"Food allergy/intolerance testing" in dermatology - science or hype?

[1]**Liam Mercieca** MD, MRCP(UK)
[1]**Lawrence Scerri** MD, FRCP (Lond), FRCP (Glasg), CCST Derm (UK)

[1]Department of Dermatology and Venereology, Sir Paul Boffa Hospital, Malta
Email: liam.mercieca@gov.mt
[1]Department of Dermatology and Venereology, Sir Paul Boffa Hospital, Malta
Email: lawrence.scerri@gov.mt

Educational aims

- To understand food allergies, their presentation and to differentiate it from food intolerance
- To clarify the proper diagnosis and management of food allergies and give a brief overview of the tests available and their appropriateness
- To outline the association of food with common skin conditions namely eczema, acne and urticaria

Key words
Food, allergy, intolerance, eczema, acne, urticaria

Abstract

Food allergies are becoming an increasingly recognized clinical problem and patients frequently ask if their health complaints are related to their diet. There has been a recent phenomenon of food allergy or intolerance testing leading to dietary alterations and restrictions. This article gives a brief overview of the latest evidence and current guidelines for proper diagnosis and management. A distinction between food allergies and food intolerance or sensitivity should be made. It focuses on the association of the common skin conditions: eczema, acne and urticaria, to food and whether dietary changes are indicated. The currently available tests and their appropriateness are also discussed.

Introduction

Health care providers should be aware of food allergies and food intolerance, their presenting symptoms, diagnosis and management. In the past years a variety of tests have been made easily available and it is important to know how to use these tools appropriately. We should be able to educate patients and follow appropriate diagnostic and management pathways to give the best care based on published research.

Food allergies have become a common clinical problem in the Western world. Studies report that they are likely to affect nearly 5% of adults and 8% of children with increasing prevalence.[1] Research in this area is growing and guidelines have been published by various organizations on how to investigate and manage these patients.

This article gives a brief overview on the differences between food allergies and food intolerance, the tests available, their use and misuse. It is also gives an outline of the food associations with commonly implicated skin conditions namely eczema, acne and urticaria. It is based on the latest evidence and guidelines and aims to give the latest updates on a topic which has received increased public interest.

Food Allergies and testing

What is a food allergy? How does it present?

Food allergy is defined as an immune system reaction that occurs soon after eating a certain food. Even a tiny amount of the allergy-causing food can trigger signs and symptoms. The food allergen causes an immunoglobulin E (IgE) – mediated response and symptoms typically manifest within a few minutes to a couple of hours after ingestion.

The clinical features can be mild to severe and include symptoms such as skin rashes, a stuffy or itchy nose, sneezing, itchy and tearful eyes, wheezing and chest tightness. It might also present with gastrointestinal symptoms such as vomiting, stomach cramps and diarrhoea. More severe symptoms include angioedema or swelling, hoarseness, troublesome breathing and anaphylaxis.

While any food can trigger an allergic response, common culprits include cow's milk, eggs, wheat, soy, peanut, tree nuts, fish and shellfish.[2]

Food allergy vs food intolerance/sensitivity

Food intolerance/sensitivity should not be confused or labelled as a food allergy. Food intolerance occurs when a person has difficulty digesting a particular food and can lead to symptoms such as intestinal gas, abdominal pain or diarrhoea. An example includes lactose intolerance due to the deficient enzyme lactase. Food intolerance involves the digestive system and is not immune mediated whilst food allergies involve the immune system.[3]

How to diagnose and tests available

A detailed clinical history is critical to correct diagnosis. Laboratory tests should support clinical diagnosis and not vice versa. Available laboratory tests have limitations not least poor positive predictive value and limited repertoire.[4]

Diagnosis of IgE-mediated food allergy is typically made using the clinical history in combination with skin prick testing (SPT) and/or immunoassays of serum food-specific IgE (sIgE) levels. These tests tend to be sensitive tools in the detection of IgE-mediated food allergy, but have a number of disadvantages, including that positive test results to tolerated foods are not uncommon; and test results do not accurately predict the severity of an allergic reaction.[5]

The EAACI (European Academy of Allergy and Clinical Immunology) food allergy guidelines recommendations on the diagnosis of food allergy include a careful and detailed

dietary history and standardised tests.[6] Specific IgE blood testing should be guided by the history and large screening panels are not recommended.

Skin prick testing demonstrates an allergic response to a specific allergen. In conjunction with an allergy focused history, SPT can help to confirm the presence of an allergy to either a food or inhaled substance (allergen). The skin prick test introduces a tiny amount of allergen into the skin, eliciting a small, localised allergic response, in the form of a wheal (bump) and flare (redness) at the site of testing.

Interestingly in a recent meta-analysis to determine the accuracy of tests to diagnose food allergy, the authors concluded that SPT and sIgE testing have good sensitivity but poor specificity for diagnosing clinically confirmed food allergy (Table 1). They highlight the fact that evidence base is limited and weak and result interpretation can be difficult. This underlines the importance of using these tests in a clinical context and keeping in mind their poor specificity.[7]

Component-resolved diagnostic testing is a new methodology which utilises purified or recombinant allergens for identification of specific molecules causing sensitisation or allergy. This is mentioned in the guidelines but is not widely available and further research on its clinical relevance is needed.[5,6]

Elimination diets for diagnostic purposes and an oral food challenge can also be considered after careful patient selection. These should be undertaken with caution and with emergency support cover.[6]

Recently there has been a surge of various other tests offered in the community to diagnose food intolerance. These tests include total immunoglobulin G (IgG) antibody binding to each food and also the IgG subclass 4 (IgG4) binding may be measured. IgG antibodies signify exposure to products, not allergy. Some research suggests that IgG may actually be a marker for food tolerance, not intolerance.[8]

Patients are given lists of foods which they are allergic to, instructions on which foods to avoid and possible medical associations. At times the diets suggested are extremely difficult to follow and very restricting since multiple allergens are listed. Recently, testing kits have become available and are directly sold to consumers. In addition these tests can be quite expensive.

Table 1: Showing good sensitivity but poor specificity of skin prick testing (SPT) and specific Immunglobulin (sIgE)

		Sensitivity	Specificity
Cow's milk	SPT	88%	68%
	sIgE	87%	48%
Egg	SPT	92%	58%
	sIgE	93%	49%
Wheat	SPT	73%	73%
	sIgE	83%	43%
Peanut	SPT	95%	61%
	sIgE	96%	59%

Evidence and guidelines

Various official associations have elected to issue a formal statement supporting the opinions expressed by the American Academy of Allergy Asthma and Immunology (AAAAI) and by the European Academy of Allergy and Clinical Immunology (EAACI) regarding the use of IgG testing.[9,10] Both of these organizations warn about the inappropriate measurement of food-specific IgG or IgG4 to suggest the presence or potential of adverse reactions to food. Recent guidelines emphasize that such testing plays no role in the diagnosis of food allergy or intolerance.[11]

For example, IgG measurements cannot be correlated with any clinical symptoms or disease. Food-specific IgG4 levels indicate that the atopic individual has been repeatedly exposed to high doses of food components, which are recognized as foreign proteins by the immune system. Therefore, EAACI gave a clear recommendation not to use these tests.

Interestingly the CSACI (Canadian Society of Allergy and Clinical Immunology) has issued a statement with a number of concerns. These included the fact that tests were widely available through complementary health providers, paramedical clinics, and some physicians. Furthermore testing kits were being sold directly to customers and are very expensive with lack of supporting evidence. Such tests might lead to exclusion diets which might cause malnutrition and poor growth in children. It also went further to discourage their use and recommended health care providers not to offer such testing.[9]

Misuse of food allergy tests

Unconventional tests are becoming increasingly common and, according to the latest evidence and research, cannot be recommended. These tests might lead to patients being misinformed and labelled as allergic to specific foods. This can cause considerable impairment in quality of life due to exaggerated restricted diets. These diets can be harmful to patients leading to malnutrition and deficiencies especially in children. Inappropriate dietary advice based on food allergy testing can also lead to micronutrient deficiency. These include vitamins, minerals, phytochemicals and antioxidants. They are all essential components of skin structure responsible for multiple biological functions. Such deficiencies can lead to skin barrier and function abnormalities.[12]

IgG testing has already been discussed. Other examples include bioresonance (electromagnetic waves used to diagnose and treat human illness), Vega electrodermal tests, iridology (determines information on patient's health based on iris characteristics) and hair analysis amongst many others. These tests are not currently validated and cannot be recommended in diagnosing food allergy.

Probiotics

Probiotics have been investigated as another option for the management of patients with food allergy, particularly cow's milk allergy, either added to formulas or given as a supplement.

Evidence that probiotic supplements have preventative or therapeutic activity for

food allergy is lacking and further research is needed to make recommendations in this area.[13]

Probiotics are not an effective treatment for eczema and may, in fact, carry a small risk of adverse events such as infections and bowel ischaemia.[14]

Diet and the skin

Eczema

Health practitioners are constantly asked by patients if certain foods could be the cause or exacerbating their eczema. This is a common concern of parents with atopic children. It should be noted that many children outgrow atopic dermatitis (eczema) by the time they reach adolescence.

In a 5-year multicenter study in infants age 3-18 months it found that even in reported mild cases of atopic dermatitis (AD), roughly 15% of infants had definite food allergies.[15] Patients with AD typically have higher levels of immunoglobulin E (IgE) antibodies. Elevated IgE antibodies are evidence only for sensitization to a food but are not proof of a food allergy. It is postulated that the presence of antibodies is a consequence of the pruritic nature of AD, causing children to scratch their skin, allowing food allergens to be absorbed via this disrupted skin barrier, and inducing the development of antibodies. AD usually comes on in infancy, before any possible food reactions.

The evidence suggests that in most cases food exclusion does not prevent or improve atopic dermatitis.[16] Some diets may actually be harmful to the skin and be associated with higher eczema prevalence in the United States. E.g. Herbal therapy, Homeopathic therapy, Vegan diet.[17]

On the other hand several studies have found an association between clinical food allergy and AD. Diet elimination trials in patients who are clinically allergic to eggs have shown promise in reducing symptoms. Elimination of certain foods (chocolate, cheese, coffee, yoghurt) in a subgroup of patients was found to be beneficial.[18]

Research clearly shows that food allergies are commoner in AD patients. Wheat, milk, soy, fish, eggs and peanuts are the commonest culprits. There was no benefit of an egg and milk-free diet in unselected participants with atopic eczema.[19]

It is still common to see food allergy testing done or referrals after a single bout of atopic dermatitis. This is neither practical nor useful.

The NIAID (National institute of allergies and infectious diseases) guidelines recommend two indications for consideration of food allergy testing (milk, egg, peanut, wheat, and soy) in children younger than 5 years with moderate-to-severe AD:

- A child who has persistent AD despite optimized management; or
- A child who has a *reliable* history of an immediate reaction after eating a specific food.

Before embarking on these tests, parents should be educated about food allergies and that positive tests are not necessarily diagnostic. In some cases dietary restrictions can lead to malnutrition and nutrient deficiencies adversely affecting growth and causing harm.[20]

Patch Testing

Another pitfall is the referral of patients with eczema for patch testing to exclude food allergies. Dermatologists apply patch tests in patients with dermatitis, to find out whether their skin condition may be caused or aggravated by a contact allergy. Patch tests are not the same as skin prick tests. Patch testing helps identify which substances may be causing a delayed-type allergic reaction (Type IV hypersensitivity reaction) in a patient.

A range of substances can be used for patch testing. A routine screen such as the European Baseline Series of allergens is applied to nearly every patient, together with specific tests appropriate to the individual. These allergens are applied on the back and may identify allergens causing contact dermatitis. It is intended to produce a local allergic reaction on a small area of the patient's back.

The top allergens from 2005–06 were: nickel sulfate, Myroxylon pereirae (Balsam of Peru), fragrance mix I, quaternium-15, neomycin, bacitracin, formaldehyde, cobalt chloride, methyldibromoglutaronitrile/ phenoxyethanol, p-phenylenediamine (PPD), potassium dichromate, carba mix, thiuram mix, diazolidinyl urea, and 2-bromo-2-nitropropane-1,3-diol.[21]

It is interesting to note that some foods and preservatives contain these substances e.g. nickel and paraben. This might lead to a systemic contact dermatitis; when a person who is already sensitized to a substance through skin contact is exposed to that substance (allergen) via a systemic route. An example is the Latex fruit syndrome; patients who are sensitized and allergic to latex develop symptoms when eating certain fruits such as avocado, banana, chestnut, kiwi, peach, tomato, potato, bell pepper, turnip, zucchini and cassava. This is due to cross reactivity where similar structural epitopes exist in different allergens.

In summary, there is scanty evidence to justify the use of food allergy tests in most patients with atopic dermatitis. Elimination diets based on these tests are not recommended and might actually be harmful. Patient reassurance and education is paramount to quell this misconception. Patch tests are indicated when there is a suspicion of allergic contact dermatitis.

Acne

Acne is a common skin condition mostly seen in adolescents and can cause considerable distress. Invariably most patients with acne and their relatives ask if certain foods could cause or exacerbate acne. Some patients will be convinced that certain specific foods cause worsening of their acne. What does the current evidence say?

Studies have shown a positive association between the intake of skimmed milk and acne.[22] The role of chocolate and other dietary factors in acne development has also been reported but not enough evidence is present to date. A particular study reported that acne is absent in populations consuming low glycaemic load and no consumption of milk or dairy products e.g. Eskimo, Okinawa islanders. Genetic differences could explain these findings.[23] Two randomized controlled studies have provided evidence for the beneficial therapeutic effects of low glycaemic load diets.[24]

There is little evidence to suggest a definite pathogenic role of specific foods in relation to acne. Advising patients to restrict particular foods is not based on robust scientific evidence. A balanced healthy diet should be recommended.

Urticaria

Urticaria is a skin condition characteristed by wheals which last less than 24 hours and/or angioedema. It is important to differentiate between acute (< 6 weeks) and chronic urticaria (> 6 weeks).

Urticaria can be triggered by a variety of factors causing histamine release. These include infections, drugs, stress, food allergies and insect bites amongst others. In a study up to 63% of patients with acute urticaria suspect food as the eliciting factor but this is much lower in clinical practice.[25]

In more than half of the cases a cause is never found. A detailed history should help elucidate the cause especially in individuals with repeated episodes. Testing for food allergies should be guided by the clinical context and 'mass' testing should be avoided.

In patients with chronic urticaria (lasting more than 6 weeks) food is rarely the cause. This should only be suspected in patients who suffer from intermittent attacks of whealing lasting for a few hours shortly after the ingestion of food.

Conclusion

Attributing skin diseases to food allergies or intolerance should be undertaken with caution. In recent years there has been increased public concern and misconceptions regarding this subject. Patients constantly asked if certain skin diseases could be attributed to food and a recent phenomenon of unregulated food allergy testing has emerged. These tests might lead to unnecessary rigorous diet regimes without any proven benefit, in addition to being expensive. Health practitioners should be aware of food allergies, intolerance/ sensitivity and follow a structured diagnostic and management pathway.

Current evidence suggests that a detailed history is invaluable in diagnosis of food allergies. Proper validated tests can help elucidate these allergies but should be guided within the clinical context. Serum IgE testing and skin prick testing are first line investigations but still have significant false positive and false negative results and should be interpreted with caution. Elimination diets and oral food challenge tests should be undertaken under specialist care and in selected patients.

Food allergies should be distinguished from food intolerance/sensitivity. At present, there are no reliable or validated tests for the diagnosis of food intolerance. Even though IgG testing has become increasingly common there is no scientific rationale behind them and there is no proven correlation between results and symptoms. Various international official immunology organisations have issued statements against IgG testing. Moreover these tests can lead to harmful diets, especially in children, causing malnutrition and retarded growth.

Currently there is limited evidence linking common skin conditions such as eczema and acne to particular food allergens. Acute urticaria is associated with certain foods but this is grossly overestimated by affected patients.

Key points

- Food allergies and food intolerance are distinct
- Diagnosis should be based on a detailed clinical history aided with appropriate testing and not vice versa
- Based on the latest evidence and published research IgG measurements for food allergies or intolerance cannot be recommended
- Patch testing is used to identify allergens in allergic contact dermatitis and not food allergies
- In general, restrictive diets are not recommended in eczema and acne since there is not any robust evidence. Acute urticaria can be triggered by food and should be investigated appropriately

Future considerations could include increased public awareness and educational campaigns. Involving all the related specialties to draft and implement local guidelines on the proper use of food allergy testing would also be beneficial.

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