

Celiac disease CD (gluten-sensitive enteropathy)

Definition: It is a chronic digestive disorder caused by an immune reaction to gluten -gliadin and glutenin. in patient's **genetically susceptible children and adults**. The toxins result from the immune reaction to gluten damage the villi decreases absorb nutrients (malnutrition) .

What are causes of Coeliac disease?

- 1-Coeliac disease caused by a reaction to gliadin, a prolamin found in wheat.
- 2- **Two** specific genes associated with CD. these **genes- HLA DQ2 and HLA DQ8**.
- 3- Autoantibody against **TG (Transglutaminase)** detected in over 95% of CD.

Immune Mediated Mechanism :-

The **gluten** (as Ag) is presented by antigen-presenting cells (APCs) in the lamina propria to **CD4⁺ T cells** after it has been **deamidated** by transglutaminase 2 (TG2). There is increased local production of antibodies. Immunoglobulin A (IgA) antibodies are secreted to the gut lumen as secretory IgA (SIgA). The epithelial **compartment of IL-15** activated natural killer (NK) cell receptors.

What are the main Signs and symptoms of CD?

Chronic diarrhea (greasy stool (**steatorrhoea**)) Weight loss ,Anemia In children with classic celiac disease: failure to thrive, weight loss, short stature, Vomiting , Diarrhea greasy stool (**steatorrhoea**) ,Hypoproteinemia.

pathogenesis of CD, that leads to:

1-Anti-Tissue transglutaminase(tTG) : autoantibodies to the enzyme tissue transglutaminase (tTG) are found in majority of cases. Tissue transglutaminase **modifies gluten peptides** (deamidation or transamidation) that stimulate the I.s more effectively.

2- enterocyte destruction are related to gluten.

3- **Gliadin is directly toxic to the enterocytes** ,primarily through the **overexpression of IL-15 and IL2** in the intestine with activation of lymphocytes, .

Diagnosis: Screening tests (patient is on a **gluten-containing diet**). Diagnosis of celiac disease is usually by slandered tools:

1-Electrolytes and chemistries - Electrolyte imbalances; evidence of malnutrition

2-Hematologic tests - Anemia, low serum iron level, prolonged prothrombin time (PT)

3- **Biopsy of the small intestine by upper intestinal endoscopy** . Histology will show some degree of villous atrophy and crypt hyperplasia.

4- **Presence of TG autoantibodies.**

Serologic, testing in celiac disease:

IgA: (IgA-tTG) or endomysium (IgA-EMA) are recommended for **initial testing**.

- ✚ **IgA or IgG anti-gliadin** antibody tests: are no longer recommended as a screening test for CD because of their very poor positive and negative predictive values.
- ✚ **IgA anti-endomysial antibodies** : remain the most specific test for coeliac disease. It is Ab bind to endomysium the connective tissue located around smooth muscle. The technique of indirect immunofluorescence for IgA EMA
- ✚ **Anti-tTG** is autoantibodies against the transglutaminase . **Anti-tTG are highly sensitive and specific for diagnosis of CD.** ELISA tests are used for detection.
- ✚ **Anti-gliadin IgE.** The IgE antibodies are more typically found in allergy-related conditions such as urticaria, asthma, and exercise-induced anaphylaxis.
- ✚ **Anti-deamidated Gliadin IgA and IgG** :directed against deamidated gliadin peptides in human serum or plasma, using ELISA technique.

What are the genetic predisposing factors for CD? Which of them is more specific?

Test	Sensitivity	Specificity
HLA-DQ2	90%	70%
HLA-DQ8	12%	80%

Treatment:

- 1- **strict gluten-free diet** is essential in the treatment and follow-up of CD.
- 2- **TG inhibitors**, which reduce the pathogenicity of gliadin .

(Refractory celiac disease): is the failure to respond to a gluten-free diet called

What is Wheat allergy? It characterizes by:

1. IgE- **and mast cell** response mediated food allergy
2. Diagnosed by RAST (Radio allegro sorbent test), skin prick or patch testing, dietary elimination/challenge

Causes of Villous Atrophy Other Than Celiac Disease

- Giardiasis
- Radiation enteritis
- Tuberculosis
- Eosinophilic gastroenteritis
- Intestinal lymphoma
- Crohn's disease

Crohn's disease

Crohn's disease, is a type of inflammatory bowel disease characterized by mucosal ulceration and inflammation, which may occur anywhere along the gastrointestinal tract but most commonly affect the distal small intestine.

Signs and symptoms:

The usual onset is between 15 and 30 years of age, but can occur at any age.

- 1- Abdominal pain may be the initial symptom of Crohn's disease.
- 2- It is often accompanied by diarrhea. The diarrhea may or may not be bloody.
- 3- **Visible bleeding in the feces is less common in Crohn's disease .**
- 4- Fistulization or abscess around the anal area .
- 5- Mouth may be affected by non-healing sores (aphthous ulcers). These can cause symptoms including difficulty swallowing (dysphagia).
- 6- Bowel obstruction also occurs and patients are at high risk of bowel cancer.

Causes: Crohn's disease seems to be caused by a combination of (three main factors (genetics, gut immune response, and the microbiota) In Crohn's disease **a malfunction in the innate immune system** and the chronic inflammation caused by disorder in adaptive immune system.

Pathogenesis: It was found that impaired cytokine secretion by macrophages, which contributes to impaired innate immunity and leads sustained microbial-induced inflammatory response in the colon. **Microbes like Mycobacterium and invasive E.coli ,clostredium. may lead to this disease.**

Diagnosis :

There are same tests used for diagnosis of Ulcerative colitis, and must differentiate between these two disease.

Antibody blood tests (biomarkers)

There are **two antibodies** used in diagnosis of Crohn disease and UC:

1. **Perinuclear anti-neutrophil antibodies (pANCA)**
2. **Anti-Saccharomyces Cerevisiae antibody (ASCA)** are antibodies against antigens presented by the cell wall of the yeast Saccharomyces cerevisiae.

These antibodies are considered biomarkers for diagnosis of Crohns Disease and UC.

- **patients with ulcerative colitis have the pANCA antibody in their blood;**
- **Patients with Crohn's disease are more likely to have ASCA in their blood.**
- p-ANCA may be positive in Crohn's Disease.
- High levels of C-reactive protein (CRP) predict in patients.

Ulcerative colitis

Ulcerative colitis is a form of inflammatory bowel disease (IBD). Ulcerative colitis is a one of disease of the colon (colitis), that includes characteristic ulcers. **The main symptom of active disease is usually constant diarrhea mixed with blood.** They may also have weight loss, leads to increased rates of anaemia.

Ulcerative colitis shares much in common with Crohn's disease, but ulcerative colitis only attacks the large intestine. Ulcerative colitis is an autoimmune disease characterized by T-cells infiltrating the colon tissue.

Causes:

Vitamin D deficiency by lack of sunlight and dietary deficiencies as a major cause of ulcerative colitis. Presence of sulfate-reducing bacteria , **Environmental factors (Diet , Smoking, drinker)**.

Treatment:

Treatment with anti-inflammatory drugs, immunosuppression, and biological therapy targeting specific components of the immune response. Colectomy (partial or total removal of the large bowel through surgery) is occasionally necessary if the disease is severe