

# DOWNLOAD PDF GLUTEN INTOLERANCE (THE FOOD SENSITIVITY SERIES)

## Chapter 1 : Healthy Eating Series: Gluten Intolerance and Celiac Disease

*A gluten intolerance is the body's inability to digest or break down the gluten protein found in wheat and certain other grains. Gluten intolerance (also known as a gluten sensitivity) can range.*

This image has been modified. FACLM on February 18th, In , researchers in England reported a series of women with no evidence of celiac disease the autoimmune disorder associated with gluten intolerance , who nevertheless resolved their chronic diarrhea on a gluten-free diet. The medical profession was skeptical at the time that non-celiac gluten sensitivity existed, and even 30 years later , such patients were commonly referred to psychiatrists. Psychological testing of such patients, however, found no evidence that they were suffering from any kind of psychosomatic hysteria. Despite resistance from the prevailing medical community at the time, these health problems have subsequently been confirmed to be credible physiologically-based disorders rather than psychologically-based confabulations. What sort of evidence do we have for the existence of a condition presumed to be so widespread? The gold-standard for confirming non-celiac gluten sensitivity requires a gluten-free diet, followed by a double-blind, randomized, placebo-controlled food challenge. We never had that level of evidence until , when a double-blind, randomized placebo-controlled trial was published, which tested to see if patients complaining of irritable bowel symptoms who claimed they felt better on a gluten free dietâ€”despite not having celiac diseaseâ€”actually could tell if they were given gluten containing bread and muffins or gluten-free bread and muffins. Subjects started out gluten-free and symptom-free for two weeks and then were challenged with the bread and muffins. In my video, Is Gluten Sensitivity Real? Just the thought that they may be eating something that was bad for them made them feel crampy and bloated. The placebo effect is when you give someone something useless and they feel better; the nocebo effect is when you give someone something harmless and they feel worse. On the other hand, the small group that got the actual gluten, felt even worse still. The researchers concluded that non-celiac gluten intolerance may therefore indeed exist. It was a small study, though, and even though the researchers claimed the gluten-free bread and muffins were indistinguishable, maybe at some level the patients could tell which was which. So, in , researchers in Italy took patients that had been diagnosed with non-celiac gluten sensitivity and put them to the test with a double-blinded wheat challenge by giving them capsules filled with wheat flour or filled with placebo powder. More than two-thirds failed the test, such as getting worse on the placebo or better on the wheat. But of those that passed, there was a clear benefit to staying on the wheat-free diet. The researchers concluded that their findings confirmed the existence of a non-celiac wheat sensitivity. Most people with wheat sensitivity have a variety of other food sensitivities. We find the same increase in symptoms with high gluten, low gluten, or no gluten diets, calling into question the very existence of non-celiac gluten sensitivity. Indeed, short-term exposure to gluten appeared to induce feelings of depression in these patients. Whether non-celiac gluten sensitivity is a disease of the mind or the gut, it is no longer a condition that can be dismissed. More than 10, articles have been published on gluten in medical journalsâ€”intimidating even for me! Combined with the multi-billion dollar financial interests on both sides, it makes for a difficult task. But I think I did it! This is the first of a 3-part series summarizing the best available science on gluten. What can we do about preventing so-called atopic diseases like allergies, asthma, and eczema? In health, Michael Greger, M.

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### Chapter 2 : 10 Signs You Have a Gluten Allergy - RM Healthy

*If you experience symptoms due to a gluten intolerance or sensitivity, you probably want to steer clear of gluten - and for good reason! And there are plenty of gluten-free alternatives on the market today.*

Last Updated on Saturday, 21 July Symptoms are delayed onset reactions caused by the inability to digest Gluten contained in wheat, rye barley and oats and other grains. Reactions can be hours or days later. FAQs on Wheat intolerance Wheat allergy: It affects less than 0. When most people speak of wheat allergy they are really referring to the inability to digest wheat gluten - or gluten intolerance. FAQs on Allergies Gluten intolerance inc. Celiac Disease The symptoms for wheat intolerance are various and usually have a delayed onset - many hours after eating - or up to 2 or 3 days later. This is why it is difficult for doctors to diagnose. Skin rashes, eczema, psoriasis, itching flaky skin General: Some people choose to treat the symptoms of Wheat sensitivity or other food sensitivity with medications like anti-histamines or supplements. But this gives only a few hours relief - and it means you have to keep buying and taking pharmaceuticals your whole life - and keep tolerating their side effects. Choose the natural no-drug solution. That is - identify your food intolerance and then substitute that food for another delicious food. Yes, there are lots of symptoms of gluten intolerance! The trouble is however - many of these symptoms are also common to Dairy intolerance, Fructose intolerance and Yeast sensitivity. So how do you differentiate between them? And what if you have more than one food intolerance? Food substitution guides are included - so you can enjoy a wide variety of great foods. What should I do? Beginning with our free e-book, we can help you establish if you are suffering from gluten or wheat intolerance or if your symptoms indicate an intolerance to dairy, fructose or yeast. You may even be suffering from more than one food intolerance. The research indicates doing nothing can be a risk. Undiagnosed food intolerance can cause serious long-term health problems like osteoporosis, anaemia and many others.

### Chapter 3 : Gluten intolerance overview - Food and Food Allergies

*Check out this series of Q&As with leading researchers about non-celiac gluten sensitivity. Learn more about the symptoms of non-celiac gluten sensitivity. Download: Celiac Disease vs. Non-Celiac Gluten Sensitivity.*

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although they did not test positive for celiac disease. These individuals were sensitive to wheat not necessarily just gluten because of specific physiological factors that improved when they eliminated gluten from their diets. This may be particularly beneficial if a traditional elimination diet reveals you are not actually sensitive to wheat products. Follow a Gluten-Free Diet According to the Celiac Disease Foundation, there is no cure for gluten sensitivity, and the only treatment is to follow a gluten-free diet. A gluten-free diet is one without wheat, rye and barley. This means you must avoid most baked products found in stores, flour-containing foods like pizza or pasta at restaurants , the majority of packaged foods bread, cereals, pastas, cookies, cakes, etc. Check ingredient labels carefully since gluten is hiding in many packaged foods. With gluten out of the picture, focus on including more anti-inflammatory foods in your diet to repair your digestive system and heal any nutrient deficiencies. These include organic animal products, raw dairy products, vegetables, fruits, nuts, seeds and probiotic foods.

*Gluten Sensitivity vs. Celiac Disease*  
*Celiac Disease*  
*Gluten Sensitivity*  
*Do Cold Sores Have a Connection to Gluten?*  
*Is Celiac Disease a Cold Sore Trigger?*  
*Which Food Allergies Trigger Cold Sores?*  
*What is the Difference Between Celiac Mouth Sores and Cold Sores?*  
*How Do You Treat Gluten Intolerance Naturally?*  
*Conclusion*  
*References*  
*Born from the herpes virus, cold sores are NOT the direct result of gluten.*

References Born from the herpes virus, cold sores are NOT the direct result of gluten intolerance. Gluten-related issues can take a toll on your immune health. This can result in the appearance of canker sores in the mouth as well as a host of more significant issues within the small intestine. You will also learn about food allergies and which selections can make the problem worse. Celiac Disease The physical response to gluten protein found in barley, rye, and wheat causes both gluten sensitivity as well as celiac disease. However, these conditions are entirely different even though their symptoms are virtually identical. Only medical testing can determine which one is responsible. Celiac Disease This severe medical issue is caused when your immune system attacks the lining of your small intestine. Causing intestinal damage over time, celiac disease can lead to malnutrition and osteoporosis. In extremely rare cases your small intestine can become so riddled with problems that cancer can occur. All of these issues are the result of your body rebelling against gluten intake. Classified as an autoimmune condition, celiac disease is not caused by gluten, but rather how your body reacts to the protein itself. Research shows that roughly 1 in 100 people have celiac disease. Gluten Sensitivity The medical jury is still very much out on this condition. In fact, there is a question as to whether it is a condition at all. The consensus is that a person with sensitivity has a direct reaction to gluten consumption. Unlike celiac disease, gluten sensitivity causes inflammation of the digestive tract rather than your own body turning against you. Since there is no real test for gluten sensitivity, you must be tested for celiac disease to establish a general conclusion. It has become common practice to use deductive reasoning when dealing with sensitivity. If you experience inflammation within your digestive system when eating gluten but yet are symptom-free while entertaining a gluten-free diet, the conclusion could be gluten intolerance. Celiac disease is a condition in which your body begins to attack the small intestine in response to gluten consumption. Inflammation of the small intestine is the hallmark concern. Celiac disease is an autoimmune condition. Gluten sensitivity is an issue in which your stomach and digestive tract respond poorly to gluten consumption. In this condition, unlike celiac disease, the gluten is to blame rather than your body turning against you. The only way to diagnose this ailment is to first rule out celiac disease. While there is no direct medical connection between cold sores and gluten the possibility is not zero. Because poor immune health can lead to a fever blister outbreak, stomach and digestive issues could be a trigger for some people. Whenever your body is forced to deal with a condition, regardless of what it is, your immune system becomes compromised. If your health is in turmoil, then you often become susceptible to other ailments. In the case of gluten concerns, if your body is having to deal with gastrointestinal issues it might not have the means to prevent a cold sore outbreak. Because HSV-1 is indeed a virus, not having all hands on deck can be an issue. This is why it is vital to stay healthy. Even something as seemingly innocent as the common cold can potentially awaken HSV-1 and result in a cold sore outbreak. While gluten concerns will never be the direct cause a cold sore, the general wear and tear it could have on your immune system could cause a fever blister to develop. While gluten issues will never cause a cold sore in the literal sense, the taxing of your immune system could lead to problems. Whenever your body is having to fight off the attack, it can be left open to other attacks. It is possible for HSV-1 to be triggered while your body deals with your gluten condition. Unlike gluten sensitivity, celiac disease is a severe autoimmune issue where the body begins to attack itself. This type of alarming disease would naturally leave the body open to attack by a host of internal and external forces causing variety of extraintestinal manifestations. So are dietary concerns. When discussing the topic of celiac disease, all three of these issues are at the forefront. Dietary concern that can act as a trigger. The worry

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and general concern over your celiac diagnosis. As your small intestine continues to come under fire, your body is taxed and worn down. This alone can weaken your system enough to allow HSV-1 to become active. Unfortunately for HSV-1 sufferers, arginine is found in many favorite foods across the board. These foods and drink selections include:

### Chapter 5 : Gluten-Free Foods | Celiac Disease Foundation

*Gluten Sensitivity Put to the Test* Written By Michael Greger M.D. FACLM on February 18th, In , researchers in England reported a series of women with no evidence of celiac disease (the autoimmune disorder associated with gluten intolerance), who nevertheless resolved their chronic diarrhea on a gluten-free diet.

Send us your health questions Do home allergy and intolerance tests work? With allergies on the rise, many people are worried about whether they, or their children, may have an allergy, or an intolerance to certain foods. There are many companies that offer home testing – either in the form of a kit that can give you an instant result, or by testing samples that you send off. Home tests for coeliac disease Coeliac disease is not an allergy or an intolerance but an autoimmune disease. It causes severe gut problems when people who suffer from it eat gluten, and can lead to damage to the gut lining. Therefore people with coeliac disease need to avoid all gluten for the rest of their lives. There are a few home test kits available for coeliac disease that involve taking a finger prick of blood. You will get a result in a few minutes. Your doctor can also do the blood test for free. It is also crucially important that you have been eating gluten regularly for at least 6 weeks before taking the blood test. If you have already excluded gluten from your diet then the blood test will not be able to tell you whether or not you have coeliac disease. Home test for allergies Allergies are an over-reaction of your immune system to something which it wrongly identifies as a threat. One of the most common is hayfever – a reaction to pollen – and it involves a sudden release of antibodies called IgE antibodies. These cause a release of chemicals called histamines in your body which give the classic signs of itching, sneezing and runny eyes and nose. An allergic reaction to something will be quick – sometimes almost immediate. There are a few companies that sell tests for allergies. Some claim to be able to do this from samples such as a hair sample, others from things like your grip strength. None of these have any scientific validity at all. Only a blood sample can be used to identify an allergy. A blood test for IgE antibodies can be helpful in diagnosing an allergy, but IgE levels vary enormously between individuals and are also specific to particular things like pollen, or foodstuffs. A general measure of your overall IgE levels will not be very helpful. If you think you have an allergy to something, and are concerned about it, then you should visit a medical professional there are allergy clinics all over the UK. They will help identify it firstly through identifying the symptoms that you have and what triggers them, and then doing a specific test for the IgE antibodies that seem most likely, from your medical history, to be causing the trouble. Home test for intolerances Intolerances are very different from allergies. They cause symptoms that take hours, or even days, to manifest and can be difficult to diagnose. They are often caused by someone not having the right enzyme to digest a food properly, although can have other causes too, which can be difficult or impossible to test for. These have no scientific basis whatsoever. Blood tests for intolerances usually measure the levels of antibodies called IgG antibodies in the blood different from the IgE antibodies involved in an allergic reaction. These are the most common antibodies we have, and are involved in fighting disease and infection from viruses, bacteria and fungi. There has been a lot of interest in linking the gut symptoms that people suffer when eating some foods with IgG antibodies, but despite some researchers finding links, no diagnosis of a food intolerance can be made from an IgG test. Your IgG antibody levels will fluctuate daily depending on what you have been eating recently. In fact, some researchers have been working on a way of using IgG tests as a means of telling exactly what someone has been eating! The advice from expert groups around the world is that IgG tests should not be used as an attempt to diagnose an intolerance. This involves removing a single foodstuff from your diet for a period of time, and recording changes in symptoms. Then you should re-introduce the food and continue to monitor symptoms. It is very important not to eliminate common foodstuffs from your diet without consulting a medical professional – especially in growing children.

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### Chapter 6 : Gluten-free diet - Mayo Clinic

*(also known as non-celiac gluten sensitivity, or non-celiac wheat sensitivity) Some individuals who experience distress when eating gluten-containing foods and show improvement when following a gluten-free diet may have what is commonly referred to as gluten sensitivity (GS), instead of celiac disease (CD). It is important to keep in mind that GS is not well understood.*

They overlap with many other chronic conditions. Researchers are still trying to discover the exact biological cause of this condition, known as NCGS. As more and more people go to their doctor reporting unpleasant symptoms after eating gluten, researchers are trying to characterize these conditions so that NCGS can be better understood. The most common symptoms of NCGS are: They may ask you to keep a food and symptom journal to determine that gluten is the cause of your problems. After this cause is established and your tests come back normal for wheat allergy and celiac disease, your doctor may advise you to begin a gluten-free diet. There is a correlation between autoimmune disorders and gluten sensitivity. An allergist or gastroenterologist can run tests and discuss your history with you to help reach a diagnosis. Celiac disease can lead to severe health complications, especially in children. More than 83 percent of Americans who have celiac disease are undiagnosed and unaware they have the condition, according to the advocacy group Beyond Celiac. Getting diagnosed To diagnose celiac disease or wheat allergy, your doctor will need to conduct a blood or skin prick test. These tests are dependent on the presence of gluten or wheat in your body in order to work. Remember, NCGS has no formal diagnosis. Living a gluten-free or wheat-free lifestyle The treatment for celiac disease is adhering to a strict gluten-free diet. The treatment for a wheat allergy is to adhere to a strict wheat-free diet. If you have NCGS, the extent to which you need to eliminate gluten from your lifestyle depends on the severity of your symptoms and your own tolerance level. Many gluten-free and wheat-free alternatives to common foods are available such as bread, pasta, cereals, and baked goods. Be aware that wheat and gluten can be found in some surprising places. You might even spot them in ice cream, syrup, vitamins, and food supplements. Your allergist, gastroenterologist, or primary care doctor can advise you on which grains and products are safe for you to eat. Takeaway Wheat allergy, celiac disease, and NCGS have many similarities in their causes and symptoms. Understanding which condition you may have is important so that you can avoid the proper foods and follow appropriate treatment recommendations.

*Gluten intolerance (inc. Celiac Disease): Delayed onset symptoms caused by the inability to fully digest Gluten - a very large and complex protein found in wheat and other grains. Gluten intolerance affects around 15% of people and is marked by dozens of seemingly unrelated symptoms.*

Sign up now Gluten-free diet To follow a gluten-free diet, you must avoid wheat and some other grains, while choosing substitutes that provide nutrients for a healthy diet. Gluten is found in grains such as wheat, barley, rye, and a cross between wheat and rye called triticale. A gluten-free diet is essential for managing signs and symptoms of celiac disease and other medical conditions associated with gluten. A gluten-free diet is, however, popular among people without gluten-related medical conditions. The claimed benefits of the diet are improved health, weight loss and increased energy. Most clinical studies regarding gluten-free diets have been conducted with people who have celiac disease. Therefore, there is little clinical evidence about the health benefits of a gluten-free diet in the general population. Removing gluten from your diet likely changes your overall intake of fiber, vitamins and other nutrients. Your doctor or a dietitian can help you make appropriate dietary choices to maintain a well-balanced diet. Purpose The gluten-free diet is essential for managing the signs and symptoms of some medical conditions: Celiac disease is a condition in which gluten triggers immune system activity that damages the lining of the small intestine. Over time this damage prevents the absorption of nutrients from food. Celiac disease is an autoimmune disorder. Non-celiac gluten sensitivity causes some signs and symptoms associated with celiac disease – including abdominal pain, bloating, diarrhea, constipation, "foggy brain," rash or headache – even though there is no damage to the tissues of the small intestine. Gluten ataxia, an autoimmune disorder, affects certain nerve tissues and causes problems with muscle control and voluntary muscle movement. Wheat allergy, like other food allergies, is the result of the immune system mistaking gluten or some other protein found in wheat as a disease-causing agent, such as a virus or bacteria. The immune system creates an antibody to the protein, prompting an immune system response that may result in congestion, breathing difficulties and other symptoms. Claims about the general health benefits of a gluten-free diet are the motivation for other people to avoid wheat and other grains with gluten. Very little clinical research has been conducted, however, about the benefits of the diet for people who do not have a gluten-related medical condition. Diet details Following a gluten-free diet requires paying careful attention to both the ingredients of foods and their nutritional content. Allowed fresh foods Many naturally gluten-free foods can be a part of a healthy diet: Fruits and vegetables Beans, seeds and nuts in their natural, unprocessed forms Eggs Lean, nonprocessed meats, fish and poultry Most low-fat dairy products Grains, starches or flours that you can include in a gluten-free diet include:

### Chapter 8 : Can Cold Sores Be Caused by a Gluten Intolerance (or Sensitivity)?

*Does gluten intolerance (inclusive of both celiac disease and gluten sensitivity) cause one to develop more food intolerances? The answer is definitely yes, but perhaps not in the way that you think.*

It is not just one specific illness, but a series of conditions where a person has a reaction, not necessarily sufficient enough to call it an allergy. However, the intolerance is sufficient to cause damage over time to the intestines, even affecting the chemistry of the blood. In some people, with autoimmune diseases, this intolerance can make them harder to treat and in others, show the opposite effect. Each person is definitely affected differently, but very few people are aware that they have an intolerance at all. Some notice subtle changes – their pants do not fit as well as they used to. They put it down to getting older. They feel intense fatigue, as well as more headaches, but put it down to insufficient rest and too much stress. Some try diet after diet to find that their belly fat just will not budge. Overall, each one of them feels unwell, though they never consider the fact that they might be suffering from gluten intolerance. Gluten is a natural protein found in triticale, wheat, malt, rye, barley, spelt, wheat and kamut. However, unlike these, oats, which do contain lower levels of gluten, do not always affect gluten intolerance sufferers, and if they do, this is usually because the oats have been processed in an area where contamination from the other gluten grains is possible. If the person is suffering from Celiac Disease, any type of gluten can cause problems, further damaging the intestines. Within just days, symptoms start to improve and dissipate. As a result, gluten can have a negative impact on the body, most especially the immune system and digestive tract. Celiacs respond to gluten by attacking the hairy-like projections in their intestines, preventing them from absorbing important nutrients. Damage to the intestines from gluten might show no symptoms for many years, or be ignored as something else until symptoms become so severe that either Celiac Disease occurs a serious gluten allergy or damage has been done. Long-term gluten intolerance can make the body very sick. Severe intolerances include symptoms such as vitamin deficiencies, anaemia and unexplained loss of weight. Eventually, with medical supervision, it might be possible to reintroduce gluten, but this is not guaranteed. Gluten Intolerance and the Future No one yet knows what causes gluten intolerance; only that it exists and is caused by grain proteins. However, even if gluten grains cannot be reintroduced, there are many non-gluten alternatives that can be eaten instead. These include quinoa, amaranth, millet, buckwheat, corn, wild rice and rice. As a result, life without regular grains does not mean going without bread, cake and other treasures that many people take for granted in their daily lives.

## Chapter 9 : Wheat, Gluten Intoler.

*People with celiac disease need to avoid gluten, which is also found in rye and barley, and people with wheat allergies need to avoid wheat, but people with what is termed as non-celiac gluten.*

Published online Jun Elli L, Branchi F and Tomba C contributed equally to this work and wrote the manuscript; Ferretti F contributed to the writing of the manuscript and collected bibliography; Norsa L wrote the pediatric paragraph and Villalta D wrote the paragraph on allergy; Roncoroni L elaborated the paragraphs on gluten and gluten-free diet; Bardella MT developed the editorial scope and wrote the manuscript. Sforza 35, Milan, Italy. Published by Baishideng Publishing Group Inc. This article has been cited by other articles in PMC. In the recent years gluten ingestion has been linked with a range of clinical disorders. Celiac disease, wheat allergy and non-celiac gluten sensitivity represent different gluten-related disorders. Similar clinical manifestations can be observed in these disorders, yet there are peculiar pathogenetic pathways involved in their development. Celiac disease and wheat allergy have been extensively studied, while non-celiac gluten sensitivity is a relatively novel clinical entity, believed to be closely related to other gastrointestinal functional syndromes. On the other hand, non-celiac gluten sensitivity is still mainly a diagnosis of exclusion, in the absence of clear-cut diagnostic criteria. A multimodal pragmatic approach combining findings from the clinical history, symptoms, serological and histological tests is required in order to reach an accurate diagnosis. A thorough knowledge of the differences and overlap in clinical presentation among gluten-related disorders, and between them and other gastrointestinal disorders, will help clinicians in the process of differential diagnosis. Although they are characterised by peculiar pathogenetic pathways involved in their development, they share similar clinical manifestations making their differential diagnosis challenging. Surveys conducted among the general population confirm that increasing numbers of consumers worldwide avoid gluten-containing food, irrespective of the presence of a known illness or allergy[ 5 , 6 ]. Switching to a gluten-free diet GFD is often viewed as a lifestyle change rather than a proper dietary treatment. Accordingly, the market for gluten-free products is constantly growing, with the latest European reports estimating a compound annual growth rate of Different mechanisms are involved in the pathogenesis of gluten-related disorders. Gluten is the main structural protein of wheat, composed of two main fractions depending on their solubility in aqueous alcohols: Homologous proteins have been found in rye and barley. In celiac disease CD a T-cell mediated autoimmune reaction is triggered by gluten-derived peptides[ 9 ]. The autoimmune inflammatory cascade is localised in the small bowel, where it leads to the classical enteropathy and malabsorption syndrome. Among the gluten-related disorders CD is the best known one to date: Wheat allergy WA represents another type of adverse immunologic reaction to proteins contained in wheat and related grains, with different clinical presentations depending on the route of exposure. Patients affected by NCGS usually report a wide range of intestinal and extra-intestinal symptoms arising shortly after the ingestion of gluten-containing food in the absence of CD or WA[ 1 , 10 ]. Although the pathogenetic mechanisms leading to the onset of NCGS are far from being clearly understood, the current opinion is that there is a non-autoimmune non-allergic process[ 11 ]. To date, a complete definitive diagnostic flowchart for gluten-related disorders has yet to be established. Gliadins are supposed to be the active fractions of gluten; in fact, they contain the immunogenic peptides especially the 33mer and are able to exert a direct cytotoxic effect on the cell[ 16 , 17 ]. Non-classical features include irritable-bowel-type symptoms, hypertransaminasemia, cerebellar ataxia and peripheral neuropathy[ 18 ]. In the past, most patients diagnosed with CD were children with severe organic manifestations, but in more recent years there has been an increase in diagnosis of adults and pauci-symptomatic patients[ 10 ]. The history of CD can be rarely complicated by refractory celiac disease or malignancies including lymphoproliferative disorders and carcinoma of the small bowel[ 19 - 24 ]. The adherence to a restrictive GFD leads to the resolution of symptoms and to the gradual healing of histological abnormalities[ 26 ] even if the complete recovery of the intestinal mucosa is rare and low-grade mucosal

inflammation seems to persist in many treated celiac patients as shown by follow-up duodenal biopsies[ 27 ]. However, there is strong interest among both patients and physicians in the development of alternative treatments for CD, with the aim of achieving mucosal healing and symptoms resolution in those patients with incomplete response or inadequate compliance to the GFD[ 28 ]. Many options are currently under investigation through clinical trials, including oral proteases, zonulin-inhibitors, gluten-binding agents and desensitization strategies[ 17 , 29 ]. TTG test has a wide diffusion as enzyme linked immunosorbent assay or radioimmunoassay commercial kits and gained an important efficiency since the introduction of human recombinant substrates. However, EMA test is expensive monkey esophagus or human umbilical cord are used as substrates and operator dependent due to the interpretation of immunofluorescent pattern[ 32 ]. Multiple biopsies of the duodenum at least four are recommended as a critical component of the diagnostic evaluation and represent the gold standard in adults. CD damage in the duodenal mucosa is not uniformly distributed so multiple biopsies are necessary to reduce the probability of false negative results[ 34 ]. The signs of gluten-related enteropathy out of duodenal biopsy range from an increase in the intraepithelial lymphocytes to villous atrophy, as staged by Marsh et al[ 14 ] and successively by Oberhuber et al[ 35 ]. However, the lymphocytic infiltration of the intestinal epithelium in the absence of villous atrophy Marsh 1 is considered a non-specific finding, warranting further investigations[ 36 ]. In fact the diagnosis of CD is not always clear-cut: Moreover, other causes of villous atrophy, such as common variable immunodeficiency, autoimmune and chronic inflammatory disorders, drugs and neoplasia, Giardiasis have to be excluded in all patients with particular attention in case of negative serology[ 41 , 42 ]. It is recommended to assess serology and duodenal histology while the patient is still on a gluten-containing diet[ 18 ]. Patients with suspected but unproven CD who are already on a GFD at the time of referral, may not show histologic changes or antibody titers consistent with CD due to the improvement of the standard diagnostic tests caused by the GFD itself[ 43 ]. For a long time, the guidelines have recommended to prescribe 10 grams of gluten per day for a duration of wk[ 44 ]. The new proposed low-dose 14 d long gluten challenge has shown higher compliance and tolerability. The added diagnostic sensitivity of extending the low-dose challenge from 2 to 8 wk is yet to be known. Ingested wheat can cause IgE-mediated wheat allergies in both children and adults. Although the sensitization to wheat assessed by serum IgE is more prevalent in adults, WA shows greater prevalence in children[ 45 , 46 ]. Immediate wheat allergy is mainly seen in children who commonly outgrow it by school-age, the same as with egg or milk allergy[ 47 , 48 ]. The majority of wheat allergic children suffer from moderate-to-severe atopic dermatitis and wheat ingestion may elicit typical IgE mediated reactions, including urticaria, angioedema, bronchial obstruction, nausea and abdominal pain, or in severe cases systemic anaphylaxis[ 47 ]. In adults FA to ingested wheat is infrequent: In adults, FA gastrointestinal symptoms could be mild and difficult to recognize, the most common are diarrhea and bloating. Some patients may develop symptoms also after eating meals contaminated by uncooked wheat flour, otherwise no problems are usually reported after the ingestion of cooked wheat[ 50 ]. However, they are affected by a low predictive value. In addition, some authors have showed that commercial wheat flour SPT solutions differ in protein content showing that the improvement and standardization of SPT for wheat is highly recommended[ 53 ]. The identification of molecular allergens for laboratory methods has profoundly changed the diagnostic approach to allergic diseases in the recent years. Molecular-based allergy MA diagnostics could overcome some limitations of sIgE in vitro assays using wheat flour extracts. If SPT and the sIgE assays with flour extracts or molecular allergens are inconclusive, functional assays are required. They are considered the gold standard for the diagnosis but are accompanied by a risk of severe induced reactions and are impractical in busy practice settings. In the recent years a flow cytometry-assisted basophil activation test BAT has been introduced as an in vitro functional test for the diagnosis of immediate-type allergy, and it seems a good alternative for those patients at risk of severe anaphylactic reactions or with contradictory test results. Some authors have recently showed the usefulness of BAT for the diagnosis of WA and in particular its ability to discriminate tolerant vs. Although BAT is more expensive and technically challenging compared to conventional in vitro tests, its use

has been gradually increasing in clinical practice. In conclusion, WA is not easily diagnosed with conventional SPT or sIgE assays using wheat flour extracts, since their diagnostic predictivity is unsatisfactory. Challenge tests remain the gold standard for WA diagnosis, but they are cumbersome and potentially dangerous. MA diagnostics and BAT represent new useful tools for the in vitro diagnosis of WA and in some cases may effectively replace the in-vivo functional tests. Nowadays, the overall prevalence of the condition is difficult to estimate. According to a study performed by the National Health and Nutrition Examination Survey in the United States, the prevalence of self-prescribed GFD in an unselected population of subjects aged 6 years or older was 0. The clinical presentation of NCGS includes gastrointestinal symptoms, such as abdominal pain, bloating and altered bowel habit, and systemic symptoms, such as fatigue, headache, bone or joint pain, mood disorders and skin manifestations e. Symptoms usually closely follow the consumption of gluten and disappear after gluten withdrawal. Contrary to CD and wheat allergy, there are no clear serologic or histopathologic criteria for clinicians to confirm the diagnosis of NCGS. As far as any intestinal damage is concerned, an increase in the number of lymphocytes infiltrating the epithelium has been described in a subset of NCGS patients[ 64 ]. In fact, NCGS has often been described as an IBS-like entity, given the apparently functional nature of both syndromes and the evident overlap of symptoms[ 65 ]. The recent evidence about the efficacy of a low-FODMAPs diet in this subsets of patients suggests the hypothesis that some components of wheat other than gluten may be responsible for triggering symptoms[ 68 , 69 ]. In fact, oligosaccharides like fructans, contained in wheat and related grains, have been proven able to exert an osmotic effect in the intestinal lumen and increase gas production from bacterial fermentation[ 70 , 71 ]. Other plant proteins contained in wheat, such as lectins, agglutinins and amylase-trypsin inhibitors, may have a role in the development of symptoms after the ingestion of cereals by triggering the innate immune response[ 72 - 74 ]. In a recent study by Biesiekierski et al[ 77 ] the concept of NCGS as a syndrome has been questioned. A more appropriate standard for the confirmation of NCGS would be an elimination diet followed by double-blind placebo-controlled gluten challenge[ 62 ]. Recently Kabbani et al[ 78 ] have proposed a diagnostic algorithm based on the combination of absence or presence of various clinical, serologic and histological markers with the purpose of identifying NCGS and distinguishing it from CD. This algorithm may prove a useful tool in clinical practice because it provides suggestions for the effective evaluation of patients with gluten-related symptoms already undertaking a GFD, for whom the exclusion of CD and confirmation of NCGS may be a cumbersome task[ 78 ]. In patients with suspected NCGS, a short-term low-dose gluten challenge as discussed above can turn out to be a more suitable pragmatic approach than the traditional 8 wk long approach[ 43 ]. Nowadays, due to the absence of any reliable biomarker for NCGS diagnosis, a double-blind placebo-controlled gluten challenge could be considered a possible gold standard to compare other algorithms or markers. The clinical suspicion of CD should be raised in children with unexplained chronic gastrointestinal symptoms, as well as extraintestinal manifestations such as growth retardation, iron deficiency anemia, weight loss, chronic fatigue, delayed puberty, amenorrhea, recurring bone fractures or alterations of liver function tests. In the case of positive serology, the current guidelines suggest to follow two different paths for the diagnostic confirmation. If these criteria are not met, similarly as in adult patients, an upper endoscopy with duodenal biopsies should be performed to confirm the presence of histological signs of enteropathy[ 33 ]. Two studies, both published in by Tanpowpong et al[ 81 ] deal with gluten avoidance in children in New Zealand[ 6 , 81 ]. In the second one, several clinical features such as irritability, poor temper, diarrhea, weight issues, pervasive developmental disorder and family history of CD were found to be independent predictors of gluten avoidance[ 81 ]. The relationship between autism and gluten has also been broadly studied, with a single double-blind cross-over study not demonstrating any GFD benefit in autistic children who were not affected by CD[ 82 ]. The suggested approach is similar to the adults, recommending a gluten challenge after at least 8 wk on GFD[ 83 ]. Due to the lack of evidence, however, no guidelines are available on NCGS in children. Wheat allergy Epidemiological studies report a prevalence of WA in children of around 0. A United States study estimated the resolution rates of pediatric wheat allergy at: The guidelines published in by the American

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National Institute of Allergy and Infectious Disease recommend that food allergies including WA should be considered in those individuals presenting with anaphylaxis or a combination of clinical symptoms occurring within minutes to hours after ingesting food, especially in young children or if it is the second episode after the ingestion of specific food. A SPT enables the identification of food categories responsible for triggering IgE-mediated allergic reactions, but a positive SPT alone cannot be considered diagnostic [ 85 ]. Similarly, the sole presence of allergen-specific IgE in the serum is not sufficient to confirm the diagnosis of WA. The reference standard for the diagnosis of food allergies is the double-blind placebo-controlled food challenge as for NCGS. An expanding body of evidence sustains the on-going debate on the appropriateness of gluten elimination from the diet in the absence of CD or WA. Table 1 Diagnostic tests for gluten related disorders Serology.