By special permission of the author, these extracts from her latest book, *Dealing with Food Allergies,* help us to understand the commonly used – often mis-used – terms encountered by anyone struggling to overcome food allergy problems.

THE ALLERGENIC POTENTIAL OF FOODS

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To what extent should a person who has a known food allergy avoid the culprit food? For example, if someone is allergic to soy, should he or she eliminate *all* forms of soy from the diet, including hydrolysed soy protein, lecithin made from soy, fermented soy (soy sauce), and so on? This is a question that few practitioners can answer with certainty. So, for safety, the allergic person is usually advised to avoid all forms of the food, even when this may lead to a great deal of work, possible nutritional deficiency, social and economic stress, annoyance, and fear, especially when foods are inadequately labelled as to the source of the ingredients.

Authorities in the field seem to agree that someone who is *mildly* allergic to a food needs to take less stringent precautions in detecting the food as a "hidden ingredient" than if the food is likely to cause a life-threatening anaphylactic reaction. The degree to which an allergic person will react to a food allergen depends on a number of factors, especially the atopic (allergic) potential of the person and the allergenic potency of the food. **Egg, cow's milk, soy, and peanut proteins** in babies and young children; **peanut, tree nuts, shellfish, and fin fish** in adults tend to be the foods that are most likely to cause a severe, and sometimes anaphylactic, reaction in hypersensitive people. *All sources of these foods should be strictly avoided if the allergic person has shown signs of an anaphylactic reaction to them.* What about other foods that may not have triggered an anaphylactic reaction, but are known to cause symptoms of allergy, albeit mild ones? How do we determine the degree of vigilance required in avoiding the food, and how do we assess its potential to trigger a life-threatening reaction in the future? Before we can answer these questions, we need to know exactly what a food allergen is.

WHAT IS A FOOD ALLERGEN?

This is a question that many scientists have tried to answer, but at the present time we do not have a precise definition, only that a **food allergen** is "an antigen present in a food that causes an allergic reaction". (Just a reminder to the reader that an **antigen** is the part of the food that triggers the immune system to respond as if the food were capable of causing a disease.) Several

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controversial aspects of food allergy present difficulties in reaching consensus on a precise definition:

❖ There is a lack of agreement about the frequency, severity, and symptoms caused by foods.

❖ Some food-induced reactions persist for years, whereas others do not. The majority of children outgrow most of their early food allergies by the age of five years.

❖ The target organ for many food allergies varies from person to person: The same food can induce a reaction in entirely different organ systems in different people. For example, cow's milk protein may induce digestive tract symptoms in one child, atopic dermatitis (skin rash) in another, and an anaphylactic reaction in a third child.

❖ Some foods are more common in provoking allergic reactions than others that are very similar. For example, peanut has a greater allergic potential than lentil, although both are legumes.

❖ Immunological processes other than Type 1 hypersensitivity (IgE-mediated) reactions can trigger allergy to food. Many clinicians restrict their definition of allergy to those reactions that can be proven to be triggered by IgE.

Because most traditional allergists define food allergy as an immediate-onset IgE-mediated reaction, a food allergen is usually defined as "a food component that induces the production of, and reacts with IgE antibodies to cause mediator release from mast cells and basophils resulting in an immediate hypersensitivity reaction". These characteristics allow scientists to identify, separate, and study the food component. Once they isolate the antigen/allergenic component, they can determine its structure and molecular characteristics.

Scientists are beginning to determine the structure of some specific molecules that cause the immune system to produce IgE antibodies. This is certainly increasing our understanding of what an allergenic food component looks like. However, there is still not enough scientific data to determine why one particular molecule rather than another will trigger an allergic reaction or why one person will respond to the molecule while another does not.

CHARACTERISTICS OF FOOD ALLERGENS

Chemical Structure

Most food allergens are either proteins or glycoproteins. **Glycoproteins** are proteins in which a carbohydrate chain is attached to the protein or peptide structure. Another frequent characteristic of allergens is that they

tend to be soluble in water. Although huge numbers of different proteins and glycoproteins are consumed in the diet, only a few are capable of causing an allergic reaction. In addition, only *sensitised* persons will show symptoms of allergy. A person who is **sensitised** to an allergen is one whose immune system has responded to that same specific allergen in the past and treated the food as if it were going to cause disease in the body - in other words, the food is deemed "foreign and a threat". Most food is considered "foreign but safe" and the immune system leaves it alone. The latter situation is called **tolerance**.

Haptens

A few nonprotein molecules can cause an allergic response; these are called **haptens.** Haptens are small molecules and may even be inorganic compounds or elements such as nickel. Haptens become allergens when they attach to a protein. The "carrier protein" with its attached molecule forms a new antigen, or **neoantigen.** The carrier protein may be part of the food in which the hapten exists, or it may be a protein from the body, to which the hapten attaches itself after it is consumed. The neoantigen is then capable of triggering a Type 1 hypersensitivity response, leading to allergy. The IgE antibodies are specific to the hapten part of the new antigen: therefore, if the hapten is nickel or sulfite, the IgE is produced against the nickel or sulfite, not against the protein to which it is attached.

Attributes of Food Allergens

In order for a molecule to initiate a Type 1 hypersensitivity reaction (allergic response), it must have the following attributes:

❖ The molecule must be the appropriate *size* to bridge two adjacent IgE molecules on the surface of the mast cell. The **mast cell** is the key to allergy: It contains the **inflammatory mediators** that are responsible for the symptoms of allergy. These are released in the process called **degranulation** when the mast cell is activated by IgE attached to its own allergen. The molecule must have a molecular weight of between 10,000 and 80,000 daltons. However, much smaller molecules may be allergenic when they act as haptens. The neoantigen formed when the hapten combines with a carrier protein is the correct size to bridge two IgE molecules.

❖ Two or more antigenic sites along the length of the protein molecule must be available for attaching to two adjacent IgE molecules. This may depend on the *shape* of the allergenic molecule because it needs to form a bridge between the two IgE molecules. The wrong shape would not fit properly.

❖ The molecule must pass the barrier of the intestinal lining in order to reach

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cells of the immune system. Proteins over 80,000 daltons in molecular weight are unlikely to pass through a healthy mucosa. The increased mucosal permeability resulting from certain conditions (e.g. intestinal inflammation; immaturity in young infants), however, may allow much larger molecules to pass through.

❖ The molecule must retain its allergenicity through various food-processing treatments. Many food allergens are heat- and acid-stable.

❖ The molecule must survive the digestive process and reach the intestinal lining in an immunogenic form. This means that it must be resistant to the effects of digestive **enzymes** that would break it down in the acidic environment of the stomach.

Function of Allergenic Molecules in Foods

Many laboratories are studying the molecule structure and characteristics of food allergens after they have been separated from the whole food. By a variety of analytical methods, researchers have determined the size (measured in kilo-daltons, kD) and the activity of the antigenic component of the food. Based on this data, they have been able to assume or suggest the possible function of the molecule in the food. Several important allergens have been separated and studied in this way. This type of research has become important in recent years because of the growing number of novel, genetically engineered foods being produced all over the world. Because of the potential for incorporating allergens into, or developing new allergenic molecules within, the new species, methods for their detection need to be available to scientists. Most of the research into the function of the allergenic molecules has been carried out on plants.

Proteins consist of amino acids linked together to form the specific protein coded for in the DNA of the plant or animal. Up to 22 different amino acids combine in numerous different sequences to form all of the proteins in nature. Based on the amino acid structure of the allergenic molecules, current research indicates that a surprisingly small number of amino acid sequences within the enormous range of proteins in plant foods can initiate a hypersensitivity response of the immune system. Furthermore, the functions of these proteins within the plant seem to be restricted to a very small number of categories. These include:

❖ Seed storage proteins, especially in nuts, seeds, and cereal grains. These are proteins that are stored in seeds to allow them to germinate and grow.

❖ Enzyme inhibitors that may be destructive to storage components. For example, inhibitors of alpha amylase,

the enzyme that breaks down plant starch, might break down starches, and the enzyme trypsin might destroy proteins in cereal grains.

❖ Structural proteins - the proteins that make up the structures of plants and allow them to keep their shape (in contrast to storage proteins).

❖ Regulatory proteins, such as profilins, that are important in plant fertilisation.

❖ Pathogenesis-related proteins, which are involved in the defence-related activities of the plant and allow it to combat plant-destroying microorganisms and some chemicals.

It appears that many of the food allergens belong to the class of proteins called **albumins.** Albumins tend to be storage proteins in animals, fish, and plants. Eggs of all species contain ovalbumin; milk of all species contains lactalbumin; fish contain parvalbumin; and plants contain seed storage albumins. Because a great deal of our plant foods come from seeds (grains, flour, peas, beans, lentils, nuts, seeds), many plant albumins are consumed by most of us daily. Albumins from different species are distinct, so allergy to one species does not predict allergy to another even within the same genus. Albumins are resistant to a variety of adverse conditions. For example, they

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tend to resist enzymes that break down proteins, such as trypsin, chymotrypsin, and pepsin, which are released in the digestive tract to digest food proteins. They also tend to be highly resistant to heat and survive cooking temperatures as high as 88°C (190°F).

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Although any food protein can be potentially allergenic, relatively few are known to cause most allergic reactions. In addition, *an allergenic protein can induce an allergic reaction only in an atopic person who has been sensitised to it.* Most of the severe allergic reactions to food occur in response to a surprisingly small number of foods. The foods most commonly associated with allergic reactions in **children** are **milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish.** Allergies to milk, egg, wheat, and soy are usually outgrown in early childhood. **Adults** tend to experience allergic reactions to foods that persist as allergens beyond infancy; these are **peanuts, tree nuts, shellfish, and certain species of fish.**

Lists of the most common allergenic foods vary according to the source of the data. In general, the "top eight" allergenic foods include:

1. Peanut and peanut products
2. Soy and soy products
3. Egg and egg products
4. Milk and milk products
5. Tree nuts and tree nut products, the most allergenic of which are:
   - Almond
   - Brazil nut
   - Cashew
   - Filbert (hazelnut)
   - Macadamia
   - Pecan
   - Pine nut
   - Pistachio
   - Walnut
6. Fish and fish products (not all species have the same allergic potential)
7. Shellfish: crustaceans (shrimp, prawn, lobster, crab, crayfish or crawfish) and molluscs (clam, mussel, oyster, scallop)
8. Wheat and wheat products

However, the *severity* of reactions associated with these foods varies. For example:

- ❖ Peanuts, tree nuts, shellfish, fish, milk, and egg account for most reported cases of anaphylactic reactions in children and adults.

- ❖ Soy is less frequently reported as a highly allergenic food, although it is often associated with severe cases of allergy and atopic dermatitis (eczema) in childhood.

- Gluten-sensitive enteropathy, more frequently known as coeliac disease, is a chronic disorder of the intestines. It is caused by an immunologically-mediated reaction to gluten, an important protein that occurs principally in wheat, rye, barley, and to some extent in oats. A person who has coeliac disease develops a number of symptoms that may include digestive-tract upset such as diarrhoea, abdominal cramping and distress, and inadequate absorption of food. In children, this may cause inadequate growth, and in adults an inability to gain weight. Other symptoms may include anaemia, infertility, recurrent sores in the mouth, and sometimes skin rashes known as dermatitis herpetiformis. Coeliac disease is a distinct medical condition, unrelated to allergy, and has its own diagnostic tests. Treatment is strict avoidance of wheat of all forms, rye, barley, and oats.

Other allergenic foods, present on some lists, absent on others, include:

- Sesame seed and products containing sesame seed
- Mustard seed
- Corn
- Kiwi fruit

Food additives rarely cause IgE-mediated hypersensitivity reactions and therefore do not appear on allergen lists.

The Allergen Scale

Every allergic person will react differently to foods, with diverse symptoms of varying severity, and will develop symptoms in response to various portions of foods. However, it is possible to summarise the more commonly allergenic foods in the form of a scale of "relative reactivity".

A scale of this type has several advantages:

- Used as a "reactivity chart" it allows people to see the number of foods that are available to them after their allergens have been crossed off. So often patients are overwhelmed when told that they must avoid a number of staple foods (eg. wheat, milk and milk products, and eggs), and the common response is "But there is nothing left to eat!" A glance at the remaining foods on the chart reassures them, and counselling can proceed in a less anxiety-provoking fashion.
- The foods most likely to cause an allergic response (the "top eight") are apparent in this

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scale. This is useful for the atopic individual because so often chronic reactivity to these foods in particular seems to lead to "hidden food allergy". *Hidden food allergy* is a term doctors use to refer to symptoms that disappear when foods are removed and appear when the food has been reintroduced, but were not apparent when the food was eaten regularly. Often the symptoms of hidden food allergy are chronic and mild and usually ignored until they become very noticeable during a food challenge. As people begin to make alternative choices, their symptoms are more readily identifiable when they eat the culprit food less frequently.

❖ If there is a risk of severe or anaphylactic reactions, the culprit foods can be marked in red on the scale. This makes family members more aware of the allergic individual's needs and alert to sources of the problem food. Many people like to keep a copy of the scale on the fridge; for this reason, the printed scale is limited to a single page.

HOW MUCH FOOD CAUSES AN ALLERGIC REACTION?

The amount of food that needs to be eaten in order to cause an allergic reaction depends on the potency of the allergen and how sensitive the person is to it. Unfortunately, data is scarce on this topic and rarely reported in the literature. A few studies have attempted to define a threshold level for a variety of food allergens. For example, tests have shown that:

- ❖ 10 milligrams of ovalbumin was required to elicit symptoms in egg-allergic children
- ❖ 6 milligrams of cod was required to elicit symptoms.
- ❖ 0.1 to 0.2 milligrams of peanut was required to elicit an allergic reaction.

The Food and Drug Administration (FDA) Ad Hoc Committee on Hypersensitivity to Food Constituents attempted to define "allergenic levels" of foods in their 1986 report. [1]

- ❖ The usual amount of food that causes an allergic reaction in a sensitised adult is 20 grams (0 to 7 ounces).
- ❖ Shrimp allergy will be produced by 1 to 2 grams (0.03 to 0.07 ounce) of shrimp.

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❖ Peanut allergy can be caused by as little as 25 milligrams (0.0009 ounce) of peanut.

However, there are reports that *inhaling* food components (such as being in a room where fish is being cooked) or merely *handling* food can cause a reaction in highly sensitive individuals.

As more sophisticated analytical tests become available, more data on this important subject will be collected.

In the meantime, the directive is that ***all*** *sources of the most highly allergenic foods, especially those that have previously caused a severe or anaphylactic reaction in an individual, should be completely avoided.* To achieve this, a sensitive person must be aware of:

- ❖ all types of natural foods that would be expected to contain the allergen,
- ❖ all terms in a food ingredient list that would indicate the presence of the allergen or its derivatives, and
- ❖ foods and non-food products that are likely to contain the culprit allergen.

In a number of cases, ingredients in processed and manufactured foods are derived from natural food sources, but their origins are somewhat obscure. Highly sensitive people should obtain information from food manufacturers concerning "hidden sources" of their particular allergens. They should also become familiar with terms on food ingredient labels that would indicate the presence of their allergens.