



# Intestinal pathology, part 1

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# Diseases of the intestines

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



# Intestinal obstruction

## Mechanical obstruction:

Intussusception

Hernias.

Adhesions.

Volvulus

Tumors.

Diverticulitis

Infarction

## Non-mechanical obstruction

Hirschsprung disease

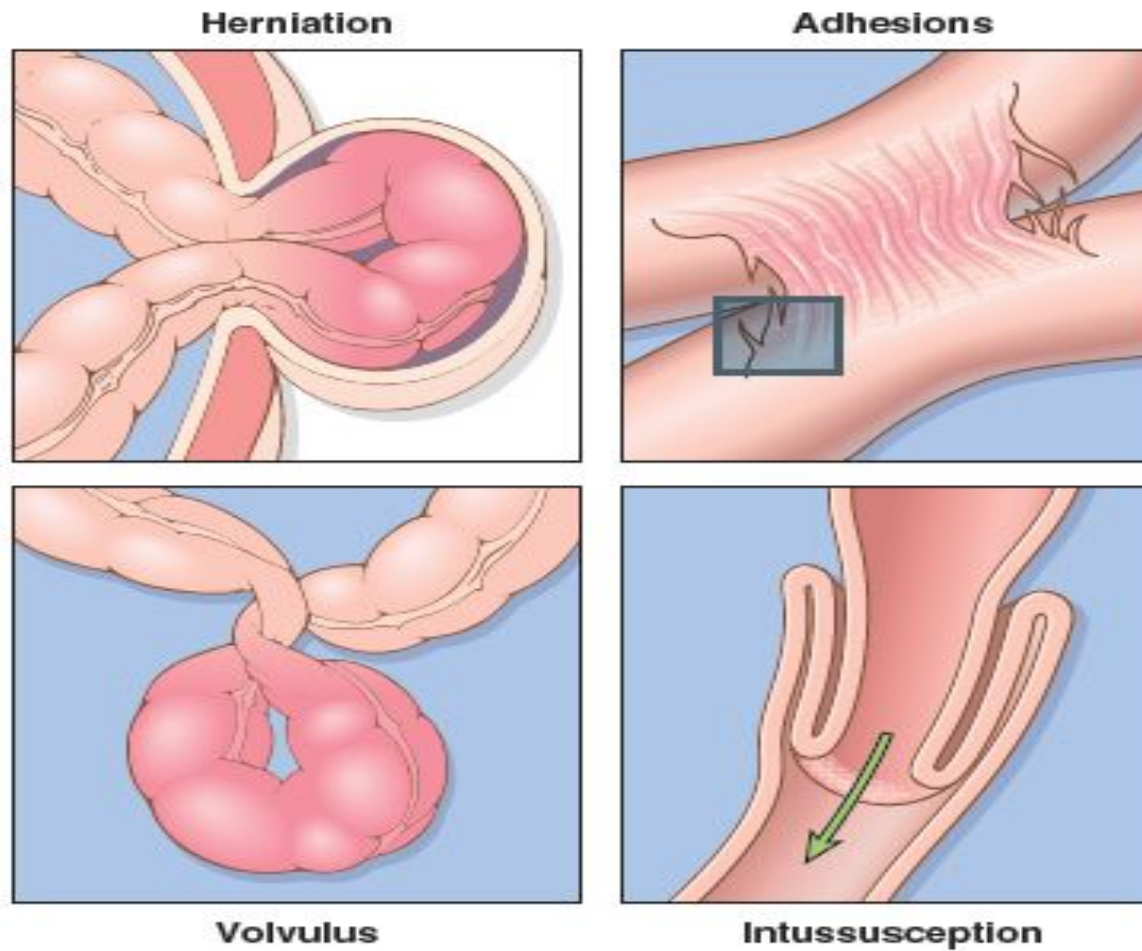
Neurological disorders.

Drugs....etc

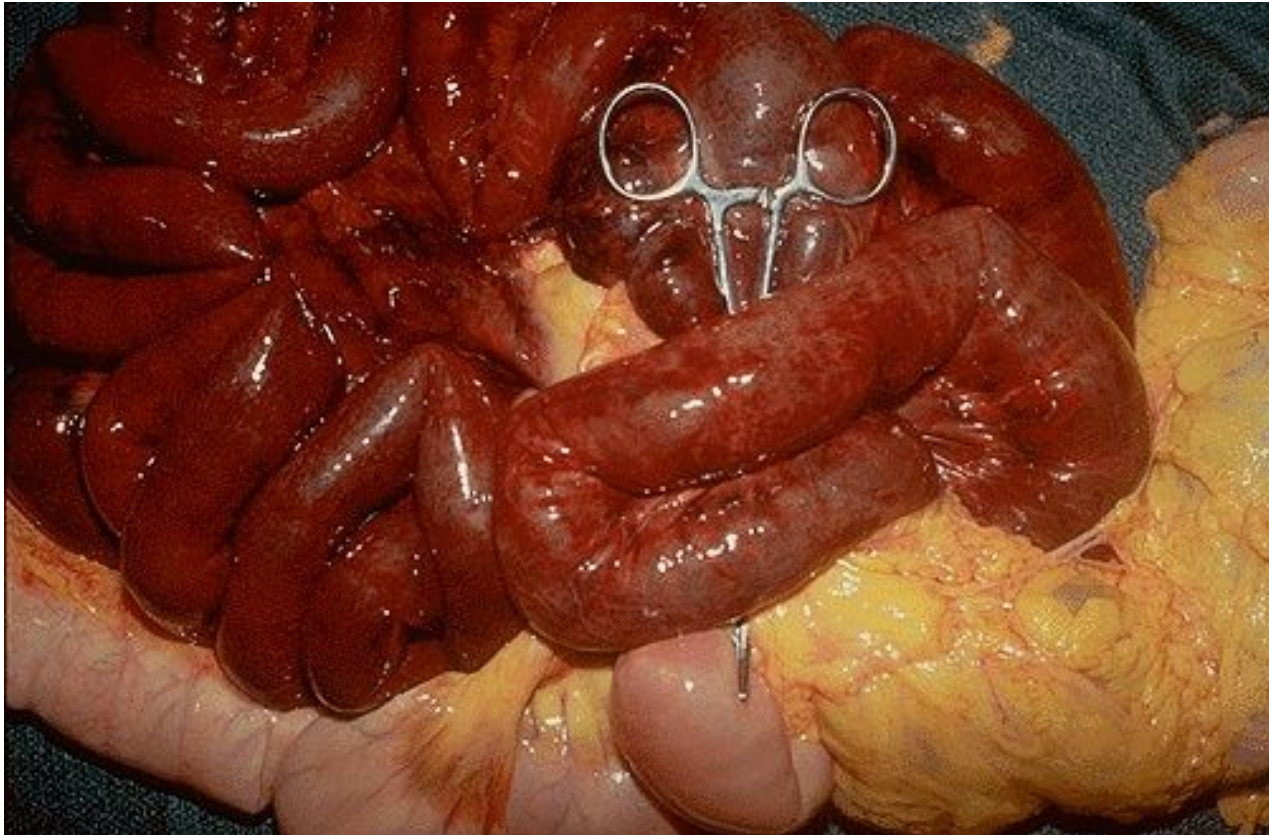
# Clinical picture of intestinal obstruction.

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

## 80% of mechanical obstructions



# Bowel 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.



# Causes of intussusception

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

# Clinical features:

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

# Management

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

# Meckel's diverticulum

- ▶ The most common congenital anomaly of the GI tract
- ▶ Incomplete obliteration of omphalomesenteric duct
- ▶ True diverticulum.
  
- ▶ **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).
- ▶ Most common cause of lower GI bleeding before age of 2.



# Meckel's diverticulum



# 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.

# 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
- ▶ Later: Obstructive constipation.



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

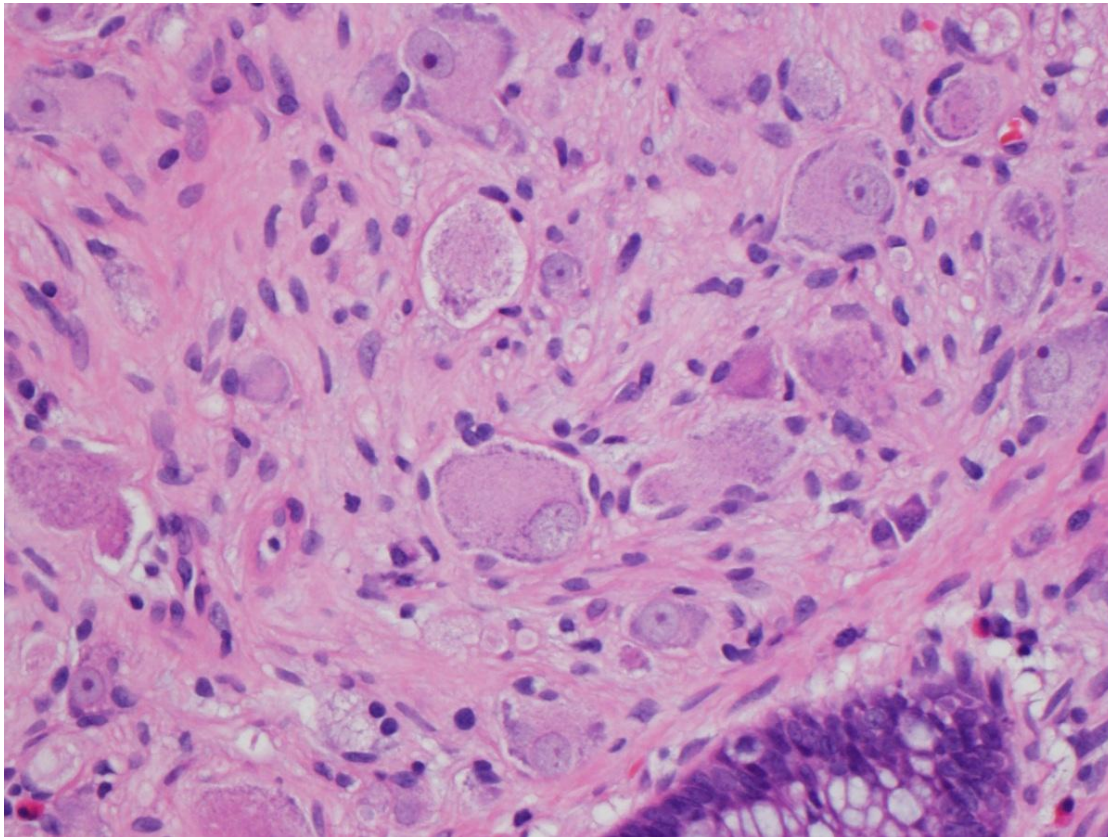
# Morphology

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



Robbins Basic Pathology 11th edition

# ganglion cells



<http://www.pathologyoutlines.com>

# 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**
- ▶ **Angiodysplasia.**
- ▶ **Hemorrhoids**



# Angiodysplasia.

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



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

▶ **Morphology:**

- ▶ Thin -walled, dilated, submucosal vessels beneath anal or rectal mucosa.

▶ **Symptoms:**

- ▶ Bleeding (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: painful , bloody, small volume diarrhea.
- ▶ Secretory, osmotic, malabsorptive, exudative.
- ▶ **Malabsorptive Diarrhea**
- ▶ Pancreatic insufficiency.
- ▶ Celiac disease
- ▶ Crohn disease
- ▶ Cystic Fibrosis
- ▶ Lactase (Disaccharidase) Deficiency
- ▶ Abetalipoproteinemia
- ▶ **Infectious Enterocolitis**
- ▶ **Ischemia.**
- ▶ **Inflammatory bowel diseases.....**

# Malabsorptive Diarrhea

- ▶ **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)

# Malabsorptive diarrhea

## Defect in one of the following:

- ▶ Intraluminal digestion.
- ▶ Terminal digestion.
- ▶ Transepithelial transport.
- ▶ Lymphatic transport.



# Manifestations:

- ▶ Weight loss, anorexia,
- ▶ Flatus, abdominal distention,
- ▶ Borborygmi (intestinal noise), 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

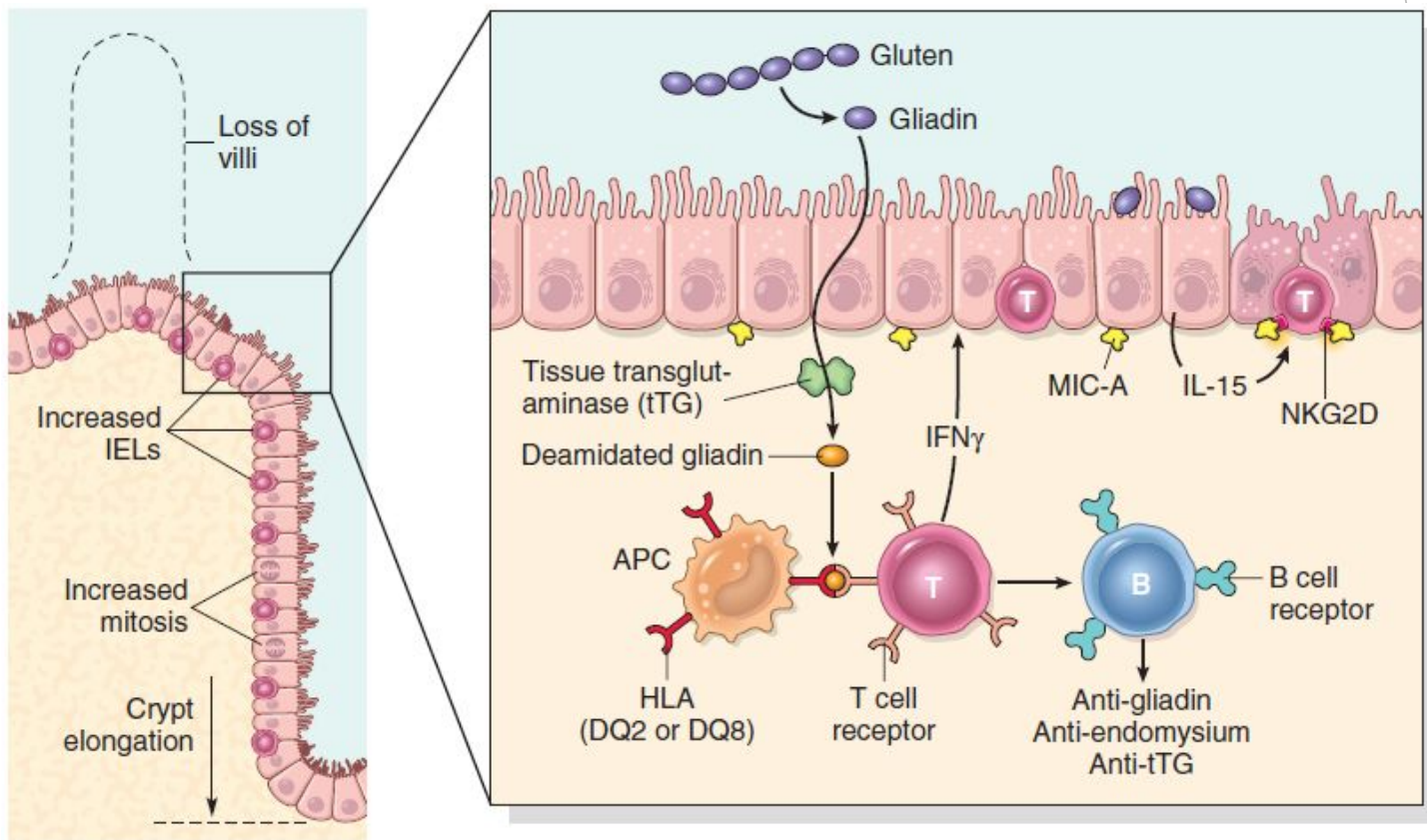
- ▶ Mutations in cystic fibrosis transmembrane conductance regulator (CFTR)
- ▶ Defects in ion transport across intestinal and pancreatic epithelium.
- ▶ Thick viscous secretions.
- ▶ Mucus plugs in pancreatic ducts >>> pancreatic insufficiency (80% of patients)
- ▶ Meconium ileus in neonates.
- ▶ Defect 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: type 1 diabetes, thyroiditis, and Sjogren syndrome

# Pathogenesis

- ▶ Gluten >>> gliadin >> deamidated by TTG >> react with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells >>> CD4+ T cells activation >>> cytokines >>> tissue damage >> B cell activation >> antibodies
- ▶ Serology:
  - ▶ Anti- tissue transglutaminase antibodies
  - ▶ Anti-gliadin antibodies.
  - ▶ Anti -endomysial antibodies



edition

Robbins Basic Pathology 10th

# 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.

# Normal intestine



**Normal**



**Celiac Disease**




UCLA

# 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.



- 
- ▶ Adults (30-60 years)
  - ▶ Anemia: iron deficiency
  - ▶ B12 and folate deficiency: less common.
  - ▶ Diarrhea , bloating, and fatigue.
  - ▶ Missed diagnosis: Silent celiac (positive serology and biopsy but asymptomatic).
  
  - ▶ Increased risk of enteropathy associated T cell lymphoma & Small intestinal adenocarcinoma.

# Diagnosis:

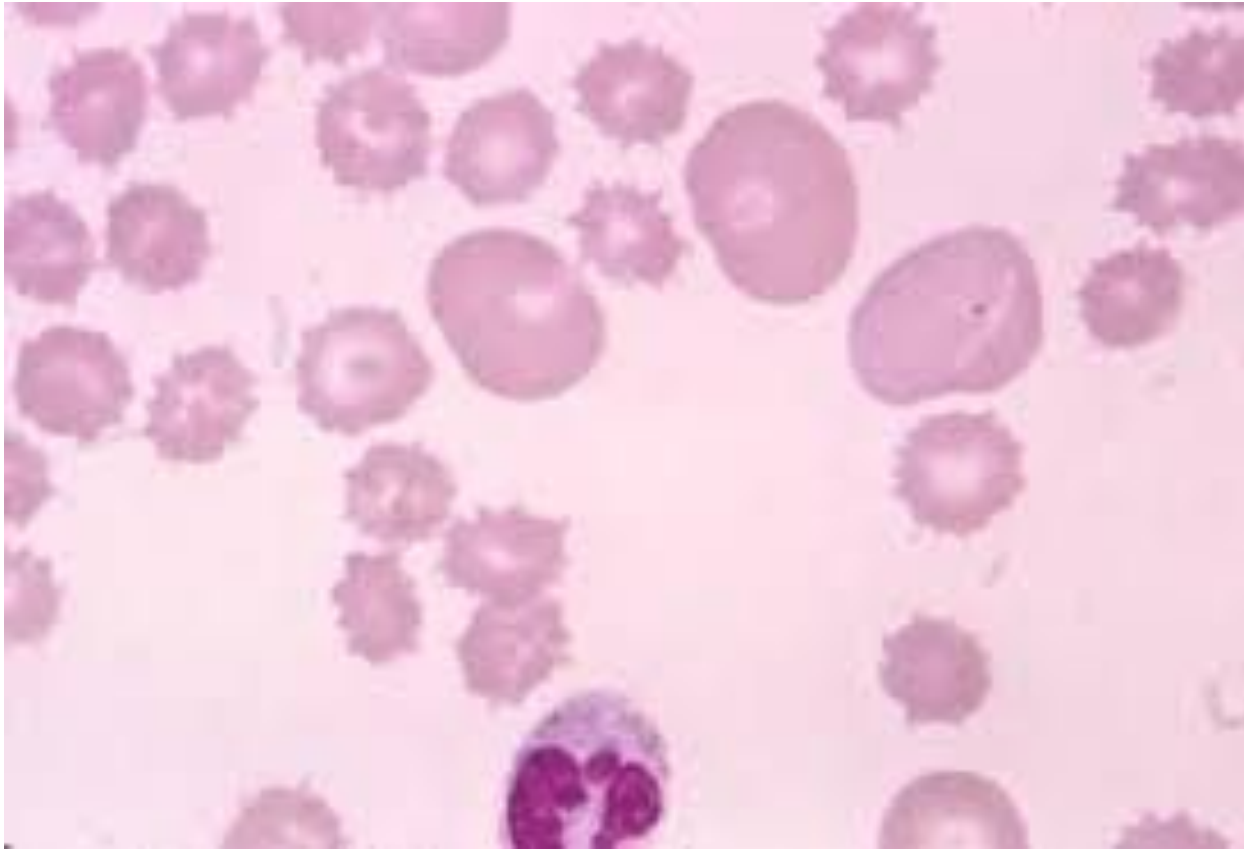
- ▶ **Non invasive serologic tests:**
- ▶ **Most sensitive:**
- ▶ Anti tissue transglutaminase antibody, IgA
- ▶ Anti deamidated gliadin antibodies, IgA & IgG
  
- ▶ **Most specific, but less sensitive**
- ▶ Antiendomysial antibody.
  
- ▶ **Invasive tests: small bowel biopsy.**

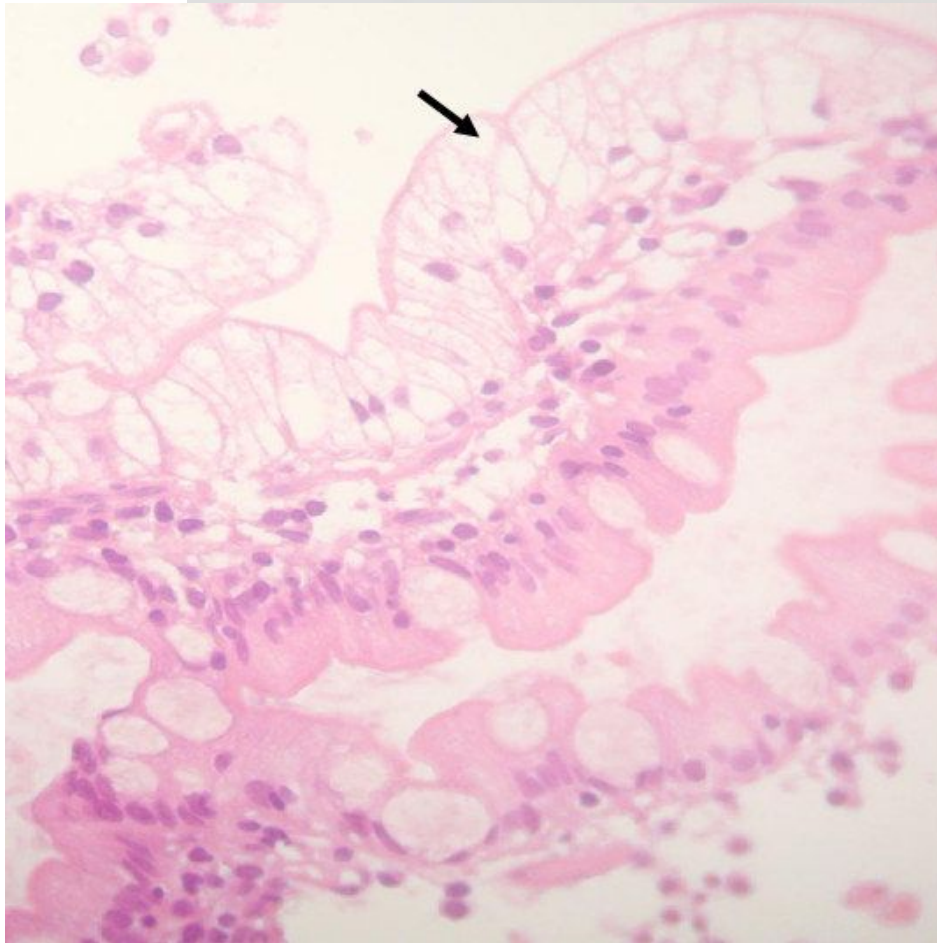
# Lactase (Disaccharidase) Deficiency

- ▶ 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*** : very common, downregulation of gene, after weaning. Affects 2/3 of world's population (50% of USA population).
  - ▶ **Transient**: caused by injury after infectious or inflammatory insults (reversible)

# Abetalipoproteinemia

- ▶ Autosomal recessive, rare.
- ▶ Inability of enterocytes to secrete triglyceride-rich chylomicrons.
- ▶ Lack of absorption (Transcellular transport defect of lipoproteins, FAs and fat-soluble vitamins).
- ▶ Infants' w/ failure to thrive, diarrhea, and steatorrhea
- ▶ Vitamin K deficiency, skeletal CNS and retinal abnormalities.
- ▶ Spur cells in peripheral blood.
- ▶ Monoglycerides and triglycerides accumulate in epithelial cells.





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