An update on food allergy: What every practitioner should know

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Summary

Adverse reactions to food are a common occurrence in clinical practice. Some of these reactions are "true food allergies" while others represent various forms of "food intolerance", or toxicity.

There has been a real increase in true food allergies, e.g. peanut allergy, which has accompanied the general increase in allergic diseases worldwide. In practice, however, more frequently doctors encounter patients with "atypical" or delayed adverse reactions to food which, are not Type I IgE dependent reactions, and in whom conventional allergy tests are usually unhelpful. The identification of the triggers of such reactions requires careful history taking and in some cases can be confirmed by new tests. The corner stone of the management of food allergies is identification and avoidance. No commercial immunotherapy vaccines are available for clinical use for food allergy.

It is important to take care with influenza or yellow fever vaccinations in egg allergy subjects. MMR by contrast, may be safely administered to egg allergic subjects for the future, novel genetically engineered proteins have a real potential for allergenicity.

(SA Fam Pract 2004;47(8): 42-48)

Early diagnosis of food allergy

Food allergy is on the increase worldwide. Food allergy may occur in infants from birth when infants may be sensitised through the cord blood, in utero, to proteins such as peanut and milk via the maternal diet. Specific IgE does not cross the placenta, but allergen specific cord IgE of foetal organ may be induced. However, low levels of specific IgE response to food allergens may be part of a **normal** TH2 responder phenotype in the first year of life, and many never manifest as clinical food allergies.

Thus, screening for food allergies in asymptomatic infants is unnecessary and usually results in low false positive test results which cause confusion and could lead to unnecessary food restriction.

The prevalence of true food allergy in early childhood is about 7% in developed countries and falls to 1-2% in children going to school.[1,2] By contrast the prevalence of true food allergy in children with atopic dermatitis is about 20% with Specific IgE sensitization to foods being present in 33-40%.[3]

Early diagnosis of food allergy in infants with atopic dermatitis is important for 2 reasons: The first is to avoid the food triggers in the pathogenesis of the flares of atopic dermatitis. The second reason is a long term one.

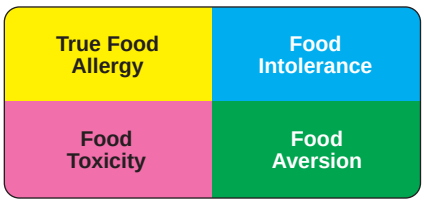
Children with atopic dermatitis who have food allergy or inhalent allergies are more likely to go on and develop asthma and other inhalant allergies in the future. In this group interventional strategies for the prevention of asthma (e.g. Avoidance of dust mite exposure) may be more relevant.

Confirmation of the diagnosis of food allergy by testing with challenges is seldom necessary where anaphylactic events have previously occurred. Predictive cut-off values for true clinical sensitivity for skin tests and RASTs have been determined in children with atopic dermatitis (Table I and II). Important allergens include peanut, milk, egg, wheat, soya and fish allergens.[1]

Allergic reactions to foods in older children and adults

In older children and adults adverse reactions are conveniently divided into 4 possible groups:

Figure 1



Important true food allergies in older children and adults include peanut, fish, crustaceans, molluscs, tree nuts and tropical fruits. True food allergies manifest within 30 minutes to an hour of exposure. Manifestations of food allergy affect the skin in 60-70%, the gastrointestinal tract in 20% and the respiratory tract in 20%.

Asthma and/or rhinitis are unusual manifestations of true food allergy, but may be part of an anaphylactic reaction, especially if preexisting asthma due to other inhalents is present.

In the case of seafood allergy,

Table I: 100% predictive value of skin prick tests for food allergies

	Size of wheal	
Over 2 years	>8mm	Cow milk
	>7mm	Egg
	>8mm	Peanut
Under 2 years	>6mm	Milk
	>6mm	Egg
	>4mm	Peanut

Ref.: Sporik, Hill et al. Clin Exp Allergy 2000; 30: 1540-1546

Table II: 95% predictive value of CAP RASTs for food allergies in children

	Predictive value
Egg	6Ku/L
Milk	32Ku/L
Peanut	15Ku/L
Fish	20Ku/L
Soya	65Ku/L
Wheat	80Ku/L

Ref.: Sampson H, L to D. JACI 1997; 100: 444-454

mollusc allergy (e.g. mussels, abalone) is as common as crustacean allergy in South Africa. Allergy to "line fish" (e.g. sole, hake, cob, salmon, Kingklip) is also frequently encountered, particularly at the coast, and is often a very severe allergy. Sensitisation can occur via the inhaled route during cooking of fish.

Variations in the reactions to seafoods are common and may depend on whether the seafood is cooked or raw, cooked by boiling or grilling, or contaminated with toxins, or with nematodes, such as Anisakis species. These parasites are found in up to 90% of fish caught on South African shores.

Specific IgE to commercial allergens (e.g. cod, hake, langoustine, shrimp) is readily determined using the Immuno CAP RAST, or using Western Blotting for some of our indigenous fish (e.g. Kingklip, abalone [Perlemoen], Alikreukel, snoek, etc.). Indigenous Western Blotting tests are performed at the Allergy Diagnostic and Clinical Research Unit of the UCT Lung Institute in Cape Town and serum for these tests can be sent to Cape Town through the local pathologists. This unit specialises in identification of Specific IgE to indigenous seafood and inhalent allergens of the African continent.

IgE tests are fairly reliable for confirming true food allergy for the heat stable allergens in peanut, milk, seafood and tree nuts. For fruit and vegetable allergies, skin testing with fresh extracts would be much more sensitive. This is particularly important for the diagnosis of allergies to apple, melon, peach and some unstable seafood allergies.

The adverse reactions to foods

Most adverse reactions to foods are not true allergies. A delayed reaction to a food is very rarely a true allergy, but has been reported with abalone allergy in which symptoms developed about 4 hours after exposure. Delayed reactions may occur if the allergen is released slowly in the gastrointestinal tract.

The majority of delayed adverse reactions to food are food intolerances. Occasionally they are due to contaminants (bacteria or toxins) in foods.

Food intolerances often manifest with gastrointestinal symptoms, usually starting a few hours after ingestion. However, food intolerances may also manifest with urticaria, angioedema and bronchospasm, when exposure is significant. Tingling of the mouth and pharynx usually precedes a more severe reaction.

Food intolerance may result from sensitivity to food proteins, sugars (e.g. lactose intolerance), but often is induced by the contaminants, preservatives and colourants found in processed and preserved foods supplied in packets, bottles and tins.

Important triggers of such reactions include sodium metabisulphite, sulphur dioxide, sodium benzoate, yellow colorants and occasionally Tartrazine and sodium nitrate. Testing patients for sensitivity to these agents is possible using the CAST test (sulphido leukotriene release test). The CAST test sensitivity and cut off values are still being investigated for most of the preservatives. A cut off value of above 40 picograms/ml for sodium metabisulphite and a cut off value of 90 picograms/ml for sodium benzoate is currently regarded as a positive result.

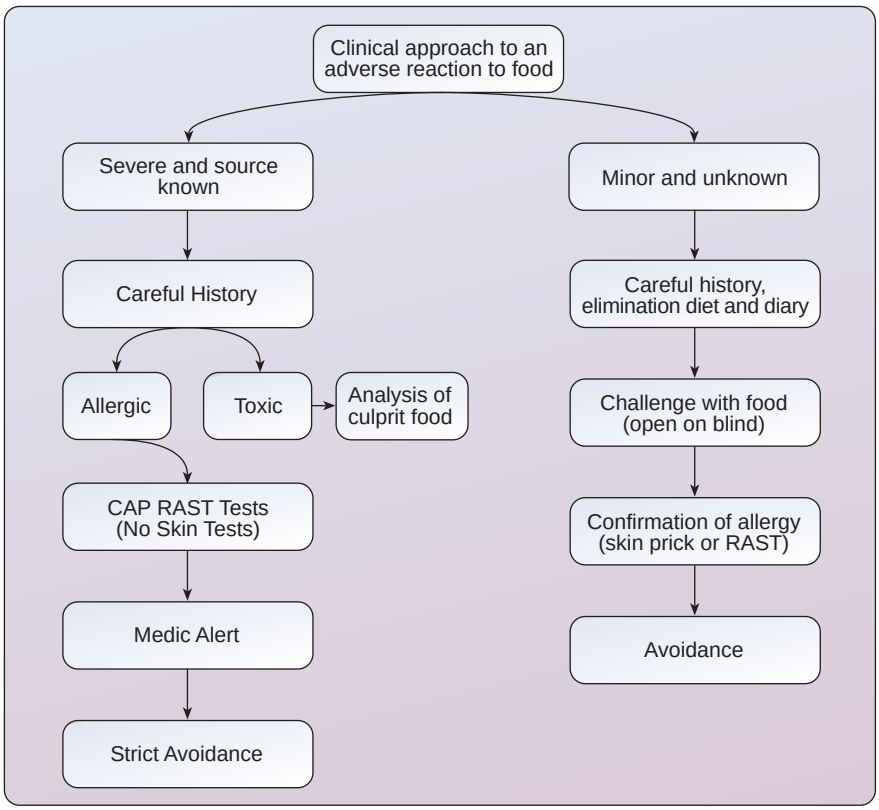
Where preservatives and colourants are suspected, the implementation of a diet avoiding exposure to such foods, with a daily diary record card often results in a cessation of the symptoms. This should be explored in all cases, before embarking on expensive screening tests, using the CAST system.

Patients need to identify the suspicious "preservative" by reading labels on processed foods first, before providing a blood sample for testing. Used in this way, the CAST test is proving to be more useful for true Type I reactions, the Cap RAST or skin test is more sensitive than the CAST.

If reactions to foods are due to toxins or contaminants, encouraging the patient to vomit, using Ipecacuana or activated charcoal is appropriate in such circumstances, particularly when symptoms occur within a short period of exposure (within an hour).

Food "aversion" often develops following true food allergies, when patients associate the food with an unpleasant allergic reaction they have experiences before and "avoid it", or feel "nauseas" at the thought of ingesting such a food. In some cases

Figure 2:



the food aversion can be overcome by a challenge test, particularly when the aversion does not follow a true allergy.

The clinical approach to an adverse reaction to a food is summarised in Figure 2.

Elimination and challenge diets

In many cases the history is unconvincing and vague and the doctor has no real direction from the patient as to which tests should be ordered. In such cases, an elimination challenge diet is most informative. The diet avoids all legumes, nuts, most grains, preservatives, colourants, seafood and allergenic fruits (Table III). It is administered for 2-3 weeks with a diary card. It is useful if symptoms are occurring more than 2-3 times a week.

Table III: Basic 2-week elimination diet (allowed foods)

Rice (all forms), Sago
Fruit: Pear, Apple, Grape
Meat: Lamb, Chicken
Vegetables: Asparagus, Beetroot, Carrots,
Lettuce, sweet Potatoes, Butternut, Squash
Other: Black tea, Rooibos
Olive oil, Sunflower oil, Sugar, Salts
NB: No preservatives, No tinned or packet foods

On this diet the patient should record a decrease or cessation of the symptoms. This confirms that a "food" or "additive" is indeed responsible for the symptoms (e.g. urticaria) and the food or additive causing such symptoms can be identified by re-introducing the eliminated foods one by one. Reading labels on processed foods is essential to identify the culprit "additive" and to plan further confirmatory testing either by RAST, skin prick test, CAST or repeat challenge test under controlled conditions.

New issues in food allergy

1. Influenza vaccination

Since flu vaccines may be prepared using egg embryo tissue, there have been concerns that subjects allergic to eggs may have severe allergic reactions if given the vaccine. The safety of influenza vaccination in egg allergen subjects has recently been reviewed by Zeiger.[4]

Adverse allergen reactions have been seen in egg allergic patients injected with inactivated influenza vaccines. Thus, the inactivated vaccine should **not** be administered to patients who have had generalised or anaphylactic reactions to egg.

In a study by James et al [5] of 83 subjects allergic to eggs as documented by a positive IgE or skin prick test with convincing history and challenges (in 25 of the cases), it was found that the influenza vaccine would be safely given to such subjects without systemic reactions, using a 2-dose injection protocol (one tenth dose followed in 30 minutes with nine-tenth dose with vaccines which no more than 1.2µg/ml of protein) in all 83 patients. All 34 patients who needed a second dose tolerated a single booster injection one month later.

Based on the above studies the following approach is recommended by Zeiger. (Figure 3)

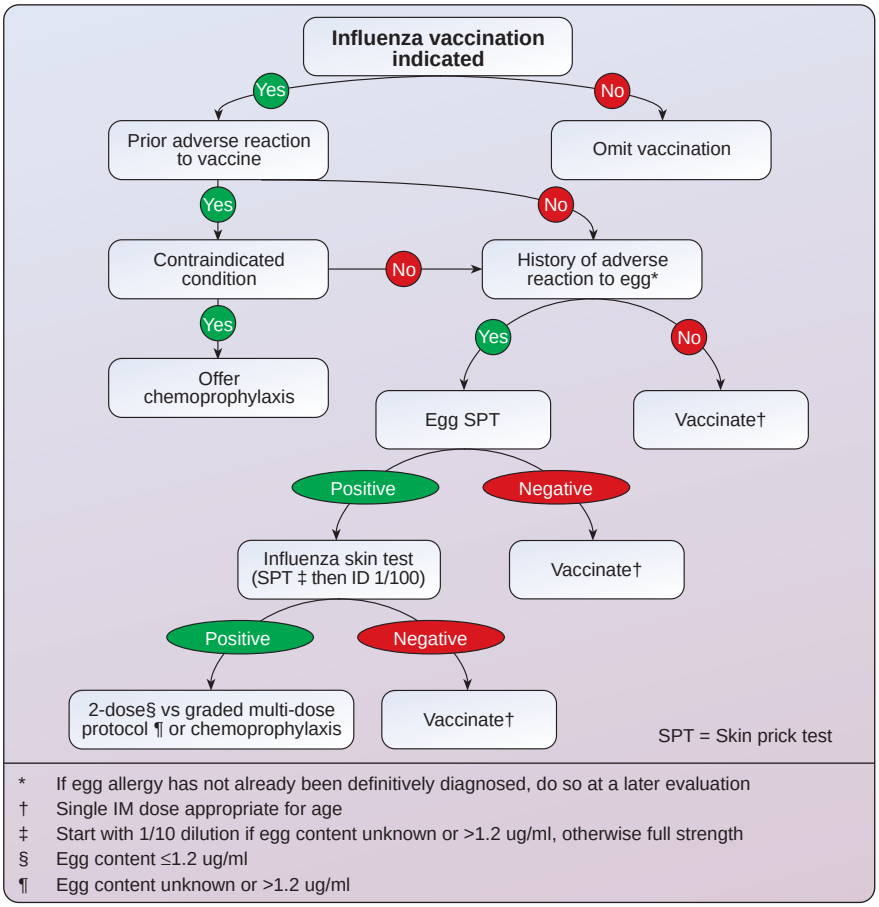
2. Measles vaccination in egg allergic subjects

The majority of life threatening reactions to MMR (measles, mumps, rubella vaccine) have been reported in children who are **not** allergic to eggs. Most of the reactions to vaccines previously attributed to egg allergy are in fact allergic reactions to gelatin, neomycin or other contaminants. Children with egg allergy may receive MMR without any special precautions. Prior skin testing is unnecessary and the injection should be given in a single injection rather than in a series of increasing doses.[6]

3. Yellow fever vaccination and egg allergy

Since yellow fever vaccines often contain egg proteins they may cause

Figure 3: Algorithm for administering influenza vaccination in patients with egg allergy



* If egg allergy has not already been definitively diagnosed, do so at a later evaluation
† Single IM dose appropriate for age
‡ Start with 1/10 dilution if egg content unknown or >1.2 ug/ml, otherwise full strength
§ Egg content ≤1.2 ug/ml
¶ Egg content unknown or >1.2 ug/ml

immediate hypersensitivity reactions in severely egg sensitive individuals. Prior skin prick testing is recommended in such individuals and if strongly positive vaccines should be withheld. In patients with less severe or localised manifestations of egg allergy, the vaccine is not contra-indicated.[6]

4. Genetically engineered foods and allergy

Foods produced through agricultural biotechnology must be assessed for safety and potential allergenicity before they are approved by worldwide regulatory agencies for entry into the food supply.[7]

Potential allergens include soybeans, nuts and fish. For example, glyphosate tolerant soybean (GTSs) has been modified to be broad spectrum herbicide glyphosate. These beans have had a gene inserted into them which results in expression of a bacterial enzyme (CP4 EPSP5) not normally found in soya beans.

Since this enzyme is readily digested by PEPSIN it has not resulted in allergies in humans although the potential for allergy does still exist.

By contrast high methionine soybeans were created by inserting a gene from Brazil nuts. A Brazil nut protein was expressed in the beans, to which 3 Brazil nut sensitive individuals reacted on skin tests. Thus it was decided internationally, not to commercialise this variety of soybeans.

Thus in the field of new genetically engineered foods, allergy potential and surveillance is essential in the future.

Conclusion

The key to the accurate diagnosis following adverse reactions to foods is the history. Food diaries, reading labels on processed foods, close attention to the interval between exposure and symptoms and knowledge of the important new food allergens is essential. Laboratory and skin tests are extremely useful for confirming a food allergy if one knows how to interpret the result.

Absolute values, e.g. Ku/L or wheal size have varying significance depending on the allergen and the age of the subject. Testing should be **history** based and wide food screening panels are expensive and produce confusing results with low-level false positivity and are not an intelligent thing to do.

Care must be taken with highly sensitive individuals who should always carry injectable Adrenaline and Antihistamines on their person and wear a *Medic Alert*. Avoidance is the key to management.

With certain vaccines, e.g. yellow fever and influenza, care should be taken in certain high-risk groups (e.g. egg allergic subjects). In the future certain novel genetically engineered proteins may pose a problem for allergic subjects.

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