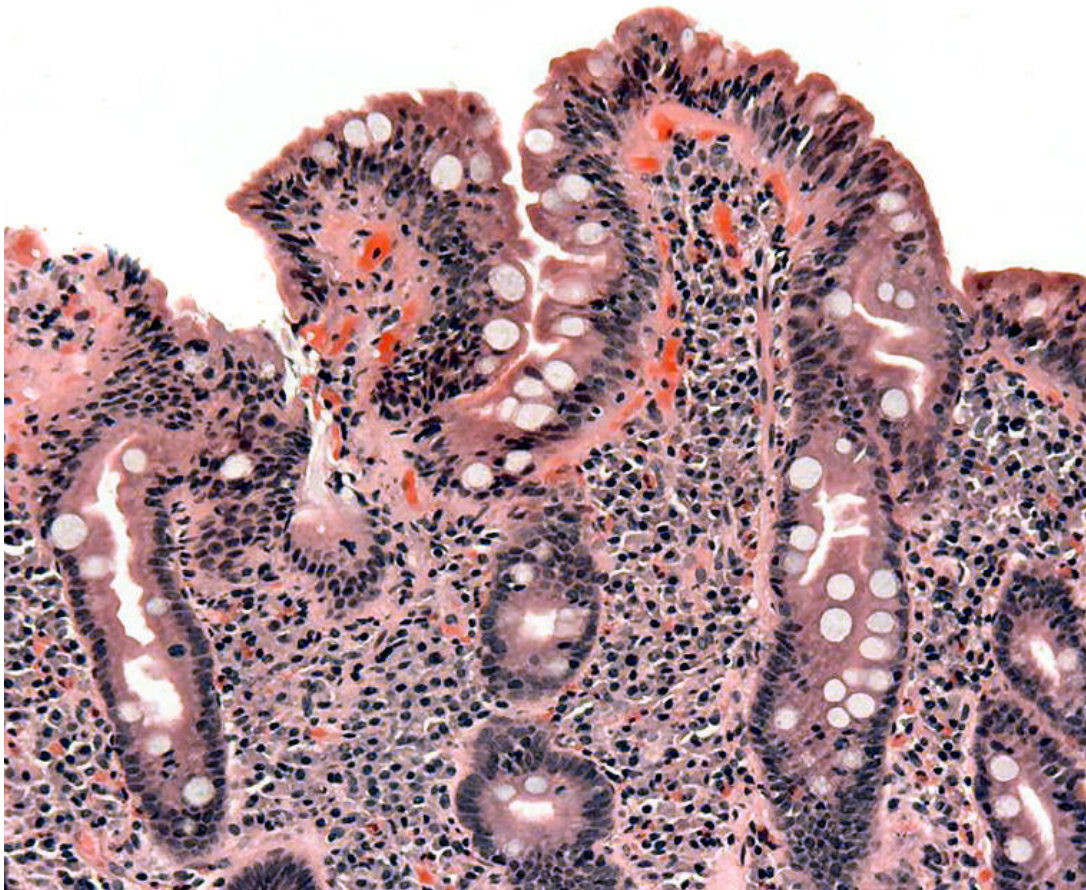


Celiac Disease (Celiac Sprue, Gluten Enteropathy) — Symptoms and Treatment

[See online here](#)

Celiac disease, also called gluten-sensitive enteropathy or nontropical sprue, is a type of malabsorption syndrome. Relevant exam topics include the symptoms of gluten sensitivity and the clinical presentation of chronic malabsorption. Diagnosis is led by the characteristic histological findings and specific autoantibodies.



Definition of Celiac Disease

Celiac disease: A type of gluten sensitivity

Celiac disease is the intolerance to gliadin, a component of the protein gluten. When a person with celiac disease ingests gliadin, it triggers an inflammatory response in the intestinal mucosa, resulting in the malabsorption of food nutrients.

Almost all of the cereal types that are cultivated and consumed in Europe and the United States contain gluten.

Cereals containing gluten: Wheat, rye, barley, spelt and green spelt, kamut wheat, emmer and einkorn wheat

Gluten-free cereals: Rice, corn, millet, buckwheat, quinoa and amaranth

Epidemiology of Celiac Disease

In the Western population, it is estimated that about 1 in 100 people have celiac disease. However, the incidence rates vary strongly between regions, with the highest rates found among white Europeans. The trend is rising and it is assumed that there is a high number of undiagnosed cases due to very mild forms or delayed courses of the disease.

Etiology of Celiac Disease

Genetic predisposition for celiac disease

What causes celiac disease has not been conclusively clarified. There is, however, a strong genetic disposition: The receptor proteins **HLA-DQ2 or HLA-DQ8** can be found in almost all patients with celiac disease.

Note: Many autoimmune diseases are associated with celiac disease.

Gliadin triggers an inflammatory response in the lamina propria of the [small intestine](#). An often tested fact: In gluten-sensitive persons, the **enzyme tissue transglutaminase (tTG)** connects gliadin with proteins of the connective tissue, forming new antigen structures. These structures, in turn, trigger destructive inflammation processes in the mucosa of the small intestine which results in **lymphocyte infiltration and villous atrophy**.

UPPER JEJUNAL MUCOSAL IMMUNOPATHOLOGY

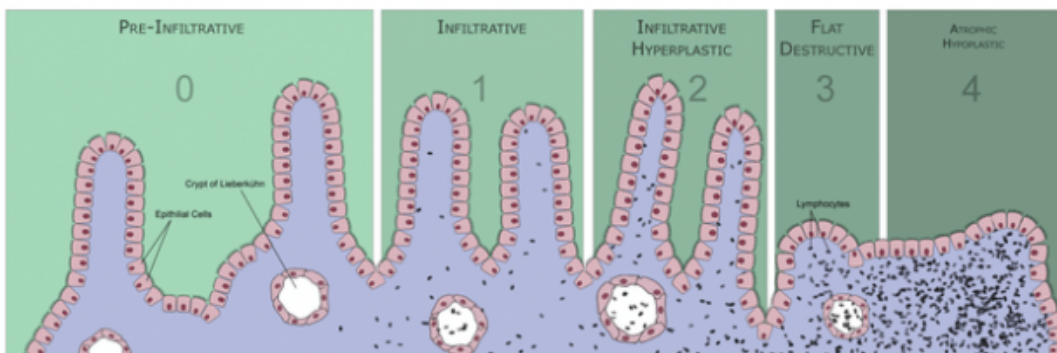


Image: "Diagram to show the different stages of Coeliac Disease." by WikipedianProlific at en.wikipedia. License: [CC BY-SA 3.0](#)

The inflammation diminishes the resorptive surface of the intestine and leads to **severe malabsorption** and maldigestion of all food nutrients.

Pathology of Celiac Disease

Mucosal changes in celiac disease

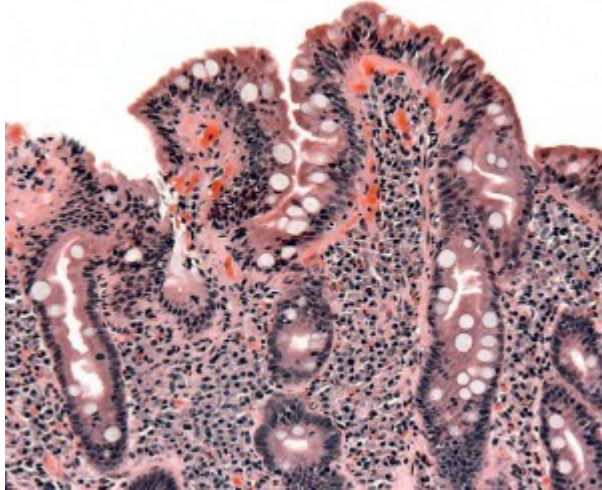


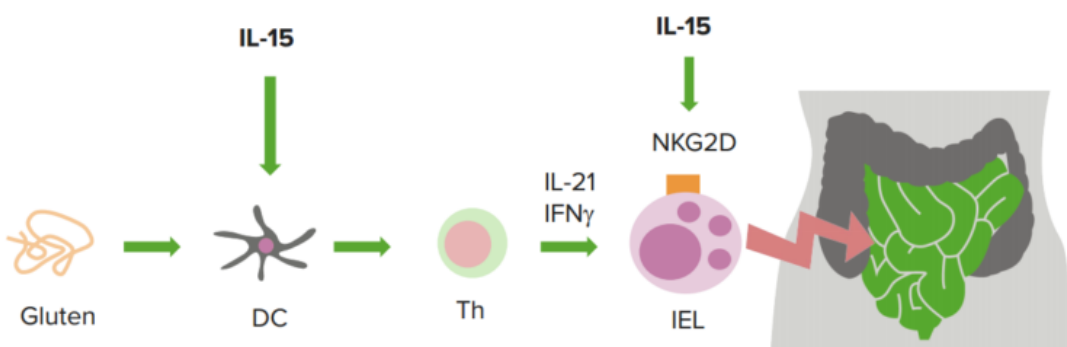
Image: „Biopsy of small bowel showing coeliac disease manifested by blunting of villi, crypt hyperplasia, and lymphocyte infiltration of crypts, consistent with Marsh classification III.“ by [Samir](#) at en.wikipedia. License: [CC BY-SA 3.0](#)

Celiac disease is characterized by mucosal changes, especially the blunting of villi, crypt hypertrophy, and inflammatory infiltration of cell structures into the mucosa.

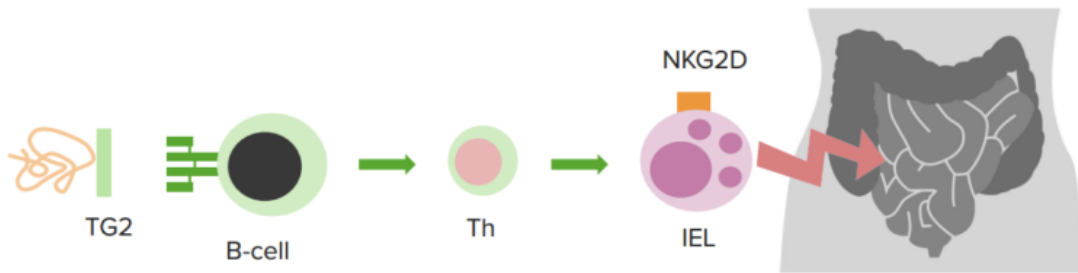
The appearance of the mucosa can vary, from inconspicuous mucosal folds to fold scalloping and even completely reduced mucosal folds.

In a much progressed stage, even a narrowing of the Kerckring folds can be found.

- T-cell reactivity to the gliadin component of wheat gluten in the small intestine
- Gluten absorbed from gut is taken up by dendritic cells
- Processed and presented to T-cells in mesenteric lymph nodes
- IL-15 stimulates dendritic cells to activate proinflammatory Th cells secreting IL-21 and IFN γ
- Induction of gluten-specific Th and B-cells
- Lymphocytes home to gut lamina propria
- IL-15 also induces expression of the cytotoxicity-activating receptor NKG2D on CD8⁺ IELs
- NKG2D recognizes stress-induced self-ligands such as MICA/B
- NKG2D⁺ CD8⁺ IELs destroy gut epithelial cells



- Autoantibodies against transglutaminase 2 (TG2) are also present
- Gluten binds to TG2
- Therefore, IgA B-cells specific for TG2 may process and present gliadin to Th cells



Note: Villous atrophy, crypt hyperplasia, and lymphocyte infiltration are characteristic histological findings for celiac disease.

Symptoms of Celiac Disease

Clinical presentation of celiac disease

About 3 to 4 months after introducing an infant to cereal products such as porridge or bread, i.e. starting with the second year of life, first symptoms may manifest. If celiac disease is not recognized as such, serious sequelae might develop.

Initial symptoms include:

- Lack of weight gain
- Loss of appetite
- Reduced tolerance to stress
- Increasing [diarrhea](#)

If the disease has already progressed, the following **cardinal symptoms** may become apparent:

- Protuberant abdomen
- Lipodystrophy of the buttocks
- Dermatitis herpetiformis
- Muscle wasting
- [Iron deficiency anemia](#) caused by the malabsorption
- Hypoproteinemic [edema](#)

If left untreated, celiac disease can result in **severe sequelae**, such as:

- Short stature
- Hypoproteinemia
- Rickets (vitamin D deficiency)
- Coagulation defects (vitamin K deficiency)
- Joint pain
- Delayed puberty
- Absence of menarche

Note: Also with adult patients or when the clinical presentation is not comprehensive, celiac disease should still be considered.

Diagnosis of Celiac Disease

Tentative diagnosis of celiac disease through close observation

As mentioned above, starting with the second year of life, attention should be paid to any failure to thrive and to unusual signs of mood swings or severe diarrhea.

Important hint: The first clinical diagnostic evidence for suspected celiac disease can consist in the detection of IgA and IgG endomysial antibodies against gliadin (gluten-sensitive enteropathy).

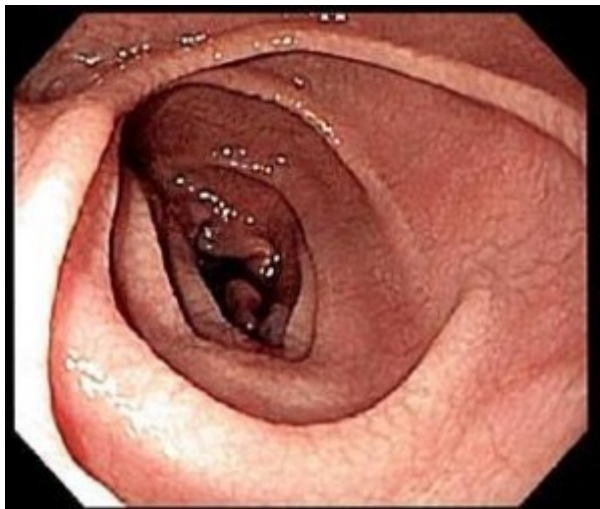


Image: "Endoscopic image of duodenum in individual with celiac disease, showing scalloping of the folds and cracked-mud appearance of the mucosa.." by [Samir](#) at en.wikipedia. License: [CC BY-SA 3.0](#)

Increased levels point to celiac disease and can cause dermatitis herpetiformis, a chronic skin disease marked by herpes-like vesicles and strong pruritus.

Positive evidence of IgA antibodies against tissue transglutaminase can be a further indication for the autoimmune celiac disease. Transglutaminase antibodies are autoantibodies that are directed against certain structures on the inside of muscle cells.

General screening for antibodies can increase the chance of detecting celiac disease early, but only a biopsy of the small intestine can provide a definitive diagnosis.

Note: For exams, it is important to know about tTG antibodies, anti-gliadin antibodies, and endomysial antibodies.

Differential Diagnosis of Celiac Disease

Similar disease patterns to celiac disease

Based on dietary history, weight gain patterns, and clinical findings including laboratory and imaging studies, further diagnostic considerations can be explored.

The following conditions should be considered as possible differential diagnoses:

- Infectious diseases (e.g., [Whipple's disease](#))
- Chronic inflammatory diseases (e.g., [Crohn's disease](#))
- [Irritable bowel syndrome](#)
- Food allergies
- Diarrheic diseases (e.g., fructose malabsorption or [lactose intolerance](#))
- Hereditary diseases (e.g., [cystic fibrosis](#))

Treatment of Celiac Disease

Gluten-free diet for celiac disease



Logo of a gluten-free certification program

Celiac disease is incurable; however, the right diet and lifestyle can provide for the unproblematic management of this disease.

Gold-standard treatment is a permanent gliadin-free diet, which excludes any food products that are based on cereal grains like wheat, rye, oat or barley.

At the beginning, an additional substitution of vitamins and iron accompanies this diet, and soon, the mood should improve, the appetite increases and diarrhea should be diminished.

Prevention and Prognosis of Celiac Disease

Food products based on rice, corn, soy beans, potatoes, nuts, or carob flour are unproblematic.

A gluten-free diet should result in normalization of the IgA endomysial antibody titers.

There are investigations into supplemental medication, especially for oligosymptomatic patients, to increase their tolerance of minor amounts of gluten. Most efforts are currently aimed at the **development of transglutaminase inhibitors**.

A protective influence has been attributed to breastfeeding—also against other allergic diseases. Currently, there is a European study being performed regarding a possibly protective effect the **introduction of minimal doses of gluten** into baby food might have.

Review Questions

Solutions can be found below the references.

1. Which antibodies should be screened for when suspecting celiac disease?

- A. Anti-gliadin antibodies, tTG antibodies, endomysial antibodies
- B. c-ANCA and tTG antibodies
- C. RF
- D. Cardiolipin and anti-gliadin antibodies
- E. p-ANCA

2. What are characteristic histological findings for celiac disease?

- A. Villous hyperplasia
- B. Crypt atrophy
- C. Lymphocyte infiltration in the lamina propria
- D. Villous atrophy and no lymphocyte infiltration
- E. Crypt and villous hyperplasia

3. In which year of life do the initial symptoms of celiac disease typically, but not necessarily, occur?

- A. 13th to 18th year of life
- B. 20th year of life
- C. 2nd year of life
- D. 5th to 6th decade of life
- E. 12th year of life

References

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Correct answers: 1A, 2C, 3C

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