INTRODUCTION

Food allergy and intolerance rank as some of the most difficult clinical problems to elucidate. With the exception of milk intolerance, coeliac disease and peanut allergy many medical practitioners still deny their existence.

Fourteen years ago my personal experience forced me to recognise that food allergy and intolerance were indeed very real problems, capable of causing symptoms in almost any part of the body. Since then, knowledge of immunological mechanisms involved has improved and this has allowed a more logical explanation and classification of adverse reactions to food (Figure 1).

This article relates only to those problems with a recognised immunological basis. These may be either Type 1 IgE-mediated resulting in an immediate reaction within seconds to minutes, or cell-mediated slower immunological reactions, with the formation of immune complexes and/or activation of lymphocytes. These latter reactions may cause symptoms within hours or sometimes days.

AETIOLOGY

There is good evidence that allergic diseases such as asthma, eczema, hay fever and food allergies have increased over recent years in more affluent societies. The reasons for this are probably multifactorial. The prerequisite is undoubtedly an underlying genetic susceptibility. Subsequent factors include age at presentation of the offending food, the state of the immune system and the integrity of the gut barrier. There is increasing evidence that healthy gut microflora, ie lactobacilli and bifidobacteria, may stimulate the development of the immunoregulatory pathways. Factors which may adversely affect this include antibiotics and acute gastro-enteritis. Breastfeeding is protective.

The allergies causing a reaction are proteins, characterised by their specific amino acid sequence. Most proteins have many different potential allergens, eg cow's milk has about 20, including beta-lactoglobulin, casein, and lactalbumin. These will remain allergenic after pasteurisation and after digestion, though they may be modified by heat treatment and hydrolysis. If the offending amino acid sequence is shared with other foods then that individual may have cross-reactions, eg latex in rubber cross-reacts with banana, kiwi, chestnut, potato and avocado; birch pollen allergy cross-reacts with the oral allergy syndrome in which sufferers experience acute pain, swelling and blisters in the mouth after eating apples.

ALLERGENS AND SYMPTOMS AT DIFFERENT AGES

(a) Infancy

Seventy percent of type I IgE-mediated reactions present below two years of age. Cow's milk is the commonest allergen, accounting for over 90% of reactions seen. Other allergens include egg, soy, seafoods and nuts. Classic symptoms are urticaria, swelling of the lips and eyes and wheeze within seconds to minutes of contact.

Many of these infants will also exhibit delayed non-IgE-mediated reactions, including atopic dermatitis, gastro-esophageal reflux, infant colic, abnormal bowel habit and failure to thrive. Foods responsible include cow's milk, soya and wheat.

Once the offending food is removed from the diet then the disease improves immediately for Type 1 reaction, but may take up to six weeks for delayed reactions.

Atopic dermatitis (AD) is one of the most common clinical manifestations of food allergy in infancy. There is a strong relationship between food hypersensitivity and the severity of AD. The majority will improve by about two years of age, but persistence of AD is often associated with persistence of IgE food allergy and inhalant allergy later in life.

(b) Over 12 months

1 peanut - This causes a classic Type I IgE-mediated reaction with symptoms ranging from swelling of the lips and eyes through to anaphylaxis. There does appear to be an increase in frequency, but it may relate to increased exposure. Studies demonstrate no relationship with breastfeeding or maternal
ingestion of peanuts during pregnancy. However, there is a significant relationship with weeping eczema in infancy and this possibly relates to the application of topical arachis oil. It used to be thought that peanut allergy was lifelong, but we now know that at least 20% of youngsters will outgrow it. This is more likely to happen in children who have no other atopic symptoms. Skin prick tests, or alternatively the specific IgE blood test (formally RAST), may be helpful in confirming this diagnosis (see below).

Peanut allergic individuals at greatest risk of an anaphylactic reaction are those with severe asthma. It is essential that their asthma treatment be optimised.

2 milk and dairy – Although most children will have outgrown milk and dairy allergy by two years of age, some will continue to be troubled well beyond childhood. The exceptional case may continue to demonstrate an acute type 1 reaction, but for the majority, symptoms will be of abdominal pain, vomiting, loose stools, constipation, tiredness and atopic dermatitis.

It is important to recognise that for intolerances the reaction may not be an ‘all or none’ response. The points below illustrate how various factors may influence the reaction, even in the same individual.

(i) When an individual develops tolerance to a food previously not tolerated, they are likely to have a ‘threshold’ of intake below which they will not exhibit symptoms, eg a quarter of a pint of milk per day and one portion of yoghurt or cheese. Exceeding this limit will precipitate symptoms. It is important that parents are aware of this. Otherwise parents imagine their child has outgrown the intolerance and feed the child large amounts of the food every day, only to be disappointed that the symptoms have recurred.

(ii) It is well recognised that modification of the food by heating reduces the allergenicity, eg a child with milk intolerance can be expected to tolerate cheese and yoghurt better than raw uncooked milk. Similarly an egg allergic person will tolerate a small amount of cooked egg yolk first, followed a while later by cooked egg white, but it may be several years, if ever, before they are able to tolerate raw egg such as in pavlova or salad dressing.

(iii) A previously dairy allergic child may have grown to tolerate these foods normally, but an episode of gastroenteritis, stress, vigorous exercise or a combination of high allergen foods may cause a relapse. Parents need to be aware of this.

3 wheat – Although less common than milk and dairy, wheat intolerance which is not coeliac disease appears to be on the increase. Symptoms are usually of abdominal pain, distension, and altered bowel habit – either diarrhoea or constipation.

If wheat intolerance is considered as a possible diagnosis it is essential that a coeliac screen be performed before removing wheat from the diet. Failure to do this causes great difficulties in the food clinic as parents are naturally reluctant to put their child back on wheat if exclusion has caused a significant improvement in symptoms. Coeliac disease is an important diagnosis with significant implications which must not be missed. However, once gluten has been removed from the diet of an individual with coeliac disease, then the antibody screen and small intestinal biopsy revert to normal, so the opportunity to make the diagnosis is lost. In untreated wheat intolerance, the coeliac screen is negative, though the IgA Gliadin Ab is not uncommonly positive, and the small intestinal biopsy is normal.

As with milk and dairy, the majority of wheat intolerant children will improve in time. A light white bread is more likely to be tolerated initially than heavy fibre and wholemeal. Weetabix and pasta are noted for causing symptoms.

4 colourants and preservatives – Children are often referred for allergy testing for these, usually said to be causing behavioural problems. To date there is no ‘test’ for them. There is, however, indisputable evidence that some children (and adults) demonstrate a variety of symptoms after ingestion of certain ‘e’ numbers, particularly the bright colourants and the sweetener aspartame. There is indisputable evidence that, in some individuals, these can cause hyperactivity, aggressive behaviour or a feeling of being ‘spaced out’. A recent paper suggests that these are more likely to be pharmacological reactions rather than allergic. They are equally common in non-atopic and atopic children.

5 NSAIDs – This is being increasingly recognised, probably because of the increasing availability of these preparations, both as antipyretics and topical anti-inflammatory agents. The specific symptoms I have seen to date have been type 1 allergic reactions (see case histories below).

**TESTS**

In the majority of cases of food allergy and intolerance, no testing is performed. This is either because there is no test available, or the results would be of limited benefit. It is rare for tests to be performed below two years of age as milk, dairy and nuts are known to be responsible for 95% of allergic reactions in this age group, so testing is unlikely to provide additional information.

The gold standard test for food intolerance is the ‘double blind food challenge’. However, this is not practical for the majority of foods, and in cases of IgE-mediated reactions may be potentially dangerous. In practice, therefore, the decision to test or not depends on the history of symptoms and the food responsible.

A thorough history of precise events surrounding the reaction is essential. This includes foods ingested at the time, exposure to environmental inhalants, state of health and medication, exercise and altitude. It is also important to enquire about previous atopic symptoms and family history.

Situations where testing is useful include confirmation, or indeed disproval of nut allergy, chronic severe atopic dermatitis often associated with other type 1 reactions, and inhalant allergy.

For gastrointestinal manifestations of food intolerance, the diagnosis depends on resolution of symptoms on exclusion of the food(s), which is generally recommended to be for six weeks in the first instance. If there is still doubt, then a challenge is appropriate.

Where testing is appropriate, the test most commonly done is the skin prick test (SPT), though the blood measurement of specific IgE will give similar results. SPTs are reliable for IgE-mediated reactions with specificity and sensitivity being 85% to 95%. They are not, however, helpful in the diagnosis of delayed/T cell-mediated reactions.

It is important to remember that a positive result indicates that the person has antigen-specific IgE, but does not prove that exposure to that allergen is responsible for the symptoms.