


# Celiac disease: Understandings in diagnostic, nutritional, and medicinal aspects

International Journal of  
Immunopathology and Pharmacology  
Volume 35: 1–22  
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DOI: 10.1177/20587384211008709  
journals.sagepub.com/home/iji  


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## Abstract

Celiac disease (CD) is characterized by clinical polymorphism, with classic, asymptomatic or oligosymptomatic, and extra-intestinal forms, which may lead to diagnostic delay and exposure to serious complications. CD is a multidisciplinary health concern involving general medicine, pediatric, and adult gastroenterology, among other disciplines. Immunology and pathology laboratories have a fundamental role in diagnosing and monitoring CD. The diagnosis consists of serological testing based on IgA anti-transglutaminase (TG2) antibodies combined with IgA quantification to rule out IgA deficiency, a potential misleading factor of CD diagnosis. Positive TG2 serology should be corroborated by anti-endomysium antibody testing before considering an intestinal biopsy. Owing to multiple differential diagnoses, celiac disease cannot be confirmed based on serological positivity alone, nor on isolated villous atrophy. In children with classical signs or even when asymptomatic, with high levels of CD-linked markers and positive HLA DQ2 and/or DQ8 molecules, the current trend is to confirm the diagnosis on basis of the non-systematic use of the biopsy, which remains obligatory in adults. The main challenge in managing CD is the implementation and compliance with a gluten-free diet (GFD). This explains the key role of the dietitian and the active participation of patients and their families throughout the disease-management process. The presence of the gluten in several forms of medicine requires the sensitization of physicians when prescribing, and particularly when dispensing gluten-containing formulations by pharmacists. This underlines the importance of the contribution of the pharmacist in the care of patients with CD within the framework of close collaboration with physicians and nutritionists.

## Keywords

Celiac disease, diagnosis, gluten-free diet, gluten-free drugs

Date received: 24 February 2021; accepted: 18 March 2021

## Introduction

Celiac disease (CD) is an immune-mediated systemic disorder triggered by gluten consumption, occurring in genetically predisposed individuals.<sup>1–3</sup> Gluten refers to insoluble cereal proteins, including prolamins found in wheat (gliadins), rye (secalins), barley (hordein), and oats (avenins). However, the amino acid sequences inducing CD-associated immune reactions are less prevalent in avenins, which explains the tolerance of small amounts of oats by patients with CD.<sup>4</sup>

Unlike CD, recently described gluten sensitivity is characterized by negative serological tests and the absence of villous atrophy, and despite the

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presence of intestinal or extra-intestinal symptoms, it can be resolved by a gluten-free diet (GFD).<sup>5,6</sup>

In spite of the classical symptoms strongly suggestive of CD, the last decades have seen the emergence of asymptomatic, oligosymptomatic, or extra-intestinal often misleading forms; hence, the diagnostic delay and the risk of potentially serious complications<sup>7–10</sup> can be avoided by implementing GFD.<sup>8,11</sup> In addition to medical care for patients with CD, the role of the nutritionist is essential in initiating and adhering to implementing GFD. Physicians and pharmacists often fail to check for gluten when prescribing and dispensing medications; yet, it is frequently a component in the solid phase of certain galenic forms. Therefore, these drugs represent a potential source of hidden gluten.<sup>12</sup>

The aim of this review is to shed light on the diagnostic, nutritional, and medicinal aspects of CD with an emphasis on practical issues in the management of celiac patients.

## Epidemiological data

The overall prevalence of CD among the general population varies from region to region; it fluctuates between 0.5% and 1% in Europe and North America,<sup>6,13,14</sup> and surprisingly ranges from 2% to 3% in Finland and Sweden.<sup>15</sup> High rates are recorded in North Africa, Middle East, and Asia-pacific regions.<sup>16</sup> Similarly, the prevalence of the disease is reported to be high in Arab countries, reaching 3.2% in Saudi Arabia, due to dietary habits such as excessive consumption of barley and wheat, and to a higher frequency of DR3-DQ2 haplotypes.<sup>17</sup> It is probably underestimated in South East Asia and Sub-Saharan Africa, and is almost unknown in many other countries.<sup>18</sup>

The disease is more prevalent, with large discrepancies between series in the so called high risk groups, such as type 1 diabetes (1–12%);<sup>19,20</sup> autoimmune thyroid disease (2–6%);<sup>16,21</sup> Down syndrome (2–6%);<sup>22,23</sup> autoimmune hepatitis (3–7%);<sup>24,25</sup> Turner syndrome (4–5%);<sup>26,27</sup> CD first-degree family members (10–20%);<sup>28,29</sup> individuals with iron deficiency anemia (3–15%);<sup>29,30</sup> patients with osteoporosis (1–3%),<sup>29</sup> and many other clinical conditions.<sup>16,28</sup>

In addition, The incidence of CD has significantly increased over the past 30 years, from 2–3 to approximately 9–13 new cases per 100,000 inhabitants per year.<sup>31</sup> This likely reflects a fortuitous discovery of non-classic and asymptomatic forms

of the disease through serological testing.<sup>10,13,29</sup> Indeed, sero-epidemiological studies suggest that for each diagnosed CD case, there could be 3–7 undiagnosed cases.<sup>32</sup>

## Immunopathologic aspects

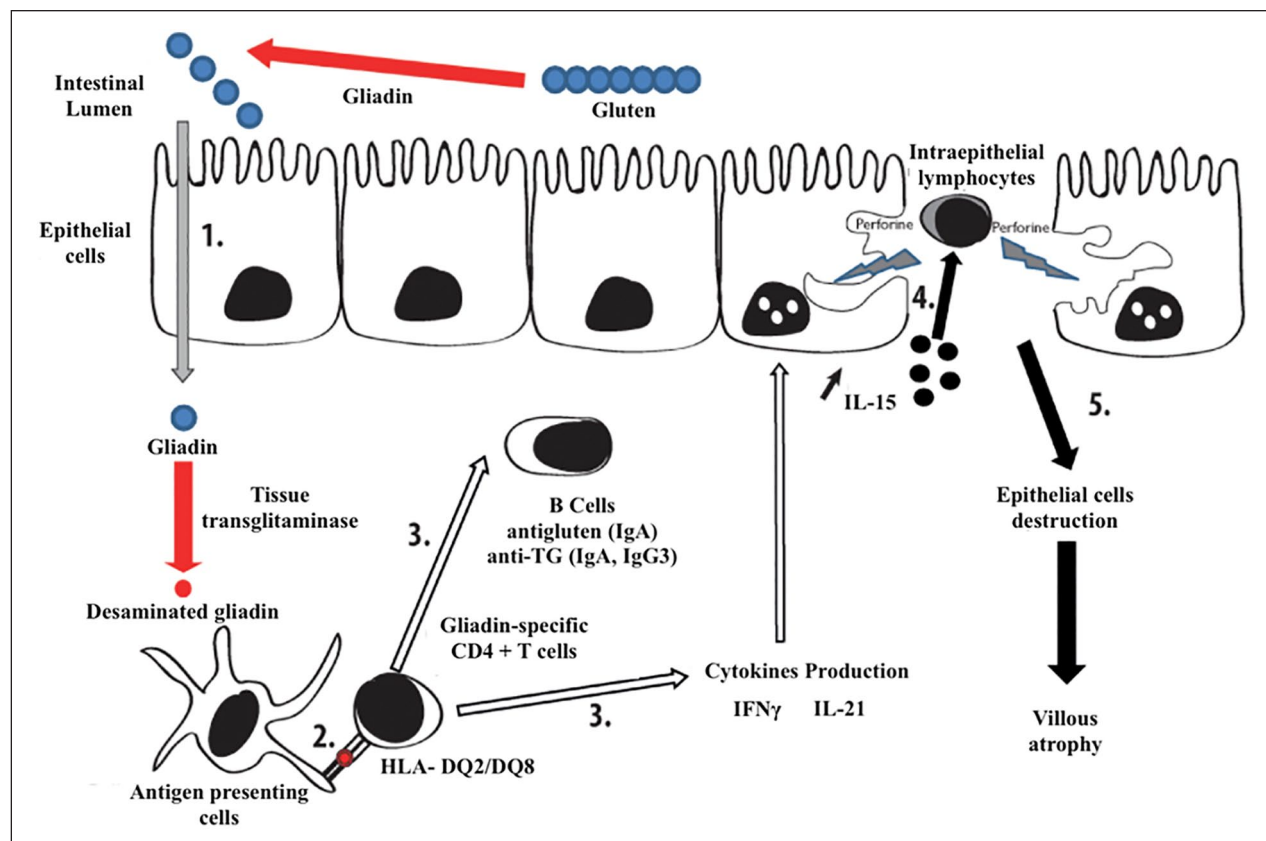
The pathogenic process of CD, as described in Figure 1, takes place in five main steps: (1) the glutamine residues of the ingested gliadin are converted into glutamates by tissue transglutaminase. (2) The modified gliadin is taken up by antigen-presenting cells carrying Human Leukocyte Antigen (HLA)-DQ2 or DQ8, thus activating gliadin-specific CD4<sup>+</sup> T cells. (3) These cells produce pro-inflammatory cytokines, such as interleukin (IL)-15, IL-21, and interferon-gamma (IFN $\gamma$ ), and allow specific anti-gliadin and anti-transglutaminase responses. (4 and 5) IFN $\gamma$  and IL-21 induce a massive release of IL-15, which leads to the proliferation and survival of intraepithelial lymphocytes (IEL), the activation of which alters epithelial cells, thus provoking villous atrophy.<sup>7,33</sup>

## The new face of CD

CD status has gradually changed from a rare enteropathy to a common systemic disease, and as a clinical chameleon, the CD presents in symptomatic, asymptomatic, potential, and refractory forms affecting all age groups.<sup>34</sup>

In its classic form, the disease usually starts at the age of 6 months, a few weeks after introducing gluten into the diet. It manifests as chronic diarrhea with abundant stools, accompanied by anorexia and apathy. Other clinical symptoms such as recurrent vomiting, anorexia, chronic constipation, growth or puberty delay, short stature, and irritability, are fairly characteristic and require prompt screening for the disease.<sup>35</sup> Physical examination often shows abdominal meteorism, signs of undernutrition, loss of muscle and fat tissues, a break in the weight curve, and sometimes, slower growth in height. However, non-classic forms are more frequent than classic ones, with extra-intestinal symptoms (Table 1), thus suggesting CD.<sup>36,37</sup> Even obese children may have CD, which undoubtedly contributes to the failure and delay of diagnosis.<sup>38</sup>

In adults, most patients with CD do not present with diarrhea, but rather “atypical or extra-intestinal”



**Figure 1.** Simplified immunopathological mechanism of celiac disease (adapted from<sup>7</sup>).

**Table 1.** Main circumstances justifying serological testing for CD.<sup>7,35–37,39–44</sup>

Digestive disorders	Extra-digestive disorders	Associated pathologies
Chronic diarrhea	Refractory iron deficiency anemia	CD in first degree relative
Irregular stools	Vitamin or mineral deficiencies: Vit B12, Vit B6, Vit D, folate, zinc	Type I diabetes
Malabsorption	Hypoplasia of tooth enamel	IgA deficiency
Abdominal bloating	Growth retardation	Sjögren syndrome
Chronic constipation (more common in children)	Chronic fatigue	Autoimmune thyroiditis
Recurrent abdominal pain	Puberty delay	Autoimmune liver diseases
Irritable bowel syndrome	Amenorrhea	Down syndrome
Poor weight gain	Early menopause	Turner syndrome
Decreased appetite	Unexplained liver cytolysis	Williams syndrome
Anorexia	Bone pain, Fractures on osteopenia	CVID (common variable immune deficiency)
vomiting	Osteoporosis	Neurologic disorders (neuropathy, ataxia, migraine, epilepsy, headache, abnormal EEG*)
Gastro-esophageal reflux	Recurrent aphthous stomatitis	Sleep disordered breathing
	Peripheral neuropathy	
	Ataxia	
	Unexplained hemorrhagic syndrome	
	Herpetiform dermatitis	
	Hyposplenism	

\*Electroencephalography abnormalities: spike/sharp wave discharges, especially in the occipital lobes and in the central-temporal sites, and in diffuse distribution.

symptoms such as anemia, osteoporosis, dermatitis herpetiformis, abdominal pain, and neurological disorders.<sup>45</sup> Furthermore, in children and adults alike,

serological testing should be routinely ordered in the presence of clinical conditions with a high potential for association with CD (Table 1).

The classical forms of CD are characterized by different laboratory findings such as anemia due to iron and/or folate deficiency, hypoprotidemia, hypoalbuminemia, decreased prothrombin time, and vitamin K-dependent factors, and lowered cholesterol mainly related to lipid leakage in the stool.<sup>46,47</sup> In fact, biological abnormalities, such as hypocalcemia and hypophosphatemia with decreased alkaline phosphatase owing to vitamin D malabsorption, or hypertransaminasemia, may be the only suggestive signs of CD.<sup>48–50</sup>

### Immunoserological tests

Immunoserological tests are excellent diagnostic and monitoring tools for CD; they allow for the identification of patients at risk of developing the disease, better selection of patients requiring intestinal biopsy, and monitoring adherence to GFD.<sup>47,49,51</sup> These tests aim to detect auto-antibodies recognizing two main antigens:

- Transglutaminase 2: targeted by anti-tissue transglutaminase 2 (anti-TG2) and anti-endomysium (EmA) Abs, which are very sensitive and specific for CD.<sup>51–54</sup>
- Gliadin: targeted by the conventional anti-gliadin Abs, which are now obsolete owing to their low sensitivity and specificity. However, Abs against deamidated gliadin peptides (DGP) perform just as well as anti-TG2.<sup>55,56</sup>

### Immunobiological diagnostic approach

In daily practice, when CD is suspected, whether symptomatic or not, or in high-risk individuals, the first line of screening is based on the detection of IgA anti-TG2, followed if positive by EmA, a highly specific marker, which improves the positive predictive value (PPV) of serological tests.<sup>57–60</sup> Indeed, the simultaneous positivity of several tests makes the diagnosis of CD very likely.<sup>61,62</sup> In addition, a combination of IgA anti-TG2 with IgG anti-TG2 allows the exclusion of CD potentially occulted by IgA deficiency.<sup>57,58,63</sup> Additionally, the PPV of these tests in populations at low risk for CD depends on antibody titers. Low titers (less than three times the cut-off) in asymptomatic patients should be retested after 3–6 months under a gluten-rich diet before considering endoscopy and

**Box 1.** Possible false negative serological tests in celiac disease.<sup>39</sup>

- Age <2 years
- Selective IgA deficiency
- Reduction or elimination of gluten in the diet
- Use of corticosteroids or immunosuppressive agents
- Possible laboratory error

biopsies.<sup>2,57</sup> Moreover, the sensitivity of these tests is lower in children under 2 years of age; therefore, besides IgA anti-TG2, IgA DGP testing is recommended for this age group.<sup>39,64</sup>

As a reproducible, non-invasive, and highly sensitive test, the salivary anti-transglutaminase testing is a promising screening tool for CD.<sup>65,66</sup>

Notably, serological tests can be falsely negative in certain circumstances as listed in Box 1.

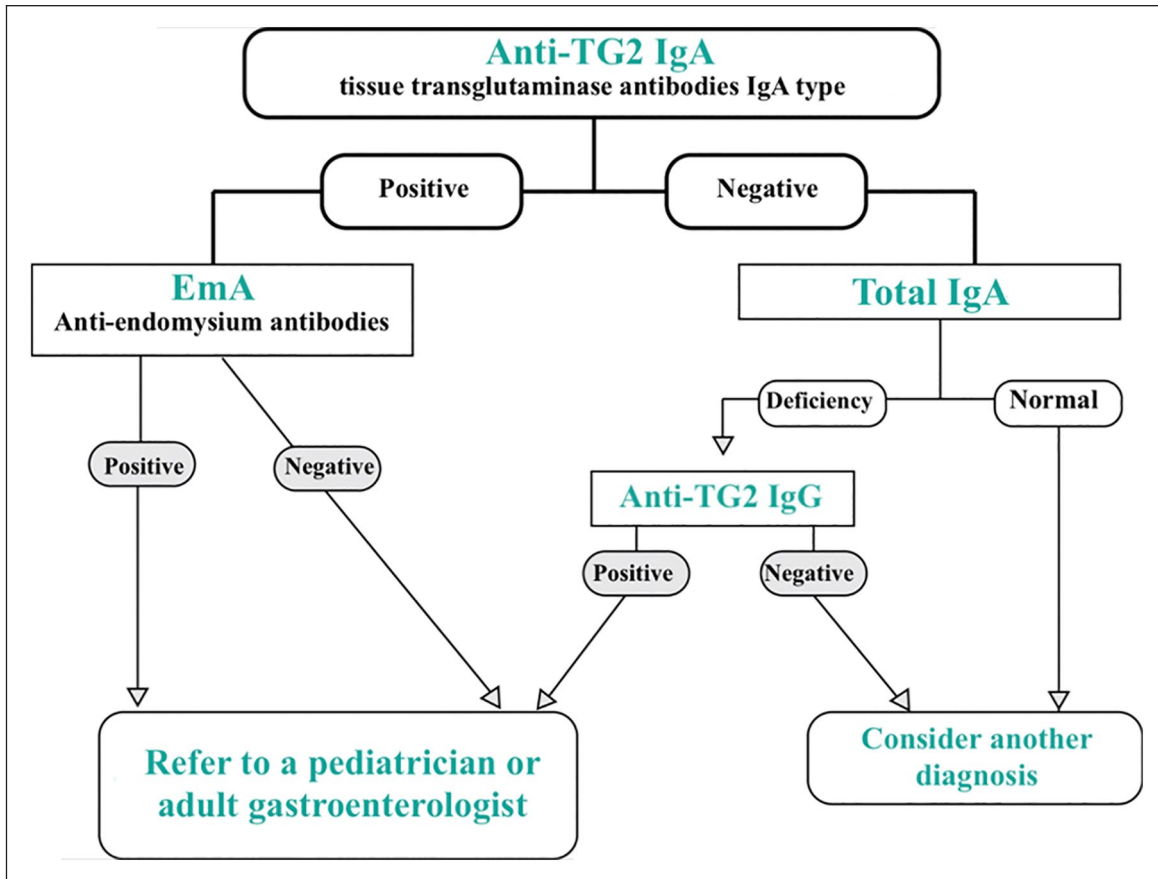
### Rapid test screening for CD

Physiologically present in the intracellular compartment of erythrocytes,<sup>67</sup> TG2 made it possible to develop rapid tests based on a chromatographic method using an endogenous TG obtained from the erythrocytes of patients. However, the performance of the rapid tests remains slightly lower than that of serological tests.<sup>68,69</sup> Several studies have demonstrated an interest in rapid tests showing a relatively good correlation with whole blood tests, and good positive and negative predictive values for ambulatory CD screening, particularly in the pediatric population.<sup>70</sup> They could, therefore, be used for diagnostic purposes by the physician, even in an office setting.<sup>68</sup>

### Role of the general practitioner in the management of CD

In their daily practice, general practitioners (GP) often encounter patients with CD, regardless of their location. These doctors must rely on specific diagnostic criteria; however, this is difficult because of the wide range of clinical manifestations that patients present with.<sup>39</sup>

GPs must know which serological screening tests to order, how to interpret the results, and which patients are to be referred to a specialist.<sup>39</sup> Thus, according to the diagnostic algorithm proposed in Figure 2, they must refer to a pediatrician or adult gastroenterologist, any patient whose serological tests are positive, for further evaluation.



**Figure 2.** Immunoserological diagnosis procedure of CD.

Indeed, the presence of specific antibodies in patients with CD-like symptoms is not sufficient to establish diagnosis owing to many clinical and laboratory circumstances (Box 2) mimicking CD.<sup>40,71</sup>

### HLA typing

CD is linked to a strong genetic predisposition, chiefly represented by the HLA-DQ2 and DQ8 systems, which have a high negative predictive value. In fact, less than 1% of patients with CD are negative for both HLA-DQ2 and DQ8, as these are present in approximately 95% and 5% of the cases, respectively, and sometimes both molecules are found in patients.<sup>2,72,74</sup> HLA typing cannot be performed as a CD diagnosis tool, since approximately 30–40% of the general population carry HLA-DQ2 and/or DQ8 molecules, and only about 4% of them will develop CD.<sup>74–76</sup> On the other hand, HLA-DQ2 and DQ8 typing can be useful when the results of the biopsy are uninformative, or in patients who had initiated GFD on their own prior to serologic testing. CD can also be ruled out

in symptomatic patients with negative serological tests as well as in patients considered at high risk, such as first-degree relatives of a patient with CD.<sup>74,77</sup>

### Histopathological diagnosis of CD

Pathologic diagnosis is established or confirmed according to the modified Marsh-Oberhuber and Corazza-Villanacci classifications, with different scales based on the number of intraepithelial lymphocytes, crypt hyperplasia, and villous atrophy<sup>78,79</sup> (Table 2). The Corazza score has less variability and benefits from more agreement between pathologists.<sup>77</sup>

In order to appropriately assess the histological abnormalities of CD according to commonly used criteria, it is recommended to correctly orient the endoscopic sampling (four to six staged biopsies of the bulb and/or the second duodenum) and to repeat levels of biopsy sections. In fact, an imperfectly oriented sample can give a false appearance of villous atrophy (VA).<sup>5,80</sup>

**Box 2.** Differential diagnoses of celiac disease.<sup>40,71–73</sup>

• Anorexia nervosa	• Cystic fibrosis
• Autoimmune enteropathies	• Cow's milk protein intolerance
• Intestinal microbial swelling	• Tropical sprue
• Collagen sprue	• Whipple's disease
• Crohn's disease	• Zollinger-Ellison syndrome
• Giardiasis	• Eosinophilic gastroenteritis
• HIV enteropathy	• Alpha chain disease
• Hypogammaglobulinemia	• Graft versus host disease
• Infectious gastroenteritis	• Intestinal transplant rejection
• Intestinal lymphoma	• Malnutrition
• Post-radiation enteritis	• Enteritis (rotavirus, adenovirus, cryptosporidiosis, microsporidiosis, strongyloidosis)
• Ischemic enteritis	• Microvillous atrophy
• Intestinal tuberculosis	• Epithelial dysplasia
• Lactose intolerance	• Abetalipoproteinemia
• CVID	• Post-drug enteropathy (ex. Olmesartan)
• IgA deficiency	

**Table 2.** Summary of the histological classifications commonly used for CD diagnosis.<sup>72</sup>

March modified-Oberhuber	Histological criterion			Corazza-Villanacci
	Increased intraepithelial lymphocytes*	Crypt hyperplasia	Villous atrophy	
Type 0	No	No	No	None
Type 1	Yes	No	No	Grade A
Type 2	Yes	Yes	No	
Type 3a	Yes	Yes	Yes (partial)	Grade B1
Type 3b	Yes	Yes	Yes (subtotal)	
Type 3c	Yes	Yes	Yes (total)	Grade B2

\*>40 intraepithelial lymphocytes per 100 enterocytes for Marsh Modified (Oberhuber).

\*>25 intraepithelial lymphocytes per 100 enterocytes for Corazza.

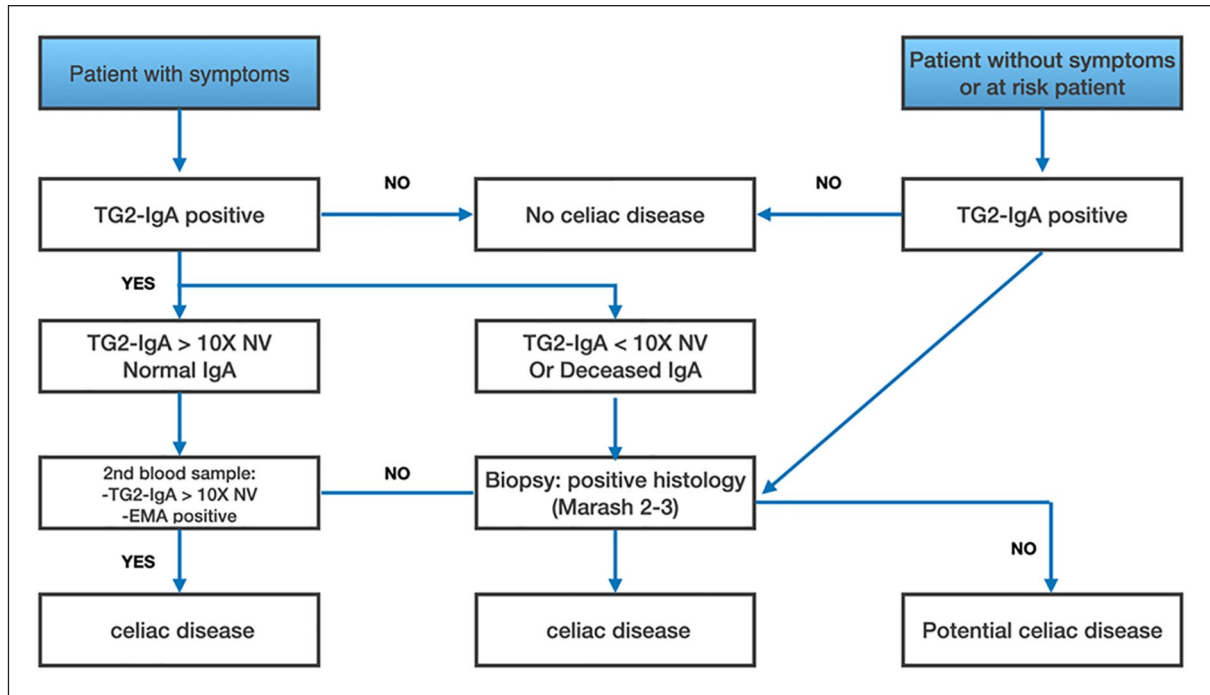
The major histological criteria of CD include VA of varying degrees with an increased number of IEL. These two signs, although nonspecific, strongly suggest CD and are associated with crypt hyperplasia and increased chorion cell density.<sup>81,82</sup> However, VA and increased IEL can be associated with various pathologies, as listed in Box 2.<sup>83</sup> In addition, patients with an isolated increase in IEL with positive serological tests are considered as potential candidates for CD as an asymptomatic latent form, while in the majority of cases, the presence of lonely intraepithelial lymphocytosis does not correspond to CD.<sup>84</sup>

On the other hand, almost all VAs associated with IEL, crypt compensatory hyperplasia, chorion hypercellularity (increased density of inflammatory cells and IgA plasma cells), and positive serological tests, correspond to silent forms of CD.<sup>81,85</sup>

### What can we do without the intestinal biopsy?

In children with suspected CD, the current trend is the unsystematic use of intestinal biopsy.<sup>86</sup> Notably, the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition has proposed a biopsy-free approach in symptomatic children meeting the following four criteria: typical clinical signs, anti-TG2 10-fold or more the upper limit of normal (ULN), positive EmA, and positive HLA DQ2 and/or DQ8.<sup>87,88</sup>

More recently, a group of experts assume that even asymptomatic children can be accurately diagnosed with CD without biopsy, but only on basis of high titers of IgA anti-TG2 (10-fold or more the ULN), positive EmA tests on 2 blood samples. They also consider that HLA analysis is not required for accurate diagnosis.<sup>89</sup> Conversely,



**Figure 3.** Proposal for a CD diagnostic approach to overcome intestinal biopsy in symptomatic children with positive anti-TG2 (TG2-IgA) and EMA testing. In asymptomatic or at-risk children, the positivity of TG2-IgA antibodies should lead to a biopsy and histological analysis. Adapted from.<sup>86</sup>

intestinal biopsy becomes necessary in the event of clinical manifestations suggestive of CD with negative or discordant serological tests, associated with the positivity of HLA DQ2/8 typing.<sup>2,37,90,91</sup> In addition, patients at risk of CD with positive anti-TG2 testing cannot be exempted from the intestinal biopsy.<sup>86</sup> In accordance with the above-mentioned guidelines, Husby et al.<sup>86</sup> highlighted situations where intestinal biopsy is unnecessary to diagnose CD, particularly in children (Figure 3).

In all cases, the decision to perform or not biopsies in this category should be made collegially with the parent (s) and, if applicable, with the child.<sup>92</sup>

In adults, the positivity of serological tests is insufficient to establish the diagnosis of CD, since false-positive cases are frequent in this group.<sup>93</sup> It is, therefore, necessary to complement the serological testing with an intestinal biopsy to confirm the disease before initiating a lifelong GFD.<sup>94-96</sup>

### Diet and gluten-free products

GFD can only be prescribed once the diagnosis of CD has been made with certainty.<sup>97</sup> Rigorous

adherence to the GFD results in the absence of functional symptoms within a few days and rapid weight gain. The diet also leads to the decrease or even the disappearance of the VA, thus, avoiding the occurrence of complications.<sup>97</sup>

In general, GFD consists of excluding the four categories of cereals that contain gluten and any food derived from them. Patients with CD must, therefore, systematically exclude bread, pasta, pizza, pies, cakes, and other pastries made from wheat flour as well as industrial food products and preparations, whose composition may contain gluten.<sup>98,99</sup> Moreover, patients should be encouraged to consume whole grain gluten-free foods (e.g. quinoa, gluten-free oats, and teff) and avoid gluten-free cereals (e.g. white rice and ground corn).<sup>100</sup>

The GFD which seems easy in theory, is in fact complicated and difficult to follow, especially in nurseries and schools, restaurants, and even at home.<sup>101</sup> Gastroenterologists, pediatricians, and GPs must therefore convince the patient to follow this diet and emphasize the importance of its life-long compliance.<sup>97,98</sup> In this regard, the involvement of the dietitian in the care of patients with CD is fundamental.

**Box 3.** Clinical conditions justifying the referral of celiac patient to the dietitian.<sup>100</sup>

- At the time of diagnosis: initial assessment, followed by 2–3 visits during the first year, then 1–2 annual visits
- Suspected gluten exposure (positive serology after 1 or more years of GFD)
- Lactose intolerance
- Fructose intolerance
- Food allergy
- Constipation/Diarrhea/Gastroesophageal reflux
- Weight fluctuations (gain and loss)
- Deficits or toxicity of Micronutrients
- Gastroparesis
- Hypercholesterolemia
- Type 1 diabetes
- Refractory celiac disease

### When to refer a patient with CD to a dietitian

After confirmation of CD, the clinical conditions listed below (Box 3) require a systematic referral of the patient to an experienced dietitian as part of a collaborative approach.

### Role of the dietitian in the care of a patient with CD

The initiation of a GFD should preferably be entrusted to an experienced dietitian who is perfectly familiar with this type of diet that requires clear and detailed explanations, with particular attention to its pitfalls.<sup>9,100</sup>

During the first consultation, the dietitian explains the GFD and insists on the importance of complete and definitive exclusion of gluten from the diet.<sup>97,98</sup>

The ubiquitous character of gluten in foods requires providing the patients and their families with the most exhaustive possible list of authorized and prohibited foods. Table 3 presents the main categories of foods containing gluten that the dietitian should explain to the celiac patient and/or to his family.

At the second consultation (scheduled 1 month after the first), the dietitian will answer questions related to any difficulties the patient may encounter, and ensure that a balanced diet is maintained and the weight is regained. The dietitian must also inquire about the social integration of the patient into the new lifestyle, and about the implementation of meals, particularly in nurseries, schools, and in the workplace.

The following consultations are usually coupled with a medical follow-up of the patient at 3 and 6 months, and then once a year. However, they can be more frequent depending on patient needs.<sup>98</sup>

To ensure smooth progress of GFD, the dietitian is in charge of educating the patient or his family to:

1- Avoid the risk of contamination by gluten-containing products through the following precautions:

Gluten-free products should be meticulously separated from those containing gluten, reserving an appropriate space in the pantry and the refrigerator

Work surfaces, appliances, toasters or bread makers, cooking utensils, and dishes used to prepare other meals should be thoroughly cleaned before use, or should preferably not be used

Frying baths should only be used for breaded products or donuts.<sup>97,100,102</sup>

2- Read the product labeling carefully:

Patients with CD should be encouraged to routinely read product labels to check for the presence of cereals containing gluten; some ingredients may even change over time. It is also necessary to be vigilant toward foods sold in bulk or catering products.<sup>99,103</sup>

In addition, terms found on the labels of many products indicate that some ingredients contain gluten and should not be consumed; for example, starch from wheat, barley, rye, or oats; unleavened bread (wheat flour); kamut (ancient wheat), bulgur; malt, and others. A precise list of terms appearing in the composition of a product, which indicate the presence or absence of gluten must also be made available to the patients and their families.<sup>4,97,103</sup> A comprehensive list of ingredients and additives that may contain gluten is provided in Table 4, making it easy to identify gluten in food products through their labels.

### Medical follow-up for patients with CD

A strict follow-up and a multi-disciplinary approach are needed to ensure harmonious growth



**Table 3.** List of allowed and prohibited foods for celiac disease.<sup>4,99,102</sup>

Food	Allowed	Prohibited
Milk and dairy products	<ul style="list-style-type: none"> <li>- Whole milk, semi-skimmed, skimmed, growth milk</li> <li>- Sweetened or unsweetened condensed milk</li> <li>- Fresh, pasteurized, powder, UHT sterilized milk</li> <li>- Goat and sheep milk</li> <li>- Plain fermented milk</li> <li>- Yogurts, flavored white cheeses</li> <li>- Soft, hard, cooked, melted cheeses</li> </ul>	<ul style="list-style-type: none"> <li>- Flavored milk</li> <li>- Cereal and fiber yogurts and dairy products</li> <li>- Fruit yogurts</li> <li>- Fool Epi Cheese</li> <li>- Industrial milk-based preparations (custards, creams, gelling agents, desserts, foam, etc.)</li> <li>- Mold and spread cheeses</li> <li>- Cereal-based dairy desserts</li> </ul>
Meats	<ul style="list-style-type: none"> <li>- All fresh meats, natural frozen, or natural canned</li> <li>- Ground beef "pure beef"</li> </ul>	<ul style="list-style-type: none"> <li>- Commercial ready-made preparations based on meat or poultry</li> <li>- Breaded, crusted, or flaky preparations</li> </ul>
Eggs	<ul style="list-style-type: none"> <li>- All</li> </ul>	<ul style="list-style-type: none"> <li>- Industrial scrambled eggs</li> </ul>
Fish	<ul style="list-style-type: none"> <li>- All fresh, smoked, frozen fish, canned fish</li> <li>- Natural crustaceans and mollusks</li> </ul>	<ul style="list-style-type: none"> <li>- Breaded or floured fish</li> <li>- Commercial preparations based on fish or fish butter</li> <li>- Fish dumplings</li> </ul>
Cold meat	<ul style="list-style-type: none"> <li>- White ham or country ham</li> <li>- Cooked shoulder</li> <li>- Unbreaded ham</li> <li>- Salted or smoked breast, bacon</li> <li>- Rillettes</li> <li>- Canded and natural foie gras</li> <li>- Plain sausage meat</li> <li>- Sausages from Strasbourg, Morteau, Frankfurt, Montbéliard</li> <li>- Mortadella, head cheese, snout</li> <li>- Andouille and andouillette</li> <li>- Tripe</li> </ul>	<ul style="list-style-type: none"> <li>- Surimi</li> <li>- Breaded ham</li> <li>- Meat stuffing</li> <li>- Foams and foie gras cream</li> <li>- Dough and galantine</li> <li>- Pies, sweets, quiches, queen bites</li> <li>- Dry sausages</li> <li>- Garlic sausages, dry sausages, salami, chorizo, cervelas, dumplings</li> <li>- White and Caribbean sausages</li> <li>- Black pudding</li> </ul>
Cereals and starchy foods	<ul style="list-style-type: none"> <li>- Rice and rice products: rice cream, pure rice semolina, rice cakes</li> <li>- Corn and derivatives: maizena, semolina</li> <li>- Cassava and derivatives: tapioca, tapiocaline</li> <li>- Buckwheat and pure buckwheat flour (without wheat flour)</li> <li>- Soy and soy flour</li> <li>- Sorghum</li> <li>- Millet</li> <li>- Sesame</li> <li>- Quinoa</li> <li>- Maranta</li> <li>- Sweet potatoes</li> <li>- Yam</li> <li>- Gluten-free infant flour</li> <li>- Certain breakfast cereals made only from rice and/or corn and without malt</li> </ul>	<ul style="list-style-type: none"> <li>- <b>Wheat or wheat, rye, barley, oats, spelled, kamut, triticale, and their derivatives:</b></li> <li>- Flour</li> <li>- Semolina</li> <li>- Pasta, vermicelli, ravioli, gnocchi</li> <li>- Bulgur</li> <li>- Flakes</li> <li>- <b>All types of bread:</b></li> <li>- White, rye, bran, crumb, brioche, toast, Swedish bread</li> <li>- Rusks, biscotti</li> <li>- Breadcrumbs</li> <li>- Any breaded food</li> <li>- <b>Shortcrust pastry, shortbread, puff pastry, puff pastry</b></li> <li>- <b>All sweet and savory cakes and cookies:</b></li> <li>- All aperitif cookies</li> <li>- All products sold in bakeries</li> <li>- All the commercial pastries</li> <li>- All the pastries</li> <li>- Unleavened bread</li> </ul>

(Continued)

**Table 3. (Continued)**

Food	Allowed	Prohibited
Vegetables and dried vegetables	<ul style="list-style-type: none"> <li>- Potato and potato starch</li> <li>- All fresh green vegetables, canned or frozen naturally, cooked under a vacuum</li> <li>- All dried vegetables</li> <li>- Small jars of homogenized vegetables mentioned gluten-free</li> </ul>	<ul style="list-style-type: none"> <li>- All commercial cooked vegetables (canned, frozen, catering)</li> <li>- Soups in sachets or in boxes</li> <li>- Dauphine potatoes, duchess potatoes (check the coating of the hazelnut apples and pre-cooked fries)</li> <li>- Flavored crisps</li> <li>- Instant mashed potato</li> <li>- Dried figs (flour that can be used for drying)</li> <li>- Glazed chestnuts and candied fruit (handling possible with floured fingers)</li> <li>- Dry grilled oil seeds</li> </ul>
Fruits	<ul style="list-style-type: none"> <li>- Fresh or natural frozen fruit</li> <li>- Fruits in syrup</li> <li>- Frozen or canned compotes</li> <li>- Chestnuts, natural chestnuts</li> <li>- Oilseeds not dry roasted (nuts, hazelnuts, peanuts, almonds)</li> <li>- Small jars of homogenized fruit without cereals</li> <li>- Oil, butter, fresh cream, Vegetal, margarine, Bacon, bacon, tallow, goose fat</li> </ul>	
Fat		
Sweet products	<ul style="list-style-type: none"> <li>- White sugar, brown sugar, cane, vanilla</li> <li>- Jelly, jam, pure fruit chestnut cream</li> <li>- Honey</li> <li>- Pure, tablet, dark, or milk chocolate</li> <li>- Pure cocoa</li> <li>- Sour candies and lollipops</li> <li>- Pure vanilla extract</li> <li>- Pure licorice</li> </ul>	<ul style="list-style-type: none"> <li>- Wheat germ oil</li> <li>- Low-fat butters or margarines</li> <li>- Nougat</li> <li>- Sugared</li> <li>- Banania chocolate powder</li> <li>- All loose candy</li> <li>- Eskimos and ice cream in cornet</li> <li>- Packaged candy</li> <li>- Commercial ice creams and sorbets</li> <li>- Filled chocolates</li> <li>- Icing sugar</li> <li>- Chocolate powders</li> </ul>
Drinks	<ul style="list-style-type: none"> <li>- Tea, coffee, chicory, infusions</li> <li>- Fruit juice, fruit syrup</li> <li>- Sodas and lemonade</li> </ul>	<ul style="list-style-type: none"> <li>- Beers (most are made from malt and, therefore, germinated barley)</li> <li>- Plume</li> <li>- Instant drink powders</li> </ul>
Condiments and various	<ul style="list-style-type: none"> <li>- Aromatic herbs, pure spices, salt, pepper</li> <li>- Garlic, onion, shallot, pickle</li> <li>- Some mustards</li> <li>- Baker's yeast</li> <li>- Sodium carbonate to replace baking powder</li> </ul>	<ul style="list-style-type: none"> <li>- Spice mixes</li> <li>- All other commercial condiments and sauces (Curry, soy sauce, mayonnaise, etc.)</li> <li>- Savora mustard</li> <li>- Baking powder</li> </ul>

**Table 4.** List of ingredients and names indicating the presence or absence of gluten on product labels.<sup>4,103,104</sup>

Presence of gluten	Absence of gluten
<ul style="list-style-type: none"> <li>• Starch from prohibited cereals (wheat, barley, rye, oats)</li> <li>• Starchy material</li> <li>• Vegetable proteins from prohibited cereals</li> <li>• Vegetable protein binder</li> <li>• Malt or malt “extract”</li> <li>• Anti-Caking agents in fruit pastes certain thickeners in light products</li> <li>• Unleavened Bread (wheat flour); wheat, spelled</li> <li>• Kamut (old wheat)</li> <li>• Bulgur</li> <li>• Oatmeal (preparation of cereal grains), vegetable amino acids (without further details)</li> <li>• Gelling agents (without further details)</li> <li>• Plant polypeptides or proteins</li> <li>• Protein binder (without further details)</li> <li>• Triticale (wheat and rye hybrid)</li> </ul>	<ul style="list-style-type: none"> <li>• Starch from authorized cereals</li> <li>• Flavor of malt</li> <li>• Dextrin</li> <li>• Maltodextrin</li> <li>• Glucose syrup</li> <li>• Glutamate</li> <li>• Gelatin</li> <li>• Lecithin</li> <li>• Plant amino acids</li> <li>• Vegetable protein binders</li> <li>• Thickeners (carob, xanthan gum)</li> <li>• Texturing agents (alginates, carrageenan)</li> </ul>
<p>Additives which may contain gluten (E1400 to I451)</p> <ul style="list-style-type: none"> <li>• E1400: Dextrins, roasted starch</li> <li>• E1401: Acid-treated starch</li> <li>• E1402: Starch treated with alkalis</li> <li>• E1403: Bleached starch</li> <li>• E1404: Oxidized starch</li> <li>• E1405: Starches treated with enzymes</li> <li>• E1410: Starch phosphate</li> <li>• E1411: Diamidon glycerol</li> <li>• E1412: Diamidon phosphate</li> <li>• E1413: Phosphate of diamidon phosphate</li> <li>• E1414: Acetylated diamidon phosphate</li> <li>• E1420: Acetylated starch</li> <li>• E1421: Acetylated vinyl acetate starch</li> <li>• E1422: Acetylated diamidon adipate</li> <li>• E1413: Acetylated diamidon glycerol</li> <li>• E1440: Hydroxypropylated starch</li> <li>• E1442: Hydroxypropylateddiamidon phosphate</li> <li>• E1443: Hydroxypropylateddiamidon glycerol</li> </ul>	<p>All E + 3-digit additives</p> <ul style="list-style-type: none"> <li>• E 620 to 625: Glutamate (flavor enhancer)</li> <li>• E 406: Agar agar</li> <li>• E 407: Carrageenans</li> <li>• E 410: Carob seed flour</li> <li>• E 412: Guar gum</li> <li>• E 440a: Pectins</li> <li>• E 460: Cellulose</li> <li>• E 413: Eraser, tragacanth</li> <li>• E 414: Gum arabic</li> <li>• E 415: Xanthan gum</li> <li>• E411: Oat gum (not suitable for gluten intolerant)</li> <li>• All E+3 digits+ 1 letter additives</li> </ul>

and prevent CD-related complications.<sup>38</sup> As summarized in Table 5, the medical follow-up is generally based on clinical evaluation, serological testing, nutritional assessment, bone density measurement, liver and thyroid exploration, intestinal biopsy and cancer screening.

Patients with CD should be examined at least twice during the first year after diagnosis, to monitor clinical and biological manifestations, nutritional status, body mass index (BMI), serological tests, and to assess compliance with GFD.<sup>2,72,74</sup> BMI can be a reliable reflection of the impact of GFD on the nutritional status of celiac patients: underweight patients typically gain weight and overweight or obese patients lose weight.<sup>38</sup> The efficiency of a GFD is thus attested by clinical and biological improvement (1–3 months), the negativity of specific Ab tests, and the regression

of histological abnormalities (12 months).<sup>3,105,106</sup> Regular monitoring of serology makes it possible to detect diet deviations, whether voluntary or not; and patients whose serological tests do not improve should be reassessed for continued exposure to gluten.<sup>40,72,97</sup>

One of the most controversial aspects of CD is the value and the timing of the intestinal biopsy when monitoring the disease. To better appreciate the evolution of intestinal damage, a biopsy is generally recommended 1–2 years after GFD initiation. However, intestinal healing is often slow, incomplete, and age-dependent.<sup>70,107</sup> Moreover, intestinal biopsy remains essential if symptoms persist.<sup>70</sup>

In general, the management of CD must include a nutritional assessment in order to detect deficiencies such as autoimmune thyroiditis (T3, T4, TSH,

**Table 5.** Guidelines for medical monitoring of patients with celiac disease.<sup>40</sup>

Test	Time interval	Comments
Clinical evaluation	Annually or if recurring symptoms	
Serology	Every 3–6 months until normalization Then every 1–2 years	Normal titers are insensitive to continuous exposure to gluten or enteropathy. The continuous increase in titers indicates significant exposure to gluten.
Nutritional assessment	Every 3–6 months until normalization Then every 1–2 years	Iron deficiency, 25-OH vitamin D, vitamin B12, folate, and zinc. Monitoring of weight gain, low fiber intake, and constipation.
Bone density	Once during the first 2 years	Significant increases in bone density are often seen during the first year after diagnosis. Several experts therefore recommend the test 1 year after the GFD.
Liver transaminases (ALT/AST)	At the time of diagnosis Then every 1–2 years	Increased levels of ALT and AST are common during celiac disease. Their constant increase indicates an associated hepatic co-morbidity.
Functional exploration of the thyroid	At the time of diagnosis Then every 1–2 years	Autoimmune thyroiditis is the most common autoimmune disorder found in approximately 15%–20% of celiac adults.
Intestinal biopsy	To be considered 1–2 years after diagnosis	Repeated biopsies to assess healing are frequently performed. However, their interest remains controversial in celiac patients responding well to GFD with a good clinical course.
Cancer screening	As for the general population	Even if the rate of certain cancers is high, they are not frequent enough to justify a specific systematic screening.

anti-thyroperoxidase, and anti-thyroglobulin antibodies) and justify replacement therapy (hemoglobin, albumin, calcium, folate, vitamin B12, zinc, magnesium, and vitamin D).<sup>9</sup>

It is also recommended to evaluate bone mineral density during the first year of follow-up, using densitometry.<sup>9,72</sup>

In the pediatric population, the late childhood is particularly critical for the conduct of GFD. In fact, this diet impacts daily life and can be a source of frustration or even depression, and often experienced as “dissocializing,” especially among adolescents.<sup>101,108</sup> Closer follow-up by both the specialist and the dietitian is, therefore, necessary to re-explain the disease and its complications, to understand the difficulties of the adolescent in accepting the diet, and to help them overcome social or academic constraints, thus, preventing potential abandonment of the diet.<sup>109</sup>

On the other hand, the transition to adulthood is often a period of slackening during follow-up, and sometimes of GFD. Consequently, the orientation toward the adult specialist becomes necessary to ensure continuity in care and avoid the insidious

installation of serious complications, mainly, osteopenia and fracture osteoporosis, increased risk of autoimmune diseases (type I diabetes, thyroiditis, and others), hypofertility, or even sterility, neuropathies, and particularly the risk of cancers such as adenocarcinomas and intestinal lymphomas.<sup>3,11,108</sup>

Medicines are a potential source of gluten concealment, which is commonly introduced into the solid phase of drugs such as tablets and pills when the starch used is extracted from wheat, rye, and/or barley, serving as a diluent or binder.<sup>12,103</sup> Starch is also used as a carrier for controlled or sustained-release dosage forms as well as to form nanoparticles, nanogels, and microcapsules.<sup>110</sup> The excipients of some drugs may also contain gluten in small quantities, especially those based on wheat starch, wheat germ oil, wheat bran, wheat flour, barley bran, and vegetable amylase, which can be extracted from barley.<sup>104</sup> The type of excipients can also be different between generic and branded drugs, and those with a known effect (lactose and gluten) must be indicated in the leaflet intended for patients.<sup>111</sup> Thus, even if the brand name is

determined to be gluten-free, the gluten-free status of each generic must be verified by the pharmacist and the celiac patient as well.

Unfortunately, drug manufacturers may not disclose the source of the starch used or indicate whether their products are free from gluten contamination.<sup>12</sup> Indeed, all medicines can be made gluten-free since alternatives to starch can be used during production. This highlights the importance of adopting a new policy for the manufacture of gluten-free drugs by pharmaceutical companies and excipient producers.<sup>12</sup>

Since 2017, Food and Drug Administration (FDA) has issued a draft guidance on Gluten in Drug Products and Associated Labeling, recommending to drug manufacturers a statement to include in their labeling when truthful and properly supported: “Contains no ingredient made from a gluten-containing grain (wheat, barley, or rye)”.<sup>112</sup>

Hence, the pharmacist has an essential role in the management of gluten-intolerant patients. He must check whether the medicine contains gluten, even in very small quantities, especially in excipients. The following components indicate the presence of gluten in the drug: starch, glycerol starch, starch glycolate, carboxymethyl starch, partial hydrolysate of hydrogenated starch, modified/soluble/pregelatinized starch, precooked/processed wheat germ oil, wheat bran, barley, and vegetable amylase. An exception is made for the specialties of Maxilase® or Megamylase® (possibly extracted from barley), which have been authorized by the French association of gluten intolerants after investigations in pharmaceutical laboratories.<sup>113</sup> Box 4 reports a non-exhaustive list of medications containing gluten, drawn from the Vidal dictionary, indicating both the generic and the brand name. A complementary list of drugs that may or may not contain gluten depending on the concentration and formulation of the drug is displayed in Table 6. Indeed, the generic name of drugs may differ depending on the country of origin and distribution. These lists must also be regularly updated with the development of new generic drugs. Thus, both pharmacists and patients with CD should constantly check the composition of the drugs.<sup>113</sup> Determining the gluten status of generic drugs is challenging owing to changes in manufacturers, drug shortages, and wholesale product variability. These factors make identifying the gluten content in generic medications difficult, even for the manufacturers themselves.<sup>114</sup>

Additionally, even low gluten intake can irritate sensitive individuals.<sup>104</sup> In contrast, the ointment forms, effervescent tablets, drinkable drops, oral solutions, eye drops, suppositories, nasal drops, and injectable ampoules are gluten-free regardless of the specialty name.<sup>113</sup> Some medications are the only ones to contain the active principle, and the benefit/risk ratio of these drugs must therefore be evaluated by the prescriber before use or exclusion in any therapy.<sup>104,114</sup>

To sum up, this overview suggested an integrated approach to the main practical aspects of CD (clinical and laboratory diagnosis; implementation and monitoring of gluten-free diet; delivering and use of gluten-free medications), which represent concerns for physicians, biologists, nutritionists and pharmacists during the process of CD management. However, as limitations, some aspects have not been or insufficiently developed, such as the role of innate immunity in the pathogenesis of CD, the comparative performance of serological testing, the seronegative and refractory CD and possible immunotherapeutic approaches. We have also been faced to the scarcity of scientific data related to drugs and gluten.

## Conclusion

Despite its polymorphism with many differential diagnoses, CD benefits from a standardized diagnostic approach based on serology, intestinal biopsy, and possibly HLA typing. The management of CD is a multidisciplinary concern, involving general practitioners, different clinical and biological specialists, as well as dietitians and pharmacists.

The implementation and monitoring of GFD remains a challenge, which reflects the incontestable role of the dietitian as well as that of the pharmacist, considering the risk of the existence or concealment of gluten in the various stages of drug manufacturing.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

**Box 4.** Pharmaceutical specialties containing gluten or marked “wheat starch” in their composition.<sup>104,113</sup> (Brand names of drugs are put between brackets).

- ABUFENE (Beta-alanine) 400 mg tablet
- ACEBUTOLOL WINTHROP (acebutolol) 200 mg coated tablet
- ACEBUTOLOL ZENTIVA (acebutolol) 400 mg coated tablet
- ADENYL (Adenosine phosphate) 60 mg tablet
- ADIAZINE (Sulfadiazine) 500 mg tablet
- ALFATIL (Céfaclor) 250 mg/5 ml powder for oral suspension
- ALLOPURINOL ARROW (allopurinol) 100 mg tablet
- ALLOPURINOL ARROW (allopurinol) 200 mg tablet
- ALLOPURINOL ARROW (allopurinol) 300 mg tablet
- ALLOPURINOL EG (allopurinol) 100 mg tablet
- ALLOPURINOL EG (allopurinol) 200 mg tablet
- ALLOPURINOL EG (allopurinol) 300 mg tablet
- ALLOPURINOL SANDOZ (allopurinol) 100 mg tablet
- ALLOPURINOL SANDOZ (allopurinol) 200 mg tablet
- ALLOPURINOL SANDOZ (allopurinol) 300 mg tablet
- APAROXAL (phenobarbital) 100 mg tablet
- ARTANE (trihexyphenidyl hydrochloride) 2 mg tablet
- ARTANE (trihexyphenidyl hydrochloride) 5 mg tablet
- ARTICHAUD BOIRON (Cynara scolymus) capsule
- ATHYMIL (mianserin hydrochloride) 10 mg coated tablet
- ATHYMIL (mianserin hydrochloride) 30 mg coated tablet
- ATHYMIL (mianserin hydrochloride) 60 mg coated tablet
- ASPIRINE RICHARD (aspirin) 500 mg tablet
- BECILAN (pyridoxine hydrochloride) 250 mg coated tablet
- BELUSTINE (lomustine) 40 mg capsule
- BENEMIDE (probenecid) 500 mg tablet
- BEVITINE (thiamine hydrochloride) 250 mg coated tablet
- BI-PROFENID LP (ketoprofen) 100 mg tablet
- BOURDAINE BOIRON (frangula alnus) capsule
- BUFLOMEDIL ARROW (buflovedil) 150 mg tablet
- BUFLOMEDIL ARROW (buflovedil) 300 mg tablet
- BUFLOMEDIL EG (buflovedil) 150 mg coated tablet
- BUFLOMEDIL EG (buflovedil) 300 mg coated tablet
- BUFLOMEDIL GNR (buflovedil) 150 mg tablet
- BUFLOMEDIL GNR (buflovedil) 300 mg tablet
- BUFLOMEDIL IREX (buflovedil) 150 mg tablet
- BUFLOMEDIL IREX (buflovedil) 300 mg tablet
- BUFLOMEDIL RPG (buflovedil) 150 mg tablet
- BUFLOMEDIL RPG (buflovedil) 300 mg tablet
- BUFLOMEDIL RATIOPHARMA (buflovedil)
- BUFLOMEDIL TEVA (buflovedil) 150 mg coated tablet
- BUFLOMEDIL TEVA (buflovedil) 300 mg tablet
- BUFLOMEDIL ZYDUS (buflovedil) 150 mg tablet
- CANTABILINE (hymecromone) 400 mg tablet
- CERIS (trospium chloride) 20 mg coated tablet
- CASSIS BOIRON (ribes nigrum) capsule
- CLARITHROMYCINE SANDOZ (clarithromycin) 50 mg/ml powder for oral suspension
- CHLORHYDRATE D'HEPTAMINOL RICHARD (Heptaminol hydrochloride) 187.8 mg tablet
- CIRKAN (Hesperidin Methyl Chalcone) coated tablet
- COLIMYCINE (colistimethate sodium) 1.5 M UI tablet
- CYNOMEL (liothyronine sodium) 25 µg tablet
- DANTRIUM (dantrolene sodium) 100 mg capsule
- DANTRIUM (dantrolene sodium) 25 mg capsule
- DENISICAL VITAMINE D3 (cholecalciferol) powder for oral suspension
- DESINTEX (sodium thiosulphate) coated tablet
- DEXAMBUTOL (ethambutol) 500 mg coated tablet
- DIAMOX (acetazolamide) 250 mg tablet
- DICYNONE (tranexamic acid) 500 mg tablet
- DI-HYDAN (phenytoin sodium) 100 mg tablet

(Continued)

**Box 4. (Continued)**

- DISULONE (dapsone) tablet
- DOLIPRANE LIB (paracetamol) 500 mg tablet
- DOLIRHUME (paracetamol + pseudoephedrine) 500 mg/30 mg tablet
- DOLIRHUMEPRO (paracetamol, pseudoephedrine & doxylamine) tablet
- DOXYLAMINE (doxylamine) tablet
- ENTECET (germinated barley + amylase) coated tablet
- ENTEROPATHYL (sulfaguanidine) 500 MG
- ENZYMICINE (Neomycin) cone for dental use
- ESIDREX (hydrochlorothiazide) 25 mg tablet
- EXACYL (tranexamic acid) 500 mg coated tablet
- FAGOPYRUM ESCULENTUM
- FLAGYL (metronidazole) 250 mg coated tablet
- FLAGYL (metronidazole) 500 mg coated tablet
- FURADANTINE (nitrofurantoin) 50 mg capsule
- FURADOINE (nitrofurantoin) 50 mg tablet
- GARDENAL (phenobarbital) 10 mg tablet
- GARDENAL (phenobarbital) 50 mg tablet
- GARDENAL (phenobarbital) 100 mg tablet
- GINSENG BOIRON (ginseng) capsule
- GLUTAMINOL B6 (glutamic acid + Pyroxidine) tablet
- HEPTAMYL 187.8 (heptaminol) mg tablet
- HEXASTAT (altrétamine) 100 mg capsule
- IMOVANE (zopiclone) 3.75 mg coated tablet
- IMOVANE (zopiclone) 7.5 mg coated tablet
- INSADOL (corn) 35 mg coated tablet
- ISOPRINOSINE (inosine acedoben dimepranol) 500 mg tablet
- KETOPROFENE ZENTIVA LP (ketoprefen) 100 mg tablet
- LARGACTIL (chlorpromazine hydrochloride) 100 mg coated tablet
- LARGACTIL (chlorpromazine hydrochloride) 25 mg coated tablet
- LEGALON (silymarin) 70 mg coated tablet
- LIORESAL (baclofen) 10 mg coated tablet
- MALOCIDE (pyriméthamine) 50 mg tablet
- MEGAMAG (magnesium) 45 mg capsule
- MEPROBAMATE RICHARD (meprobamate) 400 mg tablet
- METHOTREXATE BELLON (methotrexate) 2.5 mg tablet
- MODUCREN (timolol maleate + amiloride chlorhydrate + hydrochlorothiazide) tablet
- MUCITUX (eprazinone dihydrochloride) 50 mg coated tablet
- NEO-CODION (codeine) coated tablet
- NEOCONES (neomycin sulfate + benzocaine) cone for dental use
- NEULEPTIL (propériciazine) 25 mg coated tablet
- NIVAQUINE (Chloroquine) 100 mg tablet
- NORDAZ (Nordazepam) 15 mg tablet
- NORDAZ (Nordazepam) 7.5 mg tablet
- NOTEZINE (diethylcarbamazine) 100 mg tablet
- NOZINAN (levomepromazine) 100 mg coated tablet
- NOZINAN (levomepromazine) 25 mg coated tablet
- PARACETAMOL SANDOZ (paracetamol) 1 g tablet
- PARACETAMOL SANDOZ (paracetamol) 500 mg tablet
- PARACETAMOL ZYDUS (paracetamol) 500 mg tablet
- PASSIFLORE BOIRON (passiflora) capsule
- PEFLACINE (pefloxacin) 400 mg coated tablet
- PEFLACINE MONODOSE (pefloxacin) 400 mg coated tablet
- PERUBORE INHALATION (plant essences) inhalation tablet
- PHENERGAN (promethazine) 25 mg coated tablet
- PHOLCODYL (pholcodine) liquid mixture
- PIPORTIL (pipotiazine) 10 mg coated tablet
- PIPRAM FORT (piperacillin + tazonaactum) 400 mg coated tablet
- PRAZINIL (carpipramine) 50 mg coated tablet
- PREVISCAN (fluindione) 20 mg tablet
- PROFEMIGR (ketoporofen) 150 mg tablet

(Continued)

**Box 4.** (Continued)

- PYOREX (sodium ricinoleate + thacridine) toothpaste
- PYOSTACINE (pyostacine) 250 mg coated tablet
- PYOSTACINE (pyostacine) 500 mg coated tablet
- QUININE CHLORHYDRATE LAFRAN (quinine) 224.75 mg tablet
- QUININE CHLORHYDRATE LAFRAN (quinine) 449.50 mg tablet
- QUININE SULFATE LAFRAN (quinine) 217.2 mg tablet
- QUININE SULFATE LAFRAN (quinine) 434.4 mg tablet
- RASILEZ HCT (hydrochlorothiazide) 150 mg/12.5 mg coated tablet
- RASILEZ HCT (hydrochlorothiazide) 300 mg/12.5 mg coated tablet
- RASILEZ HCT (hydrochlorothiazide) 300 mg/25 mg coated tablet
- REINE DES PRES BOIRON (spiraea ulmaria) capsule
- RHUMAGRIP (acetaminophen + pseudoephedrine) tablet
- RITALINE (methylphenidate) 10 mg tablet
- RUBOZINC (zinc) 15 mg capsule
- SECTRAL (acebutolol) 200 mg coated tablet
- SECTRAL (acebutolol) 400 mg coated tablet
- SPASFON (phloroglucinol) coated tablet
- SPOTOF (tranexamic acid) 500 mg coated tablet
- SULFARLEM (anetholtrithione) 12.5 mg coated tablet
- SULFARLEM S (anetholtrithione) 25 mg coated tablet
- SURMONTIL (trimipramine) 100 mg coated tablet
- SURMONTIL (trimipramine) 25 mg tablet
- TANGANIL (acetyllicine) 500 mg tablet
- TARDYFERON B9 (iron + folic acid) coated tablet
- TARDYFERON B9 (iron + folic acid) coated tablet
- TERALITHE (lithium) 250 mg tablet
- TERCIAN (cyamemazine) 100 mg coated tablet
- TERCIAN (cyamemazine) 25 mg coated tablet
- TERGYNAN (metronidazole + neomycin sulfate + nystatin) vaginal tablet
- THERALENE (ternidazole + neomycin sulfate + nystatin) coated tablet
- TONILAX (frangula alnus) coated tablet
- TOPREC (ketoprofen) 25 mg tablet
- TRIHEXY RICHARD (trihexyphenidyl hydrochloride) 2 mg tablet
- TRIHEXY RICHARD (trihexyphenidyl hydrochloride) 5 mg tablet
- TRIMEBUTINE BIOGARAN (trimebutine) 100 mg tablet
- TRIMEBUTINE MERCK (trimebutine) 100 mg tablet
- TRIMEBUTINE MYLAN (trimebutine) 100 mg tablet
- TRIMEBUTINE QUALIMED (trimebutine) 100 mg tablet
- TRINITRINE SIMPLE LALEUF (nitroglycerin) 0.15 mg coated pill
- VIBTIL (dry extract of lime sapwood) 250 mg coated tablet
- VISCERALGINE (tiemonium Iodide) 50 mg coated tablet
- VITAMINE B6 RICHARD (piroxidin) 250 mg tablet
- VITATHION (ascorbic acid + thiamine + inositolcalcium) effervescent granule
- VOGALENE (metopimazine) 15 mg capsule
- ZOPICLONE ZENTIVA or RPG (zopiclone) 7.5 mg coated tablet

**Table 6.** Gluten status of medications (adapted from<sup>114</sup>).

Drug (Manufacturer)	Strength and formulation	Gluten status
- Allopurinol (Mylan)	- 300 mg tablet	- Gluten free
- Amino acid solution (B. Braun)	- 10% and 15% injections	- Gluten free
- Azacitadine (Celgene)	- 100 mg injection	- Gluten free
- Barium sulfate contrast dye (EZ EM CANADA)	- 9.5 g in 23.5 g suspension	- Gluten free
- Dextrose solution (Hospira)	- 5% injection	- Gluten free
- Diphenoxylate /atropine (Mylan)	- 2.5 mg/0.025 mg tablet	- Gluten free
- Doxycycline hyclate (Mylan)	- 100 mg tablet	- Gluten free
- Endure handsoap (Ecolab)	- Not applicable	- Gluten free

(Continued)



**Table 6.** (Continued)

Drug (Manufacturer)	Strength and formulation	Gluten status
- Levocetirizine (Dr. Reddy's)	- 5 mg tablet	- Gluten free
- Linezolid (Pfizer)	- 100 g/5 mL suspension	- Gluten free
- Lipid emulsion (Fresenius kabi)	- 10%, 20%, and 30% injections	- Gluten free
- Loperamide (Mylan)	- 2 mg capsule	- Gluten free
- Losartan (Mylan)	- 25 and 50 mg tablets	- Gluten free
- Magnesium oxide (McKesson Packaging)	- 400 mg tablet	- Gluten free
- Menthol/camphor (Geritrex)	- 0.5%/0.5% lotion	- Gluten free
- Metaxalone (Amneal)	- 800 mg tablet	- Gluten free
- Morphine (Hospira)	- 2 and 4 mg injections	- Gluten free
- Pomalidomide (Celgene)	- 1, 2, 3, and 4 mg capsules	- Gluten free
- Prochlorperazine (Mylan)	- 5 mg tablet	- Gluten free
- Rosuvastatin (AstraZeneca)	- 5, 10, 20, and 40 mg tablets	- Gluten free
- Salsalate (Amneal)	- 500 and 750 mg tablets	- Gluten free
- Acetaminophen (McNeil)	- 325 mg tablet	- Possibly contains gluten
- Acetaminophen (McNeil)	- 500 mg caplet	- Possibly contains gluten
- Acyclovir (Teva)	- 200 mg capsule	- Possibly contains gluten
- Acyclovir (Teva)	- 400 mg tablet	- Possibly contains gluten
- Allopurinol (Watson)	- 300 mg tablet	- Possibly contains gluten
- Amlodipine (Teva)	- 5 mg tablet	- Possibly contains gluten
- Amoxicillin (Sandoz)	- 400 mg/5 mL suspension	- Possibly contains gluten
- Amoxicillin/clavulanate (Sandoz)	- 500 and 875 mg tablets	- Possibly contains gluten
- Apixaban (Bristol-Meyers Squibb)	- 2.5 and 5 mg tablets	- Possibly contains gluten
- Aripiprazole (Otsuka)	- 2, 5, 10, 15, 20, and 30 mg tablets	- Possibly contains gluten
- Atazanavir (Bristol-Meyers Squibb)	- 150, 200, and 300 mg capsules	- Possibly contains gluten
- Butalbital/acetaminophen/caffeine (Qualitest)	- 325 mg/50 mg/40 mg tablet	- Possibly contains gluten
- Celecoxib (Pfizer)	- 50, 100, 200, and 400 mg capsules	- Possibly contains gluten
- Cephalixin (Teva)	- 500 mg capsule	- Possibly contains gluten
- Ciprofloxacin (Watson)	- 250 and 500 mg tablets	- Possibly contains gluten
- Clindamycin (Watson)	- 150 mg capsule	- Possibly contains gluten
- Dabigatran (BoehringerIngelheim)	- 75 and 150 mg capsules	- Possibly contains gluten
- Darunavir (Janssen)	- 75, 150, 400, 600, and 800 mg tablets	- Possibly contains gluten
- Darunavir (Janssen)	- 100 mg/mL suspension	- Possibly contains gluten
- Dextran/hydroxypropyl methylcellulose (Alcon)	- 0.1%/ 0.3% ophthalmic solution	- Possibly contains gluten
- Diphenhydramine (Major)	- 25 and 50 mg tablets	- Possibly contains gluten
- Diphenhydramine (Qualitest)	- 12.5 mg/5 mL liquid	- Possibly contains gluten
- Diphenoxylate/atropine (Greenstone)	- 2.5 mg/0.02 mg tablet	- Possibly contains gluten
- Emtricitabine/tenofovir (Gilead)	- 200 mg/300 mg tablet	- Possibly contains gluten
- Ethinyl estradiol/levonorgestrel (Watson)	- 0.03 mg/0.15 mg tablet	- Possibly contains gluten
- Ethinyl estradiol/norethindrone (Watson)	- 0.035 mg/1 mg tablet	- Possibly contains gluten
- Ethinyl estradiol/norgestimate (Janssen)	- Varies	- Possibly contains gluten
- Ethinyl estradiol/norgestimate (Watson)	- Varies	- Possibly contains gluten
- Ethinyl estradiol/norgestrel (Watson)	- 0.03 mg/0.3 mg tablet	- Possibly contains gluten
- Etravirine (Janssen)	- 25, 100, and 200 mg tablets	- Possibly contains gluten
- Fluconazole (Teva)	- 400 mg tablet	- Possibly contains gluten
- Hydrocortisone cream (Fougera)	- 0.5% cream	- Possibly contains gluten
- Hydrocortisone cream (Wyeth)	- 1% cream	- Possibly contains gluten
- Hydrocortisone sodium succinate (Pfizer)	- 100 mg injection	- Possibly contains gluten
- Intravenous immune globulin (CSL Behring)	- 3, 6, and 12 g injections	- Possibly contains gluten
- Levofloxacin (Lupin)	- 250 and 500 mg tablets	- Possibly contains gluten
- Linezolid (Pfizer)	- 600 mg tablet	- Possibly contains gluten
- Lopinavir/ritonavir (AbbVie)	- 100 mg/25 mg and 200 mg/50 mg	- Possibly contains gluten
- Lopinavir/ritonavir (AbbVie)	- 80 mg/20 mg/mL solution	- Possibly contains gluten
- Magnesiumtrisilicylate (Silarx)	- 500 mg solution	- Possibly contains gluten
- Maraviroc (ViiV Healthcare)	- 150 and 300 mg tablets	- Possibly contains gluten
- Multivitamin with fluoride (Qualitest)	- 0.25, 0.5, and 1.0 mg chewable tablets	- Possibly contains gluten
- Nimodipine (Arbor)	- 3 mg/mL solution	- Possibly contains gluten

(Continued)

**Table 6.** (Continued)

Drug (Manufacturer)	Strength and formulation	Gluten status
- Oxycodone immediate release (Actavis)	- 15 and 30 mg tablets	- Possibly contains gluten
- Pantoprazole (Dr. Reddy's)	- 20 and 40 mg tablets	- Possibly contains gluten
- Potassium chloride (Upsher-Smith)	- 20 meq tablet	- Possibly contains gluten
- Rabeprazole (Eisai)	- 20 mg tablet	- Possibly contains gluten
- Ritonavir (AbbVie)	- 100 mg tablet	- Possibly contains gluten
- Ritonavir (AbbVie)	- 100 mg tablet	- Possibly contains gluten
- Ritonavir (AbbVie)	- 80 mg/mL solution	- Possibly contains gluten
- Rivaroxaban (Janssen)	- 10, 15, and 20 mg tablets	- Possibly contains gluten
- Saquinavir (Genentech)	- 200 and 500 mg capsules	- Possibly contains gluten
- Sitagliptin (Merck)	- 25, 50, and 100 mg tablets	- Possibly contains gluten
- Sulfamethoxazole/trimethoprim DS (Amneal)	- 800 mg/160 mg tablet	- Possibly contains gluten
- Telmisartan (BoehringerIngelheim)	- 20, 40, and 80 mg tablets	- Possibly contains gluten
- Tramadol (Mylan)	- 50 mg tablet	- Possibly contains gluten
- Triazolam (Greenstone)	- 0.125 and 0.25 mg tablets	- Possibly contains gluten
- Valsartan (Novartis)	- 40, 80, 160, and 320 mg tablets	- Possibly contains gluten
- Vancomycin (Baxter)	- 1 g injection	- Possibly contains gluten
- Nebivolol (Forest)	- 2.5, 5, 10, and 20 mg tablets	- Contains gluten
- Tramadol (Amneal)	- 50 mg tablet	- Contains gluten

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**References**

- Roujon P, Sarrat A, Contin-Bordes C, et al. (2013) Diagnostic sérologique de la maladie cœliaque. *Pathologie Biologie* 61: e39–346.
- Husby S, Koletzko S, Korponay-Szabó IR, et al. (2012) European society for pediatric gastroenterology, hepatology, and nutrition guidelines for the diagnosis of coeliac disease. *Journal of Pediatric Gastroenterology and Nutrition* 54: 136–160.
- Malamut G and Cellier C (2010) Celiac disease. *La Revue de Médecine Interne* 31: 428–433.
- Tounian P and Sarrio F (2011) Prise en charge diététique de certaines pathologies. In: Masson E (ed.) *Alimentation De L'enfant De 0 à 3 Ans*. Collection Pédiatrie au Quotidien, Elsevier, pp.73–89.
- Bruneau J, Cheminant M, Khater S, et al. (2018) Importance of histopathology in coeliac disease diagnosis and complications. *Revue Francophone des Laboratoires* 2018: 30–38.
- Fasano A and Catassi C (2012) Clinical practice. Celiac disease. *The New England Journal of Medicine* 367: 2419–2426.
- Godat S, Velin D, Aubert V, et al. (2013) An update on celiac disease. *Revue Médicale Suisse* 9: 1584–1589.
- Malamut G, Verkarre V, Suarez F, et al. (2010) The enteropathy associated with common variable immunodeficiency: The delineated frontiers with celiac disease. *The American Journal of Gastroenterology* 105: 2262–2275.
- Lepers S, Couignoux S, Colombel J-F, et al. (2004) La maladie cœliaque de l'adulte : Aspects nouveaux. *La Revue de Médecine Interne* 25: 22–34.
- Riznik P, De Leo L, Dolinsek J, et al. (2021) Clinical presentation in children with coeliac disease in Central Europe. *Journal of Pediatric Gastroenterology and Nutrition* 72(4): 546–551.
- Cosnes J and Nion-Larmurier I (2013) Complications of celiac disease. *Pathologie Biologie* 61: e21–e26.
- Shah AV, Serajuddin ATM and Mangione RA (2018) Making all medications gluten free. *Journal of Pharmaceutical Sciences* 107: 1263–1268.
- Nenna R, Tiberti C, Petrarca L, et al. (2013) The celiac iceberg: Characterization of the disease in primary schoolchildren. *Journal of Pediatric Gastroenterology and Nutrition* 56: 416–421.
- Lebwohl B, Sanders DS and Green PHR (2018) Coeliac disease. *Lancet* 391: 70–81.
- Mustalahti K, Catassi C, Reunanen A, et al. (2010) The prevalence of celiac disease in Europe: Results of a centralized, international mass screening project. *Annals of Medicine* 42: 587–595.
- Ashtari S, Najafimehr H, Pourhoseingholi MA, et al. (2021) Prevalence of celiac disease in low and high risk population in Asia-Pacific region: A systematic review and meta-analysis. *Scientific Reports* 11: 2383.
- El-Metwally A, Toivola P, AlAhmary K, et al. (2020) The epidemiology of celiac disease in the general population and high-risk groups in Arab Countries: A systematic review. *BioMed Research International* 2020: 6865917.
- Gujral N, Freeman HJ and Thomson ABR (2012) Celiac disease: Prevalence, diagnosis, pathogenesis and treatment. *World Journal of Gastroenterology* 18: 6036.
- Costa Gomes R, Cerqueira Maia J, Fernando Arrais R, et al. (2016) The celiac iceberg: From the clinical spectrum to serology and histopathology in children and adolescents with type 1 diabetes mellitus and Down

- syndrome. *Scandinavian Journal of Gastroenterology* 51: 178–185.
20. Oujamaa I, Sebbani M, Elmoumou L, et al. (2019) The prevalence of celiac disease-specific auto-antibodies in type 1 diabetes in a Moroccan population. *International Journal of Endocrinology* 2019: 7895207.
  21. Minelli R, Gaiani F, Kayali S, et al. (2018) Thyroid and celiac disease in pediatric age: A literature review. *Acta Biomedica* 89: 11–16.
  22. Du Y, Shan L-F, Cao Z-Z, et al. (2018) Prevalence of celiac disease in patients with Down syndrome: A meta-analysis. *Oncotarget* 9: 5387–5396.
  23. Pavlovic M, Berenji K and Bukurov M (2017) Screening of celiac disease in Down syndrome-old and new dilemmas. *World Journal of Clinical Cases* 5: 264.
  24. Hoffmanová I, Sánchez D, Tučková L, et al. (2018) Celiac disease and liver disorders: From putative pathogenesis to clinical implications. *Nutrients* 10: 892.
  25. Najafi M, Sadjadei N, Eftekhari K, et al. (2014) Prevalence of celiac disease in children with autoimmune hepatitis and vice versa. *Iranian Journal of Pediatrics* 24: 723–728.
  26. De Sanctis V and Khater D (2019) Autoimmune diseases in Turner syndrome: An overview. *Acta Bio Medica Atenei Parmensis* 90: 341–344.
  27. Kılınç S (2019) Associated clinical abnormalities among patients with Turner syndrome. *Nothorn Clinics Of Istanbul* 7: 226–230.
  28. Kumral D and Syed S (2020) Celiac disease screening for high-risk groups: Are we doing it right? *Digestive Diseases and Sciences* 65(8): 2187–2195.
  29. Dubé C, Rostom A, Sy R, et al. (2005) The prevalence of celiac disease in average-risk and at-risk Western European populations: A systematic review. *Gastroenterology* 128: S57–S67.
  30. Mahadev S, Laszkowska M, Sundström J, et al. (2018) Prevalence of celiac disease in patients with iron deficiency anemia—A systematic review with meta-analysis. *Gastroenterology* 155: 374–382.e1.
  31. Lohi S, Mustalahti K, Kaukinen K, et al. (2007) Increasing prevalence of coeliac disease over time. *Alimentary Pharmacology & Therapeutics* 26: 1217–1225.
  32. Rewers M (2005) Epidemiology of celiac disease: What are the prevalence, incidence, and progression of celiac disease? *Gastroenterology* 128: S47–S51.
  33. Ettersperger J, Montcuquet N, Malamut G, et al. (2016) Interleukin-15-dependent T-cell-like innate intraepithelial lymphocytes develop in the intestine and transform into lymphomas in celiac disease. *Immunity* 45: 610–625.
  34. Rampertab SD, Pooran N, Brar P, et al. (2006) Trends in the presentation of celiac disease. *The American Journal of Medicine* 119: 355.e9–355.e14.
  35. Hill ID, Dirks MH, Liptak GS, et al. (2005) Guideline for the diagnosis and treatment of celiac disease in children: Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *Journal of Pediatric Gastroenterology and Nutrition* 40: 1–19.
  36. Mouterde O, Hariz MB and Dumant C (2008) Le nouveau visage de la maladie cœliaque. *Archives de Pédiatrie* 15: 501–503.
  37. Fasano A (2005) Clinical presentation of celiac disease in the pediatric population. *Gastroenterology* 128: S68–S73.
  38. Nenna R, Mosca A, Mennini M, et al. (2015) Coeliac disease screening among a large cohort of overweight/obese children. *Journal of Pediatric Gastroenterology and Nutrition* 60: 405–407.
  39. Rashid M and Lee J (2016) Serologic testing in celiac disease: Practical guide for clinicians. *Canadian Family Physician* 62: 38–43.
  40. Kelly CP, Bai JC, Liu E, et al. (2015) Advances in diagnosis and management of celiac disease. *Gastroenterology* 148: 1175–1186.
  41. Nion-Larmurier I and Cosnes J (2009) Celiac disease. *Gastroentérologie Clinique et Biologique* 33: 508–517.
  42. Bushara KO (2005) Neurologic presentation of celiac disease. *Gastroenterology* 128: S92–S97.
  43. Nenna R, Petrarca L, Verdecchia P, et al. (2016) Celiac disease in a large cohort of children and adolescents with recurrent headache: A retrospective study. *Digestive and Liver Disease* 48: 495–498.
  44. Parisi P, Pietropaoli N, Ferretti A, et al. (2015) Role of the gluten-free diet on neurological-EEG findings and sleep disordered breathing in children with celiac disease. *Seizure* 25: 181–183.
  45. Lebwohl B, Ludvigsson JF and Green PHR (2015) Celiac disease and non-celiac gluten sensitivity. *BMJ* 351: h3447.
  46. Ehsani-Ardakani MJ, Nejad MR, Villanacci V, et al. (2013) Gastrointestinal and non-gastrointestinal presentation in patients with celiac disease. *Archives of Iranian Medicine* 16: 78–82.
  47. Olives JP (2001) Nouvelles stratégies diagnostiques de la maladie cœliaque. *Archives de Pédiatrie* 8: 403–405.
  48. Vajro P, Maddaluno S and Veropalumbo C (2013) Persistent hypertransaminasemia in asymptomatic children: A stepwise approach. *World Journal of Gastroenterology* 19: 2740.
  49. Sharma M, Singh P, Agnihotri A, et al. (2013) Celiac disease: A disease with varied manifestations in adults and adolescents. *Journal of Digestive Diseases* 14: 518–525.
  50. Admou B, Essaadouni L, Krati K, et al. (2012) Atypical celiac disease: From recognizing to managing. *Gastroenterology Research and Practice* 2012: 637187.

51. Hill ID (2005) What are the sensitivity and specificity of serologic tests for celiac disease? Do sensitivity and specificity vary in different populations? *Gastroenterology* 128: S25–S32.
52. Bai JC, Fried M, Corazza GR, et al. (2013) World Gastroenterology Organisation global guidelines on celiac disease. *Journal of Clinical Gastroenterology* 47: 121–126.
53. Bossuyt X (2014) Le diagnostic de la maladie cœliaque au laboratoire: Recommandations actuelles. *Revue Francophone des Laboratoires* 2014: 15–20.
54. Van Meensel B, Hiele M, Hoffman I, et al. (2004) Diagnostic accuracy of ten second-generation (human) tissue transglutaminase antibody assays in celiac disease. *Clinical Chemistry* 50: 2150–2135.
55. Volta U, Granito A, Parisi C, et al. (2010) Deamidated gliadin peptide antibodies as a routine test for celiac disease: A prospective analysis. *Journal of Clinical Gastroenterology* 44: 186–190.
56. Agardh D (2007) Antibodies against synthetic deamidated gliadin peptides and tissue transglutaminase for the identification of childhood celiac disease. *Clinical Gastroenterology and Hepatology* 11: 1276–1281.
57. Webb C, Norström F, Myléus A, et al (2015) Celiac disease can be predicted by high levels of anti-tissue transglutaminase antibodies in population-based screening. *Journal of Pediatric Gastroenterology and Nutrition* 60: 787–791.
58. Sandström O, Rosén A, Lagerqvist C, et al. (2013) Transglutaminase IgA antibodies in a celiac disease mass screening and the role of HLA-DQ genotyping and endomysial antibodies in sequential testing. *Journal of Pediatric Gastroenterology and Nutrition* 57: 472–476.
59. Rostom A, Dubé C, Cranney A, et al. (2005) The diagnostic accuracy of serologic tests for celiac disease: A systematic review. *Gastroenterology* 128: S38–S46.
60. Giersiepen K, Lelgemann M, Stuhldreher N, et al. (2012) Accuracy of diagnostic antibody tests for coeliac disease in children: Summary of an evidence report. *Journal of Pediatric Gastroenterology and Nutrition* 54: 229–241.
61. Sugai E, Hwang HJ, Vázquez H, et al. (2015) Should ESPGHAN guidelines for serologic diagnosis of celiac disease be used in adults? A prospective analysis in an adult patient cohort with high pretest probability. *The American Journal of Gastroenterology* 110: 1504–1505.
62. Oyaert M, Vermeersch P, De Hertogh G, et al. (2015) Combining antibody tests and taking into account antibody levels improves serologic diagnosis of celiac disease. *Clinical Chemistry and Laboratory Medicine* 53: 1537–1546.
63. Rashtak S, Ettore MW, Homburger HA, et al. (2008) Combination testing for antibodies in the diagnosis of coeliac disease: Comparison of multiplex immunoassay and ELISA methods. *Alimentary Pharmacology & Therapeutics* 28: 805–813.
64. Hoerter NA, Shannahan SE, Suarez J, et al. (2017) Diagnostic yield of isolated deamidated gliadin peptide antibody elevation for celiac disease. *Digestive Diseases and Sciences* 62: 1272–1276.
65. Condò R, Costacurta M and Docimo R (2013) The anti-transglutaminase auto-antibodies in children's saliva with a suspect coeliac disease: Clinical study. *ORAL & implantology* 6: 48–54.
66. Bonamico M, Nenna R, Montuori M, et al. (2011) First salivary screening of celiac disease by detection of anti-transglutaminase autoantibody radioimmunoassay in 5000 Italian primary schoolchildren. *Journal of Pediatric Gastroenterology and Nutrition* 52: 17–20.
67. Bergamini CM, Dean M, Matteucci G, et al. (1999) Conformational stability of human erythrocyte transglutaminase. Patterns of thermal unfolding at acid and alkaline pH. *European Journal of Biochemistry* 266: 575–582.
68. Korponay-Szabo I, Nemes E, Vecsei Z, et al. (2008) Rapid bedside detection of humoral IgA deficiency and celiac disease antibodies from capillary blood. In: *2008 World congress of pediatric gastroenterology, hepatology, and nutrition*, Chutes d'Iguazu, Brésil, 16–20, Bologna: Medimond International Proceedings, <https://journals.lww.com/jpgn/Documents/WorldCongress2008abstracts.pdf>
69. Raivio T, Kaukinen K, Nemes É, et al. (2006) Self transglutaminase-based rapid coeliac disease antibody detection by a lateral flow method. *Alimentary Pharmacology & Therapeutics* 24: 147–154.
70. Costa S, Astarita L, Ben-Hariz M, et al. (2014) A point-of-care test for facing the burden of undiagnosed celiac disease in the Mediterranean area: A pragmatic design study. *BMC Gastroenterology* 14: 219.
71. da Silva TSG and Furlanetto TW (2010) Diagnosis of celiac disease in adults. *Revista da Associação Médica Brasileira* 56: 122–126.
72. Rubio-Tapia A, Hill ID, Kelly CP, et al. (2013) ACG clinical guidelines: Diagnosis and management of celiac disease. *The American Journal of Gastroenterology* 108: 656–676.
73. Ramos ATP, Figueirêdo MM, de Aguiar APB, et al. (2016) Celiac disease and cystic fibrosis: Challenges to differential diagnosis. *Folia Medica (Plovdiv)* 58: 141–147.
74. Ludvigsson JF, Bai JC, Biagi F, et al. (2014) Diagnosis and management of adult coeliac disease: Guidelines from the British society of gastroenterology. *Gut* 63: 1210–1228.
75. Abadie V, Sollid LM, Barreiro LB, et al. (2011) Integration of genetic and immunological insights

- into a model of celiac disease pathogenesis. *Annual Review of Immunology* 29: 493–525.
76. Rostom A, Murray JA and Kagnoff MF (2006) American Gastroenterological Association (AGA) Institute technical review on the diagnosis and management of celiac disease. *Gastroenterology* 131: 1981–2002.
77. Shannahan S and Leffler DA (2017) Diagnosis and updates in celiac disease. *Gastrointestinal Endoscopy Clinics of North America* 27: 79–92.
78. McCarty TR, O'Brien CR, Gremida A, et al. (2018) Efficacy of duodenal bulb biopsy for diagnosis of celiac disease: A systematic review and meta-analysis. *Endoscopy International Open* 6: E1369–E1378.
79. Adelman DC, Murray J, Wu T-T, et al. (2018) Measuring change in small intestinal histology in patients with celiac disease. *The American Journal of Gastroenterology* 113: 339–347.
80. Pais WP, Duerksen DR, Pettigrew NM, et al. (2008) How many duodenal biopsy specimens are required to make a diagnosis of celiac disease? *Gastrointestinal Endoscopy* 67: 1082–1087.
81. Verkarre V and Brousse N (2013) Le diagnostic histologique de la maladie cœliaque. *Pathologie Biologie* 61: e13–e19.
82. Patey-Mariaud De Serre N, Verkarre V, Cellier C, et al. (2001) Etiological diagnosis of villous atrophy. *Annales de Pathologie* 939: 301–367.
83. Pallav K, Leffler DA, Tariq S, et al. (2012) Noncoeliac enteropathy: The differential diagnosis of villous atrophy in contemporary clinical practice. *Alimentary Pharmacology & Therapeutics* 35: 380–390.
84. Aziz I, Key T, Goodwin JG, et al. (2015) Predictors for celiac disease in adult cases of duodenal intraepithelial lymphocytosis. *Journal of Clinical Gastroenterology* 49: 477–482.
85. Schmitz J and Garnier-Lengliné H (2008) Celiac disease diagnosis in 2008. *Archives de Pédiatrie* 15: 456–461.
86. Husby S, Murray JA and Katzka DA (2019) AGA clinical practice update on diagnosis and monitoring of celiac disease—Changing utility of serology and histologic measures: Expert review. *Gastroenterology* 156: 885–889.
87. Bouteloup C (2016) Digestive diseases related to wheat or gluten: Certainties and doubts. *Cahiers de Nutrition et de Diététique* 51: 248–258.
88. Catassi C and Fasano A (2010) Celiac disease diagnosis: Simple rules are better than complicated algorithms. *The American Journal of Medicine* 123: 691–693.
89. Werkstetter KJ, Korponay-Szabó IR, Popp A, et al. (2017) Accuracy in diagnosis of celiac disease without biopsies in clinical practice. *Gastroenterology* 153: 924–935.
90. Gidrewicz D, Potter K, Trevenen CL, et al. (2015) Evaluation of the ESPGHAN celiac guidelines in a North American pediatric population. *The American Journal of Gastroenterology* 110: 760–767.
91. Murch S, Jenkins H, Auth M, et al. (2013) Joint ESPGHAN and coeliac UK guidelines for the diagnosis and management of coeliac disease in children. *Archives of Disease in Childhood* 98: 806–811.
92. Husby S, Koletzko S, Korponay-Szabó I, et al. (2020) European society paediatric gastroenterology, hepatology and nutrition guidelines for diagnosing coeliac disease 2020. *Journal of Pediatric Gastroenterology and Nutrition* 70: 141–156.
93. Leffler DA and Schuppan D (2010) Update on serologic testing in celiac disease. *The American Journal of Gastroenterology* 105: 2520–2524.
94. Rahmati A, Shakeri R, Sohrabi M, et al. (2014) Correlation of tissue transglutaminase antibody with duodenal histologic marsh grading. *Middle East Journal of Digestive Diseases* 6: 131–136.
95. Alessio MG, Tonutti E, Brusca I, et al. (2012) Correlation between IgA tissue transglutaminase antibody ratio and histological finding in celiac disease. *Journal of Pediatric Gastroenterology and Nutrition* 55: 44–49.
96. Zanini B, Magni A, Caselani F, et al. (2012) High tissue-transglutaminase antibody level predicts small intestinal villous atrophy in adult patients at high risk of celiac disease. *Digestive and Liver Disease* 44: 280–285.
97. Tounian P and Sarrio F (2017) Prise en charge diététique de certaines pathologies. In: *Alimentation De L'enfant De 0 à 3 Ans*, 3rd edn. Paris, France: Elsevier Masson, pp.97–116. <https://www.sciencedirect.com/book/9782294748530/alimentation-de-lenfant-de-0-a-3-ans>
98. Fayet L, Guex E and Bouteloup C (2011) Gluten free diet: The practical points. *Nutrition Clinique et Métabolisme* 25: 196–198.
99. Cegarra M (2006) Gluten-free diet: A challenging follow-up. *Archives de Pédiatrie* 13: 576–578.
100. Simpson S and Thompson T (2012) Nutrition assessment in celiac disease. *Gastrointestinal Endoscopy Clinics of North America* 22: 797–809.
101. Schmitz J (2013) Le régime sans gluten chez l'enfant. *Pathologie Biologie* 61: 129–133.
102. Faure S, Pineau S, Amar É, et al. (2012) Pathologies et régimes alimentaires. *Actualités Pharmaceutiques* 51: 1–24.
103. Battu C (2017) L'accompagnement nutritionnel d'un patient souffrant d'une maladie cœliaque. *Actualités Pharmaceutiques* 56: 55–58.
104. Weber AL (2012) *La maladie cœliaque: physiopathologie et traitement. "Guide" de conseils pour le pharmacien d'officine*. Université de lorraine. Available

- at: <https://hal.univ-lorraine.fr/hal-01733878> (accessed 14 March 2018).
105. Lee SK, Lo W, Memeo L, et al. (2003) Duodenal histology in patients with celiac disease after treatment with a gluten-free diet. *Gastrointestinal Endoscopy* 57: 187–191.
  106. Fotoulaki M, Nousia-Arvanitakis S, Augoustidou-Savvopoulou P, et al. (1999) Clinical application of immunological markers as monitoring tests in celiac disease. *Digestive Diseases and Sciences* 44: 2133–2138.
  107. Lebowitz B, Murray JA, Rubio-Tapia A, et al. (2014) Predictors of persistent villous atrophy in celiac disease: A population-based study. *Alimentary Pharmacology & Therapeutics* 39: 488–495.
  108. Olives JP (2013) Should the whole population be screened for coeliac disease? *Pathologie Biologie* 61: e57–e60.
  109. Rashid M, Cranney A, Zarkadas M, et al. (2005) Celiac disease: Evaluation of the diagnosis and dietary compliance in Canadian children. *Pediatrics* 116: e754–e759.
  110. Ochubiojo EM and Rodrigues A (2012) *Scientific, Health and Social Aspects of the Food Industry*. InTech. <https://www.intechopen.com/books/scientific-health-and-social-aspects-of-the-food-industry/starch-from-food-to-medicine>
  111. Le Jeune C (2013) Les médicaments génériques. *Revue Francophone des Laboratoires* 4028: 5–53.
  112. U.S. Department of Health and Human Services Food and Drug Administration (2017) *Gluten in Drug Products and Associated Labeling Recommendations Guidance for Industry*. Available at: <https://www.fda.gov/drugs/ensuring-safe-use-medicine/medications-and-gluten> (accessed 12 December 2017).
  113. Bousquet A (2015) *La maladie cœliaque, du diagnostic à sa prise en charge: un nouvel espoir thérapeutique?* Université Toulouse III-Paul Sabatier. <http://thesesante.ups-tlse.fr/948/1/2015TOU32063.pdf>
  114. Cruz JE, Cocchio C, Lai PT, et al. (2015) Gluten content of medications. *American Journal of Health System Pharmacy* 72: 54–60.