

ADVANCES IN ALLERGY

Alimentary tract and distant organs

The symptoms can be divided into two groups, those occurring in the alimentary tract itself and those which occur in some other organ. Of the former, the most spectacular are the rapid urticaria and itching that arises in and around the mouth, almost as soon as a sensitised individual raises the food to his lips. The most common provoking foods are said to be nuts, citrus fruits and vegetables. Reactions in the lower alimentary tract take a little longer to develop, but nausea and vomiting, possibly accompanied by diarrhoea, may occur within 30 minutes of eating seafood or eggs. It may be accompanied by flushing and headaches, itching and palpitations, though it generally resolves within 1-2 hours.

But foods can precipitate an allergic response in other organs as well. Those specialists who have seen food-induced asthma attacks

describe them as being quite as bad as attacks which are produced by inhaling the antigen. And as well as local urticaria around the mouth, food intake can aggravate urticaria elsewhere. In one Swedish hospital, 330 consecutive patients with recurrent urticaria were asked what made their conditions worse. Foods were said to worsen their woes in 30% of cases, and 18% also mentioned drinks. Fruits, vegetables, nuts and fish were the most frequent offenders.

Mechanisms of food allergy

And what are the mechanisms involved? It is generally assumed that the commonest is the Type I reaction, with histamine release from mast cells leading to inflammation and increased vascular permeability. An unresolved question is how the patient became sensitised in the first place. There is no doubt that food

molecules can pass through the intestinal wall into the circulation. Many normal individuals have circulating IgM and IgG antibodies to food proteins. But the food-sensitive individual appears to make IgE antibodies as well.

The secretory IgA in the gut is probably responsible for reducing the amount of food antigen gaining access to the circulation, and IgA antibody complexes are thought not to activate the complement system. These may therefore be harmless, cleared by the liver.

However, patients with atopic eczema (which sometimes improves when certain foods are removed from the diet) have food antigen complexes which do bind and activate the complement system. This activation may be responsible (at least in part) for the skin eruptions themselves.

So in addition to Type I reactions, the food allergic individual might also show Type III responses.

Not only that, but his cell-mediated system (Type IV) may become activated as well, at least in cases where contact with food is via the skin.

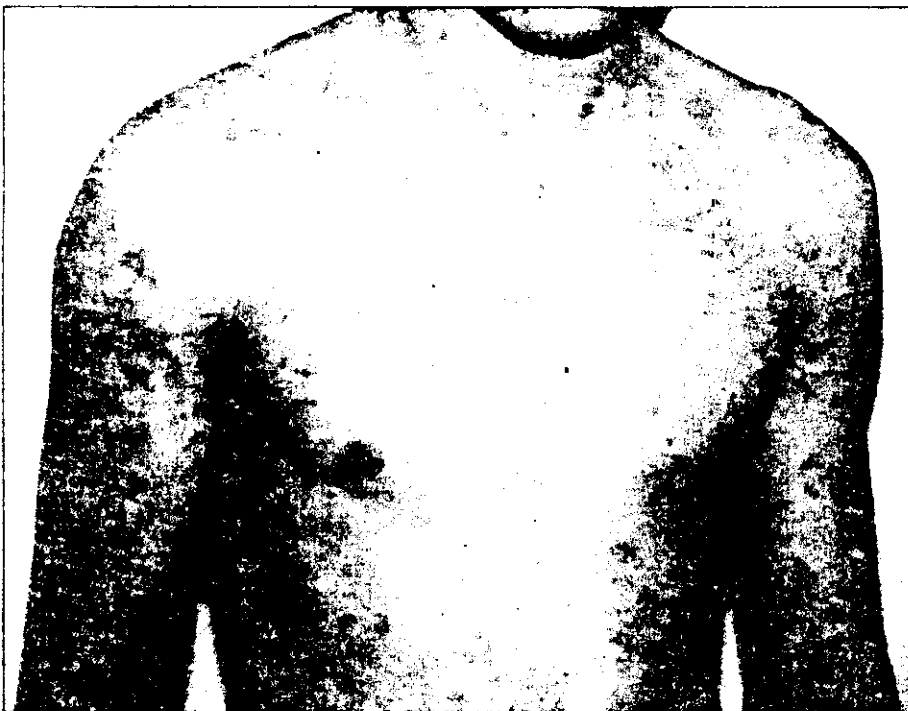
Bakers, bar workers and caterers can all suffer from food-induced contact dermatitis.

But whatever the effect of these other mechanisms, the direct hypersensitivity reaction is probably the most important, and with this in mind efforts have been made to identify the actual food antigens present in, say, fish or milk.

They turn out to be proteins or glycoproteins of remarkably similar size, with molecular weights of 15-35,000, similar to those of inhalant allergens.

They are also remarkably resistant to enzyme attack, though this finding itself is not new.

In the 1920s, Dr Heinz Küstner showed that his allergy to fish



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(an immediate urticaria as soon as he put it in his mouth) could be transferred to his colleague Dr Karl Prausnitz by injecting him with Küstner's serum.

This was once the basis of the "passive transfer" test for hypersensitivity (though in these days of transferable hepatitis it is not used any longer).

Küstner himself, over 50 years ago, showed that the haddock antigen to which he responded was resistant to digestion by both trypsin and pepsin.

Breast is best?

If hypersensitivity to foods depends on food antigens escaping from the gut into the circulation, then it is obviously desirable to reduce this escape to a minimum.

And since it probably occurs most extensively in the infant, there is now a strong move among many paediatricians to ensure that babies, and particularly the babies of atopic parents, are fed nothing but breast milk for the first 3-6 months of their lives.

The recommendation is made for 3 reasons.

By avoiding cow's milk altogether, the cow's milk antigen cannot sensitize the infant's immune system.

Secondly, breast milk is thought to have a factor which helps to seal the infant's gut mucosa, thus reducing antigen access later in life, and thirdly, breast milk protects against gastrointestinal infections which tend to have the opposite effect and increase gut permeability. In this way, the baby stands the best chance of being protected during the most vulnerable period of its life, and hence of tolerating cow's milk (and other potentially antigenic foods) when they are introduced at a later stage.

Colitis and IBS

Certainly there seems no doubt that such allergy to foreign proteins is a major cause of infantile colitis. When a group of eight infants with colitis were examined in London, the doctors were struck by the closeness in time of the babies being put on artificial feeds and the onset of the complaint. They found that switching to a diet that excluded probable antigens cleared the colitis very rapidly. The major allergen to be avoided was cow's milk, though some babies reacted to soya and beef proteins.

To investigate what was happening in the gut itself, they performed a series of colonoscopy studies and saw IgE plasma cells in the colon wall. These fell in number as the disease subsided. They were left with only one conclusion: "These results provide compelling evidence that food allergy is the major source of inflammatory bowel disease in infancy, and that an exclusion diet is

the treatment of choice.

And is food intolerance a major cause of bowel complaints in adults as well? Some studies of the adult **irritable bowel syndrome** or IBS (in which abdominal pain is accompanied by diarrhoea or constipation but no radiological abnormalities) suggests that it is. A research team in Cambridge put 21 sufferers from IBS onto an elimination diet consisting of meat, fruit and water, and no less than 14 of them found that their symptoms cleared. Foods were then reintroduced to see which were responsible for provoking the IBS. Wheat was found to be the most common, followed by corn and then dairy products.

Six of the patients who had benefited from the restricted diet were then brought into hospital and "challenged" in a double-blind test to see whether they could tell from the symptoms they felt, whether the substance they were given by nasogastric tube was one of the

ALLERGENIC FRACTIONS IDENTIFIED IN COLIC

Food	Active component	Concentration (mg/100 g food)	Molecular weight	Sensitivity index
Fish (cod)	Sarcoplasmin protein	200	12,000	0.001
Egg white	Ovomucoid	225	32,000	0.0025
Cow's milk (pasteurized)	β -lactoglobulin	100	36,000	0.10
Tomatoes	Glycoprotein fraction	2.5	20-30,000	0.15

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"allergenic" foods or a placebo. They were able to identify when they were receiving an offending food in the vast majority of cases. So food intolerance can lead to IBS. But is it due to allergy? Possibly not. Tubes were inserted to collect secretions from the colon during the food challenges. During provocation with foods, but not when a placebo was being given, the levels of prostaglandin E₂ showed a marked increase. In contrast, there was no rise in serum histamine, IgE or immune complexes. Since prostaglandins stimulate smooth muscle contraction, the cause of the IBS symptoms may be pharmacological rather than immunological. But the lesson of the study is the same - that although it is difficult to identify the offending foods, it is well worth while trying to remove them from the diet. In this case, two patients out of every three received benefit from doing so.

The "oligoallergenic" diet

The difficulty in identifying an allergenic food is two-fold. Patients may react not just to one but to several different foods. Their allergy is multiple. At the same time, the foods that they eat may contain a wide range of allergenic ingredients. Bread, for example, may have wheat, soya, yeast and milk, all of which are potential allergens. To get round these problems an exclusion diet used for diagnosis should ideally consist only of water, and a mixture of elemental nutrients, and some clinicians actually recommend such a mixture. However, for infants particularly, there is the question of whether such a diet will lead to nutrient deficiency, even when used over a period of only days or weeks. Some specialists therefore compromise by giving an **oligoallergenic** diet, consisting of well-defined unprocessed foods

such as turkey, apple, rice, and rhubarb, that generally produce few allergic reactions.

Patients are put on the diet for a number of weeks, and if their symptoms improve they then start cautiously to reintroduce the foods that they used to eat, one at a time, and preferably under medical supervision, to look for the reappearance of symptoms. As the tell-tale reactions appear the provoking food is recognised and eliminated.

Since children tend to outgrow their food allergies, some doctors recommend reintroducing the offending food each year to see whether the child has become tolerant to it.

The results of such dietary manipulation have sometimes been impressive.

For example, atopic eczema which is certainly related to food intolerance, though the question of actual allergy remains open.

Doctors in London found that two-thirds of children aged 2-8 showed benefit in their eczema symptoms when eggs and milk were withheld in a double blind trial.

They were in no doubt that "... it is time for us to accept that the aetiological relationship between food and eczema is a real one".

Migraine is another complaint in which striking benefits have been claimed for dietary regulation.

A number of theories have been advanced to explain the periodic headaches, sometimes accompanied by nausea and vomiting, that are experienced by migraine sufferers.

One of the most popular is the inability of brain tissues to break down dietary amines because of selective enzyme deficiencies. But a clinical group at the Institute of Child Health in London found that

Turkey	Lamb
Potatoes and potato flour	Rice and rice flour
Carrots	Cabbage
Cooked apple	Rhubarb
Olive oil	Kosher (milk-free) margarine
Soya milk	Kosher (milk-free) cream

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Allergy and intolerance

There are at least five reasons why some people may not be able to tolerate certain foods. Allergy is only one. The most obvious is simple toxicity. Additives or contaminants may make such foods poisonous, and anyone ingesting them will suffer the same ill effects. More subtle, however, are adverse reactions which only a few people will experience because they are unable to break down say, lactose or phenylalanine, since inborn metabolic errors have deprived them of the relevant enzymes. The majority of the population with the appropriate enzyme systems will suffer no ill effects from ingesting either of these substances and this effect is perhaps best described as an **idiosyncrasy**.

A third, and hardly investigated area, is our psychological reaction to foods. If we are convinced, perhaps because of our past experience, that we cannot tolerate this or that food, then we avoid it. One survey of 580 adults found that two-third of them avoided some specific foods because of their taste or texture or because of adverse reactions in the past. Fourth come the foods that produce **pseudo-allergic** reactions. Old cheese may actually contain histamine, whilst strawberries and shellfish can liberate histamine by a direct action on the body's mast cells, and certain plant products (lectins) can directly influence T-lymphocytes.

More common in atopics

Of particular interest to this Series are those food reactions which have a truly allergic basis.

They stimulate a genuine immune response.

The first thing to say about them is that they are not very common.

Prevalence figures for the general population are difficult to arrive at, but estimates vary from a 0.2% in Denmark to about 1% in France and the United States.

Secondly, it seems clear that real allergic reactions to food are usually (though not invariably) seen in atopic individuals, who also suffer from other allergic complaints such as asthma or rhinitis.

A study of 23 adult patients complaining of food allergy symptoms in Manchester found only four of them to be truly hypersensitive when the appropriate immunological tests were carried out. All four had allergic rhinitis and a history of urticaria; three had asthma and two suffered from atopic eczema.

Among the non-allergic patients nearly half were found to be suffering from neurotic depression, which might explain why the most common presenting symptoms were feelings of lethargy and general ill-health, not symptoms that one generally associates with truly allergic reactions.

It is also interesting that six of them only became convinced that they were allergic after reading Dr Mackareness's book.

The psychological dimension in this type of suspected allergy is enormously important, as we shall see in the last Issue, when we look at the so-called **Total Allergy Syndrome**.

It has been suggested that as many as half the patients who present with "food allergy" have no allergic symptoms at all.

They simply think that they have, and satisfying these people can be a difficult task for any doctor. But anyone concerned with reactions to food for which a truly allergic mechanism can be established has to ask, firstly, what are the symptoms of real food allergy, and secondly, what are the allergic mechanisms involved?

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The trouble with you doctors is you don't believe in fairies".

This parting shot was made by a mother as she left a London allergy clinic, still convinced that her child had an allergy problem although all the diagnostic tests had been negative. Another mother at the same clinic became so abusive when told that her child was not suffering from allergy that she had to be threatened with police action before she would leave the hospital. Yet a third, in her attempts to protect her children from allergens in the air, made them both sleep on an upturned wardrobe, wrapped in silver foil.

Allergy: the new disease

There is no doubt that allergy, and particularly allergy to foods, has captured the imagination of the general public, many of whom are now convinced that it lies at the root of their health problems, whatever those problems may be. They have reached this conclusion partly through a flood of popular books and articles with titles like *Not All in the Mind* by Dr Richard Mackarness, and partly because doctors had suggested that "allergy" might have been at the root of the patient's problem, without actually looking for real allergic signs. The situation has become serious enough, in Britain at least, for the influential Royal College of Physicians to produce a special report in April 1984, trying to put the problem into perspective. And perspective is certainly necessary, when another popular book written by medical journalist

Robert Eagle, can list as "diseases which have been attributed to food or chemical allergy", not only respiratory, intestinal and skin complaints, but also high blood pressure, depression and panic attacks. Food allergy has even been implicated in heart disease and cancer.

According to Eagle "Food and chemical allergy may not be the only cause, or even the most common cause of these diseases but it is almost certainly the most unrecognized cause".

He goes on to say "I am of course using the term 'allergy' in its widest meaning; only a minority of the complaints listed fit the orthodox description of allergy... Allergy here means intolerance".

In short, he is admitting to a basic confusion which lies at the root of this whole popular movement. When patients talk about being **allergic**, what they really mean is that certain foods make them ill.

