.

Our results for individual foods suggest that the consumption of milk, butter, and nuts was negatively associated with AD.

Current scientific evidence indicates that the consumption of ω-6 PUFAs is associated with the prevalence of atopy [8]: the increase in arachidonic acid levels enhances the formation of proinflammatory cytokines and IgE [7,8]. In industrialized countries, vegetable fats and oils, a primary source of PUFAs, are increasingly used. Consumption of saturated fats has decreased as a result of public health measures to reduce coronary heart disease [9,14], and this reduction may contribute to an increase in the prevalence of allergic diseases [7].

While ω-6 intake has been linked to an increased risk of AD, several authors suggest that butter, a source of saturated

fatty acids, is associated with a lower risk of atopic diseases [15,16]. The authors of a study in East Germany found an inverse relationship between increased butter intake and hay fever and atopic sensitization among schoolchildren aged 9 to 11 years [15]. Bolte et al [17] compared the type of fat consumed by 5 to 14-year-old children and concluded that boys who consumed margarine were at higher risk of allergic sensitization than boys who consumed butter. A study in Finland found that atopic children consumed more margarine and less butter than nonatopic children [16].

Milk is a source of saturated fat and has been associated with a lower risk of atopic diseases. In fact, some studies have suggested that increased consumption of milk can protect against AD [18]. Our study reported a negative association between milk and AD.

We expected to find a positive association between the consumption of margarine and AD, since this food contributes to the intake of ω-6 (linoleic acid) [19]. However, our results produced odds ratios of 1.01 and 0.97, with no statistical significance. One possible explanation for our findings is that individuals with AD may change their diet after being diagnosed with this disease.

The potential anti-inflammatory capacity of ω-3 PUFAs may also play a role in atopy. While ω-6 fatty acids enhance the development of inflammatory reactions, ω-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid) competitively inhibit the formation of prostaglandins and leukotrienes derived from arachidonic acid [7].

The anti-inflammatory properties of ω-3 could partly explain the negative association found between AD and nuts, a source of ω-3. Black and Sharpe [7] indicated that decreasing the intake of foods rich in ω-3 could contribute to the increased prevalence of atopic diseases.

Our results must be interpreted with caution, because there may be considerable differences in the proportion of fatty acids in foods included in this group. Furthermore, the term nuts employed in the original version of the questionnaire was translated as *frutos secos*, which, in Spanish, includes dried fruits (eg, raisins, sultanas, currants, dates) and not just walnuts, peanuts, hazelnuts, almonds, and cashew nuts.

We found that consumption of seafood and fish was not positively associated with AD. In a study on the association between dietary fats and the occurrence of atopic diseases, Dunder et al [16] found no significant differences between atopic and nonatopic children with regard to the intake of fish.

However, other studies revealed an association between the consumption of fish and AD. Tabak et al [20] found a potentially protective effect of a high intake of fish against asthma in children, while Nafstad et al [21] showed that fish consumption in the first year of life lowers the risk of developing asthma and allergic rhinitis in childhood.

In our study, the lack of association between the consumption of seafood and fish with AD may have been influenced by the variety of foods included in this group. As with nuts, the nutritional composition of seafood and fish can vary considerably in relation to the profile of fatty acids, thus complicating the interpretation of our findings. Although scientific evidence suggests that ω-3 fatty acids are present in greater quantities in certain fish and therefore protect against atopy, the design of our study did not allow us to evaluate the specific contribution of the nutrients of each food investigated. In addition, fish is a potentially allergenic food, and is the third most frequent allergen consumed in some European countries [22]: even contact or inhalation of cooking vapors can induce allergic reactions with IgE [23].

The lack of association between intake of vegetables and AD was unexpected. Many studies indicate that the consumption of foods containing antioxidants (eg, fruit and vegetables) acts as a protective factor against atopy [9,24], although other studies found a positive association [25] or none at all [26].

Although the present study did not identify an association between the Mediterranean diet score and AD, Garcia-Marcos et al [27] found that the Mediterranean diet was a potentially protective factor against severe asthma in girls, probably because it was a source of both antioxidants and cis-monounsaturated fats.

We identified an association between obesity and AD. Although evidence for an association between obesity and atopic diseases is growing [28], little is known about the underlying mechanisms. Some authors hypothesize that the increased prevalence of these diseases is caused in part by reduced immunological tolerance as a consequence of changes in the immune system induced by adipokines (leptin and adiponectin), cytokines (interleukin [IL] 6), and tumor necrosis factor alfa secreted by white adipose tissue. Increased body weight leads to higher levels of circulating IL-6, leptin, and tumor necrosis factor alfa. IL-6 and leptin downregulate the activity of regulatory T lymphocytes. Additionally, adiponectin levels, which decrease as obesity increases, down-regulate secretion of interleukin 10 from macrophages and adipocytes. These changes in IL-6, leptin, and IL-10 decrease the regulatory effect of T lymphocytes, resulting in decreased immunological tolerance to antigens [29,30].

In conclusion, although our study results do not illustrate cause and effect, they do reveal a consistent negative association between AD and milk, butter, and nuts. The fact that the findings published in this area are contradictory supports the need to conduct longitudinal research and to assess food consumption quantitatively. Nonetheless, studies such as ours, which are based on the qualitative aspects of food consumption, are important, because they show which foods could potentially contribute to development of AD.

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References

1. Rance F. Quelle est l'útilité des examens complementaires pour le diagnostic et la prise en charge de la dermatite atopique? Ann Dermatol Venereol. 2005;132:53-63.
2. Taiëb A. Dermatite atopique. Ann Dermatol Venereol. 2005;132:535-43.
3. Adinoff AD, Clark RAF. Management of skin disease. In: Bierman VCW, Pearlman DS, Shapiro GG, Busse WW, editors. Allergy, Asthma, and Immunology from Infancy to Adulthood. Philadelphia: B W Saunders Co; 1996. p. 613-32.
4. Eichenfield LF, Hanifin JM, Beck LA, Lemanske RF Jr, Sampson HA, Weiss ST, Leung DY. Atopic dermatitis and asthma: parallels in the evolution of treatment. Pediatrics. 2003;111:608-16.
5. Asher MI, Montefort S, Bjorksten B, Lai CK, Strachan DP, Weiland SK, Williams H. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multi-country cross-sectional surveys. Lancet. 2006;368:733-43.
6. Maziak W, Behrens T, BraskY TM, Duhme H, Rzehak P, Weiland SK, Keil U. Are asthma and allergies in children and adolescents increasing? Results from ISAAC, Phase I and phase III surveys in Munster, Germany. Allergy. 2003;58:572-9.
7. Black PN, Sharpe S. Dietary fat and asthma: is there a connection? Eur Respir J. 1997;10:6-12.
8. Calder PC. Polyunsaturated fatty acids and cytokine profiles: a clue to the changing prevalence of atopy? Clin Exp Allergy. 2003;33:412-5.
9. Devereux G, Seaton A. Diet as a risk factor for atopy and asthma. J Allergy Clin Immunol. 2005;115:1109-17.
10. Sausenthaler S, Koletzko B, Heinrich J. Dietary fat intake and allergic diseases. Curr Nutr Food Sci. 2006;2:351-9.
11. García-Marcos L, Castro-Rodriguez JA, Suarez-Varela MM, Garrido JB, Hernandez GG, Gimeno AM, González AL, Ruiz TR, Torres AM. A different pattern of risk factors for atopic and non-atopic wheezing in 9–12-year-old children. Pediatr Allergy Immunol. 2005;16:471-7.
12. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320:1240-3.
13. García-Marcos L, Canflanca IM, Garrido JB, Varela AL, Garcia-Hernandez G, Guillen Grima F, Gonzalez-Diaz C, Carvajal-Urueña I, Arnedo-Pena A, Busquets-Monge RM, Morales Suarez-Varela M, Blanco-Quiros A. Relationship of asthma and rhinoconjunctivitis with obesity, exercise and Mediterranean diet in Spanish schoolchildren. Thorax. 2007;62:503-8.
14. Simopoulos AP. Essential fatty acids in health and chronic disease. Am J Clin Nutr. 1999;70(Suppl):560-9.
15. Von Mutius E, Weiland SK, Fritzsch C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. Lancet. 1998;351:862-6.
16. Dunder T, Kuikka L, Turtinen J, Räsänen L, Uhari M. Diet, serum fatty acids, and atopic diseases in childhood. Allergy. 2001;56:425-8.
17. Bolte G, Frye C, Hoelscher B, Meyer I, Wjst M, Heinrich J. Margarine consumption and allergy in children. Am J Respir Crit Care Med. 2001;163:277-9.
18. Woods RK, Walters EH, Raven JM, Wolfe R, Ireland PD, Thien FC, Abramson MJ. Food and nutrient intakes and asthma risk in young adults. Am J Clin Nutr. 2003;78:414-21.
19. Willet WC, Ascherio A. Trans fatty acids: are the effects only marginal? Am J Public Health. 1994;84:722-4.
20. Tabak C, Wijga AH, de Meer G, Janssen NA, Brunekreef B, Smit HA. Diet and asthma in Dutch school children (ISAAC-2). Thorax. 2005;61:1048-53.
21. Nafstad P, Nystad W, Magnus P, Jaakkola JJ. Asthma and allergic rhinitis at 4 years of age in relation to fish consumption in infancy. J Asthma. 2003;40:343-8.
22. Crespo JF, Pascual CY, Burks AW, Helm RM, Esteban MM. Frequency of food allergy in a pediatric population from Spain. Pediatr Allergy Immunol. 1995;6:39-43.
23. Pascual CY, Reche M, Fiandor A, Valbuena T, Cuevas T, Martin EMM. Fish allergy in childhood. Pediatr Allergy Immunol. 2008;19:573-9.
24. Farchi S, Forastiere F, Agabiti N, Corbo G, Pistelli R, Fortes C, Dell'Orco V, Perucci CA. Dietary factors associated with wheezing and allergic rhinitis in children. Eur Respir J. 2003;22:772-80.
25. Kim JL, Elfman L, Mi Y, Johansson M, Smedje G, Norbäck D. Current asthma and respiratory symptoms among pupils in relation to dietary factors and allergens in the school environment. Indoor Air. 2005;15:170-82.
26. Nagel G, Linseisen J. Dietary intake of fatty acids, antioxidants and selected food groups and asthma in adults. Eur J Clin Nutr. 2005;59:8-15.
27. García-Marcos L, Canflanca IM, Garrido JB, Varela AL, Garcia-Hernandez G, Guillen Grima F, Gonzalez-Diaz C, Carvajal-Urueña I, Arnedo-Pena A, Busquets-Monge RM, Morales Suarez-Varela M, Blanco-Quiros A. Relationship of asthma and rhinoconjunctivitis with obesity, exercise

and Mediterranean diet in Spanish schoolchildren. Thorax. 2007;62:503-8.
28. Kusunoki T, Morimoto T, Nishikomori R, Heike T, Ito M, Hosoi S, Nakahata T. Obesity and the prevalence of allergic diseases in schoolchildren. Pediatr Allergy Immunol. 2008;19:527-34.
29. Hersoug LG, Linneberg A. The link between the epidemics of obesity and allergic diseases: does obesity induce decreased immune tolerance? Allergy. 2007;62:1205-13.
30. Nagel G, Koenig W, Rapp K, Wabitsch M, Zoellner I, Weiland SK. Associations of adipokines with asthma, rhinoconjunctivitis, and eczema in German schoolchildren. Pediatr Allergy Immunol. 2009;20:81-8.

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