

## ATTACHMENT:

Useful remarks for patient and doctor, to be associated to the analytical results. Your doctor should interpret this report.

**Cod. ID: 123456**

**CCV: 000**

**Date: 01/01/2014**

**Patient: Rossi Mario**



Rapport de:

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Aut.n. 67 del 26.01.10

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# **GLUTEN SENSITIVITY (Immunoassay for gluten sensitivity)**

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## **GLUTEN SENSITIVITY**

Gluten Sensitivity (GS), also defined as non-coeliac gluten sensitivity, is a syndrome characterized by multiple bowel and/or out-of-the-bowel symptoms which show up after gluten consumption and which improve or disappear after being excluded from the diet. This condition is found in subjects in which the diagnosis of coeliac disease has been ruled out on the basis of negative serologic tests and/or non-atrophic bowel villi, as well as in cases of non-allergy (IgE) to wheat.

Gluten Sensitivity exists, it is a clinical reality of which the scientific world is quickly becoming aware. It is a condition that shows up with a high frequency, mostly in adults rather than in children, though the prevalence still has to be defined with certainty. It appears to be more frequent in females and is common in relatives of coeliacs.

GS is a chronic condition that entails the appearance of IgA and IgG antibodies to gliadin, a molecule found in gluten. Gluten sensitivity often occurs in people who suffer from irritable colon and bowel inflammation, as undigested food comes into contact with the immune system more easily and triggers an inflammatory response which, unless continuously monitored, can lead to the onset of more serious diseases, such as coeliac disease, Crohn's disease,...

Adverse reactions to gluten-containing food are increasingly present and frequent in Western societies, as eating habits are oriented to buying ready-to-eat, pre-packed and industrial food, or to choosing quick meals that are easy to cook. Wheat is probably on our tables at least 3 times a day.

There are still no accurate estimates available for the frequency of gluten sensitivity, yet preliminary data from Prof. Fasano's studies (Director of the center for coeliac research – University of Maryland, USA) have shown that 6% of the American population has a certain degree of gluten sensitivity.

The causes of increased gluten diseases are due to:

- Higher gluten load subsequent to the adoption of a diet increasingly rich in cereal content;
- Increased mechanization and industrial production, which promotes the creation of new qualities of wheat (modified more for productive than for nutritional reasons), which are richer in toxic peptides compared to wheat qualities produced in the last century;
- The increasingly pronounced reduction of bread leavening times brings about a significant increase in the concentration of toxic peptides.

## **GLUTEN**

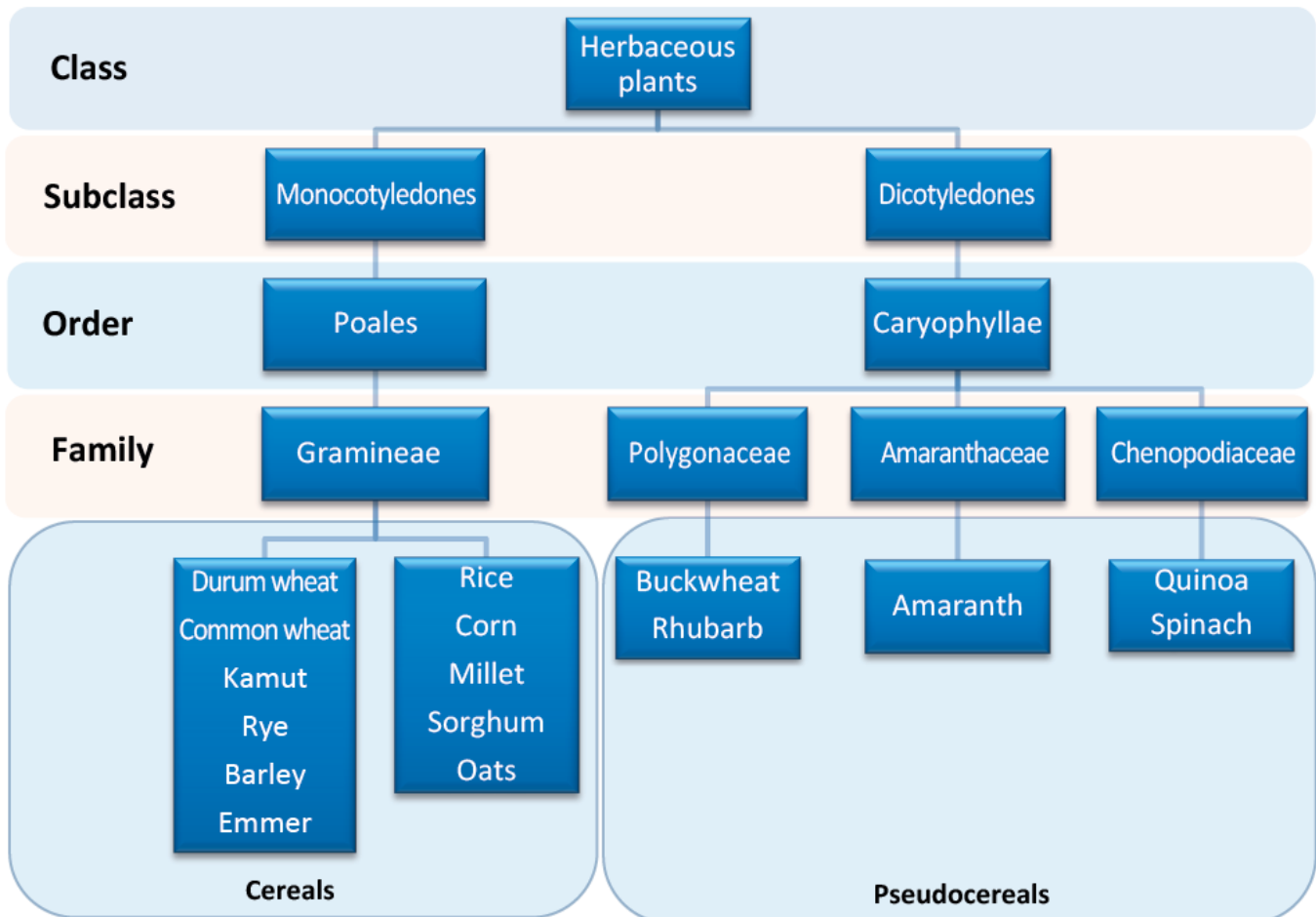
Gluten does not exist as a natural product, but it forms when flour is kneaded with water, from a few proteins, gliadins and glutenins naturally occurring in the grains of several cereals, which organize into a three-dimensional protein lattice that provides elasticity and resistance to the stretching of the dough and promotes bread leavening and baking.

Glutelins (or glutenins) and prolamins (or gliadins) account for 80% of the proteins present in the caryopsis (grain) of wheat, with the remaining 20% being composed of soluble proteins, such as albumins and globulins.

Gluten is used a lot in the modern food industry and is found in bread, pasta, biscuits, pizza and in other products containing certain cereals. Moreover, it is also used as an ingredient, although in low concentrations, in sauces, soups, precooked food, and as a thickener in tablet or lozenge formulations of several drugs.

## CLASSIFICATION OF CEREALS

Herbaceous plants, generally from the Gramineae family, such as wheat, rye, oats, barley, rice, corn, with fruit rich in starch and proteins. The seeds, subjected to grinding, provide flour suitable for bread making, and are one of the basic foods of mankind. Also derivatives from other plant species, and for this reason defined as pseudo-cereals, are included in cereals from the commercial and cultivation viewpoints.



### • Gluten-containing cereals

**WHEAT:** The most important wheat species are represented by common or bread wheat (*Triticum vulgare*), the flour of which is used for making bread and bakery products (breadsticks, crackers, biscuits, desserts) and durum wheat (*Triticum durum*), used in the kneading of dough. In addition to the above-indicated food, wheat is also found in such products as cuscus, semolina, breakfast cereals, breadcrumb-coated precooked or deep-frozen food, sausages, canned food, sauces and dressings, drinks such as chocolate, beer, gin, whiskey, and vodka.

**KAMUT:** Kamut® is a registered trademark of the American Kamut International company, which denotes a variety of durum wheat. Thus, Kamut® is a gluten-containing cereal, used for preparing breakfast cereals, muesli, broths and thick soups. The flour derived therefrom is used for making bread, pasta, biscuits, snacks, flat bread, pancakes.

**EMMER:** A very popular kind of wheat in ancient Rome. It is currently very common both in the form of grains (in deep-frozen thick soups, mixed with dry legumes for the preparation of thick soups, etc. ...), and in the form of flour for the preparation of pasta, desserts, etc. ... There are several varieties of emmer, one of which is *Triticum Spelta*, another is *Triticum Monococco*, also called *ENKIR*. The nutritional value of emmer is very similar to that of common wheat, and as such it contains gluten.

**RYE:** The typical cereal of Northern European countries where it is used alone or mixed with wheat for the

making of rye bread characterized by its dark colour. It contains a wheat gliadin homologue named secalin, therefore in case of gluten sensitivity, food made of rye flour such as bread, cakes, biscuits or snacks should be excluded.

**BARLEY:** (*Hordeum vulgare*) has a high content of mostly soluble fibres. Predominantly used as a malt for making beer, whiskey, and bread; as a post-roasting coffee substitute, and for the preparation of dietetic products. It contains a wheat gliadin homologue called hordein, therefore in case of gluten sensitivity, barley flour and coffee, beer, Irish and Scotch Whiskey should be excluded from the diet. It contains gluten in the form of hordein.

**OATS:** (*Avena sativa*) the most well-known species of the *Avena* genus. It contains many proteins (up to 17%) and very few carbohydrates, and is the cereal with the highest content of fats of all. When added to 11% fibres, we are looking at one of the cereals with the lowest glycaemic index, which makes it particularly suitable for diabetics. The scientific community does not have a common view of oats. Historically, oats have always been excluded from *gluten free* diets due to the presence of avenin as a reserve protein. Today it is advised to include in the diet, although in small doses, only oats which are known not to be contaminated by gluten-containing cereals.

- **Non gluten-containing cereals**

**CORN:** (*Zea mays*) Corn is a cereal used in the diet as: popcorn and cornflakes, germ-extracted oil, snacks and products from caryopsis grinding. Corn may be used instead of barley for the production of beer. Consumed in the form of flour (maize porridge), thus hulled, it is deprived of important nutritional factors. Corn is a naturally gluten-free cereal.

**RICE:** (*Oryza sativa*) is one of the cereals most rich in starch of all (over 75%), and poor in proteins (6-7%). Not naturally containing gluten.

**MILLET:** (*Panicum miliaceum*) Herbaceous plant belonging to the Gramineae family, with a composition similar to that of wheat, but without gluten. It may be found in cereal-based soups.

- **Pseudocereals**

**AMARANTH:** Gluten-free, suitable for people suffering from gluten sensitivity. The seeds may be found in legume- and cereal-based soups.

**QUINOA:** Herbaceous plant of the Chenopodiaceae family, such as spinach and beet, without gluten and very rich in proteins. The seeds may be found in legume- and cereal-based soups.

**BUCKWHEAT:** (*Fagopyrum esculentum*) for its characteristics and its use in food, buckwheat has always been commercially included amongst cereals, although it does not belong to the Gramineae family. A good store of fibres and minerals, and it is gluten-free.

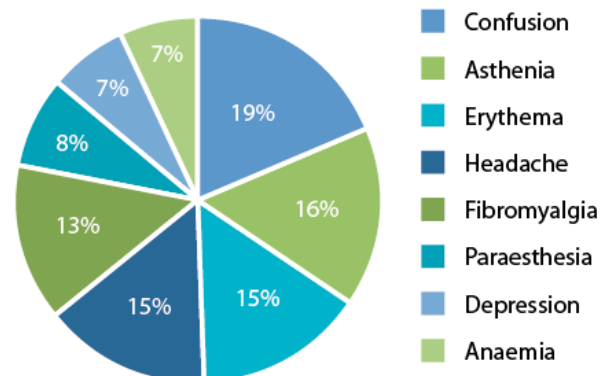
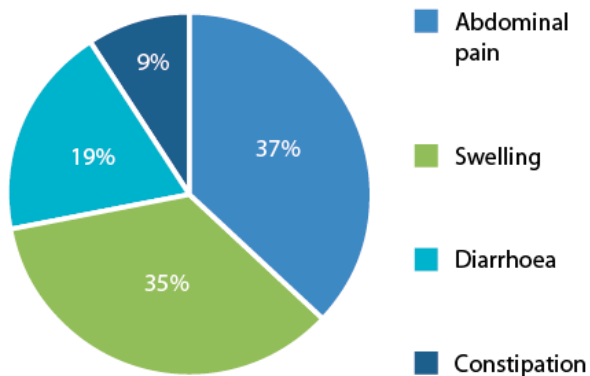
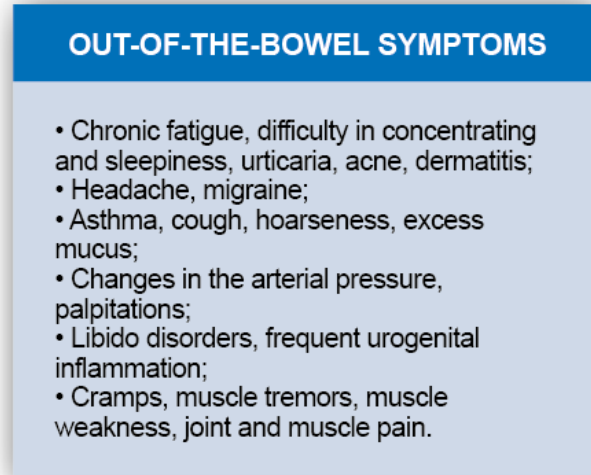
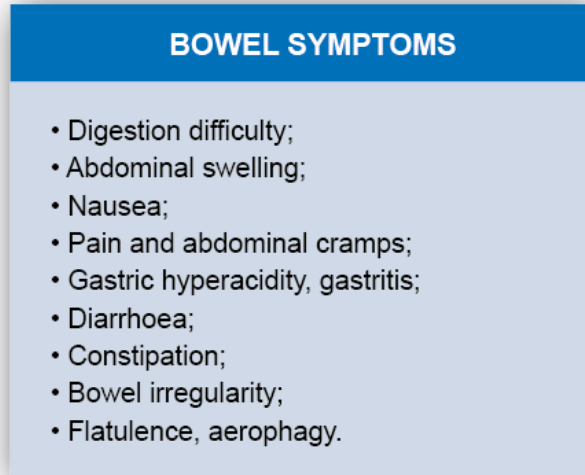
## **WHAT DOES IT CAUSE AND HOW DOES IT SHOW UP**

Unlike coeliac disease, where ingestion of gluten causes damage to the bowel mucosa with consequent malabsorption, in gluten sensitivity the symptomatology is more connected to that given by adverse reactions to food, the so-called “delayed allergies”, or better known but incorrectly defined as “food intolerances”. In this case too the reaction is dose dependent, and symptoms may appear even many hours after the consumption of the gluten-containing food.

Symptoms improve or disappear after gluten elimination, occurring again just as quick if gluten is reintroduced in the diet.

Changes in the bowel wall (inflammation, modified permeability) and the gut microbiota (dysbiosis vs. eubiosis) appear to play a crucial role in the onset of symptoms.

The most frequently detected symptoms are:



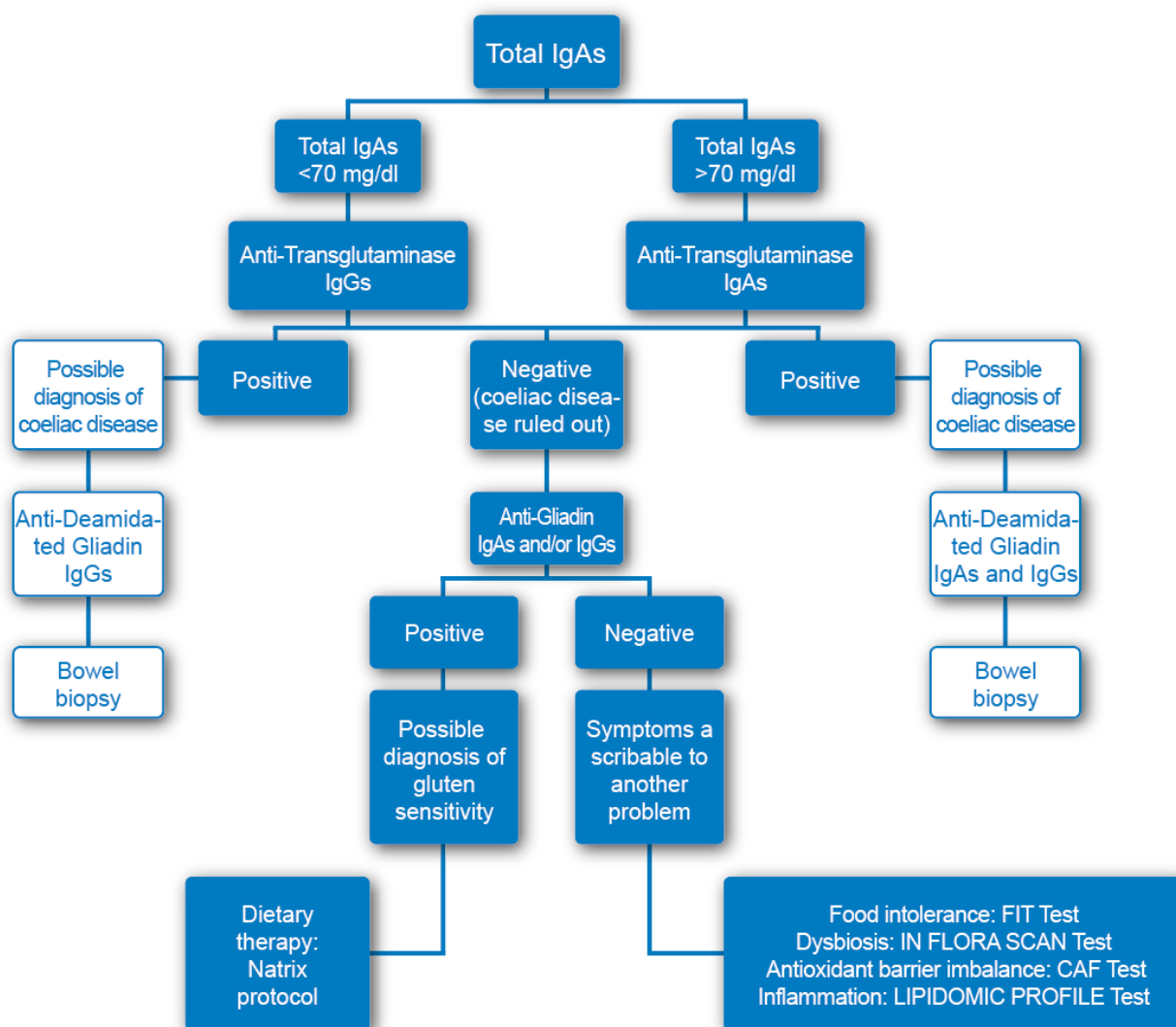
It is very important to undergo periodic checkups and to monitor symptoms in order to reveal the progress made and improvements obtained with a correct nutrition.

All this happens because gluten-derived gliadin is poorly digested in the human stomach and, when still intact or as large fragments, often comes into contact with the gut wall, and is thus able to trigger immune reactions with consequent inflammation of the bowel lumen and mucosa.

## HOW IS IT DIAGNOSED

The "Gluten Sensitivity" test uses the standard ELISA method which affords a high level of sensitivity and specificity for the gluten sensitivity markers tested.

The specific tests performed are assessments for the presence of total IgA antibodies, anti-transglutaminase IgA antibodies (or IgGs in case of low titers of total IgAs) to exclude a possible diagnosis of coeliac disease, and anti-gliadin IgA and IgG antibodies to reveal a potential Gluten Sensitivity.



**Figure 2:** Diagnostic protocol for gluten sensitivity test GST

## TOTAL IgAs

Immunoglobulins are proteins synthesized by lymphocytes B, with antibody activity, which act as sentinels in the body by checking the presence or absence of pathogens or exogenous substances to be removed. They are specific for certain portions of the agent they have to recognize (epitope), and once the agent has been recognized, they bind to it making it detectable, allowing for recognition and elimination thereof by other cells of the immune system (macrophages and cytotoxic cells).

**Immunoglobulins** of Class A are antibodies normally produced at mucous-associated lymphoid tissues of the digestive and respiratory tracts, and thus are prevalent in secretions, representing an important defense mechanism against local infections and preventing colonization by pathogens. Lower yet quantifiable levels thereof are also detected in blood. An increased titer of total IgAs could be caused by infections or inflammations at mucous membranes, and is therefore to be investigated. In case of low IgA positivity, which is possible in subjects with a primary immunodeficiency, other immunoglobulin classes may be investigated, such as IgGs or IgMs.

## **ANTI-TRANSGLUTAMINASE**

Transglutaminase is an enzyme found in cells, and is implicated in cell death and tissue repairing processes. As a result of cell wall damage, as in the case of inflammation of the gut mucosa, this enzyme is released in the extracellular environment. It has a repairing action on the mucosa tissue, yet also has a high affinity for gluten peptides, causing a partial digestion of gliadin and generating peptides that can induce a specific antibody response. In subjects prone to coeliac disease, anti-transglutaminase (anti-tTG) antibodies develop which induce the inflammatory process and the pathological changes in the bowel villi.

Anti-tTG IgAs and IgGs are sought in the test in order to exclude a possible diagnosis of coeliac disease. In the presence of high titers of total IgAs, anti-tTG IgAs will be sought, whereas in case of deficiency of total IgAs, anti-tTG IgGs will be analysed. In children of under 3 years of age a negative test result to anti-tTG immunoglobulins does not rule out a possible diagnosis of coeliac disease. Therefore, specific anti-deamidated gliadin (anti-DPG) antibodies must be sought.

## **ANTI-GLIADIN**

As previously described, gliadin is one of the protein components that together with glutenin form gluten. Together they account for 80% of wheat proteins.

From recent studies, gliadin was shown to be a powerful immunogen capable of triggering an immune response that causes the symptoms of the gastrointestinal system. IgGs are a more sensitive, but less specific, marker of the utmost importance in cases of IgA deficiency, which is often present in gluten-sensitive subjects. In the active phase of the disease, the anti-gliadin IgA and IgG values will be high, whereas a few months later and up to one year on the gluten-free diet only the IgG values can still be high.

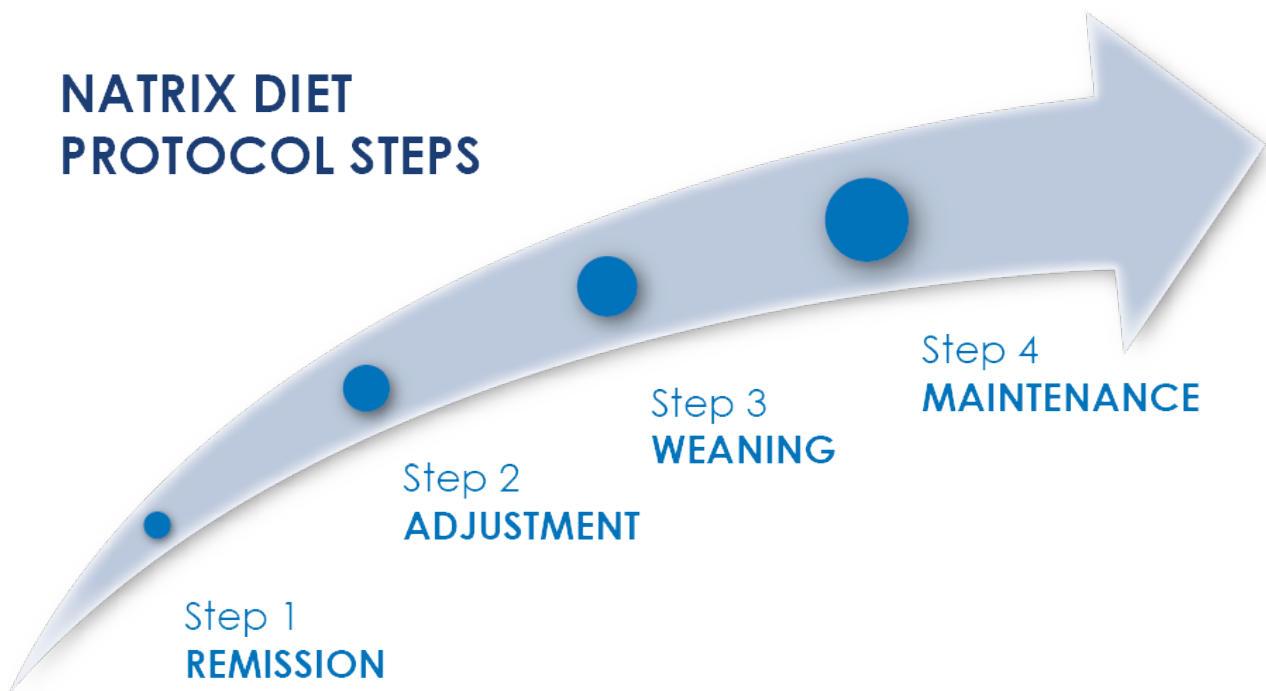
For this reason, anti-gliadin IgGs are used as a marker both for the assessment of a potential Gluten Sensitivity and for monitoring improvements consequent to the gluten-free diet, and thus are indicators of remission of gluten sensitivity. The dosing of these antibodies is also recommended in children of under 5 years of age.

## **TREATMENT**

The only effective treatment currently known for relieving or improving symptoms of this sensitivity is to follow a diet protocol that induces remission of gluten sensitivity (or tolerance recovery). Natrixlab has been studying these problems related to inflammation from food for over a decade and has established tolerance recovery protocols that have been tried and tested. The telenutrition service provided for by Natrixlab enables the patient to be given instruction on correct, healthy nutrition and to become aware that food can and must be seen as an ally and no longer as an enemy. By means of the telenutrition service, the patient will be followed step by step through the various steps of the path by a team of physicians and nutritionists who lead him/her to recovery.



## NATRIX DIET PROTOCOL STEPS



Ask for the service at the centre where you were tested or call the number +39 0522-232606 for information. Correct nutrition not only allows for the swift disappearance of the disorders experienced (regression in the symptoms is already seen in the first month), but it also prevents the development of other allergies or sensitivities or the potential establishment of true coeliac disease or of even more serious bowel diseases (inflammation).

### REPETITION OF THE TEST

It is recommended to repeat the test after 6-8 months. In case of therapeutic monitoring, it is recommended to repeat the test following the advice of the attending physician. In the case of difficulty in interpreting the report or diseases in progress, it is recommended to seek advice from a specialist who can give targeted therapeutic support.

### RELATED TESTS

In the case of a negative result of the test, yet persistency of the symptoms, the cause of the illness could be ascribable to other gastrointestinal problems that can be investigated with the following tests:

**FIT (Food Intolerance Test)** - Test for assessment of IgG-mediated adverse reactions to food.

It can be considered as a screening secondary to GST:

- Positive GST => The FIT test is useful for identifying the presence of further problematic food, in order to make the diet protocol more specific.
- Negative GST => The FIT test is useful for identifying other causes of the symptoms (food intolerances).

**INFLORA SCAN** - Test for assessment of the condition of the intestinal bacterial flora.

It can be considered as a screening secondary to GST: when negative, useful for identifying other causes of the symptoms, such as dysbiosis, or the potential presence of pathogen bacteria.

**C.A.F. (Cellular Antiaging Factor)** - Test for assessment of the overall inflammatory and oxidative status. It can be considered as a screening secondary to GST:

- Positive GST => The C.A.F. test is useful for identifying the body's extent of inflammation partly induced by gluten sensitivity.
- Negative GST => The C.A.F. test is useful for identifying other possible causes of the symptoms.

**LIPIDOMIC** - Test for assessment of cell oxidative status.

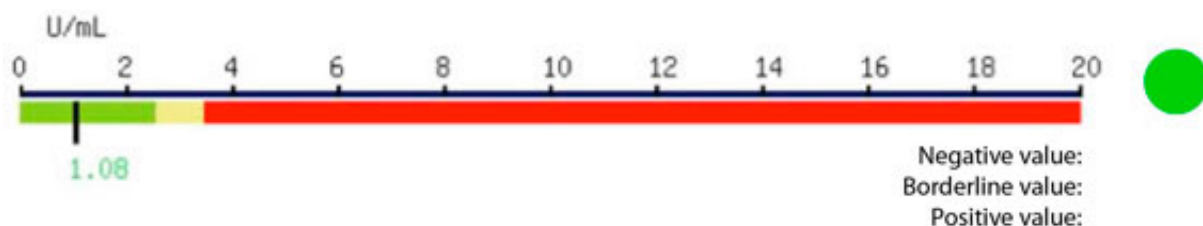
It can be considered as a screening secondary to GST which, when negative, is useful for identifying other possible causes of the symptoms, such as a fatty acid imbalance.

## IMPORTANT

The test results must however always be contextualized by the physician to the medical condition of the individual patient. This test must not be reproduced in a partial way. The laboratory results, charts, and explanations contained in this brochure are not to be construed as a medical diagnosis. They solely represent a tool available to the attending physician who may use them as a supplement to what is noticed during the medical examination or through other diagnostic tests, in order to formulate the proper therapy and the correct diagnosis of the subject's condition.

## GUIDANCE TO THE READING OF THE TEST

- **RESULT WITHIN THE GREEN BAR** - value inside the reference range
- **RESULT WITHIN THE YELLOW BAR** -borderline value
- **RESULT WITHIN THE RED BAR** - value outside the reference range



# TEST RESULTS:

**Cod. ID: 123456**  
**CCV: 000**  
**Date: 01/01/2014**  
**Patient: Rossi Mario**



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## **GS TEST** **(Gluten Sensitivity Test)**

Dott.ssa Ausilia Rausa

A handwritten signature in black ink, appearing to read "ARausa", written in a cursive style.

Rossi Mario

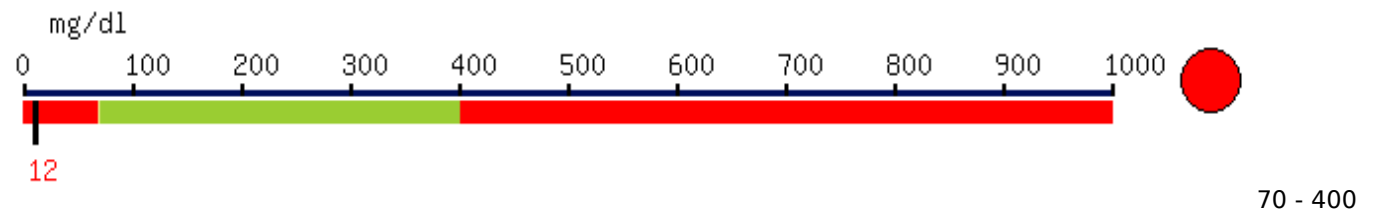
Cod. ID: 123456  
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## Results

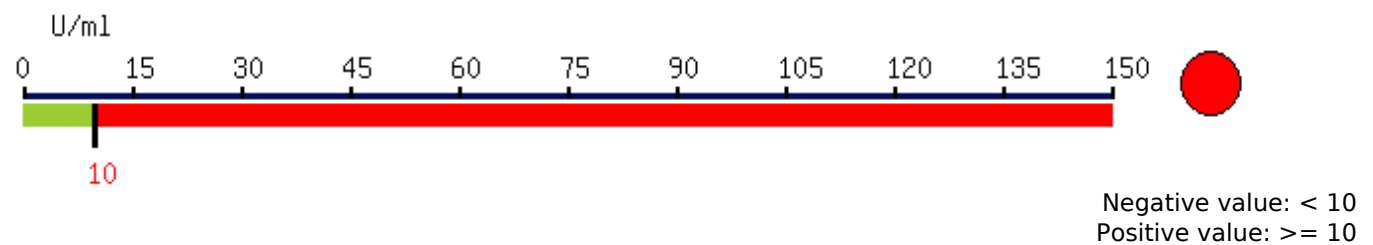
Total IgAs

12 mg/dl



IgG ANTI-TRANSGLUTAMINASE

10 U/ml



Gliadin IgGs

7 U/mL

