PATHOLOGY

بسم الله الرحمن الرحيم

MID | Lecture #5

Intestinal diseases pt.1

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا

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On gastric diseases pt.2

اللهم علّمني ما ينفعني وانفعني بما علّمتني وزدني علمًا

Intestinal pathology, part 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
- Inflammatory intestinal disease.
- Polyps and neoplastic diseases

Intestinal obstruction

Is divided into two types:

Mechanical obstruction:

Intussusception

Hernias.

Adhesions.

Volvulus

Tumors.

Diverticulitis

Infarction

Mechanical obstruction: there is something we see it causing the obstruction (more common)

Non-mechanical obstruction

Hurschsprung disease

Neurological disorders.

Drugs….etc

Some drugs can affect peristaltic movement and causes constipation for patients

Non mechanical obstruction are neurological disorders (problem in the innervation or peristaltic movements)
Hurschsprung disease is an important cause of non mechanical obstruction in the pediatric age group.

Clinical picture of intestinal obstruction.

- Abdominal pain
- Distention
- Vomiting
- Constipation.

- All the diseases that we will discuss in this lecture share the same clinical features.
- They vary in severity and whether they are acute(sudden onset) or chronic (over a prolonged period of time, but the symptoms tend to be less severe)

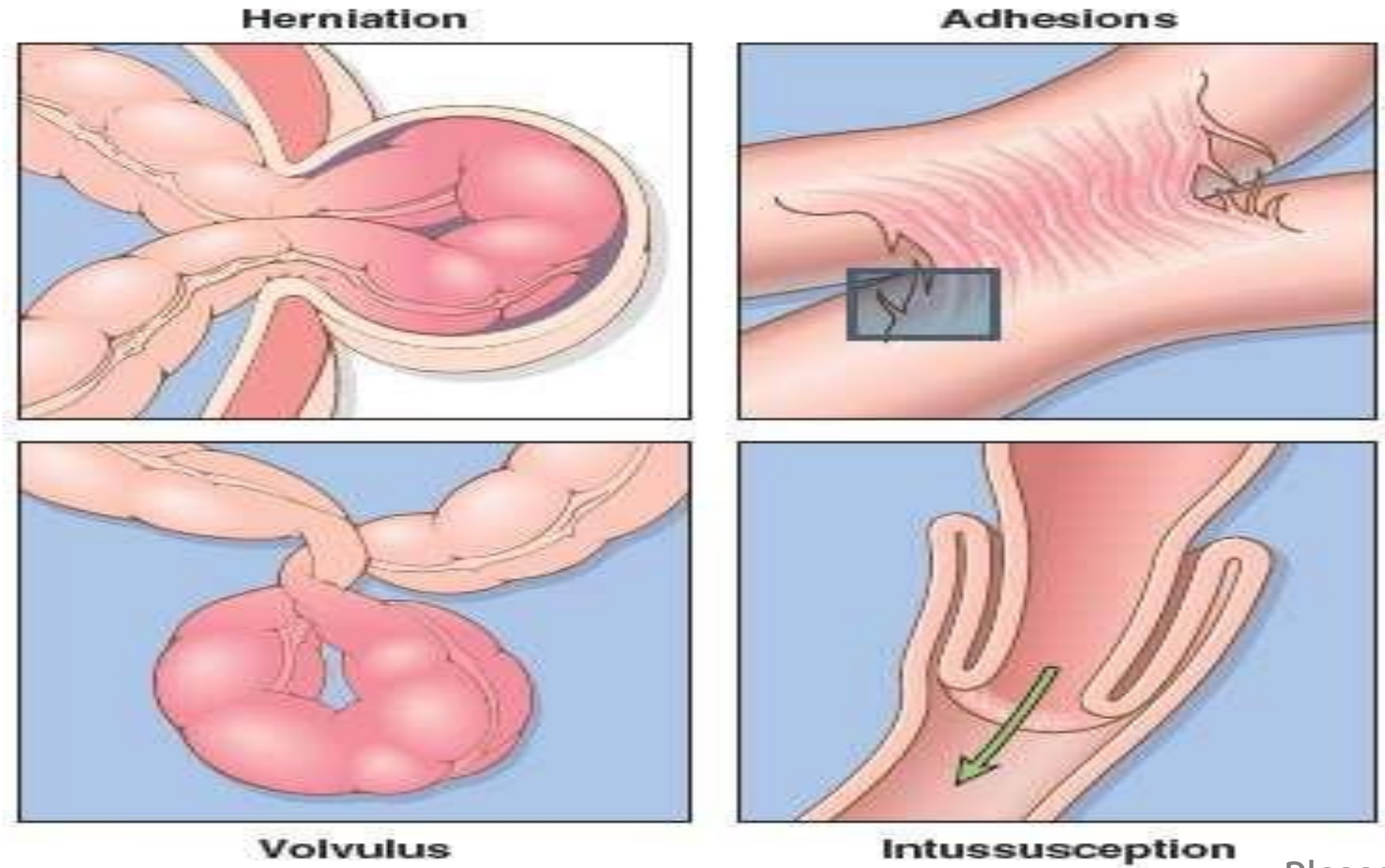
- Acute or chronic.

Intestinal obstruction means that there is something imbedding the peristaltic movement or the passage of the stool in the intestine.

Symptoms are :

- Constipation (the most important feature, most common in patients with chronic obstruction)
- Dilation above the obstruction may occur
- Vomiting (in patients with acute obstruction)
- Abdominal pain
- Abdominal distension

80% of mechanical obstructions



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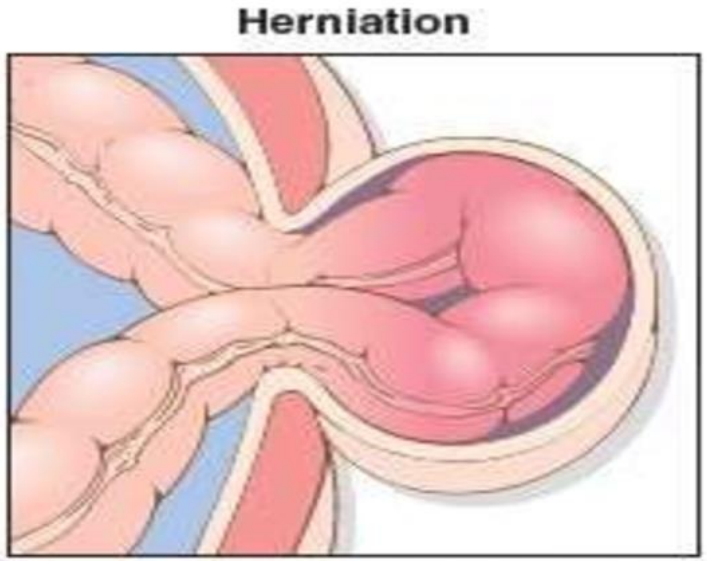
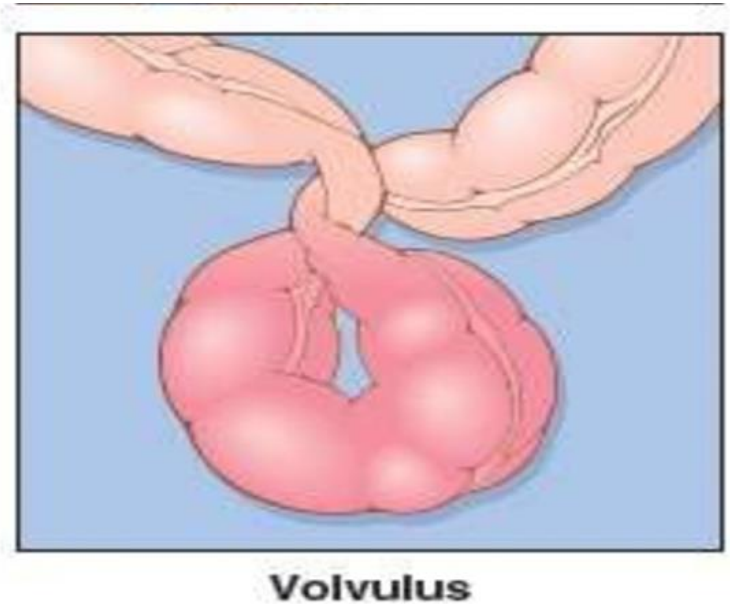


Herniation :

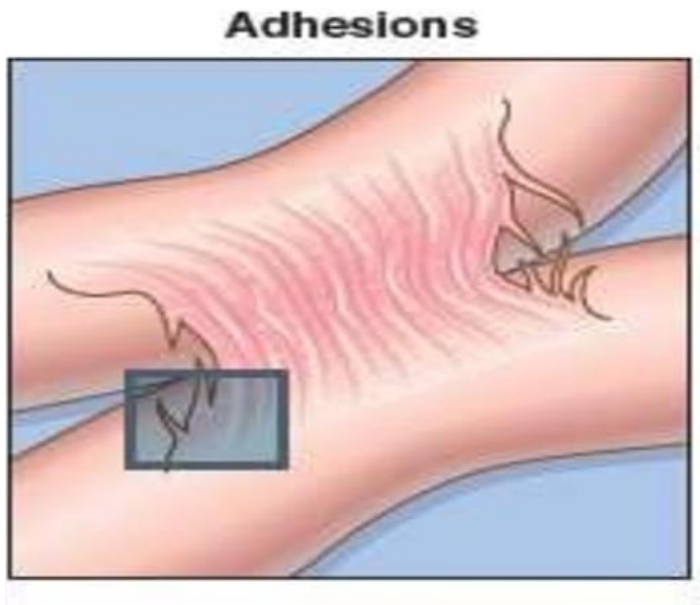
there is many types of herniations like: femoral hernia, inguinal hernia, umbilical hernia.

Bowel hernia happens when there is a point of weakness in abdominal wall where the intestine and part of omentum herniate through it. Sometimes its reducible , the bowel can be reduced again if the neck of herniation was wide. But as you see in this picture, the neck is small, so the color of bowel is purple or red which means we have ischemic changes due to the pressure on the venous return if we don't solve these herniations from the start, hemorrhagic infarction of the bowel could be developed



Volvulus :

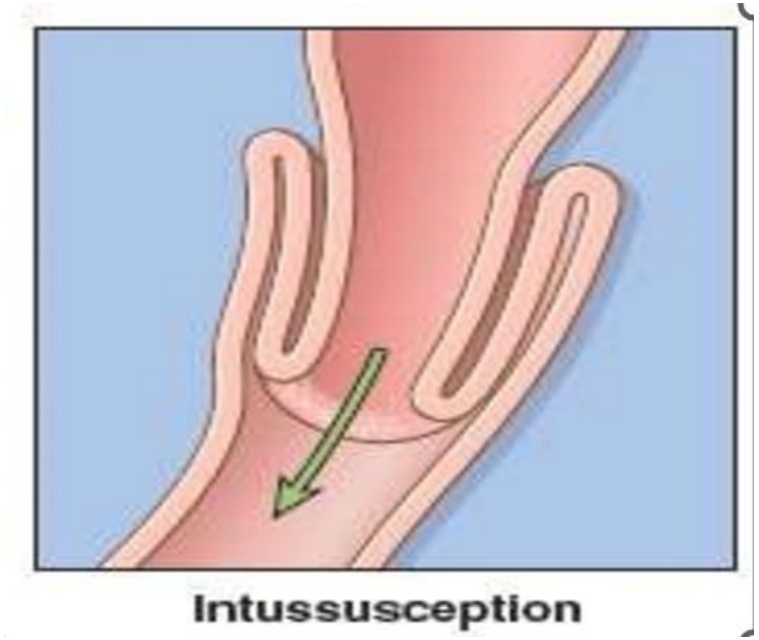
it is the similar concept of the hernia . when it occurs,embedence of venous return will occur, then there will be decrease in the blood supply (we call it incarceration or haemorrhagic necrosis and also lead to infarction of bowel)



Adhesions :

fibrotic connections between bowel loops ,so this will affect the peristaltic movement

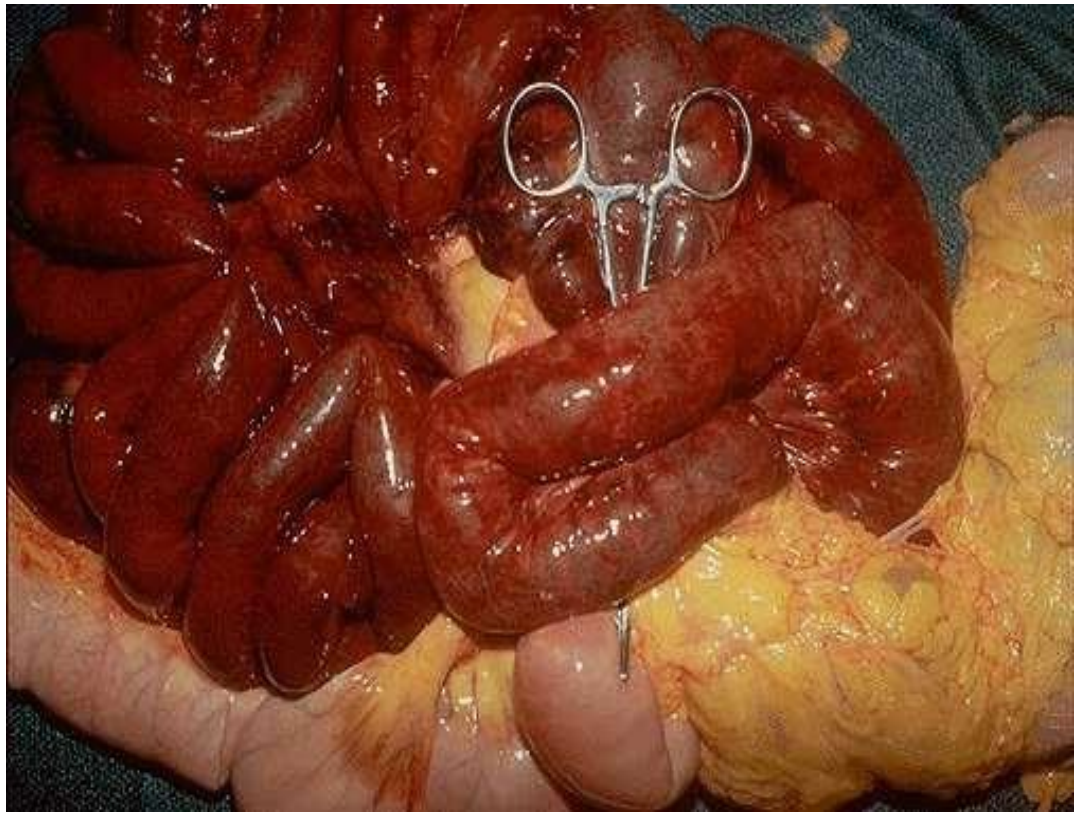
When do we predict the patient to have adhesions ?
If the patient had a previous surgical procedure in the abdomen (cesarean section ,previous ulcer perforated , previous perforation of the bowel)



Intussuscpetion:

The case when the proximal part of the bowel invaginates into the distal part.
the proximal part is contracted and the distal part is dilated.

Bowel infarction



- The cause of bowel infarction might be hernia or volvulus or intussusception (anything that lead to cut of blood supply to the bowel)
- this makes it gangrenous bowel as we see in the figure.

- In acute obstruction, most important thing is the high index of suspicion before the bowel becomes infarcted or necrotic.

Why does bowel infarction appear red instead of pale?
Because there is a lot of anastomosis that handle out the decrease in blood flow or ischemia so the infarction doesn't appear pale as we might expect ,it will appear haemorrhagic infarction.

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.

If a child under the age of two comes to the emergency with abdominal destination, vomiting, and constipation, and sometimes the mother says that there is passage of current jelly stool (stool mixed with the blood and mucus) don't forget the intussusception, high index of suspicion is important.

Causes of intussusception

- **Idiopathic in most cases.**
- **Other causes:**
- Peyer patches hyperplasia (rotavirus vaccine, viral infections)
- Meckles diverticulum (ileum)

Because the lymph nodes will be enlarged by lymphoid follicular hyperplasia and this will act as the leading point to the intussusception.

- Old children & adults: Intraluminal mass or tumors

In older children (more than two years old)and adults we have always to suspect an underlying cause . It's tumor until proven otherwise!

Clinical features:

- **Abdominal** swelling
- **Vomiting**
- Passing stools mixed with blood and **mucus (currant jelly stool)**
- **Pain.**

Clinical features comes in acute presentation. The children will have pain which is(irritable , crying,abdominal swelling , disetnation, and constipation with vomiting ,passage of current jelly stool)

Management

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

- First you have to suspect.
- second, if it is early on and not complicated, give the patient rectal enema (حقنة شرجية) to reduce the intussusception .

The fluid pushes the bowel out of the intussusception, so we remove it.
But in complicated cases , if there is infarction the case needs surgical intervention

Meckel's diverticulum

rare

- The most common congenital anomaly of the GI tract
- Incomplete obliteration of omphalomesenteric duct
- True diverticulum. Diverticulum means: out pouching ,part of bowel's wall is pouched out

- **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 will produce acid and pepsin, pancreatic mucosa will produce enzymes, so the patient may develop ulcerations which will cause the complain from GI bleeding

Meckel's diverticulum

Clinical presentation

- Can be asymptomatic and discovered incidentally.

The surgeon performs an operation to remove the appendix in the case of appendicitis, and he found Meckel's diverticulum.

- 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.

Can be confused with acute appendicitis , specifically with ulceration and pain, in this situation the patient will come with pain in the right lower quadrant which is the same location for appendix. Sometimes it is misinterpreted in the emergency room as an acute appendicitis

Non mechanical obstruction

Hirschsprung Disease

- Congenital defect in colonic innervations
- Congenital aganglionic megacolon
- More common in males
- More severe in females
- Risk increase in siblings.

It cause obstruction because the absence of ganglion cells (which forms the internal neurological system of the bowel and are responsible for peristaltic contraction) will inhibit peristalsis.

- **Typical presentation:**

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

Meconium : is the first stool passed by the baby

Pathogenesis

- **During embryogenesis:** 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.

The Intramuscular plexus between the muscle layers of the small bowel is called myenteric plexus

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

Morphology

- Rectum always involved, Most cases in rectosigmoid
- Extent is variable.

- Aganglionic region normal or contracted
- Proximal normal segment progressively dilated.
- **BIOPSY to confirm absence of ganglion cells.**

Because of the accumulation of stool and there is a risk of developing perforation.

- **Diagnostic workup: barium enema, biopsy.**

Biopsy is the gold standard for diagnosis and it must contain: submucosa and muscularis layers to confirm the absence of ganglion cells. Once it's confirmed, the patients undergo surgical procedure

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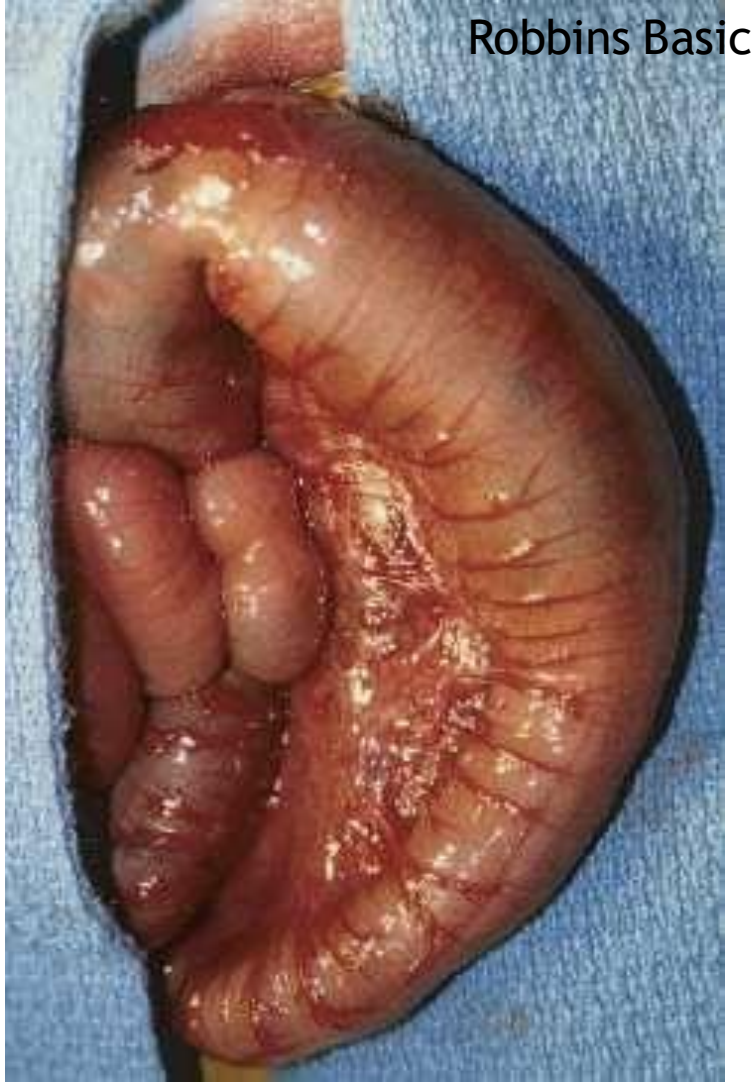
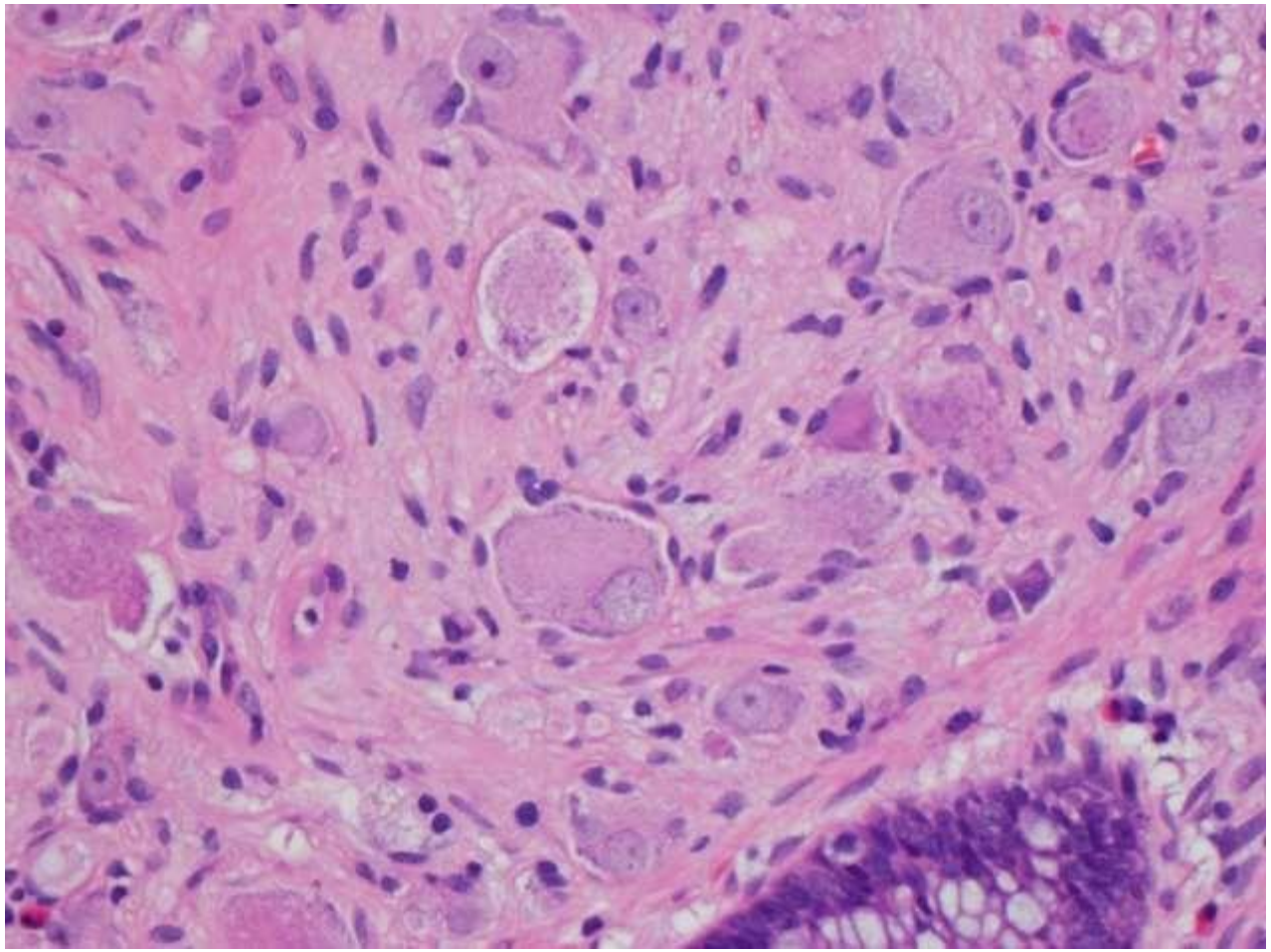


This is a barium enema (enema means through the anal canal). the barium will give white color in the x-ray .
The lower part in the figure which is contracted, this is the region aganglionic
Look at the upper part and notice how much it's dilated in both pictures due to the accumulation of stool.
So this patients will came with abdominal distension and risk of perforation if it's not detected.

ganglion cells



Ganglion cells are neuronal cells
Have eccentric, prominent nucleolus with abundant eccentric cytoplasm.

http://www.pathologyoutlines.com

Complications

- Enterocolitis
- Fluid and electrolyte disturbances Due to the vomiting
- Perforation
- Peritonitis

Perforation will lead to peritonitis

- **Treatment:**
- Surgical resection of aganglionic segment and anastomosis of normal segments. The surgery usually involves the anal canal

VASCULAR DISORDERS OF BOWEL

- Ischemic Bowel Disease
- Angiodysplasia.
- Hemorrhoids

Ischemic bowel disease : the doctor will not talk about it, because it happens with the elderly.

Angiodysplasia : because it is an important cause of Lower GI bleeding, we should know about it.

Angiodysplasia.

- Malformed submucosal and mucosal blood vessels.
- Most often in cecum and right colon.
- 6^{th} decade of life.
- Less than 1% of adult population.
- 20% of cases of lower GI bleeding.
- Blood is bright red in color.

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

Hemorrhoids

The anus has an anastomosis between the systemic venous circulation and portal venous circulation, so anything that elevates the portal pressure will lead to dilation of these BV, which results in hemorrhoids.
Patients with portal hypertension or liver cirrhosis commonly present as hemorrhoids.

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

- **Predisposing factors:**
- Chronic Constipation (the most imp) and straining
- Venous stasis of pregnancy (happens commonly due to the pressure of the uterus).
- 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.

- **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), (mostly painless) pain due to thrombosis and inflammation (or infection of the hemorrhoid).

- **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** (below are a some problems that lead to maldigestion which will result in malabsorption)
- Pancreatic insufficiency
- **Celiac disease**
- Crohn disease
- **Cystic Fibrosis** is an inherited multisystem disease that includes the GIT.
- **Lactase (Disaccharidase) Deficiency**
- **Abetalipoproteinemia**
- **Infectious Enterocolitis**
- **Ischemia** colitis -> If an elderly patient (60-70) with hypertension & diabetes & risk factors for atherosclerosis presents to you with diarrhea then it might be ischemic colitis.
- **Inflammatory bowel diseases…..**

Malabsorptive Diarrhea

Chronic and has sequels (consequences).

- **Chronic.**
- Defective absorption of fats, fat- and water-soluble vitamins, proteins, carbohydrates, electrolytes, minerals and water.
- **Hallmark is**: steatorrhea (excessive fat, bulky, frothy, yellow, greasy stool, foul-smelling).

Malabsorptive diarrhea
Defect in one of the following:

- **Intraluminal digestion** like pancreatic enzymes
- **Terminal digestion** like lactase deficiency
- **Transepithelial transport.**
- **Lymphatic transport** like lymphatic obstruction

Manifestations:

- Weight loss, anorexia.
- Flatus due to the action of microflora on the nutrients that are not absorbed, abdominal distention.
- Borborygmi (intestinal noise), Muscle wasting esp in children and mostly seen in the gluteus region.
- Anemia and mucositis (iron, pyridoxine (VB6), folate, or vitamin B12 deficiency)
- Bleeding (vitamin K deficiency)
- Osteopenia and tetany or rickets (calcium, magnesium, or vitamin D deficiency)
- Neuropathy (vitamin A or B12 deficiency)
- Skin and endocrine disorders like iodine deficiency which leads to hypothyroidism.

Cystic Fibrosis

- Mutations in cystic fibrosis transmembrane conductance regulator (CFTR) this mutation makes secretions viscous not fluid.
- Defects in ion transport across intestinal and pancreatic epithelium.
- Thick viscous secretions.
- Mucus plugs in pancreatic ducts >>> pancreatic insufficiency & pancreatitis (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 result in obstruction.
- Defect in intraluminal digestion.

Celiac Disease

- *Gluten sensitive enteropathy*
- Immune mediated enteropathy **(Antibodies formed by the body against certain antigens). It is not considered an allergy as allergies involve IgE.**
- Wheat, rye or barley.
- Genetically predisposition, HLA-DQ2 or HLA-DQ8.
- Treatment: gluten free diet.

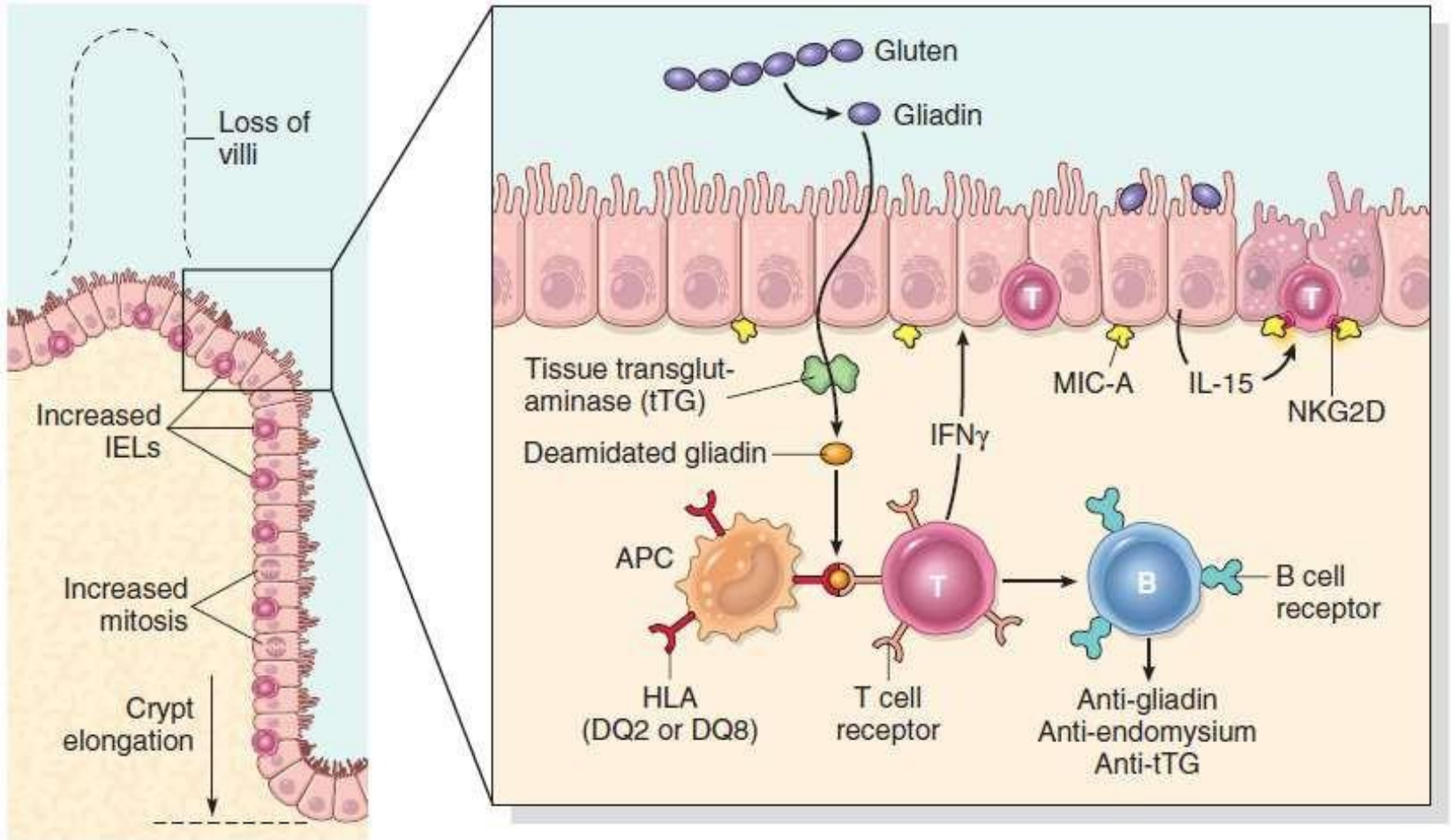
- Association with **(autoimmune diseases)** : type 1 diabetes, thyroiditis, and Sjogren syndrome

Pathogenesis

- Gluten >>> gliadin >> gliadin enters between enterocytes 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 then CD8+ T cells (cytotoxic T cell) >> 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

Treatment with gluten free diet for 3-6 months will result in the absence of these antibodies from serum and the absence of all the changes in the bowel (next slide).



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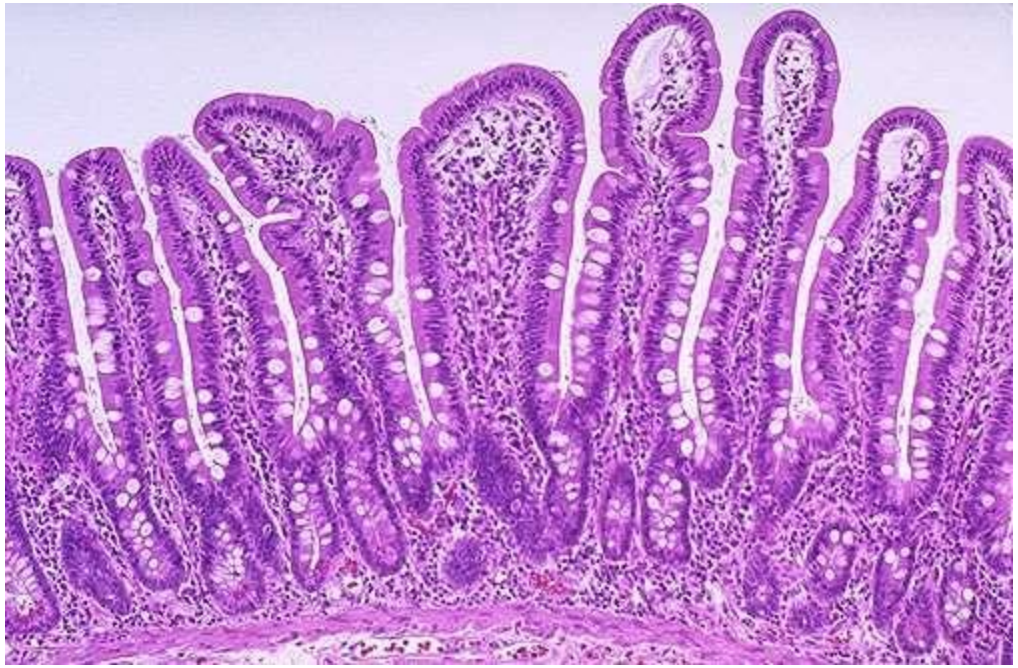
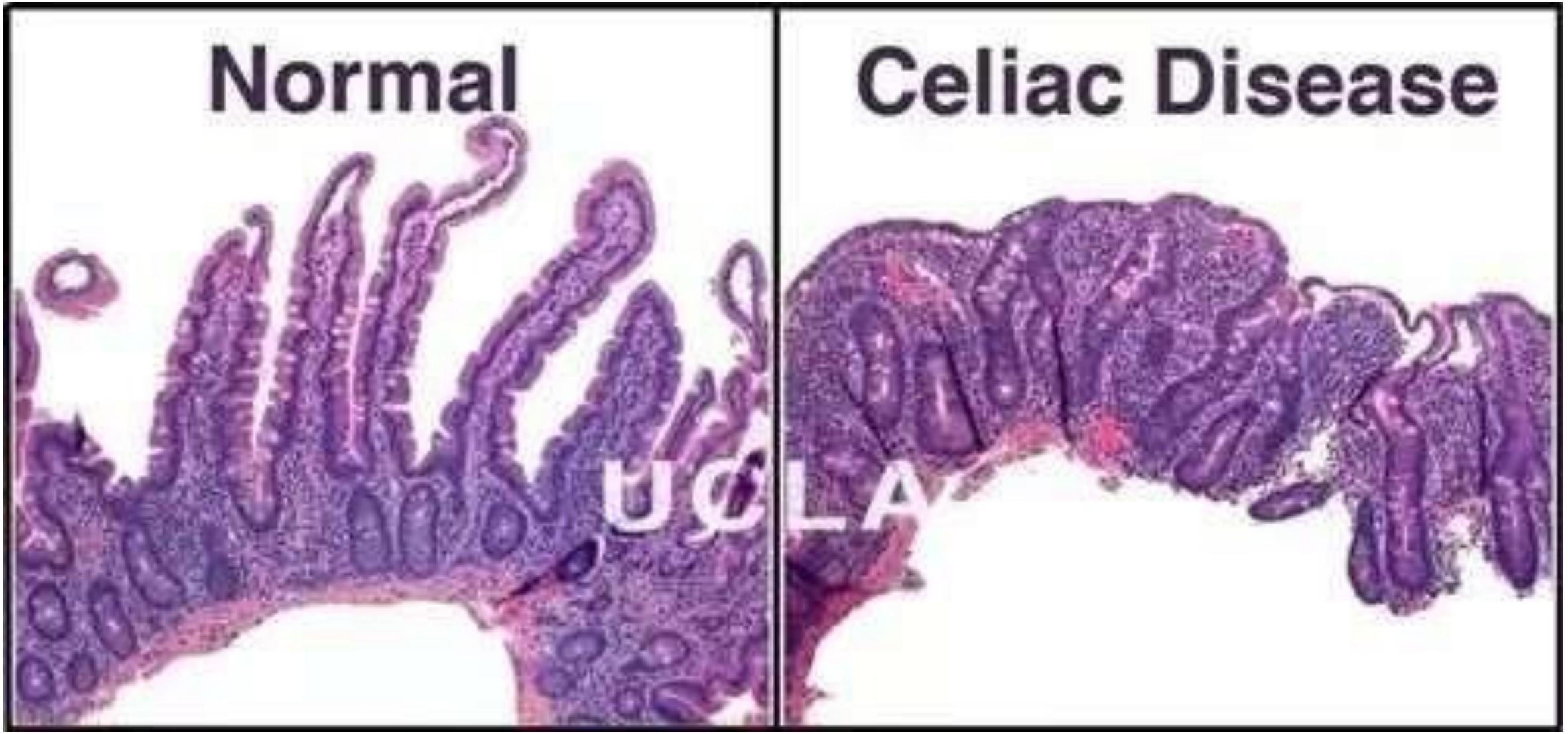
MORPHOLOGY

- Second portion of the duodenum or proximal jejunum. These are important sites for iron absorption so patients can present with iron deficiency as the only manifestation.
- **Microscopic features:** **Triad:** Earliest feature is (IEL) intraepithelial lymphocytosis "The bowel has finger like projections lined by absorptive enterocytes which lymphocytes (T cells) attack these cells "(CD8+ T cells), crypt hyperplasia, and villous atrophy is the most important and leads to a decrease in the surface area.
- Lamina propria: lymphocytes, plasma cells, eosinophils…….
- IEL & villous atrophy are not pathognomonic (celiac disease cannot be diagnosed based on these features only especially if the biopsy is taken from the first portion of the duodenum as the villous atrophy can be from gastric acid secretions not celiac disease. Biopsy should be taken from the second portion of the duodenum), seen in viral enteritis.

- Diagnosis: Clinical, histologic and serologic correlation. (clinical, serological, and pathological correlation).

Normal intestine





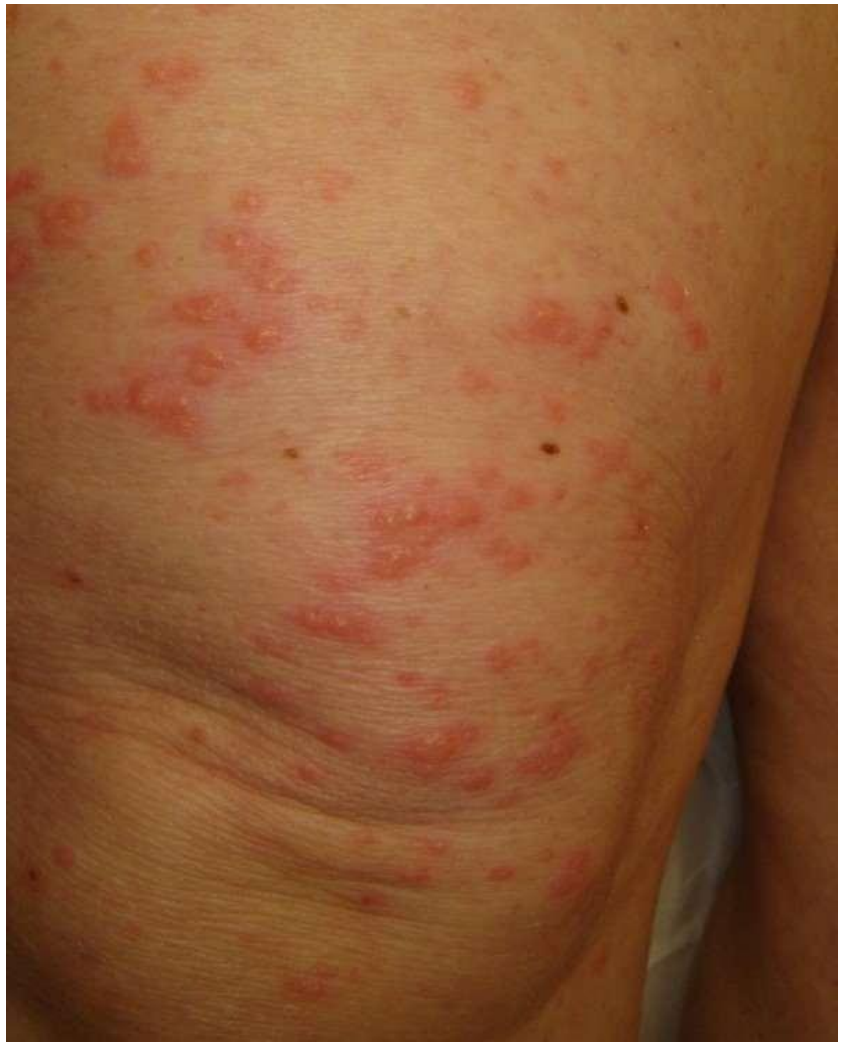
Total villous atrophy

Clinical Features

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

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

Dermatitis herpetiformis.



- Adults (30-60 years)
- Anemia: iron deficiency
- 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).

- Increased risk of enteropathy associated small intestinal T cell lymphoma & Small intestinal adenocarcinoma due to T cell activation.

Diagnosis:

- **Non invasive serologic tests:**
- **Most sensitive:**
- Anti tissue transglutaminase antibody, IgA
- Anti deamidated gliadin antibodies, IgA & IgG

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

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

Sensitive: they are found in all cases of celiac disease, but are also found in other diseases.

Sensitive -> if positive then its not diagnostic, except if patient has symptoms and the biopsy is positive.

Specific: they are not found in all cases of celiac disease, but if found then diagnosis is celiac disease 100%.

Lactase (Disaccharidase) Deficiency

- Osmotic diarrhea because the lactose in the bowel will absorb water.
- Lactose remains in the gut lumen.
- Lactase found at apical brush border membrane.
- Normal biopsy findings.

Deficient enzyme responsible for the digestion of lactose which is present on the terminal brush border.

- Three types:
- ***Congenital*** : AR, genetic mutation, rare, explosive diarrhea, watery, frothy stools & abdominal distention, after milk ingestion. Treatment include lactose free milk.
- ***Acquired*** : very common, downregulation of gene (Lactase is present but in decreased amount, so if patient consumes more milk than the amount of enzyme they have, they will experience symptoms), after weaning. Affects 2/3 of world's population (50% of USA population).
- **Transient:** caused by injury after infectious or inflammatory insults (reversible). In inflammation of the bowel like viral enterocolitis or gastroenteritis causes the brush border to get damaged. The patient will experience symptoms for a short period of time that is until the brush border regenerates.

Abetalipoproteinemia

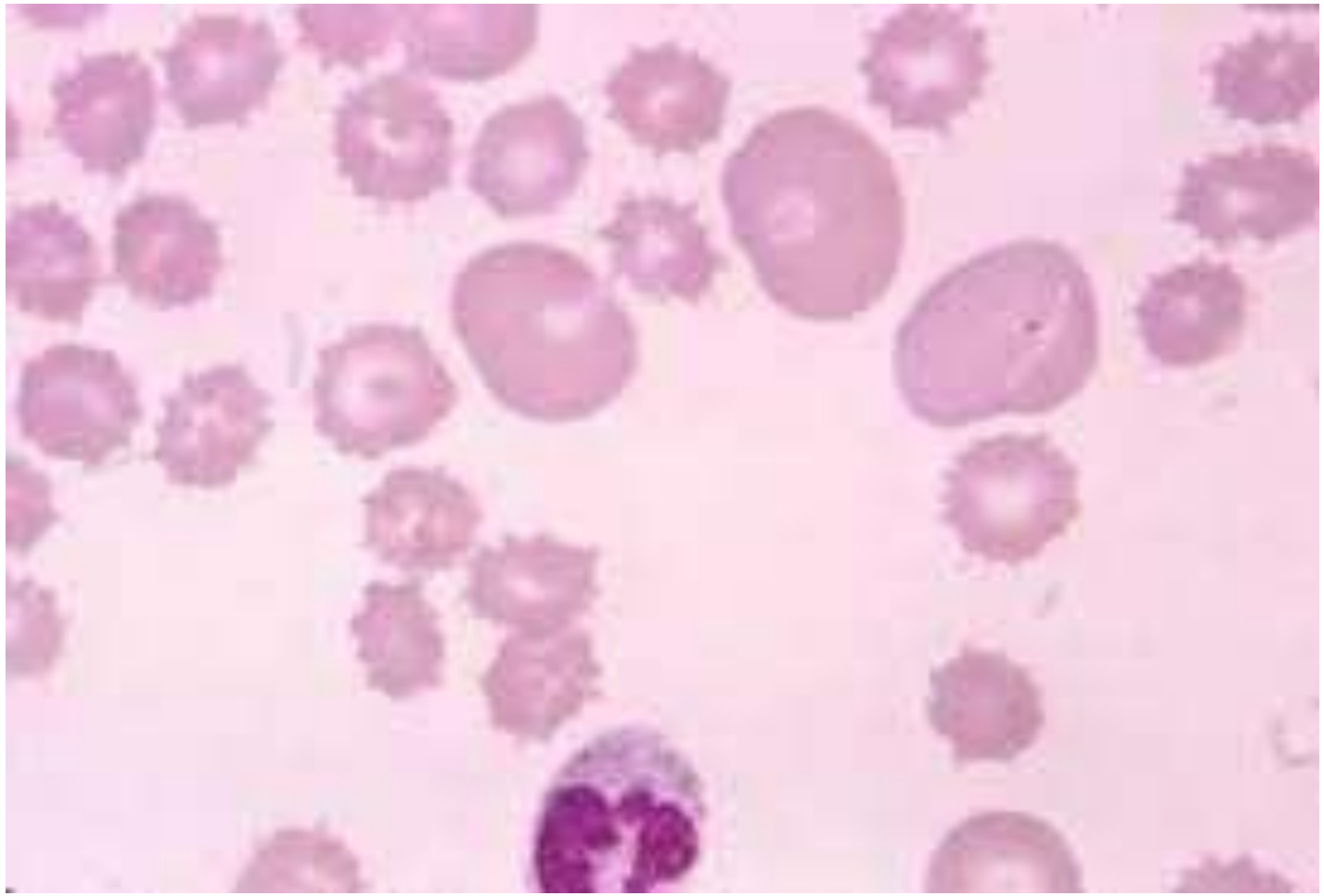
Absence of lipoproteins due to malabsorption

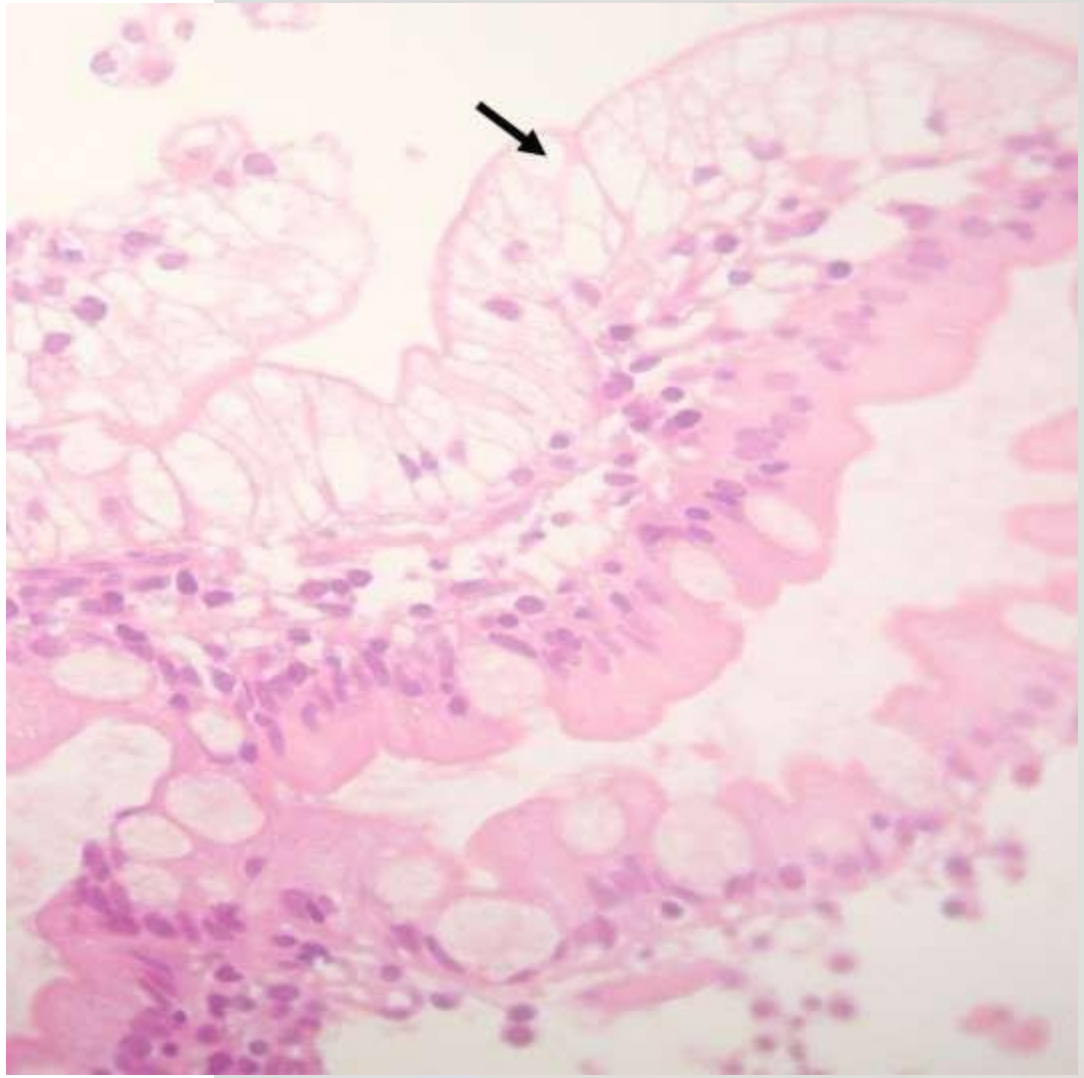
Lipoproteins enter the enterocytes, but can't be transported to lymphatics due to a defect in the transport. Lipoproteins, FA, and fat-soluble vitamins will accumulate in the enterocytes which results in a white color in the cytoplasm of the enterocytes under the microscope.

- Autosomal recessive, rare.
- Inability of enterocytes to secrete triglyceride-rich chylomicrons.
- Lack of absorption (Transepithelial transport defect of lipoproteins, FAs and fat-soluble vitamins).
- Usually effects Infants' w/ failure to thrive, diarrhea, and steatorrhea.
- Vitamin K deficiency (Symptoms include anything affected by the fat-soluble vitamins "AKED"; Vit A effects skin and retina, Vit D might cause rickets), skeletal CNS and retinal abnormalities.
- Spur cells in peripheral blood because FAs are needed to produce the phospholipids in the wall of the all cells including RBCs. We use RBCs because they can be easily seen on peripheral blood smear.
- Monoglycerides and triglycerides accumulate in epithelial cells.

Spur cells in peripheral blood

Notice the star-like appearance due to the disruption of the plasma membrane of the cells.





Micrograph showing enterocytes with a clear cytoplasm (due to lipid accumulation) characteristic of abetalipoproteinemia.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slides 10 & 20 Slide 11	Repeated twice Ganglionic bowel	Deleted slide 10 Gangrenousbowel
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

ما تنسوا أهلنا في غزة من دعائكم