

Adverse Reactions To Food



European Federation
of Asthma and Allergy
Associations

Adverse Reactions To Food



Pharmacia
& Upjohn

Scientific justification

The Brochure on Adverse Reactions to Food provides food allergic subjects and the parents of food allergic children with accurate scientific information that is in agreement with the viewpoint expressed by the Subcommittee on Adverse Reactions to Food of the European Academy of Allergy and Clinical Immunology (EAACI), in the Position Paper published in *Allergy* 1995, 50, 623-635.

We believe that the present Brochure can be useful for the food allergic patients as well as the patients suspected of being food allergic, inasmuch as it explains the often complex problems that face food allergy/intolerance and provides the reader with appropriate measures for prevention.

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Preface and acknowledgement

Dear Reader,

Every day you and your child have to eat. Breakfast, lunch and dinner. Food will be present throughout the week, when on holiday, at school or at parties. For the average person this is part of life's routine but for you or your child who have to follow a diet this routine can never be taken lightly, you may never take a day off.

I know from personal experience that it helps to know that you are not the only one or the only parent who has this problem. I would encourage you to talk to your fellow sufferers, it helps. On page 35 you will find the address of The European Federation of Asthma and Allergy Associations (EFA), where you can ask for the address of a patient organisation in your country. I hope that this brochure will go some way to giving you the information you are looking for and I trust that it will contribute to your understanding with your doctor or dietician.

The text in this brochure is based on the 'Position paper on adverse reactions to food', published in 1995 by the Subcommittee on Adverse Reactions to Food of the European Academy of Allergy and Clinical Immunology (EAACI) in the scientific magazine 'Allergy' and on publications of Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden.

I would like to thank the following persons for their help and comments on preparing this brochure:

Prof.dr. C.A.F.M. Buijnzeel-Koomen and Prof.dr. R.C. Aalberse, The Netherlands, Mrs. G. Plambek, Denmark, Mr. and Mrs. R. Golding, France, Prof. K. Nékám, Hungary, Mrs. E. Malmberg and Mrs. K. Wall, Pharmacia & Upjohn in Sweden.

Also I am greatly indebted to the members of EAACI Subcommittee on Adverse Reactions to Food for their support.

The financing of this brochure by Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden, is gratefully acknowledged.

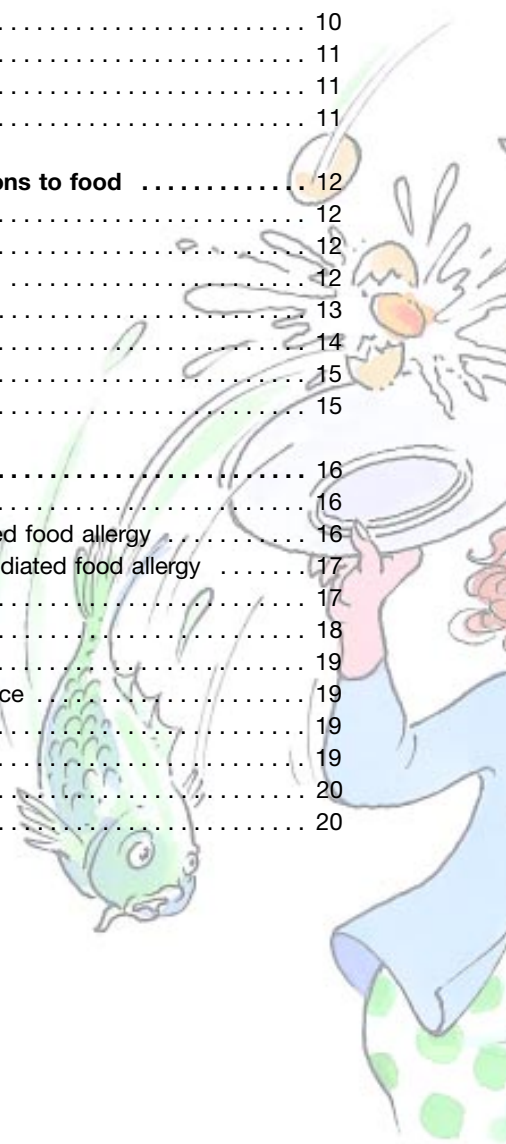


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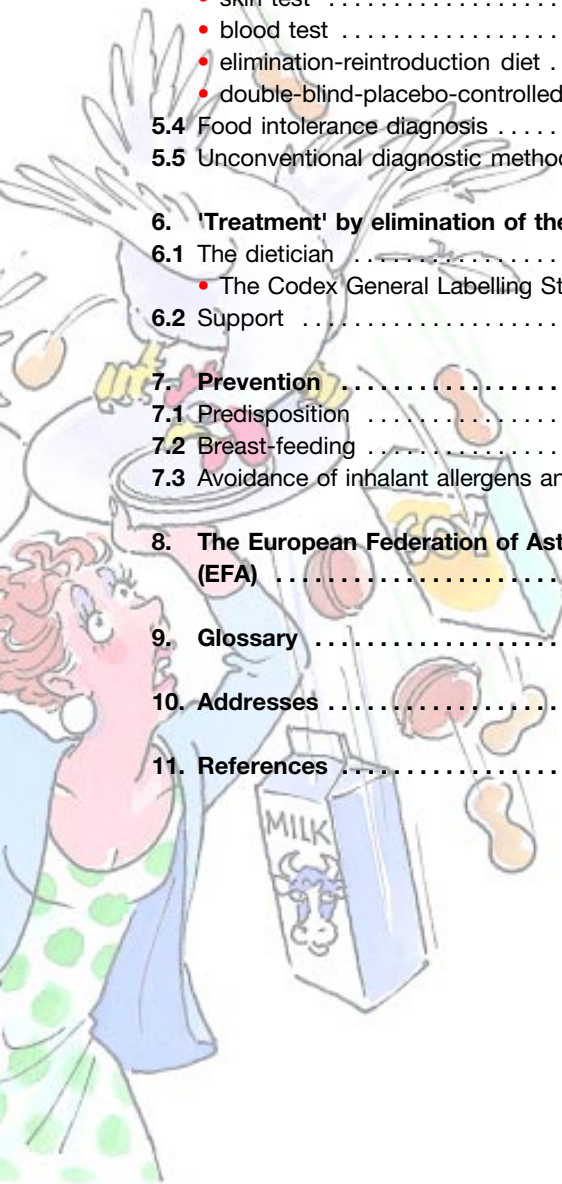
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1. Adverse reactions to food are fashionable

For years it has been fashionable to say: "No, thank you, I am allergic to that". Not only as an excuse to refuse things one does not like to eat, but often to refuse certain foods to which one believes he or she is allergic. It is known that many people complain of adverse reactions to foods but only a few people are in fact allergic.

In the United Kingdom about 20% of 20,000 people thought they had adverse reactions to food, but in fact this study shows that only 1.4% had a food allergy. Other European studies suggest that 0.3 to 7.5% of children have a food allergy, 2% of European adults are thought to have a food allergy. The prevalence of food allergy amongst people with an atopic constitution (see page 11) is 10%.

How many people have food intolerance is not known. It is certain that misunderstanding about adverse reactions to food result in unnecessary elimination of some foods. To prevent this, this booklet provides information about adverse reactions to food, the related symptoms and products that can cause these symptoms. Also information on cross-reactivity is given (see page 17). Information on diagnostic methods, treatment, how a dietician can be of help and also the prevention of allergies is dealt with.



2. Defining adverse reactions to food

The classification reported is that proposed by the European Academy of Allergy and Clinical Immunology (EAACI) in its Position Paper on Adverse Reactions to Food.

2.1 Toxic food reactions and psychosomatic food adverse reactions

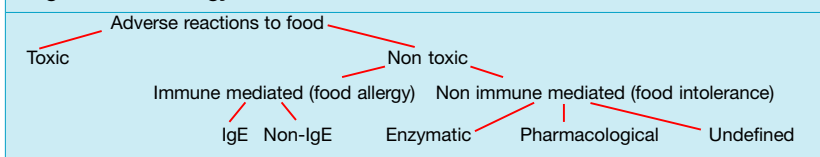
This booklet does not give information on *toxic food reactions*. Almost everyone experiences toxic reactions when the dose of the toxic food is high enough or, for example, after eating poisonous mushrooms. Neither does it give information on *psychosomatic food adverse reactions*, which are related to a primary mental disorder. This food aversion may mimic allergic or food intolerance symptoms. These reactions are not immune mediated and are caused by emotional factors which are interpreted by the patient as allergic or food intolerance symptoms. Double-blind-placebo-controlled food challenge (when the flavour, the smell and colour of food is unknown to the patient and the doctor also does not know which food is involved) is negative when these emotional factors are involved (DBPCFC, see page 23).

2.2 Immune (food allergy) and non immune-mediated reactions (food intolerance)

The information given here is restricted to non-toxic adverse reactions to food. These reactions are divided into *immune-mediated reactions (food allergy)* and *non immune-mediated reactions (food intolerance)*.

The term *food allergy* is commonly used for any adverse reaction to an otherwise harmless food or food component that involves the *body's defense (immune)* system and is therefore referred to as immune-mediated reaction. The substances which cause this abnormal reaction of the defense (immune) system are called *allergens* (such as cow's milk, eggs or peanuts). Reactions in which there is no evidence that the defense (immune) system is involved are referred to as *food intolerance*.

Diagram Terminology ¹⁾



¹⁾ The classification reported is that proposed by the EAACI-Position Paper on Adverse Reactions to Food.

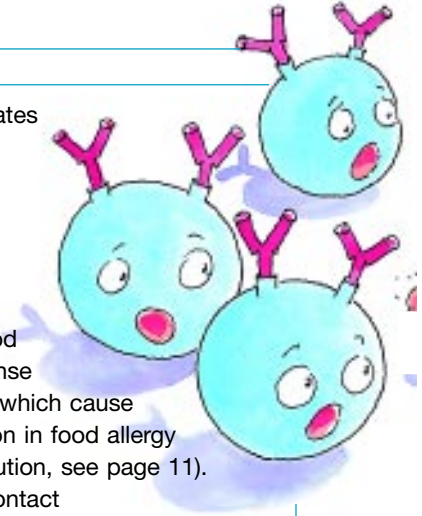
2.3 Food allergy

As can be seen in the diagram there are two different types of food allergic reactions involving the defense (immune) system, namely reactions that are *immunoglobulin E (IgE)-mediated* and *non IgE-mediated reactions*. So far as we know non IgE-mediated reactions to food are scarce. The majority concerns IgE-mediated reactions.

Food allergen

A food allergen is the part of a food that stimulates the defense (immune) system of food-allergic individuals, to make IgE antibodies specific to certain proteins in food.

The most important task of the body's defense (immune) system is to protect against foreign substances via the formation of antibodies. Food proteins are substances which the body's defense (immune) system can recognize as foreign and which cause antibody formation. The most significant reaction in food allergy is genetically determined allergy (atopic constitution, see page 11). Symptoms usually appear within one hour of contact with the allergy-including substance.



• IgE-mediated food allergy

Allergens which enter the body are detected by the body's defense (immune) system. The defense (immune) system produces a specific allergy-associated antibody known as *Immunoglobulin E (IgE)* (IgE-mediated food allergy). The IgE becomes attached to cells called *Mast cells* situated in different parts of the body, most commonly in the skin, gastrointestinal tract and respiratory tract.

When allergic individuals eat certain foods, their defense (immune) system is stimulated by these so called *food allergens*, to make IgE antibodies specific to certain proteins in food. For instance, proteins that appear in cow's milk, chickens eggs or peanuts.

The allergens react with IgE attached to cell surfaces, resulting in the release from these cells of biologically potent chemical substances, called *mediators*. The most well known mediator is called *histamine*.

Histamine affects the surrounding tissues and the result is intense swelling, spasm of muscles in the wall of the affected organ, and the production of

watery mucus. These reactions may occur in any part of the body distant from the gastrointestinal tract, because the food allergens are absorbed in the intestine and carried to these distant parts.

- **Non IgE-mediated food allergy**

In non IgE-mediated food allergy an immune mediated mechanism other than IgE against the suspected food (allergen) is involved.



- **Atopic constitution**

A person with an 'atopic constitution' has inherited the susceptibility to develop one or more illnesses, caused by IgE-mediated allergy, like allergic asthma, allergic rhinitis, atopic dermatitis or food allergy. These illnesses are often seen in 'allergy-prone families'.

Someone with an atopic constitution who has a food allergy, can also become asthmatic or develop allergic rhinitis or atopic dermatitis.

Which kind of allergy an '*atopic person*' will develop, depends on the allergens with which this person comes in contact with.

During lactation an adapted diet for the mother of an atopic child may have, at least temporarily, a preventive effect on the development of the atopic syndrome until 18 months. It may also reduce the severity of allergy in the child.

2.4 Food intolerance

The definition 'food intolerance' is used when the history and/or the provocative tests clearly prove a food is the cause but there is no evidence that the defense (immune) system is involved.

Food intolerance is subdivided into reactions in which *enzymes* play a role (see enzymatic food intolerance, page 19), or in pharmacological and undefined reactions. Pharmacological reactions can be caused by certain natural constituents like *biogenic amines* which are present in, for example, wine and shell-fish or food additives, such as preservatives, flavourings or colouring. When the mechanism is not known, the reactions are classified in the group of undefined reactions, for instance intolerance to additives.

Some reactions after ingesting food or food additives belong to the group of psychic or psychosomatic reactions.

3. Symptoms related to adverse reactions to food

Adverse reactions to food can occur locally, for example, in the intestine or mouth, or be wide spread, like urticaria (hives). The reactions are divided into immune mediated (food allergic) and non-immune mediated (food intolerant) reactions to food.

The symptoms of adverse reactions to food differ from person to person and can be acute or chronic. The same food can cause different symptoms to different people and the symptoms a patient has may change.

3.1

Allergic reactions to food

- **IgE-mediated allergic reactions to food**

Allergic reactions to food in which IgE antibodies play a role, usually begin within minutes or a few hours after eating the offending food (allergen). But in very sensitive people, simply touching or smelling the food may produce an allergic reaction.

The most severe allergic reactions to food are anaphylaxis (see page 13), and other more common symptoms are from the gastrointestinal tract, symptoms from the respiratory tract and symptoms from the skin. Usually these symptoms occur in combination with each other.

The role of food allergy in atopic dermatitis is controversial, but there is no doubt that food allergens, particularly in young children, can induce atopic dermatitis lesions or at least cause a flare-up of existing lesions.

IgE-mediated allergic reactions to food

gastrointestinal tract:	oral allergy syndrome (see page 18), infantile colic, cramps, nausea, vomiting, diarrhoea, abdominal pain
respiratory tract:	allergic rhinitis, larynx oedema, allergic asthma
skin:	urticaria, angioedema, atopic dermatitis, protein contact dermatitis

- **Non-IgE-mediated allergic reactions to food**

Non-IgE-mediated allergic reactions to food include food-induced enterocolitis and food-induced colitis in young children. These symptoms disappear often after cow's milk, wheat or soy protein are eliminated from the diet of the child.

- **Anaphylaxis**

Anaphylaxis is a most severe form of a whole body (systemic) reaction in which several different parts of the body experience **allergic reactions to foods** at the same time. In individuals highly sensitive to foods, even airborne exposure to food allergens can produce anaphylactic reactions. Anaphylaxis is a reaction resulting from sudden release of multiple chemical mediators, as a result of events mediated by IgE antibodies. The effects of these mediators are severe itching, hives, swelling of the throat, broncho-constriction, lowered blood pressure, unconsciousness and sometimes even death.

The time taken for a reaction to show after food has been eaten varies, however symptoms show normally within a few minutes.

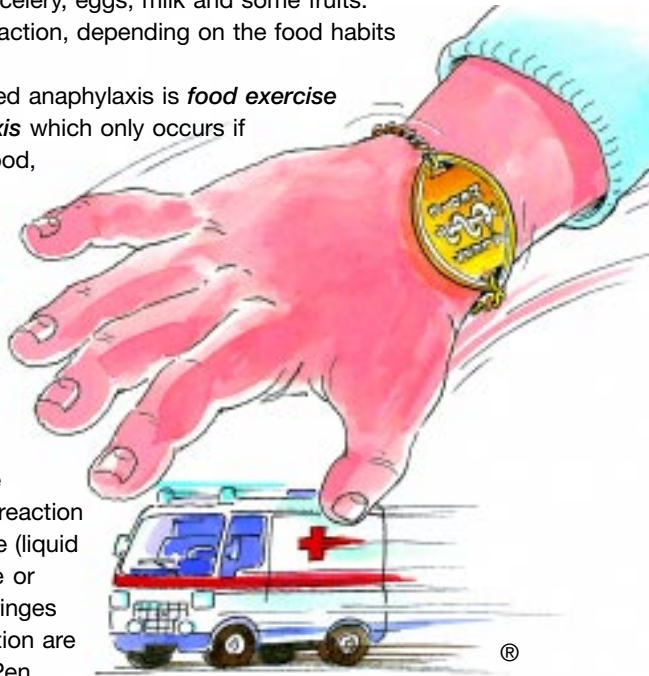
The foods most frequently associated with anaphylaxis are peanuts, tree nuts, seeds, seafood, spices, celery, eggs, milk and some fruits. Other foods can cause this reaction, depending on the food habits in different countries.

An unusual form of food-related anaphylaxis is **food exercise induced asthma or anaphylaxis** which only occurs if

the person eats a particular food, such as molluscs, shrimps or celery, prior to exercising.

Because food induced anaphylaxis can be life threatening, persons with this condition need to be instructed when and how to use prophylactic drugs and to give themselves a shot of epinephrine (adrenaline) in the event of this severe systemic reaction and when to use antihistamine (liquid diphenhydramine, hydroxyzine or clemastine). Ready-to-use syringes with epinephrine for self-injection are available, like Ana-Kit or Epi-Pen.

These syringes are easy to use and should always be carried by persons with a history of anaphylaxis. Medihaler Epi, which is an aerosol of adrenaline, can be a good alternative to adrenaline via injection. A Medic-Alert bracelet should also be worn at all times.



- **Peanut, nut and anaphylaxis**

Sensitization to peanuts, member of the pea family, is occurring in very young children, and multiple peanut and nut allergies appear progressively. Peanuts are believed to be one of the leading causes of food allergic reactions in the United States, and together with tree nuts, are probably the leading cause of fatal and near fatal anaphylaxis induced by food. However, it is not longer an American problem. In Great Britain the press reported in 1993 six deaths due to peanut allergy.

People with severe peanut allergy must be aware of the relationship between peanut and soybean and other members of the pea family. Some children and teenagers have died after eating hamburgers, sausages etc. because this allergy was unknown to doctors, parents and school staff.

People who are allergic to peanut also have an increased risk to develop nut allergies. The prevalence of peanut and nut allergy is increasing. Peanut allergy is also occurring in very young children. Peanut and nut allergy are rarely 'outgrown'.

Young atopic children should avoid peanuts and nuts to prevent the development of this allergy. All peanut products should be eliminated from the child's diet for at least three years, and mothers who are breast-feeding should eliminate peanut products from their own diet.

Peanuts, peanut butter and nuts can be easily avoided, but peanut and nut products can be 'hidden' in other products. Peanut allergen can be found in for instance cold-pressed peanut oil, vitamin supplements, sweets, Chinese and Indian foods, chili and spaghetti sauces, breakfast cereals, gravies, pastries, ice cream and desserts. If there is any doubt about a food's ingredients, a person with a peanut and nut allergy should not eat it.

People with a nut or peanut induced anaphylaxis should have prophylactic drugs to hand at all times, see anaphylaxis.

3.2 Food intolerant reactions

Non-immune mediated adverse reactions to foods are divided in *enzymatic food intolerance*, *pharmacological food intolerance* and some other *undefined reactions*.

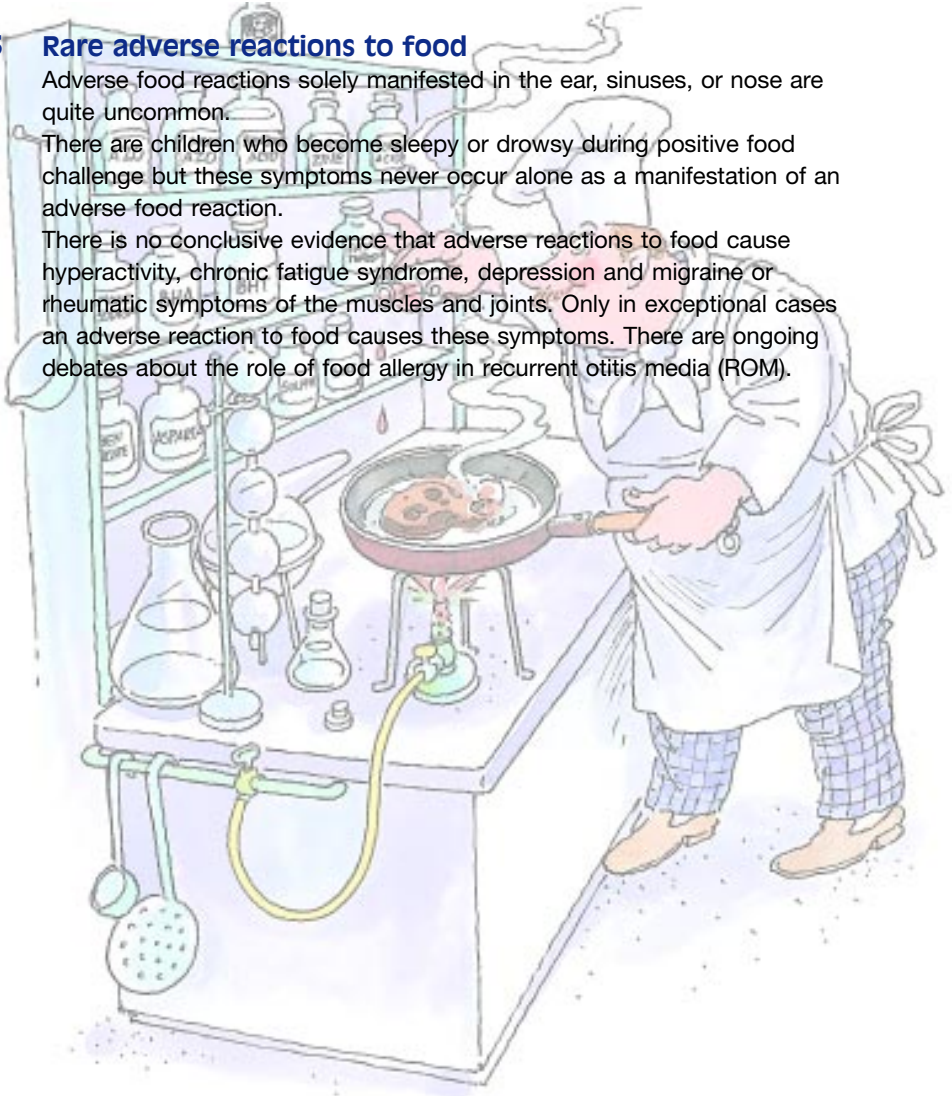
These food intolerant symptoms can be the same as food allergic symptoms and also can be related to the gastrointestinal and respiratory tract and/or the skin.

3.3 Rare adverse reactions to food

Adverse food reactions solely manifested in the ear, sinuses, or nose are quite uncommon.

There are children who become sleepy or drowsy during positive food challenge but these symptoms never occur alone as a manifestation of an adverse food reaction.

There is no conclusive evidence that adverse reactions to food cause hyperactivity, chronic fatigue syndrome, depression and migraine or rheumatic symptoms of the muscles and joints. Only in exceptional cases an adverse reaction to food causes these symptoms. There are ongoing debates about the role of food allergy in recurrent otitis media (ROM).



4. Products that can cause symptoms

Although adverse reactions can occur virtually to any food, most reactions are caused by a limited number of foods.

The prevalence of adverse reactions to specific foods may depend on the eating habits or other peculiarities of a given population; for example soybean allergy is more common in Japan and fish allergies are more prevalent in Scandinavian countries. Maize (corn) and maize products are extensively used in the United States and the incidence of maize allergic people is higher in that country. Allergy to dairy products is probably the most common food allergy in children. Especially cow's milk allergy, because this is commonly introduced to the child's diet at an early age and often given repeatedly and in large quantities.

4.1 Products that can cause food allergy

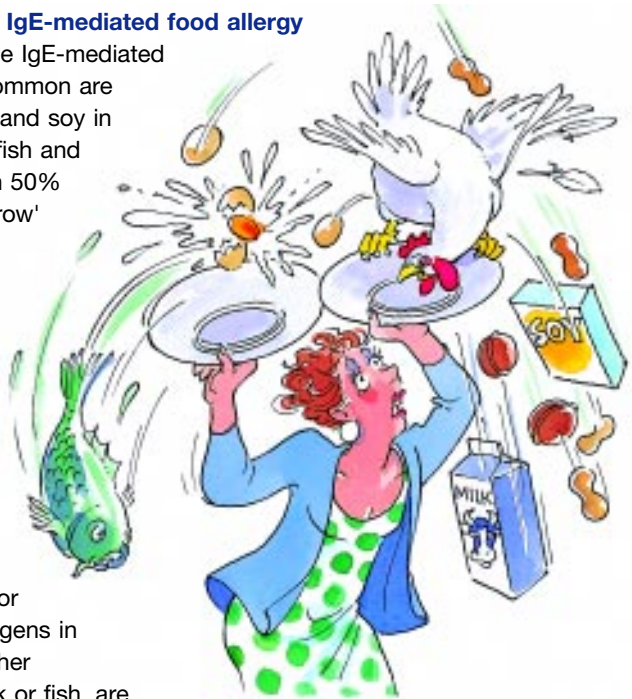
- **Products that can cause IgE-mediated food allergy**

All food can potentially cause IgE-mediated food allergy, but the most common are egg, milk, peanut, nuts, fish and soy in children and peanuts, nuts, fish and shellfish in adults. More than 50% of the allergic children 'outgrow' their allergy to cow's milk, egg and soy between one to three years of age.

An allergy to fish and peanut can persist longer, whereas allergic reactions to fruits and vegetables in pollen-allergic people tend to be permanent.

The allergenic activity of some food allergens is easily destroyed by heating or denaturing, such as the allergens in fruit like apples. However other allergens, for instance in milk or fish, are resistant to denaturation as happens in cooking and digestion.

Only a few cases of IgE-mediated food allergy to additives are known.



- **Products that can cause non-IgE-mediated food allergy**

Non-IgE-mediated food allergy can be caused by milk, soy, but reactivity to egg and pork has also been reported. Food additives belong to this group of reactions.

- **Cross-reactivity**

Sensitization to a certain fruit or vegetable is often associated with sensitization to other foods belonging to the same or a *closely related botanical family*.

The most frequent clusters are various nuts, apple and pear, potato, and carrot; melon, watermelon and tomato; peach, apricot, plum and cherry.

Another cross-reactivity is that of *inhalant allergens* (aeroallergens) and *food allergens*. When the atopic (see page 11) patient grows older, and sensitization to common inhalants such as pollen and the allergens of house-dust mite and pets occur, there is an ever increasing possibility of becoming allergic to food allergens that cross-react with inhalant allergens. For example patients allergic to birch pollen are frequently sensitized to numerous fresh fruits (apple, kiwi, orange, peach, apricot, cherry), vegetables (carrot, potato, celery, fennel) and hazelnuts.

Many mugwort-sensitive patients react to vegetables of the Umbelliferae-family: celery, fennel, carrot, parsley and spices (like anise, coriander).

This reaction is called the Mugwort-Celery-Spice syndrome. The symptoms of this syndrome can be very severe, like angioedema (see Glossary).

Other cross-reacting allergens between pollen and foods are for example ragweed pollen, melon, banana, watermelon and the gourd family (pumpkin).

Or between grass pollen and potato, peanut, buckwheat, wheat and tomato.

Another cross-reactivity occurs between hazel pollen and hazelnuts. A less common cross-reactivity, that is induced by sensitization to house-dust mite, is that of house-dust mite and vineyard snail or shrimp.

Over the past several years the prevalence of immediate allergic reactions to natural latex products has increased. Natural rubber latex contains allergens which cross-react with various foods, such as chestnut, avocado, kiwi, pineapple and banana. Patients primarily allergic to latex may have a secondary allergy to these foods which can lead to an anaphylactic reaction following food ingestion; several deaths have been reported.

The presence of specific IgE in blood is evidence of sensitisation to that specific food or due to cross reactivity. The development of symptoms vary greatly between individuals. In some cases there are no immediate clinical symptoms. For example, all apple allergics are not necessarily allergic to birch pollen. Therefore, cross-reactivity never can be assumed. Under no circumstances should important foods be eliminated from the diet without appropriate testing and clinical diagnosis.

Food	Claimed cross-reactivity
apple	potato, carrot, birch pollen
carrot	celery, anise, apple, potato, rye, wheat, birch pollen, avocado, pineapple
cereals	wheat, rye, barley, oats, maize/corn, rice, corresponding pollen, grass pollen
cod	eel, mackerel, salmon, trout, tuna, bass, dentex, sole, haddock
cow's milk	mare's milk, goat's milk, cow's milk-based formulas
egg	egg yolk, egg white, lysozyme, ovalbumin, ovomucoid, inhaled bird antigens
garlic	onion, asparagus
honey	contamination by pollen
pea	soybean, white bean, peanut, lentil, fennel, guar gum, carob bean, tragacanth, chick pea, liquorice
peach	apricot, plum, guava, banana
pecan nut	walnut
rice	wheat, rye, barley, oats, maize/corn, rye pollen
shrimp	crab, lobster, squid, crayfish, dust mite

- **Oral Allergy Syndrome**

Patients suffering from allergies to certain pollen more often react with the Oral Allergy Syndrome (OAS) to certain fresh fruits and vegetables, like apple, peach, cherry, nuts, celery, carrot and tomato. Seafood, milk and egg may also be involved in the OAS.

In the OAS the lips, cheeks, tongue or throat may swell or itch within 15 minutes of contact with a specific food. Usually these symptoms disappear very quickly.

In adults suffering from pollen allergy the prevalence of this syndrome has been estimated to be about 40%, making it a very common condition. Approximately 50% of patients allergic to birch pollen and having a cross

reaction to apple, peach and hazelnut, especially suffer from OAS. In patients with OAS blood tests for specific IgE antibodies are nearly always positive (see page 23).

- **Occupational food allergens**

Occupational food allergens can also cause symptoms. A grain dust lung is one of the oldest occupational diseases described in Sweden.

Occupational asthma can, for instance, be caused by seafood or by soybean allergens causing sensitization of occupationally exposed bakers. Occupational allergy can also be caused by buckwheat flour that is used in the baking industry in most Western countries.

4.2 Products that can cause food intolerance

Lactase deficiency is well known and food additive intolerance receives a lot of publicity, but not only lactose or additives can cause a non-IgE-mediated food intolerance.

Which food can play a role in the intolerant reaction, depends whether one has an *enzymatic, pharmacological or undefined food intolerance*.

- **Enzymatic food intolerance**

'Enzymatic food intolerance' means an adverse reaction to food or food additives resulting from an enzymatic defect which becomes clinically evident after eating certain foods. The most well known enzymatic food intolerance is *lactase deficiency*, at which people cannot tolerate lactose (milk sugar) as a result of a deficiency of the intestinal enzyme lactase which is needed to digest this milk sugar. This may be an inherited defect or a temporary consequence of an intestinal infection.

Other enzymatic food intolerances are very rare conditions.

- **Pharmacological food intolerance**

'Pharmacological food intolerance' can be caused by food additives or may depend on the direct effect of *vasoactive amines* naturally found in foods. In this case some individuals may have symptoms after eating even a very small amount of food containing one or more amines. The threshold of susceptibility to vasoactive amines, like histamine, tyramine, phenylethylamine and serotonin, may be lowered in these individuals.

The largest amounts of histamine and tyramine are found in fermented foods, such as cheese, alcoholic beverages, canned fish, fish autolysates (Nuoc-Mam), sauerkraut and tuna.

Vasoactive amines may have direct or indirect effect on the vascular system. Tyramine may play a role in migraine and chronic urticaria, especially in patients treated with Mono Amino Oxydase (MAO) inhibitor (f.e. Moxlobemide), an anti depressant.

- **Undefined food intolerances**

Undefined food intolerances to compounds such as additives which cause intolerance are for example food colourings like azo dyes (f.e. tartrazine) and non-azo dyes (f.e. erythrosine), flavours (like aspartame or monosodium glutamate which can cause the 'Chinese

restaurant syndrome'), preservatives (like sulphites, benzoates, benzoic acid and sorbic acid) and antioxidants (like butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT)). Even if the symptoms are caused by an additive intolerance, not all additives should be suspected.

In subjects intolerant to NSAID (non-steroidal anti-inflammatory drugs) certain food additives (benzoic acid derivatives, azo and non-azo dyes and sulphites) can elicit symptoms, especially in the back of the throat (oropharynx).



- **Chinese restaurant syndrome**

In the Chinese Restaurant Syndrome symptoms - including numbness, burning, pressure and tightness in the upper chest, neck and face - shortly occur after the start of a meal in a Chinese restaurant and are caused by the flavour enhancer monosodium glutamate (MSG).

5. Diagnostic methods

Diagnosis of adverse reactions to food may be easy if a person always has the same reaction after eating a certain food.

But more often the diagnosis of food allergy or food intolerance is difficult, because many symptoms can have other underlying causes.

The same food can cause different symptoms to different persons and different foods can cause different symptoms in the same person. And the symptoms one person has may change after a while.

It is therefore important to consult an *allergist* or an other qualified specialist who can examine whether the symptoms are related to adverse reactions to food or have other causes.

Diagnosis begins with a complete physical examination followed by laboratory tests to exclude any medical condition not related to adverse reactions to food.

5.1 Medical, family and food history

In order to ascertain the type and cause of symptoms and how serious symptoms are and to identify the suspected food or to exclude other causes, the *medical history* of the patient has to be known.

The *family history* is also important, in order to know if someone has a predisposition to one or more illnesses caused by allergy, such as asthma, allergic rhinitis, atopic dermatitis or food allergy, seen in 'allergy-prone families'. This predisposition to develop allergies is called 'atopic constitution' (see page 11).

With the help of a doctor or dietician the *food history* of a person has to be revealed. Therefore information on the personal food pattern is needed and persons may be required to keep a food diary of foods eaten and to record symptoms over a specified period.

5.2 Supplementary tests

After the medical, family and food history are known and adverse reactions to food are suspected, supplementary tests are needed to reach a final diagnosis. In a food allergic person the defense (immune) system is sensitized (immune mediated), but in a person with food intolerance there is no evidence that the defense (immune) system is involved (non immune mediated).

Therefore for diagnosis of food allergy, skin tests and blood tests for detecting specific IgE can be used to provide extra information. For the diagnosis of food intolerance however, these tests do not give a positive answer.

The medical, family and food history, and selective elimination diet regime, may give evidence supporting the diagnosis.

5.3 Food allergy diagnosis

- **Skin test**

Different types of *skin tests* can be used to diagnose food allergy.

In the skin-prick test a diluted extract or fresh part of the suspected food is placed on the skin of the forearm or the back, which is then scratched or punctured. The skin test is more sensitive and reproducible when fresh food items are used, rather than extracts from most manufacturers. The fresh food is punctuated with a special needle and then the skin. This is called the '*prick-prick method*'.

If after the prick a wheal (swelling) surrounded by redness (flare) forms within 15 minutes, similar to a mosquito bite or larger, then the skin test is positive and the person may be allergic to the tested food.

Because food allergen extracts currently available are not standardized, and their stability often remains poorly established, it is important that only experienced doctors interpret results of the skin tests. Skin prick testing should be performed only in places equipped to treat anaphylaxis in case of a risk of a systemic reaction.

When a patient has extensive eczema, skin tests are unreliable. Another problem can be medication that will interfere with the result of a skin test and that cannot be discontinued because of the severity of the illness, like antihistaminica.



- **Blood test**

Allergic or potentially allergic people may have abnormal high levels of IgE in their blood and this can be measured and used as an indicator when allergy is suspected. These blood tests may confirm IgE-mediated allergy and can be done at any age, even on babies. The advantage of the blood test is that many determinations can be done on a single blood sample, it is also highly reproducible and it is not affected by any drugs e.g. antihistamines. Pharmacia & Upjohn Diagnostics launched the first test for *specific IgE*, **RAST®**, more than 20 years ago. UniCAP®, the system today offers many of different allergy tests; Phadiatop® test can be used to determine if someone has a predisposition to develop an allergy (atopic individual) or already has an allergy. *Total IgE* can be used in the same way also for looking for more uncommon allergies. For specific food allergy measurements there are more than 200 different allergens available, single tests for specific foods, or panels for groups of food.

Whether a blood test or a skin prick test is used depends on which type of doctor the patient is visiting, i.e. general practitioners more often use blood tests than specialists due to its simplicity.

- **Elimination-reintroduction diet**

When food allergy to one or more foods is suspected based on results of the skin test and/or blood test, *elimination-reintroduction diets* can be used. This is done for two reasons.

The first reason is that allergens used for skin and blood tests can be affected by loss of allergenicity during preparation. The second reason is that a substantial number of patients with IgE to foods do not present any symptom when ingesting the food.

- **Double-blind-placebo-controlled food challenge (DBPCFC)**

Only when a patient has clinical symptoms like urticaria, atopic dermatitis or asthma, they are asked to register their symptoms daily for two weeks. Then an elimination diet, in which the suspected allergens are excluded, is given for the next two weeks. During this time the patient must avoid even minute quantities of these allergens.

Sometimes patients who are suspected of having food allergy but have negative skin or blood tests result, are asked to use a diet with no allergens (*oligoallergic diet*) for this period.

During this elimination diet period the patient keeps a record of the symptoms. If the symptoms do not clearly improve within two weeks, it is unlikely that food allergy is involved or there could be multiple sensitivities.

If the symptoms clearly improve and the patient has an isolated adverse reaction to a certain food(s), the diet period is followed by an **open oral challenge**, in which both the doctor and patient know which suspected food is involved. If the open challenge is negative food allergy is excluded. If the open challenge is positive, the diagnosis food allergy ideally should be confirmed by a **double-blind-placebo-controlled food challenge (DBPCFC)**, at which both doctor and patient do not know which food is involved in the **provocation**.

DBPCFC excludes psychological reactions associated with adverse reactions to food, and eliminates the doctor's and patient's bias and prejudice and provides objective evidence. Therefore DBPCFC is regarded as the 'gold standard' in the confirmation of food allergy or food intolerance.

Persons with severe reactions such as anaphylactic shock, should not be subjected to a provocation. Provocation tests should only be carried out by a doctor, as severe reactions can never be predicted beforehand.

5.4 Food intolerance diagnosis

If the defense (immune) system is not involved, food intolerance cannot be diagnosed by performing a skin or blood test. IgE tests only demonstrate IgE-mediated adverse reactions to food and do not give any positive results when food intolerance is involved. Therefore food intolerance is further diagnosed with the help of the medical history and food history, followed by elimination and reintroduction or provocation of the suspected food or groups of food. **DBPCFC** is also of great importance for the diagnosis of food intolerance.

5.5 Are unconventional diagnostic methods reliable?

Diagnostic methods used by 'clinical ecologists' to diagnose and treat patients with the so called environmental illness (or food and chemical sensitivity / environmentally induced disease / ecologic illness / total allergy syndrome), are expensive and lack scientific foundation in detecting adverse reactions to food and should be avoided.

The theory is that multiple food or chemical sensitivity leads to common somatic complaints such as headache, fatigue, malaise, disorientation and dizziness, among others. This theory has not been proven.

6. 'Treatment' by elimination of the offending food

When it becomes clear which foods cause the various symptoms, the only proven therapy is to **eliminate the offending food**. This means giving up the food that causes the symptoms. If the items are multiple or when the item is an essential part of the basic food stuff, such as milk, then a doctor or dietician with expert knowledge in this area must be consulted. A registered dietician can be of help in providing long term meal planning and can make suggestions for alternative food or ingredients. The dietician should also be involved in evaluating the diet in order to avoid deficiencies and in assessing the need of supplementary food.

Long-term dietary guidelines are only justified after a proper diagnosis has been made and in children the diagnosis should be reconsidered at intervals, as very young children 'outgrow' many food allergies. For milk and egg, this should be done yearly, because at the age of 5-6 years the levels of IgE antibodies to offending food allergens usually start to decline (for milk this can be at the age of 1 - 3 years), while levels of IgE antibodies to inhalant allergens can increase at that age.

The elimination regime does not mean that the diet has to be boring. Creative preparation of food can make adhering to the diet easier. Sometimes minute amount of food substances are present as hidden allergen or carried over in production of processed food. Avoiding these foods is best in order not to suffer from unexpected reactions. In some special situations the use of prophylactic medication is beneficial.

6.1 How can a dietician be of help?

It is possible that the diet may impose too many restrictions to the patient's life. The drawbacks of dietary regimens must always be balanced against the intended benefits. Also, the diet must be affordable.

In order to obtain the desired extent of elimination, it is often necessary that a dietician explains the prescribed diet to the patient and helps patients to become familiar with reading food labels. Many foods and food additives are present in processed foods in a hidden form. For example, bread improver may contain cow's milk.

The food industry should list on labels all ingredients, including any additives with E-number and category or E-number and name. However, the present policy of the European Union requires only listing of compounds - not being

additives - comprising more than 25% of the contents of the food. The dietician should therefore point out hidden sources to insure a full dietary prescription.

Some European countries, such as the Netherlands and the United Kingdom, do have *manufactured food product lists* which can be of help with shopping. For instance, 'the list free from cow's milk'. The dietician can also explain how to use a manufactured food product list.

Hopefully the result of the project 'Europe-wide Food Intolerance Databanks' (EFID) will be launched in 1997, so most European countries could have a Databank. In 1997 the following countries are involved in the project: United Kingdom, the Netherlands, Belgium, Austria, Denmark and Portugal.

• The Codex General Labelling Standard

"Where an ingredient is itself the product of two or more ingredients, such a compound ingredient may be declared, as such, in the list of ingredients provided that it is immediately accompanied by a list in brackets of its ingredients in descending order of proportion (m/m = with the necessary changes). Where a compound ingredient for which a name has been established in a Codex standard or in national legislation constitutes less than 25% of the food, the ingredients other than food additives which serve a technological function in the finished product need not be declared."

Use of the '25% rule' leads to the situation that a substance added to food in small amounts as an ingredient must be declared on the label, whereas the same substance can be present in larger amounts in another product (as a compound ingredient), without being declared on the label.

The worldwide Committee on Food Labelling proposed to the Codex Committee to label all ingredients, that can cause adverse reactions to food, like milk, egg, peanut, fish, soybean and tree nuts. Ingredients used in a product in minimal quantities or carried over from other products should also be mentioned on the label. Some countries consider to abolish the '25% rule' or reduce it to 5%. A '5%-rule' however does not ensure the declaration of potent allergens which can induce allergic reactions in small amounts.

6.2 Support

Elimination diets, particularly extensive ones, may impose a heavy burden on patients and their family members. Eating habits have to be changed, as well as food-buying habits. Substitutions have to be found to make life more pleasant for the patient.

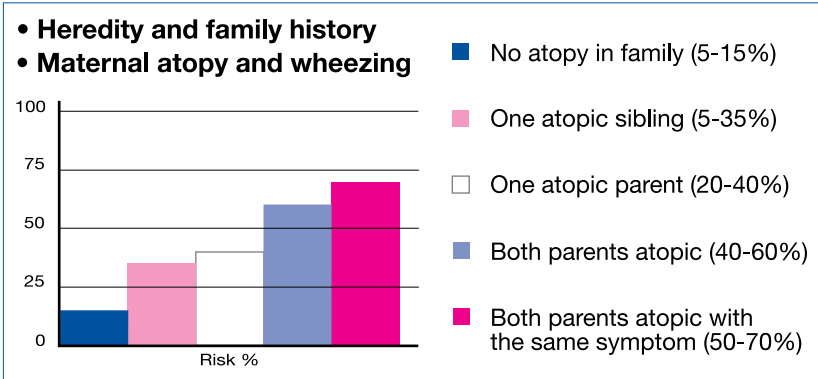
Meals must be planned in advance and the diet may severely restrict social activities and may cause isolation. Psychological, social and practical support from the doctor as well as from a dietician therefore play an important role in the successful treatment of adverse reactions to food!



7. Prevention

Genetic Predisposition

Predisposition/Pediction



Reference: Kjellman

7.1 Predisposition

Allergies to specific substances such as pollen or certain foods, are not inherited. But children with parents or other relatives who suffer from allergies will be more inclined to have allergies themselves. If one parent is allergic the child has 20-40% chance of developing allergy, but when both parents suffer from an allergy, there is a 40-60% chance that their child may develop an allergy. Only a small percentage of children from families showing no history of an allergy will develop allergic symptoms.



7.2 Breast-feeding

Allergen exposure to a child with an atopic constitution (see page 11) may be an important factor in the induction of food allergy. Apart from the exposure to allergen and the nature of the allergen (not all allergens have the same allergic potential), the permeability of the gastrointestinal tract plays an important role in the development of food allergy. The permeability may temporarily be increased by infections or allergic reactions in the gastrointestinal tract. On the basis of this phenomenon **breast-feeding** ought to be stimulated as much as possible, preferably until 6 months of age, whereas introduction of known potent food allergens at this stage of life ought to be avoided where possible.

Because proteins of allergenic foods like cow's milk and egg can be transferred into the breast milk after consumption by the mother, the mother of a breast-fed infant with a confirmed allergy should try to reduce the intake of these allergens. The mother of this allergic child should not stop breast-feeding, because breast-feeding has nutritional, immunological and psychological advantages for the child.

If breast-feeding is not successful, a child with an atopic constitution should be given a hypoallergenic formulae, which have a greater lower allergenic potential compared with regular cow's milk

formula. Soy-based formulae are not a good alternative, because between 4 and 10% of the children with cow's milk allergy become allergic to soy protein as well.



In children from families with a history of atopic disease (see page 11), an adapted diet for the mother during breast feeding may have at least temporarily a preventive effect on the development of the atopic syndrome. It may also reduce the severity of allergy in infants if a positive family history is present.

A maternal diet during pregnancy, however, has little influence on sensitization of the infant to foods. Sensitization of the infant in the womb has been shown only in rare instances.

7.3 Avoidance of inhalant allergens and tobacco smoke

Not only an adapted diet for the mother during breast-feeding for the 'atopic' child is important as a preventive measure. Other measures are also strongly advised, such as the avoidance of exposure to tobacco smoke. It is therefore strongly advised not to smoke in the presence of the mother. It is also important to limit exposure to inhalant allergens, for example to pets and house-dust mite, as much as possible.



8. The European Federation of Asthma and Allergy Associations (EFA)

The purpose of the European Federation of Asthma and Allergy Associations (EFA) is to promote better health for people with asthma and allergy throughout Europe.

EFA represents the views and interests of people who have asthma and allergy, to ensure a continuing improvement in their quality of life, and that of their carers.

EFA promotes prevention, research and education on asthma and allergy. The federation provides a forum for debate within Europe between individuals and national organisations which represent, work with, or serve people with asthma and allergy.

EFA strives to improve the quality of management through health care professionals and patient education programmes and campaigns on behalf of people with asthma and allergy.

EFA aspires to increase awareness of asthma and allergy and to ensure that decision makers within Europe and particularly the European Union, are kept well informed.

EFA aims at working in conjunction with existing international and national societies involved in asthma and allergy research and management, and together implement programmes of the highest scientific standard and social relevance.

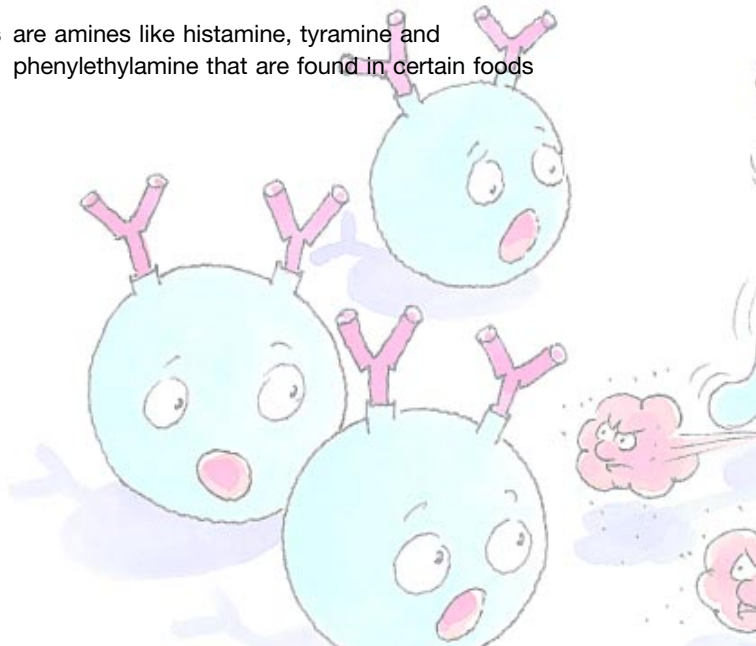


9. Glossary

Allergen	antigen such as food that causes an allergic reaction
Allergist	a doctor who has completed a specialist training program in allergy and immunology
Anaphylaxis	severe systemic reaction to an (food) allergen
Angioedema	local swelling of the skin and underlying tissues. This happens when urticaria affects deeper skin layers and causes swelling. The areas most commonly affected are the mouth, eyes, tongue, genitals, hands and feet. Normally angioedema does not itch like urticaria
Antigen	a non-self molecule, generally (part of) a protein, that can provoke the body into producing antibodies or to cell-mediated reactions
Atopic	prone and liable to develop IgE-mediated allergies
Atopic dermatitis	or atopic eczema, is a chronic relapsing dermatitis in the flexures of arms and legs. 85% of these patients have an atopic constitution. It is part of the atopy syndrome (asthma, rhinitis, eczema)
Atopic eczema	see Atopic dermatitis
Biogenic amines	like histamine, phenylethylamine, tyramine are chemical compounds which are naturally present in the human body and are responsible for for example digestion, body temperature, blood circulation, respiration and bio rhythms. Biogenic amines are also naturally present in certain foods. Foods produced through fermentation or by ripening and decayed protein rich products also contain a high amount of biogenic amines.
Colitis	inflammatory disease of the large intestine

Contact dermatitis	dermatitis after direct skin contact with an allergen
DBPCFC	double-blind-placebo-controlled food challenge
Enterocolitis	inflammation of the mucosa of the small and large intestine
Enzymes	substances enhancing biochemical reactions
Food additive	a substance which is added to, or used in or on, food at any stage for purposes of maintaining quality, texture, consistence, taste, odour, alkalinity or acidity, or to serve any other technological function in relation to food
Food allergen	the part of a food that stimulates the immune (defense) system of food-allergic individuals, to make IgE specific to certain proteins in food. The majority are proteins, not carbohydrates or fats.
Food allergy	any adverse reaction to an otherwise harmless food that involves the body's immune (defense) system and production of IgE antibodies.
Food aversion	dislike and avoidance of a particular food for purely psychological reasons
Food intolerance	general term for any adverse reaction to a food or food component that probably does not involve the body's immune (defense) system
Ig	immunoglobulin, or antibody
IgE	immunoglobulin E is an antibody in the immune (defense) system that reacts with allergens
Immune reactions	reactions which are directed against 'foreign' substances which have entered the body

Immune system	body's defense system
Inhalant allergen	allergen present in the environment that we inhale
Mast cell	a type of cell which is present below the surface and lining membranes of the body and can be triggered into releasing inflammatory substances (mediators), for example during the course of an allergic reaction
Mediators	inflammatory substances which are released from for example mast cells after previous contact with an allergen and thereby cause the allergic reaction. Other mediators play a role in the normal immune regulation
Oral Allergy Syndrome (OAS)	swelling or itching of the lips, cheeks, tongue or throat within 15 minutes after contact with a specific food
Rhinitis	a term loosely applied to any condition accompanied by a running nose or sneezing
Toxic	poisoning
Urticaria	a skin reaction with elevated white centre and raised red surrounding. Intensively itching (wheals and welts)
Vasoactive amines	are amines like histamine, tyramine and phenylethylamine that are found in certain foods



10. Addresses

European Federation of Asthma and Allergy Associations (EFA)

Letters should be send to:

P.O. Box 5

3830 AA Leusden

The Netherlands

European Food Intolerance Databanks (EFID)

Leatherhead Food RA

Randalls Rd

Leatherhead

Surrey KT22 7RY

United Kingdom

11. References

The text of this booklet is based mainly on the 'Position paper on adverse reactions to food', published in 1995 by the Subcommittee on Adverse Reactions to Food of the European Academy of Allergy and Clinical Immunology and on publications of Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden. Also on the Committee report from the American Academy of Allergology and Immunology 'Topics related to controversial practices that should be taught in an allergy and immunology training program' that was published in the Journal of Allergy and Clinical Immunology in 1993 and on the text of the 'Consensus Food Hypersensitivity' of the Netherlands National Organisation for Quality Assurance in Hospitals, published in 1990.

More than 80 scientific articles on adverse reactions to food, published in the past few years, in The Lancet, British Medical Journal, Allergy, Journal of Clinical Immunoassay, Journal of Allergy and Clinical Immunology, Journal of Pediatrics and Pediatric Allergy and Immunology, have been consulted to write this booklet.

The references can be applied for through the secretariat of the European Federation of Asthma and Allergy Associations (EFA), address for correspondence: P.O. Box 5, 3830 AA Leusden, The Netherlands.

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Illustrations: Wim Dolk, The Netherlands

Layout: De Jong Creatieve Communicatie, The Netherlands

An electronic version of the brochure may be found on Internet on the Home-page of The Netherlands Asthma Foundation (Astma Fonds):

<http://www.astmafonds.nl/astmafonds/brochure/allergie.phtml>

ISBN 90-9010537-9

