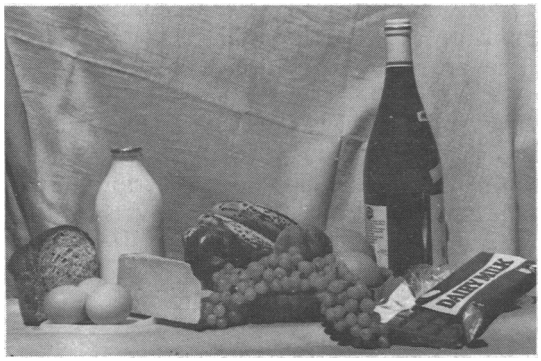
ABC of Nutrition

A STEWART TRUSWELL

FOOD SENSITIVITY

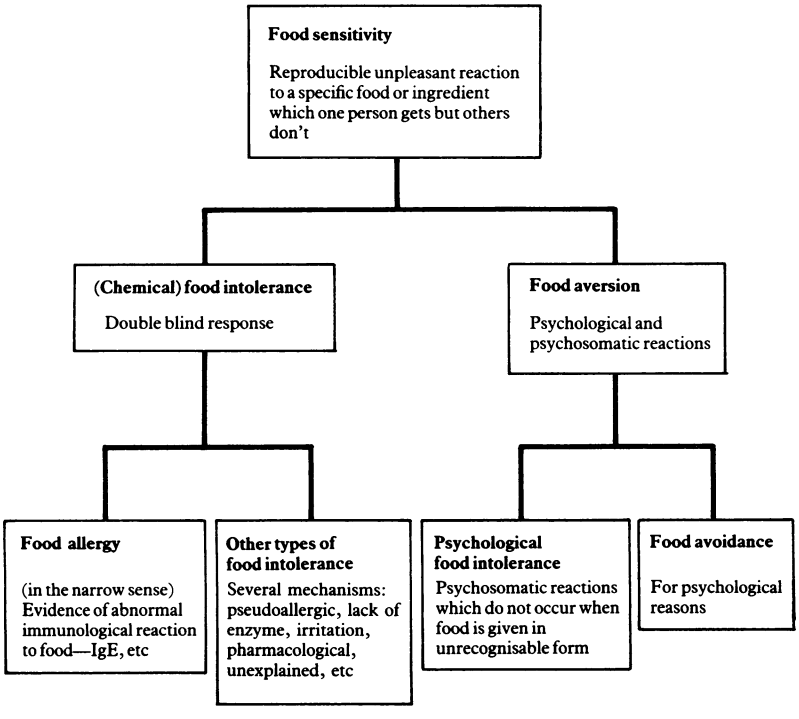


One man's meat is another's poison—LUCRETIUS 96-55 BC

In affluent countries the idea is now widespread that a variety of symptoms (not just those of classical allergy) are caused by individual (hyper)sensitivity to certain foods or substances in them; that such sensitivity has become more common; and that food processing has something to do with it. The media, various unorthodox practitioners, and some groups of lay people have spread the "news." Medical practitioners meanwhile are equipped with little information, most of it confusing, and no reliable diagnostic test to answer their patients' needs.

The subject is at the interface between scientific immunology, food technology, and quackery. Good clinical research has been lacking, but recently a few academic departments have started to apply the methods of clinical science to unravel this confusing area. Four authoritative reviews were published in 1983.[1-4] All are recommended for further reading.

Terminology



The words describing food sensitivity are imprecise and often used to mean different things.

Food allergy is commonly used by lay people (and by doctors talking to patients) as the broad term, including non-immunological (and sometimes even psychosomatic) reactions. In technical communication the term "allergy" should be confined to immunological reactions.[1-4]

Food sensitivity or hypersensitivity is sometimes used in the narrow sense to mean only immunological reactions.

Adverse reaction to food is not used in this article because it conveys no meaning of individual susceptibility and includes food poisoning (dealt with in another article).

Pseudoallergic and *anaphylactoid* reactions are used for, for example, asthma or angio-oedema after food with no immunological abnormalities detectable in the patient.

Food idiosyncrasy is used in some classifications for non-allergic food intolerance.

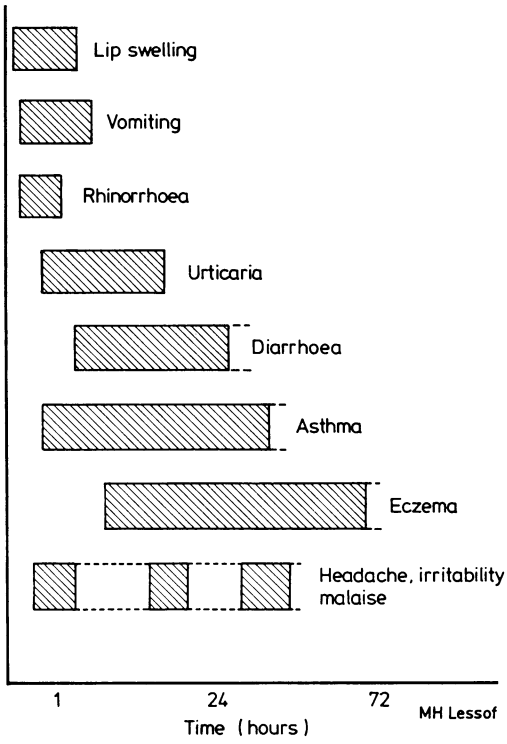
The classification used here is developed from and compatible with the definitions in the report of the Royal College of Physicians.[3]

Diagnosis

Four ways of presentation:

- "Whenever I eat persimmons I get swollen lips, then itchy spots and I sometimes vomit."
- "I can't eat persimmons" (reason why vague or based on a single episode long ago).
- "I wonder if this rash could be caused by something in my diet?"
- "I've given up eating persimmons because the lady in the health food shop (or the lady next door) says I must be allergic to them."

Time course of symptoms of food intolerance



Elimination diets

The meat least likely to cause reactions is *lamb*

The least antigenic cereal is *rice*

Vegetables: *peeled potatoes*, *carrots*, and *lettuce*

Fruits: *pears*

Fat: a refined vegetable *seed oil*, eg *sunflower*

Drink: *water* and *sugar*

Other foods are included in some elimination diets, depending on the type of reaction and the suspected ingredients.

Diagnosis of food sensitivity is easy when there is a characteristic early response to a food that is eaten at least occasionally. The patient often notices the association and its reproducibility and tells the doctor the diagnosis.

Diagnosis is more difficult, however, if the clinical reaction is delayed or varies or does not always happen. Such reactions are also made more difficult to judge if someone else has already incriminated a food on circumstantial evidence or because of prejudice.

There are no straightforward diagnostic tests for food sensitivity comparable with the electrocardiogram for coronary disease or the blood urea concentration for renal failure.

Skin tests—Drops of extracts of one or more suspected food antigens are dropped on to the skin and the skin is then pricked or scratched through the drop. A positive response is a wheal and flare within 20 minutes. This indicates the ability of skin mast cells to degranulate in response to the antigen, presumably because they have on their surface IgE specific to the food antigen. False positive and false negative responses are common. Skin tests are most reliable for urticarial skin reactions that are immunologically mediated. They are less useful for delayed reactions or reactions in other organs and not at all useful for reactions that are not immunologically mediated. The results also depend heavily on the quality and concentration of the antigens.

The *radioallergosorbent test* (RAST) is a radioimmunoassay performed on serum to show the presence of IgE specific for the food antigen. It is positive in association with IgE mediated food sensitivity but even here false positive and false negative results may occur. People may also have IgE antibodies to a food that they used to react to as a child but can now tolerate.

Dietary manipulation

The more general diagnostic procedure to indicate food sensitivity is dietary manipulation and recording of symptoms. Such procedures give diagnostic information in food sensitivity of all types. There are several strategies.

Diet diary—The patient or parent keeps a list of all foods eaten and notes any symptoms. This is simple and cheap and can be done at home for several weeks. It is liable to subjective bias, not suitable if the reaction was serious, and difficult to interpret if the responsible agent is present in several foods.

Temporary elimination of one or a few suspected foods—Elimination can be for about a week each time. This is an open trial, liable to subjective bias, but it causes little inconvenience. The method is not suitable if the reaction was serious.

Elimination diet followed by reintroduction of foods one by one—All the foods that commonly provoke sensitivity reactions are eliminated from the diet for two or three weeks. One food is then added back every three to seven days. Elimination diets carry a risk of nutritional deficiency if taken for long or not properly managed.

Patient blind or double blind challenges—After the patient has been stabilised on a standard or elimination diet foods or ingredients are given in capsules or incorporated into oligoantigenic masking foods. The patient is "blind" to what the foods are. The tests may be carried out in hospital or (more economically but less reliably) at home with the patient recording reactions.

Responses expected with different types of food sensitivity

Type of food sensitivity	Open trial	Blind trial	Immune response
Food allergy	+	+	+
Food intolerance	+	+	–
Psychosomatic	+	–	–
Food aversion	–	–	–

Clinical reactions

Foods with a high content of natural salicylate include:

dried fruits
berry fruits
oranges
apricots
pineapples
cucumbers
gherkins
endive
olives
grapes
almonds
liquorice
peppermints
honey
many herbs
thyme
mint
paprika
rosemary
oregano
curry
tomato sauce
Worcester sauce
tea
wines
port
liqueurs

For more details see: Swain A, Dutton S, Truswell AS. *J Am Diet Assoc* (in press).

Foods likely to contain tartrazine (food colour E102) include:

fruit squash and cordial
coloured fizzy drinks
pickles
bottled sauces
salad cream
cakes (shop bought)
cake mix
soups (packets and tins)
custard
instant puddings
coloured sweets
filled chocolates
jelly
ice cream and lollies
jam
marmalade
curry powder
mustard
yoghurt

Tartrazine is water soluble and gives a pleasant lemon yellow colour to foods. It is also used in some medicine capsules. Incidence of sensitivity is between 1 in 10 000 and 1 in 1000.

Foods likely to contain sulphur dioxide

Salads in salad bars*
Fresh fruit salad in hotels*
Wines, chilled fruit juices
Pickled onions, dried fruits
Commercial precut chips

*From "stay fresh" spray

Urticaria and angio-oedema

Urticaria and angio-oedema may be caused by collagen diseases, serum sickness drug reactions, physical agents, and contact with dusts, among other things. Urticaria may be provoked by foods in four ways.

(1) It may occur as an IgE mediated food allergy, especially to egg (ovalbumin in the white of hen's eggs), peanuts, fish, or cows' milk. These may also cause anaphylaxis.

(2) Large amounts of food which contain histamine releasing agents—for example, strawberries, shellfish, and paw paw—may provoke urticaria.

(3) Foods which contain histamine itself may also provoke urticaria—for example, some wines, fermented cheeses, and sausages. Again, large amounts are needed.

(4) The above foods usually provoke an acute reaction, but chronic urticaria may result from intolerance to salicylates in aspirin and naturally occurring in foods, or to tartrazine, a commonly used yellow food colour, or to benzoates (preservatives in some foods). Cross sensitivity is common between salicylates and tartrazine.

Diagnosis of types 1-3 is often clear from the history, but in chronic urticaria an elimination diet followed by challenge of aspirin and tartrazine in capsules is necessary to prove the diagnosis. Physical factors—for example, exercise and warmth—tend to cause urticaria on their own and may exacerbate a reaction to food.

Rhinitis and asthma

Foods can precipitate some attacks of asthma in infancy but come well behind infections. The role of foods in asthma diminishes during childhood and they are uncommon precipitants in adults. Inhalants, irritants, infections, pollens and moulds, changes in the weather, and exercise are then all more important. Food sensitivity asthma in adults is largely confined to those exposed to dusty grain, flour, coffee, etc, in their work.

Eggs, fish, nuts, and chocolate are among the foods most likely to provoke asthma in children. Skin tests are usually positive, indicating that IgE is implicated, but, if the skin test is positive for a food in an asthmatic child, asthma may not follow a double blind challenge. In addition, the response to foods is sometimes psychosomatic.

Tartrazine, the yellow azo dye, and benzoates, used as food preservatives, may sometimes cause àsthma. This usually occurs in patients sensitive to aspirin. The role of tartrazine can be difficult to unravel because it is present to varying degrees in different types of food, and blind challenge tests are useful.

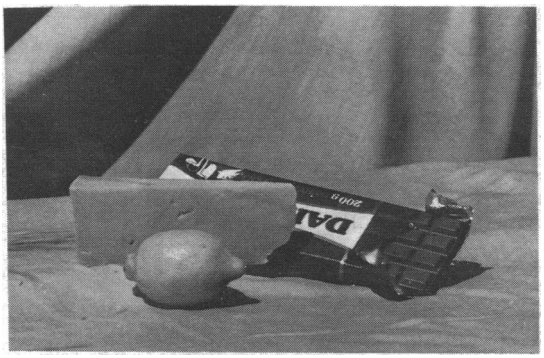
The food preservatives sulphur dioxide (SO_2) and sodium metabisulphite can aggravate bronchospasm in established asthmatics. These patients are very sensitive to the irritant effect of SO_2 gas which is liberated from sodium metabisulphite in acid foods and inhaled in low concentration as the food is swallowed.

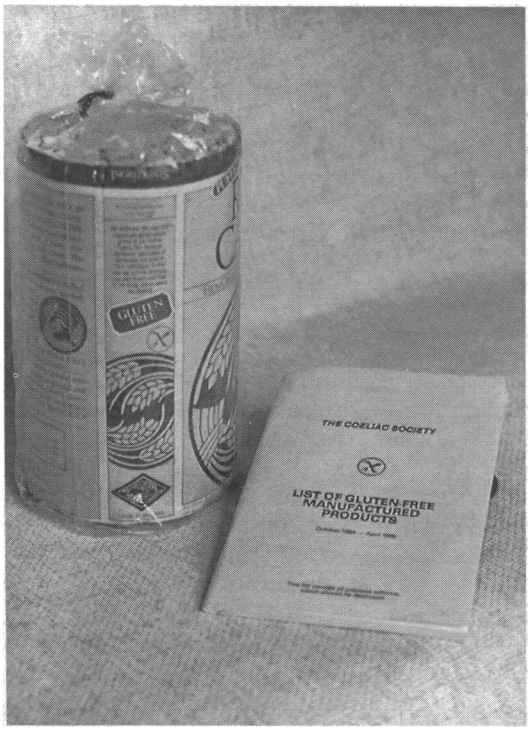
Eczema

Infantile eczema and flexural eczema in adults are associated with high serum titres of IgE and often with multiple positive skin tests. In infantile eczema the response to food taking or elimination is slower and less clear cut than in urticaria.

Statistically significant responses to skin tests have been reported in infants apparently sensitive to a food—for example, exacerbation after milk or improvement after withdrawing egg. A controlled trial showed improvement in 14 out of 20 children with infantile eczema when egg and milk were removed. Elemental diets (glucose, oil, amino acid mixture, vitamins, and minerals), though expensive, have been helpful in severe infantile eczema. Breast feeding reduces the chance of eczema but only partly in babies with a strong atopic family history.

In adults with eczema response to elimination diets is less likely. Milk, eggs, and wheat are the most powerful antigens.





Some less common food sensitivities

Favism—Haemolytic anaemia after eating broad beans. The basic defect is red blood cell glucose-6-phosphate dehydrogenase deficiency.

Bitter lemon purpura—"Bitter lemon" contains quinine, which may rarely precipitate thrombocytopenic purpura.

Chinese restaurant syndrome—Facial pressure, burning sensation in upper trunk and shoulders, and chest pain soon after eating foods rich in monosodium glutamate, particularly Chinese wonton soup.

Sensitivity to tea or coffee, or both—These common social beverages can cause a variety of pharmacological effects, eg vomiting, headaches, tachycardia, which have sometimes been proved by objective tests.[5]

Migraine

Tension, relaxation, menstruation, bright lights, and hypoglycaemia are among the major precipitants of migraine. Foods can also precipitate attacks. The different factors can be cumulative; several may be needed before an attack occurs. Attacks may come on many hours after a provoking food. Suggestibility and placebo effect have been well established in the responses of migraine sufferers.

Cheese, chocolate, and citrus fruits are often reported to precipitate migraine. They contain pressor amines—tyramine, phenylethylamine, and synephrine, respectively. Alcoholic drinks are another precipitant, notably related to cluster headaches: red wines and some other drinks contain histamine. Other attacks may come about from foods that produce nausea, such as fatty foods. Nitrates, found in some sausages, occasionally cause headaches ("hot dog headache").

True food allergy via IgE is not the usual mechanism in migraine. In a recent trial in children with severe recurrent migraine at Great Ormond Street most recovered on an exclusion diet. Reintroduction of foods, first "open," later disguised, showed that cow's milk, eggs, chocolate, orange, and wheat were most likely to provoke an attack and tartrazine less commonly.

Gastrointestinal reactions

Many different gastrointestinal sensitivity reactions to food are known and they can act through several different mechanisms. Early symptoms are lip swelling, tingling in the mouth or throat, and vomiting. Later symptoms include diarrhoea, bloating, or even steatorrhoea. Remote symptoms—urticaria, asthma, headache, joint pains—can be associated.

In children immediate intolerance is not uncommon to cows' milk or egg white, nuts, seafood, and some fruits. Tolerance increases with age. Cows' milk allergy can produce a variety of effects, including gastrointestinal bleeding or protein losing enteropathy; eosinophilia may be present.

Coeliac disease—Sensitivity to wheat gluten is the cause of coeliac disease with jejunal atrophy. It took from 1888, when coeliac disease was classically described, to 1953 before it was found that a fraction of wheat was responsible. A few other foods have been linked with occasional mucosal damage in children, such as cows' milk and soya.

Three month colic occurs as much in breast fed as in bottle fed infants and there is debate whether in breast fed infants it is associated with maternal consumption of cows' milk.

Irritable bowel syndrome—Evidence for food sensitivity in the irritable bowel syndrome is conflicting. One study, which performed exclusion and double blind challenge, indicated that food sensitivity was common: wheat, dairy foods, maize, some fruits, tea, and coffee were mostly responsible. Another study could not show food sensitivity in most patients.

Intestinal lactase insufficiency is the rule in most adults of Asian and African origin and seen in a minority of white people. There is diarrhoea, abdominal distension, discomfort, and flatus after milk, usually a cupful or more.

Hyperactivity

Feingold in the USA suggested that children (usually boys) with overactivity, short attention span, and impulsive behaviour might improve on a diet which omitted foods containing artificial colours or natural salicylates, or both. Although organisations of parents of difficult children have faith in this hypothesis, objective confirmation is sparse. Most double blind tests with food colours reported significant effects in either none or only one or two of the hyperactive children tested, and some of the information Feingold used on the salicylate content of foods was wrong. Nevertheless, there are some children with a combination of overactivity and physical symptoms (rashes, rhinitis, headaches) suggestive of food sensitivity that have improved on an elimination diet at Great Ormond

1 Lessof MH, ed. *Clinical reactions to food*. Chichester: John Wiley, 1983.
2 Marabou Symposium. Food sensitivity. *Nutrition Reviews* 1984;42:65-139.
3 Royal College of Physicians and the British Nutrition Foundation. Food intolerance and food aversion. *J R Coll Physicians London* 1984;18:2.
4 American Academy of Allergy and Immunology Committee on Adverse Reactions to Foods. National Institute of Allergy and Infectious Diseases. *Adverse reactions to food*. Bethesda, Md: National Institutes of Health, 1984. (NIH Publication No 84-2442.)
5 Finn R, Cohen HN. "Food allergy": fact or fiction? *Lancet* 1978;i:426-8.

Street. They appeared on challenge to be sensitive to different foods, but tartrazine and benzoic acid were top of the list.

Arthritis

Gouty arthritis is aggravated by alcohol and by high purine and high protein diets. Although most patients with rheumatoid arthritis do not respond to food exclusions or challenges, a patient was reported from the Hammersmith Hospital whose arthritis was clearly shown to be aggravated by milk and cheese.

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The illustration showing the true course of symptoms of food intolerance is reproduced, by permission, from Lessof MH. *Clinical Reactions to Food*. Chichester: John Wiley.

Lesson of the Week

Prolonged hypoparathyroidism presenting eventually as second trimester abortion

R EASTELL, C J EDMONDS, R C S DE CHAYAL, I R McFADYEN

Idiopathic hypoparathyroidism is an uncommon condition that is rarely diagnosed during pregnancy. The patient described here had symptoms for many years and an abortion during the second trimester before the diagnosis was suspected and established during a second pregnancy.

Hypocalcaemia due to hypoparathyroidism can go undetected in spite of untoward physical effects. If the condition remains untreated during pregnancy second trimester abortion may occur

Case report

A 23 year old white woman had noticed spontaneous carpal spasms for 10 years but had never brought them to medical attention. She had suffered from episodes of depression and had attempted suicide three years previously. In May 1983 she went into labour at 27 weeks of pregnancy. The pregnancy had seemed normal, and there was no evident reason for abortion. The female infant weighed 790 g and died after 26 hours. Necropsy showed that she had bilateral intraventricular haemorrhages, bilateral pneumothoraces, and the respiratory distress syndrome. A radiograph of the neonate did not show any signs of parathyroid dysfunction.

In October 1983 the patient was admitted during the 16th week of a second pregnancy for insertion of a cervical suture to prevent premature labour. She was observed to have Chvostek's and Trousseau's signs and snowflake opacities of the lens. She did not have signs of monilial infection, and her knuckles and feet looked normal. She was short, with a height of 1·48 m compared with the mean parental height of 1·68 m. Her teeth were normal. Initial investigations showed a plasma calcium concentration of 1·61 mmol/l (6 mg/100 ml), phosphate concentration of 1·61 mmol/l (5 mg/100 ml), magnesium concentration of 0·68 mmol/l (2 mg/100 ml), and alkaline phosphatase activity of 110 U/l (upper limit of normal 280 U/l). Urinary excretion of calcium was 1·2 mmol (48 mg)/24 h. Radiographs of the hands and skull were normal. Plasma parathyroid hormone concentration was 50 ng/l (upper limit of normal 120 ng/l) and thus was not increased in response to the hypocalcaemia; plasma 25-hydroxycalciferol concentration was normal for the season. Idiopathic primary hypoparathyroidism was diagnosed, but before the hypocalcaemia could be corrected she went into labour and was delivered at 18 weeks. At necropsy the fetus was found to have a polymorphic leucocyte infiltration of the lungs and chorioamnionitis consistent with a three day labour. During the puerperium the patient underwent a modified Ellsworth-Howard test, which measured the response of plasma cyclic adenosine 3',5' monophosphate to 100 IU of bovine parathyroid hormone given intravenously. The plasma concentration rose from a base value of 8 nmol/l (0·27 mg/100ml) to a peak value of 98 nmol/l (3·2 mg/100 ml) (normal peak value 100-280 nmol/l (3·3-9·3 mg/100 ml)), confirming the diagnosis.

Subsequently, treatment with alfacalcidol 2 μg daily increased the plasma calcium concentration to 2·25 mmol/l (9 mg/100 ml). A hysterocervicogram showed cervical incompetence. She remained well without any recurrence of depression or carpal spasms. Ten months after the second abortion she had a third pregnancy, at which time she was receiving treatment and the plasma calcium concentration was consistently normal. The pregnancy was unremarkable. Spontaneous rupture of the membranes occurred at 36 weeks, and a normal infant was delivered.

Discussion

Our patient evidently had severe hypocalcaemia due to hypoparathyroidism for at least 10 years before it was identified. Until her pregnancies, however, the untoward effects of recurrent carpal spasms, opacities of the lens, stunted growth, and possibly episodes of depression had been unrecognised. The pregnancy itself may have exacerbated her condition.

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