

Management of food allergy

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Our present options for the management of food allergy are avoidance and pharmacotherapy. There are, however, many promising perspectives for better future management such as the more extensive use of hydrolyzed and elemental formulas for therapy and prevention, or greater emphasis on diagnosis and treatment of accompanying diseases linked with increased gut permeability. In selected situations, specific immunotherapy might be helpful. Rapid progress is expected in the search for the conditions of induction of oral tolerance. The latest results in genetic engineering can give us very effective tools for mass production of less allergenic foods with high nutritional value - if all safety, stability, productivity, and antigenicity problems can be solved.

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The management of food allergy consists overwhelmingly of avoidance and, if that is unsuccessful (mainly because of the failure of identification of the offending food), pharmacotherapy. Very few attempts have been made in the past to change the underlying pathologic immune reaction in either an antigen-specific or nonspecific way, or the antigenic composition of main food components. The importance of the problem can be characterized by Sampson's calculation of 4 million food allergies in the USA alone (1).

Management options today

None of the approaches used in everyday practice are really effective. The identification of the allergenic food, the prerequisite for effective avoidance, is often frustrating, not only because of the shortage of relevant, cheap, and easy-to-perform diagnostic methods, but also because of unknown structural changes due to food processing and storage, unidentified cross-reactivities, "hidden" components, etc. (2, 3).

Other methods of allergen avoidance on broader terms are the use of partially or extensively hydrolyzed formulas and that of elemental diets. Partially hydrolyzed cow's milk or soy milk is suitable for prevention in children of atopic prone families after the breast-feeding period, while extensively hydrolyzed (and sometimes also elemental) formulas can replace mother's milk if it is not available for any reason (4, 5). Elemental diet

without any obvious benefit, but its use in food allergy, especially where gastrointestinal inflammation coexists, can be justified for a short period (6, 7). The possible benefits of a non-antigen-specific restriction in the diet are disputed, and it is not advised generally. Some investigators, however, have found that symptoms of asthma or food-sensitive enteropathy are reduced parallel to the increased intake of n-3 polyunsaturated fatty acids, and that proinflammatory leukotriene synthesis is suppressed (8, 9). The avoidance of passive smoking, mites, and pets at an early age might also reduce the prevalence of food allergy (10, 11). Pharmacotherapy is purely symptomatic and, therefore, individual. Its main disadvantages are that it does not offer any means to cure food allergy, has no preventive effect, and is not specific for food allergy or for the gastrointestinal tract. Consensus exists on the emergency treatment of food-induced anaphylaxis: epinephrine must be given first in severe cases, while the use of antihistamines or steroids is restricted to milder systemic symptoms (12).

Difficulties in today's management of food allergies can be partially explained by the individual character of the disease. There are important differences not only in the agriculture, climate, food processing, or culture influencing the list of nutrients in a region or country, but also in atopic predisposition, age of the patients, length of breast-feeding, date of weaning of a given population: in local mucosal immunity; in general hygiene and

of concomitant diseases such as helminthiasis, or other gastrointestinal diseases – from *Helicobacter*-positive chronic gastritis to inflammatory bowel disease (13–15). All these factors may substantially influence the clinical symptoms of food allergy and cause resistance to therapy, unless the underlying disease is diagnosed and cured at the same time as the food allergy itself.

Management options for tomorrow: remodeling the allergic response or remodeling the antigen?

There are two practical ways to change the food-allergic immune response: specific immunotherapy and the induction of oral tolerance.

So far, no convincing and long-lasting clinical improvement has been observed after food-specific immunotherapy, but the situation may change with the production of biotechnologically modified epitopes. If the new epitopes will have less allergenicity, less IgE-binding capacity, will not induce mediator-release from basophils, and will activate T cells rather than B cells, at least the following issues remain to be considered: optimal routes of immunization, vaccination schemes, and possible vectors. In addition to new protein epitopes, the use of DNA vaccines is a possibility also (1, 16, 17).

The (re)induction of oral tolerance might be necessary in case of defective digestive functions. Gastrointestinal inflammation or infection means, in addition to changes in optimal pH of the gastric juice, less activity of digestive enzymes, and so more unprocessed allergenic epitopes. It is followed, at least temporarily, by defective antigen presentation (via enterocytes), substantial changes in the cell composition of the gut, and an increased proinflammatory mediator synthesis and release. Transforming growth factor-beta further increases permeability; this facilitates unlimited antigen presentation, and, finally, instead of oral tolerance, an enhanced, harmful immune response occurs (18). Attempts to restore oral tolerance are numerous in animal models of autoimmunity and are expected in man also in the near future (19).

The remodeling of the antigen means the introduction of the achievements of genetic engineering in plants into the management of food allergy. For example, hypoallergenic rice has been produced on this way, and there are controversial results in increasing the nutritional quality of soybean (20, 21). At present, the immense future advantages of biotechnology in the mass production of hypoallergenic food seem to be limited by

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Finally, there is an opportunity and a need for the “remodeling” of the psyche of food-allergic patients and their relatives – by improved dietetic counseling, education, emergency planning, consumer protection, and information – at school, work, and home (1, 4, 23).

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