

Small and Large Intestinal pathology, part 2

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Diseases of the intestines

- ▶ **Intestinal obstruction**
- ▶ **Vascular disorders**
- ▶ **Malabsorptive diseases and infections**
- ▶ Inflammatory bowel disease.
- ▶ Polyps and neoplastic diseases

Intestinal obstruction

- ▶ Mechanical obstruction:

- ▶ Intussusception
- ▶ Hernias.
- ▶ Adhesions.
- ▶ Volvulus

- ▶ Tumors.
- ▶ Diverticulitis
- ▶ Infarction

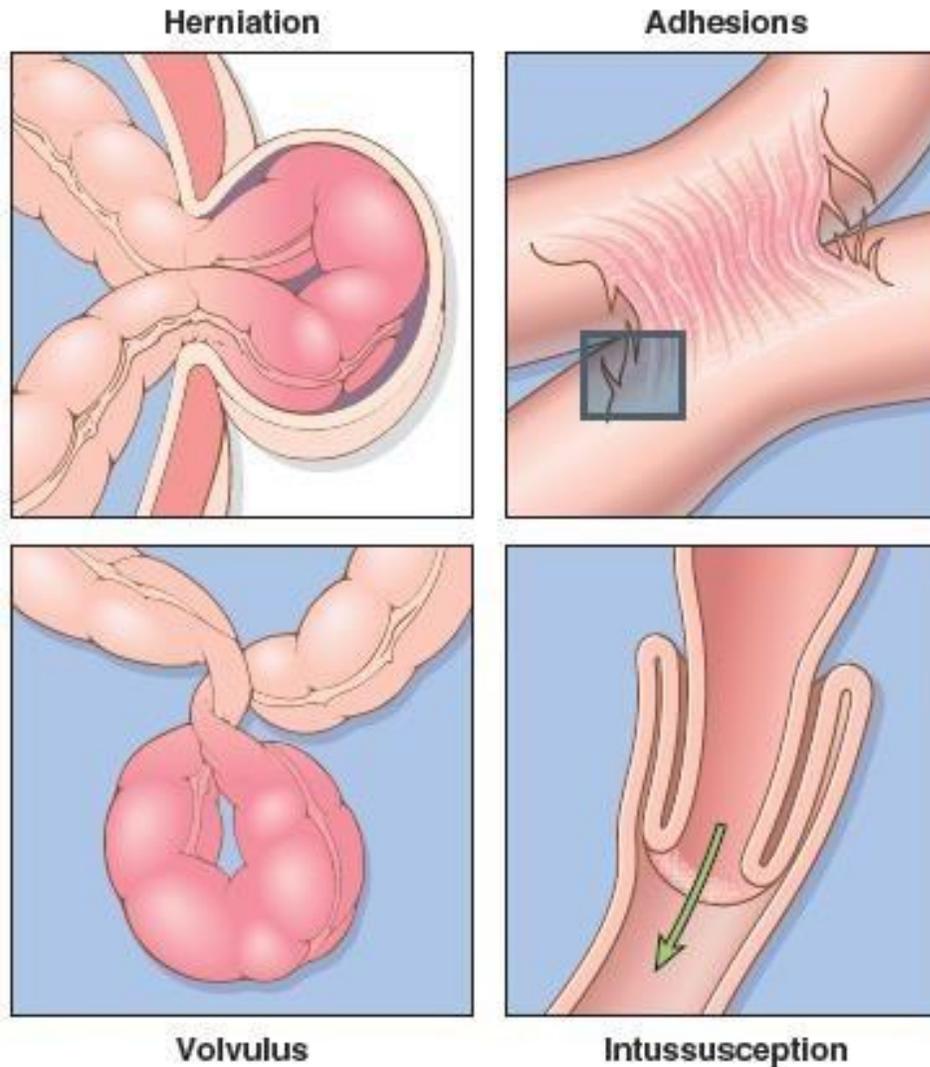
- ▶ Non-mechanical obstruction

- ▶ Hirschsprung disease
- ▶ Neurological disorders.
- ▶ Drugs....etc

Clinical picture of intestinal obstruction.

- ▶ Abdominal pain
 - ▶ Distention
 - ▶ Vomiting
 - ▶ Constipation.
-
- ▶ Acute or chronic.

80% of mechanical obstructions



Intussusception

- ▶ **Segment of the intestine constricted by a wave of 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 infarction.**

Causes of intussusception

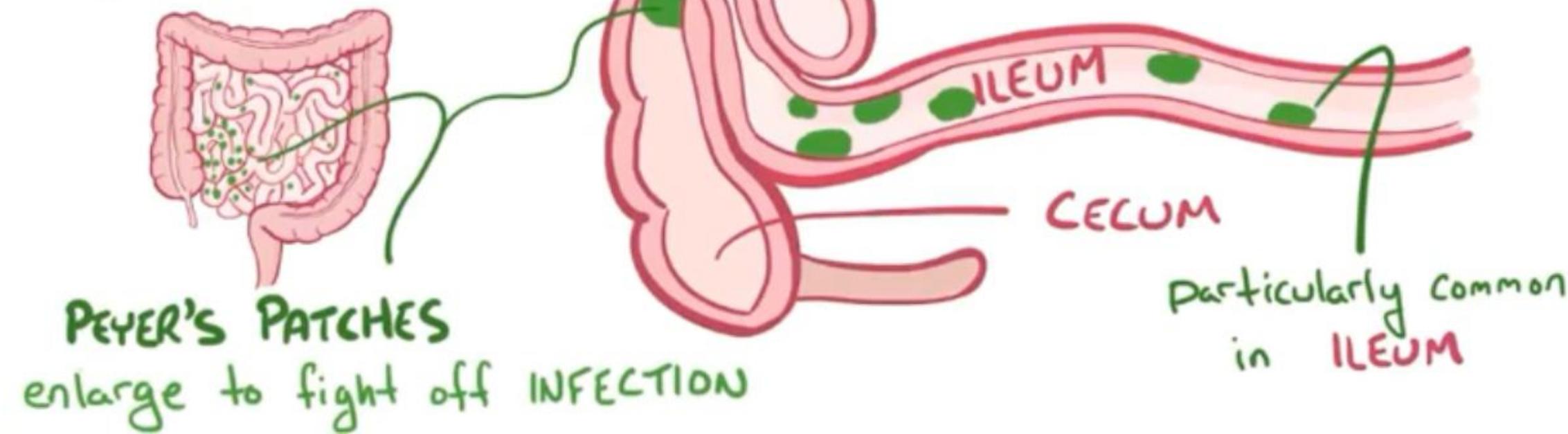
- ▶ **< 2years : Idiopathic in most cases.**
- ▶ **Peyer patches hyperplasia (rotavirus vaccine, viral infections)**
- ▶ **Meckles diverticulum (ileum)**
- ▶ **Old children & adults: Intraluminal mass or tumors**

INTUSSUSCEPTION

(usually happens in ILEOCECAL region)

* in BABIES the
LEADING EDGE is often
LYMPHOID HYPERPLASIA
enlargement of lymph tissue

ALMOST ALL INTUSSUSCEPTIONS
happen when the
ILEUM folds into the CECUM



INTUSSUSCEPTION

(usually happens in ILEOCECAL region)

* in ADULTS is often caused by:

L POLYP

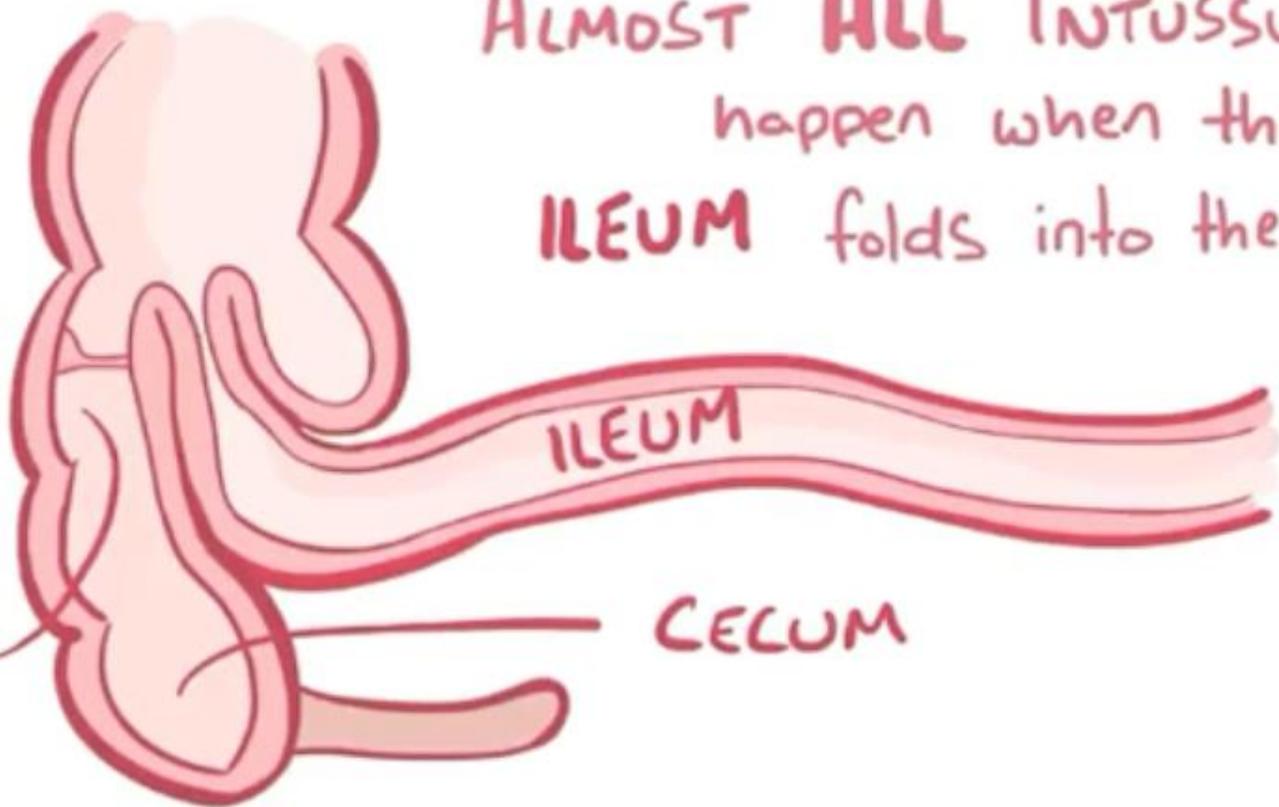
L TUMOR

Serve as LEADING EDGE

CONTRACTING INTESTINES
can grab leading edge

& pull it ahead

ALMOST ALL INTUSSUSCEPTIONS
happen when the
ILEUM folds into the CECUM





Clinical features:

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

Management

- ▶ **Contrast enemas in uncomplicated idiopathic cases.**
- ▶ **Surgery if complicated or if masses are the leading point.**

Hirschsprung Disease

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

- ▶ **Typical presentation:**
- ▶ Neonatal failure to pass meconium
- ▶ Obstructive constipation.

Pathogenesis

- ▶ **During embryogenesis**
- ▶ Disrupted migration of neural crest cells from cecum to rectum.
- ▶ Lack of **Meissner submucosal plexus** and the **Auerbach myenteric plexus**.
- ▶ Failure of coordinated peristaltic contractions.
- ▶ Mutations in RET: in familial cases and 15% of sporadic
- ▶ Other genes and environmental factors play role.

Morphology

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

- ▶ **Macroscopic**
- ▶ Aganglionic region normal or contracted
- ▶ Proximal normal segment progressively dilated.

- ▶ **Diagnosis: BIOPSY, microscopic.**

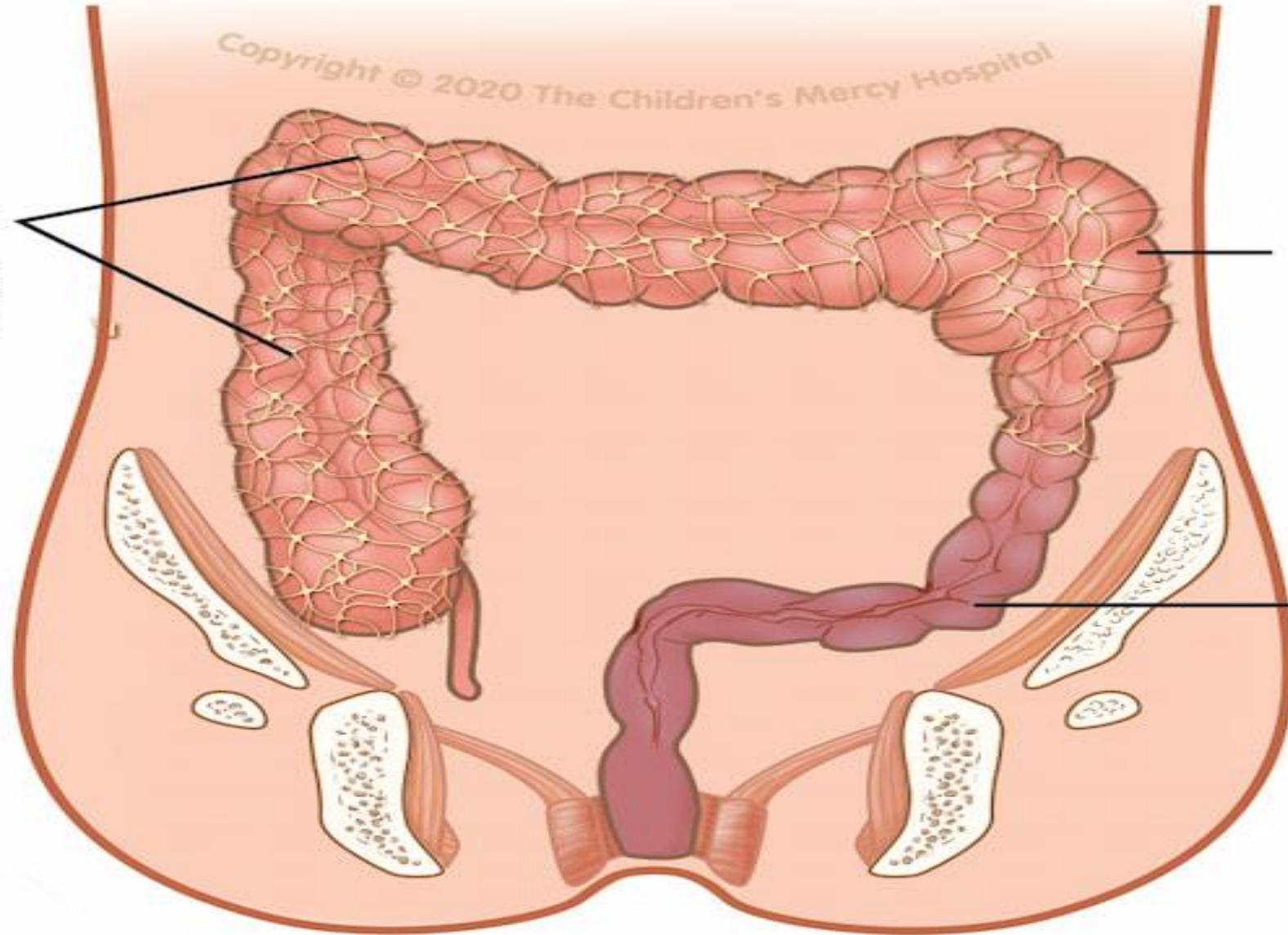
HIRSCHSPRUNG DISEASE

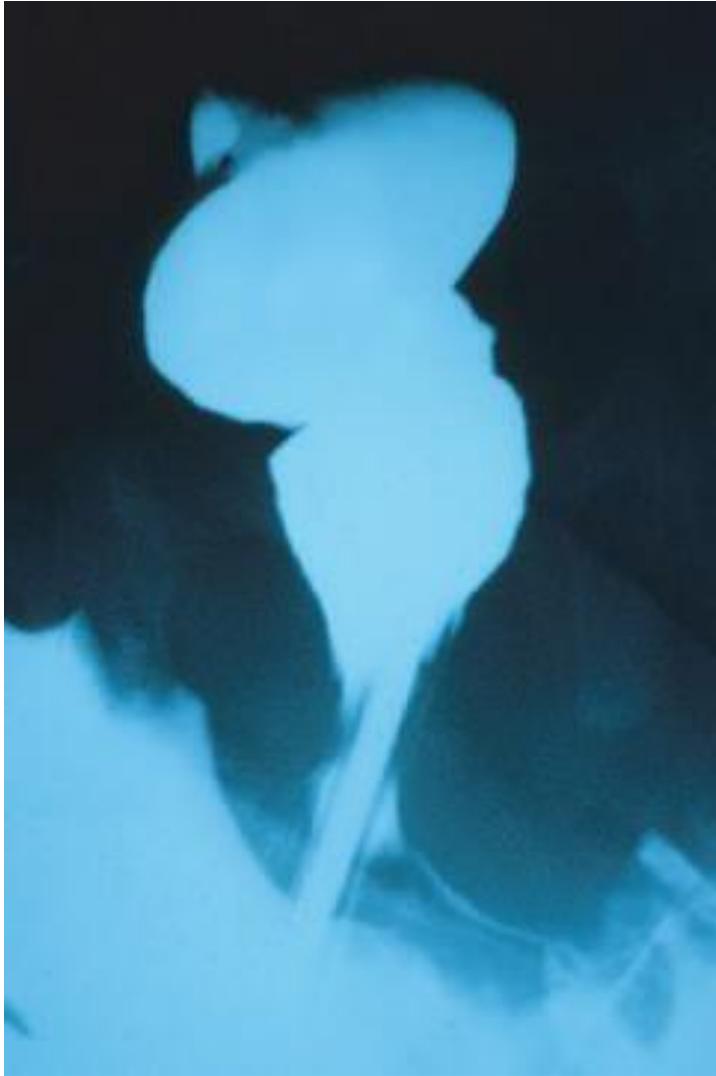
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Ganglion
innervating
colon

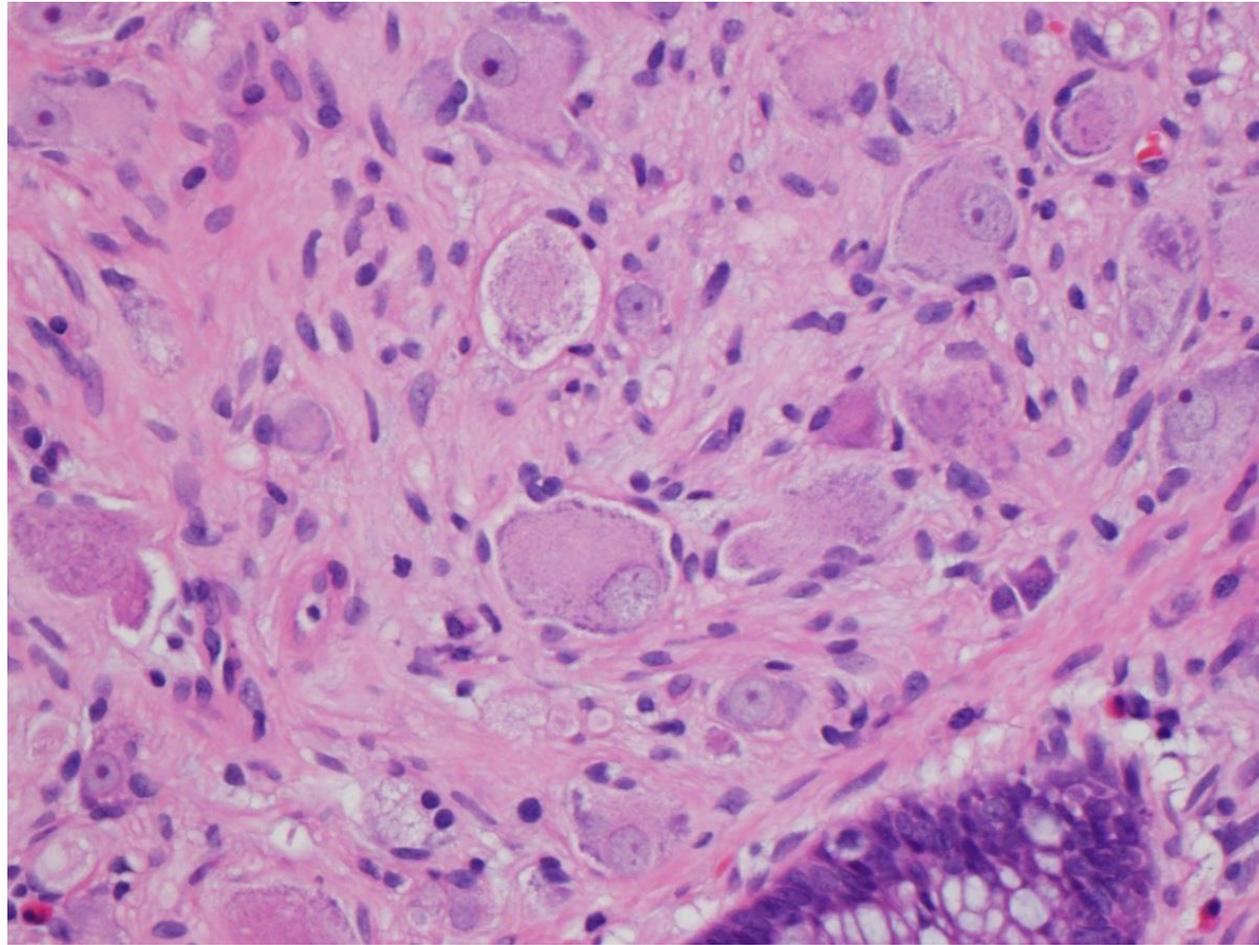
Normal colon

No ganglion
No colon
movement





ganglion cells



Complications

- ▶ Enterocolitis
- ▶ Fluid and electrolyte disturbances
- ▶ Perforation
- ▶ Peritonitis

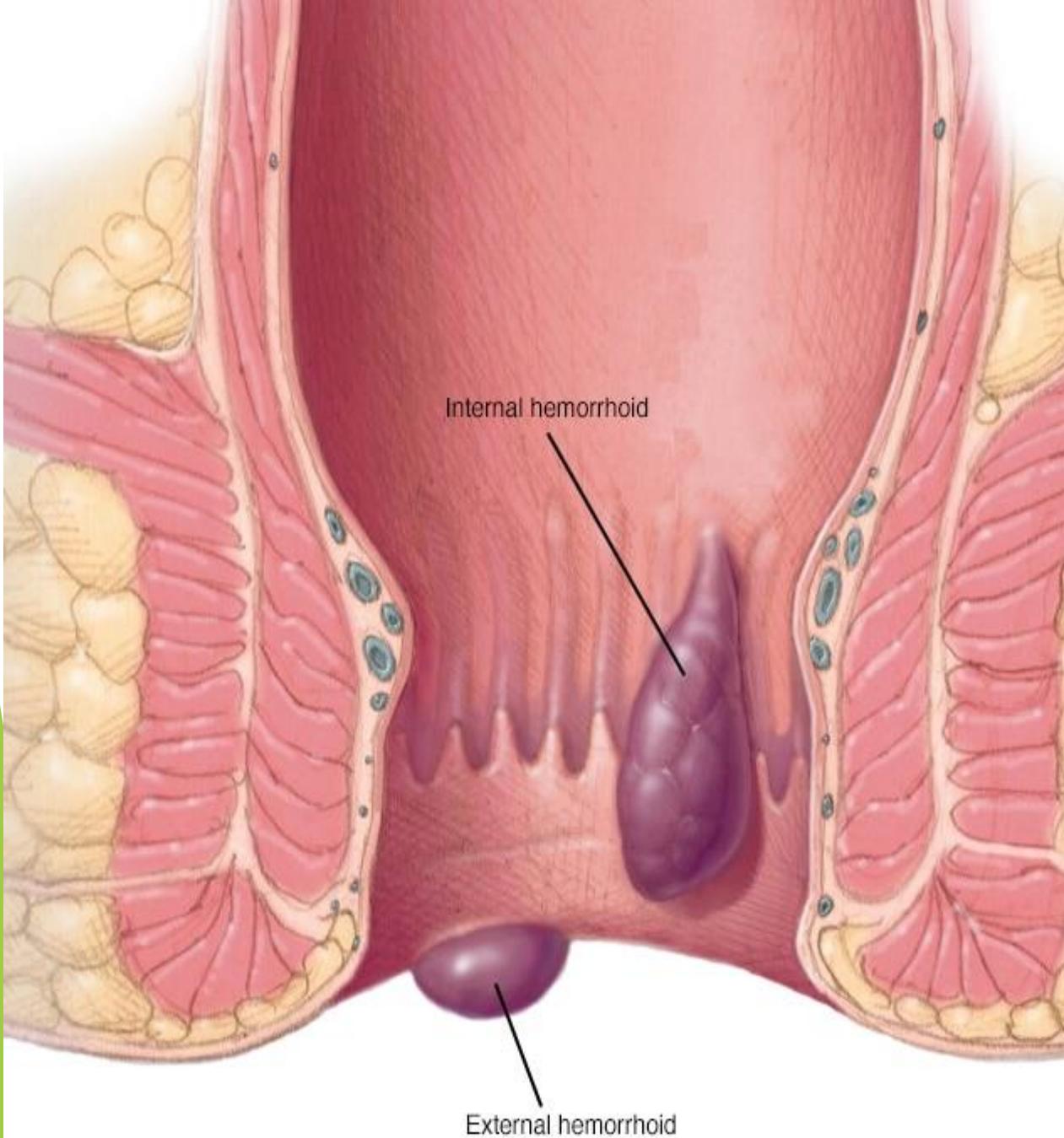
- ▶ **Treatment:**
- ▶ Surgical resection of aganglionic segment and anastomosis of normal segments.

VASCULAR DISORDERS OF BOWEL

- ▶ **Ischemic Bowel Disease**
- ▶ **Hemorrhoids**

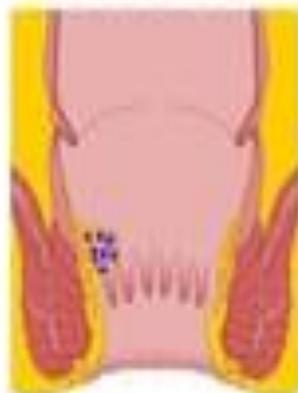
Hemorrhoids

- ▶ Dilated anal and perianal collateral vessels that connect the portal and caval venous systems.
- ▶ **Predisposing factors:**
 - ▶ Constipation and straining
 - ▶ Venous stasis of pregnancy,
 - ▶ Portal hypertension.
- ▶ External and internal hemorrhoids



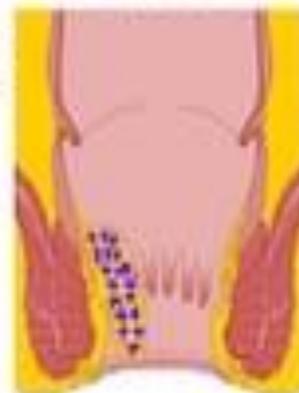
INTERNAL HEMORRHOID GRADES

Grade I



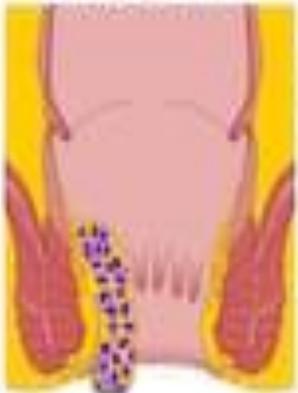
No prolapse, just prominent blood vessels

Grade II



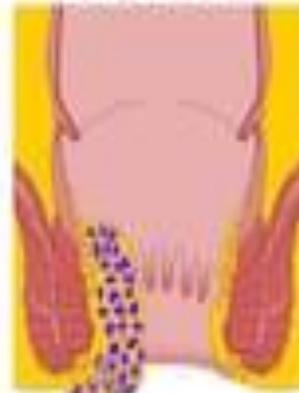
Prolapse upon bearing down, but spontaneous reduction

Grade III



Prolapse upon bearing down requiring manual reduction

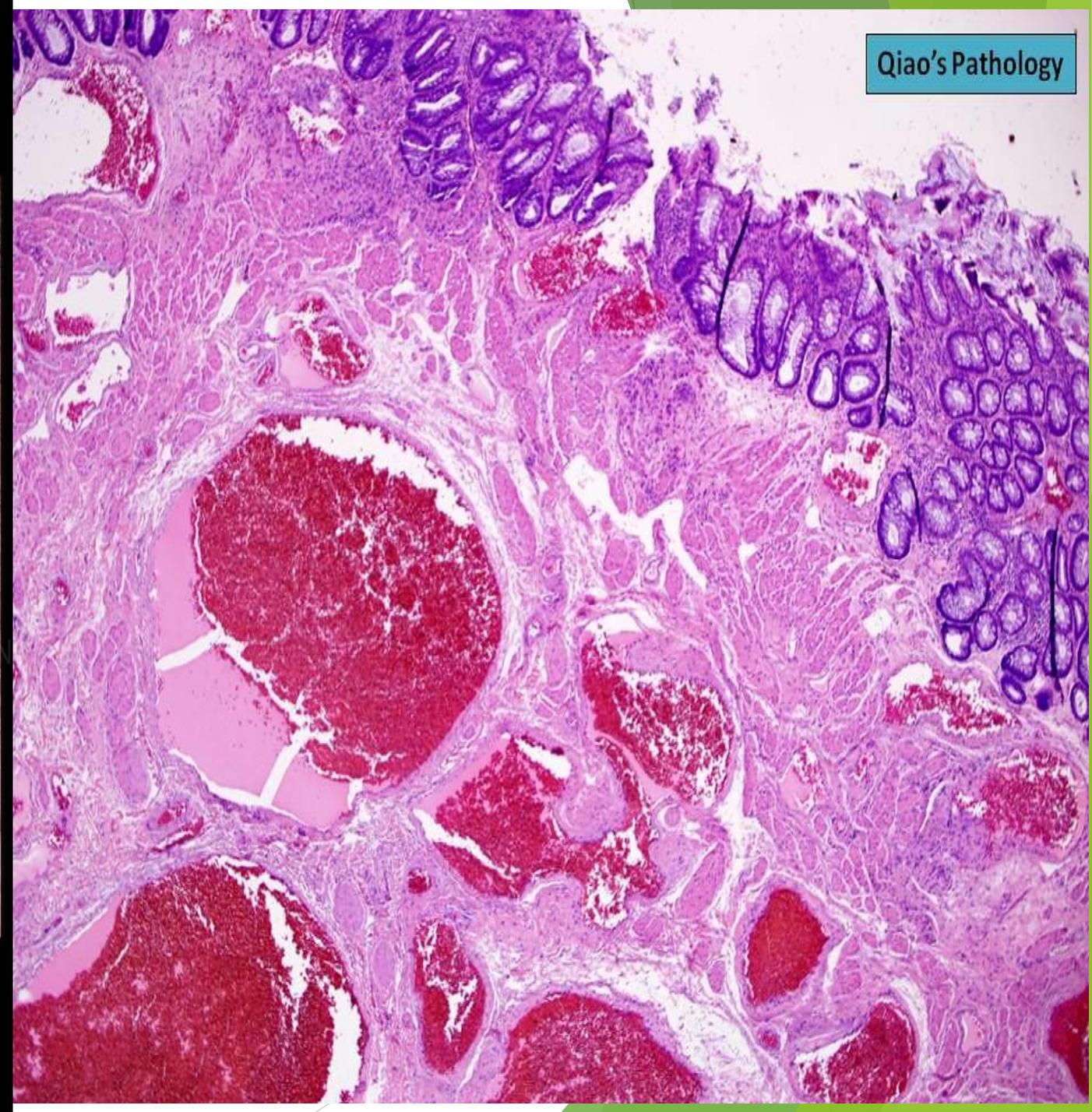
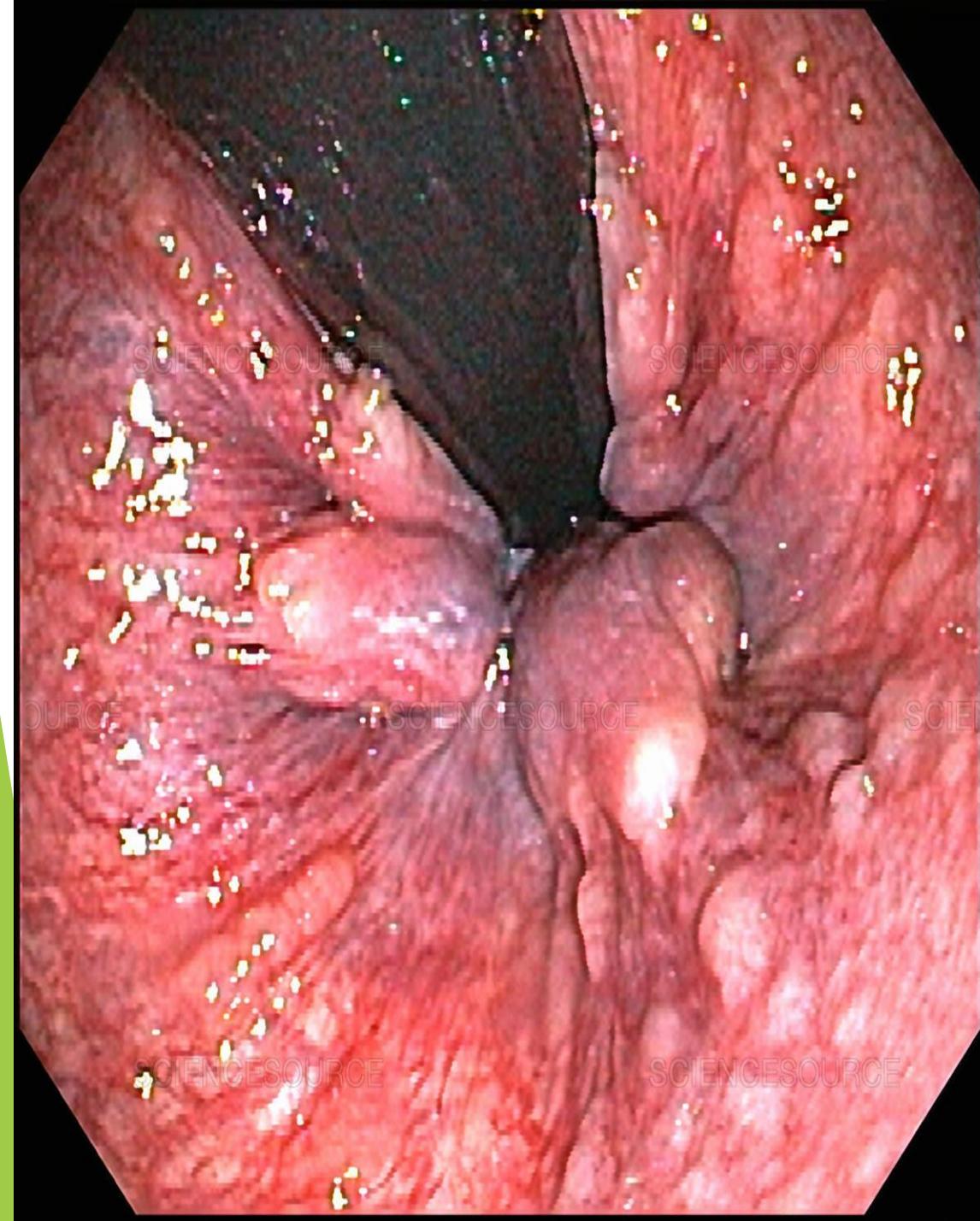
Grade IV



Prolapse with inability to be manually reduced

Microscopic findings

- ▶ Dilated, thick walled, congested submucosal vessels and sinusoidal spaces, often with thrombosis; variable hemorrhage into connective tissue
- ▶ Dilated spaces may show exuberant vascular proliferation confined to vessel known as papillary endothelial hyperplasia
- ▶ Internal hemorrhoids are lined by rectal or transitional mucosa, external hemorrhoids have a squamous lining
- ▶ Surface may show ulceration



Clinical features

- ▶ Patients usually have **painless bleeding**, noticing blood in the toilet or on lavatory paper
- ▶ Patients may experience **pain** or discomfort, especially with thrombosis, strangulation or ulceration
- ▶ **Anemia** from hemorrhoids is unusual - patients should undergo hematologic evaluation

- ▶ Clinically four grades:
 - ▶ **First degree**, anal cushions that slide down past dentate line with straining at stool, that bleed with defecation
 - ▶ **Second**, anal cushions that prolapse with straining, but reduce spontaneously
 - ▶ **Third**, hemorrhoids that remain outside of the anal canal unless manually replaced
 - ▶ **Fourth**, hemorrhoids that cannot be reduced

DIARRHEAL DISEASE

- ▶ **Diarrhea**: increase in stool mass, frequency or fluidity (more than 200 grams per day)
- ▶ In severe cases, stool volume can exceed 14 L per day and, without fluid resuscitation, result in death.
- ▶ Worldwide, diarrheal diseases account for greater than 700,000 deaths of children under 5 years of age, making them the second leading cause of death in this age group.
- ▶ Painful, bloody, small-volume diarrhea is known as **dysentery**.
- ▶ Diarrhea is a common symptom of many intestinal diseases, including those due to infection, inflammation, ischemia, malabsorption, and nutritional deficiency

DIARRHEAL DISEASE

- ▶ It can be classified into four major categories:
- ▶ 1• **Secretory diarrhea** is characterized by isotonic stool and persists during fasting.
- ▶ 2• **Osmotic diarrhea**, such as that occurring with lactase deficiency, is due to osmotic forces exerted by unabsorbed luminal solutes more concentrated than plasma, and the condition abates with fasting.
- ▶ 3• **Malabsorptive diarrhea** caused by inadequate nutrient absorption is associated with steatorrhea and is relieved by fasting.
- ▶ 4• **Exudative diarrhea** is due to inflammatory disease and characterized by purulent, bloody stools that continue during fasting.

Malabsorptive Diarrhea

- ▶ Malabsorption manifests most commonly as chronic diarrhea
- ▶ Characterized by defective absorption of fats, fat- and water-soluble vitamins, proteins, carbohydrates, electrolytes
- ▶ Chronic malabsorption causes weight loss, anorexia, abdominal distention, borborygmi, and muscle wasting.
- ▶ A hallmark of malabsorption is **steatorrhea**, characterized by excessive fecal fat and bulky, frothy, greasy, yellow, or clay-colored stools.

Malabsorptive Diarrhea

- ▶ **Pancreatic insufficiency.**
- ▶ **Celiac disease**
- ▶ **Crohn disease**
- ▶ **Cystic Fibrosis**
- ▶ **Lactase (Disaccharides) Deficiency**
- ▶ **Abetalipoproteinemia**
- ▶ **Infectious Enterocolitis**
- ▶ **Inflammatory bowel diseases.....**

Malabsorptive diarrhea

Defect in one of the following:

- **Intraluminal digestion**, in which proteins, carbohydrates, and fats are broken down into absorbable forms
- • **Terminal digestion**, which involves the hydrolysis of carbohydrates and peptides by disaccharidases and peptidases, respectively, in the brush border of the small-intestinal mucosa
- • **Transepithelial transport**, in which nutrients, fluid, and electrolytes are transported across and processed within the small-intestinal epithelium
- • **Lymphatic transport** of absorbed lipid

Table 15.3 Defects in Malabsorptive and Diarrheal Disease

Disease	Intraluminal Digestion	Terminal Digestion	Transepithelial Transport	Lymphatic Transport
Celiac disease		+	+	
Tropical sprue		+	+	
Chronic pancreatitis	+			
Cystic fibrosis	+			
Primary bile acid malabsorption	+		+	
Carcinoid syndrome			+	
Autoimmune enteropathy		+	+	
Disaccharidase deficiency		+		
Mycobacterial infection, Whipple disease				+
Abetalipoproteinemia			+	
Viral gastroenteritis		+	+	
Bacterial gastroenteritis		+	+	
Parasitic gastroenteritis		+	+	
Inflammatory bowel disease	+	+	+	

+, Indicates that the process can be abnormal in the disease indicated. Other processes are not typically affected.

Manifestations:

- ▶ Weight loss, anorexia,
- ▶ Flatus, abdominal distention,
- ▶ Borborygmi, Muscle wasting
- ▶ 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)
- ▶ Skin and endocrine disorders.

Cystic Fibrosis

- ▶ **Mutations in cystic fibrosis transmembrane conductance regulator (CFTR)**
- ▶ **Individuals with cystic fibrosis have defects in intestinal and pancreatic ductal ion transport.**
- ▶ **This abnormality interferes with bicarbonate, sodium, and water secretion, ultimately resulting in inadequate luminal hydration.**
- ▶ **The viscous luminal contents may result in meconium ileus, which is present in up to 10% of newborns with cystic fibrosis.**

Cystic Fibrosis

- ▶ In the pancreas the ducts are plugged by thick mucus.
- ▶ This leads to obstruction, low-grade chronic autodigestion of the pancreas, and eventual exocrine pancreatic insufficiency in more than 80% of patients.
- ▶ The result is failure of the intraluminal phase of nutrient absorption, which can be effectively treated in most patients with oral enzyme supplementation.

Celiac Disease

- ▶ Celiac disease, also known as **celiac sprue** or **glutensensitive enteropathy**, is an immune-mediated enteropathy triggered by the ingestion of gluten-containing cereals, such as wheat, rye, or barley, in genetically predisposed individual
- ▶ Genetically predisposition, HLA-DQ2 or HLA-DQ8.
- ▶ Treatment: gluten free diet.
- ▶ Association with: type 1 diabetes, thyroiditis, and Sjogren syndrome

Pathogenesis

- ▶ Celiac disease is an intestinal immune reaction to **gluten**, the major storage protein of wheat and similar grains.
- ▶ Gluten is digested by luminal and brush border enzymes into amino acids and peptides, including a 33–amino acid gliadin peptide that is resistant to degradation by gastric, pancreatic, and small-intestinal proteases
- ▶ Gliadin is delaminated by tissue transglutaminase and is then able to interact with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells and be presented to CD4+ T cells.
- ▶ These T cells in lamina propria produce cytokines that likely contribute to the tissue damage and characteristic mucosal histopathology

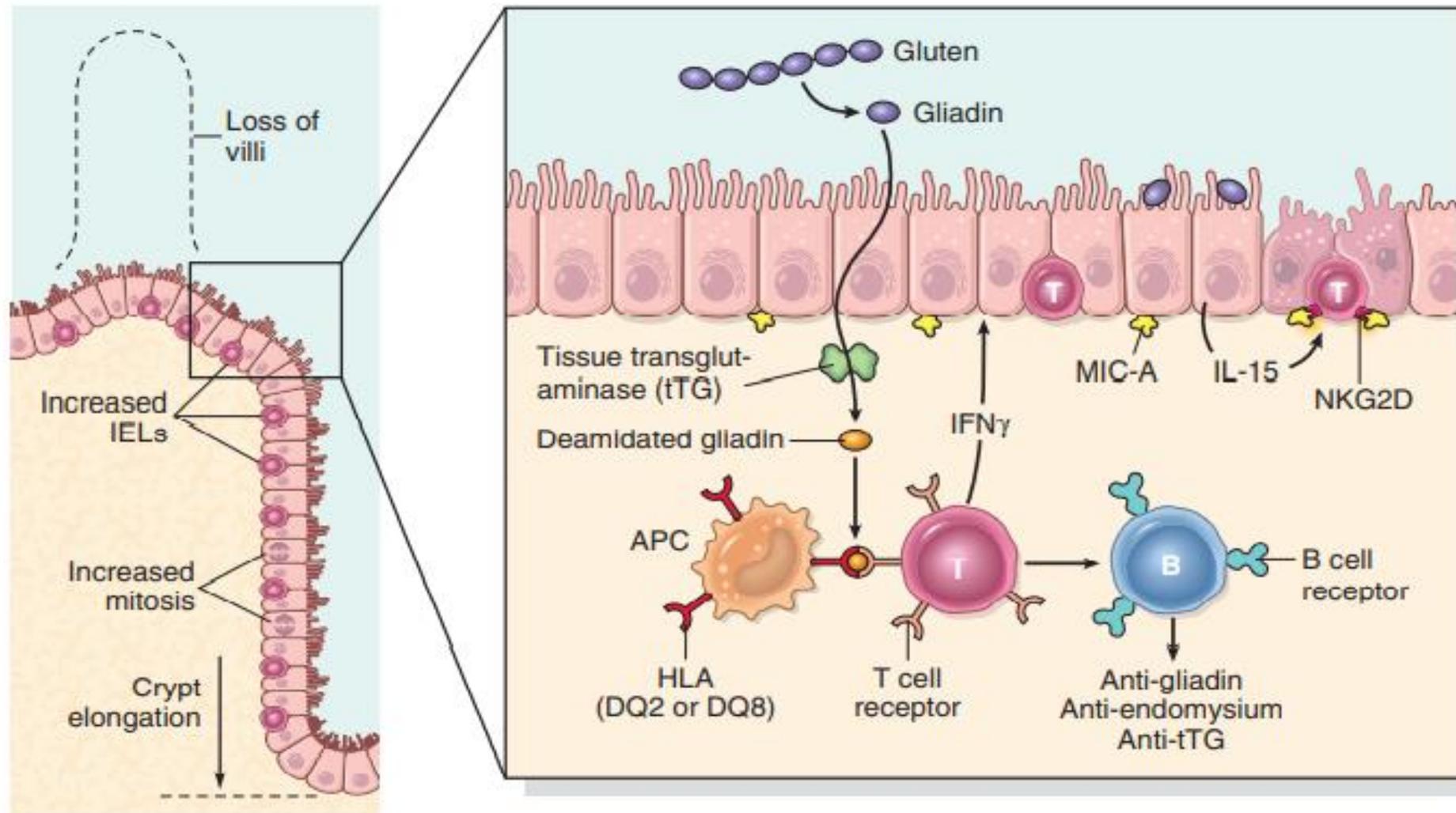


Fig. 15.21 The morphologic alterations that may be present in celiac disease, including varying degrees of villous atrophy, increased numbers of intraepithelial lymphocytes (IELs), and epithelial proliferation with crypt elongation (left). A model for the pathogenesis of celiac disease (right). Note that both innate and adaptive immune mechanisms are involved in the tissue responses to gliadin. CD4 T cells (producing IFN γ) are shown in lamina propria and CD8 T cells, expressing NKG2D receptor, in between epithelial cells.

Serology:

- ▶ **Anti- tissue transglutaminase antibodies**
- ▶ **Anti-gliadin antibodies.**
- ▶ **Anti -endomysial antibodies**

NORMAL

CELIAC DISEASE

Enterocyte

Villous

Celiac Disease

1. Villous Blunting

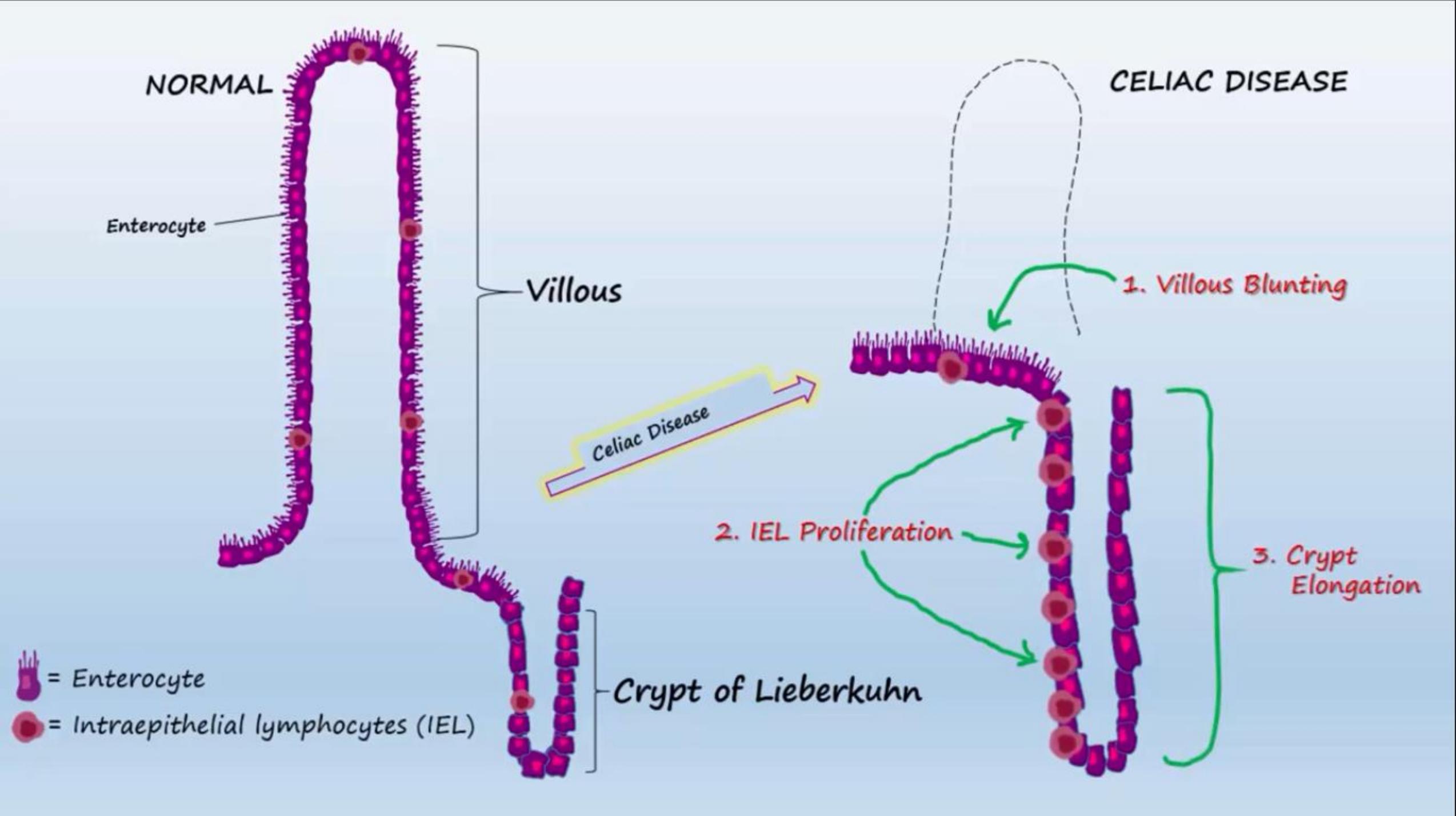
2. IEL Proliferation

3. Crypt Elongation

Crypt of Lieberkuhn

= Enterocyte

= Intraepithelial lymphocytes (IEL)

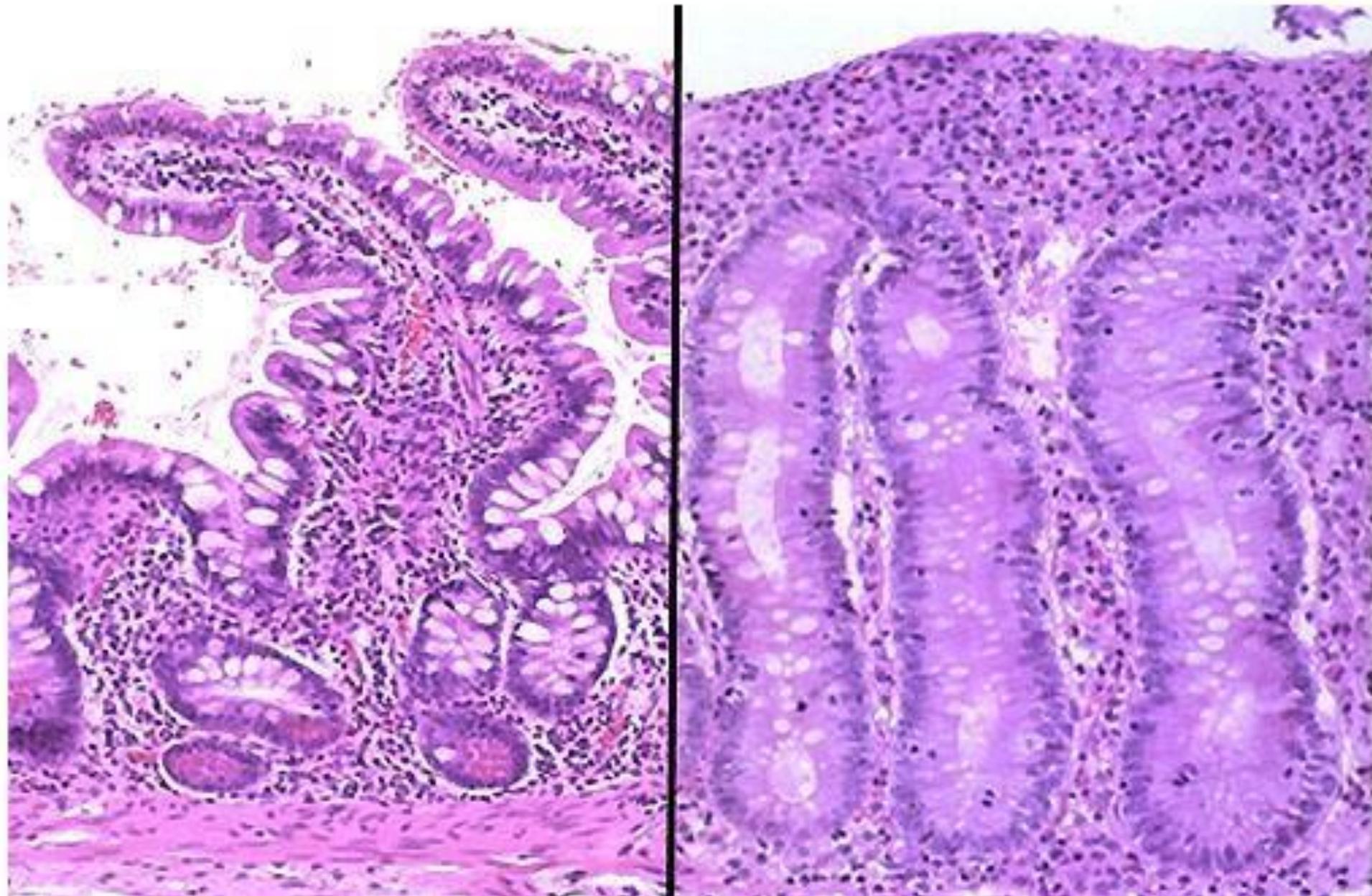


MORPHOLOGY

- ▶ Second portion of the duodenum or proximal jejunum.
- ▶ **Triad:** intraepithelial lymphocytosis (CD8+ T cells), crypt hyperplasia, and villous atrophy.
- ▶ Lamina propria: lymphocytes, plasma cells, eosinophils.....
- ▶ IEL & villous atrophy are not pathognomonic, seen in viral enteritis.

- ▶ **Diagnosis:** Clinical, histologic and serologic correlation.





webpathology

Clinical Features

- ▶ **Children 6-24 months : classical or non classical symptoms**
- ▶ **Classical:** Irritability, abdominal distention, anorexia, diarrhea, failure to thrive, weight loss, or muscle wasting
- ▶ **Non-classical:** abdominal pain, nausea, vomiting, bloating, or constipation.
- ▶ **Blistering skin lesion, dermatitis herpetiformis, in 10% of Pnts.**

Dermatitis herpetiformis.



Clinical Features

- ▶ **Adults (30-60 years)**
- ▶ **Anemia: iron deficiency**
- ▶ **B12 and folate deficiency: less common.**
- ▶ **Diarrhea , bloating, and fatigue.**
- ▶ **Missed diagnosis: Silent celiac or latent celiac.**

- ▶ **Increased risk of enteropathy associated T cell lymphoma & Small intestinal adenocarcinoma**

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.**

Lactase (Disaccharidase) Deficiency

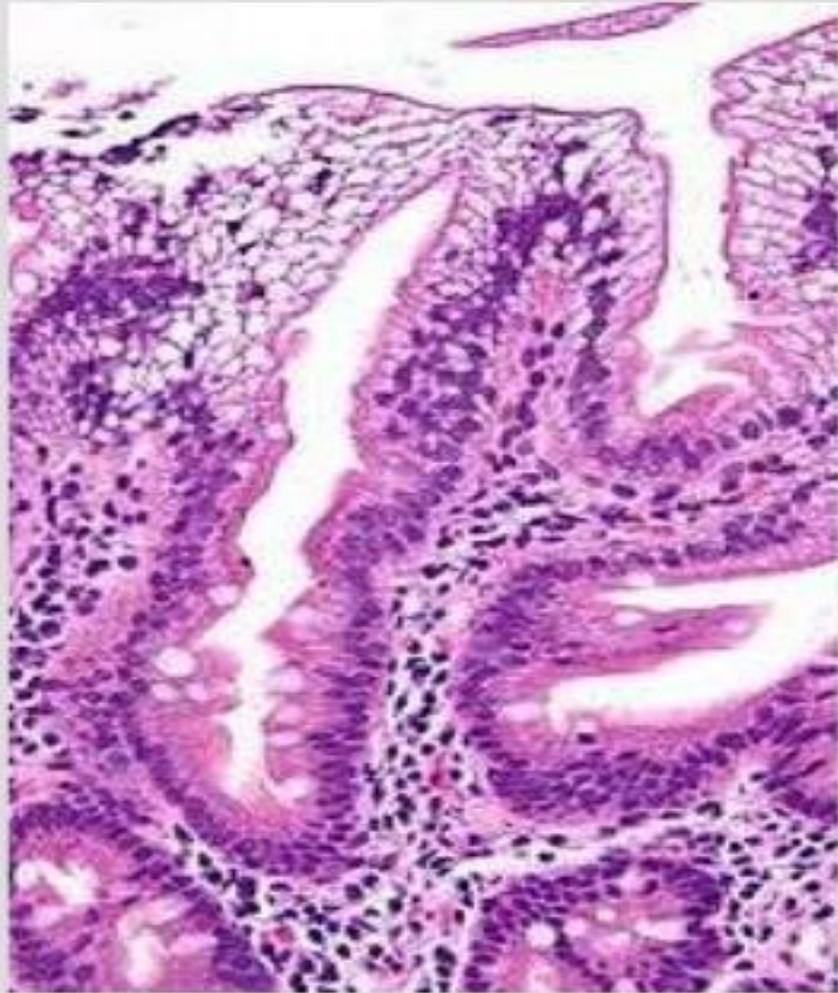
- ▶ Osmotic diarrhea
- ▶ Lactose remains in the gut lumen.
- ▶ Lactase found at apical brush border membrane
- ▶ Normal biopsy findings.
- ▶ Two types:
- ▶ ***Congenital*** : AR, genetic mutation, rare, explosive diarrhea, watery, frothy stools & abdominal distention, after milk ingestion
- ▶ ***Acquired*** : follow viral or bacterial enteritis, downregulation of gene, after childhood.

Abetalipoproteinemia

- ▶ **Beta apolipoproteins are very large apolipoproteins. They are critically important for the secretion and formation of chylomicrons (CMs) and VLDL.**
- ▶
- ▶ **Abnormalities that impede this process result in abetalipoproteinemia and hypobetalipoproteinemia**
- ▶ **Autosomal recessive, rare.**
- ▶ **The underlying defect is a mutation in the microsomal triglyceride transfer protein (MTP) responsible for lipoprotein and fatty acid export from mucosal cells.**

Abetalipoproteinemia

- ▶ Infants w/ failure to thrive, diarrhea, and steatorrhea
- ▶ Lack of absorption of fat and fat soluble vitamins
- ▶ Inability to secrete triglyceride-rich lipoproteins.
- ▶ Transepithelial transport defect of TG and FAs.
- ▶ Monoglycerides and triglycerides accumulate in epithelial cells.



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



Acanthocytosis is a hallmark feature of this disease.

Acanthocytes are abnormally spiked RBCs due to the defective phospholipid cell membrane.

They are also seen in liver dysfunction

The end

Good luck