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Diet regimen in the treatment of food allergy

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Summary. - Adverse reactions to food may be mediated by immunological or non immunological mechanisms. The term "food allergy" describes an event in which a definite immunopathological process can be demonstrated and a cause and effect relationship must be present. Symptoms and signs of food allergy may appear in any organ system, depending in part on the age of the subject and on the allergen involved. At present it is generally agreed that the only effective therapy for food allergy is strict elimination of the offending food antigen. Institution of a food elimination diet should be considered comparable to prescribing a medication, which carries along definite risk-benefit ratio. Consequently, appropriate diagnostic measures based on history, skin test, or radioallergosorbent test (Rast) and blind food challenges, must be utilized before implementing special diets. The allergist and other health care professionals must recognize the advantages of elimination diets (improvement of symptoms) as well as disadvantages (increase of the time required to purchase food and prepare meals, impossibility to eat at restaurants, at friends' houses or at school with consequent possible social isolation, nutritional disorders) and choose the most appropriate elimination diet.

Key words: diet, food allergy, children.

Riassunto *(Terapia dietetica delle allergie alimentari).* - Le reazioni indesiderate da alimenti possono essere mediate attraverso un meccanismo immunologico, tossico, infettivo, metabolico o neuropsicologico. Con il termine di allergia alimentare si intendono attualmente solo le reazioni in cui sia dimostrata una relazione causa-effetto fra l'ingestione di un cibo e sintomo clinico e che siano mediate da un definito meccanismo immunopatologico. Il più semplice ed efficace trattamento delle allergie alimentari consiste nella eliminazione dalla dieta dell'alimento "offending". Prima di considerare l'impiego di una terapia dietetica, specialmente se questa è molto ristretta, un particolare rigore deve essere posto nella diagnosi (anamnesi, test cutanei e/o *in vitro*, test di provocazione) e nella valutazione del rapporto costo-beneficio. Si deve in sostanza valutare se i vantaggi della dieta (miglioramento o scomparsa dei sintomi) siano superiori ai possibili svantaggi (aumento del tempo necessario alle madri per il reperimento e la preparazione dei cibi, condizionamento psicologico dei bambini con possibile isolamento sociale, possibilità di carenze nutrizionali).

Parole chiave: dieta, allergia alimentare, bambini.

Introduction

Although food allergy has been known since the time of Hippocrates (who described cow's milk allergy around 370 BC), this kind of pathology continues even today to be an object not only of study, but also of remarkable controversy with regard to its clinical and diagnostic aspects as well as its prevention and therapy. The food allergy prevalence can be found in about 1.4% (from 0.5% to 3.8%) of children and 0.3% (from 0.1% to 1.0%) of adults [1]. The adverse reactions to foods may be subdivided into toxic and not toxic reactions (in which both food allergy or an immunomediated reaction and a non immunomediated food intolerance can be found) [2]. One source of confusion is constituted by the fact that often what are labelled as "allergies" are in fact "intolerances" to food which may be pharmacological (caused by substances present in the food which, if taken in subtoxic amounts, can cause symptoms in some intolerant individuals), indefinite (as in the case of adverse reactions to food additives), or enzymatic, as for example in the case of intolerance to lactose. Currently the term "food allergy" is used only for those pathological manifestations in which an IgE or non IgE mediated immunological cause can be found.

However, even so, the difficulty in diagnosing pathological reactions different from those of type I (since even in normal subjects both IgG4 anti foods as well as IgG and IgE class circulating immunocomplexes containing food antigens can be found), has made practitioners base their diagnoses almost exclusively on IgE mediated reactions.

From a clinical point of view it is often difficult to distinguish strictly "allergic" reactions from those stemming from food intolerance.

The development of allergic diseases (also called atopic diseases) is influenced by genetic factors (in fact, if both parents suffer from allergies, so will 60-80% of their children) as well as environmental ones.

An association between particular HLA phenotypes and specific allergens exists.

In fact the specific responses to the allergenic peptides re-expressed in the antigen presenting cells (APCs) are

controlled both by aminoacid sequences located in the variable parts of the alpha I and beta 2 chains of the hystocompatibility antigens of class II, as well as by the levels of expression of these molecules on the APCs membrane, and finally, by the structure of the variable parts of the alpha and beta chains of the T cell receptors and the corresponding genes controlling them [3].

Clinical aspects of food allergy

There are various clinical manifestations of food allergy, and they can practically affect every organ or apparatus. According to Ventura, the gastroenteric apparatus is affected in 62% of cases, skin in 49% and the respiratory apparatus in 8%. The gastroenteric apparatus only would be affected in 43% of cases [4]. The most common clinical manifestations are listed in Table 1.

Symptoms may affect one or more apparatus. It appears obvious that the most common allergy during the first year of life is to the proteins of cow's milk and to the other foods precociously introduced into the diet.

Among these, eggs, citrus fruits, tomatoes, and cereals are considered the allergens which may easily cause precocious allergies. Moreover, eating habits play an important role in the manifestation of a food allergy. Presumably, the high incidence of undesired reactions to soybean in Japan, to peanuts in the USA, and to fish in Scandinavia is due to the great use of these products in early childhood [5].

According to 1988 data gathered by the research group of the Società Italiana di Pediatria (SIP, Italian Society of Pediatrics) on the allergy to cow's milk proteins, symptoms such as continuous vomiting, chronic diarrhoea with or without malabsorption, colitis, gaseous colics can be attributed to cow's milk allergy in almost 30% of cases in the first year of life [6]. The acquisition of a "tolerance" to the allergen in a certain period of time can be considered a predictor of food allergy. As far as cow's milk allergy is concerned, the acquisition of this tolerance seems to be negatively influenced by various anamnestic, clinical, and laboratory parameters. Dannaeus demonstrated that, after 2 years and 4 months of an elimination diet, tolerance to cow's milk was present in less than one third of children with total and increased specific IgE and atopic inheritance and in more than two thirds with low IgE and familiar anamnesis to negative atopy [7]. Even in Host's case histories the presence of specific IgE was a marker for a later acquisition of the tolerance to cow's milk [8]. Our experience confirms these IgE antibody characteristics. In 37 children suffering from cow's milk allergy which appeared in their first year of life and without specific IgE towards the proteins of cow's milk, the acquisition of tolerance, by the age of 5, was manifested in the majority of cases (86%). Whereas in 35 children still suffering from cow's milk allergy as above but with specific IgE towards cow's milk protein, in only about half of the cases (57%), the intake of cow's milk did not produce clinical disorders at the age of 5. Ventura and Panizon pointed out that, in children with a diagnosed cow's milk allergy in their first year of life, the prognosis was better in those patients who presented a "pure" intestinal manifestation (diarrhoea, colics, malabsorption) than in those with also or only an extraintestinal manifestation (asthma, eczema): at a five year follow up the tolerance was 84% in the first group, whereas in the second it was 60% [9]. In general, as concerns the course of cow's milk allergy, atopic inheritance, the late appearance of symptoms (after the first year of life), the type of symptoms (immediate or extraintestinal), and positive reactions to skin tests and to RAST for the cow's milk proteins and other allergenic proteins are to be considered negative prognostic factors.

Diets

Diets can be used not only in the prevention, but also in the diagnosis and the therapy of food allergy [10-12]. The IgE mediate is without doubt the preferential pathogenetic mechanism through which foods induce allergy [13], but sometimes there may be associated mechanisms [1]. The presence of combined immuno-

Table 1. - Clinical manifestations frequently associated with food allergy

Gastrointestinal symptoms	- vomiting, diarrhoea, intestinal colics, dyspepsia, map tongue, stomatitis, hematemesis, etc.
Respiratory symptoms	- rhinitis, chronic cough, asthma
Skin	- eczema, urticaria, angioneurotic edema
CNS	- headache, irritability, fatigue-tension syndrome
Haematologic manifestations	- iron deficiency anemia, thrombocytopenias
Other	- anaphylaxis, recurrent fever, serous media otitis

pathogenetic reactions explains the great number of late reactions to challenge tests [14]. The definition of the etiopathogenetic role played by food is based on the combined use of anamnesis, skin and laboratory tests aimed at the determination of the involved immunopathogenetic mechanisms, of the "diagnostic" elimination diets and of the challenge tests [15]. These are considered the diagnostic "gold standard", especially by American researchers [16, 17]. Challenge tests can be open, blind, double blind [18]. In children a single blind challenge is often sufficient to obtain a reliable clinical response, and in many uncertain cases it allows us to avoid useless diets, worked out only on the basis of anamnestic and laboratory data, and to reintroduce the food allergenic once it is tolerated [15].

According to other authors [11, 19], food challenges must not be given great importance, because during these tests the food intake does not occur in the same environmental conditions in which it previously aroused the symptoms, and it is also known that various factors condition the clinical manifestation of food allergy (simultaneous intake of cross-reaction foods, compounds or drugs, physical exertion, etc.) [20]. Food challenges are also restrictive in their diagnostic accuracy because they are based on a single food intake, while in many cases the new outbreak of symptoms appears only after repeated administrations; therefore other dietotherapeutic approaches are needed.

Food allergy is mainly a pediatric disease (in 95% of cases it begins within the first 5 years), and even within the various pediatric ages there is a progressive reduction with growth. The disappearance of the food allergy during puberty varies from 10 to 50% according to case histories [21]. Therefore, when using a diet in the treatment of food allergy in a child, you must take into account that it often clears up spontaneously and so this kind of treatment must be used only in the most severe cases and/or in the ones with a significant clinical history.

The age factor becomes, for various reasons, very important when a "therapeutic" diet must be planned for many reasons: first of all, because the younger the child, the fewer the foods he eats, so the "offending" one is easier to find.

A classical example of this is that of the baby presenting an allergy to the cow's milk protein, the replacement of it leading to a quick improvement. On the other hand, in an older child with a more varied diet, the search for an allergenic food can be more difficult, especially without a clear clinical history, and can lead to very restricted diets which the child may not follow. Other factors, apart from faulty cooperation from parents and children, which interfere in the correct evaluation of the effectiveness of the diet are the accidental contaminations or "hidden foods"; these are the ones which are not mentioned in the ingredients list or those that one cannot know to be in the food [22, 23].

Besides, the incompleteness of the ingredients list on the packets, with incomprehensible definitions (such as casein, seroprotein, etc), can negatively affect the success of a diet (Table 2).

From a general point of view, the diets that may be utilized in the treatment of food allergy can be divided into aimed, empiric, rotation, oligo-antigenic, and elementary. Aimed diets are characterized by the elimination of one or more foods to which the patient proves to be allergic after a correct allergenic diagnosis based on the combined use of the patient's clinical history, skin and/or *in vitro* tests, and food challenges. These represent an ideal strategy of intervention and they are usually utilized when very important food allergenics such as milk, eggs, peanuts and fish are involved; they also usually give immediate reactions, and therefore the patient can easily notice them. The advantages of aimed diets are that they are easy to follow, and therefore they assure an adequate "compliance"; they are not very expensive and they are very effective.

The disadvantages are represented by the necessity of finding substitutes and also the "hidden" presence of these foods (Table 3).

A common example of an aimed diet is the one without milk in the baby with food allergy who is fed, at 4-5 months of age, with an adapted formula, and the one without eggs or wheat or fish in the older child.

In the baby affected by food allergy the replacement of a cow's milk formula is often a necessary means. The requirements a substitutive milk must possess are a low allergenicity, a high nutritional power, a low osmolarity, an acceptable taste and a reasonable price. Presumable substitutive milks are essentially the special ones [16, 24] (usually casein or seroprotein hydrolysates), soy milks or soy hydrolysates, alternative animal milks and aminoacid mixtures [25, 26].

The characteristics of some cow's milk substitutes are listed in Table 4. It appears obvious that the more the hydrolysis is induced the lower the allergenicity will be, but the price is higher and the taste worse. When wanting to introduce a casein or seroalbumin hydrolysate it is

Table 2. - Factors that may influence the outcome of the elimination diet

- identification of all foods suspected of an adverse reaction
- possibility of an elimination from the diet
- hidden foods
- defective ingredients lists on the packaging
- marketing with incomprehensive definitions
- degree of family compliance
- degree of patient's sensitization
- type of current symptomatology
- presence of inhalation allergy
- association with other factors (physical exercise, gastroenteric disorders, emotional factors, hormonal changes, etc.)

Table 3. - Advantages and disadvantages of the most common dietary regimens in the food allergy treatment associated with atopic dermatitis

Dietary regimens	Advantages	Disavantages
aimed diet	easy follow-up inexpensive very effective	precise diagnosis need for substitutes "hidden" foods
empiric diet	easy prescription	"empiricism" need for substitutes family cooperation
oligo-antigenic diet	good compliance for short periods low cost	tedious diet empiric evaluation of the outcome
elemental and half elemental diet	utility in serious cases high specificity defining the role of food	high cost unpalatable nutritional

Table 4. - Characteristics of cow's milk substitutes used in the prevention of food allergy and atopic dermatitis

	Soy	Casein hydrolysate	Whey protein hydrolysate	Amino acid formulas	Hypoallergenic formulas
Low allergenicity	++	+++	++±	++++	+±
High nutritional power	++±	++	++	+±	+++
Low osmolarity	+++	+±	++	+±	++
Good palatability	++±	+	+±	±	+++
Low cost	++	+	+	-	++

preferable to use the ones with an extensive hydrolysis, and the allergenicity of the product must be evaluated with a prick test [27, 28]. Although special milks with a partial hydrolysis possess many of the characteristics required (good taste, high nutritional power and low price), they still tend to conserve a certain allergenicity; therefore, they may be used in prevention, but not in the therapy for cow's milk allergy. From a nutritional point of view, soy milk seems adequate [29], but 30% of patients subsequently develop an allergy [9].

In some cases, and where available, other animal milks such as ass's, goat's, etc. may also be utilized as cow's milk replacements in the treatment of food allergy [25, 26], but their different composition and the possibility of cross-reactions (30-40% with goat's milk) must be taken into consideration [25]. Ass's milk seems to be the most similiar to maternal milk [26].

Moreover, the aimed diet without eggs is frequently and successfully used in pediatrics; but it is important to point out that usually, especially during the first year of life, the allergy to eggs is related to the cow's milk allergy, so both foods must be eliminated. Since milk and eggs are considered to be the most common food allergenics, diets without these are used with success in an "empirical" way in the first year of life. But after this period it becomes difficult to use these diets again without a correct etiological diagnosis because of the great effort they require from the family.

An aimed diet with the elimination of wheat is usually used on its own, but sometimes it is associated to a diet without milk and eggs in patients with more severe food allergies. Various products without wheat (based on rice, corn starch, potato flour, etc. usually used in patients who suffer from celiac disease) that are very useful for this purpose may be easily found on the market. Oligo-antigenic diets are more restrictive, they are based on the intake of a small quantity of food which possesses a low allergenicity. At the beginning the diet is characterized by one source of carbohydrates (one type of flour or amid and cane sugar), one type of meat (usually lamb or rabbit), one type of fruit (usually apple or pear) and one kind of oil. The most common example of this type of diet in Italy is represented by the one based on lamb [30-32]. One of the most common diets (Rezza's diet) is described in Table 5. On the other hand we must take into consideration the existence of a phylogenetic similiarity between the ovine and the bovine seroalbumin which causes a percentage of cross-reactions, which would make the use of this type of diet in patients with cow's milk allergy questionable [33].

British countries have employed other types of oligo-antigenic diets [34]. In Italy even more "bizarre" diets, based on pork [35] or chicken [36], have been used but only in rare cases of patients with untreatable diarrhoea caused by food allergy.

Even the casein or seroprotein or soy hydrolysates should be included among the oligo-antigenic foods, keeping in mind, however, that in subjects with more severe forms (those for whom the diet is used) even these foods can cause anaphylactic reactions [37, 38].

The "initial" oligo-antigenic diet, chosen on the basis of the anamnesis, skin and *in vitro* tests, and the severity of symptoms, is prescribed for a period of time that varies from 2 to 4 weeks; if there is an improvement in the symptoms (at least 50%) other foods are reintroduced, one at a time, every 7 days the symptoms are recorded in a notebook (Table 6). The "definitive" diet will eliminate only those foods which are definitely harmful: "therapeutic diet". In doubtful cases, before deciding to discontinue the food, a blind challenge test is advised.

Oligo-antigenic diets are used when the symptoms are more evident, and the anamnesis and allergy tests are not very revealing. The advantages of this type of dietetic approach are the compliance (good for brief periods) and the low cost; the disadvantages can be considered the monotony of the diet itself and a certain empiricism in evaluating results (Table 3). Furthermore, if these diets are used for a prolonged period, there may be nutritional risks (inadequate number of calories, inadequate calcium supply) [39, 40].

The rotation diet is another not very objective but useful dietotherapic approach in some food allergy situations with an uncertain diagnosis, or cases in which patients do not provide an adequate compliance in putting into practice an elimination diet: members of the same food family are introduced at intervals of not less than 1 day, and the minimum interval between the intake of each single food is not less than 4 days [19].

Table 5. - Rezza's diet

Homogenize the following foods in one litre of water:	
- lamb meat	100 g
- pre-cooked rice-flour	70 g
- olive-oil	40 g
- calcium gluconate	300 mg
Composition in one litre:	
- calories	740 kcal
- carbohydrates	58.8 g
- fats	45.3 g
- proteins	24.6 g
- calcium	310 mg
- iron	2 mg
- sodium	100 mg
- potassium	350 mg
- phosphorus	196 mg

Table 6. - Example of oligo-antigenic diets

Diet A
1 hydrolysate milk (casein, whey, soy)
1 carbohydrate source (wheat, rice, maize)
1 meat (lamb, rabbit, horse)
1 fruit (apple, pear, preferably cooked)
1 oil (olive, or corn)

Diet B
1 hydrolysate milk
1 carbohydrate source

Diet C
1 carbohydrate source
1 meat
1 oil

The different diets (A, B, C) must be worked out in relation to clinical history, age, seriousness of symptoms, and used in sequence if necessary.

The theoretical assumption (not demonstrated) is that in these cases, repeated intakes of the same food are necessary to induce the food allergy.

Elementary diets are used for children with severe food allergies (often associated with severe atopic dermatitis) [41] who do not respond either to other dietotherapy approaches or intensive treatments which use other conventional measures (local treatment with emollients and steroids, antibiotics for infections, antihistamines).

In hospital diets, patients are exclusively fed with aminoacid mixtures (Nutrinaut, Nutricia); in order to minimize the possibility of osmotic diarroea, a low concentration is initially used (6-7 g/100 ml, 140 mOsm/kg) and gradually increased on the third day up to 13 g/100 ml (280 mOsm/kg) and then, if well-tolerated, it is continued up to a maximum of 26.7 g/100 ml (560 mOsm/kg).

After 28 days, if there is no improvement, the diet is abandoned and systemic corticosteroids are used. But if there is an improvement, treatment is continued by reintroducing the foods for which there is an apparently negative clinical history.

This type of dietetic approach has shown [38] improvement in 73% of food allergies associated with atopic dermatitis; often reactions to the challenges are quite delayed, up to as much as 2-7 days after the introduction of the food and towards those foods (lamb, rice, corn, casein hydrolysate) which are normally used at the beginning of oligo-antigenic diets.

Long hospitalization, weight loss, loss of the seroalbumin concentration, and the possibility of inducing anaphylactic shock during the reintroduction phase are the restrictions involved in this type of dietetic treatment. Furthermore, these mixtures do not have a good taste, they are very expensive, and there is no information available on their true nutritional adequacy [15]. Recently,

aminoacid preparations with a lower osmolarity and a lower energy value (Nutri-Junior, Nutricia) have been proposed. Maltodextrin and lipid mixtures are also on the market, and could be useful (Duocal).

Diet duration

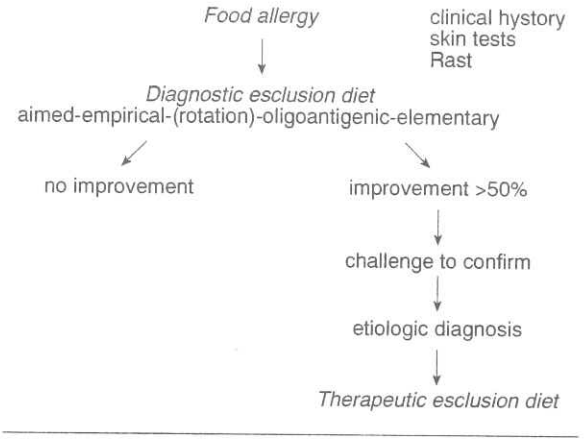
A diet, even the easiest, should last as long as is strictly necessary and must always be supervised by a nutrition expert, in order to ensure a sufficient supply of the various nutrients. It is also very important that the parents are conveniently informed about the possibility of finding the necessary products for the particular type of diet their child must follow, and that they received proper assurance on the validity of the dietotherapy as well as advice and suggestions for using the permitted foods based on simple recipes. Diets that are too long lasting may cause maternal overprotection with the subsequent social isolation of the child, problems with family relationships and between the family and the doctor [42].

The introduction of an elimination diet is similiar to prescribing a medicine, and in the same way, it must be evaluated in terms of risk-benefit ratio. Pediatricians, as well as specialists in diagnosing and treating food allergies, must however recognize the enormous emotional impact the prescription of a diet has on a family. The time required to purchase the tolerated foods and to prepare meals increases and the impossibility of eating at restaurants, enjoying parties at friends' houses or even having a snack can be sources of anxiety and family arguments.

Some parameters, such as the severity of the symptoms at the onset, the degree of allergic sensitivity, the type of food concerned, can indicate either the anticipation or postponment of the reintroduction of the eliminated food. It is usually recommended to reintroduce the food allergenic every 6-12 months. The modality of such reintroduction (at home or controlled challenge in a medical environment) is established case by case, on the basis of the clinical history and the course of the allergy tests.

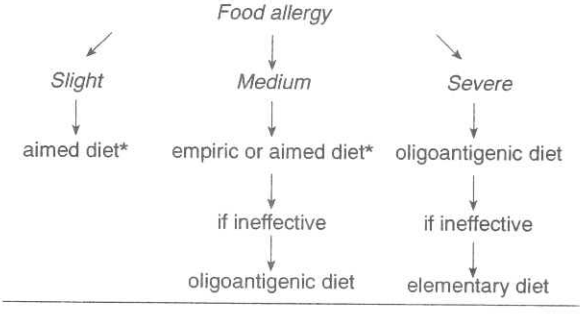
In some patients the tolerance reached is only partial and dose dependent; furthermore, approximately 50-70% of the cases with current atopic dermatitis associated to food allergy also develop asthma and sensitivity to airborne allergens (acarids, animal furs) [43]. Diets are difficult to use in children over 4-5 years of age, because the child usually does not understand this restriction and the chances of transgression are very high (at home, at school, at friends' houses, at grandparents' houses, etc.). Therefore, especially in patients with immediate and severe reactions, it is preferable to evaluate from time to time the stage of tolerance by using challenges contolled by a doctor, who may direct the more or less restrictive behaviour of parents as regards that particular food.

Table 7. - Clinical-diagnostic approach to diets in children with food allergy with or without atopic dermatitis



Modified from [44].

Table 8. - Use of diets in relation to severity of food allergy



*If clinical history is quite indicative
Modified from [44].

In conclusion, it is very important to make good use of diets both from a diagnostic and a therapeutic point of view in the treatment of a child with food allergy and a probable associated atopic dermatitis (Table 7). The correct use of diets is closely linked to a careful evaluation of the risk-benefit relationship.

Light and episodical forms of food allergy do not need particular diets, unless the anamnesis and the food allergenic are relatively important from a nutritional point of view (Table 8).

More severe forms of food allergy should be treated with adequate dietotherapy programmes administered by qualified personnel and continued for limited periods.

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