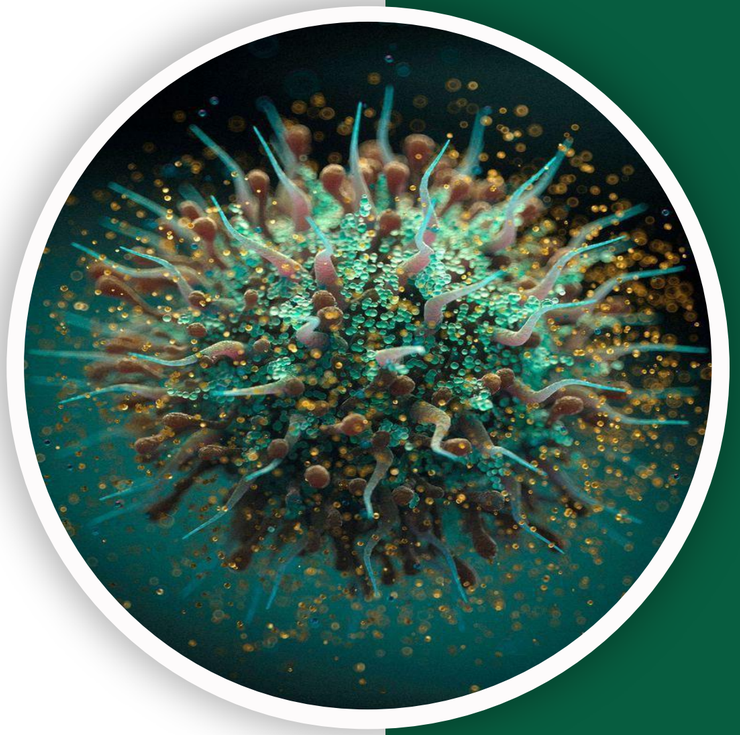
بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

GIS Pathology | MID 5

Intestinal Diseases Pt.1



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On gastric diseases pt.2

Intestinal pathologypart 1

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Diseases of the intestines

- Intestinal obstruction
- Vascular disorders
- Malabsorptive diseases and infections The infections will be covered in the Microbiology course.
- Inflammatory intestinal disease.
- Polyps and neoplastic diseases

Intestinal obstruction

Divided into two types:

1- Mechanical obstruction:

Intussusception

Hernias.

Adhesions.

Volvulus

Tumor causing obstructions that prevent the passage of stool in the small and large intestines.

Diverticulitis

Infarction

2- Non-mechanical obstruction:

Hirschsprung disease

Neurological disorders.

Drugs….etc (medications)

Some drugs can affect peristaltic movement and cause constipation for patients.

1- Mechanical obstructions happen when there is something seen preventing the passage of stool and other materials through the small and large intestines.

2- Non-mechanical obstruction are due to neurological disorders (problems in the innervation). You can't see anything causing the obstruction with your naked eye.

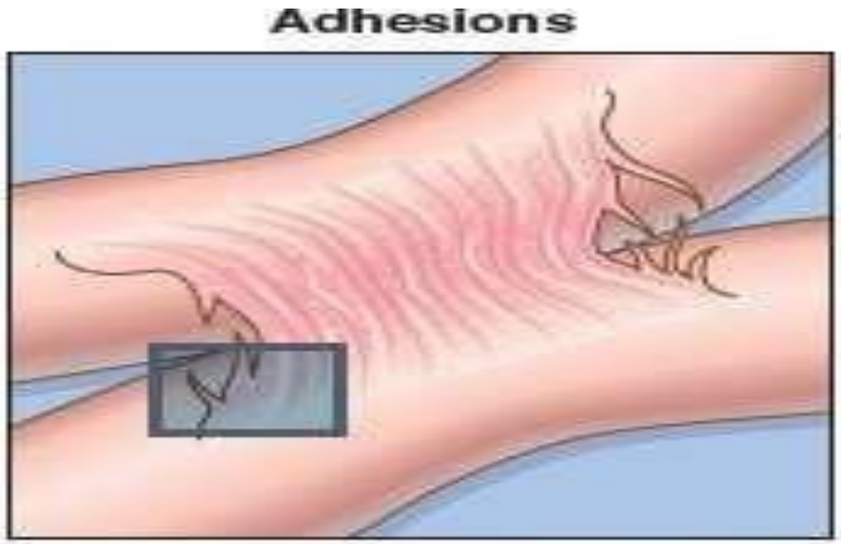
Clinical picture of intestinal obstruction:

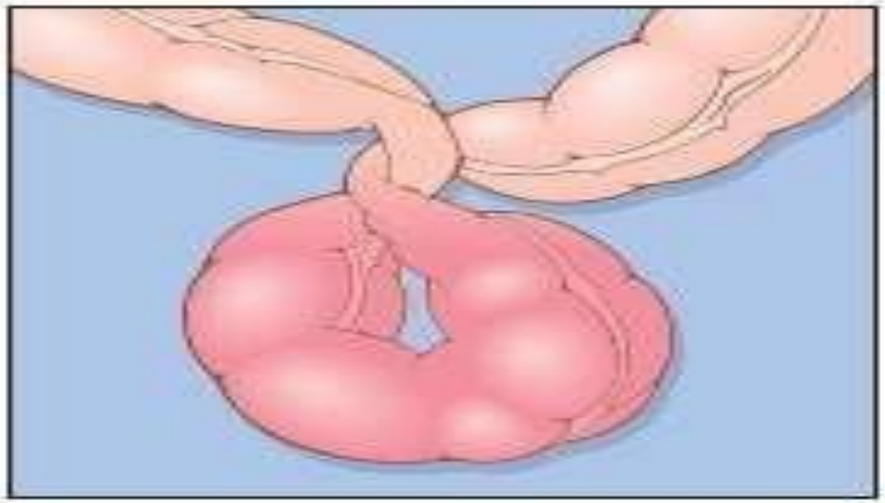
- **Abdominal pain** due to peristaltic contractions being stronger to aid passage, resulting in colic (severe, cramping pain that comes and goes in waves).
- **Distention**
- **Vomiting**
- **Constipation.**
- **Acute or chronic.**

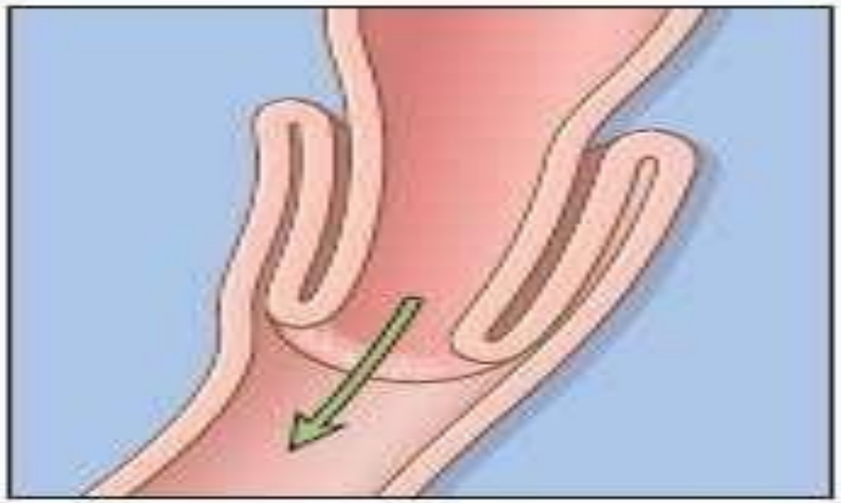
Both mechanical and non-mechanical diseases discussed in this lecture share the exact same clinical features.They only vary in:

- **Severity**
- **Duration**: Presenting as either acute (sudden, short-term symptoms) or chronic (prolonged, generally milder symptoms).

80% of mechanical obstructions are due to these 4 causes:







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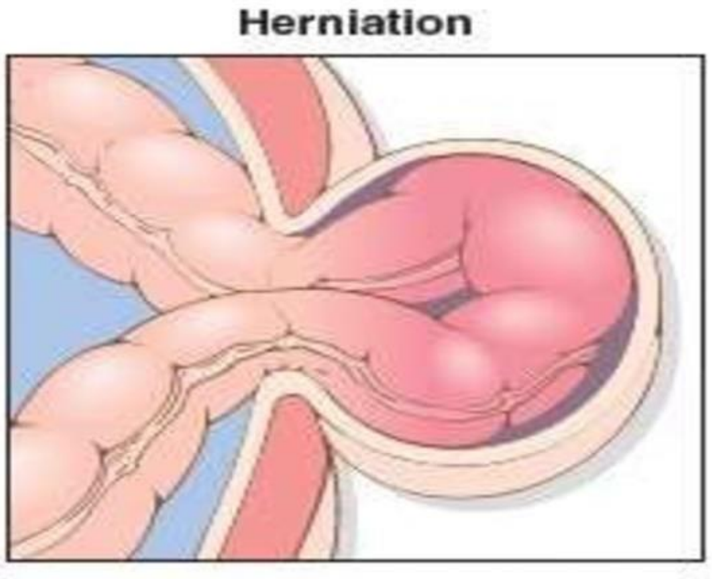
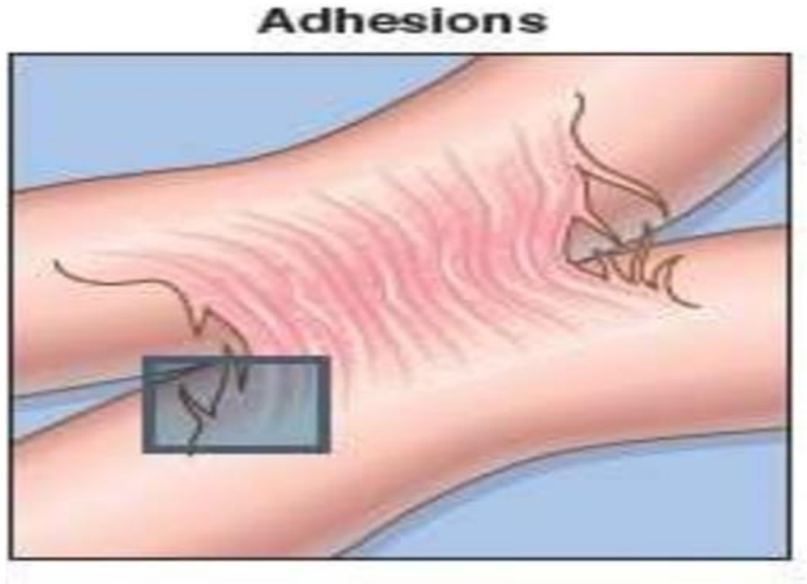


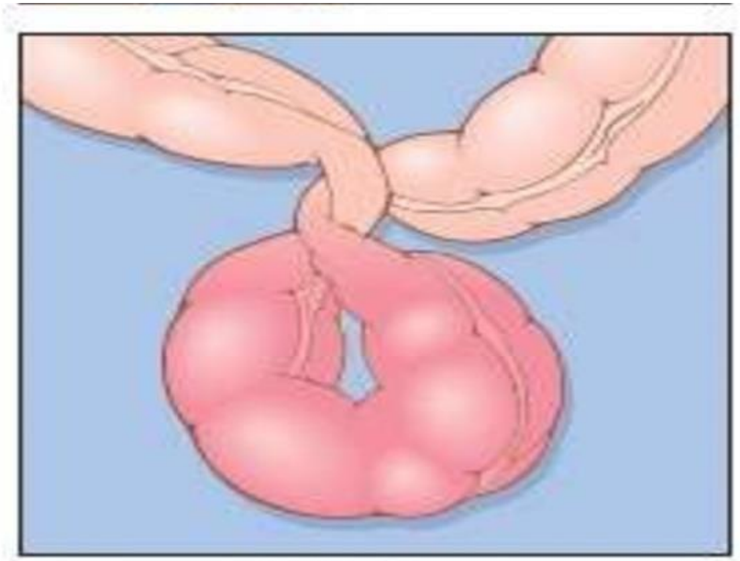
Herniation :

Herniation is the **protrusion** of a bowel segment through a defect or opening in the abdominal wall, such as the inguinal canal, femoral canal, umbilicus, or a surgical incision. Once the bowel passes through this opening, it gets trapped, which **impedes venous outflow and blood supply.** This results in ischemia which turns the bowel into a **dusky color** and leads to **bowel infarction**, causing severe pain and constipation.



Adhesions :

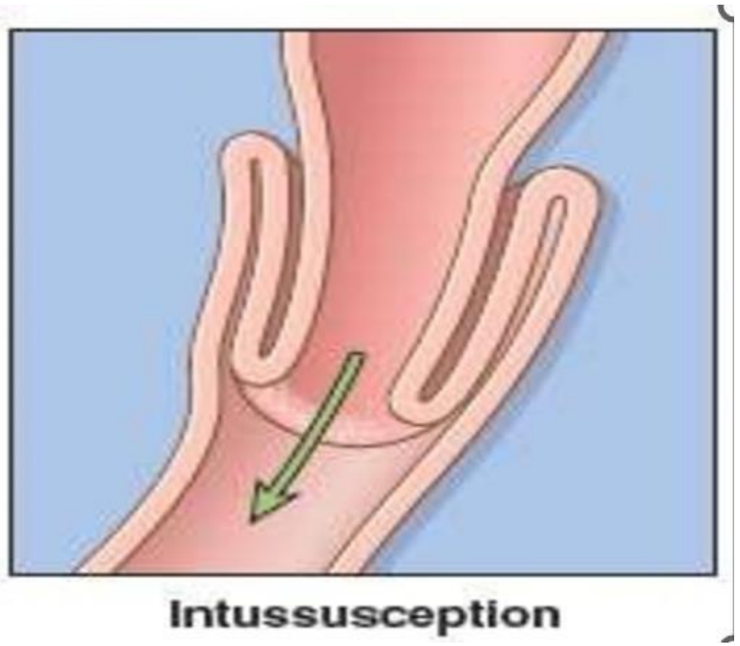
Adhesion is the **abnormal sticking together** of different bowel regions, which often happens in people who have had previous surgery in that area. This occurs because of the **fibrosis and scarring** after surgery impair normal peristalsis, leading to constipation.



Volvulus

Volvulus :

Volvulus is the **twisting** of the bowel upon itself, which typically occurs in **mobile segments**, especially the small bowel or sigmoid colon. This twisting produces the same effects as herniation by compromising venous outflow and blood supply, leading to severe pain, ischemia, and **bowel infarction**.

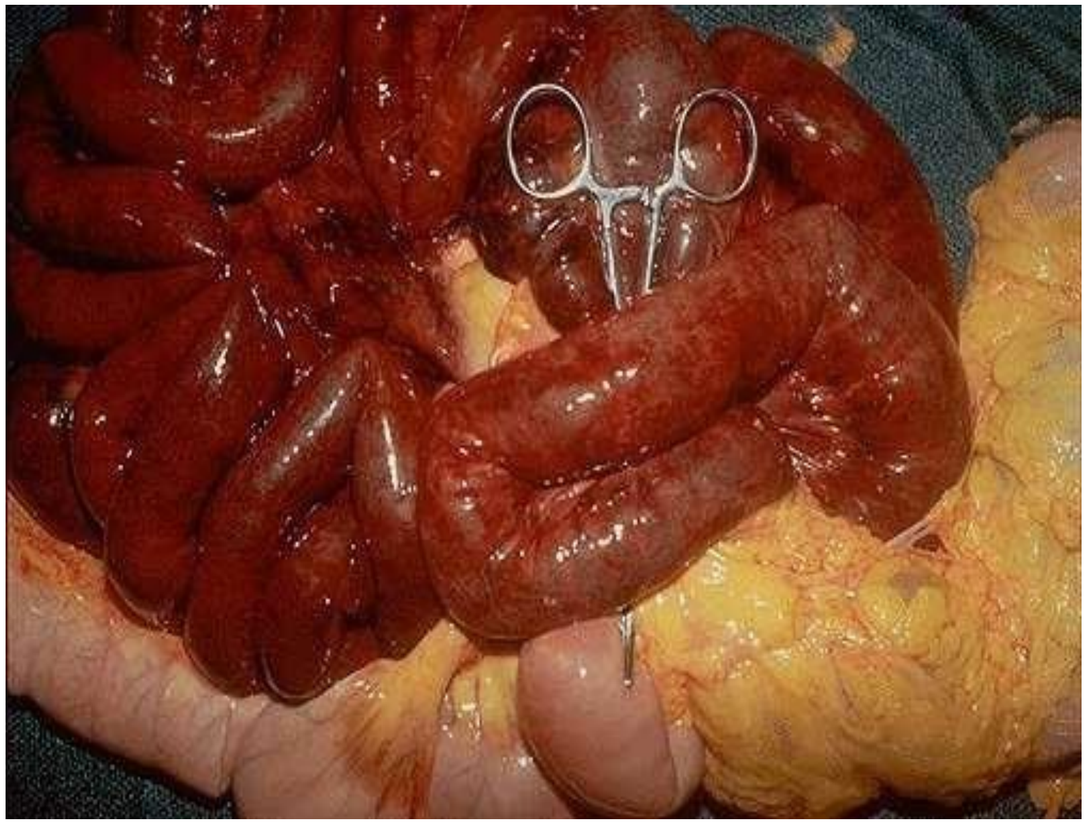


Intussusception

Intussuscpetion:

Intussusception occurs when a **proximal part** of the bowel **telescopes**, or slides directly into a **distal bowel segment**. With each peristaltic contraction, the bowel is propelled further inside, which compresses the blood supply and ultimately causes **infarction**.

Bowel infarction



Because intussusception, herniation, and volvulus **all present acutely**, the primary goal is to save the bowel from infarction. To achieve this, it is essential to maintain a high index of suspicion, consider intestinal obstruction as the top differential diagnosis, and secure an early diagnosis.

Why do bowel infarctions appear red instead of pale?

Bowel infarction is **hemorrhagic** rather than pale due to the **great anastomosis** between the blood vessels supplying the bowel.

Intussusception

- Segment of the intestine constricted by peristalsis, telescopes into the immediately distal segment.
- Once trapped, invaginated segment is propelled by peristalsis, and pulls mesentery with it.
- **Most common cause of intestinal obstruction in children younger than 2 years of age**.
- Untreated progresses to obstruction and infarction.

When a child under the age of two presents to the emergency department with abdominal distension, vomiting, constipation, and pain, maintaining a high index of suspicion for **intussusception** is crucial.

Causes of intussusception:

- **Idiopathic (unknown cause) in most cases.**

  Other causes:

- Peyer patches hyperplasia (rotavirus vaccine, viral infections) Following a viral infection, the lymphoid follicles in the small intestine can enlarge, a condition known as Peyer's patch hyperplasia. This enlargement can subsequently act as a starting point that leads to intussusception.

- Meckles diverticulum (ilium)

- Old children & adults: Intraluminal mass or tumors

Intussusception is rare in adults. When it does occur, it strongly indicates the presence of an underlying tumor or mass (acting as a lead point) that must be investigated and identified.

Clinical features:

- **Abdominal swelling**
- **Vomiting**
- **Passing stools mixed with blood and mucus (currant jelly stool)** **(The most important)**
- **Pain.** (In pediatric patients, a crying and irritable child is a primary clinical indicator of pain)

Management

- Contrast enemas (diagnostic and therapeutic) in uncomplicated idiopathic cases.
- Surgery if complicated by infarction or if masses are the leading point.

- The management of intussusception depends on the **time of diagnosis**. In early, uncomplicated cases, a **contrast enema** can be used as it is both **diagnostic and therapeutic**; the pressure from injecting the contrast material physically pushes the telescoped bowel back into its normal position. However, in complicated cases involving bowel infarction, **surgical intervention** is required.

Meckel's diverticulum

- The most common congenital anomaly of the GI tract (terminal ilium)
- Incomplete obliteration of omphalomesenteric duct
- True diverticulum. A diverticulum is an **outpouching** of the bowel wall. A **true diverticulum** is one that involves all **layers of the bowel wall**, specifically the mucosa, submucosa, muscularis propria, and serosa.
- **Remember (rule of 2):**
- About **2%** of people have them;
- Located **2 feet** from the ileocecal valve.
- **2 inches** in length.
- **2 types** of heterotopic mucosa (gastric or pancreatic). **Heterotopia** is a tissue presented in location that's not native to it.
- Most common cause of lower GI bleeding **before age of 2.**

Because the gastric mucosa produces acid and pepsin, and the pancreatic mucosa produces enzymes, the patient may develop **peptic ulcerations**. These ulcerations can ultimately cause the patient to present with **lower gastrointestinal (GI) bleeding.**

Meckel's diverticulum (thin bowel lumen of a child):

Clinical presentation:

- Can be asymptomatic and discovered incidentally.

- Ulceration, lower GI bleeding or perforation from ectopic gastric mucosa.
- Bowel obstruction due to the intussusception, volvulus or adhesive band.
- Can be confused with acute appendicitis, because of pain present in the lower right quadrant where the appendix is located.

Hirschsprung Disease

Non mechanical obstruction

- Congenital defect in colonic innervations
- Congenital aganglionic megacolon
- More common in males
- More severe in females
- Risk increase in siblings. (Familial cases)
- **Typical presentation:**

Congenital aganglionic megacolon: The absence of ganglion cells, which act as the **pacemaker** for the bowel's intrinsic nervous system, **prevents normal contraction and peristalsis.** Normally, these cells are found within two plexuses: one located in the submucosa and the other situated between the two muscle layers. Without these cells to drive motility, the bowel cannot propel contents forward, ultimately resulting in **constipation**, so the bowel will **dilate (megacolon)** because of the build up of stool, so the bowel may rupture

- Neonatal failure to pass meconium
- Later: Obstructive constipation.

Meconium : is the first stool passed by the baby.
Neonatal: 0-28 days after birth.

Pathogenesis

- **During embryogenesis (congenital anomaly):** disrupted migration of neural crest cells from cecum to rectum.
- **Aganglionosis: Distal intestinal segment lacks both: Meissner submucosal plexus and the Auerbach (myenteric) plexus**.
- Failure of coordinated peristaltic contractions.

- RET Mutations: in familial cases and 15% of sporadic.
- Other genes and environmental factors play role.
- More in Down syndrome.

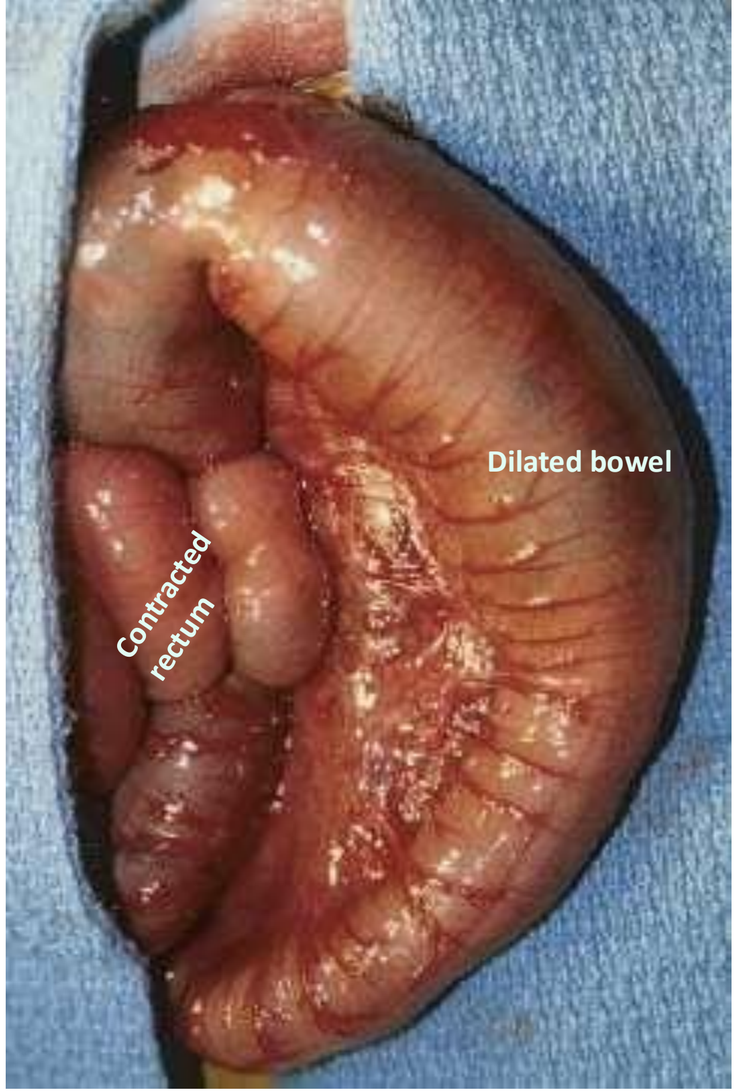
During fetal development, neural crest cells may prematurely stop their migration at various points, leaving different lengths of the bowel without innervation. The severity of the condition depends on where this migration arrests: the lack of ganglion cells may involve only the rectum, extend into the rectosigmoid region, or, in the worst-case scenario, affect the entire colon all the way up to the cecum

Morphology

- Rectum always involved, Most cases in rectosigmoid
- Extent is variable.
- **Why is the rectum always involved in this condition?**
  Because neural crest cells **migrate downwards** (from proximal to distal) during development, if they stop early and fail to innervate a higher segment of the bowel, they will inevitably fail to reach the rectum at the very end of the pathway.

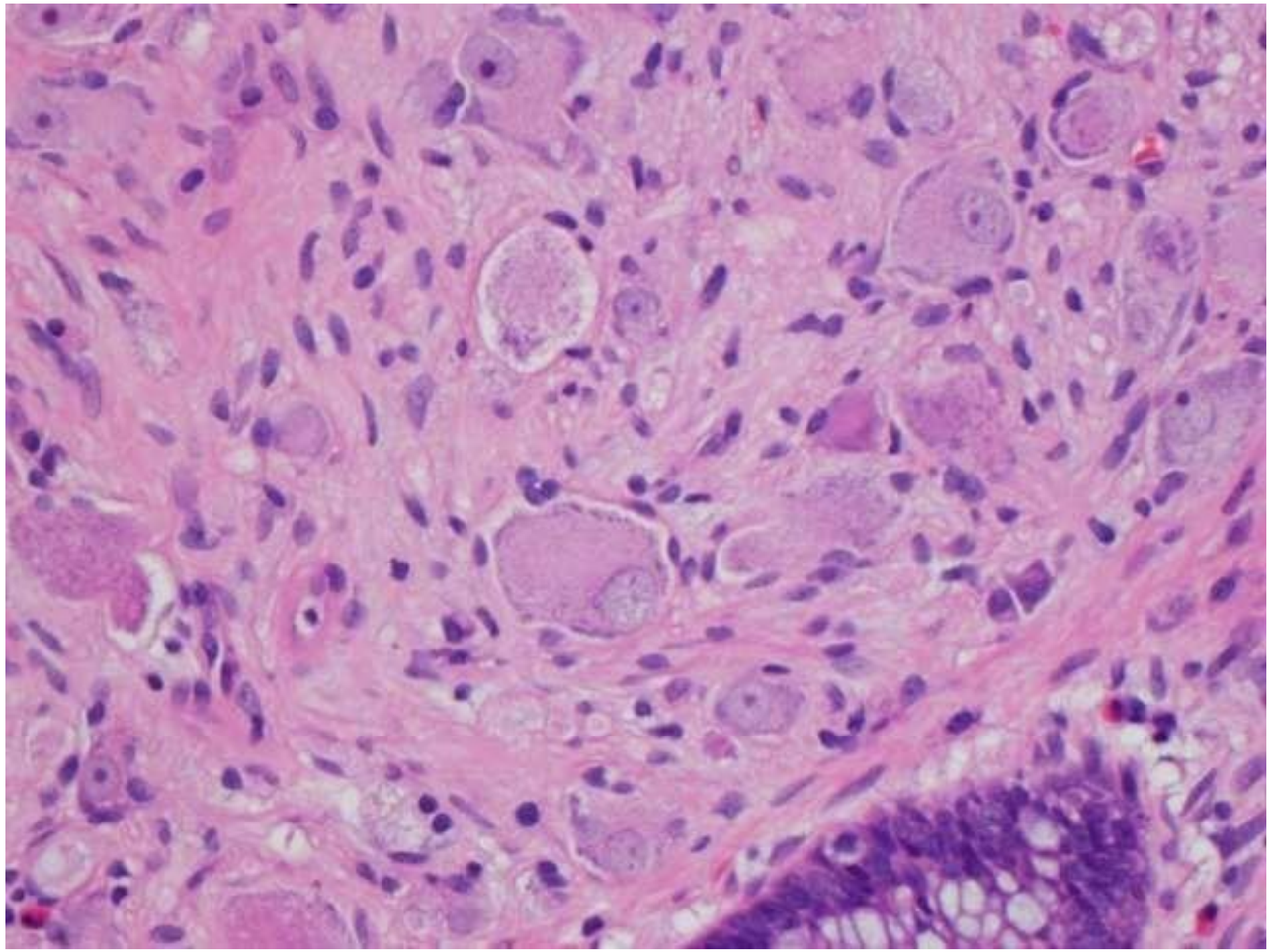
- Aganglionic region normal or contracted (semi-contracted due to nerve bundles hypertrophy, but not efficient peristalsis and passage of stool)
- Proximal normal segment progressively dilated. (**Megacolon**)
- **Biopsy** is the gold standard for establishing the initial diagnosis. Additionally, during surgery, a frozen section biopsy is performed to confirm the presence of ganglion cells at the resection margin. It is crucial to ensure that the remaining bowel being left behind has normal innervation; otherwise, the patient will continue to experience symptoms and pain.

  Diagnostic work up: barium enema, biopsy



During a **barium enema**, contrast material is injected through the anal orifice into the rectum, appearing bright **white** on an X-ray. The image on the right clearly highlights the characteristic gross appearance of the condition: the healthy, innervated proximal bowel becomes massively **dilated** from backed-up contents, while the aganglionic (uninnervated) rectum appears either **normal in size or contracted.**

ganglion cells:



Under the microscope, the pathologist searches for the presence of a ganglion cell, to rule out Hirschsprung disease. Histologically, these ganglion cells are identified by their distinct features: a peripherally located nucleus containing a prominent nucleolus, along with peripherally located Nissl substance.

http://www.pathologyoutlines.com

Complications

- Enterocolitis due to stagnation of stool
- Fluid and electrolyte disturbances
- Perforation
- Peritonitis

Perforation will lead to peritonitis

- **Treatment:**
- Surgical resection of aganglionic segment and anastomosis of normal segments.

VASCULAR DISORDERS OF BOWEL

- Ischemic Bowel Disease
- Angiodysplasia.
- Hemorrhoids

Angiodysplasia.

- Malformed submucosal and mucosal blood vessels. (Congenital, can be sporadic)
- Most often in cecum and right colon.
- 6th decade of life. Because vascular walls become more fragile with time
- Less than 1% of adult population. Uncommon
- 20% of cases of lower GI bleeding.
- Blood is bright red in color. Not melena as in upper GI bleeding

Hemorrhoids

- They are found at the left side, in the anal canal.
- More common than Angiodysplasia.

- Dilated anal and perianal &anal collateral vessels that connect the portal and caval venous systems (circulation).

- **Predisposing factors:**
- Chronic Constipation and straining (difficulty in defecation)
- Venous stasis of pregnancy
- Portal hypertension

- External (below anorectal line, inferior hemorrhoidal plexus) and internal (above anorectal line, superior hemorrhoidal plexus).

External &internal does not refer to there actual presence out of the anal canal or not, but according to where they originate.

The anus has an anastomosis between the systemic (caval) venous circulation and portal venous circulation as in lower part of esophagus, anorectal region and around umbilicus, so anything that elevates the portal pressure (liver cirrhosis, schistosomiasis, portal vein thrombosis) will lead to dilation of these BV, which results in hemorrhoids.
Patients with portal hypertension or liver cirrhosis commonly present as hemorrhoids.

- **Morphology:**
- Thin-walled (Thin walled so risk of rupture is high so bleeding occurs fast), dilated, submucosal vessels beneath anal or rectal mucosa.

- **Symptoms:**
- Bleeding in lower GI (bright red), pain due to thrombosis and inflammation

- **Treatment:**
- Sclerotherapy, rubber band ligation, infrared coagulation. Hemorrhoidectomy.

DIARRHEAL DISEASE

- Diarrhea: increase in stool mass, frequency or fluidity.
- Dysentery (mostly with infections): painful, bloody, small volume diarrhea.
- Diarrheal disease is divided into: Secretory, osmotic, malabsorptive, exudative (mostly with infections or inflammatory bowel disease).
- **Malabsorptive Diarrhea**
- Pancreatic insufficiency
- **Celiac disease**
- Crohn disease
- **Cystic Fibrosis**
- **Lactase (Disaccharidase) Deficiency**
- **Abetalipoproteinemia**
- **Infectious Enterocolitis**
- **Ischemia**
- **Inflammatory bowel diseases…..**

Malabsorptive Diarrhea

When a patient presents with acute diarrhea, it can be enterocolitis, enteritis or ischemic bowel but not malabsorptive diarrhea.

- **Chronic.**
- Defective absorption of fats, fat- and water-soluble vitamins, proteins, carbohydrates, electrolytes, minerals and water.
- **Hallmark is**: steatorrhea (excessive fat), bulky,)due to malabsorption) ,frothy, yellow, greasy stool).
  *Steatorrhea is usually found with in fat malabsorption cases.

Malabsorptive diarrhea

Defect in one of the following:

- **Intraluminal digestion**
- **Terminal digestion** which happens in brush borders (enzymatic digestion) like disaccharidases
- **Transepithelial transport.**
- **Lymphatic transport** like lymphatic obstruction

Manifestations: Variable depending on diseases (iron malabsorption, fat malabsorption, vitamins malabsorption…)

- Weight loss especially in protein and fat malabsorption, anorexia due to vitamins malabsorption
- Flatus due to the action of microflora on the non-absorpable nutrients mainly carbs, abdominal distention.
- Borborygmi (intestinal noise), Muscle wasting in protein malabsorption.
- Anemia and mucositis (iron, pyridoxine (VB6), folate, or vitamin B12 deficiency)
- Bleeding (vitamin K deficiency)
- Osteopenia and tetany (calcium, magnesium, or vitamin D deficiency)
- Neuropathy (vitamin A or B12 deficiency) tingling , numbness and in severe cases to paraplegia esp with vit B12
- Skin and endocrine disorders like iodine deficiency which leads to hypothyroidism.

Cystic Fibrosis multisystem disease

- Mutations in cystic fibrosis transmembrane conductance regulator (CFTR)
- Defects in ion transport across intestinal and pancreatic epithelium and in respiratory tract
- Thick viscous secretions.
- Mucus plugs in pancreatic ducts >>> pancreatic insufficiency (80% of patients)
  Pancreatic enzymes are very viscous they will be unable to reach the bowel which results in maldigestion.
  Treatment includes providing patients with tablets of these enzymes.
- Meconium ileus (paralysis of the bowel so no peristaltic contractions or passage of stool) in neonates due to delayed passage of the meconium so it stays in the bowel and results in obstruction.
- Defect in intraluminal digestion.

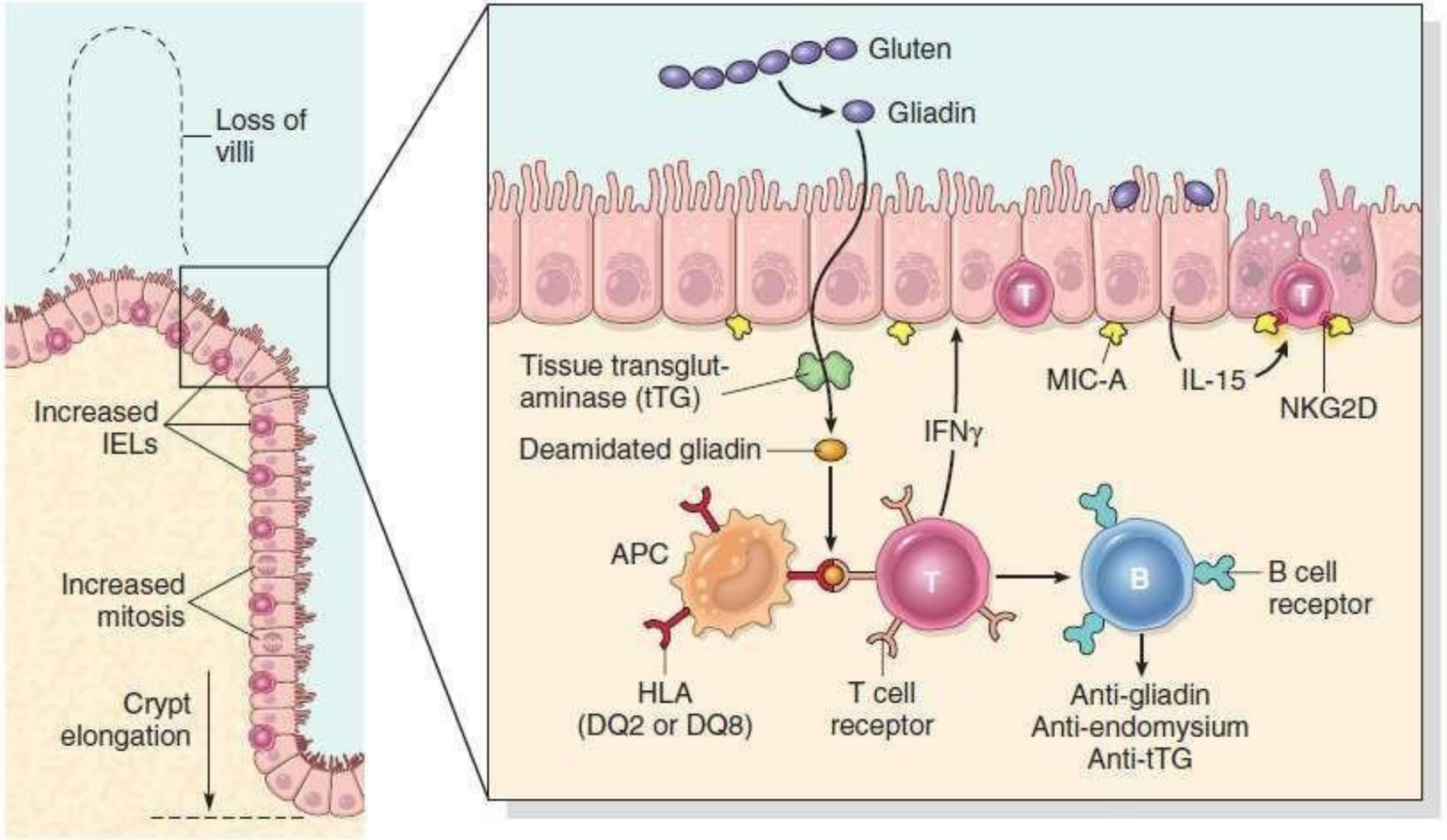
Celiac Disease

- *Gluten sensitive enteropathy*
- Immune mediated enteropathy
- Wheat, rye or barley.
- Genetically predisposition, HLA-DQ2 or HLA-DQ8
- Treatment: gluten free diet.
- Association with (autoimmune diseases) : type 1 diabetes, thyroiditis, and Sjogren syndrome

Pathogenesis

- Gluten >>> gliadin >> gliadin enters between epithelial cells to the submucosa
  >> gliadin is deamidated by TTG (Tissue TransGlutaminase)
  >> react with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells
  <<CD4+ T cells (helper T cell) activation
  >> they will induce a strong inflammatory reaction in the small bowel >>> cytokines
  << tissue damage >> B cell activation >> antibodies (anti-gliadin, anti- endomysium, & anti-TTG present in the serum of the patient).

- Serology:
- Anti- tissue transglutaminase
- antibodies Anti-gliadin antibodies.
- Anti -endomysial antibodies

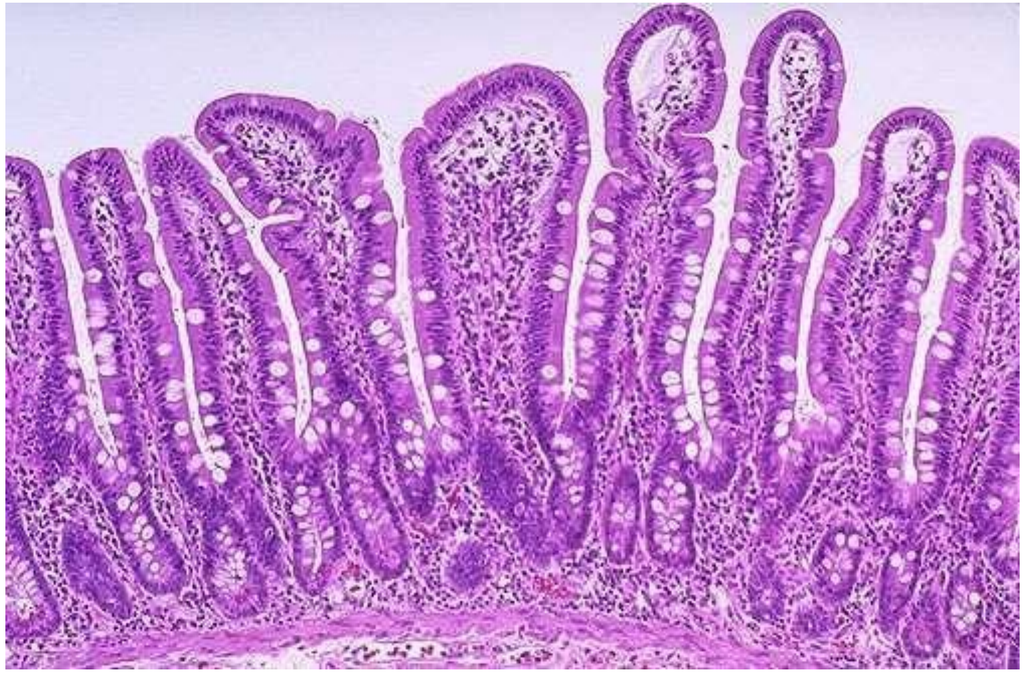


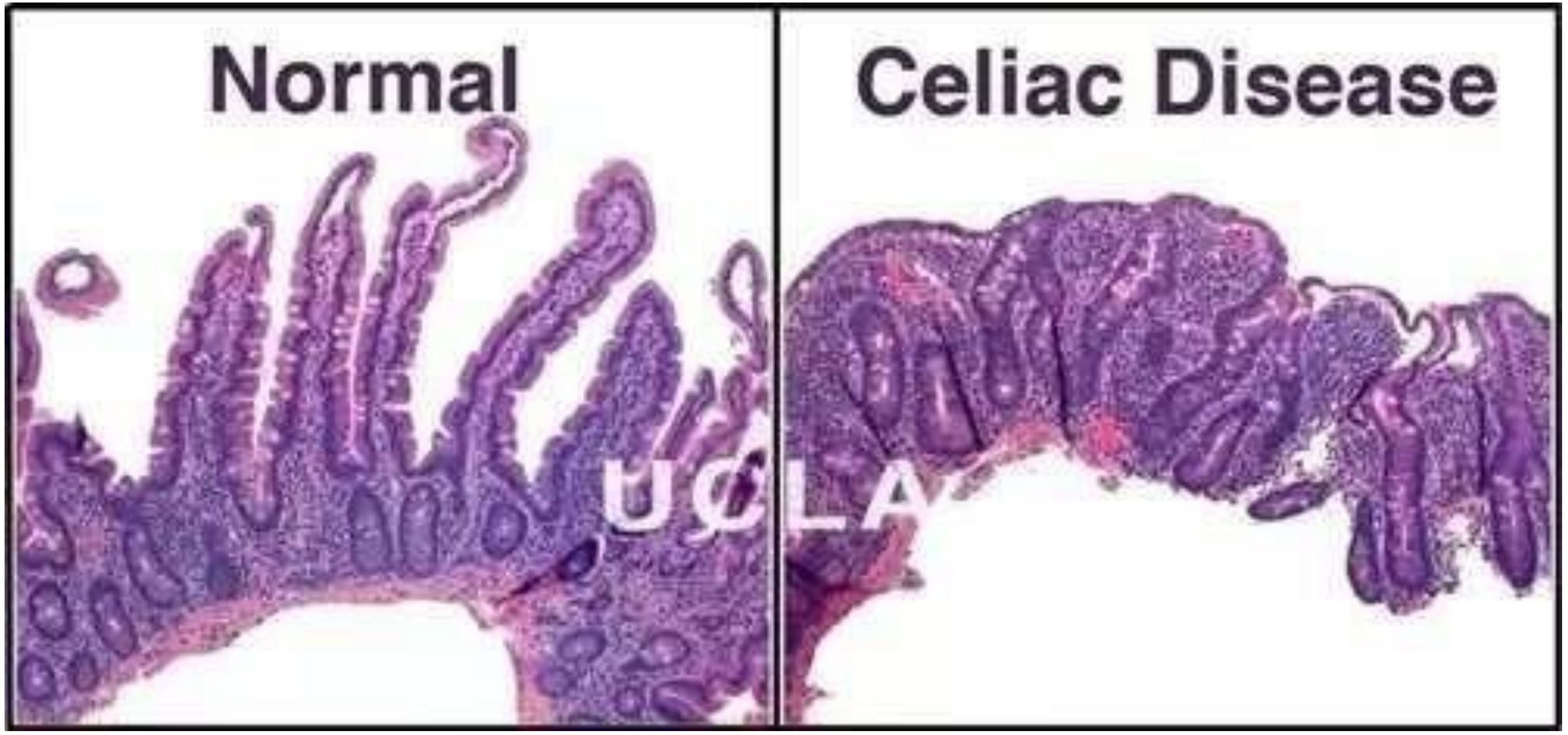
Robbins Basic Pathology 10th edition

MORPHOLOGY

- Biobsy from second portion of the duodenum (not the first portion because it is usually inflammed due to gastric secretion(or proximal jejunum.
- **Triad**: intraepithelial lymphocytosis (Cytotoxic CD8+ T cells), crypt hyperplasia, and villous atrophy is the most important and leads to a decrease in the surface area.
  These signs are not specific for celiac disease, so diagnosis is clinical, histologic and serologic.
- Lamina propria: lymphocytes, plasma cells, eosinophils…….
- IEL & villous atrophy are not pathognomonic, seen in viral enteritis.
- Diagnosis: Clinical, histologic and serologic correlation.

Normal intestine





Total villous atrophy

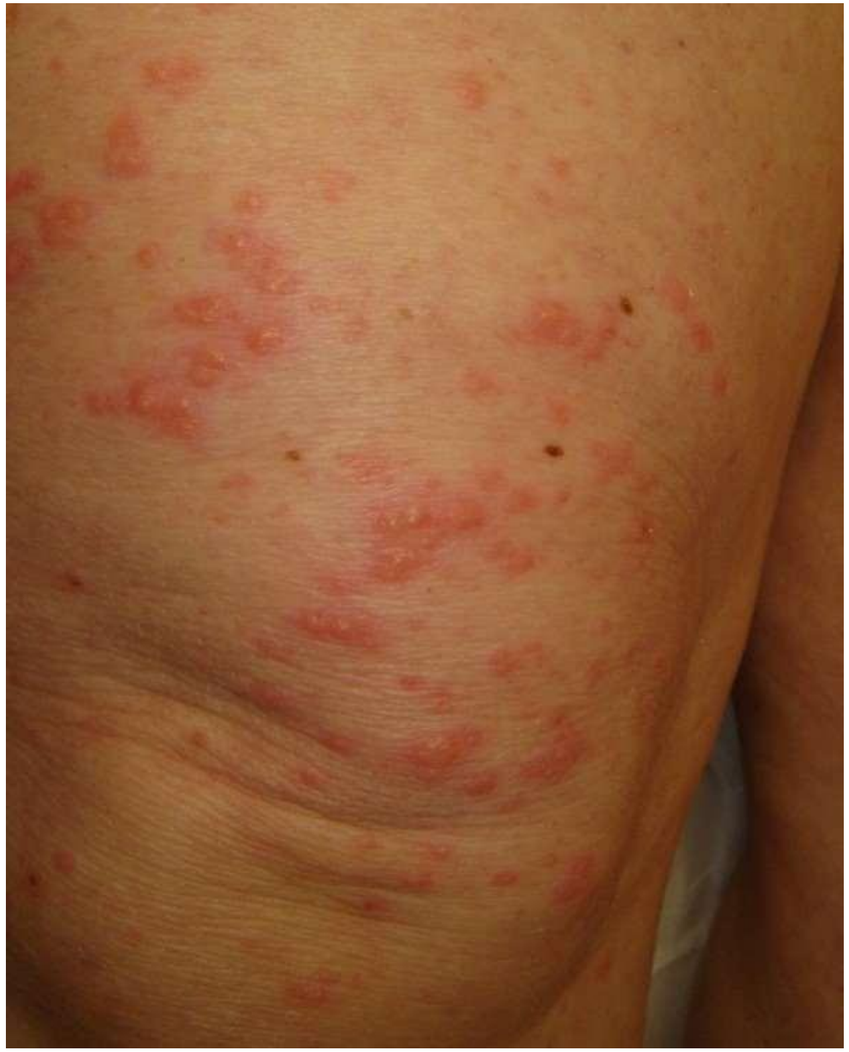
Clinical Features

Children before 6 months of age cannot get diagnosed because at this age they are not exposed to solid food like wheat, rye, or barley.

- **Children 6-24 months : classical or non-classical symptoms**
- **Classical**: Irritability, abdominal distention, anorexia due to iron deficiency, diarrhea, most important manifestation, failure to thrive, weight loss, or muscle wasting, iron deficiency) anemia(
- **Non-classical:** abdominal pain, nausea, vomiting, bloating, or constipation.
- Blistering skin lesion, **dermatitis herpetiformis** (its name comes from its similarity with herpes virus, but its not infectious) , in 10% of Pnts.

It is common for children to present with non-classical symptoms for classical diseases like in some respiratory diseases

Dermatitis herpetiformis.



- Adults (30-60 years)
- Anemia: iron deficiency because absorption of iron is mainly in the duodenum
- B12 and folate deficiency: less common because they are absorbed in the ileum.
- Diarrhea , bloating, and fatigue.
- Missed diagnosis: Silent celiac (positive serology and biopsy but asymptomatic).
  These patients can develop manifestations at any time.
- Increased risk of enteropathy associated T cell lymphoma & Small intestinal adenocarcinoma.

If a celiac disease patient is adhere to the gluten-free diet and then the symptoms begins to worsen , it is an indicator for T cell lymphoma

Diagnosis:

- **Non invasive serologic tests:**
- **Most sensitive:**
- Anti tissue transglutaminase antibody, IgA) most sensitive but not specific)
- Anti deamidated gliadin antibodies, IgA & IgG

- **Most specific, but less sensitive**
- Antiendomysial antibody.

- **Invasive tests: small bowel biopsy.** By endoscopy

رسالة من الفريق العلمي:

عن عبدالله بن عبّاس –رضي الله عنهما-، عن النبيّ - صلّى الله عليه وسلّم- أنّه قال:

"نِعمَتانِ مَغبونٌ فيهما كَثيرٌ مِنَ النَّاسِ: الصِّحَّةُ والفَراغُ"

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Corrections from previous versions:

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