The adverse reaction to foods

U11

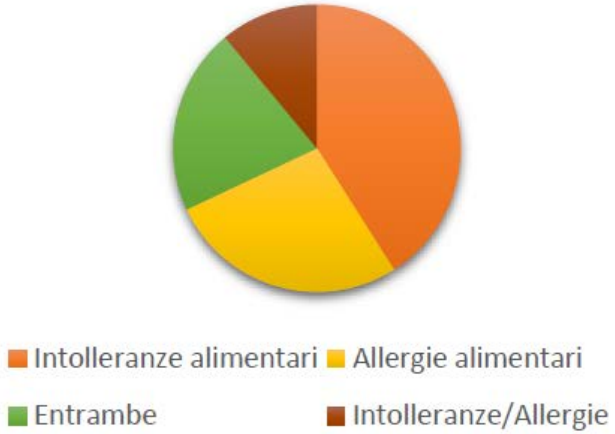
Data 2015-2016 from the scientific literature

PubMed, using "adverse food" reactions ”and“ food intolerance ” as keywords allowed to visualize the entity and the content of scientific publications in this regard. In both cases two filters were used: "Human" for the species and "Review" for the type of publication.

Keywords: "adverse food reactions"

The total results were 1592, of which 338 were relevant. Of these, 77% related to food allergies, 19% all types of adverse reactions to food, 3% food intolerances and 1% toxic reactions.

Keywords: "food intolerance"



The results obtained were 925, whose 150 were relevant. Of these, 41% concerned real food intolerances (where it does not occur an involvement of the immune system), 27% food allergies (in particular IgE-mediated allergies and celiac disease), 21% both reactions and 11% wrongly classified as food intolerances

Tesi di Laurea Magistrale in Farmacia di Letizia Savant Moton:
Le intolleranze alimentari in farmacia

The adverse reaction to foods

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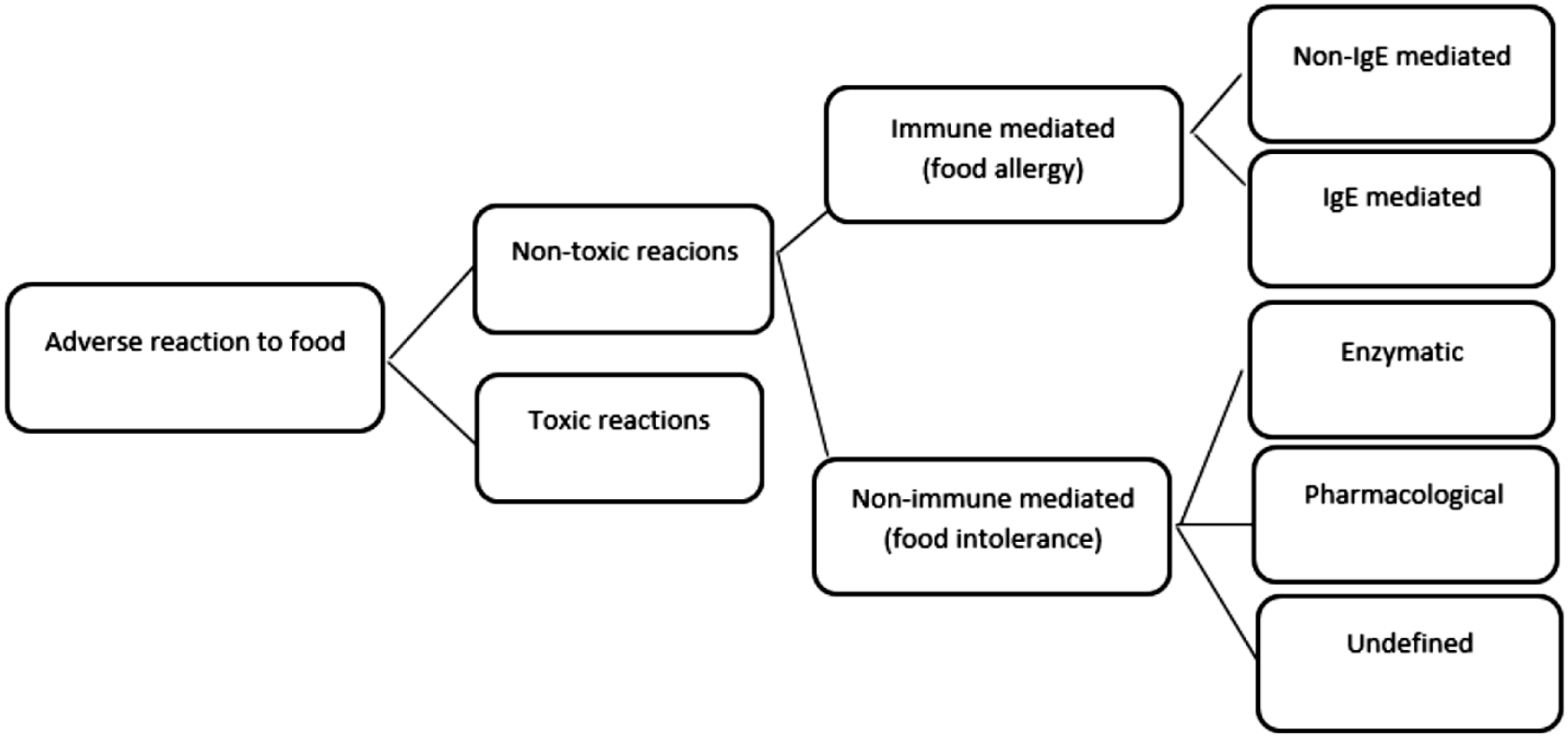
Adverse reactions to food, classification according to EAACI (European Academy of Allergy and Clinical Immunology)



Food allergy IgE mediated

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Food allergies are hypersensitivity reactions to commonly consumed foods.
Depend on an immune reaction mediated by IgE antibodies, it presents a clinical symptomatology that varies from mild skin reactions to anaphylactic shock.

Fonte: Modif. da: Evangelisti F, Restani P. *Prodotti dietetici. Chimica Tecnologia ed Impiego*. Seconda ed. Piccin Ed. 2011.

Risk factors are:

- Familiarity the symptomatology can change from parents to children allergy can develop towards different antigens
- Environmental factors exacerbated by exposure to more allergens (smoke, smog etc) too much hygiene in the neonatal age
- Gastrointestinal permeability
- Repeated exposure to antigen (GALT) Gut Associated Lymphoid Tissue

Food allergy IgE mediated

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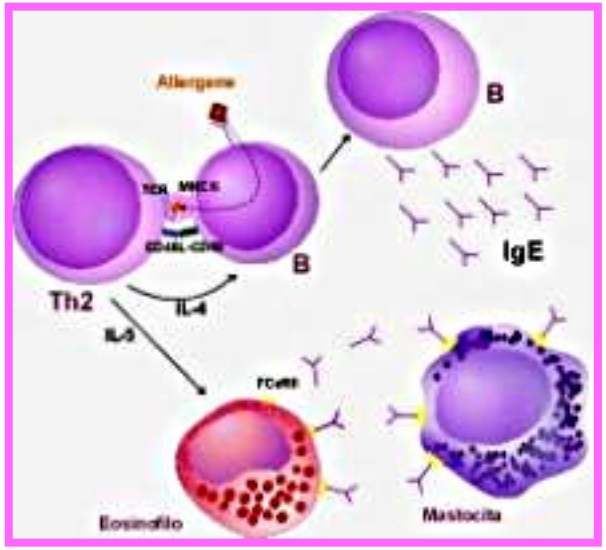
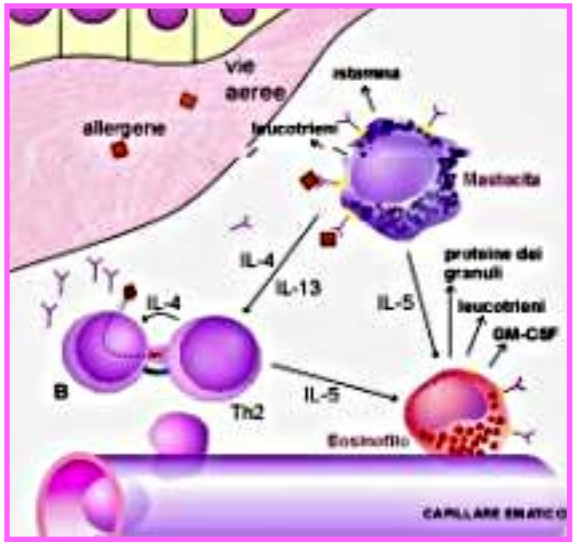
What is an allergic reaction?

An allergic reaction is the response of the body's immune system to normally harmless substances (known as allergens), such as pollens, foods, and house dust mites. When the immune system encounters these substances for the first time, it produces large numbers of antibodies, called IgE antibodies, which bind to the surface of mast cells (i.e. tissue cells). This is known as sensitisation. The next time the body encounters that particular allergen, the IgE antibodies on the surface of the mast cells are activated, causing the release of chemicals such as histamine, which cause the allergic symptoms.



Sensistisation



Allergic reaction

Food allergy IgE mediated

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What are the symptoms?

Allergic symptoms can range from mild (causing discomfort), to life threatening. Common symptoms affect the face, skin, respiratory system and the gut. Symptoms affecting the face or skin include a runny or itchy nose, dry mouth, itchy eyes, sneezing, or a rash (itchy red skin or hives). In the windpipe and lungs allergies can cause wheezing and shortage of breath, and in the gut, symptoms such as abdominal discomfort, nausea, vomiting and diarrhoea may occur.

A severe allergic reaction is known as anaphylaxis, and can be life-threatening. Anaphylaxis causes closing of the throat and difficulty breathing. It may also result in a drop in blood pressure, abdominal pain and vomiting and unconsciousness. People experiencing anaphylaxis should be treated immediately.

Table 2 | Clinical features of IgE-mediated food allergy

Local oral & orbital	Dermatological	Gastrointestinal	Respiratory	Systemic
Itching of palate/lips	Acute urticaria	Nausea	Nasal itching	Hypotension
Swelling of lips/ tongue	Flushing	Abdominal pain	Rhinorrhoea & nasal obstruction	
Eye itching, redness and watering	Angioedema	Vomiting	Sneezing	
Periorbital oedema	Exacerbation of existing eczema	Diarrhoea	Laryngospasm	
	Morbiliform rash		Dyspnoea, wheeze	

Food allergy IgE mediated

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How common are food allergies?

The prevalence of food allergy varies between different ages. In infancy, 8-10% of the population have an allergy, which decreases to around 4% during childhood. By adulthood, only about 1-2% of adults suffer from a food allergy. It is worth noting that the percentage of people who think they are allergic (i.e. are self-diagnosed) is higher than the percentage of people who are actually diagnosed. This discrepancy highlights the need for accurate diagnosis to avoid unnecessary dietary restrictions and to provide reliable prevalence data.

Frequency of food allergies in adults and children

Food	Prevalence (%)
Young children	
Cow's milk	2.5
Egg	1.3
Peanut	0.8
Soy	0.4
Tree nut	0.2
Shellfish	0.1
Adults	
Shellfish	2
Peanut	0.6
Tree nut	0.5
Fish	0.4

Is it possible to develop or lose an allergy during your lifetime?

Most allergies begin in childhood, or as a teenager, but it is possible to develop an allergy at any point in your life. Childhood allergies can be outgrown later in life, but that is not common for late onset allergies. Mild allergic reactions may become more serious over time, so it is important to see a doctor even for mild reactions.

Food allergy IgE mediated

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Which are the most common allergy-causing foods?

Although many foods or groups of foods can trigger an allergic reaction, 14 of them have been identified as the most common or serious causes of food hyper-sensitivity in the EU. They are:

Celery
Gluten
Crustaceans
Egg
Fish
Lupin
Milk
Molluscs
Mustard
Peanut
Sesame seed
Soybean
Sulphur dioxide/sulphites
Tree nuts

Almost all the food allergens are proteins present in foods

Food allergy IgE mediated

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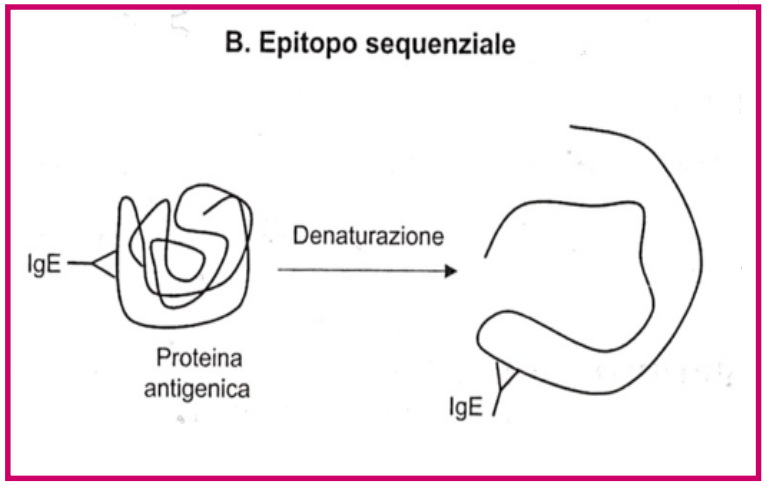
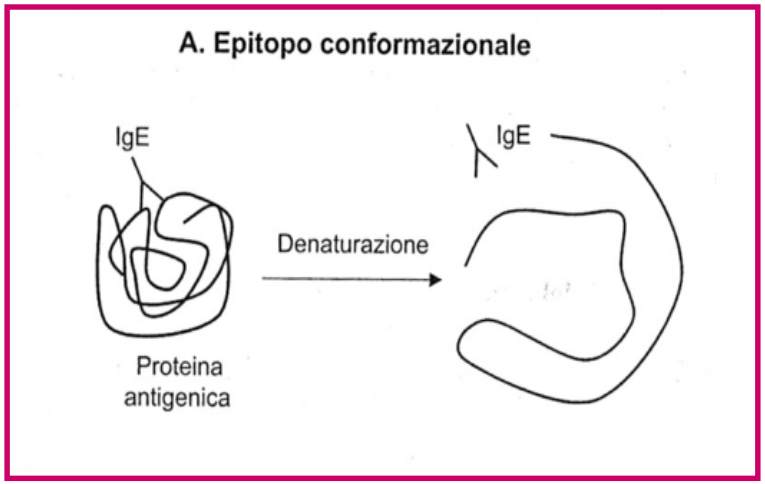
Epitopes?

Epitope is the portion of the protein (allergen) that binds specifically with the antibody

Two types of epitopes can be defined and they are differently susceptible to the foods treatments.



Neighborhood sequence of AA on the primary sequence of the protein. It resists to thermic denaturation, but it is sensitive to enzymatic attacks



Neighborhood sequence of AA in the space linked to the three-dimensionality of the protein. It is susceptible to thermic denaturation

Food allergy IgE mediated

Cross-reactivity

occurs when the proteins in one substance are like the proteins in another. As a result, the immune system sees them as the same. In the case of food allergies, cross-reactivity can occur between one food and another. Cross-reactivity can also happen between pollen and foods or latex and foods.

Because of cross-reactivity, testing and diagnosis of food allergies can be challenging. Since the immune system sees the similar proteins as the same, a positive skin test or blood test (serum IgE) can result for a food, yet the patient may be actually allergic to a substance that is cross-reactive to that food. However, the individual may or may not have any allergic symptoms from eating that food. The individual may not have allergic symptoms from a food that is cross-reactive with another food or pollen to which the individual is allergic. This is true even though they have a positive skin test or blood test to that food. This point cannot be emphasized enough. Many people end up avoiding foods because of a positive test and in some cases, they may have been eating that food before without any problems.

Cross-contact happens only through physical contact but it can happen with any allergen; *cross-reactivity* can happen without physical contact but it tends to happen in specific known patterns.

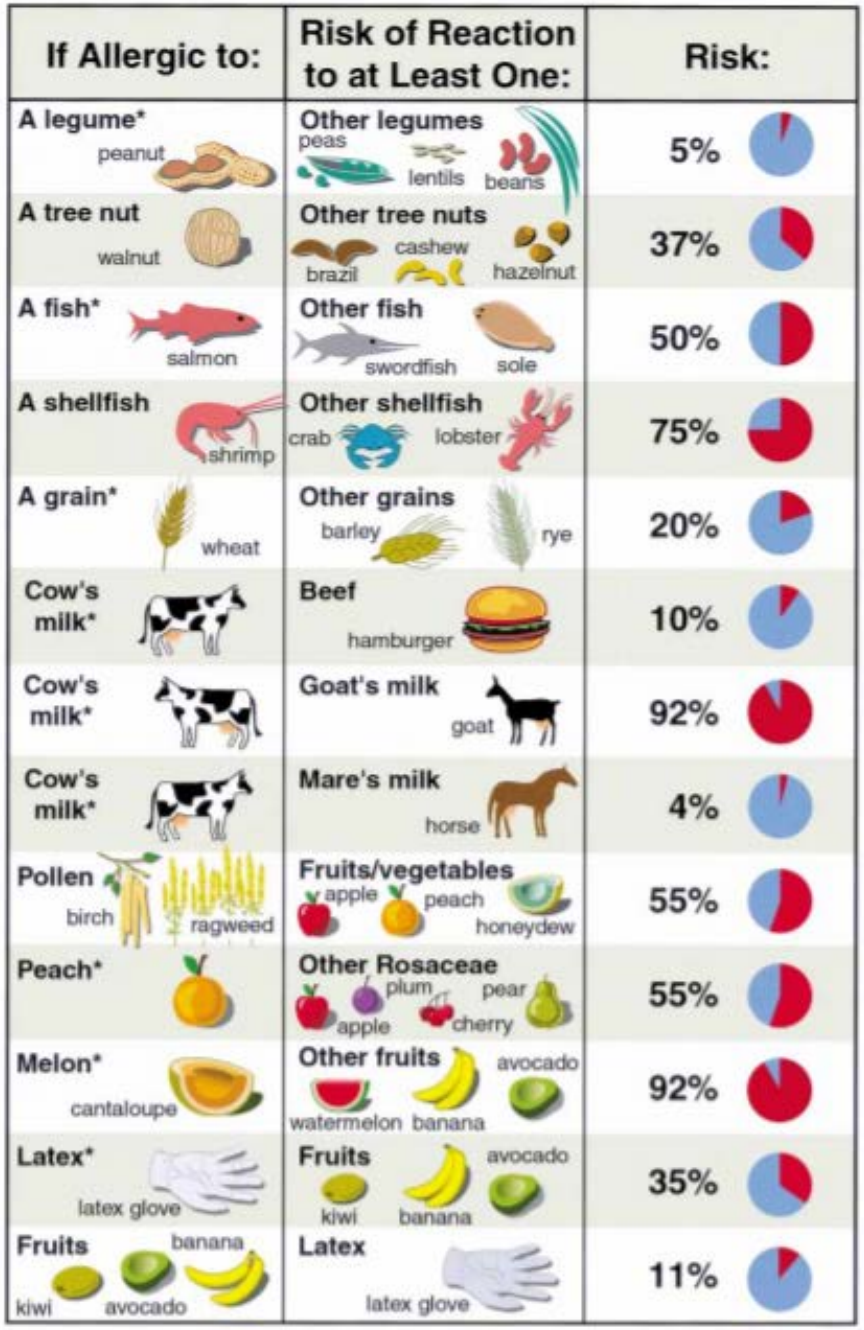


FIG 1. Approximate rate of clinical reactivity to at least 1 other related food. The probability of reacting to related foods varies, depending on numerous factors (see text). *Data derived from studies with DBPCFCs.

Food allergy non-IgE mediated

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Non-IgE-mediated food allergies

are reactions in which, following ingestion of one or more foods containing proteins to which the subject is sensitized, occurs an abnormal activation of the immune system, in which they seem to prevail Immunoglobulin production of classes A, G and M and processes mediated by lymphocytes T.

The pathophysiological mechanisms of non-IgE-mediated allergies, unlike those of the IgE-mediated, have not yet been fully defined. These are delayed reactions, of entity proportional to the amount of food introduced, which gives manifestations especially in the skin and in the gastrointestinal tract; in some cases it can be verify a symptomatology also affecting the respiratory tract (Heiner syndrome).

Gastrointestinale disorders	Diarrhea / constipation, bloating, irritable bowel syndrome (IBS), gastritis, reflux ...) Associated malabsorption and / or nutrient deficiencies
Skin symptoms	Eczema, psoriasis, rashes, keratosis pilaris, urticaria
Neurological symptoms	migraines, headaches, memory problems Chronic fatigue, mood swings and depression (in the context of the neuroendocrine immune system), ADHD, neuropathy
Respiratory disease	Chronic cough, wheezing / bronchoconstriction, sinusitis
Metabolic / endocrine / hormonal disorders	Obesity, diabetes, metabolic syndrome, inability to lose weight, weight loss, thyroid illness and diseases, infertility, irregular menstruation
Muscular-skeletal disorders	Stiff or sore joints, arthritis, tendonitis
Immune system and other favored comorbidities	Reduced immune status against viral infections, allergies, autoimmune diseases, heart problems, tumor

Food allergy IgE mediated

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How can I find out if I've got an allergy? Diagnosis

In the first phase of the diagnostic procedure, the patient must undergo a complete physical examination. After that, the specialist can take the medical history, paying particular attention to the type and frequency of symptoms, and trying to relate them to the consumption of certain foods. Subsequently, the following assessment methods can be used.

- Cutaneous tests are often in the form of skin prick tests, where the skin is pricked with a drop of the allergen on it, to see if IgE antibodies are produced (indicating an allergic reaction). Blood tests measure levels of specific IgE antibodies to suspected or known allergens. The likelihood of a clinical reaction increases with higher IgE levels.

- Food challenge tests involve the patient eating suspected allergic foods in gradually increasing amounts to see if allergic symptoms occur. These are always conducted under controlled conditions. Sometimes these tests take the form of double-blind placebo-controlled food challenge tests (DBPCFC).This is where neither the subject nor the investigator knows whether the food contains the allergen under investigation.

- In an elimination test, the suspected foods are removed from the diet. If allergic symptoms disappear, suspected foods are gradually reintroduced into the diet in very small quantities while the person is closely monitored for any symptoms. Once all the suspected foods have been checked out, foods causing problems can be avoided.

Food allergy IgE mediated

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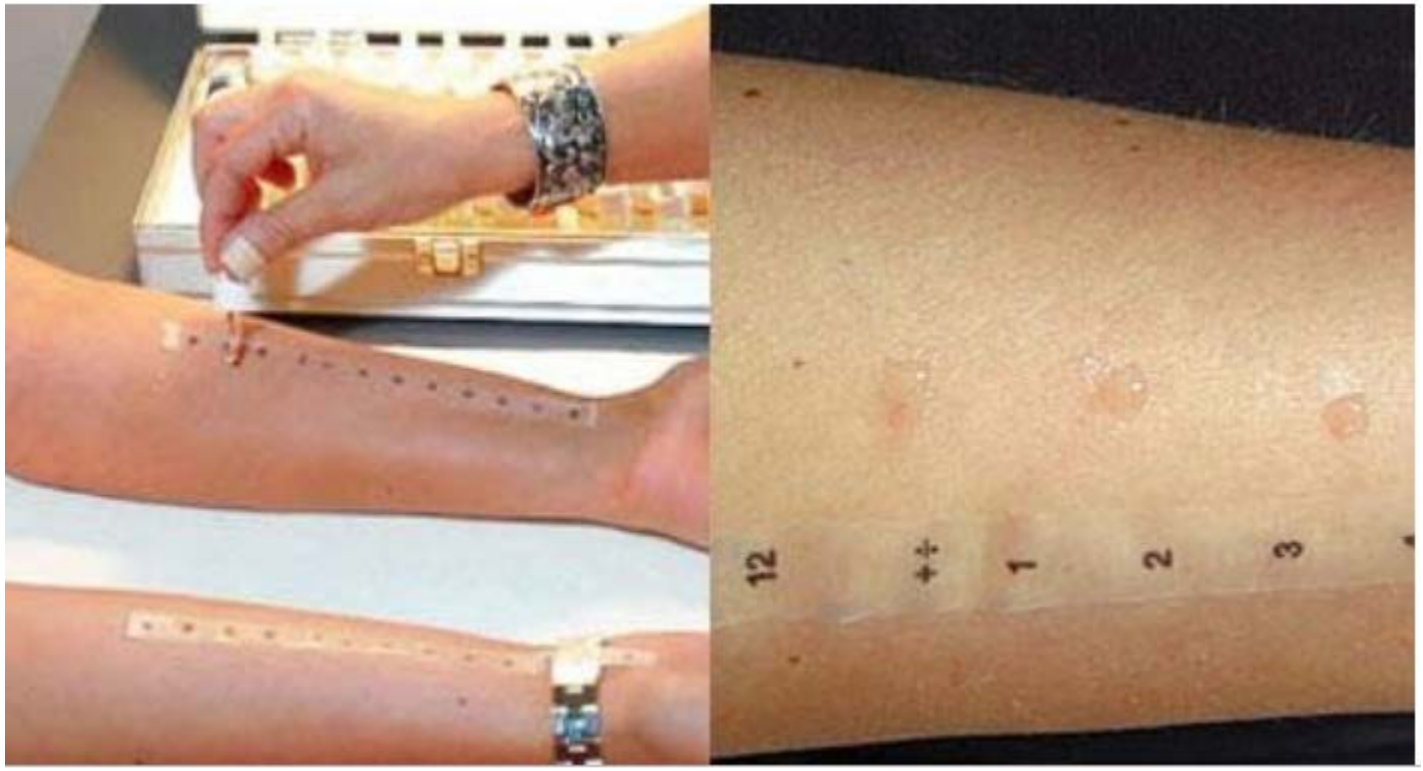
Skin prick test (+ Prick by prick Test)



Food allergy non-IgE mediated

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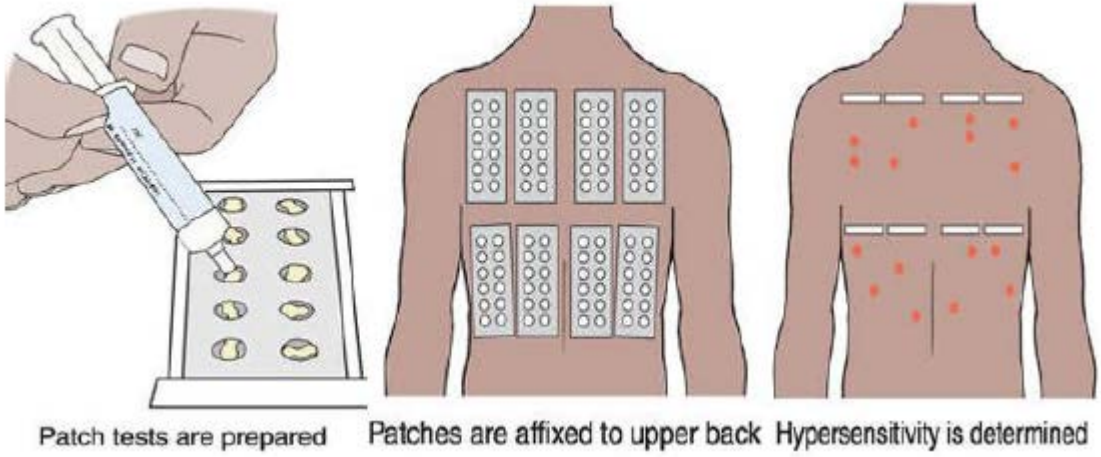
Patch test

validated diagnostic tests to detect non-IgEmediate food allergies are few. What gave the most encouraging results, especially in the dermatitis, in Heiner syndrome and in FPIES, was the patch test, which unlike of the skin prick test is useful in the diagnosis of delayed reactions. The patch test provides for the application on the patient's back of special plasters containing the suspected allergenic substances. These are plastic cells attached to a support, in which small quantities of the substances to be tested are inserted. Reading comes carried out after 48-72 hours. Possible systemic corticosteroid therapies a high dosages or for prolonged periods affect the development of the reaction



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Food allergy non-IgE mediated

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Table 4 | Unvalidated tests with no scientific evidence to support their use in the diagnosis of food intolerance

Test	Description
Allergen-specific IgG or IgG4	Serological testing for IgG or IgG4 against several foods can be performed by enzyme-linked immunosorbent assays and radioallergosorbent assays. The presence of IgG or IgG4 against foods represents exposure to that particular food and indicates immunological tolerance.[92] Therefore, increases in IgG or IgG4 concentration against food or food components are common and clinically irrelevant. However, these commercially available tests are widely available and may lead to inappropriate dietary over-restriction.
Cytotoxic assays	Cytotoxic food testing involves the addition of whole blood to a food extract and is based on the assumption that leucocytes reacting to food antigen exposure can predict intolerance to food. However, the test is not reproducible and positive cytotoxic effects are frequently obtained with foods that produce no clinical symptoms while negative results are obtained with foods that do produce clinical symptoms.[93, 94]
Electrodermal test	A galvanometer is used to measure skin conductivity. The patient holds a negative electrode in one hand and a positive electrode is placed on specific acupressure points. Food extracts in sealed glass vials are put in contact with an aluminium plate within the circuit. Food intolerance is diagnosed when there is a drop in electrical conductivity of the skin. No studies have demonstrated its usefulness to detect food intolerance.[94]
Hair analysis	Bio-resonance analysis of hair based on the belief that anything living emits electromagnetic waves that can be measured as good or bad. However, there is no explanation of how hair analysis might detect food intolerance.[95]
Iridology	Iridology involves the analysis of the iris assuming that all organs are represented in the iris and any irregularities in pigmentation represent dysfunction. There is no scientific evidence to support the use of iridology in the diagnosis of food intolerance.[96]
Kinesiology	The patient holds a sealed glass bottle that contains a test food or food extract while an investigator estimates muscle strength in the other arm. A decrease in muscle power while the food is held is considered to indicate food intolerance. Another method of kinesiology called DRIA measures a change in muscle strength in response to a food extract being placed under the tongue.[93] These tests have no scientific support and have not been validated.
Pulse test	This may be used in combination with provocation-neutralisation or independently. A 16 beats per min change in the pulse rate from baseline indicates food intolerance following sublingual or intradermal exposure to the specific food extract. There is no clinical evidence to support the use of this test.[94]
Sublingual or intradermal provocation-neutralisation	Aqueous food extract is placed under the tongue or intradermally and observed for symptoms to occur (usually 10 min). If symptoms occur, a neutralising dose (diluted dose of the same food extract) is given in the same way. Symptoms are expected to disappear in about the same time period. Adverse outcomes are rare but these tests have failed to show any usefulness in food intolerance.[94]

Food allergy IgE and non-IgE mediated

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Is there a cure?

There is currently no cure for food allergies. The condition must be managed by the susceptible individual's careful avoidance of the allergen-containing food. However, research is being undertaken to try and prevent the initial sensitisation stage in an allergic reaction.

The substantial difference between those who are "truly allergic" and those who are intolerant is one:

- in the IgE mediated, the offending food must necessarily be eliminated from one's diet and often also from the surrounding environment;
- in the non-IgEmediated, the mere fact of reducing portions and resorting to occasional consumption may suffice to avoid the onset of symptoms.

The best way to prevent symptoms is to carefully read the labels of all packaged products, find out about ingredients and cooking methods when eating away from home, and explain the particular needs to your guests or restaurateur.

Food allergy IgE and non-IgE mediated

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How do we know if a food contains an allergen?

To alert consumers to the presence of allergens in food products, food companies use allergen labels. There are two types of allergen labels: mandatory and precautionary.

Mandatory labels: A compulsory label to alert consumers to the presence of allergenic ingredients. Under EU law, the fourteen allergens listed above must be declared on the label of the foodstuff if they are used as an ingredient (including those carried over in processing aids, additives and solvents).

Precautionary labels: If a priority allergen is not used as an ingredient, but there is a chance that the allergen may be present (through cross contamination), food companies often choose to use a voluntary precautionary label, for example 'may contain X', or 'created in a factory that handles X'.

What are the problems with the current labelling system?

Precautionary labels are entirely voluntary and policies of different companies vary regarding both the level of risk required to warrant a label, and how to express or phrase that risk on the label. This can result in confusion for consumers, as the exact level of risk to them posed by that product is unclear.

As technology has advanced to detect lower traces of allergen, companies have been using precautionary labels more frequently, resulting in a limited choice of foods for allergic consumers. This can lead to a lower quality of life and a potential nutritional deficiency. Furthermore, consumer frustration with reduced food options may result in disregard of the precautionary labels and risk-taking behaviour.

Gluten disorders

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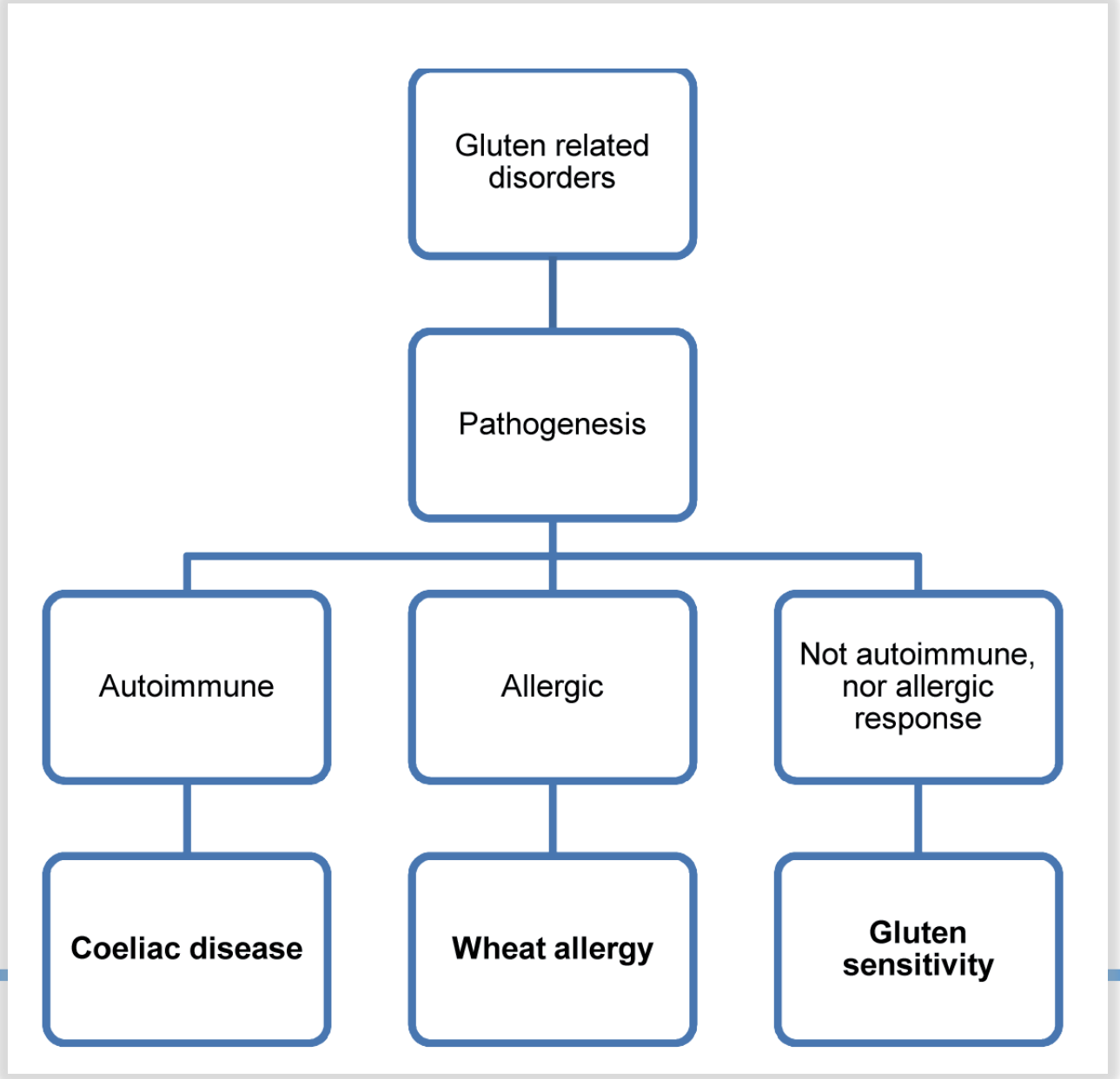

Coeliac diseases

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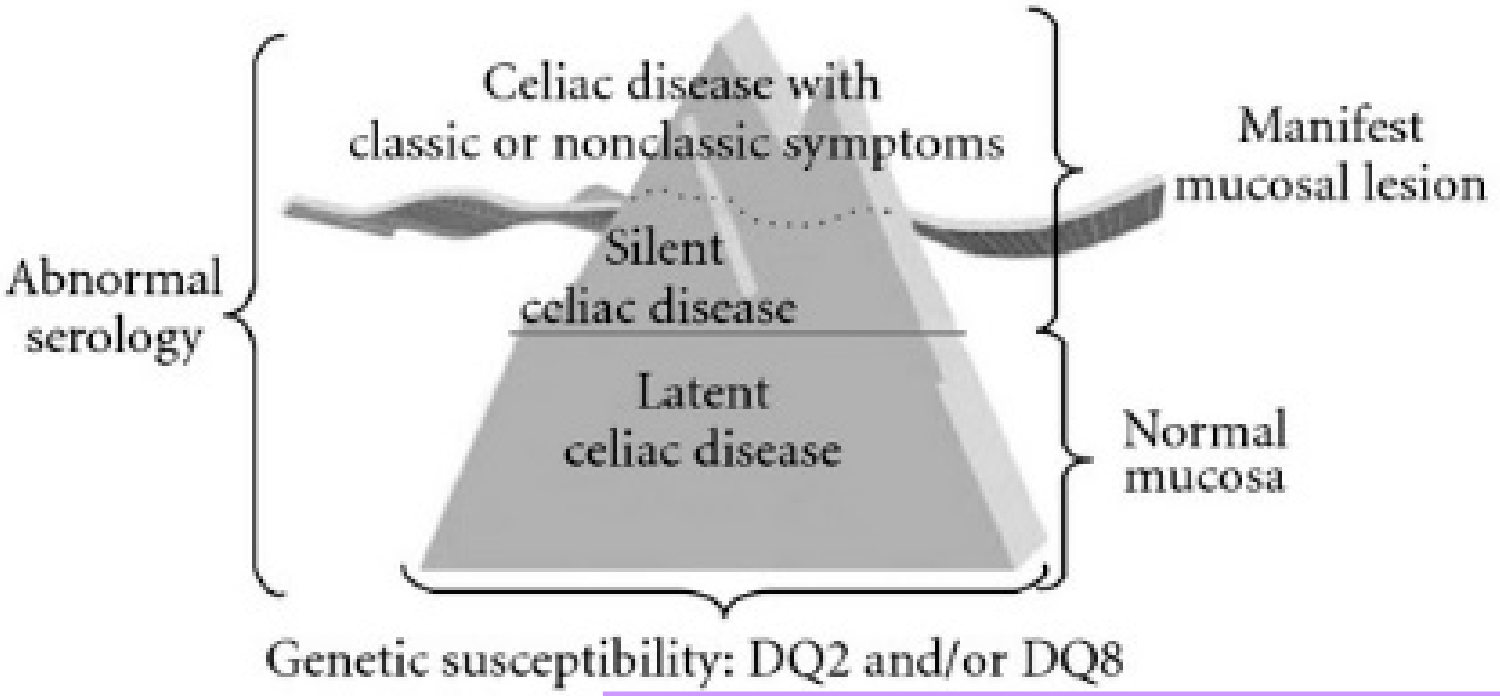
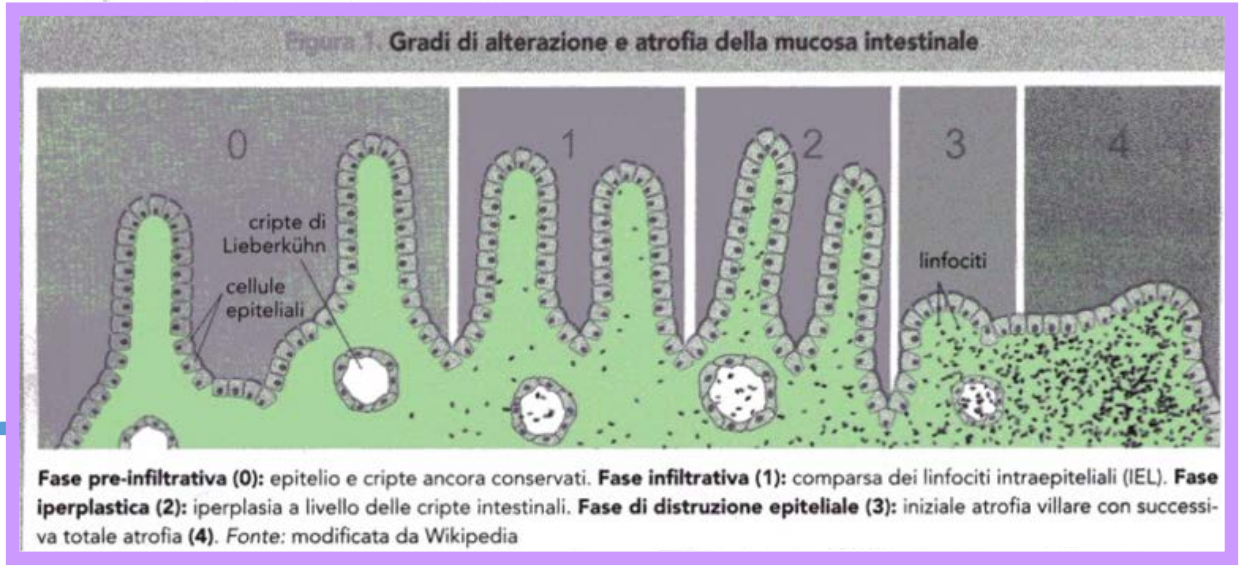
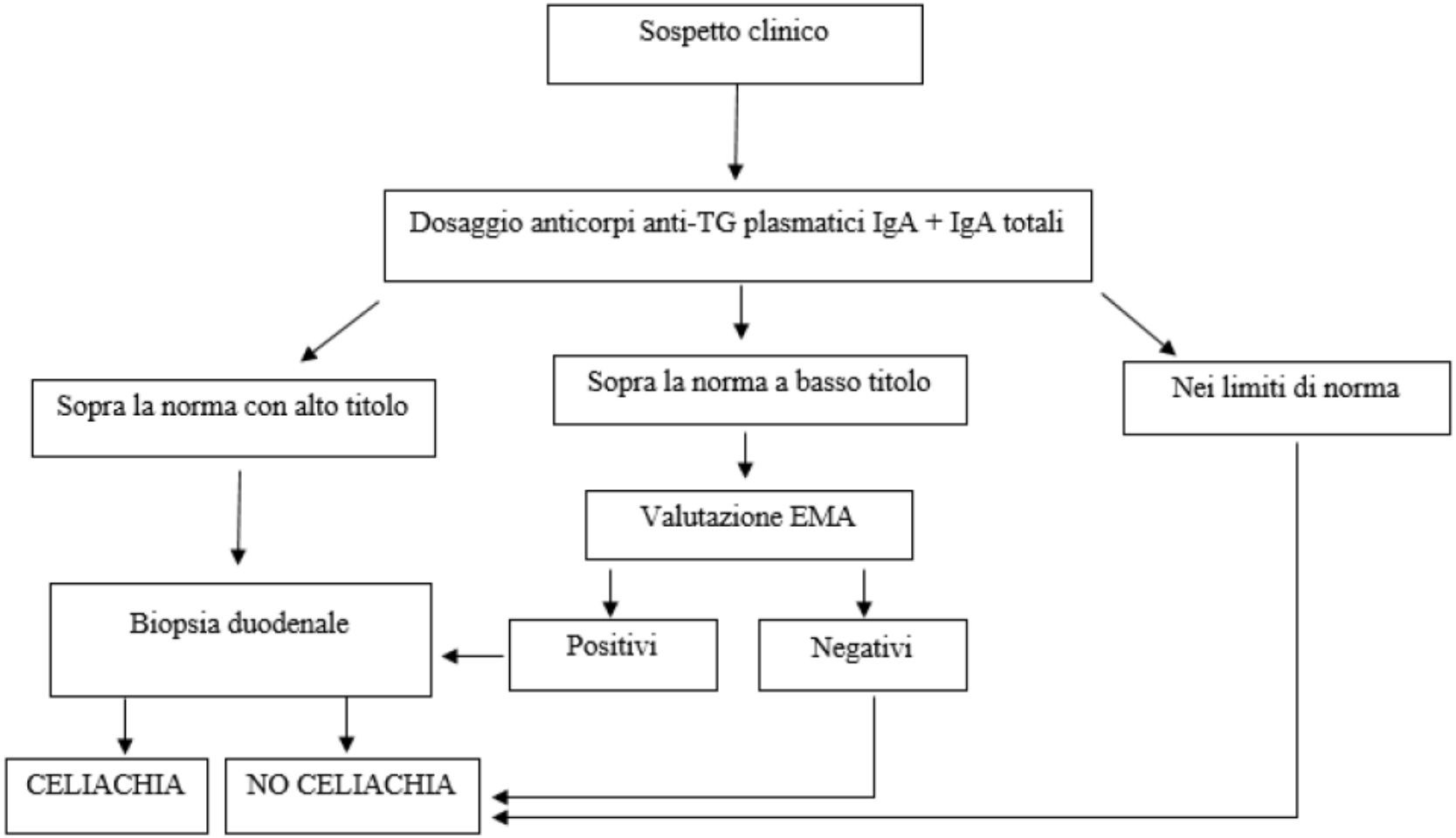




Fase pre-infiltrativa (0): epitelio e cripte ancora conservati. **Fase infiltrativa (1):** comparsa dei linfociti intraepiteliali (IEL). **Fase iperplastica (2):** iperplasia a livello delle cripte intestinali. **Fase di distruzione epiteliale (3):** iniziale atrofia villare con successiva totale atrofia **(4)**. *Fonte:* modificata da Wikipedia

Coeliac diseases- Diagnosis

U11



Coeliac diseases and gluten

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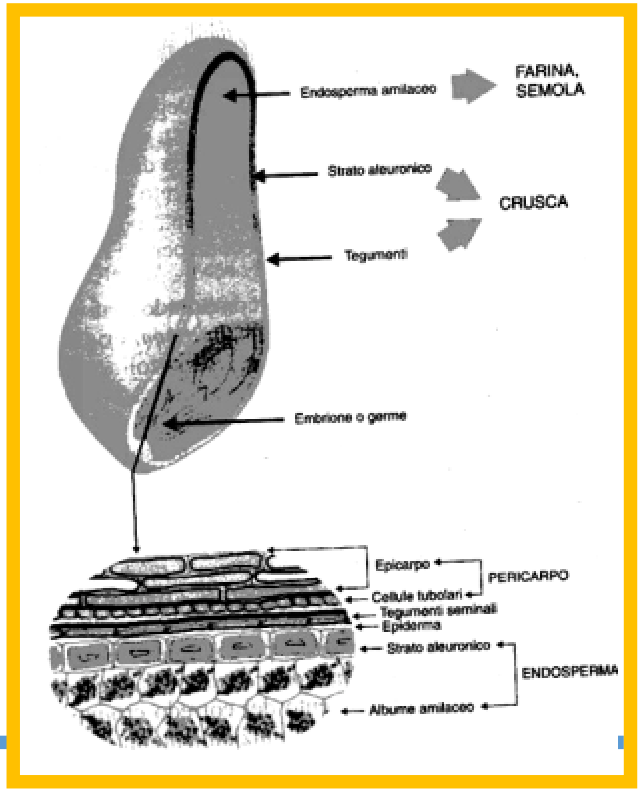
Gluten is a group of proteins, called prolamins and glutelins, which occur with starch in the endosperm of various cereal grains. This protein complex comprises 75–85% of the total protein in bread wheat
It is found in related wheat species and hybrids, such as spelt, kamut, and triticale; barley, rye, and oats as well as products derived from these grains such as breads and malts. Glutens, especially Triticeae glutens, have unique viscoelastic and adhesive properties, which give dough its elasticity, helping it rise and keep its shape and often leaving the final product with a chewy texture. These properties and its relative low cost are the reasons why gluten is so widely demanded by the food industry and for non-food uses.

The prolamines (75-95%) located in the endosperm, are composed of gliadins and glutenins, these proteins are characterized by cysteine, proline and glutamic acid, limiting AA are lysine and methionine.

In contact with water the gliadins and glutenins are joined by hydrogen bonds, disulfide bridges and ionic bonds forming gluten, a fundamental substance for bread making and pasta making.

Cereals banished in gluten disorders are any type of wheat (including flour, semolina and durum), barley, rye, bulgur, Kamut, malt, spelt, couscous

Admitted cereals and derived products are
Brown, wild or white rice, Pasta made from rice, corn, amaranth, quinoa or pure buckwheat, Corn, Quinoa, Millet, Sorghum, Legumes, chest nut



Coeliac diseases and gluten

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In celiac patient exposure to even only a small amount of gluten can lead to malabsorption of some important nutrients including calcium, iron, folic acid, and fat-soluble vitamins because of small-intestine inflammation. A strictly followed gluten-free (GF) diet throughout the patient's lifetime is the only effective treatment for celiac disease; however, elimination of gluten from cereal-based product leads to many technological and nutritional problems.

While a limited amount of gluten is permitted in a celiac patient's diet, the amount of tolerable gluten varies widely between 10 mg and 34–36 mg gluten per day. This has led to confusion about labeling "GF" products. For example, in Canada, such products must meet standards of <20 ppm gluten (20 mg gluten/1 kg), whereas other countries specify a maximum of 200 ppm. However, producing food that provides a daily gluten intake of <10 mg is acceptable. Omitting or reducing gluten lowers the quality of end products; this could be overcome with gluten substitutes.

PRODOTTI COMMERCIALI

20 ppm gluten residue

FARINE
Per pane, pizza, dolci, pasta devono avere:

Miscela di base: riso, mais, miglio, sorgo, amido di mais,patata,tapioca, fecola di patate, farina di soia glucosio,saccarosio, sciroppo di glucosio, latte scremato o siero di latte, proteine isolate della soia e o di altri legumi

Addensanti: farine di guar, semi di carrube, addensanti e/o stabilizzanti chimici, idrocolloidi

Coeliac diseases and gluten

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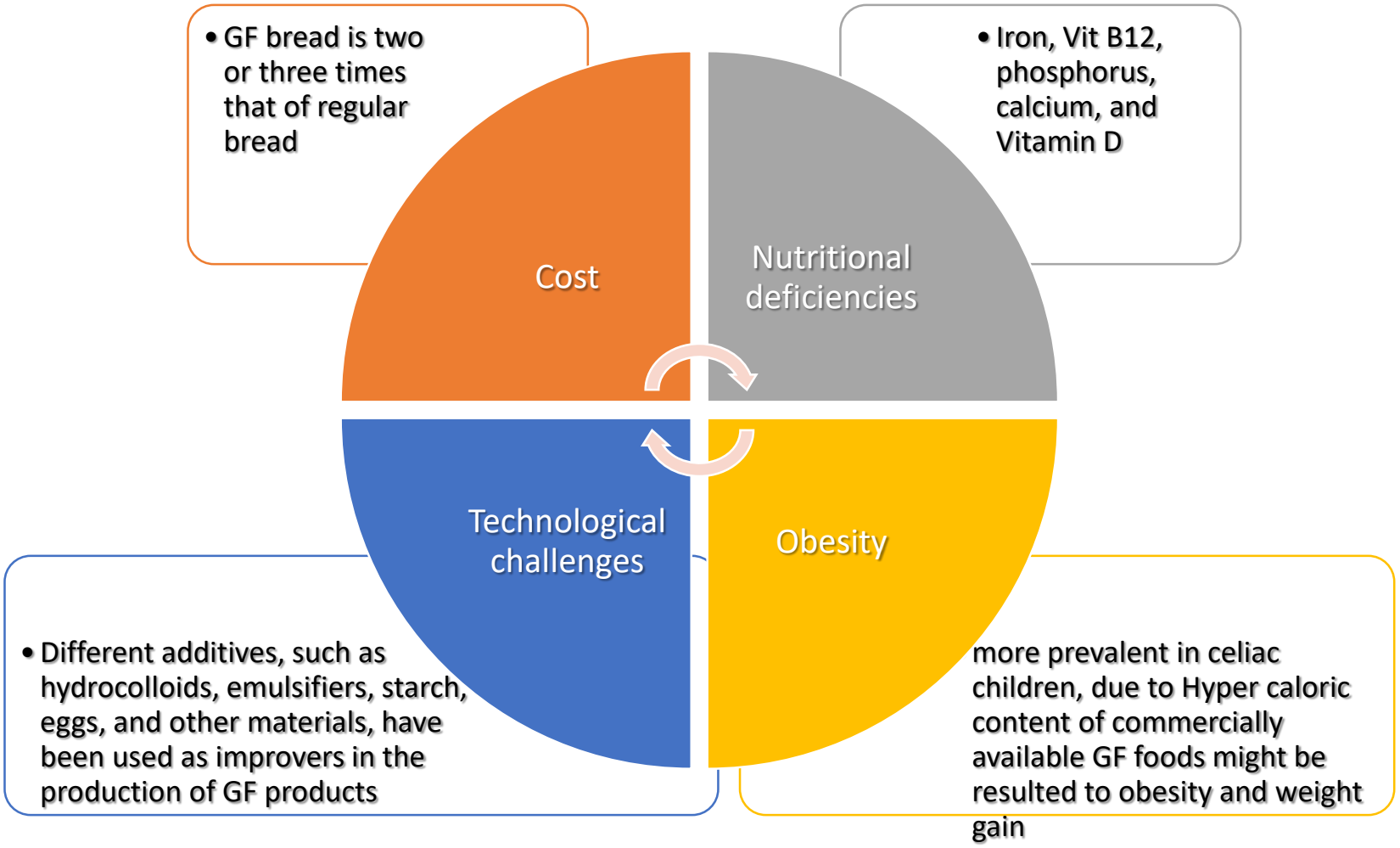

Tabella 3.9 : Confronto delle etichette dei prodotti gluten-free e di quelli tradizionali.

Contenente glutine	Gluten-free
Pasta	
1-Ingredienti: semola di grano duro,acqua **2-Ingredienti**: semola di grano duro,acqua	**1-Ingredienti**: farina di riso, farina di mais, acqua, proteine isolate di pisello, emulsionante (E471) **2-Ingredienti**: farina di mais, farina di grano saraceno, farina di riso, acqua
Base per pizza / pane (confezionato)	
Ingredienti: Farina di frumento, acqua, latte intero in polvere, sale, lievito di birra, margarina vegetale, lecitina di soia, amido modificato.	**Ingredienti:** Amido di mais, acqua, farina di riso, fecola di patate, lievito, addensante (farina di guar), emulsionante (E471), proteine del latte, sale, acidificanti
Biscotto frollino	
Ingredienti: Farina di frumento, zucchero, grassi vegetali, uova, amido di frumento, agenti lievitanti, sciroppo di saccarosio invertito, latte in polvere, sale, aromi, lecitina di soya.	**Ingredienti**: Farina di mais, amido di mais, farina di amaranto 20%, zucchero, margarina vegetale, lecitina di soya, proteine dell'uovo, miele, uova, lievito, sale, aromi, emulsionante (E471, E475)

(Fonti: Ingredienti Barilla, Mulino bianco, Schar,ds4you, BiAglut)

Le funzioni principali degli isolati proteici possono essere quindi riassunte in quattro punti:

1. **Buone proprietà emulsionanti**, schiumogene e grande stabilità in un ampio range di pH (da 3 a 9)
2. **Proprietà gelificanti e viscosizzanti** tali da poter sostituire l'uso degli idrocolloidi, modificando in modo naturale le proprietà tecnologiche dell'impasto
3. **Buona solubilità ed idratabilità**. Le proteine sono molto idrosolubili, inoltre trattenendo l'acqua permettono di mantenere nell'impasto il giusto grado di umidità
4. **Capacità di imbrunimento** (tipico delle proteine del latte e dell'uovo), che permette durante la cottura di produrre il richiesto aspetto "dorato" tipico nei prodotti da forno

Un continuativo ed eccessivo consumo di questi alimenti può modificare i rapporti tra i nutrienti, portando ad una condizione in un certo senso sfavorevole sotto il profilo metabolico. Se infatti prima della diagnosi e dell'inizio della dieta aglutinata la patologia intestinale limitava l'assorbimento dei nutrienti e rendeva ragione di una tendenza al calo ponderale, la correzione dell'alterazione intestinale attraverso l'utilizzo degli alimenti dietoterapeutici, porta ad un ripristino dell'assorbimento intestinale, sia di tutti quei nutrienti essenziali per il benessere dell'organismo che, in larga misura anche dei grassi, costituenti questi alimenti particolari. **Si stima infatti che il 15% dei soggetti celiaci che non seguono una dieta variata secondo la piramide alimentare, sviluppino dopo alcuni anni di dietoterapia alterazioni metaboliche a livello lipidico e/o glucidico**.

Coeliac diseases and gluten

U11

Regulation (EU) No 828/2014

Article 3 Information to consumers

1. Where statements are used to provide information to consumers on the absence or reduced presence of gluten in food, such information shall be given only through the statements and in accordance with the conditions set out in the Annex.

2. The food information referred to in paragraph 1 may be accompanied by the statements 'suitable for people intolerant to gluten' or 'suitable for coeliacs'.

3. The food information referred to in paragraph 1 may be accompanied by the statements 'specifically formulated for people intolerant to gluten' or 'specifically formulated for coeliacs' if the food is specially produced, prepared and/or processed to:

(a) reduce the gluten content of one or more gluten-containing ingredients; or
(b) substitute the gluten-containing ingredients with other ingredients naturally free of gluten.

Decreto 17 maggio 2016 Modifiche all'art. 1 del D.M. 8 giugno 2001

1. Il comma 1 dell'art. 1 del decreto e' sostituito dal seguente:

«1. Rientra nei livelli essenziali di assistenza sanitaria l'erogazione dei prodotti alimentari di seguito elencati:

a) alimenti a fini medici speciali per persone affette da malattie metaboliche congenite;

b) alimenti a fini medici speciali per persone affette da fibrosi cistica o malattia fibrocistica del pancreas o mucoviscidosi,

c) alimenti con dicitura «senza glutine, specificatamente formulati per celiaci» o «senza glutine, specificatamente formulati per persone intolleranti al glutine» per persone affette da morbo celiaco, compresa la variante clinica della dermatite erpetiforme

Food intolerance

U11

Food intolerances are adverse reactions that occur later ingestion of one or more foods, in which is not involved immune. The main causes are: the defect of transport mechanisms or systems enzyme; gluten sensitivity, which is not attributable to either celiac disease or to wheat allergy; the pharmacological type reactions, which can develop into following the ingestion of foods containing potentially pharmacological active substances. Non-immunological adverse reactions occurring in following the ingestion of food, which are not part of any of the previous mechanisms and for which the causes are unknown, they are called food intolerances indefinite or idiosyncratic.

Food group	Food	Percentage of subjects reporting symptoms
Cereal products	Wheat bread	4.8–34.8
Vegetables	Cabbage	9.6–57
	Onion	8.9–56
	Peas/beans	21.4–46
Dairy products	Milk	4.4–41.7
Miscellaneous	Hot spices	25.9–45
	Fatty/deep fried	13.3–44
Drinks	Coffee	26.2–39

Lactose intolerance

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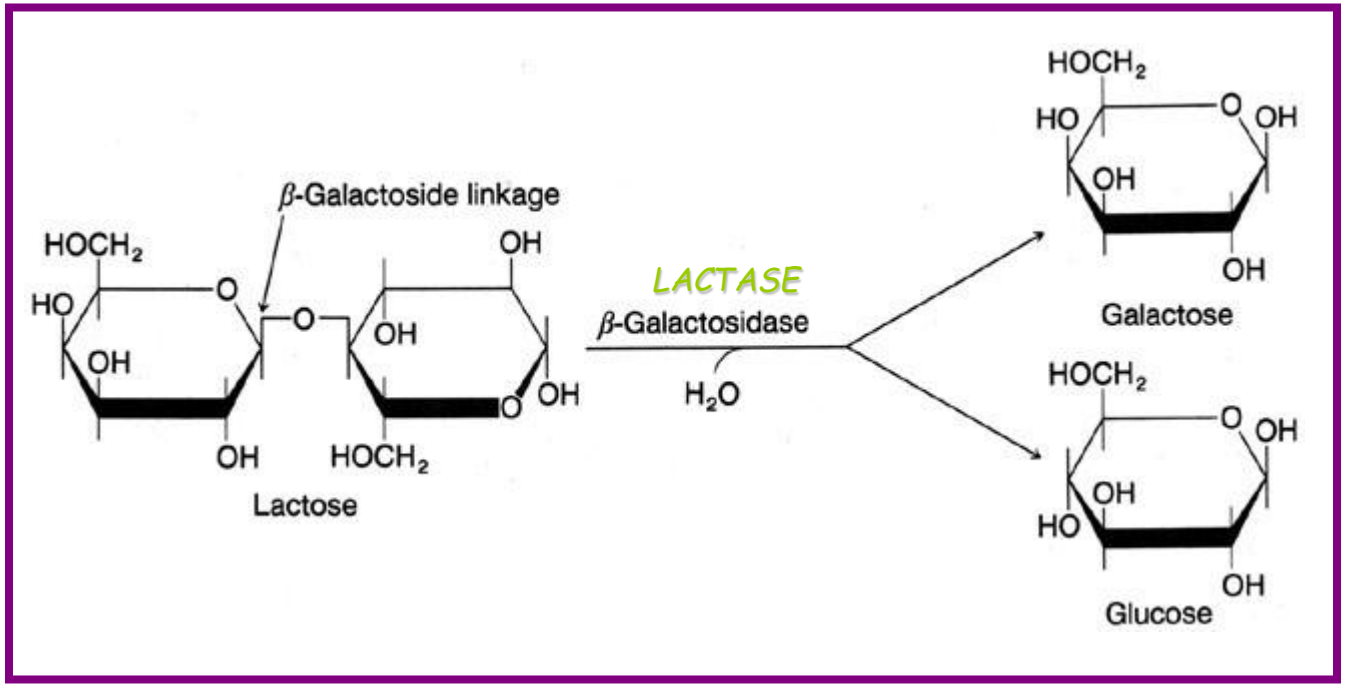


People with lactose intolerance are unable to fully digest the sugar (lactose) in milk. As a result, they have diarrhea, gas and bloating after eating or drinking dairy products. The condition, which is also called lactose malabsorption, is usually harmless, but its symptoms can be uncomfortable.

Lactose intolerance

U11

Primary lactose intolerance

This is the most common type of lactose intolerance. People who develop primary lactose intolerance start life producing plenty of lactase — a necessity for infants, who get all their nutrition from milk. As children replace milk with other foods, their lactase production normally decreases, but remains high enough to digest the amount of dairy in a typical adult diet.

In primary lactose intolerance, lactase production falls off sharply, making milk products difficult to digest by adulthood. Primary lactose intolerance is genetically determined, occurring in a large proportion of people with African, Asian or Hispanic ancestry. The condition is also common among those of Mediterranean or Southern European descent.

Secondary lactose intolerance

This form of lactose intolerance occurs when your small intestine decreases lactase production after an illness, injury or surgery involving your small intestine. Among the diseases associated with secondary lactose intolerance are celiac disease, bacterial overgrowth and Crohn's disease. Treatment of the underlying disorder may restore lactase levels and improve signs and symptoms, though it can take time.

Congenital or developmental lactose intolerance

It's possible, but rare, for babies to be born with lactose intolerance caused by a complete absence of lactase activity. This disorder is passed from generation to generation in a pattern of inheritance called autosomal recessive, meaning that both the mother and the father must pass on the same gene variant for a child to be affected. Premature infants may also have lactose intolerance because of an insufficient lactase level.

Lactose intolerance

U11

Risk factors

Factors that can make you or your child more prone to lactose intolerance include:

- Increasing age. Lactose intolerance usually appears in adulthood. The condition is uncommon in babies and young children.
- Ethnicity. Lactose intolerance is most common in people of African, Asian, Hispanic and American Indian descent.
- Premature birth. Infants born prematurely may have reduced levels of lactase because the small intestine doesn't develop lactase-producing cells until late in the third trimester.
- Diseases affecting the small intestine. Small intestine problems that can cause lactose intolerance include bacterial overgrowth, celiac disease and Crohn's disease.
- Certain cancer treatments. If you have received radiation therapy for cancer in your abdomen or have intestinal complications from chemotherapy, you have an increased risk of lactose intolerance.

The signs and symptoms of lactose intolerance usually begin 30 minutes to two hours after eating or drinking foods that contain lactose. Common signs and symptoms include:

Diarrhea
Nausea, and sometimes, vomiting
Abdominal cramps
Bloating
Gas

Lactose intolerance

U11

Complications of lactose intolerance

Milk and other dairy products contain calcium, protein and vitamins, such as A, B12 and D. Lactose also helps your body absorb a number of other minerals, such as magnesium and zinc.
These vitamins and minerals are important for the development of strong, healthy bones. If you're lactose intolerant, getting the right amount of important vitamins and minerals can prove difficult.

This may lead to unhealthy weight loss and put you at increased risk of developing the following conditions:
osteopenia – where you have a very low bone-mineral density; left untreated, it can develop into osteoporosis
osteoporosis – where your bones become thin and weak, and your risk of breaking a bone is increased
malnutrition – when the food you eat does not give you the nutrients essential for a healthy functioning body; this means wounds can take longer to heal and you may start to feel tired or depressed

Lactose intolerance

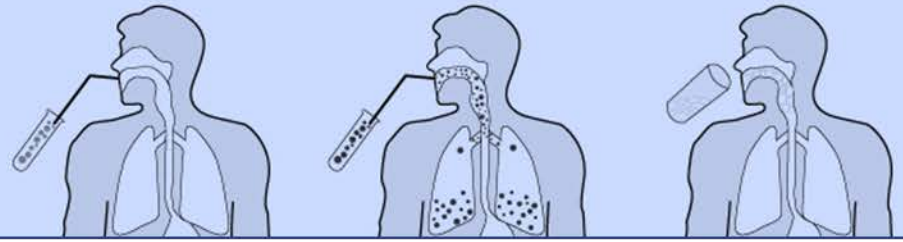
Diagnosis

- Analisi del pH fecale (Stool Acidity Test)
- Test di Tolleranza al Lattosio (Lactose Tolerance Test)
- **Test del respiro al Lattosio (Lactose Breath Test)**
- Tempo di Transito Orocecale al Lattosio (Oro-Cecal Transit Time Lactose Test)
- **Analisi Polimorfismi Gene LCT (Congenital Lactose Deficiency)**

Come si esegue il breath test?

I test del respiro sono sicuri e semplici da eseguire. Bastano 3 passi:

1. Raccogliere l'espirato (campione - BASE)
2. Assumere il pasto del test (liquido o solido)
3. Raccogliere l'espirato ad intervalli regolari (campioni - POST)



Test genetico

Lactease® DNA

Dal campione di saliva che ci hai inviato abbiamo effettuato l'analisi del tuo gene lattasi. Tutte le considerazioni relative all'intolleranza al lattosio riportate di seguito sono state elaborate dall'interpretazione del tuo profilo genetico per il gene lattasi.

Risultato genetico

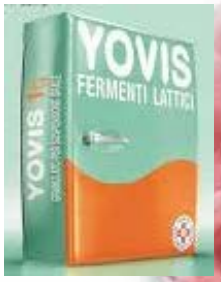
- *Forma gene LATTASI:* ***non ottimale***
- *Predisposizione:* ***intolleranza al lattosio***

La dimostrazione di malassorbimento di lattosio non indica necessariamente che un soggetto avrà i sintomi.

Alimenti con lattosio

Alimenti senza lattosio

Fonti nascoste di lattosio



Lactose intolerance

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Paese	“Senza lattosio” g/100 g	“Basso contenuto di lattosio” g/100 g
Danimarca	0.01 g/100 g	1 g/100 g
Estonia	0.01 g/100 g	1 g/100 g
Finlandia	0,01 g/100 g	1 g/100 g
Norvegia	0,01 g/100 g	1 g/100 g
Svezia	0,01 g/100 g	1 g/100 g
Germania	0,1 g/100 g	Non definito
Slovenia	0,1 g/100 g	Non definito
Ungheria	0,1 g/100 g	Non definito
Irlanda	Assenza totale	1 g/100 g

Anche in farmacia sono presenti prodotti formulati per soggetti intolleranti, quindi privi di lattosio.

Lactose intolerance

U11

INTEGRATORI di LATTASI

β-galattosidasi da

Aspergillus oryzae,

Aspergillus niger,

Kluyveromyces lactis

INTEGRATORI di PROBIOTICI

Lactobacilli,

Bifidobatteri,

Streptococchi

INTEGRATORI COMBINATI

Lattasi,

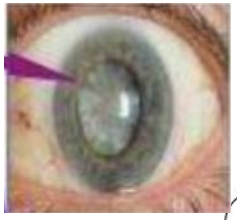
Enzimi digestivi,

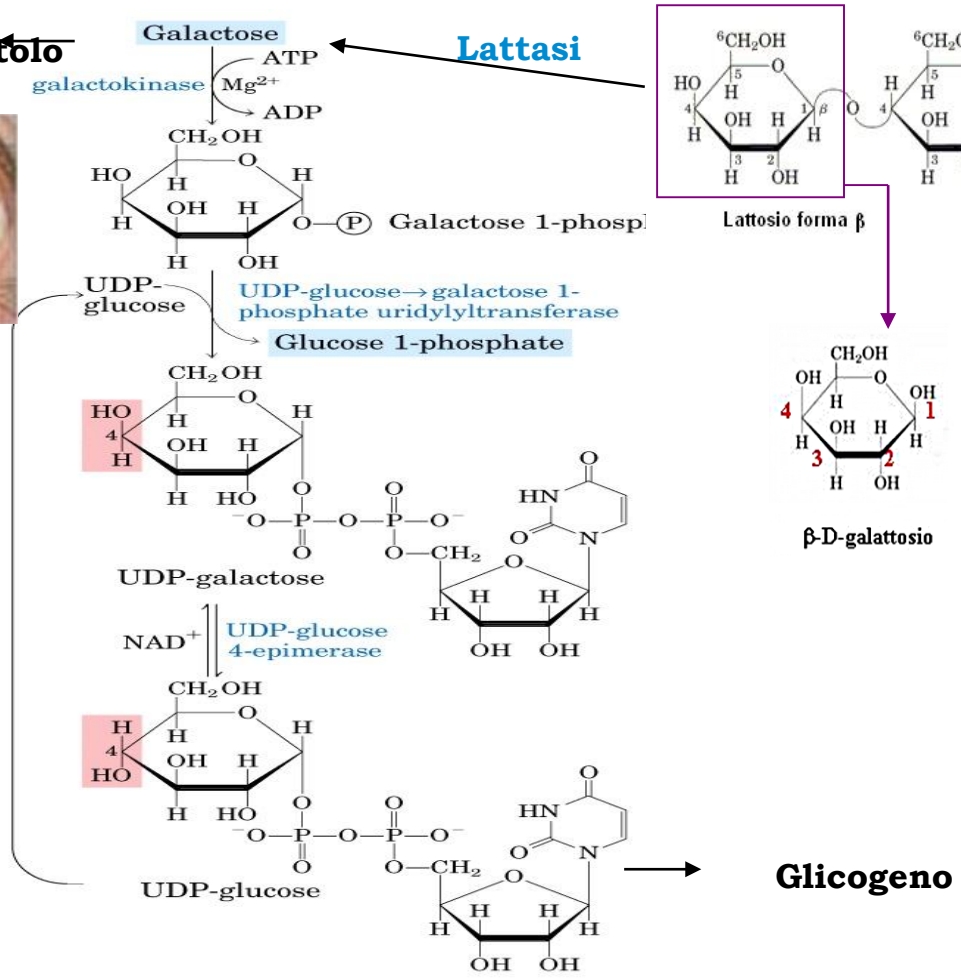
Probiotici,

Botanicals,

Metabolic carbohydrates desease Galactosemia

U11





Classic galactosemia is an autosomal recessive disorder of carbohydrate metabolism , due to a severe deficiency of the enzyme, galactose-1-phosphate uridyltransferase

- Intellectual disability
- Hepatomegaly
- Hepatic failure
- Renal failure
- Cataract
- Premature ovarian failure
- Dysmetria
- Ataxia

Metabolic carbohydrates desease Galactosemia

U11

Treatment of galactosemia in the newborn.

1) Eliminate lactose-containing formula and breastfeeding (use soy-based or elemental formula with no lactose).
2) Monitor for signs of sepsis.
3) Monitor for signs of coagulopathy (consider fresh frozen plasma).

Table 4
Long-term complications in GALT deficiency.

Speech defect	Hypergonadotropic hypogonadism or POI in females
Cognitive deficits	Reduced bone mineral density
Learning problems	Growth disturbance
Cataracts	Cerebellar ataxia/tremor/dystonia

Categoria merceologica	Alimenti permessi	Alimenti vietati
Latte e derivati	Prodotti specifici Latti di soia	Latte materno Latte di tutti i mammiferi Latti modificati per lattanti Panna, burro, margarine miste Formaggi Yogurt Gelati e sorbetti
Frutta	Frutta e verdura fresca con attenzione a quella contenente più di 10 mg galattosio/100 g (vedi colonna a fianco) Frutta secca Frutta e verdura in scatola purché si faccia attenzione all'eventuale aggiunta di lattosio o latte	Ananas Anguria Datteri Mirtilli Papaia Pomodori
Prodotti animali	Tutte le carni Uova	
Cereali e derivati	Tutti i cereali e derivati purché si faccia attenzione all'eventuale aggiunta di lattosio o latte	
Grassi	Tutti gli oli vegetali	

Problema dietetico nel neonato

⇨Idrolisati proteici privi di lattosio

⇨Formule a base di soia

⇨Formule specifiche con tenori di zuccheri <0.01g/100mL

La legislazione italiana prevede aiuti economici per i soggetti portatori di patologie metaboliche ereditarie:

Varianti a seconda della regione
Soggetti con diagnosi accertata presso enti autorizzati
Fabbisogno non superiore ai 30 gg
I prodotti dietetici ascrivibili sono i latti in polvere

Hereditary fructose intolerance

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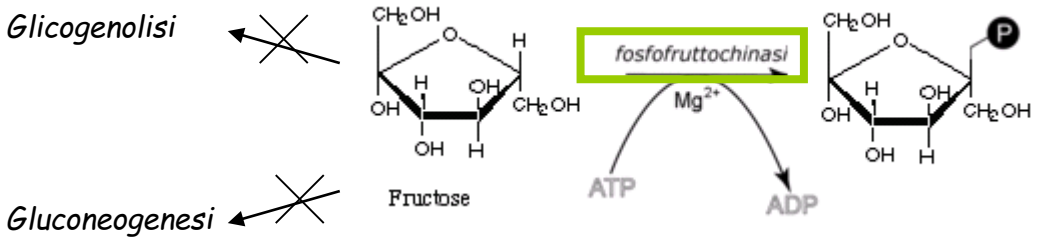
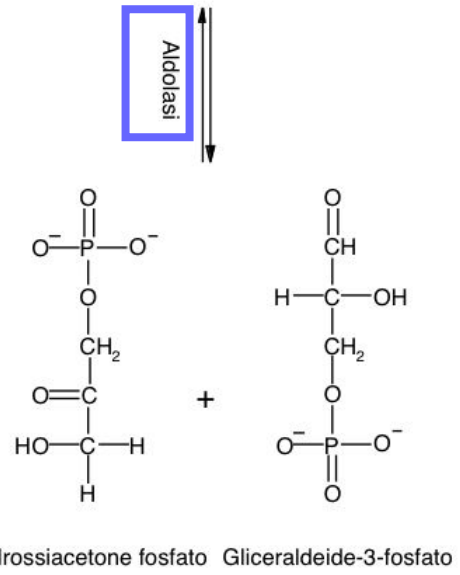


Nel fegato



- FRUTTOSEMIA
- INTOLLERANZA EREDITARIA AL FRUTTOSIO

Fructose is found mainly in honey, in all fruit, in raw vegetables, in tomatoes, however the "hidden" sources are very numerous. All sweets, drinks and baby food can contain traces. Many canned products, such as sauces, breakfast cereals, salad dressings, contain added sugars used by food industries to obtain a more pleasant taste and improve preservation.

Hereditary fructose intolerance

Symptoms include severe abdominal pain, vomiting, and hypoglycemia following ingestion of fructose or other sugars metabolized through fructose-1-phosphate.

Prolonged fructose ingestion in infants leads ultimately to hepatic and/or renal failure and death.
Patients develop a strong distaste for sweet food, and can avoid a recurrence of symptoms chronic course of the disease by remaining on a fructose- and sucrose-free diet.

HFI must not be confused with fructose malabsorption, which is a non-life threatening and much more common condition.

Dietary Guidelines for Hereditary Fructose Intolerance (HFI)

Food Category	Foods Permitted	Foods Prohibited
Dairy	Any milk, cheese, eggs	Milk products w/added sugar (sweetened yogurt, fruit yogurt, milkshake, chocolate milk)
Meat	Beef, veal, lamb, pork	Ham, bacon, hot dogs, processed meats; any other meat where sugar is used in processing
Fish	All fish	None
Poultry	Chicken, turkey	None
Cereal	Cooked or ready-to-eat cereals (except sweetened & sugar-coated cereals)	Sweetened/sugar-coated cereals
Fruit	None	All fruits, fruit juices, including squashes & cordials, & fruit extracts prohibited
Vegetables	Asparagus, cabbage, cauliflower, celery, green beans, green peppers, lettuce, nuts, onions, potatoes, spinach, wax beans	All other vegetables, including sweet potatoes
Bread	Breads prepared w/out fructose, sucrose, sugar, or sorbitol; soda crackers & saltines	Any breads or crackers prepared w/fructose/sucrose/sugar/sorbitol
Fat sources	Butter, margarine, oil, mayonnaise / mustard prepared w/out sugar	Mayonnaises, mustards, & salad dressings made with sugar
Desserts and sweeteners	Dietetic jello, dietetic ice cream, dietetic puddings; natural yogurt; glucose, dextrose, dextrin, maltose & zero-calorie sweeteners	All desserts containing sugar (cake, pie, cookies, candy, jello, ice cream, sherbet, honey, fruit juice); sugar, sucrose, sorbitol, fructose
Miscellaneous	Vegetable juices, coffee, tea, salt, pepper, broths/soups from permitted vegetables; some sugar substitutes; some dietetic beverages; pasta; rice; cinnamon, garlic, poppy seeds; peanut butter (when pure & w/out added sugars)	Ketchup & any other sauces / condiments containing sugar, jam, jelly, preserves, carbonated beverages / soda; peanut butter if prepared w/added sugars; chewing gum w/sorbitol

Adapted from www.bu.edu/aldolase/HFI/treatment/sugar_table.htm

Metabolic aminoacids desease PKU

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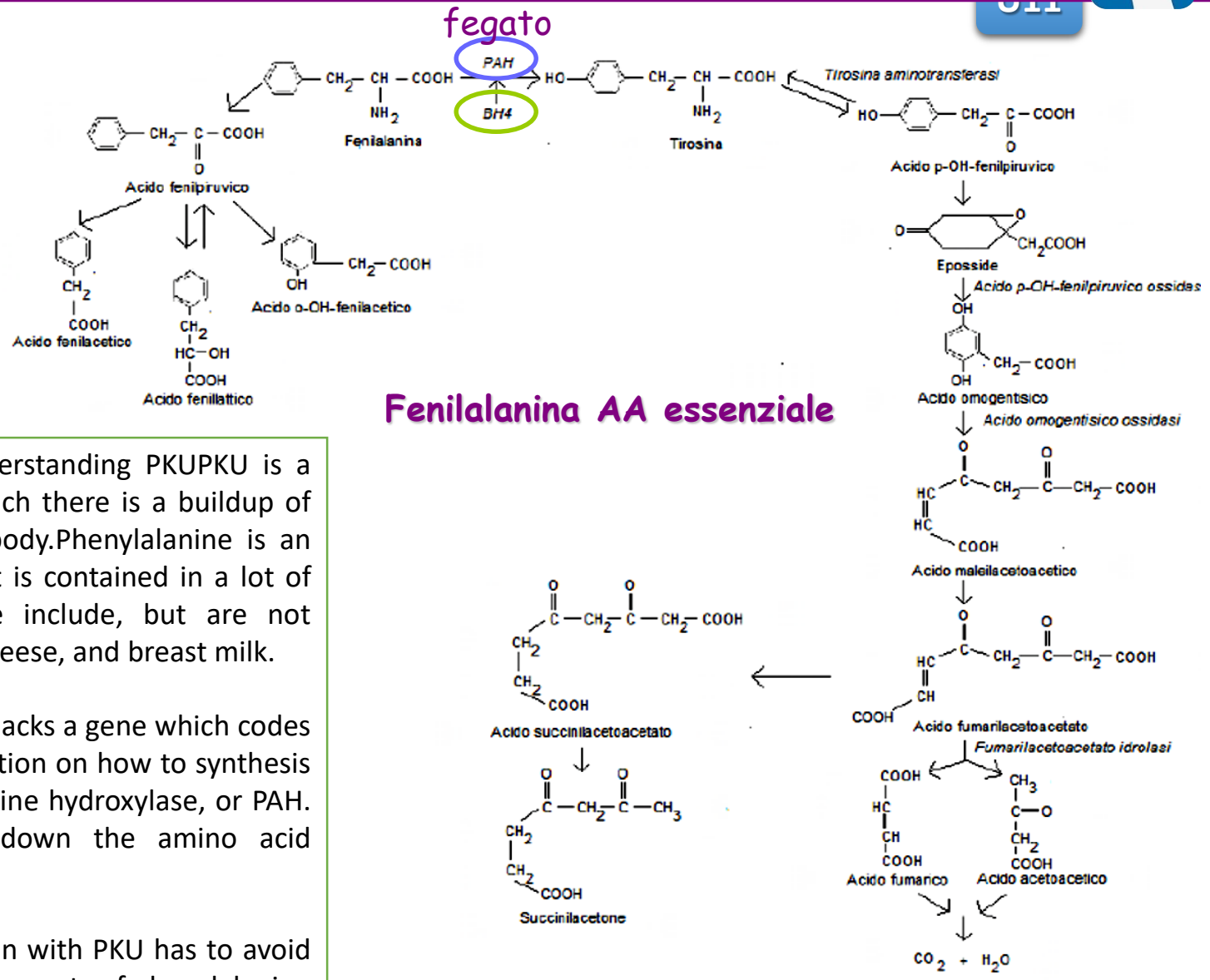

Fenilalanina AA essenziale

Phenylketonuria - Understanding PKUPKU is a genetic disorder in which there is a buildup of Phenylalanine in the body.Phenylalanine is an essential amino acid, it is contained in a lot of different foods. These include, but are not limited to, fish, pork, cheese, and breast milk.

A person who has PKU lacks a gene which codes for the genetic information on how to synthesis the enzyme phenylalanine hydroxylase, or PAH. This enzyme breaks down the amino acid phenylalanine.

Because of this a person with PKU has to avoid foods containing high amounts of phenylalanine for their entire life.

PAH: fenilalanina idrossilasi
BH4:tatraidrobiopterina, cofattore

Metabolic aminoacids desease PKU

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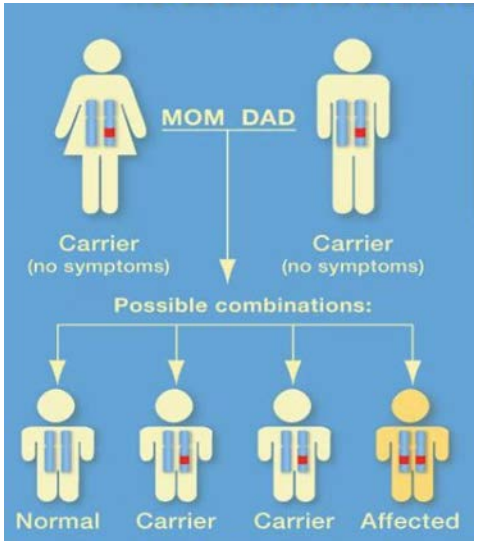

PKU is an autosomal recessive disorder. Meaning that two copies of an abnormal gene must be present in order for the disease or trait to develop.If a child is born and both parents have the same autosomal recessive mutation then there is a 1 in 4 chance of the child inheriting the abnormal gene and inheriting the disease.Often, the parents will not show signs and symptoms of the condition because they only carry one copy of the mutated gene.

Classificazione	Test urinario	Attività enzimatica media	Fenilalaninemia (mg/dL)	Trattamento raccomandato
Tipo I Fenilchetonuria classica	Positivo	<1%	≥20	Sì
Tipo II Iperfenilalaninemia persistente MILD-PKU	Positivo/ negativo	1-3%	6-20	Sì
Tipo III Iperfenilalaninemia persistente lieve	Negativo	>3%	<6	?

Iperfinilalaninemia materna

Manifestazioni cliniche	Incidenza media
– Ritardo di sviluppo neuromotorio e/o psichico	100%
– Comportamento agitato	90%
– Alterazioni aspecifiche dell'EEG	80%
– Ipertonia muscolare	75%
– Microcefalia	68%
– Iperriflessia	66%
– Deficit del linguaggio	63%
– Ipercinesia	50%
– Disturbi della deambulazione	35%
– Tremori	30%
– Autismo	30%
– Convulsioni	26%

Metabolic aminoacids desease PKU

U11

What is Included in a Low Phenylalanine Food Pattern?

The diet for PKU consists of a phenylalanine-free medical formula and carefully measured amounts of fruits, vegetables, bread, pasta, and cereals. Many people who follow a low phenylalanine (phe) food pattern eat special low protein breads and pastas. They are nearly free of phe, allow greater freedom in food choices, and provide energy and variety in the food pattern.

However, if these foods were the only foods a person consumed, his or her diet would be lacking protein, vitamins, and minerals. That is where the special formula comes in.

They contains protein, vitamins, minerals and energy (calories) with no phenylalanine.

How Long Must a Person With PKU Follow This Special Diet?

this diet should be followed for life. Keeping blood phe levels in the safe range helps to prevent problems with thinking and problem solving.

Metabolic aminoacids desease PKU

U11

CONCENTRAZIONE DI FENILALANINA NEL SANGUE E DIETA		
Fenilalanina fino a 2 mg/100ml	Condizione di normalità	Dieta libera
2-6 mg/100 ml	Iperfenilalaninemia lieve (*Mild Hpa*)	Dieta libera
6-10 mg/100 ml	Fenilchetonuria lieve (*Mild Pku*)	Dieta ipoproteica
10-20 mg/100 ml	Fenilchetonuria moderata (*Moderate Pku*)	Dieta ipoproteica
Sopra 20 mg/100 ml	Fenilchetonuria classica o severa	Dieta ipoproteica

Formulas for breastfeeding
Based on balanced free AA for other nutrients
Phenylalanine-free formulas (to supplement the needs of breast-fed infants)
Reduced phenylalanine formulas (artificial feeding)

Formulas for weaning and adulthood
Foods with low / known phenylalanine contents
Low-protein foods
Aproteic foods specific for phenylketonurics (pasta, bread, cracher)
Special formulas calibrated for gravidic status

The Italian legislation provides economic aid for the bearers of hereditary metabolic diseases:

Variations depending on the region
Subjects with a confirmed diagnosis from authorized bodies
Free regime in SSN

MILUPA PKU 2-SHAKE è una miscela di L-amminoacidi puri priva di fenilalanina con carboidrati, vitamine, minerali, oligoelementi e moderata quantità di grassi.
È indicata come sostituto proteico nella gestione nutrizionale dei bambini e adolescenti **da 8 a 14 anni** affetti da fenilchetonuria ed iperfenilalaninemia.
Il gusto di MILUPA PKU 2-SHAKE è determinato dalla presenza di ingredienti naturali per cui sono presenti tracce di fenilalanina:
gusto Fragola: 5mg
gusto Cioccolato: 15mgContiene tracce di fenilalanina a causa dell'utilizzo di ingredienti naturali Sostituto proteico a base di singoli amminoacidi liberiIdeale per l'alimentazione di soggetti affetti da fenilchetonuria e iperfenilalaninemiaCon carboidrati, vitamine, minerali, oligoelementi Non adatto come unica fonte di nutrienti

Dosaggio ed uso:La dose quotidiana di MILUPA PKU 2-SHAKE necessaria per soddisfare il fabbisogno proteico giornaliero è subordinata all'età, al peso corporeo e al livello di tolleranza individuale alla fenilalanina. Tale dose, pertanto, deve essere periodicamente regolata dal medico.MILUPA PKU 2-SHAKE nella pratica busta monoporzione consente di suddividere più facilmente la quantità giornaliera in diverse singole porzioni.

MILUPA PKU 2-SHAKE può essere utilizzato da solo o in combinazione con MILUPA PKU 2-SECUNDA, MILUPA PKU 2-ACTIVA e MILUPA PKU 2-FRUTA.

pku 2-secunda

henylalalanine free

lefined protein supplement based on free amino acids

or the dietary management of Phenylketonuria and Hyperphenylalaninemia

nriched with vitamins, minerals and trace elements in age-adapted quantities

ot to be used as a sole source of nutrition

nust be used under medical supervision

inition and indikation

pa pku 2-secunda is a mixture of pure L-amino acids free from phenylalanine, en-ed with vitamins, minerals and trace elements. It is to be used as a defined ein supplement in the dietary management of Phenylketonuria and Hyper-ylalaninemia.

2-secunda → 9 - 14 years

sage and use

daily amount of pku 2-secunda depends on age, body weight, protein requirements individual metabolic condition. The dose of pku 2-secunda must be adjusted by physician or dietician regularly.

daily amount required should be divided into 3 to 5 equal portions and should be n mixed with calculated amounts of other food (e.g. beverages, fruit puree). The protein need can be covered by pku 2-secunda alone or in combination with pku akes and pku 2-activa. Diets with pku 2-secunda require an adequate intake of ener-ssential fatty acids and phenylalanine to meet daily requirements. In beverages ximum concentration of 10 g per 100 ml should not be exceeded.

kaging

2-secunda 500 g tin (2 tins per box)

Nutrition information

Average content per 100 g		pku 2-secunda
Energy	kJ	1306
	kcal	307
Protein*	g	70
Amino Acids	g	84
of which		
Arginine	g	2,8
Cystine	g	1,9
Histidine	g	1,9
Isoleucine	g	4,8
Leucine	g	7,9
Lysine	g	5,6
Methionine	g	1,9
Threonine	g	3,8
Tryptophan	g	1,4
Tyrosine	g	4,7
Valine	g	5,6
Alanine	g	3,4
Aspartic acid	g	8,0
Glutamic acid	g	16,8
Glycine	g	1,9
Proline	g	7,6
Serine	g	4,2
Carnitine	mg	150
Fat	g	0
Carbohydrates	g	6,8

** Conversion: 1 g Protein = 1,2 g Amino acids = 17 kJ = 4 kcal*

Average content per 100 g		pku 2-secunda
Minerals		
Sodium	mg	<3
Potassium	mg	1400
Calcium	mg	1680
Magnesium	mg	350
Phosphorus	mg	990
Chloride	mg	<1
Iron	mg	20
Trace elements		
Zinc	mg	20
Copper	mg	1,4
Iodine	µg	230
Manganese	mg	2,8
Chromium	µg	42
Fluoride	mg	1,4
Molybdenum	µg	90
Selenium	µg	60
Vitamins		
Vitamin A	mg	1,07
Vitamin D_3	µg	11
Vitamin E	mg	15,0
Vitamin K_1	µg	51
Vitamin B_1	mg	1,8
Vitamin B_2	mg	2,2
Vitamin B_6	mg	2,5
Niacin	mg	13,1
Folic acid	µg	294
Biotin	µg	70
Vitamin B_{12}	µg	3,5
Pantothenic acid	mg	8,2
Vitamin C	mg	105
Choline	mg	630
Myo-Inositol	mg	315

Ingredients

phe-free L- amino acid mixture, mineral and trace element mixture, vitamin mi maltodextrin, vanillin

PKU 3-Tablets

Stampa

MILUPA PKU 3-TABLETS è una miscela di L-amminoacidi puri priva di fenilalanina con vitamine, minerali ed oligoelementi sotto forma di compresse.
È indicata come sostituto proteico nella **gestione nutrizionale di adolescenti oltre i 14 anni e adulti affetti da fenilchetonuria ed iperfenilalaninemia.**

- **Non contiene fenilalanina**
- **Sostituto proteico a base di singoli amminoacidi liberi**
- **Ideale per l'alimentazione di soggetti affetti da fenilchetonuria e iperfenilalaninemia**
- **Con vitamine, minerali ed oligoelementi**
- **Non adatto come unica fonte di nutrienti**

Tabella 3.6: Confronto ingredienti e valori nutrizionali di diverse tipologie di latte

Tipologia prodotto:	Latte vaccino per adulti	Latte liquido per neonati	Latte dietoterapeutico per adulti	Latte dietoterapeutico per neonati
Ingredienti:	Latte di vacca pastorizzato	Acqua demineralizzata, lattosio, latte scremato, olii vegetali, fibre alimentari, additivi.	Acqua, malto destrine, lattosio (4%), grassi di latte (2%), siero di latte a basso tenore di Phe (4%), emulsionanti.	Idrosilato di caseina, proteine ed aa adatti, carboidrati digeribili, grassi LCPUFA, vitamine, minerali ed oligoelementi
Composizione nutrizionale su 100ml di prodotto:	Valore energetico: 46kcal Proteine:3g Carboidrati: 4,85g Grassi: 1,55g	Valore energetico: 68kcal Proteine:1,4g Carboidrati.: 8,6g Grassi: 3,2g	Valore energetico: 70kcal Proteine: 0,3 g di cui <10mg di Phe Carboidrati: 9,2 g Grassi: 3,5	Valore energetico: 72kcal Proteine: 1,95g di cui 0g di Phe Carboidrati: 8,1g Grassi: 3.5g

(Fonti: www.parmalat.it, www.mellin.it, www.nutricia.it, www.aproten.it)

PKU e Latte
confronto per bambini ed adulti

Tabella 3.7: Ingredienti e valori nutrizionali nel pane tradizionale e nel pane "speciale"

Tipologia di prodotto:	Pan carrè tradizionale	Pan carrè dietetico
Ingredienti:	Farina di grano tenero, olio vegetale, lievito, destrosio, glutine, sale, farina di orzo maltato, alcool etilico.	Amido di frumento, amido di riso, margarina, destrosio, lievito, farina di semi di carrube, zucchero, emulsionanti
Composizione nutrizionale su 100g di prodotto:	Valore energetico: 251kcal Proteine: 10g Carboidrati: 39g Grassi: 5,5g	Valore energetico: 399kcal Proteine: < 1g di cui <50mg di Phe Carboidrati: 76,8g Grassi: 10g

(Fonti: Mulino bianco, www.nutricia.it)

PKU e prodotti da forno

Dal punto di vista tecnologico, la riduzione delle proteine viene definita "estrusione proteica". Tale tecnica, provoca alcune conseguenze negative sulle caratteristiche organolettiche del prodotto, essendo le proteine del grano importanti componenti di viscosità ed elasticità, in particolare nei prodotti da forno. Dal punto di vista nutrizionale invece, si riesce a mantenere un contenuto energetico simile, talvolta addirittura maggiore a quello degli analoghi di uso corrente.

Tabella 3.8: Confronto degli ingredienti e dei valori nutrizionali fra l' hamburger di carne e l'hamburger "speciale"

Tipologia di prodotto:	Hamburger per PKU	Hamburger di carne
Ingredienti:	Farina di mais, fecola di patate, funghi essicati, cipolle essicate, olio vegetale, aromi, aglio in polvere, erbe aromatiche, sale, antiossidante, colorante E160a.	Carne di bovino adulto 92%, pangrattato (farina di frumento, lievito di birra, sale), albume d'uovo in polvere, sale, pepe nero, antiossidante: acido ascorbico.
Composizione nutrizionale per 100g di prodotto:	Valore energetico: 409kcal Proteine: 2g di cui 80 mg di Phe Carboidrati: 71,6g Grassi: 12,7g	Valore energetico: 222kcal Proteine: 17,5g Carboidrati: 3,2 Grassi:15,5 g (di cui saturi 7g)

(Fonti: www.montanafood.it, www.dmfmetabolic.it-ingredienti -taranis-)

PKU e prodotti sostituti della carne

Per quanto riguarda invece i sostituti della carne, come per esempio l'hamburger, la formulazione si complica ulteriormente, in quanto in questo caso l'hamburger non potrà contenere davvero la carne, (una delle principali fonti proteiche), ma tutta una serie di ingredienti utili a rendere l'alimento il più possibile vicino a quello originale dal punto di vista organolettico, ma non nutrizionale. Gli ingredienti predominanti sono la farina di mais e la fecola di patate, elementi particolarmente necessari per dare la giusta consistenza all'alimento, ma hanno anche un importante valore nutrizionale, perché responsabili dell'apporto di carboidrati, fonti di energia per l'organismo.

Artefici di questo dislivello calorico, sono proprio i carboidrati: **70,6g/100g dell'alimento speciale, contro 3,2g/100g** di quello classico. **Le calorie fornite dai carboidrati sono abbondanti e sopperiscono alla mancanza di proteine dell'alimento**. Bisogna però tener conto che le proteine e i carboidrati hanno nel nostro organismo ruoli molto differenti; le prime sono necessarie per la costruzione di strutture cellulari, la sintesi di enzimi ed ormoni, oltre ad essere utilizzate a scopi energetici. Il secondo gruppo invece, costituisce la principale fonte e riserva energetica dell'organismo, fungendo da combustibile di facile e pronto utilizzo perché rapidamente assimilabile**. Per questo motivo è sempre necessario che il paziente assuma integratori proteici o di amminoacidi essenziali, in grado di sopperire alla mancanza di proteine degli alimenti dai quali si nutre quotidianamente.**