The causes of food allergy
By Pia Nørhede

The causes of food allergy are still poorly understood. Food allergies and allergic diseases in general may share many risk factors. However, there appears to be a number of both genetic and nutritional factors that are specific to food allergies. The timing of introduction into the diet and the amount of potentially allergenic foods consumed in early life appear to be important factors. Additionally, the amount of gastric acid in our stomach and the composition of bacteria in our gut may influence susceptibility to food allergies. Much more research is needed into the causes of food allergies. Such research will help to develop strategies for prevention and management that could improve health and quality of life for many people.

Why is it important to know the causes of food allergy?
Individuals with food allergy develop symptoms after eating foods that for the vast majority of the population are part of a healthy diet. Currently, the only way for allergic individuals to manage food allergy is to avoid eating the foods that cause the allergic reactions. The level of avoidance required may seriously impair their quality of life.

The number of people with allergy is increasing. Although we do not know for sure, a few studies suggest that the same is true for food allergy. We do not have a clear understanding of why more people are becoming allergic. Nor do we know whether the causes of food allergy are the same as those for allergy in general. However, some studies suggest that, in addition to the general causes of allergy, factors exist that are specific to the causes of food allergy. This article reviews the current understanding of the specific causes of food allergy.

With knowledge about the specific causes of food allergy we might be able to prevent some cases of food allergy. We also might be able to provide new advice on how to manage food allergy, which may help improve the quality of life of food allergic individuals.

What is food allergy?
Some people develop symptoms when eating certain foods that cause no problems to most people. To talk about food allergy it is a requirement that the immune system is involved in the reactions leading to the symptoms. Some allergic reactions are local causing, for example, tingling of the lips, whilst other reactions may become systemic. This means that symptoms may be triggered elsewhere, for example, as a skin rash, a fall in blood pressure or difficulty in breathing.

Different kinds of poisoning and enzyme deficiencies can provoke symptoms that are similar to the symptoms experienced in food allergy. In order to distinguish between a food allergy and other reactions to food the person with symptoms need to see a doctor.

Our immune system protects our bodies from infections, for example, by producing antibodies to fight germs. We do not understand why, but in some people the immune system mistakenly produces the IgE antibody to harmless things like some foods, giving rise to food allergies. Food allergens (the parts of food responsible for an allergic reaction) are usually proteins, and there are usually several kinds of allergens in each food. It is not yet clear what makes some food proteins allergens, and not others.
Some people have allergic reactions where IgE is not involved. This article, however, only deals with the allergic reactions mediated by IgE since these reactions can potentially be more severe.

**What do we know about the causes of food allergy?**

**Food allergy and other allergic diseases**

It is well known that infants with food allergies are more likely to develop other allergic diseases such as asthma later in life compared to infants without food allergies. One allergic disease is unlikely to cause another. A better explanation for the observation is that food allergies and allergic diseases in general probably have many risk factors in common.

**The genes of food allergy**

It is also well known that if your close family has a history of allergy you will have a higher risk of becoming allergic. Because of that observation, researchers have looked for genes that may play a role in the development of allergies. Many genes have been identified as possibly involved in different allergies. However, the studies attempting to identify allergy-associated genes have seldom provided consistent results. Very few studies have dealt directly with genes associated with food allergy, probably because most researchers believe that the same genes are involved in all allergies. However, a few genes have been identified as possibly having a specific role in allergic responses to foods. These are genes responsible for molecules with roles in the immune system or in the breakdown of food proteins in the gut.

**The food allergens**

In order to understand how food allergy might differ from, for example, allergy to pollen it is necessary to look more closely at the food allergens and how they interact with the immune system.

The food we eat needs to be digested into small molecules before our bodies can make use of it. For foods that we cook this breakdown process starts outside the body as heating helps the process. The food is further broken down when we chew it. Enzymes in the mouth and in the gut, as well as gastric acid in the stomach, are essential for the final breakdown.

Individuals with pollen or latex allergy often experience allergic symptoms when they eat certain fruits, vegetables or nuts. This “cross-reactivity” occurs because the body cannot distinguish between the allergens in pollen or latex and related proteins in food, and may react to both. Most of the allergens in cross-reacting foods are easily digested in the gut. This explains why the allergic symptoms are frequently mild and limited to the mouth. Likewise, most of the allergens in cross-reacting foods will easily be broken down if the food is cooked. This explains, for example, why many birch pollen allergic people cannot eat raw apples without experiencing symptoms, but stewed apples and pasteurised apple juice might not be a problem.

In contrast, many “true” food allergens, which cause a wider range of allergic symptoms, are hard to break down when cooked and tend to be less digestible in the stomach or gut. Because the food allergens are not well digested the gut immune system might recognise them as harmful foreign substances and start an allergic reaction.
Time and route of contact with food allergens

To acquire a food allergy we need to be in contact with the food at least once. We also need to be in contact with the food in order for our immune system to recognize it as harmless. However, we know very little about how much of an allergen we need to eat or be in contact with in other ways in order to become allergic, or how much is needed for the immune system to be adequately trained to regard the allergen as harmless. Furthermore, it is likely that the timing of the first encounter with a particular food allergen is important.

Researchers have found that breast milk may contain food allergens, and examples exist of infants who become allergic even though they have been exclusively breast fed. We also know that food allergens can, in very small amounts, reach the foetus by crossing the placenta. Other ways to come into contact with food allergens is via the skin or the respiratory tract. Based on a study with almost 14,000 pre-school children, a group of researchers concluded that children who used skin preparations that contain peanut oil might develop peanut allergy. Examples exist of people who have become allergic to foods after breathing in tiny parts of the food, for example, during cooking.

The best time for an infant to be introduced to solid foods in order to avoid food allergies remains unclear. A recent review of available studies suggested that early solid feeding might increase the risk of eczema but probably not other allergic diseases. On the other hand, recent data from wheat allergic patients showed that children who ate cereals before six months of age had a lower risk of wheat allergy than children who first ate cereals after six months of age.

Gastric acid in the stomach and food allergy

As described previously, gastric acid in the stomach is essential for the final breakdown of foods. If the food is not broken down properly, more food allergens may be available for the gut immune system to deal with. Therefore, lower amounts of gastric acid in the stomach may predispose individuals to food allergy or worsen the symptoms of an already existing food allergy. Patients with gastric ulcers are more susceptible to develop food allergy as they are often treated with drugs that lower the amount of acid in the stomach. Infants may also be more susceptible because they have lower amounts of gastric acid in the stomach than older children and adults.

The gut immune system and food allergens

Cells of the immune system are distributed all over our bodies in organs such as the bone marrow, spleen and lymph nodes. However, the highest numbers of immune cells surround our gut. This is no wonder since the gut is in contact with everything we eat. The gut immune system will try to protect us, for example, when we eat chicken infected with Salmonella bacteria.

Fortunately, in most people the gut immune system learns to correctly recognise food allergens as harmless, and no allergic reaction occurs. It is generally accepted that the gut immune system plays an important role in the development of IgE-mediated food allergy. However, we know very little about how food allergens interact with the gut. For example, we do not yet fully understand how they reach and interact with the gut immune system. How the food allergens are transported to the immune system strongly influences whether the gut immune system senses the food allergens as harmful or harmless. This means that changes in the gut’s transport of foods might change susceptibility to food allergy.
Microorganisms of the gut and food allergy

As foetuses we have a sterile gut. During birth and rapidly thereafter, bacteria and other microorganisms from the mother and the surrounding environment colonise the infant gut. Healthy children and adults end up with hundreds of different species and several kilos of beneficial bacteria in their guts. Research suggests that the microorganisms are involved in a range of useful functions, including aiding the gut immune system in recognising food allergens as harmless.

It has been noted that allergic and non-allergic infants have different mixtures of bacteria in their gut. Researchers have therefore tried to prevent allergy by changing the mixture of bacteria in the guts of infants. You can do that in two ways. You can feed the infants prebiotics, which are food substances intended to promote the growth of beneficial bacteria in the gut. As an example, human breast milk contains some sugars that do not provide nutrition directly to the infant but promote the growth of the beneficial *Bifidobacterium* bacteria in the gut. The second option is to feed the infant probiotics, which are live beneficial microorganisms such as *Lactobacillus* bacteria. The food industry uses *Lactobacillus* bacteria to ferment food, for example, to make yogurt and cheese.

Studies in animals have shown that feeding pre- or probiotics can reduce the development of allergy. Some studies in infants fed pre- or probiotics have failed to demonstrate any benefits. In other studies with pre- or probiotics, the infants developed less atopic dermatitis (a form of eczema which may be caused by food allergy). The results from the many studies probably differ because the study designs vary a lot. The infants have been fed various types of pre- or probiotics at different ages, doses and durations. In some of the studies the mothers of the infants have also eaten pre- or probiotics during pregnancy. Indications to date are that the use of probiotics is probably most useful very early in infancy. However, we need more research in the area before recommendations for allergy prevention can be made. None-the-less, numerous infant milk manufacturers incorporate both pre- and probiotics into specialized formulas to try to mimic the effect of breast milk.

When we have an infection we might eat antibiotics to kill the bacteria causing the infection. The antibiotics, however, also kill some of the bacteria in our gut. This means that antibiotics change the composition of bacteria in the gut. These changes in the gut may also be important in the development of food allergy.

Current dietary recommendations to prevent food allergy

Because of our limited knowledge, much controversy exists on possible preventive measures and strategies. In 2004 a European expert group recommended exclusive breastfeeding (no solid foods or supplementary infant formula) for the first 4-6 months of life. If breastfeeding for infants with a high risk of developing allergies is not possible, hypoallergenic formula should be used to reduce the likelihood of developing allergies. The same expert group recommended that pregnant and breastfeeding women do not need to eat a special diet. In 2000 an American expert group stated that infants with a high risk of developing allergy might benefit from late introduction of some of the common allergenic foods, namely dairy products, eggs, peanuts, nuts, and fish. Whether this practice is beneficial or might even increase the risk for food allergy is currently not known.
The above text is based on the paper:


_EuroPrevall is an EU-funded project about food allergy. The primary objective of EuroPrevall is to improve the quality of life for all food allergic consumers. To meet that objective EuroPrevall will conduct research to obtain information that we currently lack. EuroPrevall will also develop the tools necessary to manage food allergies more effectively. The 63 partners from 25 different countries include some of the leading allergy research organisations in Europe as well as clinical, patient, and industrial organisations. Visit [www.europrevall.org](http://www.europrevall.org) for more information on the project._