بسم الله الرحمن الرحيم

Chronic Diarrhea

- **Persistent diarrhea** is defined as episodes that began acutely but last for at least 14 days.

- **Chronic Diarrhea**

DEFINITION.

Diarrhea, defined as increased total daily stool output, is usually associated with increased stool water content. For infants and children, this would result in stool output >10 g/kg/24 hr. When diarrhea lasts >2 wk, it is considered chronic.

Differential Diagnosis of Osmotic Vs Secretory Diarrhea

	Osmotic diarrhea	Secretory diarrhea
Volume of stool	<200 mL/24 hr	>200 mL/24 hr
Response to fasting	Diarrhea stops	Diarrhea continues
Stool Na^+	<70 mEq/L	>70 mEq/L
Reducing substances[*]	Positive	Negative
Stool Ph	<5	>6

Common Causes of Chronic Diarrhea

- Postgastroenteritis malabsorption syndrome
- Cow's milk/soy protein intolerance
- Secondary disaccharidase deficiencies
- Chronic nonspecific diarrhea
- Giardiasis
- Celiac disease

Evaluation of Patients with Chronic Diarrhea

- Clinical history including specific amounts of fluids ingested per day
- Physical examination including nutritional assessment
- Stool exam (pH, reducing substances, smear for white blood count, fat, ova, and parasites)
- Stool cultures, Stool for *Clostridium difficile* toxin.
- 72 hr stool collection for fat determination.
- Stool electrolytes, osmolality.
- Breath H_2 tests.
- Endoscopic studies and small bowel biopsy

.Management

- The 1st principle is to ***maintain adequate nutritional intake*** to permit normal growth and development.

- The 2nd step is the treatment of underlying cause.

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Disorder of malabsorption

Disorders of malabsorption constitute a broad spectrum of diseases with multiple etiologies and varied clinical manifestations.

Classification Based on the Predominant Nutrient Which Is Malabsorbed

- **Carbohydrate malabsorption**, *e.g.* Lactose malabsorption.
- **Fat malabsorption** , *e.g.* Pancreatic exocrine insufficiency and Cholestatic liver disease
- **Amino acid malabsorption**.
- **Mineral and vitamin malabsorption**, *e.g.* Acrodermatitis enteropathica (zinc malabsorption) *and* Folate malabsorption.
- **Drug induced**, Phenytoin: calcium malabsorption

Clinical approach

- The common presenting features, especially in toddlers with malabsorption, are diarrhea, abdominal distention, and failure to gain weight, with a fall in growth chart percentiles.
- Physical findings include the disappearance of the subcutaneous fat, muscle wasting, and the appearance of skin being too loose for the child .

Evaluation of Children with Suspected Intestinal Malabsorption

- The choice of investigative studies is usually guided by the history and physical examination.

- In a child presenting with diarrhea, the **initial work-up** should include;

- **Stool** occult blood and leukocytes (inflammatory disorders),
- stool microscopy and antibody tests for parasites such as *Giardia,*
- stool pH and reducing substance for carbohydrate malabsorption.
- quantitative stool fat examination to identify fat malabsorption.
- If celiac disease is suspected, serum immunoglobulin A **(IgA)** and **tissue transglutaminase levels** should be determined.

INVESTIGATIONS FOR CARBOHYDRATE .MALABSORPTION

- Measurement of carbohydrate in the stool, using a Clinitest reagent, which identifies reducing substances.
- Acidic stool with reducing substance >2+ suggests CHO malabsorption.

- **Breath hydrogen test** is used to identify the specific carbohydrate that is malabsorbed.

  After an overnight fast, the suspected sugar (lactose or sucrose) is administered as an oral solution. In malabsorption, the sugar is not digested or absorbed in the small bowel, passes to the colon, and is metabolized by the normal bacteria flora. One of the products of this process is hydrogen gas, which is absorbed through the colon mucosa and excreted in the breath.

- **Small bowel mucosal biopsies** can directly measure mucosal disaccharidase (lactase, sucrose) concentration.

Gluten-Sensitive Enteropathy (Celiac Disease)

- Celiac disease is an immune-mediated enteropathy caused by permanent sensitivity to gluten in genetically susceptible individuals, it develops only after dietary exposure to the protein gluten, which is found in wheat, rye, and barley.

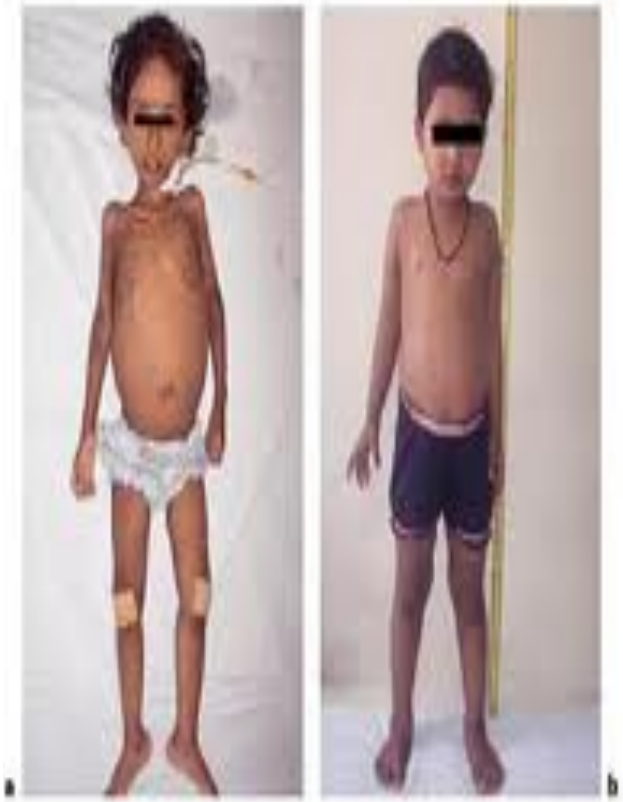
- The activity of gluten resides in the gliadin fraction, which contains certain repetitious amino acid sequences that lead to sensitization of lamina propria lymphocytes.

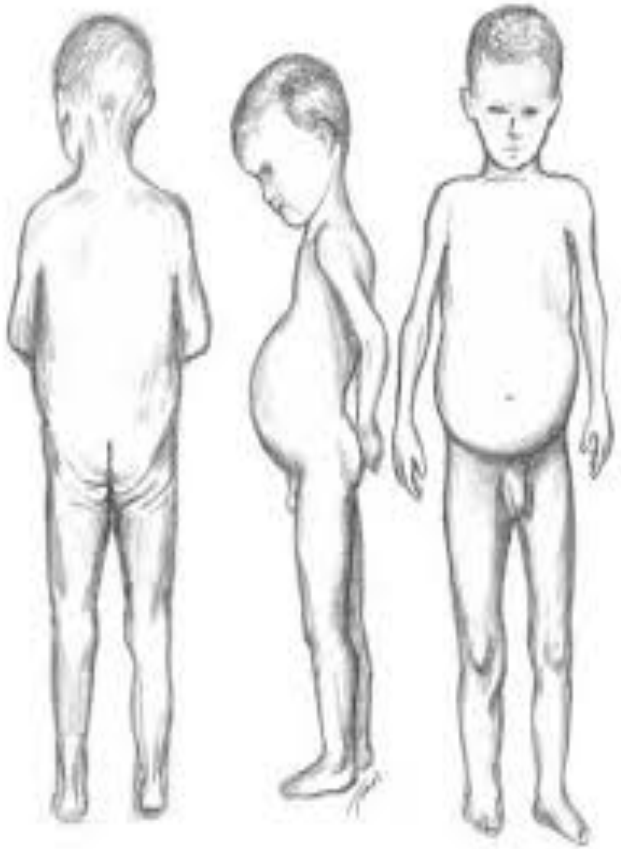
- A genetic predisposition is suggested by concordance in monozygotic twins approaching 100%. Environmental factors such as viruses may also play a role in the expression of this genetic predisposition.

Clinical presentation

- The mode of presentation of celiac disease can be quite variable .The **typical presentation** of a toddler with diarrhea, abdominal distention, and failure to thrive is becoming less common.

- **Diarrhea** is still the most common symptom and can be acute or insidious in onset. The **stools** are characteristically pale, loose, and offensive. There is often a history of **abdominal distention**, abdominal **pain**, **Muscle wasting** and **hypotonia**, and the child may be **delayed in motor milestones**.





SCREENING AND DIAGNOSIS

- The anti-endomysium IgA antibody and anti-tissue transglutaminase IgA antibody tests are highly sensitive and specific in identifying individuals with celiac disease.
- The **anti-endomysium IgA** antibody test is an immunofluorescent technique and is relatively expensive; interpretation is operator dependent and prone to errors so largely replaced by **anti-tissue transglutaminase IgA antibody tests**, which are simpler to perform. have similar sensitivity and specificity.
- **Anti-gliadin IgA and IgG** and **anti-reticulin IgA antibody** tests are no longer recommended tests due to lack of specificity.
- **Small Intestinal Biopsy. It is important for definitive diagnosis** The **characteristic histologic changes** include; partial or total villous atrophy, crypt elongation and decreased villous/crypt ratio, increased number of intraepithelial lymphocytes.
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- *The only treatment for celiac disease is **lifelong exclusion of gluten**.*

PROGNOSIS.

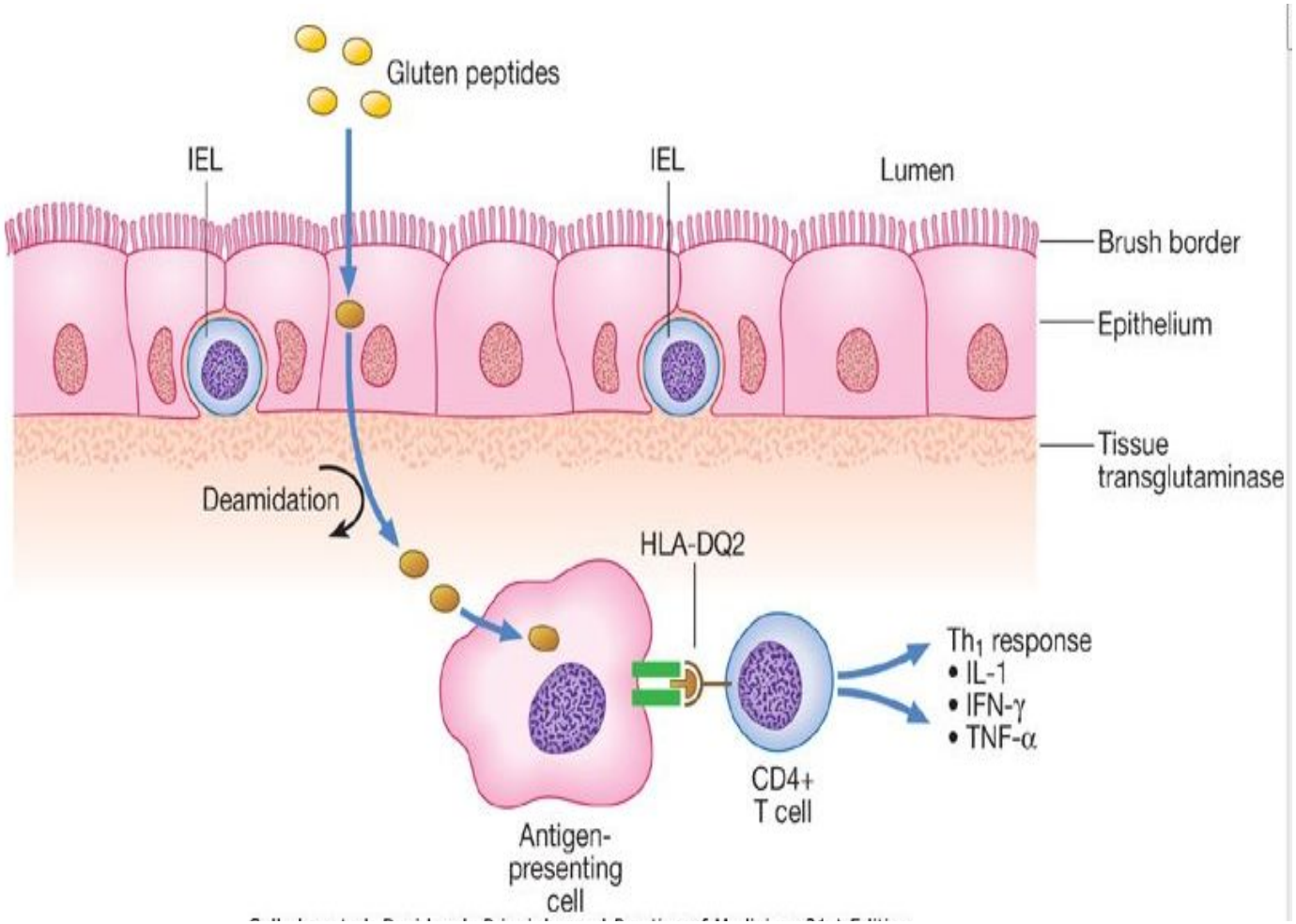
- The **clinical response** to a gluten-free diet usually results in improvement of mood, appetite, and lessening of the diarrhea within a week. **No long-term complications** from a gluten-free diet have been recognized.

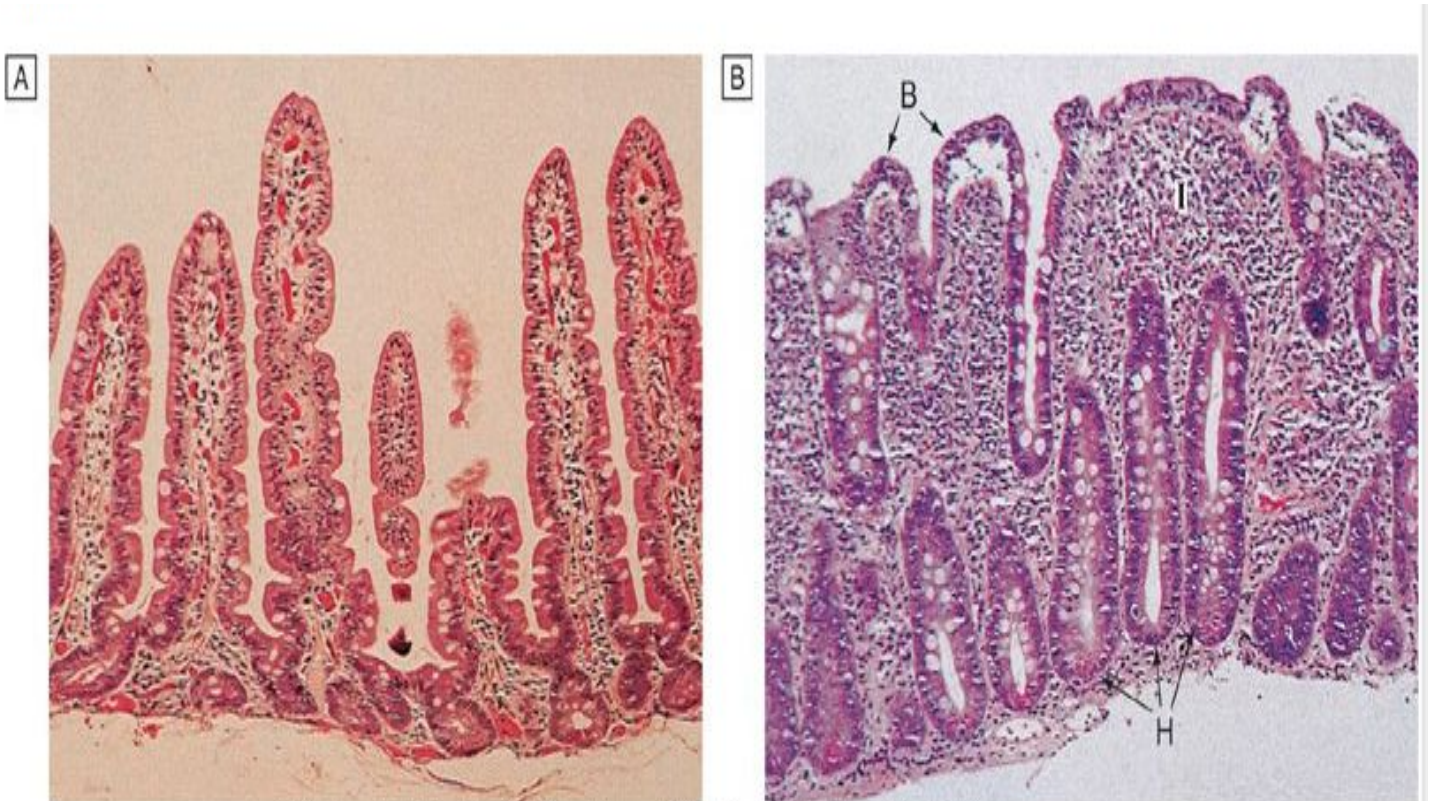
- Celiac disease is **associated with** intestinal lymphoma and other forms of cancer, especially adenocarcinoma of the small intestine, of the pharynx, and of the esophagus. Several follow-up studies suggest that a gluten-free diet protects from cancer development, especially if started in the 1st years of life.

.Pathophysiology of coeliac disease

After being taken up by epithelial cells, gluten peptides are deamidated by the enzyme tissue transglutaminase in the subepithelial layer. They are then able to fit the antigen-binding .motif on antigen-presenting cells

Recognition by these cells triggers the immune response with . generation of pro-inflammatory cytokines


Gluten peptides
IEL
IEL
Lumen
Brush border
Epithelium
Tissue transglutaminase
Deamidation
HLA-DQ2
Th1 response
• IL-1
• IFN-γ
• TNF-α
CD4+ T cell
Antigen-presenting cell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GOOD LUCK