05

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GNT pathology cases file
Don't forget to check it frequently Click

Pathology

Malabsorption

439

Color index
- Important
- Doctor's note
- Extra info
- Main text
- ★ Male's slide
- ★ Female's slide

اللهم لا سهل الا ماجعلته سهلا و انت تجعل الحزن إذا شئت سهلا

Revised & Approved

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Objective

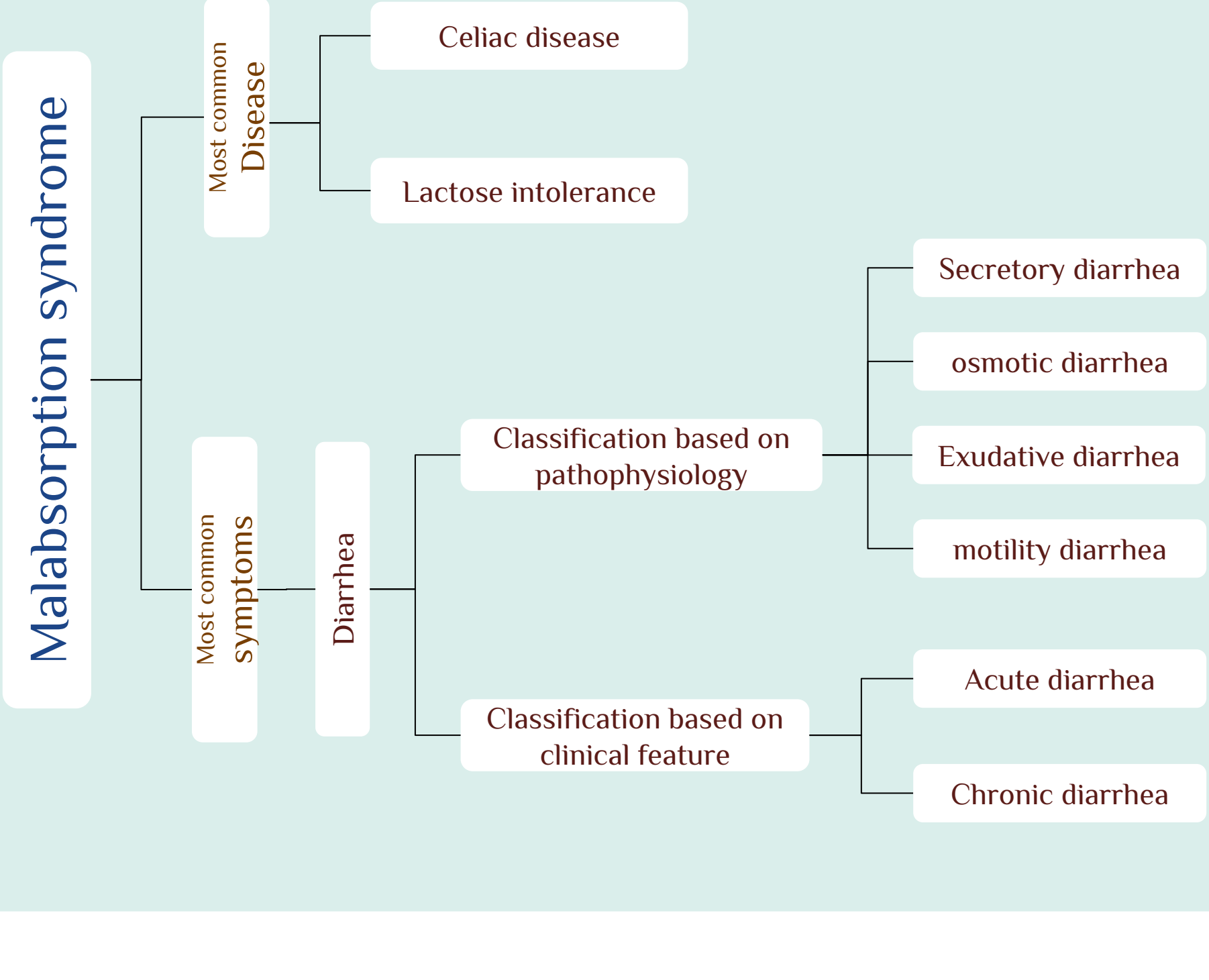
01 Understand the physiology of fluid in small intestine

02 Define diarrhea

03 Understand the four categories of diarrheal diseases, and list the major causes in each category.

04 List the causes of acute and chronic diarrhea

Overview



Normal Physiology of GI tract

- The main purpose of the gastrointestinal tract is to digests and absorbs nutrients (fat, carbohydrate, and protein), micronutrients (vitamins and trace minerals), water, minerals and electrolytes.

Malabsorption Syndrome

Definition

- it is the **inability to absorb nutrients adequately into the bloodstream**, The impairment can be of single (for certain substances like in lactose intolerance) or multiple nutrients (celiac disease) depending on the abnormality

mechanisms and their causes

Girls' doctor: You don't have to memorize them!

Inadequate Digestion:
- Postgastrectomy
- Deficiency of pancreatic lipase
- Chronic pancreatitis
- Cystic fibrosis
- Cystic fibrosis
- Pancreatic resection
- Zollinger-Ellison syndrome

Primary mucosal Abnormalities:
- **Celiac disease**
- Tropical sprue
- whipple's disease
- Amyloidosis
- Radiation enteritis
- Abetalipoproteinemia
- Giardiasis

Deficient bile salt:
- Obstructive jaundice
- Bacterial overgrowth
- Stasis in blind loops,diverticula
- Fistulas
- Hypomotility states (diabetes)
- Terminal ileal resection
- Crohn's disease
- Precipitation of bile salts (neomycin)

inadequate small intestine:
- intestinal resection
- Crohn's disease
- Mesenteric vascular disease with infarction
- Jejunoileal bypass

Malabsorption Syndrome

Pathophysiology

- Malabsorption has many mechanisms and causes, but most importantly are:
  - **Inadequate digestion**
  - **small intestine abnormalities**
- Each of these mechanisms that cause malabsorption are mainly caused by specific affected organs.

Inadequate digestion

1. Stomach
   - Postgastrectomy
2. Pancreas
   - Deficiency of pancreatic lipase
   - Chronic pancreatitis
   - Cystic fibrosis
   - Pancreatic resection e.g in case of pancreatic tumor
3. Bile
   - Obstructive jaundice
   - Terminal ileal resection, why?[1]

Small intestine abnormalities

1. Mucosa
   - Celiac disease
   - Tropical sprue[2]
   - Whipple's disease[3]
   - Giardiasis
2. inadequate small intestines
   - Intestinal resection
   - Crohn's disease[4] :fibrosis shortens the small intestine
3. Lymphatic obstruction
   - Intestinal lymphangiectasia[5]
   - Malignant lymphoma[6]

1. Normally, to digest fat we need bile salts that play a major role in fat emulsification with the help of water to get absorbed in **terminal ileum.** Thus, terminal ileal resection will prevent the bile & fat reabsorption (resulting in malabsorption) .
2. Travellers to tropical areas get exposed to bacteria that their bodies are not used to, resulting in frequent diarrhea for about a month . They return to normal with antibiotics but it will take a long time due to the villous atrophy that involves the entire intestine.
3. Infection by certain organisms (mainly protozoa "**amoeba**") leading to accumulation of inflammatory cells in the mucosa preventing the absorption process.
4. IBD : chronic disease that affect part of the intestine (mainly small intestine) leading to inflammation, fibrosis, ulceration and injury that prevent the absorption process.
5. Dilated non communicating lymphatics
6. Obstruction of the lymphatics that are needed for the absorption process.

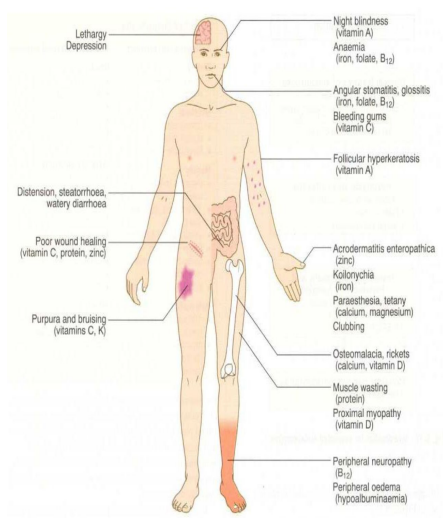
Malabsorption Syndrome

Systemic Effects

- weight loss and anorexia
- Abdominal distension and borborygmi (increased bowel sounds) due to increased gas content
- Diarrhoea (loose, bulky stools)
- **Steatorrhoea**, caused by malabsorption of fat (produces pale, foul smelling stools that characteristically float in water)
- Muscle wasting due to malabsorption of proteins

Clinical features

- **(Steatorrhea) : increase in fecal excretion of fat** soft, yellowish, greasy stools and the **systemic effects of deficiency of fat soluble vitamins (A. K,E & D), minerals, protein and carbohydrate**
- Growth retardation and failure to thrive in children.
- weight loss despite increased oral intake of nutrient



Clinical features

depends on the type of the deficient nutrient

Deficiency of Protein

-Swelling or edema
-Muscle wasting

Deficiency of Vitamin K, Other Coagulation Factors

-Bleeding tendencies
intracranial hemorrhage and bleeding under skin

Deficiency of B12, folic acid and iron

-anaemias
-fatigue and weakness

Deficiency of Vitamin D, Calcium

-Muscle cramp
-Osteomalacia
-Osteoporosis

Diagnosis

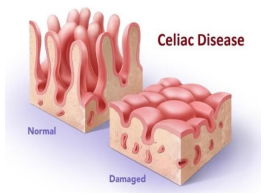
There is no specific test for malabsorption ,Investigation is guided by **Symptoms & Signs** :

1- Stool studies : Fecal fat study/content to diagnose steatorrhoea
2- Blood tests : iron deficiency anaemia ,vitamins and albumin
3- Endoscopy (for small bowel biopsy)

Celiac disease

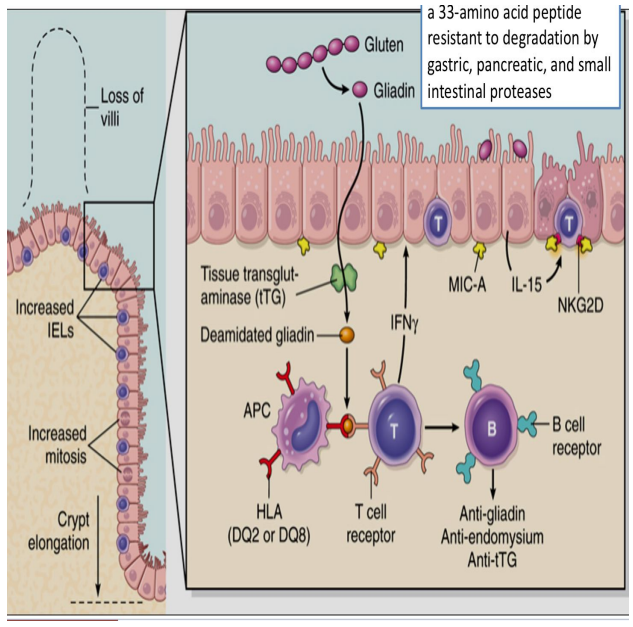
Introduction

-An immune reaction to **gliadin** fraction of the wheat protein **gluten**
-Usually diagnosed in **childhood** – mid adult.
-Patients have raised antibodies to gluten autoantibodies
-Highly specific association with class ll **HLA-DQ2 or HLA-DQ8** alleles.



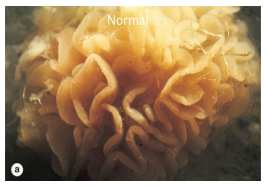
Pathophysiology

Gluten breakdown into fragments resulting of gliadin which is a (33-amino acid peptide resistant to degradation by gastric, pancreatic, and small intestinal proteases)then it get absorbed lnto intestinal mucosa ,it will become a Deamidated gliadin by the tissue transglutaminase (tTG).so people who Has HLA(DQ2 or DQ8) will recognize it by(APC) antigen presenting cell and presented to the T lymphocyte which will be activated and therefore Activate B lymphocyte to produce Anti-gliadin, Anti-endomysium and anti-tTG.Also activated T lymphocyte Will produce lFNγ and mor T lymphocytes will be infiltrated Which will increase intraepithelial lymphocyte that will Produce factors like lL-15 and NKG2D and damage the epithelium(loss of villi and crypt elongation)



Clinical feature

❖ **Typical presentation:** Gl symptoms that characteristically appear at age 9-24 months.
❖ Symptoms begin at various times after the introduction of foods that contain gluten.

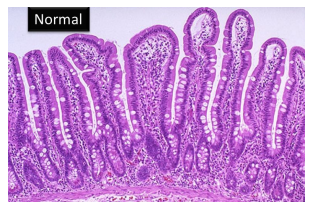


❖ A relationship between the age of onset and the type of presentation;
Infants and toddlers : (Gl symptoms and failure to thrive)
Childhood : (minor Gl symptoms, inadequate rate of weight gain)
Young adults : (anemia is the most common form of presentation)
Adults and elderly : (Gl symptoms are more prevalent)

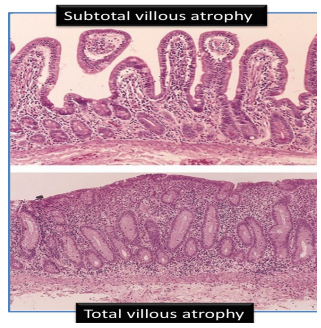
Loss of villi

Diagnosis

❖ **Clinical documentations of malabsorption.**
- Increase fat in stool **(steatorrhea)**
- Serology is **+ve for lgA** antibodies to tissue transglutaminase or **lgG** to deamidated gliadin or **anti-endomysial** antibodies
- Small intestine biopsy demonstrate vilis atrophy



❖ Improvement of symptom and mucosal histology on gluten withdrawal from diet.(wheat, barley, flour Other grains, such as rice and corn flour, do not have such an effect)

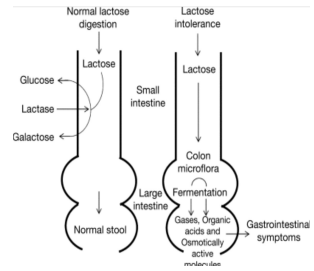


❖ **Histological appearance**
-Mucosa is flattened with marked **villous atrophy**
-Increased intraepithelial **lymphocytosis** (IELs)
-Crypt elongation

★ Complication

-Osteopenia , osteoporosis
-Infertility in women due to hypoalbuminemia
-Short stature, delayed puberty, anemia
-Malignancies: [intestinal **T-cell lymphoma**] 10 to 15% risk of developing Gl lymphoma.

Lactose intolerance

Definition and Pathophysiology	lactose intolerance low or absent activity of the enzyme **lactase**, which is needed to digest lactose to glucose and galactose.
Etiology	**1) Inherited lactase deficiency** -Congenital lactase deficiency : (extremely rare) -Childhood-onset and adult-onset lactase deficiency: (common and Genetically programmed progressive loss of the activity of the small intestinal enzyme lactase) **2) Acquired lactase deficiency** -Transient -Secondary lactase deficiency due to intestinal mucosal **injury by an infectious, allergic, or inflammatory process** -Gastroenteritis: Infectious diarrhea, particularly viral gastroenteritis in younger Acquired lactase deficiency children, may damage the intestinal mucosa enough to reduce the quantity of the lactase enzyme injury
Clinical feature	1 hour to a few hours after ingestion of milk products: - **Bloating** - **abdominal discomfort** - **flatulence / gases** Lactose will go from small intestine → large intestine (there will be bacteria) and there will be fermentation with production of gases especially hydrogen gas which will lead to ↑ motility and irritation of the bowl and then lead to the symptoms (gases and pain). 
Diagnosis	❖ **Hydrogen breath test :**specific test - An oral dose of lactose is administered - The sole source of H 2 is bacterial fermentation; - Unabsorbed lactose makes its way to colonic bacteria, resulting in excess breath H2. - Increased **exhaled H2** after lactose ingestion suggests lactose malabsorption. ❖ **Empirical treatment** : with a lactose-free diet,which results in resolution of symptoms , 3-week trial of a diet that is free of milk and milk products is a satisfactory trial to diagnose lactose intolerance

malabsorption	
Definition	●It is inability of intestine to absorb nutrients adequate into the bloodstream. ●Highly specific association with class II HLA DQ2 (haplotypes DR-17 or DR5/7) and to a lesser extent, DQ8 (haplotype DR-4).
causes	**a) Inadequate digestion:** 1) Stomach: postgastrectomy 2) pancrase : Cystic fibrosis, Chronic pancreatitis 3) bile: Obstructive jaundice , Terminal ileal resection **b) Small intestine abnormalities:** 1) Mucosa : Celiac disease,Giardiasis 2)Inadequate small intestine : Intestinal resection ,Crohn's disease. 3)Lymphatic obstruction: Intestinal lymphangiectasia ,Malignant Lymphoma
Diagnosis	Fecal fat study to diagnose steatorrhea : Blood tests Stool studies Endoscopy : Biopsy of small bowel
Celiac disease	
Definition	An immune reaction to gliadin fraction of the wheat protein gluten
Typical presentation	GI symptoms that characteristically appear at age 9-24 months.
Histology	Mucosa is flattened with marked villous atrophy.
Diagnosis	Steatorrhoea Histology Improvement of symptom and histology on gluten withdrawal from diet.
Complications	1)Osteopenia 2) Osteoporosis 3) Infertility in women Short stature 4) delayed puberty 5) anemia 6) Malignancies(intestinal T-cell lymphoma)
Lactose intolerance	
Definition	Low or absent activity of the enzyme lactase
causes	● Acquired lactase deficiency : Transient ● Inherited lactase deficiency: a) Childhood-onset and adult-onset b) Congenital lactase deficiency => infectious, allergic, or inflammatory process lactase deficiency
Clinical features	1)Bloating abdominal 2) discomfort 3) flatulence After 1 hour of consuming lactose
Diagnosis	1)Hydrogen breath test 2) lactose-free diet which results in resolution of symptoms

VI. LACTOSE INTOLERANCE

A. Decreased function of the lactase enzyme found in the brush border of enterocytes

1. Lactase normally breaks down lactose into glucose and galactose.

B. Presents with abdominal distension and diarrhea upon consumption of milk products; undigested lactose is osmotically active.

C. Deficiency may be congenital (rare autosomal recessive disorder) or acquired (often develops in late childhood); temporary deficiency is seen after small bowel infection (lactase is highly susceptible to injury).

VII. CELIAC DISEASE :

A. Immune-mediated damage of small bowel villi due to gluten exposure; associated with HLA-DQ2 and DQS

B. Gluten is present in wheat and grains; its most pathogenic component is gliadin.

1. Once absorbed, gliadin is deamidated by tissue transglutaminase (tTG).
2. Deamidated gliadin is presented by antigen presenting cells via MHC class II.
3. Helper T cells mediate tissue damage.

C. Clinical presentation

1. Children classically present with abdominal distension, diarrhea, and failure to thrive.
2. Adults classically present with chronic diarrhea and bloating.
3. Small, herpes-like vesicles may arise on skin (dermatitis herpetiformis). Due to IgA deposition at the tips of dermal papillae; resolves with gluten-free diet

D. Laboratory findings

1. IgA antibodies against endomysium, tTG, or gliadin; IgG antibodies are also present and are useful for diagnosis in individuals with IgA deficiency (increased incidence of igA deficiency is seen in celiac disease).
2. Duodenal biopsy reveals flattening of villi, hyperplasia of crypts, and increased intraepithelial lymphocytes (Fig. 10.18). Damage is most prominent in the duodenum; jejunum and ileum are less involved.

E. Symptoms resolve with gluten-free diet.

1. Small bowel carcinoma and T-cell lymphoma are late complications that present as refractory disease despite good dietary control.

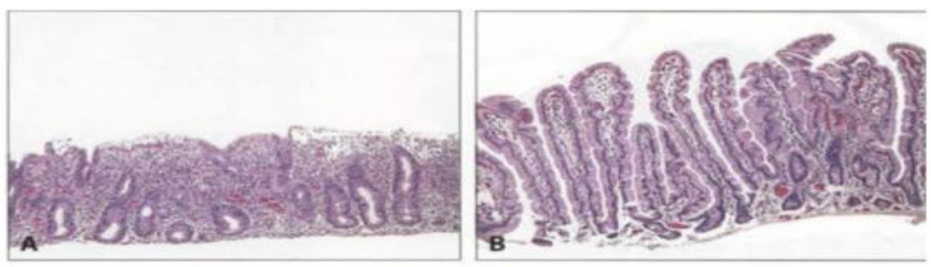


Fig. 10.18 Celiac disease. **A**, Flattened villi. **B**, Normal villi for comparison.

QUIZ!

MCQs

01 | which of the following is not a step of Celiac pathogenesis :			
A) Gluten is digested into amino acids and peptides including including “Gliadin” which will get deamidated by “tTG”	B) it will interact with HLA-DQ2/HLA-DQ8 of the antigen presenting cells which will present it to CD4 leading to cytokines release	C) B-Cell activation leading to generation of antibodies against tTG , Gliadin and CD8 will enterocytes who expresses surface MIC-A	D) all of the above are true
02 | Which is not a cause for primary mucosal abnormality mechanism of malabsorption :			
A) Crohn’s disease	B) Radiation enteritis	C) Giardiasis	D) Tropical sprue
03 | Malabsorption can cause :			
A) Photosensitivity	B) weight loss	C) depression	D) calcification
04 | which disease associated with class II HLA-DQ2 or HLA-DQ8 alleles :			
A) Lactose intolerance	B) celiac disease	C) ulcerative colitis	D) colonic polyp
05 | Which of the following complications are associated with celiac disease but not other malabsorption diseases?			
A)Osteoporosis	B) Short stature	C) Anemia	D) Malignancies
06 | A 4-year-old girl is brought to the physician because her parents noticed that she has been having pale, fatty, foul-smelling stools. The patient is at the 50th percentile for height and 10th percentile for weight. Her symptoms respond dramatically to a gluten-free diet. Which of the following is the most likely diagnosis?			
A) Celiac disease	B) Cystic fibrosis of the pancreas	C) Ménétrier disease	D) Tropical sprue

MCQs Answer key	01	02	03	04	05	06
	D	C	B	B	D	A

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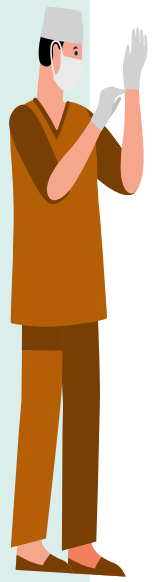

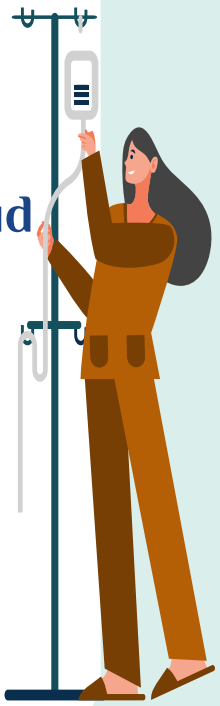

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