The mechanisms of food allergies

Allergy Fighters

Assoc. Prof. Barbara Wróblewska works on modifying food proteins, mainly those in cow milk, to derive less allergenic foods

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One fifth of Europe's population suffers from allergic reactions to a specific type of food. The prevalence of such hypersensitivity has stimulated a very intensive search for technologies yielding food products that are safe for such allergy sufferers to consume

The human body is constantly exposed to various environmental factors. Ingested food, plant pollen, dust, household chemicals, cosmetics, exhaust fume particles, microbiological contaminations, and many other substances are ceaselessly being verified by our immunological system. If they are recognized as "friendly" substances our body reacts in the correct way, but if the body's reaction is excessive, incorrect, or absent that can lead to pathologies, chiefly allergies.

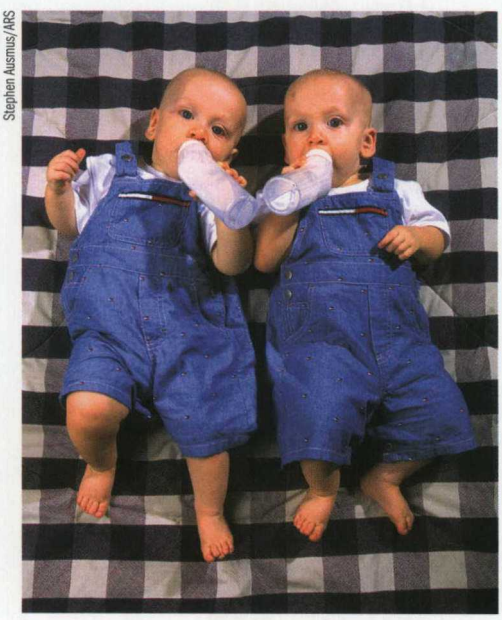
Recent years have seen a twofold increase in the occurrence of seasonal inflammations of the nose, atopic inflammations of the skin, and asthma. This upsurge is largely ascribed to the disparity between the rapid advance of human civilization and the sluggish pace of adaptation in the human immunological system. Man's natural environment has undergone vast changes due to industrial development, the introduction of new technological processes for food production, and the custom of spending time in closed or air-conditioned buildings.

The term "allergen" refers to proteins, lipo- or glycoproteins with a molecular mass of 5–50 kDa. However, hypersensitivity can also be provoked by haptens, compounds of a molecular mass of less than 1 kDa, mainly after they combine with carrier proteins that are themselves immunologically neutral or occur naturally in the body. Allergic hypersensitivity is a broader concept than that of "allergy," and encompasses any incorrect bodily reactions caused when the immunological system's comes into contact with an allergen. Such contact leads the body to mount a defensive reaction: generating special IgE antibodies (in the "acute" reaction) or sensitized lymphatic cells (in the "delayed-phase" reaction). The same allergen does not provoke any pathological consequences in healthy individuals, then being called an antigen.

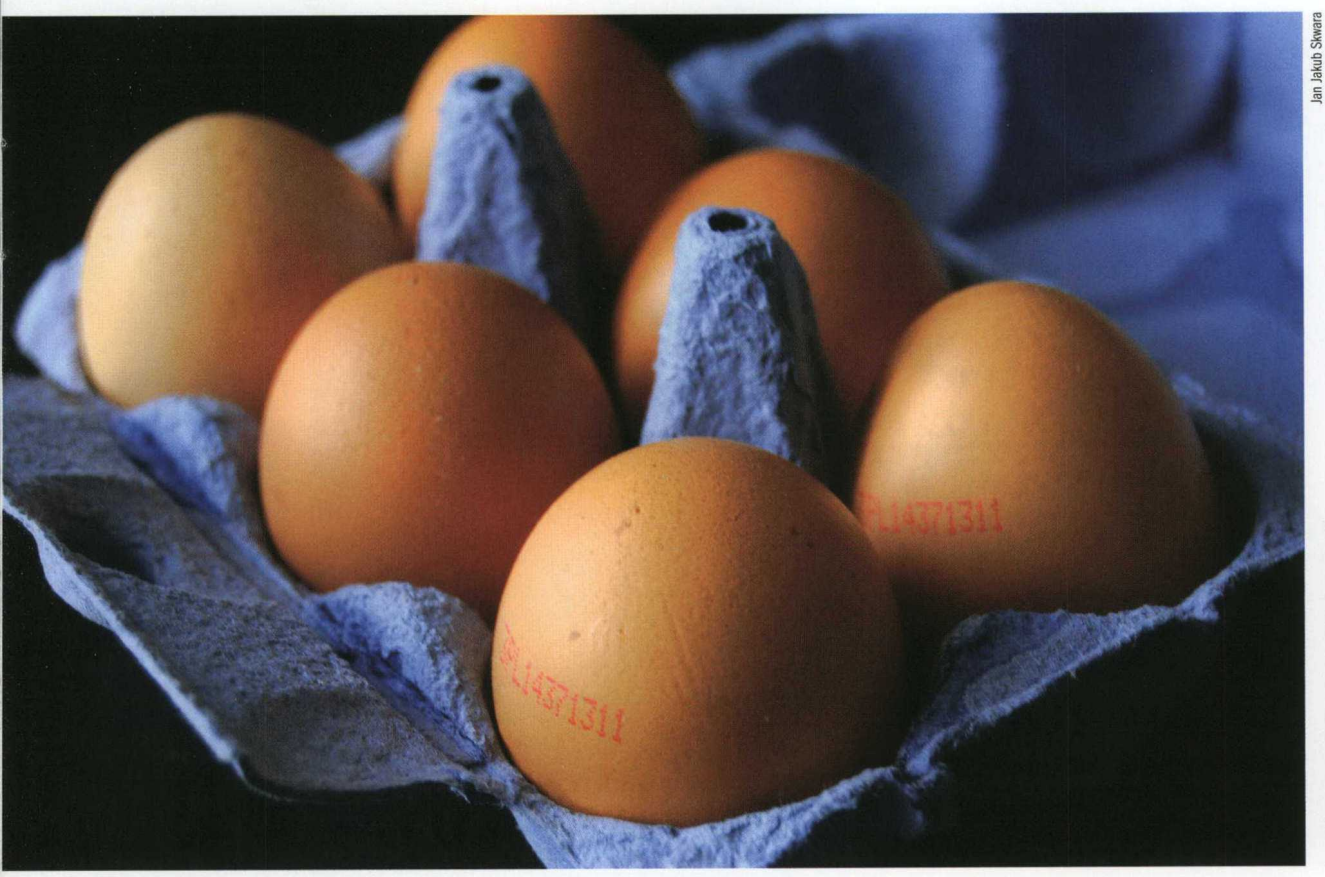
Extensive family

One of the most popular classifications of allergens categorizes them based on their origin: they may be inhaled, ingested, or bacterial; they may originate from saprophytes, parasites, and insects; or they may derive from simple chemical compounds acting as haptens (including various drugs, metals, and additives to food or animal feed). The Allergen Nomenclature Subcommittee of the International Union of Immunological Societies has developed a system of nomenclature for distinguishing allergens from other substances. Each designation is comprised of the three first letters of the Latin

Stephen Ausmus/ARS



Cow milk is usually the first food encountered by infants that comes from another species. Some 2–3% of children in their first year are allergic to such milk, and the problem unfortunately also affects adults



Jan Jakub Skewara

Soft boiled or scrambled? Unfortunately, such dilemmas are unknown to many allergy sufferers. Together with cow milk, peanuts, soy, wheat, tree nuts, fish, and shellfish, eggs are among the "big eight" allergens that cause more than 90% of all food allergies

name of the genus and one letter of the species from which the allergen originates, e.g. milk allergens are designated Bos d 4 and Bos d 5 after *Bos domesticus* (the common cow), egg allergens as Gal d 1, Gal d 2 from *Gallus domesticus* (the common chicken). The Arabic numerals reflect the order in which the specific allergens were discovered.

In EU countries, a significant percentage of the many types of allergies occurring nowadays are food-related. Studies have shown that as many as one in five individuals experience hypersensitivity to one type of food product or to whole groups of them.

In quantitative terms, allergenic proteins of animal origin are a smaller group than those of vegetable origin. The best characterized and commonplace animal allergens are those found in cow milk, usually the first food from another species consumed by infants. The main milk allergens are four fractions (mainly fraction α s 1) of casein, a protein which accounts for 3/4 of all milk proteins. These allergens occur under the common name Bos d 8. Other cow milk allergens include whey proteins like α-la (Bos d 4), β-lg (Bos d 5), and lactoferrin (a milk protein that transports iron atoms). Patients allergic to cow milk likewise exhibit reactions to goat and sheep milk.

Allergic to food

Diagnosing patients with a suspected food allergy is difficult because clinical symptoms may vary widely. The easiest symptoms to observe are those originating in the digestive system (nausea, vomiting, diarrhea, cramps, infant colic, bloating, and indigestion) or on the skin (urticaria, histamine release, and eczema). Sudden swelling of the mouth and tongue can be a very dangerous symptom, but most dangerous is called anaphylactic shock, associated with heart palpitations, dizziness, fainting with loss of consciousness, and extremely low or very high blood pressure, and potentially leading to loss of life.

Allergens of plant origin are characterized into respective groups by analyzing their sequence, 3D structure, and function. Such classification has identified super-families and families of plant allergens: prolamins, cupins, and the proteins involved in plants' defense system.

Researchers have long been seeking to render food products less allergenic, a goal

The mechanisms of food allergies

Barbara Wróblewska

Scientists are developing methods to obtain food products exhibiting lower allergenicity. The many techniques now being tested include pasteurization, microwaves, ultrasound, fermentation, hydrolysis, various protein modifications, and even genetic engineering

that can be achieved by various means. One technique that has been in use for some time involves the denaturation of proteins under high temperatures, such as pasteurization, in order to obtain a product of very good microbiological quality. This process has also been found to render foods significantly less allergenic, although the process may give rise to protein-sugar structures that are hard for the human immunological system to recognize. Allergenicity can also be lowered by means of microwaves and ultrasound.

Allergen digestion

Another method for reducing allergenicity involves the digestion (hydrolysis) of animal and/or plant proteins via the technological processing of raw foods. The enzymes used may be of animal (trypsin, chymotrypsin, pepsin, pancreatin), plant (papain), bacterial (from *Bacillus subtilis* bacteria), or fungal origin (from the species *Aspergillus oryzae*). Hydrolysis was long ago (some 50 years) proposed as a method for obtaining hypoallergenic baby food. Initially the raw material was casein; subsequently whey and soy proteins have been used. Unfortunately, none of the products so far obtained is completely devoid of allergenicity and therefore safe. The only hypoallergenic food derived consists of synthetic aminoacid mixtures (amino acids are the building blocks of proteins), intendent for parenteral nutrition. Its consumption, however, does not stimulate the body to generate natural tolerance.

Another method for obtaining safe foods is lactic acid fermentation. Here, proteins are altered by the enzymes secreted by microorganisms. Clinical research has confirmed that the consumption of fermented milk products (i.e. yoghurt or kefir) lowers the level of the antibodies that typify the allergic reaction, E-class immunoglobulins (IgE), in the blood.

Less popular methods for rendering foods less allergenic include gamma ray radiation, used for instance in the processing of shrimp, and microcapsuling. Other proposals include genetic engineering methods for developing hypoallergenic rice (whose production has been launched in Asia), the use of high-pressure technologies in the production of fruit juices, and even masking some of the proteins that evoke an allergic reaction (allergenic epitopes) by using cyclodextrin, for instance. Our research has proposed a new method: conjugating allergenic proteins with polyethylene glycol, which is a safe high molecular polymer, and binding the proteins together with epitopes so that they become inaccessible to the immunological system.

"Big eight"

As many as 90% of food allergy cases involve hypersensitivity to cow milk, peanuts,

eggs, soy seeds, wheat, tree nuts, fish, and shellfish. In 2003, the European Parliament issued directive No. 2003/98/EC, requiring that food labels pay particular attention to the "big eight" allergens. This directive's guidelines came into effect on 10 November 2005. Soon thereafter the above list was extended to include celery, mustard, sesame seeds, and sulfites, with lupine and mollusks added by another directive dated 22 December 2006. Proper information about food contents is chiefly intended to assist allergy sufferers, and the declaration made on the label must provide a guarantee of product safety.

The list of important food allergens is of course not closed and it is only a matter of time before more are added. In the Polish market, the contents of foods are listed based on declarations from the suppliers of the component raw materials. Food industry representatives are afraid of price increases if they are forced to state the actual levels of allergenic compounds based on costly analyses commissioned from specialized laboratories. The example of chocolate labeling shows how many allergens need to be marked for consumers to be fully informed. The problem of declaring food allergenicity thus poses a huge challenge for food technologists, employers, clinicians, dieticians, and consumers.

Research advances

Research carried out at the Food Enzyme and Allergen Department aims to lower the allergenicity of milk and food products from the legume family. Techniques found to be favorable include pasteurization, ultrasound, microwaves, and even proteolysis (especially involving the process of lactic acid fermentation), the conjugation of proteins, and the use of polyethylene glycol. Unfortunately, the results obtained *in vitro* have not for the time being translated into a similar reduction in allergenicity achieved *in vivo*, in patient skin tests.

We have also obtained a milk protein fraction exhibiting the lowest immunogenicity - this low molecule fraction isolated from whey protein hydrolysate (M.W.<12.4 kDa) meets the requirements to serve as the basis for deriving hypoallergenic foods. Moreover, we have proposed the use of a cross-linking enzyme, which can render the food product less allergenic and, importantly, improve its organoleptic properties.

The formation of sugar-protein adducts has turned out to be an important problem in the emergence of allergies. The immunological response to such unknown chemical structures of compounds from food products offers interesting avenues for future research.

Long road ahead

Despite much intensive work worldwide, it seems that we are still at the very outset of a long road towards resolving the problem of food allergies. The multiple technological techniques now used to obtain completely safe products still give no guarantee of success. The issue is further complicated by individual variation among patients. Research on animals enables us to conclude that the proper direction for food allergy research leads towards obtaining products which, after oral consumption, enable the body to develop its own specific tolerance. For the time being, however, we still have more questions than answers. ■

Further reading:

Wróblewska B. (2007). Alergonomika - propozycja nowej gałęzi nauki [Allergonomics - Proposing a New Field of Science]. *Przemysł Spożywczy, 2*, 2-5.

Wróblewska B., Karamać M., Amarowicz R., Szymkiewicz A., Troszyńska A., Kubicka E. (2004). Immunoreactive properties of peptide fractions of cow whey milk proteins after enzymatic hydrolysis. *International Journal of Food Science and Technology, 39*, 839-850.

The long list of food allergens is constantly getting longer, and EU directives are requiring that their presence be noted on food product labels. The example of this chocolate label shows how many allergens of varying origin would have to be indicated for consumers to be fully informed, according to our current state of knowledge, about whether a given product is safe for them

Wojciech Biedrzycki