ORIGINAL ARTICLE

Atopic Sensitization of Children with Rhinitis in Malaysia

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Summary

Atopy is defined as the genetic propensity to develop immunoglobulin E antibodies in response to exposure to allergens and assessed by skin prick test (SPT) responses to common allergens, which may contribute to the development of the clinical disorders (phenotype). Although it is generally agreed that atopy is an important risk factor for allergic diseases such as asthma, rhinitis, and eczema, the extent to which atopy accounts for these diseases is controversial. One hundred forty one children (up to 12 years) were skin prick tested to evaluate 16 foods common to the Malaysian diet and 4 common aeroallergens. Eighty-five percent of patients had positive SPT reactivity. The most commonly implicated aeroallergen and food allergen was house dust mite (HDM) and Prawn. Seventy percent had positive SPT reactivity results to HDM and 24.8% to prawns. Fifty five percent were positive to more than one allergen and 17.7% positive to single aeroallergen. The prevalence of atopy in children with history of eczema was 90%. The incidence of HDM and food allergy especially crabs and prawns, is significantly greater in Malaysian Children with rhinitis symptoms.

Key Words: Atopy, Rhinitis, Skin Prick Test, Aeroallergens, Food Allergens, Children

Introduction

Although it is generally agreed that atopy is an important risk factor for allergic diseases such as asthma, rhinitis, and eczema, the extent to which atopy accounts for these diseases is controversial. Allergic diseases affect more than 20% of the population of the United States of America[1]. The recent worldwide questionnaire survey of atopic disorders in children of 13-14 years (ISAAC) [2] showed that the prevalence of rhinoconjunctivitis ranged from 3.4% in India to 66.6% in Paraguay. A local study on perennial rhinitis in Kelantan by Elango et al shows 94% were cases of allergic rhinitis. The rising prevalence of allergic rhinitis has been reported not only in children but also in adults[3]. Another local study by Tze et al showed 96% of patients tested with skin prick test were positive to more than one allergen. Chong et al showed in 206 patients of asthma that 68% were reactive to at least one of the aeroallergens and 93.6% of which were positive to Dust mites[4]. The term Atopy should be used only when there is evidence of IgE mediated allergy. However, diseases such as asthma and perennial rhinitis may or may not be atopic. Indeed, even in atopic allergic diseases, an IgE-initiated mechanism is part of a complex cascade of cellular and humoral immune responses after allergen exposure[5]. In children, when atopy is presumed to be the cause in the vast majority of children, similar symptoms occur in nonatopic individuals[6]. The relationship of atopy to asthma and other allergic diseases is not understood clearly[6,7]. Atopic eczema is, by definition, related to atopy; however, the cause-and-effect relationship is not

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established. Eczema and sensitization to food and inhalant allergens both are common in early childhood. One birth cohort study from New Zealand examined the association of childhood asthma with sensitization to common aeroallergens, based on skin-prick testing performed at 13 years of age[8-10]. The authors report that sensitivity to house dust mite and to cat were significant risk factors for asthma, whereas sensitivity to cockroach and grass were not significant which is similar to that reported by Arshad et al[11].

Food and nutrition are essential for health and survival. Occasionally adverse reactions may occur. Adverse reactions to foods are mediated by immunologic and non-immunologic mechanisms although other immunologic mechanisms may be involved. Allergic rhinitis is the most common form of atopic disease in primary care practice affecting 10 to 20% of the general population. Total prevalence of food reactions were 19% at one year, 27% at 3 years and 8% at 6 years. On review of literature we found no previous data specific to SPT reactivity or prevalence of sensitization to common allergens in the pediatric age group in the Malaysian population.

Materials and Methods

Patient Population

The aim of this study is to describe the prevalence of sensitization to common allergens and to study the degree of association of atopy (as defined by positive skin prick test reactivity to one or more common allergens) to asthma, rhinitis, and eczema in the pediatric population presenting with nasal congestion and rhinorrhoea attending the Otorhinolaryngology clinic, Hospital National University of Malaysia (HUKM), Kuala Lumpur. This was a prospective study of 141 children (up to12 years). The skin prick test was used to evaluate 17 food items common to the Malaysian diet and 4 common aeroallergens.

This study took place as an extension of the Intensified Research in Priority areas (IRPA) project from 1993-1996. Informed consent was obtained from all parents. Information was obtained through an interview administered questionnaire for all parents on allergic symptoms mainly rhinitis, including information on gastrointestinal and dermatologic symptoms, association of foods and aeroallergens with respiratory, gastrointestinal, dermatologic, otologic and ophthalmologic symptoms and family history of allergic diseases, presence of pets etc. Those with symptoms of allergic disease underwent a skin-prick test.

Skin Prick Tests (SPT)

A total of 141 children attended the clinic and skin prick tests were performed on these children at the allergy center using the listed allergens (Table I). Standardized extracts were used when available. Histamine (0.1%) in phosphate-buffered saline and physiologic saline were used as positive and negative controls, respectively. Children were advised not to take antihistamines for one week prior to skin prick test appointment. Commercially available lancets were used to prick the epidermis through the allergen extract drops. The tests were read after 15 minutes, and mean wheal diameters were calculated (sum of the longest diameter and the diameter perpendicular to it divided by 2). In the presence of a positive control (3 mm), a mean wheal diameter of at least 3mm greater than the negative control was taken as positive. The surrounding erythema was ignored. The strength of each reaction relative to the control was recorded on a Bencard skin reaction test as follows (Table II).

Wheal of 3 mm or more in diameter were regarded as positive in the absence of a reaction to normal saline and subjects with one or more positive reactions were considered to have atopy.

Data Analysis

The statistical software SPSS Version 10.0 was used for data entry. Associations between variables were analyzed using Chi (c) Square tests. A p value of less than 0.05 was considered to be statistically significant.

Results

We performed the skin prick test as a tool to determine the skin test reactivity to different aeroallergens and food allergens on 141 children aged up to 12 years with history of at least one allergic symptom. The majority of children (54.6%) were sensitized to more than one allergen which concurs with a report by Arshad et al which reported that majority of children with allergic disorders were sensitized to more than one allergen[11]. Currently, allergic rhinitis is the most common allergic disease and one of the leading chronic conditions in children less than 18 years. It has been reported that majority of patients with nasal symptoms especially rhinitis accounted for 70% of the respiratory symptoms observed in children. In our study 69.5% were positive

to house dust mite which is the major cause of allergic rhinitis followed by Cat fur at 44%. (Fig 1 and Fig 2)

It was observed that 90.7% patients with history of asthma had positive SPT results and 85% had positivity when they presented with history of rhinitis. Children with asthma were found to have the highest positivity to Mixed Mites 79.1% followed by Cat fur 58.1% and cockroach 37.2%. (Fig 3)

Food allergy occurs approximately in 6% to 8% of children[12, 13]. In this study 35 out of 141(24.8%) of the children had skin test positivity to sea food allergens and the most common was Crab and prawns in contrast with other studies where children had allergy to cows milk, eggs, peanut, soybeans and wheat[13]. (Fig 4)

Children here in Malaysia are exposed to seafood and fishes, which is a staple diet at an early age, as early as 1 year. Seafood allergy was also found in other countries (South Africa, Scandinavian countries and Spain). Lopata et al[13] reported that people in South Africa had increased consumption of sea food due to the promotion of healthy diet which has led to more frequent reporting of allergic reactions (50% to crustaceans, 30% to mollusks and 20% to fish)[14]. We have looked into the association of 5 different variables with different disease conditions like Asthma, Rhinitis, Eczema (Table III) and we found that there was a statistical significance in the association between :-

1. Rhinitis and House Dust mite.
2. Asthma with cat fur, mixed grass and crab. Cockroach is a loose association as it is approaching significance.
3. Eczema had a significant association with crab.

No food allergens had any significance with either rhinitis or asthma.

Table I: The panel of allergens used in the skin-prick tests

Food Allergens		Aero Allergens
Milk		Dust Mites
Egg	Crab	Cockroach
Soya	Prawn	Cat Fur
Wheat	Squid	Mixed Grass
Rice	Cockle	
Mutton	Spanish Mackeral	
Banana	Indian Mackeral	
Chicken	Anchovy	
Beef		

Table II: The strength of reaction relative to the control on Bencard skin reaction test

Reaction	Size of Wheal	Strength
Negative (-)	No Wheal or Wheal <3mm	-
Positive Mild	Wheal 3mm	+
Positive Moderate	Wheal 3-5mm	++
Positive High	Wheal >5mm	+++
Positive Gross	Wheal with Pseudopodia	++++

Table III: Statistical Correlation of Allergens vs Symptoms

Allergen	Asthma (p)	Rhinitis (p)	Eczema (p)
House dust mites Positive (n=98) Negative (n=43)	0.074	0.016	0.944
Cockroach Positive (n=38) Negative (n=103)	0.055	0.160	0.702
Cat Fur Positive (n=62) Negative (n=79)	0.025	0.439	0.917
Mixed Grass Positive (n=10) Negative (n=131)	0.036	0.752	0.391
Crab Positive (n=34) Negative (107)	0.048	0.712	0.015

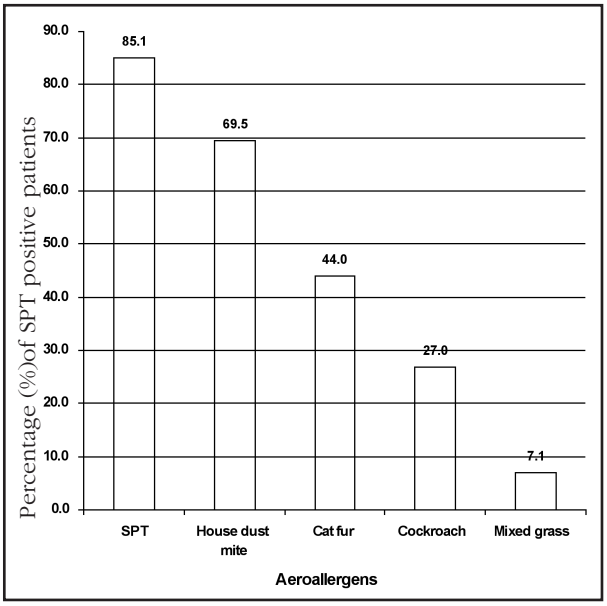

Fig. 1: SPT reactivity to common aero allergens

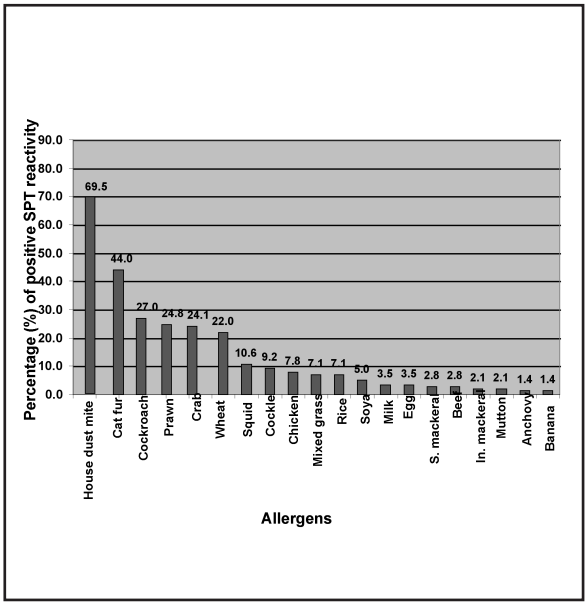

Fig. 2: SPT reactivity to common allergens in pediatric population

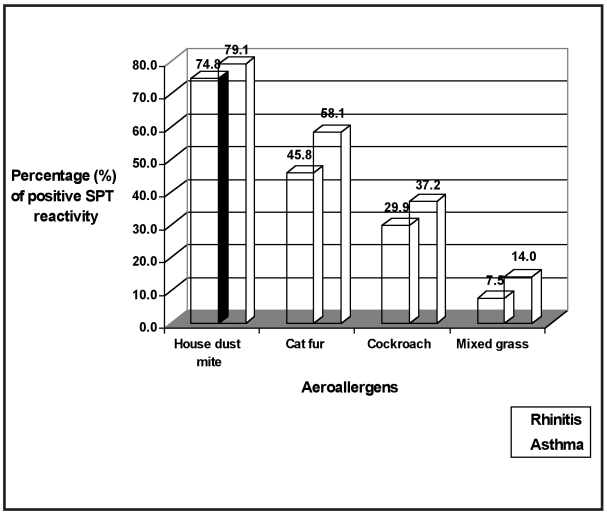

Fig. 3: Pattern of SPT aero allergens reactivity in rhinitis and asthma

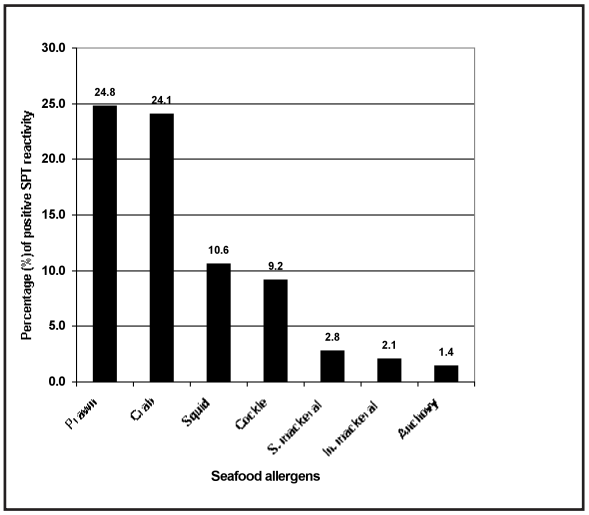

Fig. 4: SPT Seafood reactivity in pediatric population

Discussion

Allergies are common in childhood. As the child grows, foods are replaced by inhalant allergens. Allergic rhinitis usually presents in childhood. Incidence continues to increase until the fourth decade of life when symptoms begin to fade, however symptoms can develop at any age[6]. A recent report[15] describing the natural course of sensitization to food and aeroallergens showed a decrease in the sensitization to food allergen from 10% at 1 year to 3% at 6 years. At the same time, sensitization to inhalant allergens increased from 1.5% at 1 year to 26% at 6 years of age. In our study, 69.5% of the atopic children could be identified with positive skin-prick test reactivity to house dust mite alone and 72.5% when 4 common inhalant allergens were included in the skin-prick test battery. This is a useful guide when screening children for atopy. The sensitization to house dust mite is similar to the results of Arshad et al., which showed sensitivity to dust mites at 60%[11].

The prevalence of atopy may somewhat vary in other studies. Some authors, using a smaller wheal size of 2 mm as the cut-off for skin-prick test positive reactivity, reported a higher prevalence of atopy[8]. The lowest limit of skin-prick test reactivity that reliably predicts radioallergosorbent assay test positivity is, in fact, a larger wheal size of 4 to 5 mm[16]. Therefore, a 3-mm cutoff for skin-prick test positive reactivity, which is used commonly in clinical and epidemiologic studies,[17-20] was thought to be more appropriate and has been used routinely at our Allergy Center.

Although, in theory, it is possible that a child may be sensitized solely to an uncommon allergen not included in the battery, this would be a rare occurrence. We believe that by using this panel, we were able to detect most of the atopic children among those given skin-prick tests in this study. Unfortunately, serum total and specific IgE levels were not measured to strengthen the validity of skin-prick test responses. However, total IgE may be within the age-adjusted normal range in some atopic individuals[21].

In children there is evidence that symptoms of allergic rhinitis can impair cognitive functioning, which can be further impaired by use of first generation antihistamines[22]. Result of studies have shown that sensitization to indoor allergens (dust mites, animal dander's, cockroaches, molds) is a risk factor in children for developing allergic diseases[23]. Allergic sensitization to strong indoor allergens can occur when a child is as young as 2 years[24].

Food allergies affect all ages but infants are particularly susceptible especially those with allergic or atopic

parents. In our study it was found that 83.7% were atopic if mother had history of allergies and 94.2% if father had positive history. However, normal infants may also be sensitive to food allergens because of immaturity of their digestive tract or immune system.

Food allergy rarely causes symptoms of allergic rhinitis. Foods are common allergens in early childhood. As a child grows foods are replaced by inhalant allergens. Foods are among the first proteins in a child's experience that can cause allergic reactions. Subsequently, the allergic child tends to become sensitized to agents in the home such as House Dust mites, animal dander, and cockroach. Ultimately these children react to seasonal allergens such as tree, grass or weed pollens when they are exposed to the outside environment[25]. It was found that sensitization to inhalant allergens was relatively common at 19.2% as compared to food allergens as reported by Arshad et al[11]. In our study we found that it was in concordance with that of Arshad et al[11] where the incidence of aeroallergens was more than food allergens. In our study we found the incidence of aeroallergens was 72.3% and food was 54.6%.

The main symptoms from adverse reactions to foods are gastrointestinal, ophthalmologic, dermatologic and less frequently respiratory. Food allergy in most patients cannot be diagnosed by symptoms alone because symptoms can vary and often fluctuate. The foods eliciting most of the SPT-positive reactivity in this study are foods common in the everyday diet of Malaysians. Our findings of high incidence of aeroallergens are consistent with Arshad et al[11].

South East Asian homes tend to be more crowded than western homes and thus are exposed to more air pollutants, tobacco smoke and certain dietary substances that could potentially enhance allergic sensitization and increase allergic symptoms. Nitrogen dioxide from vehicle emissions, and haze from uncontrolled forest fires are major components of ambient and indoor air pollutants in South East Asian countries. Two reports revealed a synergistic effect between exposure to NO2 and HDM extract in causing broncho-constrictive responses in mite sensitive persons with asthma. The common SPT positive foods, in order of frequency were prawn, crab, wheat, squid, cockle, chicken, rice, soya, milk, egg. A common everyday food condiment in Malaysia is belachan (concentrated dried shrimp paste). Cross reactivity between tropomyosin, a protein found in shrimp and also present in HDM is possible[26]. The high incidence of food allergy in our study could be partially due to cross reactivity between foods and /or aeroallergens.

Asthma, eczema, and perennial rhinitis are more complex disorders. There is evidence to support the role of total IgE in asthma which includes the correlation of elevated serum levels of IgE with self-reported asthma symptoms [27] and airway hyperresponsiveness[27, 28]. However, other studies cast doubt on the role of total IgE as an important indicator of respiratory allergic diseases[29]. Serum IgE levels in the African population have been reported to be higher in people who do not have asthma than in people who do[30]. Similar symptoms occur in the absence of sensitization (non-allergic or intrinsic disease). Even in allergic eczema, non-IgE-mediated inflammatory mechanisms may play a significant role. For asthma, rhinitis, and eczema, it may be argued that the primary abnormality is genetically determined and affects the airway/nasal epithelium [31] and/or dermis/epidermis[32].

Conclusion

Allergies are common in children and hence allergy testing should be conducted with a common panel of both aeroallergens and food allergens. Children with allergies must be assessed in the Allergy clinic by taking a detailed history and evaluation by either skin tests or in vitro tests. Eighteen percent of children are sensitive to monoallergens and those that do not respond to pharmacotherapy and avoidance, options of Immunotherapy should be made available to appropriate candidates to prevent the allergy march.

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References

1. American Academy of Allergy, Asthma and Immunology. Task force on Allergic Disorders. Executive summary Report (1998).
2. World wide variation in prevalence of symptoms of asthma,allergic rhinoconjunctivitis and atopic eczema ISAAC. The international study of Asthma and Allergies in childhood (ISAAC Steering committee). Eur. Resp. J. 1998; 12: 315-35.
3. Lang DM. Management of Allergic Rhinitis. Geriatric Times. March/April 2002; 3(2) Special Report.
4. Liam CK, Loo KL, Wong CM, Lim KH, Lee TC. Skin prick test reactivity to common aeroallergens in asthmatic patients with and without rhinitis. Respiratory 2002; 7(4): 345-50.
5. Macaubas C, Prescott S, Smallacombe T, et al. Perinatal and Early Childhood Cytokine Responses to Environmental Allergens. New York, NY: Marcel Dekker; 1999.
6. Gergen PJ and Turkeltaub PC. The association of individual allergen reactivity with respiratory disease in a national sample: data from the second National Health and Nutrition Examination Survey, 1976-80 (NHANES-II). J Allergy Clin Immunol. 1992; 90: 579-88.
7. Pearce N, Pekkanen J, Beasley R. How much asthma is really attributable to atopy? Thorax 1999; 54: 268-72.
8. Sears MR, Herbison GP, Holdaway MD, Hewitt CJ, Flannery EM, Silva PA. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. Clin Exp Allergy 1989; 19: 419-24.
9. Sears MR, Burrows B, Flannery EM, Herbison GP, Holdaway MD Atopy in childhood I. Gender and allergen related risks for development of hay fever and asthma. Clin Exp Allergy 1993; 23: 941-48.
10. Sears MR, Burrows B, Herbison GP, Holdaway MD, Flannery EM. Atopy in childhood II. Relationship to airway responsiveness, hay fever and asthma. Clin Exp Allergy 1993; 23: 949-56.
11. Arshad SH, Tariq SM, Matthews S, and Hakim E. Sensitization to Common Allergens and Its Association With Allergic Disorders at Age 4 Years: A Whole Population Birth Cohort Study. Pediatrics. 2001; 108(2) Part 1 of 2:e33.
12. A Wesley Burks Jr. Childhood food allergy. Immunology and Allergy clinics of North America. 1999; 19(2): 398-408.
13. Sicherer SH and Sampson HA. Peanut and tree nut allergy. Current Opinion in Paediatrics 2000; 13: 567-73.
14. Lopata AL and Jeebhay MF. Seafood Allergy in South Africa-Studies in the domestic and Occupational Setting. ACI international 2001; 13: 204-10.
15. Kulig M, Bergmann R, Klettke U, Wahn V, Tacke U, Wahn U. Natural course of sensitization to food and inhalant allergens during the first 6 years of life. J Allergy Clin Immunol 1999; 103: 1173-179.
16. Pastorello EA. Skin tests for diagnosis of IgE-mediated allergy. Allergy 1993; 48: 57-59.
17. Yemaneberhan H, Bekele Z, Venn A, Lewis S, Parry E, Britton J. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. Lancet 1997; 350: 85-90.
18. Keur J, Frischer T, Karamaus W. Early childhood risk factors for sensitization at school age. J Allergy Clin Immunol 1992; 90: 358-63.
19. Leung R, Ho P, Lam CWK, Lai CKW. Sensitization to inhaled allergens as a risk factor for asthma and allergic disease in Chinese population. J Allergy Clin Immunol 1997; 99: 594-99.
20. Wickens K, Pearce N, Seibers R. Indoor environment, atopy and the risk of asthma in children in New Zealand. Pediatr Allergy Immunol 1999; 10: 199-208.
21. Williams PB, Dolen WK, Koepke JW. Comparison of skin testing and three in vitro assays for specific IgE in the clinical evaluation of immediate hypersensitivity. Ann Allergy 1992; 68: 35-45.
22. Vuurman EF, Van Veggel LM, Uiterwijk MM, et al. Seasonal allergic rhinitis & antihistamine effects on children's learning. Ann Allergy 1993; 71; 121-26.
23. Jeffrey A and German. Environmental control of Allergic diseases. American Family Physician August(1) 2002; 66: 421-6, 429-30.
24. Becker JM. Allergic rhinitis. Emedicine.com Journal, August 2004.
25. Anderson JA. Milk, Eggs and Peanuts: Food allergies in children. American Family Physician October 1997; 56(5): 1365-77.

26. Gendeh BS, Murad S, Razi AM, Abdullah N, Mohamed AS, and Khalid BK, SPT reactivity to foods in adult Malaysian with rhinitis. Otolaryngology-Head & Neck Surgery, May 2000; 122(5): 758 -62.

27. Burrows B, Martinez FD, Halonen M, Barbee RA, Cline MG. Association of asthma with serum IgE levels and skin-test reactivity to allergens. N Engl J Med 1989; 320: 271-77.

28. Sunyer J, Anto JM, Sabria J. Relationship between serum IgE and airway responsiveness in adults with asthma. J Allergy Clin Immunol 1995; 95: 699-706.

29. Tschopp JM, Sistek D, Schindler C. Current allergic asthma and rhinitis: diagnostic efficiency of three commonly used atopic markers (IgE, skin prick tests, and Phadiatop). Results from 8329 randomized adults from the Sapaldia Study. Swiss Study on Air Pollution and Lung Diseases in Adults. Allergy 1998; 53: 608-13.

30. Scrivener S and Britton J. Immunoglobulin E and allergic disease in Africa. Clin Exp Allergy 2000; 30: 304-307.

31. Doull IJM, Lawrence S, Watson M. Allelic association of gene markers on chromosomes 5q and 11q with atopy and bronchial hyperresponsiveness. Am J Respir Crit Care Med 1996; 153: 1280-1284.

32. Olesen AB, Ellingsen AR, Olesen H, Juul S, Thestrup-Pedersen K. Atopic dermatitis and birth factors: historical follow-up by record linkage. BMJ 1997; 314: 1004-1008.