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# Epidemiology of Atopy in 220 Children: Diagnostic Reliability of Skin Prick Tests, Total and Specific IgE Levels

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## Abstract

### Background

We have prospectively studied 220 children attending our Division because they suffered from atopic dermatitis (AD), asthma, and allergic rhinitis (AR) to assess the epidemiology of atopic diseases, and effectiveness of the diagnostic tests commonly used in allergic children.

### Patients and Methods

Among the 220 children there were 142 males (64.5%) and 78 females (35.5%) aged as follows: 57 (25.9%) 0-2 year old, 48 (21.8%) 2-4 year old, 49 (22.3%) 4-6 year old, 66 (30%) >6 year old. The diagnosis included family and personal history, physical examination, skin prick tests (SPT) and total and specific IgE (sIgE) levels. We tested inhalant and food allergens.

### Results

There were 101 asthmatic, 88 with AD, and 31 children with AR. The analysis of variance confirmed the age influence of PRIST with a high significance (p= 0.0001). SPTs were prevalent in all groups for Der p, but casein only in one group, and Lolium perenne only in two groups. RAST showed a higher uniformity, that is CM (cow's milk) and egg for one group, Der p and Lolium perenne for the remaining groups several correlations among diagnostic tests and the age of children were evaluated with the analysis of variance.

### Conclusion

We emphasize that atopic diseases are genetically transmitted, that AD develops at a younger age than asthma (p= 0.0052), and that SPTs have a greater effectiveness for inhalant allergens, positive at all age levels; in food allergy (FA) SPTs are less adequate and feasible

Keywords: Epidemiology of atopic diseases; Genetics of atopic diseases; Children; Skin prick tests; Total and specific IgE determination

## Introduction

The experiences stemming from daily practice and the related studies have shown an increase of atopic disease prevalence particularly accelerated in the last 20 years, and this progress is not due only to the improvement of diagnostic facilities [1-4]. Within 17 years the atopic disease prevalence in school children increased: asthma from 5% to 12%; AR from 9% to 15%, but AD from 5% to 16%. The increase by 320% of AD prevalence is not surpassed by asthma and AR [5].

SPTs are considered as the more rapid and effective tool for the diagnosis of pediatric allergies [6]. In two studies we have found that the statistical analysis has shown a high significant difference for SPTs compared with RAST (p= 0.0011) [7] and 0.0001 [8]. Concerning the possible drawbacks of SPTs, we believe that the allergenic extracts, presently at hand for diagnostic use, are better standardized although the epitopes of the major part of allergens have not yet been detected. However several food allergens have been characterized, especially with the use of recombinant allergens [9].

Total IgE levels are on average significantly elevated in atopic diseases, such as AD, allergic asthma, AR, etc [10]. Therefore the determination of IgE serum levels is widely used in the diagnostic work-up of such afflictions, to facilitate the identification of neonates at risk of atopy, and discriminate between atopic and not atopic subjects, etc [11]. Total IgE >2 SD (standard deviation) were found also in 18/53 (34%) children aged 2-5 years with serous otitis media [10]. It is known that serum sIgE antibodies (RAST) are specifically directed against certain allergens, present in the serum of individuals affected with IgE-mediated allergic disorders [12]. As for SPTs also in vitro techniques can generate false-positive or false-negative reactions.

On the other hand, both PRIST and RAST are available for the diagnosis of allergic disorders in some children. In particular in young infants it is possible to detect low concentrations of sIgE (class 1 RAST) against some foods, above all CM, even without evident clinical manifestations. This can be estimated as an indirect expression of the increased permeability of gut mucosa to the uptake of macromolecular antigens [10]. The SPT positive predictive value is reduced, but the positive predictive value is high (83.5%), whereas RAST negative accuracy is lower than that of STPs and consequently scarcely useful for FA diagnosis [13]. In this paper we have evaluated in 220 children the epidemiology of atopy, and studied the effectiveness of atopy diagnosis, as related to the reliability of in vitro tests in comparison with SPTs, in the diagnostic approach.

## Patients and Methods

### Patients

Among the children attending the Division of Allergy and Immunology of the Rome University "La Sapienza", we have consecutively examined a cohort of 220 children, coming for the first visit to our diagnostic protocol. We assessed whether the babies were "at risk" of atopic disease because of a positive family history of atopy since one or both parents and/or other siblings suffered from asthma, or AD or AR. The diagnosis of atopic diseases in the children was done according the following criteria: clinical history, physical examination and positive SPTs and/or RAST to the most common inhalant and/or food allergens.

### According to History, all Children were affected with AD, Asthma and AR

The diagnosis of AD was made according to Hanifin and Rajka criteria [14], the severity score was evaluated with body diagrams according to the SCORAD index [15]:

• For the diagnosis of asthma, 3 episodes of wheezing without fever were required.

• For the diagnosis of AR, nasal discharge and/or blockage occurring continuously for atleast 4 weeks plus the typical pale aspect of allergic mucosa on rhinoscopy, without any sign of infectious rhinitis in other relatives was required.

### Informed Consent

Informed consent was obtained from parents of each child.

### Methods: Skin Prick Test

Appropriate emergency equipment and medications were available on site. Parents were required to discontinue all oral/topical corticosteroids during the trial, antihistamines for 7 days, and all ß-agonists for 12hr before SPT application. Skin testing was done at baseline by the prick method by a doctor trained in allergy with the co-operation of a qualified nurse. The skin was marked with a ballpoint pen for the allergens to be tested. The babies were tested with: histamine hydrochloride (1 mg/ml) as a positive control, isotonic saline as a negative control, whole CM proteins, casein, lactalbumin, egg, fish (cod), Dermatophagoides pteronyssinus, Alternaria alternata, Parietaria officinalis, Lolium perenne, and Olea europea (SARM, Roma, Italy). The diagnostic extract of each individual allergen was placed on the volar surface of the forearm as drops through which the skin was superficially pricked with a straight pin for one second. A new pin was used for each SPT and then discarded, and the drop of the extract was then wiped off about one minute after the prick [16].

SPTs were read at 20 minutes and considered positive as follows:

+ when the wheal was the half of the histamine wheal;

++ when the wheal was equal to the histamine wheal;

+++ when the wheal was two-fold the histamine wheal;

++++ when the wheal was more than two-fold the histamine wheal [17].

We considered as positive only the children with a mean wheal diameter of 3 mm or larger (+++ o ++++) than the negative (saline) control. A positive (histamine, 1:1000) control was performed to ensure the absence of any anti-histamine drug interference [18].

### Total IgE

• The determination of the total serum IgE levels was done by paper radio immunosorbent test (PRIST, Pharmacia Diagnostics AB, Sweden) and results were expressed in International Units per ml.

• Specific IgE antibodies and determination of specific IgE levels by radio allergosorbent test (Phadezym RAST, Pharmacia Diagnostics).

• RAST results are expressed in » RAST Units « (PRU = Phadebas RAST Unit) as follows:

1st class= IgE levels < 0.35 IU/ml

2nd class= IgE levels > 0.35 IU/ml and lesser than 0.7 IU/ml

3rd class= IgE levels between 0.7 IU/ml and 171 U/ml

4th class= IgE levels higher than 17 IU/ml

• Only RAST results > 0.35 IU/ml were considered positive.

## Statistical Analysis

Data were statistically analyzed using the Student t test, the X2 test, and variance analysis.

## Results

• Clinical characteristics

• Sex and age

• Among the 220 children studied by us, 142 (64.5%) were males, 78 (35.5%) females; their age was as follows: Group A no. 57 (25.9%) between 0 and 2 years, Group B no. 48 (21.8%) between 2 and 4 years, Group C no. 49 (22.3%) between 4 and 6 years, Group D no. 66 (30%) between 6 and 10 years

• Atopic disease present in the parents

• Among the parents 157 were affected from atopic disease (71.4%), 87 fathers and 70 mothers, in addition to 36 brothers or sisters. Family history was therefore positive in 157, negative in 63 children (p= 0.0001)

• Atopic disease present in the children

• Asthma: 101 children (45.9%)

• AD: 88 children (40%)

• AR: 31 children (14.1%)

• The children with AD showed a mean score (SCORAD index) of 67.2

## Epidemiology of Atopic Diseases

It is outlined about prevalence of atopic disease, the progressive increase of asthma prevalence and the reduction of AD according to age (which in the study by Hattevig et al. increases more than 30% at the last follow-up) [19]. The data show that the age of AD onset is much lower than that of asthma: p= 0.0052, as confirmed by recent studies [4,19], which continues its progression along the child growth: at 6-10 years it is more frequent than AD (p= 0.0017). In particular, among 101 children with asthma, 21 (21%) belong to the A, 20 (20%) to the B, 25 (25%) to the C, and 35 (35%) to the D Group; of 88 children with AD 36 (41%) belong to the A, 23 (26%) to the B, 16 (18%) to the C, and 13 (15%) to the D Group; of 31 children with RA, none belongs A, 5 (16%) belong to the B, 8 (26%) to the C, and 18 (58%) to the D Group.

## SPTs

• SPTs were positive (+++ or ++++) for the following allergens:

• Alternaria alternata 10/82 (12%)

• Der p 89/146 (61%)

• Lolium perenne 28/107 (26%)

• Parietaria officinalis 2/73 (3%)

• CM proteins 33/206 (16%)

• Egg 11/103 (11%)

• Fish 0

• In total, 47/220 children (21.4%) had negative SPTs, 66 (30%) one negative SPT, 107/220 (48.6%) had 173 positive SPTs, so divisible: 47 (27.2%) SPTs positive for one allergen and 126 (72.8%) associated positivities.

The prevalence of different allergens according to the age classes, based on SPT results is the following:

• Group A: casein and Der p

• Group B: Der p

• Group C: Der p, Lolium perenne

• Group D: Der p, Lolium perenne

• Total IgE levels: Arithmetic mean 226.7 IU/ml ± 246.9, geometric mean (GM) 143.8 IU/ml.

• As regards the distribution of GM values according to the 4 age classes we found the following data:

Group A: 73.3 IU/ml

Group B: 118 IU/ml

Group C: 216 IU/ml

Group D: 190 IU/ml

• The variance analysis has confirmed the influence of age on PRIST values evidencing a high statistically significant difference (p< 0.0001).

## Specific IgE Levels

They resulted positive as follows:

• Alternaria alternata 20/78 (26%)

• Der p 135/155 (87%)

• Lolium perenne 70/109 (64%)

• Parietaria officinalis 7/45 (16%)

• Casein 1/13 (8%)

• CM 56/142 (39%)

• Egg 68/136 (50%)

• Fish 8/27 (30%)

• Others 18/44 (41%)

• It was observed that 38 children were RAST-negative (17.3%) and 182 RAST-positive (82.7%)

The prevalence of different allergens according to the age classes, based on RAST results is the following:

• Group A: CM and egg

• Group B: Der p

• Groups C-D: Der p and Lolium perenne

• The variance analysis did not confirm the influence of age on RAST results

The prevalence of different allergens according to the atopic diseases diagnosed by us is the following:

• Asthma: The main positivities are for Der p, as follows: SPTs 47 cases (54%), RAST 52 cases (51%), additional positivities were for pollens, as follows: SPTs 17 cases (19%), RAST 22 cases (25%)

• AD: The SPTs more significantly positive are for casein: 22 cases (34%), for RAST CM (27%) and egg (26%), altogether 60%

• AR: All SPTs and RAST were positive only for Lolium perenne

## Correlations between Diagnostic Methods

• The analysis of variance between SPTs, PRIST and RAST has elicited a statistically very significant difference between SPTs and both PRIST ($p < 0.0001$) and RAST ($p < 0.0001$) in favor of SPTs.

• As regards the correlation SPT-PRIST, there is a GM increase parallel with the increase of SPT positivity, while in children with SPTs = +/++ the PRIST GM is among 63.1 and 122.7, but in children with a +++ positivity has gone up to 233.3 and to 429.5 if ++++.

• The correlation PRIST-RAST is regulated according to the levels of pertinent concentrations, in the sense that in 92% of children who had positive RAST classes ($2^{nd}$-$3^{rd}$ class) the PRIST values were also as low as <100 IU/ml; however the concordance is not univocal, since titres of total IgE >100 IU/ml were found also in 10 children with negative RAST.

## Discussion

In this prospective study on 220 children affected with different atopic diseases we have found an important confirmation of previous data that atopic diseases increase especially in young children at risk (offsprings of allergic parents), who already in their first year of life suffer from AD and FA and exhibit wheezing: AD/FA onset is in 70-100%, AR in 69-96% and asthma in 34.5-56.2% of cases. In this study we have confirmed that the AD age of onset is earlier than that of asthma, which continues its march during the child growth: at 6-10 years the incidence is higher than that of AD. As regards AR, it is practically absent at 0-2 years, with a scarce prevalence at 6-10 years [4].

Considering the age of the four groups of children studied, the analysis of variance has confirmed the influence of the age of children on atopy development on PRIST values with a high statistically significant difference ($p< 0.0001$). Another significant difference regarded the genetically origin of atopy development ($p= 0.0001$).

An additional relevant result, is a significant difference between in vivo and in vitro tests, and a poor specificity and sensitivity of in vitro tests, that is not correlated with two milestones in the diagnosis of atopic disease in pediatrics: clinical history and examination [17]. In addition, among the comparisons done by us, the more significant one appears to be that on the prevalence of positivities of diverse allergens. With respect to SPTs, there was a prevalence of Der p in all groups, but starting already in the youngest group, foods only in Group A, and pollens only in Groups C and D. On the contrary RAST has shown a higher uniformity: foods in Group A, Der p and pollens in Groups B-D. Such data on the one hand confirms the greater specialization of SPTs for inhalant allergens, on the other their presence at all age levels; while it seems to be noteworthy that RAST correctly assigns to the younger children the greater prevalence of foods.

SPTs, when employed either correctly or with standardized extracts, are rapid, safe, sensitive, inexpensive on a per test basis and the results are reliable, since they are largely experimented: consequently SPT is the more employed method for the diagnosis of atopic disease elicited by type I immune reactions, where sensitizing antibodies are present [20,21]. SPT is more sensible and specific in respiratory allergy, therefore represents the method of first choice when an IgE-mediated disease triggered by inhalants is suspected. The diagnostic role of SPTs with foods is quite trivial in the largest part of cases [22]. Moreover in certain cases, as for example in AD, the unique skin reactivity of such children makes the SPT diagnostic interpretation quite difficult [23,24]. Children with SPTs positive for foods are often detected, however well tolerated. In FA SPTs are less reliable, due to unlike factors, as follows:

• Liability of some allergens

• Cross-reactivity between antigens belonging to different vegetal species

• Loss of antigenicity during extraction

• Short comings of allergenic extracts

We show the cases of false positivity/negativity of SPTs [17,20,21].

However SPTs are defined as fairly reliable in FA for CM, egg, soy, fish, peanuts, but Burks et al. [25] and Sampson [26] have demonstrated that SPTs elicit a greater number of false-positivities in comparison with DBPCFC (Double-blind, placebo-controlled food challenge), where the difference is increased up to 48.6% [26] and in the study by Burks et al. the concordance is 35.4% [25].

In contrast to these studies, the sensitivity and specificity of SPT and sIgE in pediatric trials is fairly good [27]: the SPT sensitivity is 1 for all foods, but 0.28 for CM, but the specificity for CM is high (0.80), and for other food is 0.59 (mean). sIgE sensitivity is high for cod (0.91), and the specificity is very high for peanut and cod, thus SPT sensitivity is better than that of RAST and the reverse is for specificity [13].

A particular problem is the exact interpretation of SPT negativity: Sampson [26] has suggested that in children with suspected FA and negative SPTs for one or more incriminated foods virtually exclude immediate food hypersensitivity, thus making the diagnosis of FA very unlikely in 99% and in 95% of cases, respectively. To evaluate whether a negative SPT to CM can be a good negative indicator of CM allergy (CMA), 35 children with AD and negative SPTs to CM among all children with suspected CMA underwent an open challenge tests to CM, however only 7 children with negative SPTs to CM had a positive CM-challenge. We conclude that a method with a 20% ineffectiveness cannot be considered as fully reliable [28]. However Rosen et al. [29] have recognized that negative SPTs to foods should be verified with DBPCFCs Allergy skin testing infants: may be a safe or risky procedure? [30] Deveney et al. [31] have reported 6 infants less than 6 months of age out of 1,152 tested during three years (0.17% for each year) who suffered from generalized allergic reactions after prick tests with fresh foods. Each infant was tested with several foods (from 2 to 4 foods) Moreover, the same food was tested in duplicate in the same baby, so it is unclear

which particular food elicited the reactions [31]. Several adverse reactions occurred, but in intradermally tested children [30]. Since about 30 years, we everyday perform SPTs in infants and children, according to fixed rules but have never seen such severe reactions. A study on 497,656 SPTs has ascertained that systemic reactions occurred in 6 adults who recovered fully within one hour [32]. In 544 children, 97 of whom aged 0-1 years [33], so about in the age-range of the 6 infants [31], in 467 children (median age 3 years, with about 38% aged < 2 years [34], and in 300 children with allergic asthma [7] no reaction to SPTs occurred [33,34].

If SPTs, expressing an IgE-mediated reaction, have gained a wide diagnostic application, PRIST is a useful diagnostic test, however not always can be employed alone [17,20,21]. However, it is suggested that when skin wheal diameter is greater than 3mm, that is CM 8mm, egg 7mm, and peanut 8mm, smaller in children aged <2 years: 6, 5 and 4mm respectively, with a 100% specificity, it could be equivalent to a challenge test positive result [34]. One major disadvantage of total IgE levels is that they can be elevated in apparently healthy individuals; furthermore high IgE titres are seen even in not allergic conditions such as helminth infestation, viral infections, rheumatoid arthritis, AIDS, etc [17,20,21], whereas low IgE levels can be observed also in allergic subjects [10,20]. In particular a concordance with the above data stems from the results of the present work, because 11 children (5%), although affected with allergic illnesses, failed to have elevated PRIST values. Nevertheless the PRIST test can also be a useful initial test: frequently high total IgE concentrations are found in allergic subjects, and may represent a useful tool in identifying specific sensibility to one or more allergens, on the contrary a normal PRIST result exclude with high probability RAST positivity [35].

The RAST characteristics are evident [17,20,21]. In the group of children studied a strict correlation exists between total and specific IgE levels, confirmed, compared with SPTs, by the analysis of variance ($p< 0.0001$). Again in 10 children (5%) we found that elevated total IgE titres were accompanied with no RAST positivity [36]. This data confirms that in the indications given from study results we should make due allowances for the existence of factors able to modify the correlation between and RAST: in the first place the false RAST positivities. These are due, among others, to the phenomenon of "aspecific binding" between the serum IgE and polyanions present on the cellulose disc utilized the test, rather frequent in the case of elevated IgE titres in the sample of serum examined for the test [37]. The substantial correlation between PRIST values and positive RAST results can partially credited to such phenomenon, underlining the necessity of taking into account an inherent degree of uncertainty, thereby confirming that the results for uncommon allergens may be misleading [21]. Returning to false RAST positivities, they are partly related to a poor purification and standardization of the allergen under exam: such a challenge, notably evident in the case of FA, is less apparent for inhalant allergens which undoubtedly form the most im-portant field of RAST application [23,38].

Recent works have suggested that there are advantages to in vitro test results with assay systems that provide results in terms of mass units of IgE for food [39] and inhalant [40] allergens. For a number of food allergens (CM, egg, peanut, fish) it was possible to define a serum IgE level above which positive DBPCFCs occurred with 95% certainty [39]. Similarly, a single test based on IgE antibodies may be effective to diagnose sensitization to common inhalant allergens [41].

## Conclusion

• SPTs are indicators of IgE-mediated allergy, do not diagnose it, as a consequence the skilled pediatrician allergist should evaluate whether the presence of IgE antibodies is responsible for the clinical illness.

• The PRIST determination, to be always appraised in correlation with the age of the child, can be utilized as a marker of an allergic state [10,34], but it is necessary to identify the offending allergen with the accomplishment of allergometric testing and completed with an accurate clinical examination.

• We deem that RAST should not be viewed, as often is the case, the first (and only) exam for the diagnosis of allergic disorders, except in cases entirely specific, such as the risk of systemic reactions following the exposition to the foreign allergen including the diagnosis of Hymenoptera sensitivity, severe AD with marked dermographism, the impossibility of discontinuing a medication, or the presence of a combative child.

• The analysis of variance between SPTs, PRIST and RAST has elicited a statistically very significant difference between SPTs and both PRIST ($p< 0.0001$) and RAST ($p< 0.0001$) in favor of SPTs.

• In conclusion, all the analyses done are in favor of SPTs.

## References


1. Aberg N, Engström I (1990) Natural history of allergic diseases in children. Acta Paediatr Scand 79: 206-211.
2. Croner S (1991) Atopic dermatitis- epidemiology. Pediatr Allergy Immunol 2 (suppl 1): 6-7.
3. Duffy DL, Mitchell CA (1991) Respiratory symptoms in Queensland school children: an association between month of birth and respiratory illness. Clin Exp Allergy 21: 231-233.
4. Cantani A (1999) The growing genetic links and the early onset of atopic diseases in children stress the unique role of the atopic march: a meta-analysis. J Investig Allergol Clin Immunol 9: 314-320.
5. Burr ML, Butland BK, King S, Vaughan-Williams E (1989) Changes in asthma prevalence: two surveys 15 years apart. Arch Dis Child 64: 1452-1456.
6. Vierucci A, Novembre E, de Martino M, Lucci A, Dini L (1989) Reliability of tests for specific IgE to foods in atopic dermatitis. Allergy 44 (Suppl 9): 90-96.
7. Cantani A, Arcese G, Lucenti P, Gagliesi D, Bartolucci M (1997) A three year prospective study of specific immunotherapy to inhalant allergens: evidence of safety and efficacy in 300 children with allergic asthma. J Investig Allergol Clin Immunol 7: 90-97.
8. Cantani A (2015) Respiratory manifestations of food allergy in babies with atopic dermatitis: a prospective study in 213 children.

9. Scheiner O, Kraft D (1995) Basic and practical aspects of recombinant allergens. Allergy 50: 384-391.
10. Businco L, Cantani A (1986) The usefulness of total and specific IgE determination in the diagnostic workup of children. In Oehling A, Cortes JL (eds) Advances in Bronchial Asthma. Madrid: Editorial Garsi, SA 105-110.
11. Kjellman NI (1976) Predictive value of high IgE levels in children. Acta Paediatr Scand 65: 465-471.
12. Hamburger RN, Berger WE, Quiva NB, Terrazas V, Casillas R, et al. (1991) Skin testing compared with in vitro testing for screening allergic patients. Ann Allergy 67: 133-137.
13. Meglio P, Giampietro PG, Farinella F, Cantani A, Businco L (1989) Personal experience in the diagnostic procedures in children with atopic dermatitis and food allergy. Allergy 44: 165-173.
14. Hanifin JM, Rajka G (1980) Diagnostic feature of atopic dermatitis. Acta Dermatovener 92: 44-47.
15. (1993) Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology 186: 23-31.
16. Pepys J (1984) Skin tests. Br J Hosp Med 32: 120,122,124.
17. (1993) Position paper: Allergen standardization and skin tests. The European Academy of Allergology and Clinical Immunology. Allergy 48: 48-82.
18. Aas K, Belin L, Backman A, Belin L, Weeke B (1978) Standardization of Allergen Extracts with Appropriate Methods. Acta Allergol 33: 130-137.
19. Hattevig G, Kjellman B, Björkstén B (1993) Appearance of IgE antibodies to ingested and inhaled allergens during the first 12 years of life in atopic and non-atopic children. Pediatr Allergy Immunol 4: 182-186.
20. David TJ (1991) Conventional allergy tests. Arch Dis Child 66: 281-282.
21. Ownby DR (1988) Allergy testing: in vivo versus in vitro. Pediatr Clin North Am 35: 995-1009.
22. Wagenpfeil S, Grabbe J, Jeep S, Czarnetzki BM (1992) Reproducibility of skin prick test reactions to common allergen in patients with atopic eczema. J Allergy Clin Immunol 89: 143-144.
23. Aas K (1978) The diagnosis of hypersensitivity to ingested foods. Reliability of skin prick testing and the radioallergosorbent test with different materials. Clin Allergy 8: 39-50.
24. Cantani A, Lucenti P (1997) Natural history of soy allergy and/or intolerance in children, and clinical use of soy-protein formulas. Pediatr Allergy Immunol 8: 59-74.
25. Burks AW, James JM, Hiegel A, Wilson G, Wheeler JG, et al. (1998) Atopic dermatitis and food hypersensitivity reactions. J Pediatr 132: 132-136.
26. Sampson HA (1988) Jerome Glaser lectureship. The role of food hypersensitivity and mediator release in atopic dermatitis. J Allergy Clin Immunol 81: 635-645.
27. Bindslev-Jensen C, Skov PS, Madsen F, Poulsen LK (1994) Food allergy and food intolerance- what is the difference? Ann Allergy 72: 317-320.
28. Cantani A, Arcese G, Lucenti P (1992) Inefficacia del prick test negativo per escludere l'allergia al latte vaccino nell'infanzia. Aggiorn Pediatr 43: 143-149.
29. Rosen JP, Selkow JE, Mendelson LM, Grodofsky MP, Factor JM, et al. (1994) Skin testing with natural foods in patients suspected of having food allergies: Is it a necessity? J Allergy Clin Immunol 93: 1068-1070.
30. Zacharien MC (2000) Allergy skin testing infants: a safe or risky procedure. Ann Allergy Asthma Immunol 85: 429-430.
31. Deveney I, Falth-Magnusson K (2000) Skin prick tests may give generalized allergic reactions in infants. Ann Allergy Asthma Immunol 85: 457-460.
32. Valyasevi MA, Maddox DE, Li JTC (1999) Systemic reactions to allergy skin tests. Ann Allergy Asthma Immunol 83: 132-136.
33. Rancé F, Kanny G, Dutau G, Moneret-Vautrin DA (1999) Food hypersensitivity in children: Clinical aspects and distribution of allergens. Pediatr Allery Immunol 10: 33-38.
34. Thompson RA, Bild AG (1983) How necessary are specific IgE antibody tests in allergy diagnosis? Lancet 1: 169-173.
35. Giampietro PG, Ragno V, Daniele S, Cantani A, Ferrara M, et al. (1992) Soy hypersensitivity in children with food allergy. Ann Allergy 69: 143-146.
36. Tang RB, Wu KK (1989) Total serum IgE, allergy skin testing, and the radioallergosorbent test for the diagnosis of allergy in asthmatic children. Ann Allergy 62: 432-435.
37. Winkler S, Pambor M, Ballke EH, Wiersbizky S (1991) Diagnostic value of skin tests in children with bronchial asthma and/or atopic eczema. Kinderarztl Prax 59: 85-87.
38. Rothe Th (1992) The clinical value of total IgE measurements. Allergologie 15: 78-84.
39. Sporik R, Hill DJ, Hosking CS (2000) Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. Clin Exp Allergy 30: 1540-1546.
40. Sampson HA, Ho DG (1997) Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. J Allergy Clin Immunol 100: 444-451.
41. Williams PB, Siegel C, Portnoy J (2001) Efficacy of a single diagnostic test for sensitization to common inhalant allergens. Ann Allergy Asthma Immunol 86: 196-202.