

## News and commentaries

# Allergy testing in children: why, who, when and how?

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## Introduction

The aim of this paper is to establish evidence-based recommendations on allergy testing in children.

Besides sound scientifically based recommendations for allergy testing, a well-organised cooperation between primary care physicians for children and specialists in allergy is crucial in order to ensure a high quality and effectiveness of allergy diagnosis and treatment to the benefit of the individual patient. It is our intention that these recommendations on allergy testing in children will be adopted by the European Society and implemented in all European countries according to local needs and possibilities. During the last decade, a new system for classification of levels of evidence and grading recommendations in evidence-based medicine has been developed. Originally, evidence classification was created for causal and intervention/treatment studies (1, 2). Based on a classification of studies in four categories of statements of evidence (I (highest)-II-III-IV) guidelines for treatment/intervention graded A (highest)-B-C-D have been developed. Typically, randomized placebo-controlled trials and meta-analyses of such trials got the highest statement of evidence (I) and accordingly the highest grade of recommendations (A). However, in many cases randomization is not possible and recommendations must be based on lower levels of evidence. Thus, for some areas

of practice such as diagnostic tests, recommendations higher than grade B are unlikely because of the type of study that can feasibly be conducted in those areas (2). Recently two well-established systems for grading of evidence for diagnostic tests have been developed (3, 4).

The prevalence of allergic diseases in childhood (atopic dermatitis, asthma, and allergic rhinitis and conjunctivitis) has increased considerably in developed countries (5, 6) in the last 20–30 years, and accordingly the need of allergy testing has increased (Table 1).

In population-based studies a cumulative prevalence of allergic diseases in childhood around 25–30% has been reported, atopic dermatitis in 15–20%, asthma in 7–10%, and allergic rhinitis and conjunctivitis in 15–20% (5–11).

In infancy the main symptoms of possible allergic nature are atopic dermatitis, gastrointestinal symptoms, recurrent wheezing, whereas bronchial asthma and allergic rhinitis and conjunctivitis are the main problems later in childhood (12, 13). Adverse reactions to foods, mainly cow's milk protein and hen's egg are most common in the first years of life, whereas allergy to inhalant allergens mostly occurs later (12, 14). Correspondingly, specific immunoglobulin E (IgE) antibodies against milk and egg are most frequent during the first 2–3 years of life, whereas IgE against inhalant allergens is predominant later in childhood (13, 15). Interestingly, IgE antibodies to allergens (hen's egg white, cow's milk) in infants

Table 1. Allergic diseases in childhood, prevalence of sensitization

Age	Diagnosis	Prevalence	IgE*-sensitization	Statement of evidence <sup>#</sup>
Early childhood	Food allergy	7–8%	40–60%	II
School age	Food allergy	1–2%	60–70%	II
Childhood	Atopic dermatitis	15–20%	33–40%	II
Early childhood	Recurrent wheeze/asthma	21–34%	30–60%	II
School age	Asthma	7–10%	70–90%	II
Childhood	Rhinitis and conjunctivitis	10–15%	60–80%	II

\* IgE-sensitization as determined by positive skin prick test (mean wheal diameter  $\geq 3$  mm larger than the negative control) or specific IgE  $\geq$  class 2 (equivalent to 0.70 kU/l as measured by Pharmacia CAP System<sup>®</sup>) to one or more relevant allergens.

The varying frequency of IgE-sensitization reflects differences as regards selection of patients and methodology.

# According to ref. 2–4.

predict sensitization to inhalant allergens and allergy before 7–10 years of life (16–19). Low levels of specific IgE to several allergens – food allergens as well as inhalant allergens – are a normal phenomenon, especially in early childhood and may have no clinical significance (20).

The field of allergy has developed rapidly during the last decades and our knowledge about immunological mechanisms has improved our understanding. However, there has been some controversies on the definition of allergic diseases and the use of different terms such as atopy/allergy and atopic/allergic (21). Recently, a revised nomenclature for allergic and related reactions that can be used independently of target organ or patient age group has been published (21). In that position paper, allergy is defined as a hypersensitivity reaction initiated by immunological mechanisms (defined or strongly suspected), whereas the term non-allergic hypersensitivity has been proposed when immunological mechanisms cannot be proven. Allergy can be antibody- or cell-mediated. In most patients, the antibody typically responsible for an allergic reaction belongs to the IgE isotype, and these patients may be said to suffer from IgE-mediated allergy. In non-IgE mediated allergy different mechanisms may be responsible (e.g. IgG, immune complexes, cell mediated). In this paper, we do not emphasize the role of other immunologically mediated diseases such as coeliac disease. Typically in IgE-mediated allergic disease exposure to a provoking allergen evokes a biphasic response, the early response within 20 min being characterized by classic IgE-mediated immediate type hypersensitivity, and followed by the late phase response after 3–6 h which is characterized by involvement of eosinophil inflammation. This is associated with prolonged hyperreactivity and in case of daily exposure to allergen, persistent inflammation resulting in structural and functional changes that cause prolonged symptoms (22–24).

## Why?

*Allergy testing* is a very important *prerequisite* for specific allergy treatment as regards:

- A. Early identification of infants at increased risk for later development of allergic diseases
- B. Specific allergy treatment
  - Specific allergen avoidance measures
  - Relevant pharmacotherapy
  - Specific allergy vaccination.

## Allergen avoidance

Avoiding exposure to relevant allergens is a logical way to treat allergic diseases, e.g. allergic asthma when the offending allergen can be identified and effective avoidance is feasible. Allergen avoidance in a mountain environment improves lung function and normalizes markers of allergic inflammation in children with allergic asthma (25–29). Controlled randomized studies have shown that allergen (especially house dust mite allergens) avoidance measures are effective both in reducing the level of allergens and improvement of disease control, e.g. by reducing the need of pharmacotherapy (29–49). Complete avoidance of pet allergens is impossible as the allergens are ubiquitous and can be found in many environments outside the home. Removal of such animals from the home is important. In pet allergic patients who persist in keeping their pets, exposure-reduction measures may be considered. However the clinical effectiveness of these measures remains unproven and there are many conflicting data on this subject (50).

## Relevant pharmacotherapy

A specific allergy diagnosis is also a prerequisite for instituting the correct antiallergic treatment, e.g. in case of allergic rhinitis and conjunctivitis, allergic skin reactions, other specific allergic symptoms (51).

## Specific allergy vaccination

Specific immunotherapy has been demonstrated in many studies to be an effective treatment for patients with allergic rhinitis and conjunctivitis. Meta-analyses show that the use of allergy vaccines can reduce asthma symptoms compared with placebo (52). There is an early clinical improvement, marked reduced skin and shock organ reactivity. Early immunological events are e.g. an IL-10 increase with T-cell anergy and reduced specific basophil histamine release. The main immunological long-term effect is a switch of allergen induced cytokine profile from TH2 to a TH1-like pattern (53). Allergy vaccination is a potential early intervention strategy. Allergy vaccinations with *subcutaneous injections* have been shown to be effective in allergic asthma in randomized controlled trials with extracts of house

Table 2. Indications for allergy testing

Gastrointestinal symptoms: Vomiting, diarrhoea, colic, failure to thrive	Persisting or intermittent symptoms without any other known reason, particularly in case of other concurrent atopic symptoms.	B
Atopic dermatitis	Persisting symptoms or allergen related symptoms, particularly in case of other concurrent atopic symptoms.	B
Acute urticaria/angioedema	Severe cases and/or at suspicion of specific allergy.	B
Chronic urticaria	Urticaria of long duration $\geq$ 6 weeks.	B
Children < 3–4 years of age with recurrent wheezing/asthma	Persisting severe symptoms and need of daily treatment. Children with long-lasting cough/wheeze/dyspnoea, particularly during play/physical activity and during the night, and children with reduced level of activity or frequent pneumoniae without other known cause should be allergy tested.	B
Children >3–4 years with asthma	Should always receive allergy testing for relevant allergens. Should be investigated for rhinitis.	B
Rhinitis	Treatment-resistant cases. There should be investigated for concurrent asthma.	B
Conjunctivitis	Treatment resistant cases.	B
Insect sting reactions	Only severe systemic reactions grade III–IV should be tested. Local reactions/urticaria are not indications for allergy testing.	B
Anaphylaxis	Should always be evaluated for allergy under special observation.	B

B: grade of recommendation according to ref. 1–4.

dust mites, pollen, and animal dander (cat). A significant reduction in asthma symptoms and medication and a reduction in both non-specific as well as allergen-specific airway hyperresponsiveness have been documented (52, 54). A recent study found that 3 years of pollen allergen vaccine treatment in children with pure seasonal allergic rhinitis resulted in significantly less children subsequently developing asthma than in an untreated parallel control group (55) and allergy vaccination may prevent the onset of new sensitizations (56). When using documented high doses sublingual–swallow immunotherapy has been shown to be efficacious in some double-blind, placebo-controlled studies in patients with allergic rhinitis due to birch pollen, grass pollen, parietaria pollen and house dust mites. In one study sublingual-swallow immunotherapy was found to be slightly less effective than subcutaneous specific immunotherapy (51). Further comparative studies are required (57).

Early identification of infants at increased risk for later development of allergic disease

Those with early development of IgE sensitization to cow's milk or hen's egg proteins or early sensitization to inhalant allergens (16–19) have an increased risk for later development of allergic diseases. Early identification of children with food allergy and atopic dermatitis may provide opportunities to prevent the development of asthma. A few studies have suggested that pharmacologic intervention with H1-antihistamines may reduce the onset of wheezing in young children who present initially with atopic dermatitis (58–60). However these studies need further confirmation.

### Who should be tested for allergy?

Generally, all individuals with severe, persisting or recurrent possible “allergic symptoms” and individuals with need for continuous prophylactic treatment should be tested for specific allergy irrespective of the age of the child (61–82), (Tables 2, 3). The extent of allergy tests will typically depend on the age of the child, positive family history, and the character of the symptomatology including possible seasonal or diurnal variations. In Table 4, proposals for allergy testing and relevant allergens at different ages are described. When children are tested according to age for specific allergy diagnosis, additional testing might be considered for assessment of sensitization reflecting the atopic constitution.

Children less than 3–4 years

- In *early infancy* food allergy with manifestations from skin, the gastrointestinal or the respiratory tract is more common than inhalant allergy.

Table 3. Insect sting reactions – severity

Large local reaction	Swelling > 10 cm diameter > 24 h
Systemic grade I	Indisposition, anxiety, generalized skin itching or urticaria
Systemic grade II <sup>1</sup>	Angioedema, vertigo, nausea, vomiting, diarrhoea, abdominal pain
Systemic grade III <sup>2</sup>	Dyspnoea, dysphagia, dysarthria, hoarseness, confusion, asthma
Systemic grade IV <sup>2</sup>	Hypotension, incontinence, cyanosis, collapse, unconsciousness

<sup>1</sup> Allergy testing only in heavily exposed patients with repeated reactions.

<sup>2</sup> Patients with such severe systemic reactions, respiratory and/or cardiovascular symptoms should be tested and specific immunotherapy considered.

- *Recurrent wheezing/asthma* and *atopic dermatitis* (Table 1) are the most common symptoms. In case of mono-symptomatology, allergy is rather uncommon except in individuals with persisting symptoms. Children with long-lasting cough / wheeze / dyspnoea, particularly during play/physical activity and during the night, and children with reduced level of activity or frequent pneumoniae without other known cause should be allergy tested.
- Children with *food allergy* almost always show symptoms from two or more organ systems concomitantly, but in some cases, e.g. atopic dermatitis, the children may only show one severe persisting symptom. Cow's milk allergy is the most common food allergy in young children followed by allergy to hen's egg, cereals, and nuts.
- A few children are sensitized to indoor inhalant allergens already during the first 1–2 year of life, and in case of persisting asthma symptoms, allergy testing for relevant indoor allergens such as mite and cat may be useful.

Children above 4 years

- With increasing age, allergy to inhalant allergens develop in childhood, especially to indoor allergens (house dust mites, pets, cockroach) and later to outdoor allergens like pollen and moulds. During childhood a high frequency of sensitization is seen in both

asthmatics and individuals with rhinitis and conjunctivitis. A great proportion of asthmatics (> 70%) also suffer from rhinitis (50), and a great proportion of individuals with rhinitis also suffer from asthma, frequently not detected. Many asthmatics suffer from persistent rhinitis and conjunctivitis and in late childhood many children with seasonal rhinitis and conjunctivitis also have developed asthma, approximately 1/3–1/2. In typical rhinitis and conjunctivitis (hay fever) in the spring or summer period symptomatic treatment can be instituted without allergy testing. In cases of associated pollen asthma and in case of treatment resistant symptoms (insufficient response to treatment according to the ARIA guidelines (51)), allergy testing should be performed in order to prove/disprove the cause of the disease and make possible specific allergy treatment, e.g. avoidance measures, allergy vaccination.

- *Asthma*. Allergy testing should be performed, where an early intervention (elimination of relevant allergens/treatment) may improve disease control and prevent progression of disease.
- *Atopic dermatitis*. Children without spontaneous improvement in the summer period and without sufficient effect of topical steroids and when food allergy is suspected should also be allergy tested.
- *Urticaria* is rarely caused by allergy except in cases of close relation to intake of specific food or exposure to specific allergens.

Table 4. Allergy testing according to age and disease/symptoms The allergen panel used should be adjusted according to allergen related symptomatology and local allergen exposure, indoor as well as outdoor

Disease/symptoms	What to test in relation to age		
Atopic dermatitis	<p>&lt;3–4 years of age</p> <p>Foods (for AD-associated food allergy):</p> <ul style="list-style-type: none"> <li>• cow's milk</li> <li>• egg white</li> <li>• (peanut, wheat, nuts, fish, etc.)</li> </ul> <p>Inhalant allergens (to test the atopic risk):</p> <ul style="list-style-type: none"> <li>• house dust mites</li> <li>• cat, dog, and other furred animals</li> <li>• pollens</li> </ul>	<p>&gt;3–4 years of age</p> <p>Foods (in case of severe persisting AD for AD-associated food allergy):</p> <ul style="list-style-type: none"> <li>• cow's milk</li> <li>• egg white</li> <li>• peanut</li> <li>• (wheat, nuts, fish, etc.)</li> </ul> <p>Inhalant allergens (for allergen-associated AD):</p> <ul style="list-style-type: none"> <li>• house dust mites</li> <li>• cat, dog, and other furred animals</li> </ul> <p>Inhalant allergens (to test the atopic risk):</p> <ul style="list-style-type: none"> <li>• house dust mites</li> <li>• cat, dog, and other furred animals</li> <li>• pollens</li> </ul>	B
Persistent and intermittent runny and stuffy nose and/or wheezing and persisting cough	<p>For allergen-specific diagnosis:</p> <ul style="list-style-type: none"> <li>• House dust mites</li> <li>• Cat, dog, and other furred animals</li> <li>• pollens</li> <li>• others*</li> </ul>		B

Teenagers with atopic dermatitis (neck and face) should also be tested for pityrosporum ovale.

B: grade of recommendation according to ref. 1–4.

\*: relevant food allergens, e.g. cow's milk, and egg, especially in young children.

- *Insect sting reactions.* Children should only be tested for allergy to insect venoms (bee or wasp) in case of severe systemic reactions (respiratory and/or cardiovascular symptoms). Local reaction and urticaria are not indications for testing because no consequence will be taken of this testing (no indication for immunotherapy/allergy vaccination) (Tables 2, 3) (83).
- *Allergy to drugs.* Allergy testing should be conducted at symptoms such as itching skin reactions, urticaria, angioedema, asthma or anaphylaxis. Maculopapulous exanthema is not an indication for testing (84).
- *Latex allergy.* Allergy testing is primarily indicated in children who belong to the risk groups for latex allergy, i.e. spina bifida, urogenital malformations (frequent operations), atopic symptoms, and other patients with early exposure to latex. The symptoms in latex allergy are like other IgE-mediated allergies. Cross-reactions in case of latex allergy may be to banana, avocado, kiwi, chestnut, papaya, figs. Even cross-reactions to potato and tomato have been reported as well as cross-reactions to *Ficus benjamina* (85).
- *Cross-reactivities* occur when two or more allergens share epitopes, or in some cases have very similar epitopes, and therefore bind to the same IgE-antibodies. Thus, patients sensitized to one of the allergens may also react to the other without previous exposure and sensitization. The most often reported cross-reactivities between pollen/foods/vegetables are shown in Table 5 (86). Symptoms caused by pollen-related cross-reactivities to foods include itching and swelling in the mouth and oropharynx, and these symptoms may often lead to cessation of intake of the offending food (oral allergy syndrome (OAS)). The knowledge about cross-reactivities is important when evaluating the need and extent of allergy testing. Often the diagnosis of OAS can be based on a typical history in pollen allergic individuals, and in unclear cases the demonstration of a positive skin prick test

or specific IgE-antibodies may be helpful. In Table 5 some more uncommon cross-reactivities are also described. Clinical reactivity to food allergens is specific, although patients may rarely react to more than one member of a botanical family or animal species. It is important to emphasize that “serological cross-reactivity” (and cross-reactivity in the skin) is not necessarily associated with clinical disease which has to be confirmed by challenge.

**Practical allergy testing**

The prevalence of allergic diseases in childhood is depicted in Table 1 including the prevalence of IgE-sensitization as determined by either positive skin prick test or specific IgE to one or more relevant allergens. Although positive skin prick test and/or positive specific IgE in serum indicate that a person has antigen-specific IgE, these findings do not prove that exposure to the allergen in question causes significant clinical allergic symptoms. Theoretically, only controlled allergen challenge can confirm the cause-effect relationship between allergen exposure and clinical symptoms. However, in daily allergy testing it is common to use a positive skin prick test (87–90) and/or presence in serum of specific IgE (91–94) to relevant environmental allergens and a suggestive clinical history as proof of allergy induced disease. The higher the specific IgE antibodies, the stronger the association with clinical disease (91–94). Both skin prick test and in vitro tests differ in their ability to detect sensitization depending on the quality of the extract used and the technical detection limit of the test. Patients referred to specialists are often selected as regards prevalence of sensitization, multiple sensitization and clinical symptoms. In general practice many children with single low degree sensitization without clinical allergy are found reducing the value of low degree responses. Therefore the clinical relevance of low specific IgE values is often limited.

Allergy testing includes the following elements:

- Case history
- Determination of IgE-sensitization
  - skin prick test (SPT)
  - total and specific IgE in serum
- Allergen challenges
  - food allergy
  - inhalant allergy
- Other tests
- Environmental investigations

Case history

A thorough history including frequency and severity of symptomatology, atopic heredity, environmental factors (housing conditions, school, and leisure time environment), exposure to pets and tobacco smoke etc. Relation between exposure to allergens and environmental factors

Table 5. Cross reactivities

Symptom related allergens	Frequently cross-reactive allergens	# Statement of evidence
Birch	Apple, hazelnut, carrot, potato, celery, cherry, pear, others	II
Mugwort (artemissia)	Celery, carrot, fennel, parsley, coriander, mustard	II
Grass	Potato, tomato, wheat, peanut	II
Cow's milk	Goat's milk, sheep's milk, beef	II
Peanut	Tree nuts, soy beans, green beans, green peas, lentils.	II
Lentils	Peanuts, soy	II

Serological cross-reactivity (and cross-reactivity in the skin) is not necessarily associated with clinical disease, which has to be confirmed by challenge if appropriate.

# According to ref. 2–4.

including seasonal and diurnal variations should be registered. Standardized questionnaires may be useful (50, 51).

#### Skin prick test

Standardized extracts and methods should be used (87–90). When testing for food allergy, fresh food material and the prick - prick method can be useful (95). There is no lower age limit for performing skin prick test. Earlier a lower age limit of 3 years has wrongly been recommended. For practical performance the guidelines for skin prick test should be followed (87–90). A mean wheal diameter  $\geq 3$  mm larger than the negative control defines a positive reaction. The number of children sensitized increases with the potency of the extract and the pressure applied to the lancet (95). The panel of allergens for skin prick testing will depend on the age of the child and the case history and varies between regions.

*Limitations* of skin prick test: should not be performed in case of active eczema on the test site (most often volar side of the forearm), or local treatment with steroid or immunomodulator ointment. Use of antihistamines should be avoided at least 3 days prior to the skin prick test.

#### Determination of IgE in serum

*Total IgE.* In children, the “normal value” for total IgE increases gradually up till prepuberty when it reaches adult levels (96, 97). A “normal” total IgE does not rule out specific allergy.

*Specific IgE.* Test for specific IgE should be conducted with a validated method (91–94) and can be performed at any age. Quantitative specific IgE tests have a high reliability, i.e. positive tests show presence of IgE, specific for the allergen tested. The specificity and sensitivity are within the range of 85–95%. Thus, specific IgE reveals sensitization to suspected allergens, and is a useful aid in allergy diagnosis since only those sensitized can develop IgE-associated allergic disease. Like the skin prick test it must be related to the clinical history and used on the same indications as the skin prick test (91, 93). Immunoassays (IgE-tests) and skin prick tests are useful and the results are in part interchangeable. In praxis either test can be used in combination with a thorough clinical history. In case of disagreement between the case history and SPT or specific IgE-test, a supplementary investigation with specific IgE or skin prick test should be conducted to document possible clinical IgE-associated allergy (93–94, 98).

#### Allergen challenges

*Food allergy.* The diagnosis of food allergy cannot be based solely on the results of case history combined with skin prick test and/or determination of specific IgE. In case of full agreement between the case history (severe systemic

reactions in relation to repeated allergen exposure) and results of specific IgE or skin prick test, there is no reason to perform allergen challenge. In general, the diagnosis has to be based on controlled elimination and food challenges (86, 99–101). The elimination period will usually last 1–4 weeks depending on the symptomatology and should abolish or at least markedly reduce symptoms. In daily clinical practice, the challenge can be performed as an open controlled food challenge when objective reactions are expected. In order to prove that a food is exacerbating atopic dermatitis, it is preferable to use a double blind placebo controlled food challenge (DBPCFC). In children older than 2–3 years, a positive open food challenge may need a confirmatory DBPCFC in order to avoid false positive reactions due to psychological/other mechanisms or Münchhausen by proxy syndrome. Negative DBPCFC should always be followed by open continued food challenge and then normal daily intake of the food in question. Food challenges should always be performed under controlled professional supervision and in adequate pediatric settings. If there is a possibility for systemic reactions, food challenges are to be made at the hospital. Parental reports only are not reliable.

The utility of food specific IgE concentrations in predicting symptomatic food allergy has been investigated in recent studies (102, 103). In selected patients with food allergy attending a highly specialized pediatric allergy department, more than 95% of food allergies were correctly identified (Pharmacia CAP System®) (102). Thus, specific IgE tests may eliminate the need for double-blind placebo-controlled food challenges in selected referred children with severe food allergy. Specific IgE showed a high sensitivity and negative predictive accuracy. Diagnostic levels of IgE that could predict immediate clinical reactivity to egg, milk, peanut, and fish with a greater than 95% certainty could be calculated (102). In young children with suspected cow's milk allergy a negative skin prick test excluded milk allergy in 97% of the patients, and a high positive predictive value (90%) was found at specific IgE levels  $\geq 2.5$  kU (A)/l (104). And in young children with egg allergy the best predictors of persisting allergy were symptoms at egg ingestion followed by the size of skin prick test, and also specific IgE antibody level in children who only had cutaneous symptoms. (105)

*Inhalant allergy.* In case of full agreement between the case history (symptoms in relation to allergen exposure) and the result of specific IgE or skin prick test, there is no reason to perform allergen provocation in the target organ. In equivocal cases and in case of continuous symptoms and/or suspected allergy to allergens present in the environment such challenges may be useful and necessary, especially before specific allergy treatment, e.g. allergy vaccination. There is a good agreement between the reactivity of shock organs, why the simple conjunctival provocation test should be preferred to the more risky and complicated nasal or bronchial challenge.

*Bronchial allergen challenges* should be performed in specialist pediatric settings and may not be performed until the age of 5–6 years, because of the necessity of good cooperation and ability of the child to perform lung function measurements with an acceptable reproducibility (6 years) (106).

*Conjunctival, nasal and bronchial challenges* should be performed with standardized allergen extracts in increasing concentrations as described (107). With standardized extracts the dose can be increased 100 to 1000-fold 10 minutes after a negative test without any risk of severe reactions (108).

#### Other tests

These tests are mainly for research purposes or in the hands of specialists.

*Histamine release test (HR test)*. This test measures the histamine release from basophile granulocytes. The results of HR test (109, 110) have been comparable to the results of SPT and specific IgE-tests. HR-test is more complicated for daily clinical practice, but may be a helpful tool in certain cases, e.g. testing for infrequent allergies, drug allergies etc.

*Patch Tests (PT)*. Patch Tests are used in delayed hypersensitivity (i.e. contact dermatitis). 'Atopy' Patch Tests have been used in recent studies for identification of cell mediated reactions to foods, particularly in children with atopic dermatitis. Some studies have shown promising results (111–113), others not (114).

There are other methods that are not validated at present and that should not be used for proper allergy diagnosis.

#### Assessment of indoor allergens

*Determination of allergen content in house dust samples*. (house dust mites, pets) may be useful in order to prove clinically important exposure to the investigated allergens and to monitor avoidance measures (40). At least in Northern Europe, cat and dog allergens are present in all official environments in concentrations high enough to cause bronchial hyperresponsiveness in sensitized children (115).

#### Conclusions

Allergy testing is a very important prerequisite for both early identification of infants at increased risk for later

development of allergic diseases and for specific allergy treatment including specific allergen avoidance measures, relevant pharmacotherapy and specific allergy vaccination.

Generally, all children with persisting/recurrent/severe "allergic symptoms" or individuals with need for continuous treatment should be tested for allergy irrespective of the age of the child. Allergy testing includes a careful case history, a determination of IgE sensitization by skin prick test with standardized extracts or allergen specific IgE in serum by validated methods. In general, the diagnosis of food allergy cannot be based solely on the results of case history and determination of IgE-sensitization, and the diagnosis has to be based on controlled elimination and food challenge procedures when there is not a full agreement between the case history (severe systemic reactions in relation to allergen exposure) and the results of determination of specific IgE-sensitization. As regards the diagnosis of inhalant allergic disease, there is no reason to perform allergen provocation in the target organ in case of full agreement between the case history and the results of determination of specific IgE-sensitization. In equivocal cases, challenges may be useful and necessary, especially before specific allergy treatment, e.g. allergy vaccination.

Implementation of evidence-based recommendations for allergy testing in children will differ between countries depending on local organisation of professionals and the level of knowledge within allergology. In general, improved education in allergology, both pre-graduate at the universities as well as post-graduate including primary care physicians and their staff, specialists, subspecialists and nurses is warranted. Furthermore, it is recommended to ensure and strengthen the co-operation between the specialist sector/hospitals, general practitioners and the local home care in order to benefit the individual patient. This will contribute to secure shared care covering both the primary and the secondary sector and make possible that the right children will get the right tests at the right time in order to ensure the best evidence-based treatment of their allergic disease.

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I-II-III-IV denote the statement of evidence according to ref. 14.