

Dietitians Association of Australia review paper

The dietary management of food allergy and food intolerance in children and adults

The following review paper was prepared by Lesley Clarke, Jenny McQueen, Ann Samild and Anne Swain on behalf of the Dietitians Association of Australia.

Abstract Adverse food reactions can be due to several mechanisms, and can be broadly divided into immunological and non-immunological reactions. Food allergy is the most common immunological reaction, producing antibodies to specific food proteins. It occurs mainly in infants and children with an atopic background, involves only a few foods (such as egg, peanut and milk, and, less commonly, soya, fish and wheat) with a reaction occurring within two hours. Reputable tests for detecting food antibodies are available. This contrasts with pharmacological food intolerance, a non-immunological mechanism resulting in a range of symptoms. Food intolerance occurs in children and adults. Many natural and artificial food chemicals can be involved and reaction times are variable, leading to a more difficult diagnosis. Food intolerance is diagnosed using an elimination diet, followed by challenge testing with relevant food chemicals (including salicylates, amines, glutamates, colours and preservatives). Allergy and food intolerance can coexist in the same individual. Approaches to preventing food allergy in infants are referred to and some recommendations made. Adverse reactions to milk are also discussed, as well as various controversial diagnoses such as hypoglycaemia, candidiasis and hyperactivity. (*Aust J Nutr Diet* 1996;53:89-98).

Keywords: adverse food reactions, food allergy, food intolerance.

Introduction

The area of adverse reactions to food is controversial and the subject of ongoing research. It is characterised by a lack of universal acceptance of definitions, diagnosis and management.

'Food allergy' is one of the most misused terms in popular and scientific literature and is used extensively to refer to all adverse food reactions, both immunological and non-immunological. Similarly, food intolerance may be used to refer to all adverse reactions including allergic reactions.

Definitions

Adverse reactions to food can be due to several mechanisms. Correct identification of the type of adverse reaction in each individual is important, as different approaches to diagnosis and dietetic management are required.

The following definitions are used in this document and summarised in Table 1.

Immunological reactions

Food allergy

An immunological hypersensitivity (usually by production of IgE [immunoglobulin E] antibodies) which occurs

most commonly to food proteins such as egg, milk, peanut and other nuts, soya, fish and wheat (1-3).

Non-immunological reactions

Food intolerance

An abnormal physiologic response to an ingested food or food component. This reaction may include pharmacologic, metabolic, toxic or psychological responses to food or food components (1,2).

1. Pharmacological food reactions

Reactions to low molecular weight chemicals which occur either as natural compounds (e.g. salicylates, amines, glutamates, monosodium glutamate [MSG]) or artificially added substances (e.g. preservatives, colours, MSG) in food. These chemicals are capable of provoking drug-like side-effects in susceptible people (4,5).

2. Metabolic food reactions

Involve an inborn or acquired error in metabolism of nutrients, for example, diabetes, phenylketonuria, lactase deficiency and favism.

3. Toxic food reactions

Adverse reactions caused by the direct action of a food or food additive without the obvious involvement of immune mechanisms. Toxins may be either present in food or released by micro-organisms or parasites contaminating food products.

4. Psychological food reactions (food aversions)

Involve the clinical manifestation of an adverse physical or psychological reaction caused not by the food itself but by emotions associated with the food or the eating of that food. It does not occur when the food is given in an unrecognisable form.

This paper will address the areas of food allergy and pharmacological food reactions, both separately and when they coexist in an individual.

Metabolic, toxic and psychological food reactions do not fall within the scope of this paper.

Table 1. Terminology of adverse reactions to food accepted by the Dietitians Association of Australia (DAA)

| <i>Immunological</i> | <i>Non-immunological</i> |
|------------------------------------|--------------------------|
| Food allergy (IgE mediated) | Food intolerance |
| | Pharmacological |
| | Metabolic |
| | Toxic |
| | Psychological |

Management of food allergy

Prevalence

Food allergy tends to occur in children under five years of age, who commonly have atopic eczema and a family history of asthma and/or eczema. It is an uncommon cause of adverse reactions to food in adults.

The prevalence of food allergy is difficult to estimate but there is general agreement that it is highest in infancy (estimates vary up to 7.5%) falling rapidly after the age of three years to 1 to 2%, and being 1% or less in adults (3,4). These adults tend to be atopic with up to 70% reporting an allergy to inhalant and contact allergens such as house dust mite, pollens, grasses, moulds and animal danders.

Symptomatology

An allergic reaction usually occurs within minutes, and up to two hours of ingesting the food protein. Acute symptoms usually begin with, 1. itching and burning around the mouth and local swelling, which may be followed by, 2. gastrointestinal symptoms such as nausea, vomiting, abdominal cramps and diarrhoea, 3. skin symptoms such as generalised urticaria, 4. respiratory symptoms such as wheezing and asthma, and, 5. fatal anaphylaxis (rare). These symptoms may occur concurrently or independently in an individual.

The onset of chronic eczema may be delayed for up to 24 to 48 hours and its relationship to food may be unrecognised until the food is withdrawn for one or two weeks and then reintroduced.

At the current time, there is no substantial evidence to support the theory that hyperactivity is caused by food allergy (6).

Clinical assessment

Food allergy is diagnosed principally by a careful history and physical examination. The history should include symptoms, suspected foods, quantity ingested, time between ingestion and development of symptoms and any other relevant factors, for example, exercise or aeroallergen exposure. When symptoms occur immediately after a single food ingestion (e.g. egg, peanut and milk), diagnosis is straightforward, and can be documented using the skin prick test (SPT) or the radioallergosorbent test (RAST).

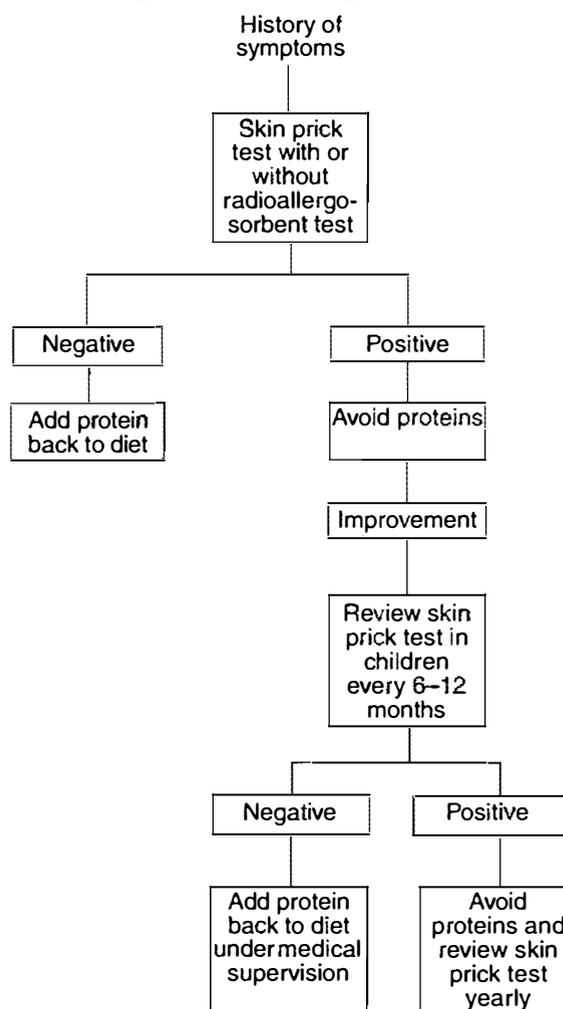
If the history is equivocal, SPT or the RAST can detect specific IgE antibodies to suspected food and aeroallergens. If the diagnosis is doubtful, oral challenge under appropriate medical supervision can be performed.

Figure 1 provides a schematic diagram of the critical steps in food allergy investigation and management.

Provoking substances

Although allergic individuals can produce IgE antibodies to almost any test food as determined by food availability and meal patterns, only a small number of foods are commonly responsible for causing food allergies. In children, egg, milk, peanut, soya, fish and wheat proteins account for around 90% of reactions, and in 80% only one or two foods are involved (3). In adults, peanut, other nuts, fish

Figure 1. Management of food allergy



and shellfish proteins account for most reactions, since allergies to egg, milk, soya and wheat proteins tend to be outgrown (7). In contrast, the incidence of reactions to contact and aeroallergens (e.g. house dust mite, pollens, grasses, moulds, animal danders) increases with age, depending on exposure (8).

Relevant tests

Carefully performed tests such as SPT and RAST are the most reliable and sensitive tests for detecting specific IgE antibodies to suspected food and aeroallergens (5,9). Negative results virtually exclude food allergy as a cause of symptoms (10). However false positive SPT results may occur with foods, so results need to be interpreted in the clinical context. Table 2 gives examples of unscientific tests.

Dietary investigation

When the diagnosis is doubtful, it may be confirmed by the exclusion of the suspected food and aeroallergens, selected on the basis of history and SPT or RAST tests. This may be followed by appropriately timed oral challenge under careful medical supervision.

If there is no change in symptoms after two to four weeks of strict avoidance of the suspected protein(s), food allergy is unlikely to be the main cause of symptoms and

Table 2. Tests for adverse reactions to food

| <i>Reputable tests</i> | <i>Unscientific tests</i> |
|---------------------------------|---|
| Skin prick test (SPT) | Leucocytotoxic test (11). |
| Radioallergosorbent test (RAST) | antigen leucocyte cellular antibody test (ALCAT) ^(a) |
| | Sublingual provocation and neutralisation test (11) |
| | Pulse test (11) |
| | Vega test (12) |

(a) Gala S, Katelaris C, Swain AR, Loblay RH. Diagnostic value of the ALCAT test. Unpublished observations.

other causes including food intolerance should be considered.

Challenge procedure

The challenge procedure involves careful reintroduction of small incremental doses of the relevant food protein under strict medical supervision, as even milligram quantities can provoke symptoms in some patients.

Challenges may take three forms: open, single-blind or double-blind, placebo-controlled challenges. The most definitive test in equivocal cases is double-blind, placebo-controlled oral food challenge (DBPCFC) carried out under careful medical supervision (6). However, there is often a limit to the staffing and equipment resources essential to the safe implementation of DBPCFC.

Challenge precautions

Where there is a history of anaphylaxis, asthma, laryngeal oedema or a large SPT reaction (4 x 4 wheal) associated with food ingestion, challenges should only be performed with extreme caution in hospital with resuscitation facilities readily available.

Individual treatment diet

The treatment diet avoids the relevant food proteins, and suitable substitutions should be recommended. In breast-fed infants the maternal diet will need modification to omit foods to which the baby has had an immediate allergic reaction or is SPT positive.

Dietary liberalisation

Management in adults involves the avoidance of the relevant food protein(s) and review as required. Management in children involves avoidance of relevant food protein(s), followed by annual review with repeat skin prick tests. If the SPT is negative, careful reintroduction of the food(s) under appropriate medical supervision should be attempted. Children are most likely to outgrow egg, milk, soya and wheat allergies (7), particularly if the reactions are relatively mild, whereas peanut (13) and fish allergies are more often severe and persistent. A history of exquisite sensitivity, severe reaction on first exposure, and/or repeated life threatening anaphylactic episodes suggests that clinical sensitivity is likely to continue into adulthood (8). In these individuals, reintroduction of the implicated food protein should never be attempted.

Nutritional considerations

To ensure nutritional adequacy, advice must be detailed and practical, taking into consideration shopping and food

preparation skills, budgeting, interpretation of food labels, eating away from home, literacy and language barriers.

In the case of milk allergy, most infants can tolerate reintroduction when the skin test is negative but children diagnosed as having a food allergy after the age of three years are less likely to outgrow the problem (7,14-17). In infants and small children an infant formula is the nutritional basis of the diet, with the addition of a few carefully selected permitted foods. Suitable milk substitutes such as infant soya formula or protein hydrolysate are recommended for these children and appropriate vitamin and/or mineral supplementation when necessary. Every effort should be made to keep in contact with patients on very restricted diets to ensure growth and general health are not compromised.

Management of pharmacological food intolerance

Prevalence

The prevalence of pharmacological food intolerance is unknown but it is estimated to occur in 10% of the population. It occurs much more commonly than food allergy.

Symptomatology

Symptoms can involve the skin, gastrointestinal tract (GIT), respiratory tract or central nervous system; either individually or in combination (4).

- Skin manifestations include urticaria, angioedema and eczema.
- Common GIT symptoms include nausea, vomiting, recurrent abdominal pain, flatulence, diarrhoea and aphthous ulceration.
- Respiratory symptoms generally involve the upper respiratory tract, with nasal congestion, excess mucus production, recurrent pharyngitis or sinusitis. Food components may also precipitate asthma in patients with bronchial hyperreactivity (18).
- Common neurological symptoms are headaches (often migrainous), generalised lethargy and myalgia. Other symptoms include impairment of memory and concentration, mental agitation or depression, visual disturbances, tinnitus, dizziness, paraesthesia and neuralgia and hyperactivity (4,19-21).
- Anaphylactoid reactions.

A family history of related symptoms is very common, and women are affected about twice as frequently as men. In some allergic individuals with eczema, asthma or rhinitis, food chemicals may aggravate their pre-existing symptoms (22).

Clinical assessment

All patients with suspected food intolerance need to be assessed by a physician to exclude any other disorder. Indications for dietary investigation include:

- severe or chronic symptoms which appear to be precipitated by foods, drinks or aspirin-containing drugs,
- a history of recurrent urticaria, mouth ulceration and/or irritable bowel syndrome symptoms,

- patient's request for investigation of diet (refusal usually results in patients seeking advice from 'fringe' or unorthodox practitioners), or
- patients who have altered their diet on the basis of misconceptions and/or fixed ideas about food allergies.

Provoking substances

Symptoms can be provoked by a variety of chemical substances, both natural and artificial. The chemicals include natural compounds such as salicylates (4,23), amines (24), glutamates (25,26), and some food additives (preservatives, artificial colours, annatto, artificial flavours and added MSG).

Chemically there is little difference between 'natural' and 'artificial' ingredients, and both may cause adverse reactions in sensitive people if sufficiently large amounts are consumed. In many plant foods, for example, benzoates and salicylates are present as natural preservatives and flavourings, some of which are identical to those added to processed foods.

These chemicals are widespread in foods and the reactions are often delayed, from one to two hours and up to 48 hours. Therefore, prior to testing, recognition of the relationship between symptoms and a particular food is often difficult for the patient, as well as the dietitian and physician. When such a relationship is recognised, multiple foods may be incriminated. Reactions to each chemical exhibit a dose-response relationship, with a triggering threshold that depends partly on recent intake, so that an individual food does not necessarily provoke the same reaction on each occasion (4).

Relevant tests

There is no currently available skin or blood test which can identify the offending chemicals. Diagnosis can only be based on the results of systematic dietary elimination and careful chemical challenge (11).

Elimination diet

The elimination diet is a diagnostic tool used to identify patients whose symptoms are likely to be diet-related.

The elimination diet must be comprehensive, containing only a few foods which are unlikely to provoke symptoms. The provoking chemicals are present in many foods, and many patients may be sensitive to more than one compound. Thorough education on the elimination diet is essential to ensure that patients and the parents of children with food intolerance understand the importance of complete adherence to the diet, and the need to maintain adequate nutrient and energy intake. Inadvertent consumption of an offending chemical often prevents complete resolution of symptoms, and may render challenge results invalid.

While on the elimination diet the patient should keep detailed records of all foods eaten, severity of particular symptoms, and medications taken. Where required, patients may need to keep these records prior to the elimination diet to establish the severity and frequency of individual symptoms.

The patient should be advised that a withdrawal reaction may occur during the first or second week on the elimination diet. Some or all of the patient's symptoms may flare or recur for a few days, usually subsiding within a week.

While on the diet some patients become more sensitive to fumes and odours, which may precipitate symptoms. Since this can complicate the elimination and challenge procedure, patients should be advised to avoid exposure to petroleum products, paints, perfumes or perfumed flowers, cigarette smoke, strong smelling cleaning agents and pressure pack sprays. Once the diet is liberalised at the end of the testing period this sensitivity to smells and fumes usually becomes less of a problem (4).

In most patients, clinical improvement occurs gradually over a two- to four-week period. If there is no change in symptoms after four weeks of strict adherence to the elimination diet, then food intolerance is unlikely to be the main factor in causing the patient's symptoms. A normal diet should then be resumed by reintroducing one suspect food or chemical group at a time (e.g. milk, wheat, salicylate, amines, preservatives and colours) in gradually increasing amounts, up to high doses for three to seven days to determine if symptoms are exacerbated.

A strict elimination diet is not advised during pregnancy. However, as adverse reactions to food chemicals are dose-related, a reduction in consumption of the major suspected chemicals during pregnancy may reduce symptoms.

Babies who are exclusively breastfed may sometimes develop symptoms (e.g. hives, colic or restlessness), due to chemicals transmitted through the milk (22). Placing the mother on a modified elimination diet may be helpful, but should only be tried if other strategies fail and only under medical and dietetic supervision. If cow's milk formula is not tolerated, an appropriate formula based on soya or a protein hydrolysate may be cautiously tried before breastfeeding is ceased. When solids are introduced, care should be taken to try the foods least likely to cause symptoms (e.g. rice, potato, pear, lamb, or chicken) and later introduce small amounts of other foods which might provoke adverse reactions.

Challenge procedure

Challenges are administered only when symptoms have cleared (or improved significantly) for five consecutive days, and patients have been on the elimination diet for a minimum period of two weeks. The elimination diet should be continued throughout the challenge procedure. Open food challenges with wheat and milk are performed first, followed by challenge with natural salicylates, amines, MSG, artificial colouring agents and a range of preservatives. Challenges may take the form of purified food chemicals or foods grouped according to their chemical composition. Two recommendations can be made:

1. It is recommended that chemical capsule challenges are used only in teaching hospitals. The chemicals and placebos are encapsulated in opaque gelatine capsules and administered double-blind at 48 to 72 hour intervals. For patients with asthma, angioedema and/or anaphylactoid reactions, these procedures can be con-

ducted in hospital or on an outpatient basis by a physician experienced in allergic disease.

- It is recommended that outside of the teaching hospital environment only food challenges, and not chemical capsule challenges, should be performed. A food challenge involves taking foods containing only one challenge compound, several times per day over three to seven days.

If a reaction occurs, the patient must wait until symptoms have subsided completely. An additional three days must be allowed before recommencing challenges since patients often experience a temporary refractory period during which they are unresponsive (4,27).

Challenge precautions

Asthma, laryngeal oedema and anaphylaxis

Patients with a history of asthma or laryngeal oedema are routinely hospitalised, as inpatients or as outpatients in a specialist clinic with resuscitation facilities available, for small incremental dose challenges with salicylate, metabisulphite, MSG and tartrazine.

In severe asthma, examination of the patient's food and symptom history may suggest a trial avoidance of one or more food chemicals, particularly metabisulphite, glutamates, salicylates or artificial colouring.

Pregnancy

The elimination diet and chemical challenges should be avoided in pregnant women because the effects on the foetus are unknown.

Individual treatment diet

When all of the challenges have been completed, careful assessment of reactions is necessary. If any results are doubtful, the challenge should be repeated. After assessment, the patient commences a modified diet based on their response to challenge. The diet restricts only those compounds to which the patient has reacted.

Liberalisation

The patient should be reassessed after four to eight weeks on their modified diet, to determine progress and to ascertain whether or not the diet should be liberalised. A gradual liberalisation of foods by chemical grouping should be encouraged as tolerated. It is important to take into account the cumulative effects of individual chemicals over time.

Nutritional considerations

During the diagnosis and management of food intolerance, care should be taken to ensure that the patient's dietary intake is adequate to sustain normal growth in children and health in adults. In most cases this goal can be achieved with careful dietary manipulation and the use of vitamin or mineral supplements when necessary.

Figure 2 provides a schematic diagram of the critical steps in pharmacological food intolerance investigation and management.

Coexisting food allergy and food intolerance

In patients with eczema, asthma and rhinitis, food allergy and intolerance may coexist in the same individual. The elimination diet for food intolerance should be the basis for dietary investigation. Suspected allergens indicated by a positive history and/or skin prick test or RAST, should also be removed from the elimination diet. Patients are challenged with the food chemicals and suspect allergens, in accordance with the procedure for investigating food intolerance and food allergy, observing the necessary precautions. A modified diet based on the positive challenge responses is then prescribed.

Table 3 summarises the distinguishing clinical features of food allergy and pharmacological food intolerance.

Prevention of food allergy

It is widely accepted that atopic diseases are inherited, although the exact mode of inheritance is not clear. Recent prospective studies indicate that a child with one atopic parent has a 50% chance of developing an allergy. When both parents are atopic, the incidence rises to about 70% (28). Manipulation of the maternal and infant diet to prevent the development of food allergy in potentially atopic children is controversial (29). Restriction of the maternal diet during the last trimester of pregnancy does not appear to be useful (30-33).

Studies indicate that sensitising food allergens are transmitted in breast milk (34-37). Several studies now suggest that avoidance of important dietary allergens (eggs, cow's milk, peanuts) by the breastfeeding mother, delaying the introduction of solids until four to preferably six months of age, and choosing low allergen solids until at least nine to 12 months, may delay the appearance of

Figure 2. Investigation and management of pharmacological food intolerance

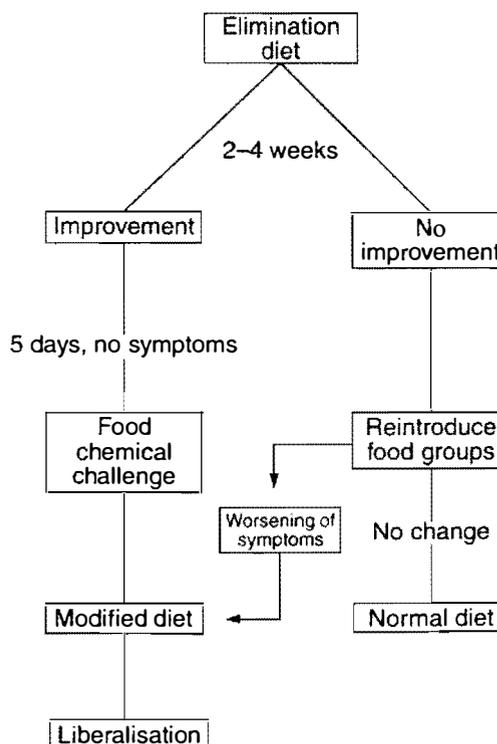


Table 3. Clinical features of food allergy and pharmacological food intolerance

| <i>Food allergy</i> | <i>Pharmacological food intolerance</i> |
|---|---|
| Immunologically mediated | Non-immune mediated (mechanisms not known as yet) |
| Uncommon | Common |
| Mostly children | All ages |
| Usually atopic | Usually non-atopic |
| One or two foods (reaction occurs whenever food is eaten) | Many foods (dose-related) |
| Protein | Low molecular weight chemicals |
| Immediate reaction | Often delayed |
| Easier diagnosis | Difficult diagnosis |
| Skin prick test (SPT), radio-allergosorbent test (RAST) | No reputable skin or blood test available. |

atopic dermatitis in the first year of life only (38–41). The long-term incidence of asthma, rhinitis and inhalant sensitisation is unaffected by dietary manipulation.

In practice, low allergen diets for breastfeeding mothers are extremely difficult to maintain even when motivation is high. In one study (39), only 10% of at-risk children were shown to benefit from manipulating the mother's diet. However, the mother of a child from a highly atopic family may choose to restrict her diet, and in this case medical and dietetic supervision is recommended. Where breastfed infants develop symptoms of eczema and have positive skin tests to major food allergens (egg, milk, peanut, wheat, soya, fish), the possibility of maternal and infant dietary manipulation should be considered.

A soya formula or protein hydrolysate should be tried for an infant who develops allergic symptoms whilst being fed a cow's milk-based formula (42).

At present it is recommended for atopic families that breastfeeding continues for 12 months, with avoidance of allergens (egg, peanut, cow's milk) in the mother's diet, followed by the introduction of low allergen foods from six months. High allergen foods such as egg, milk, peanut, soya and fish should be excluded from such an infant's diet until nine to 12 months (42). Inhalation of provoking substances such as cigarette smoke should also be avoided.

Prevention of food intolerance

In contrast to development of food allergy, avoidance of the chemicals such as salicylates, amines, glutamates, colours or preservatives does not prevent infants from developing symptoms of food intolerance on exposure.

Adverse reactions to cow's milk

Cow's milk and cow's milk-based formulas are implicated as major causes of adverse reactions to food during the first year of life. Ingestion of milk provokes symptoms after a variable period of time and may be due to several

mechanisms—lactase deficiency, cow's milk allergy, cow's milk intolerance or cow's milk enteropathy (43–46).

Lactase deficiency

It is rare to be born with primary lactase deficiency. It is mainly manifested in adults, as the intestinal lactase activity decreases with age. This is an inherited characteristic and occurs especially in populations such as Australian Aborigines, American Indians, Chinese, Japanese, Vietnamese, Arabs and South Italians. In Caucasians, primary lactase deficiency is uncommon (47).

In children, secondary lactase deficiency is the most clearly defined common cause of adverse reactions to cow's milk. It usually occurs after gastroenteritis and is generally not permanent. Lactase deficiency symptoms include watery, acid diarrhoea, abdominal cramps, distension and flatulence which may last from one to eight weeks. During this time a lactose-free formula may be used. Gradual reintroduction of cow's milk or cow's milk-based formula may then be undertaken as tolerated.

Cow's milk allergy

Cow's milk allergy is defined as an IgE mediated hypersensitivity to one or more milk proteins (44,48). Reactions develop within minutes (up to 45 minutes) of ingestion of small volumes of milk. Symptoms include acute urticaria, angioedema, anaphylaxis or exacerbations of eczema. Prevalence varies between 1 and 3% in infants (49–51). The diagnosis is often obvious from the history, and can be made from the symptoms alone. Skin tests and RAST are always strongly positive. If allergy is suspected, the most reliable approach is the withdrawal of cow's milk, followed by a cautious medically supervised challenge when the SPT becomes negative. Once a milk allergy is recognised, simple avoidance is all that is required. For children less than 12 months old, formulas based on soya or protein hydrolysate are suitable milk substitutes, although some 20 to 50% of these infants may also react to soya proteins (52).

Cow's milk intolerance

Individuals with cow's milk intolerance have delayed reactions and are non-atopic, with negative skin tests indicating normal IgE levels. Symptoms include vomiting, reflux, diarrhoea, eczema and asthma up to 72 hours after the ingestion of normal volumes of cow's milk (48,53). These infants also present with the multisystem symptoms of food intolerance.

Diagnosis is best made by the dietary elimination and challenge procedure outlined in the section on pharmacological food intolerance. Reactions are dose related so that long-term management involves the cautious reintroduction of cow's milk in small amounts as tolerated. The substances and mechanisms which cause cow's milk intolerance are unknown.

In children with eczema where true food allergy can coexist with food intolerance, cow's milk may trigger symptoms through both mechanisms.

Cow's milk enteropathy

A small number of infants present with cow's milk enteropathy. Symptoms are generally chronic and include a

delayed onset of vomiting and diarrhoea after the ingestion of small amounts of cow's milk. Mucosal damage occurs which can lead to malabsorption of nutrients and failure to thrive. These infants have negative skin tests and do not develop IgE antibodies to cow's milk. Diagnosis is made by duodenal biopsy and a favourable response to cow's milk exclusion. The risk of shock from fluid loss is very high and a milk challenge should not be attempted. Supervised reintroduction of milk should only be attempted cautiously after 12 months exclusion as recovery usually takes one to two years (54).

Nutritional management of cow's milk avoidance

Milk is an important source of protein and calcium for small children. Infants who are allergic to milk should try a soya formula, protein hydrolysate or in extreme cases an elemental formula such as Neocate. Older children should try a calcium-fortified soya beverage. If no formula is acceptable, advice on appropriate protein intake and calcium supplement should be given.

Controversial diagnoses

Hyperactivity attention deficient and hyperactivity disorder (ADHD)

In 1973 Dr Ben Feingold postulated that dietary chemicals such as salicylates and colours could cause hyperactivity (19). Controlled studies using the Feingold diet have reported doubtful benefit from dietary manipulation for patients suffering from hyperactivity (55-58).

However, the original Feingold diet failed to adequately exclude natural salicylates (22), amines and glutamates which may provoke adverse reactions in sensitive individuals (4). Later studies provide some support for the benefit of dietary manipulation for some hyperactive children (20,59,60). Therefore, a trial of the elimination diet and chemical challenge may be undertaken.

A diet high in sugar has not been confirmed as a factor adversely affecting behaviour or cognitive function in children (61).

Chronic fatigue syndrome (post-viral syndrome, myalgic encephalomyelitis)

There is no recognised dietary regimen for chronic fatigue syndrome (CFS, also known as post-viral syndrome or myalgic encephalomyelitis). However, many patients severely limit the range of foods in their diet, which may lead to an inadequate dietary intake. For some patients, food plays no discernible part in triggering symptoms, while in others, symptoms may resolve completely (62). Motivated patients may try a supervised elimination diet and challenge but, overall, only a few patients have shown any benefit from dietary manipulation.

Candidiasis syndrome (yeast allergy)

The candidiasis hypersensitivity syndrome proposed by Truss in 1978 (63) claims that overgrowth of candida organisms in the bowel releases toxins which weaken the immune system. This supposedly leads to further infections, food allergies and chemical intolerances (64).

Proposed treatment involves a special diet avoiding yeasts, sugars, and food additives, with antifungal drugs being prescribed long term to inhibit the growth of *Candida*. Recent studies have failed to confirm that there is any significant immunological disturbance (65,66) or that the response to the restricted diet is any better than placebo (67). Fungal overgrowth in the body should be treated with antifungal medications as dietary manipulation is inappropriate.

Hypoglycaemia

Genuine reactive hypoglycaemia, reversed by carbohydrate ingestion, is rare. However, orthomolecular practitioners have attributed symptoms of weakness, shakiness and fatigue to hypoglycaemia on the basis of minor fluctuations in blood sugar levels. A study by Palardy et al. (68) found that blood glucose levels measured at the time the patient's symptoms occurred, were essentially normal.

Some patients with self-diagnosed hypoglycaemia however, may have unrecognised food intolerance and may benefit from a trial of the elimination diet and challenge procedure.

The current consensus amongst orthodox physicians is that the diagnostic labels of hypoglycaemia and candidiasis have no scientific basis (69).

Recommendations

1. That professionals practising in the area should be consistent in the use of basic terms such as food allergy and food intolerance in communication with other professionals and the public.
2. Opportunities should be sought in a variety of media to provide the public with knowledge of scientifically validated tests for food allergy and food intolerance.
3. Ideally, individuals with food allergy and food intolerance should be supervised by a specialist allergy physician, in association with a dietitian.

Dietitians, in situations where there is no allergy specialist, must be aware of the valid tests and basic principles governing the dietary management of food sensitive individuals. Advice should be sought from a specialist clinic in difficult cases.
4. The child of one or two atopic parents should be exclusively breastfed for the first six months of life with the mother avoiding egg, peanut, and other nut proteins during this time. Solids should be introduced no earlier than four months using low allergen solids, preferably until the end of the infant's first year.

| Glossary | | | |
|---|---|---|---|
| Allergen | A substance, usually protein, that provokes the formation of IgE antibodies. | IgE (immunoglobulin) antibodies | Antibodies produced in response to allergens in an atopic individual. |
| Amines | Chemicals produced in food by enzymatic decarboxylation of amino acids, e.g. tyramine in cheese, β -phenylethylamine in chocolate. | Irritable bowel syndrome | A syndrome consisting of abdominal distension (with or without pain), diarrhoea and/or constipation and flatulence, in the absence of detectable organic disease. |
| Anaphylaxis | A sudden severe IgE mediated response to a foreign protein, in a previously sensitised individual. Multiple target organs are usually involved, with rapid progression through hypotension, circulatory collapse, and death if emergency treatment is not given. | Leucocytotoxic test (cytotoxic food test, antigen leucocyte cellular antibody test [ALCAT]) | An unproven test in which white blood cells are mixed with food extracts and examined under a microscope. The test is claimed to be positive, if the cells appear to be damaged. |
| Anaphylactoid reaction | A reaction resembling anaphylaxis which is not IgE mediated, e.g. severe acute reaction to MSG. | Monosodium glutamate (MSG) | The sodium salt of glutamic acid which occurs naturally in all animal and vegetable proteins, and is widely added as a flavour enhancer in savoury foods (food additive code number 621). Other glutamate salts may also be added to foods (food additive code numbers 620, 622–625). |
| Angioedema | Local swellings usually with a normal skin appearance, originating in the deep dermis and subcutaneous tissue, or in mucous membranes. This is caused by the same pathological changes as urticaria. | Preservatives | Chemicals added to processed foods to inhibit unwanted chemical reactions and the growth of micro-organisms thereby prolonging shelf life. Preservatives known to trigger adverse reactions are benzoates (food additive code numbers 210–213), sulphites (food additive code numbers 220–228), nitrite/nitrate (food additive code numbers 249–252), propionates (food additive code numbers 280–283), anti-oxidants (food additive code numbers 310–321). |
| Antigen | A substance, usually foreign to the body, that stimulates the immune system to produce antibodies, e.g. bacteria, bacterial toxins, some food proteins. | Pulse test | An unproven test in which the pulse rate is measured before and after ingestion of a food. The test is claimed to be positive if the pulse rate increases by at least 12 beats per minute. |
| Apthous ulceration (mouth ulcers) | Small painful ulcers occurring in the oral mucosa, which can be acute, recurring or chronic. | Radioallergosorbent test (RAST) | A valid test which measures the amount of a specific IgE antibody in a sample of blood. |
| Atopy (allergy) | A genetic predisposition to develop IgE antibodies to allergens, usually manifested as asthma, eczema and hayfever. | Salicylates | A group of hydroxybenzoic acid compounds which occur naturally in plant foods, and may also be synthesised for use in many artificial flavours, perfumes and medicines. |
| Atopic dermatitis (allergic eczema) | Eczema occurring in patients with a family history of atopy. | Skin prick test | A valid test which measures the amount of specific IgE antibody in the skin. |
| Candidiasis syndrome (yeast allergy) | An unsubstantiated theory of yeast overgrowth in the bowel or vagina leading to the release of toxins which weaken the immune system. | Sublingual provocation and neutralisation | An unproven treatment in which extracts of foods and chemicals are placed under the patient's tongue to provoke symptoms. Then more dilute solutions are taken daily to neutralise the reaction. |
| Chronic fatigue syndrome (post-viral syndrome, myalgic encephalomyelitis) | A distinct clinical syndrome which involves persisting or relapsing fatigue, myalgia and/or headaches, as well as a number of neuropsychiatric symptoms, in the absence of demonstrated organic disease. | Urticaria (hives) | An acute or chronic disorder involving itchy, raised, red wheals. |
| Eczema | A chronic relapsing dermatitis usually commencing in infants and children characterised by severe itching, erythema, watery discharge, exudative lesions and persistent scratching, which leads to the development of scales and crusts (lichenification). It presents classically in atopic dermatitis, but may occur from other causes. | Vega test | An unproven test, which measures the effect of food on the electrical impedance of the patient's body. |
| Hypersensitivity | May be used interchangeably with the word allergy in scientific literature. | | |

References

1. Anderson JA, Sogn DD, eds. Adverse reactions to foods. American Academy of Allergy and Immunology Committee on Adverse Reactions to Food and National Institute of Allergy and Infectious diseases. US Department of Health and Human Services, Public Health Service, National Institutes of Health Publication No. NIH 842442, July 1984.
2. Joint Committee of the Royal College of Physicians and the British Nutrition Foundation. Food intolerance and food aversion. *J R Coll Physicians Lond* 1984;18:83-123.
3. Sampson HA. IgE mediated food intolerance. *J Allergy Clin Immunol* 1988;81:516-9.
4. Loblay RH, Swain AR. Food intolerance. In: Wahlqvist ML, Truswell AS, editors. Recent advances in clinical nutrition. London: John Libbey 1986:169-77.
5. Allen DH, Van Nunen SA, Loblay RH, Clarke L, Swain AR. Adverse reactions to food. *Med J Aust* 1984;141(Suppl):S37-42.
6. Bock SA, Atkins FM. Patterns of food hypersensitivity during sixteen years of double blind, placebo-controlled, food challenges. *J Paediatr* 1990;117:561-7.
7. Bock SA. The natural history of food sensitivity. *J Allergy Clin Immunol* 1982;69:173-7.
8. Loblay RH. Food allergy in adults—state of the art. In: Wahlqvist ML, Truswell AS, editors. Recent advances in clinical nutrition. London: John Libbey 1992:163-73.
9. Yunginger JW. Proper application of available laboratory tests for adverse reactions to food and food additives. *J Allergy Clin Immunol* 1986;78:220-23.
10. Sampson HA, Alberg R. Comparison of results of skin tests, RAST, and double-blind, placebo controlled food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 1984;74:26-33.
11. Reisman, RE. American Academy of Allergy position statements—controversial techniques. *J Allergy Clin Immunol* 1981;67:333-8.
12. Katelaris CH, Werner JM, Hedde RJ, Stuckey MS, Yan KW. Position statement vega testing in the diagnosis of allergic conditions. *Med J Aust* 1991;155:113-4.
13. Bock SA, Atkins FM. The natural history of peanut allergy. *J Allergy Clin Immunol* 1989;83:900-4.
14. May CD. Food allergy—lessons from the past. *J Allergy Clin Immunol* 1982;69:255-9.
15. Sampson HA. Food allergy. *J Allergy Clin Immunol* 1989;84:1062-7.
16. Ingelfinger FJ, Lowell FC, Franklin W. Gastrointestinal allergy. *N Engl J Med* 1949;241:303-8,337-40.
17. Chiaramonte LT, Altman D. Food sensitivity in asthma: perception and reality. *J Asthma* 1991;28:5-9.
18. Baker GJ, Collet P, Allen DH. Bronchospasm induced by metabisulphite-containing foods and drugs. *Med J Aust* 1981;2:614-6.
19. Feingold BF. Why is your child hyperactive? New York: Random House, 1975.
20. Egger J, Graham PJ, Cootes CM, Grumley D, Soothill JF. Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome. *Lancet* 1985;1:540-5.
21. Swain AR, Soutter V, Loblay RH, Truswell AS. Salicylates, oligoantigenic diets and behaviour. *Lancet* 1985;2:41-2.
22. Swain AR. The role of natural salicylates in food intolerance [Thesis]. Sydney: University of Sydney, 1988.
23. Settignano GA. Aspirin and allergic disease: a review. *Am J Med* 1983;74 (Suppl6A):950-60.
24. Maga JA. Amines in foods. *CRC Crit Rev Food Sci Nutr* 1978;10:373-403.
25. Giacometti T. Free and bound glutamate in natural products. In: Filer LJ Jr, Garattini MR, Kare MR, Reynolds WA, Wurtman RJ, editors. Glutamic acid: advances in biochemistry and physiology. New York: Raven Press, 1978:25-34.
26. Allen DH, Delohery J, Baker J. Monosodium glutamate-induced asthma. *J Allergy Clin Immunol* 1987;80:530-7.
27. Zeiss C, Lockett RF. Refractory period to aspirin in a patient with aspirin-induced asthma. *J Allergy Clin Immunol* 1976;57:440-8.
28. Zeiger RS. Development and prevention of allergic disease in childhood. In: Middleton E, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, editors. Allergy: principles and practice. 4th ed. St Louis: Mosby 1993:1137-71.
29. Kramer MS. Does breastfeeding help protect against allergic disease? *J Paediatr* 1988;112:181-90.
30. Falth-Magnusson K, Oman H, Kjellman NIM. Development of atopic disease in babies whose mothers were receiving exclusion diet during pregnancy—a randomised study. *J Allergy Clin Immunol* 1987;80:868-75.
31. Falth-Magnusson K, Kjellman NIM. Allergy prevention by maternal elimination diet during late pregnancy—a 5-year follow-up of a randomised study. *J Allergy Clin Immunol* 1992;89:709-13.
32. Zeiger RS, Heller S, Mellon M, O'Connor R, Hamburger RN. Effectiveness of dietary manipulation in the prevention of food allergy in infants. *J Allergy Clin Immunol* 1986;78:224-38.
33. Lilja G, Dannaeus A, Magnusson KF, Graff-Lonnevig V, Johansson SG, Kjellman NI, Oman H. Immune response of the atopic woman and foetus: effects of high- and low-dose food allergen intake in late pregnancy. *Clin Allergy* 1988;18:131-42.
34. Van Asperen PP, Kemp AS, Mellis CM. Immediate food hypersensitivity reaction on the first known exposure to the food. *Arch Dis Child* 1983;58:253-6.
35. Gerrard JW. Allergies in breastfed babies to foods ingested by the mother. *Clin Rev Allergy* 1984;2:143-9.
36. Stuart CA, Twiselton R, Nicholas MF, Hide DN. Passage of cow's milk protein in breast milk. *Clin Allergy* 1984;14:533-5.
37. Cant A, Narsden RA, Kilshaw PJ. Egg and cow's milk hypersensitivity in exclusively breastfed infants with eczema, and detection of egg protein in breast milk. *Clin Allergy* 1984;14:533-5.
38. Hattevig G, Kjellman B, Sigurs N, Bjorksten B, Kjellman NIM. Effect of maternal avoidance of eggs, cow's milk, and fish during lactation upon allergic manifestations in infants. *Clin Exp Allergy* 1989;19:27-32.
39. Zeiger RS, Heller S, Mellon MH, Forsythe AB, O'Connor RD, Hamburger RN, Schatz M. Effects of combined maternal and infant food-allergen avoidance on development of atopy in early infancy: a randomized study. *J Allergy Clin Immunol* 1989;84:72-89.
40. Chandra RK, Puri S, Hamed A. Influence of maternal diet during lactation and use of formula feeds on development of atopic eczema in high risk infants. *B M J* 1989;299:228-30.
41. Arshad SH, Matthews S, Gant C, Hide DW. Effect of allergen avoidance on development of allergic disorders in infancy. *Lancet* 1992;339:1493-7.
42. Hill DJ, Hosking CS. Preventing childhood allergy. *Med J Aust* 1993;158:367-9.
43. National Health and Medical Research Council. Cows milk intolerance in children. Canberra: NHMRC, 1983.
44. Hill DJ, Firer MA, Shelton MJ, Hosking CS. Manifestations of milk allergy in infancy: clinical and immunological findings. *J Paediatr* 1986; 109: 270-6.
45. Diagnostic criteria for food allergy with predominantly intestinal symptoms. *J Pediatr Gastroenterol Nutr* 1992;14:108-2.
46. The Gut Foundation. Milk allergy and intolerance in infants and children. Sydney: The Gut Foundation, 1995.
47. Davidson GP. Lactase deficiency. *Med J Aust* 1984;141:442-4.
48. Hill DJ, Ball G, Hosking CS. Clinical manifestations of cows' milk allergy in childhood. I. Associations with in-vitro cellular immune responses. *Clin Allergy* 1988;18:469-79.

49. Bock SA. Prospective appraisal of complaints of adverse reactions in children during the first 3 years of life. *Paediatrics* 1987;79:683-8
 50. Host A, Husby S, Osterballe O. A prospective study of cows milk allergy in exclusively breast-fed infants. *Acta Paediatr Scand* 1988;67:663-70.
 51. Bishop JM, Hill DJ, Hosking CS. Natural history of cow milk allergy: clinical outcome. *J Pediatrics* 1990;116:862-7.
 52. Businco L, Bruno G, Gianpietro PG, Cantani A. Allergenicity and nutritional adequacy of soy protein formulas. *J. Pediatrics* 1992;121 (Suppl):S21-8.
 53. Hill DJ, Davidson GP, Cameron DJS, Barnes GL. The spectrum of cows milk allergy in childhood. *Acta Paediatr Scand* 1989;68:847-52.
 54. European Society for Paediatric Gastroenterology. Diagnostic criteria for food allergy with predominantly intestinal symptoms. *J Pediatr Gastroenterol Nutr* 1992;14:108-2.
 55. Conners CK, Goyette CH, Southwick DA, Lees JM, Andrulonis PA. Food additives and hyperkinesia: a controlled double-blind experiment. *Pediatrics* 1976;58:154-66.
 56. Harley JP, Ray RS, Tomasi L, Eichman PL, Matthwes CG, Chun R, et al. Hyperkinesia and food additives: testing the Feingold hypothesis. *Pediatrics* 1978;61:818-28.
 57. Williams JI, Cram DM. Diet in the management of hyperkinesia: a review of the tests of Feingold's hypotheses. *Can Psychiatr Assoc J* 1978;23:241-8.
 58. Lipton MA, Mayo JP. Diet and hyperkinesia—an update. *J Am Diet Assoc* 1983;83:132-4.
 59. Breakey J, Hill M, Reilly C, Connell H. Report of a trial of the low additive, low salicylate diet in the treatment of behaviour and learning problems in children. *Aust J Nutr Diet* 1991;48:89-94.
 60. Rowe, KS. Briggs DR. Food additives and behaviour: an overview. *Aust J Nutr Diet* 1995;52:4-10
 61. Wolraich ML, Lindgren SD, Stumbo PJ, Stegink LD, Appelbaum MI, Kiritsy MC. Effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children. *N Eng J Med* 1994;330:301-7
 62. Loblay RH, Swain AR. The role of food intolerance in chronic fatigue syndrome. In: Hyde BM, Goldstein J, Levine P, editors. *The clinical and scientific basis of myalgic encephalomyelitis/chronic fatigue syndrome*. Ottawa: The Nightingale Research Foundation 1992:521-8.
 63. Truss C. Tissue injury induced by *Candida albicans*: mental and neurologic manifestations. *J Ortho Mol Psychiatry* 1978;7:17-37.
 64. Crook WG. *The yeast connection*. 3rd ed. Jackson, Tennessee: Professional Books 1989.
 65. Terr AI. Environmental illness: a clinical review of 50 cases. *Arch Int Med* 1986;146:145-9.
 66. Simon GE, Daniell W, Stockridge H, Claypoole K, Rosenstock L. Immunologic, psychological, and neurophysiological factors in multiple chemical sensitivity: a controlled study. *Ann Int Med* 1993;119:97-103.
 67. Dismukes WE, Wade JS, Lee JY, Bonita K, Dockery RN, Hain JD. A randomised double-blind trial of nystatin therapy for the candidiasis hypersensitivity syndrome. *N Engl J Med* 1990;323:1717-23.
 68. Palardy J, Havrankova J, Lepage R, Matte R, Belanger R, D'Amour P, et al. Blood glucose measurements during symptomatic episodes in patients with suspected postprandial hypoglycemia. *N Engl J Med* 1989;321:1421-5.
 69. Terr AI. Unconventional theories and unproven methods in allergy. In: Middleton E, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, editors. *Allergy: principles and practice*. 4th ed. St Louis: Mosby 1993:1767-93.
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