

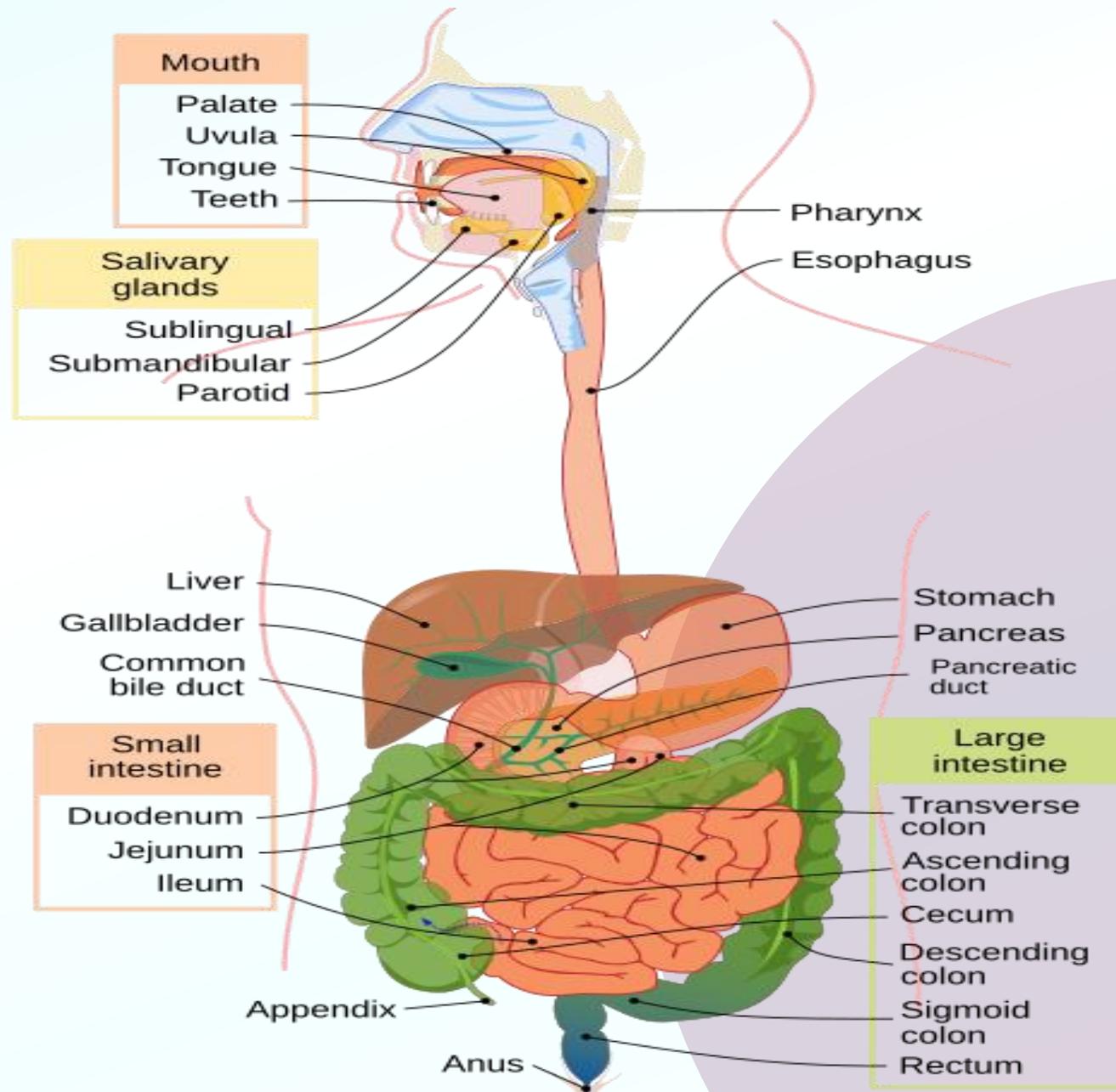


# **GASTRO-INTESTINAL SYSTEM**

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Histopathology specialist

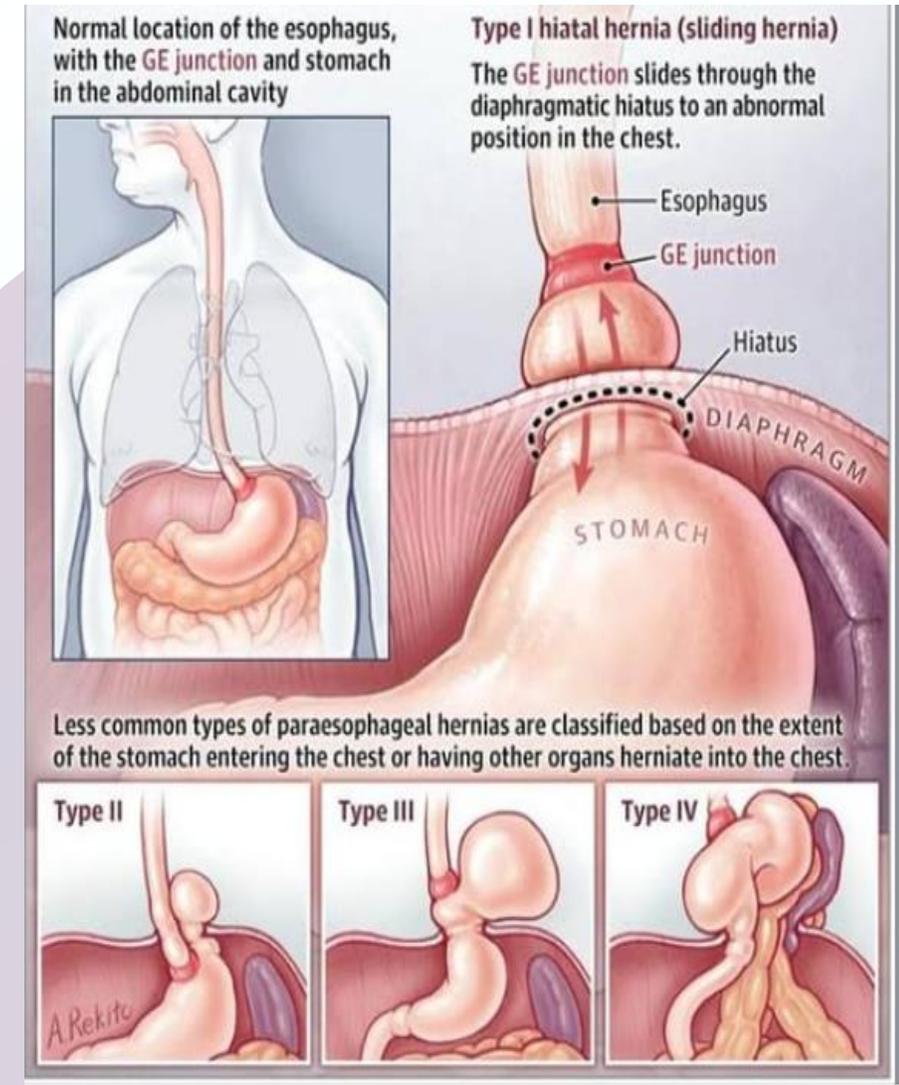
15.12.2025



# ESOPHAGUS

## # Hiatal hernia:

- **Definition:** abnormal protrusion of the upper part of the stomach through the diaphragm's hiatus.
- The region where the esophagus joins the stomach is called the "gastroesophageal junction" (GEJ).
- **Two types:**
  - 1) Sliding hernia
  - Paraesophageal hernia
- **Causes:**
  - 1) Congenital anatomical defects
  - 2) Increased intraabdominal pressure (as seen in obesity, pregnancy, and chronic coughing)
  - 3) Age-related changes in the diaphragm's muscle tone.
- **Clinically:**
  - 1) Heartburn
  - 2) Dysphagia



## # Infectious esophagitis:

- **Definition:** Inflammation of esophageal mucosa.
- **Causes:** Infections are more common in patients who are debilitated or immunosuppressed and may be caused by herpes simplex virus, cytomegalovirus (CMV), or fungal organisms.
- **Among fungi, candidiasis is most common**

## # Reflux esophagitis:

- **Definition:** Reflux of gastric contents into the lower esophagus.
- Lower esophageal sphincter (LES) is a circular muscle layer at the distal esophagus that creates a higher pressure than the intra-abdominal pressure
- **Causes:** Inappropriate relaxation of the LES, following abrupt increases in intra-abdominal pressure, e.g., after coughing, straining, or bending/ Other conditions that are associated with GERD include alcohol and tobacco use, obesity, central nervous system depressants, pregnancy, hiatal hernia.
- **Clinically:** heartburn, dysphagia, and regurgitation of sour-tasting gastric contents, most often postprandially

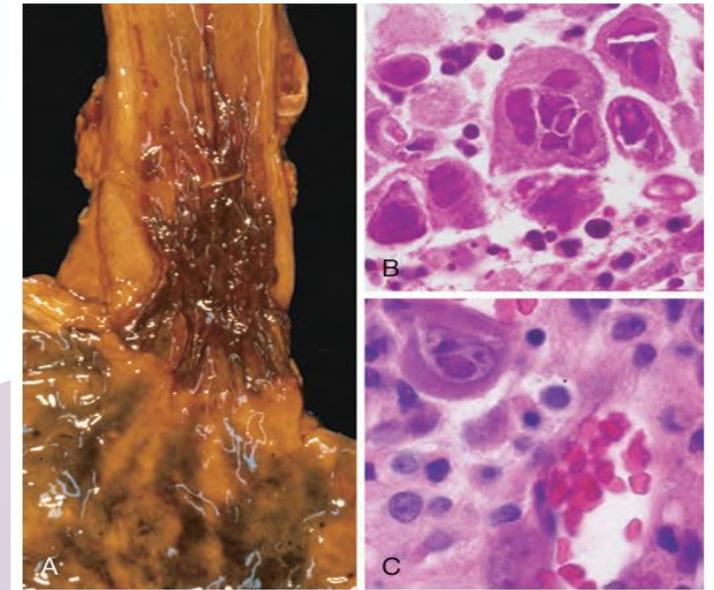
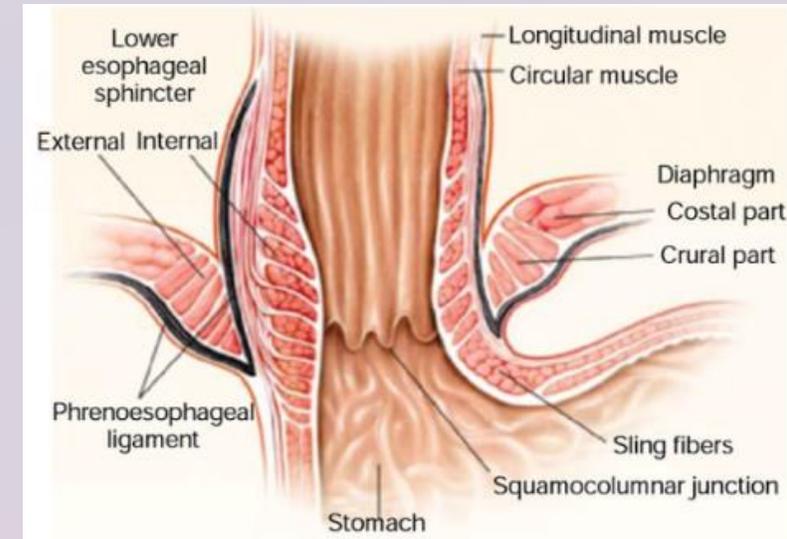


Figure 17.4 Viral esophagitis. (A) Postmortem specimen with multiple, overlapping herpetic ulcers in the distal esophagus. (B) Multinucleate squamous cells containing herpesvirus nuclear inclusions. (C) Cytomegalovirus-infected endothelial cells with nuclear and cytoplasmic inclusions.



## # Barrett esophagus:

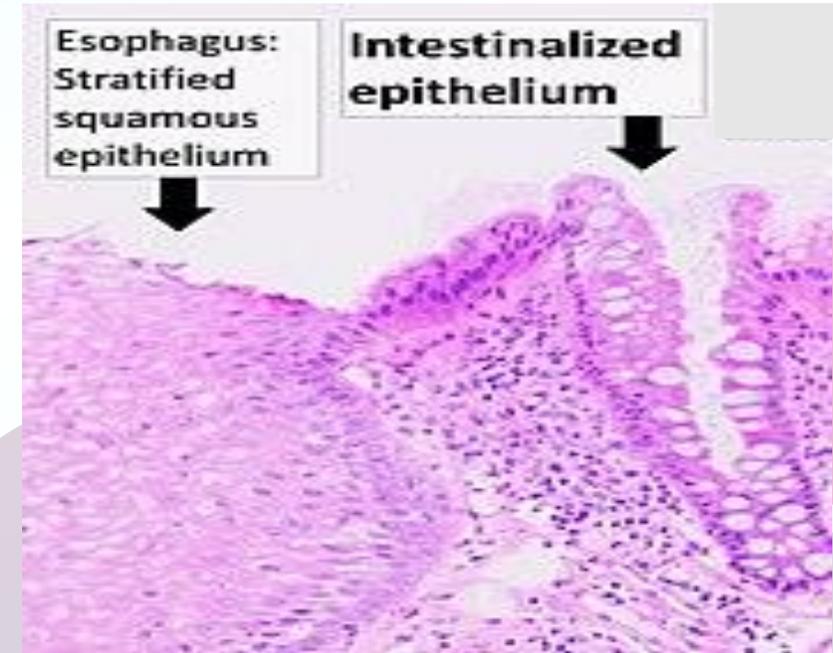
- Is a complication of chronic GERD.
- Morphology: characterized by metaplastic change in esophageal lining in which the normal squamous epithelium change into columnar (intestinal) epithelium.
- It is associated with an increased risk of cancer (adenocarcinoma)

## # Adenocarcinoma:

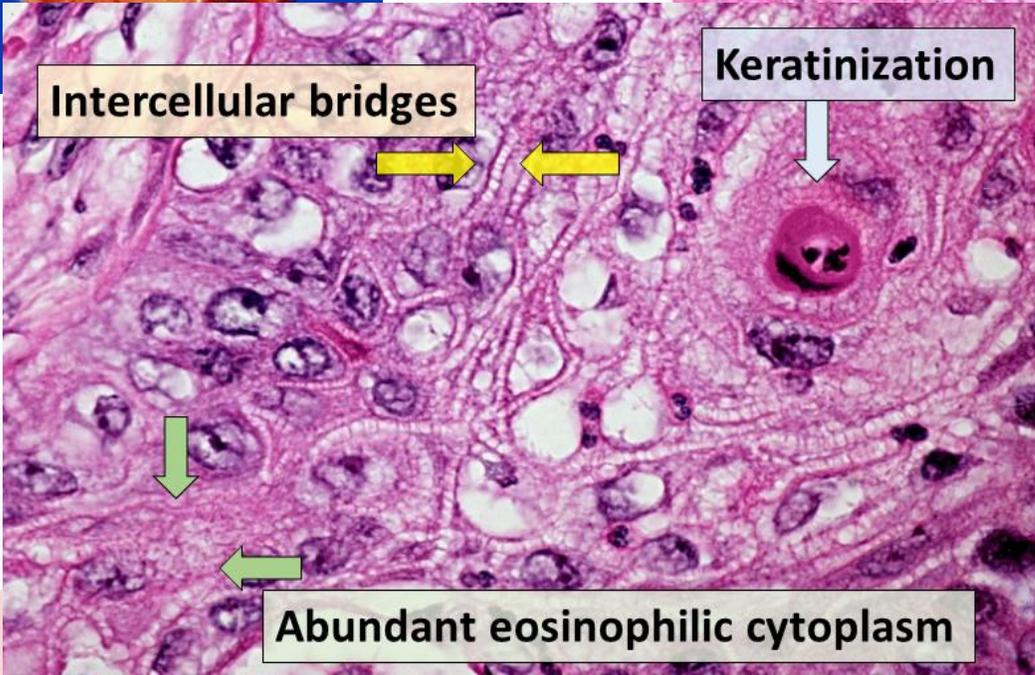
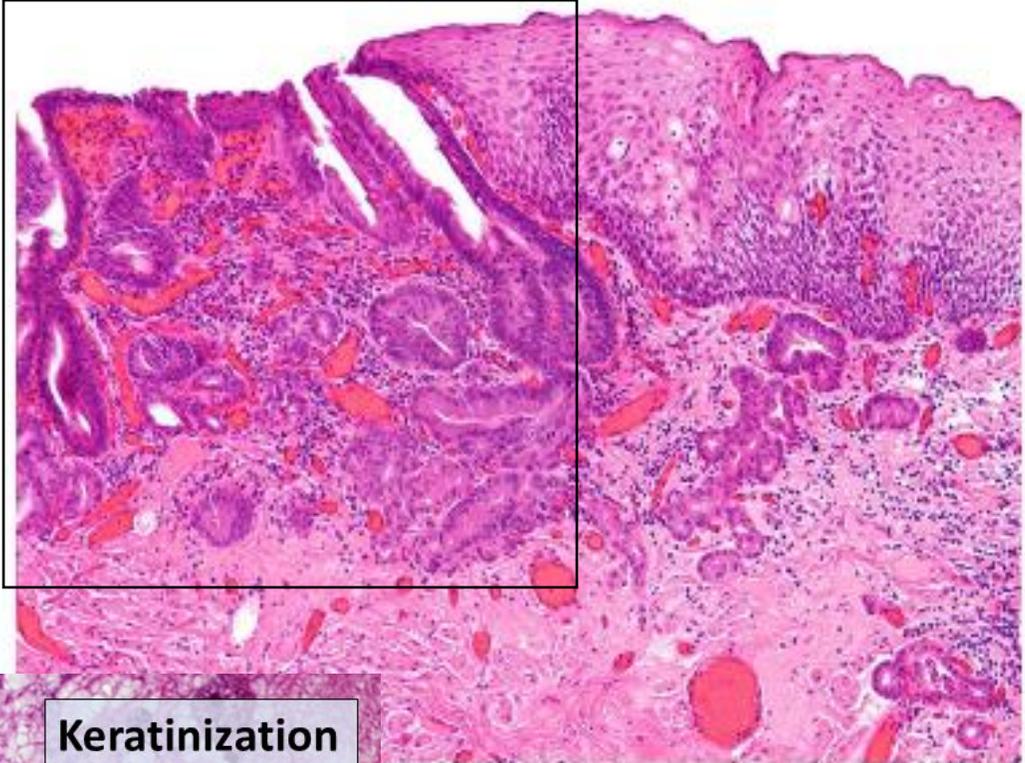
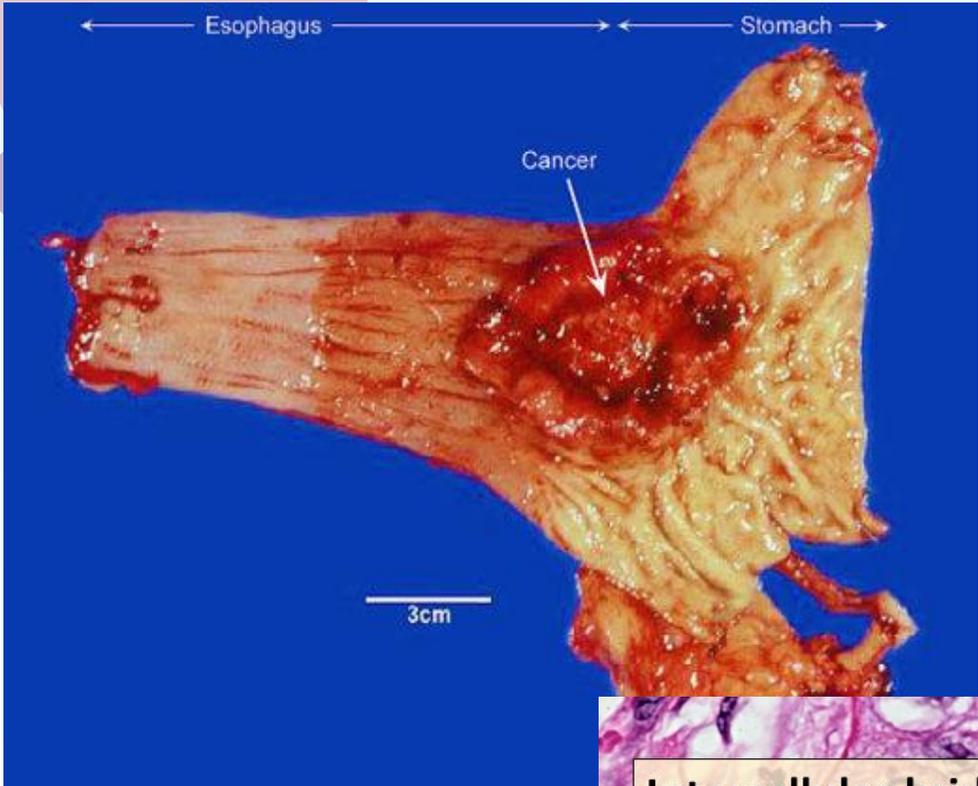
- Risk factors: Barrett esophagus and long-standing GERD/ obesity/ tobacco smoking
- Site: almost all cases occur in the lower third of the esophagus and esophagogastric junction
- Morphology: Microscopically, tumors typically produce mucin and form glands, with intestinal-type morphology.

## # Squamous cell carcinoma:

- More common than adenocarcinoma worldwide.
- Risk factors: Tobacco smoking/ alcohol
- Site: half of squamous cell carcinomas occur in the middle third of the esophagus

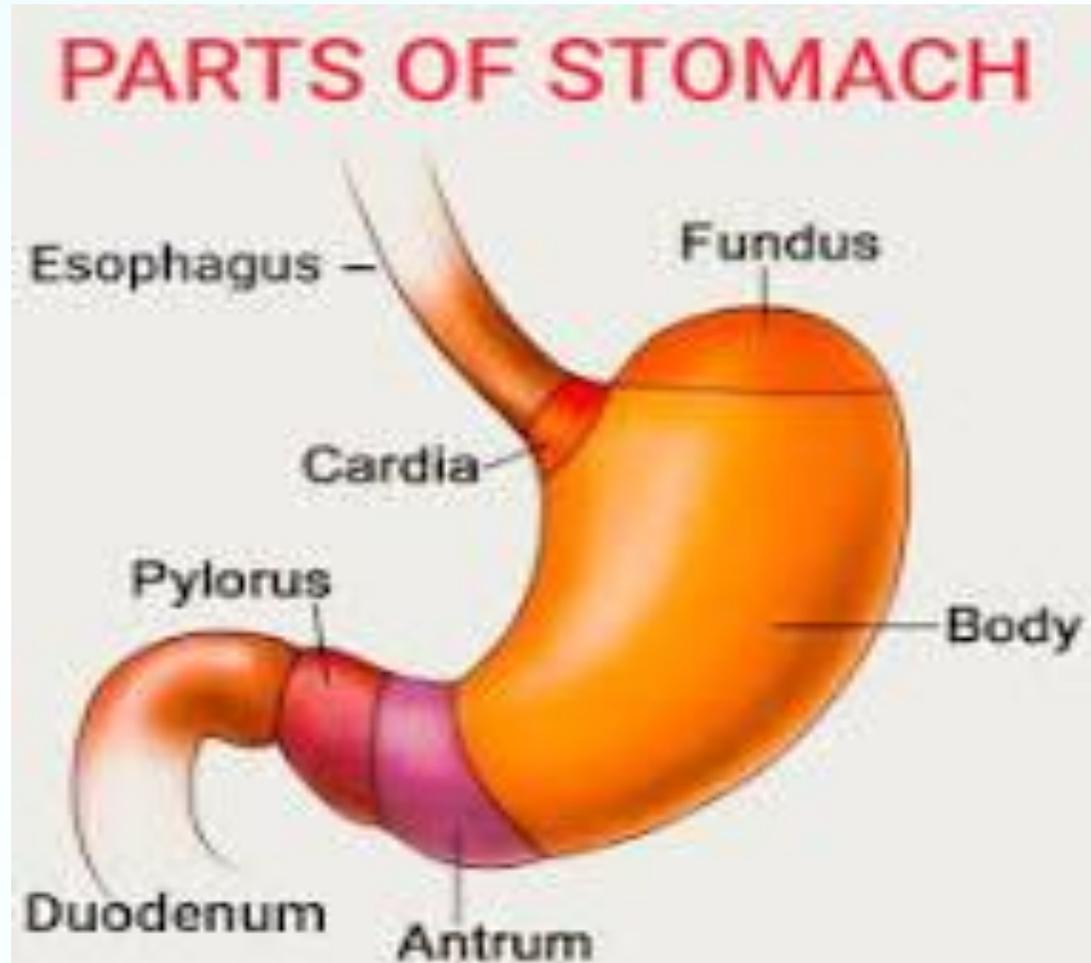


# Adenocarcinoma



Squamous cell carcinoma

# Stomach

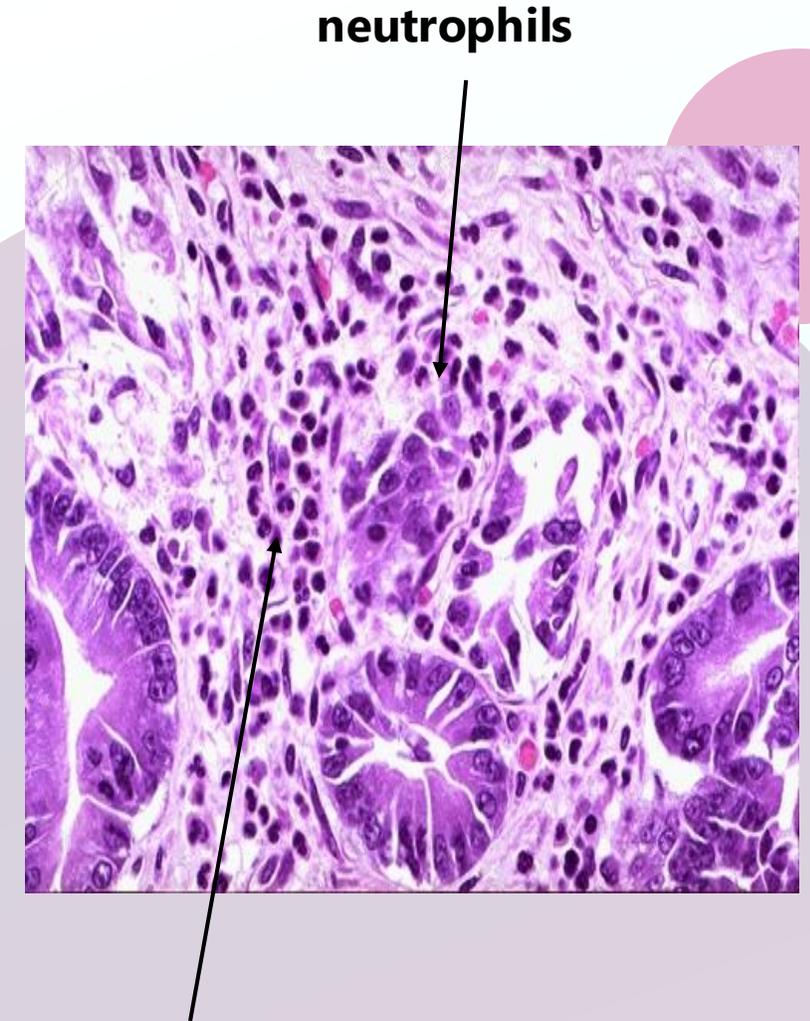


## CELLS AND THEIR SECRETIONS

Parietal (Oxyntic) cells	<ul style="list-style-type: none"><li>• <b>Secrete acid</b> (from the proton pump, <math>H^+K^+</math> ATPase)</li><li>• <b>Secrete intrinsic factor</b> (required for vitamin <math>B_{12}</math> absorption)</li></ul>
Chief (Zymogenic) cells	<ul style="list-style-type: none"><li>• Secrete the <b>proenzymes pepsinogen I and II</b> (activated to pepsin)</li></ul>
Endocrine cells	<ul style="list-style-type: none"><li>• Secrete <b>gastrin in antrum</b> (by G cells), <b>histamine</b> in the body</li></ul>
Foveolar cells	<ul style="list-style-type: none"><li>• Secrete <b>mucin layer</b> over the mucosal cells</li></ul>

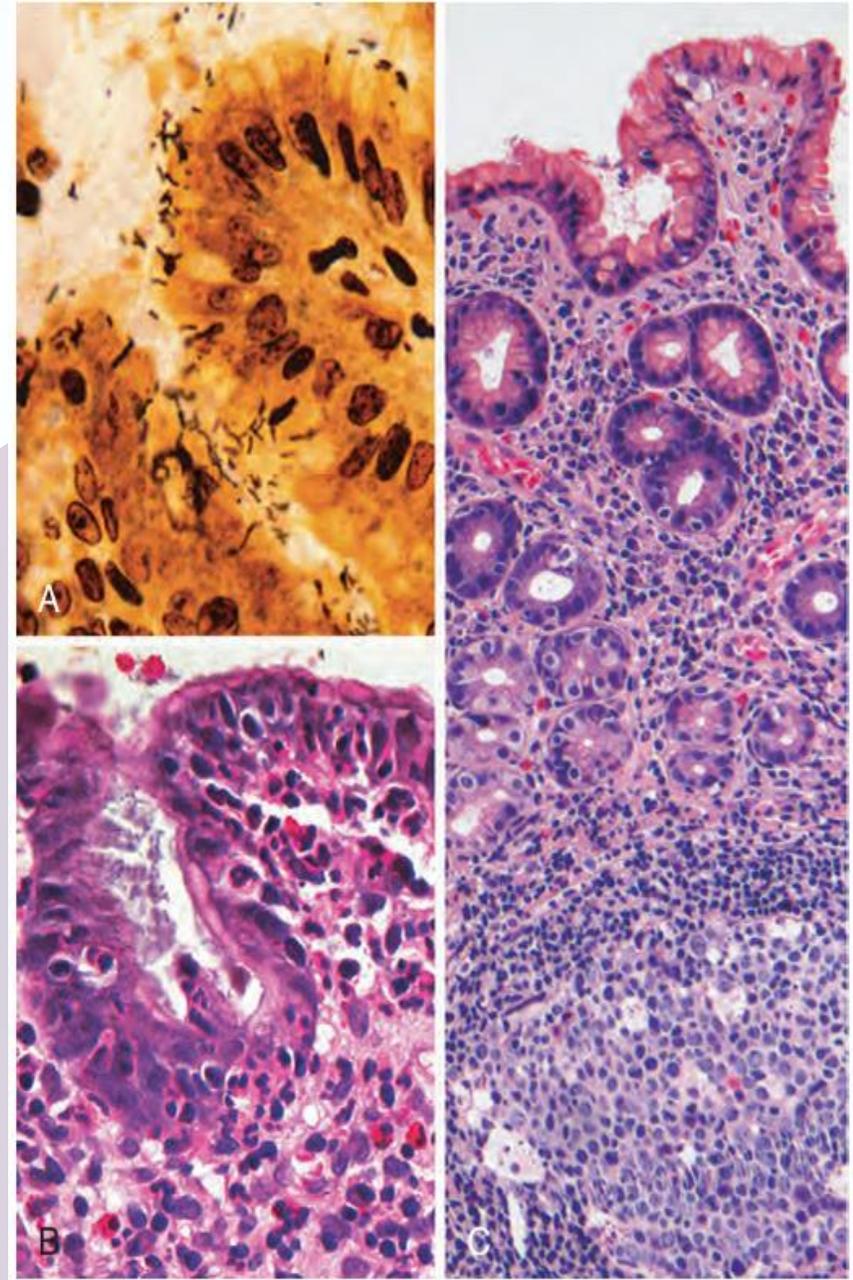
## # Gastritis:

- Definition: Inflammation of gastric mucosa. Can be acute or chronic.
- ❖ Risk factors for acute gastritis: heavy smoking/ alcohol/ excessive use of NSAIDS especially aspirin/ ischemia and shock/ stress (burn, surgery)/ Partial gastrectomy.
- Characterized by: presence of neutrophils in lamina propria and gastric glands (on gastric biopsy)
- ❖ Risk factors for chronic gastritis: chronic infection with H.Pylori/ Autoimmune cause (pernicious anemia)/ alcohol and smoking/ antrectomy.



❖ Chronic gastritis associated with H.Pylori microorganism:

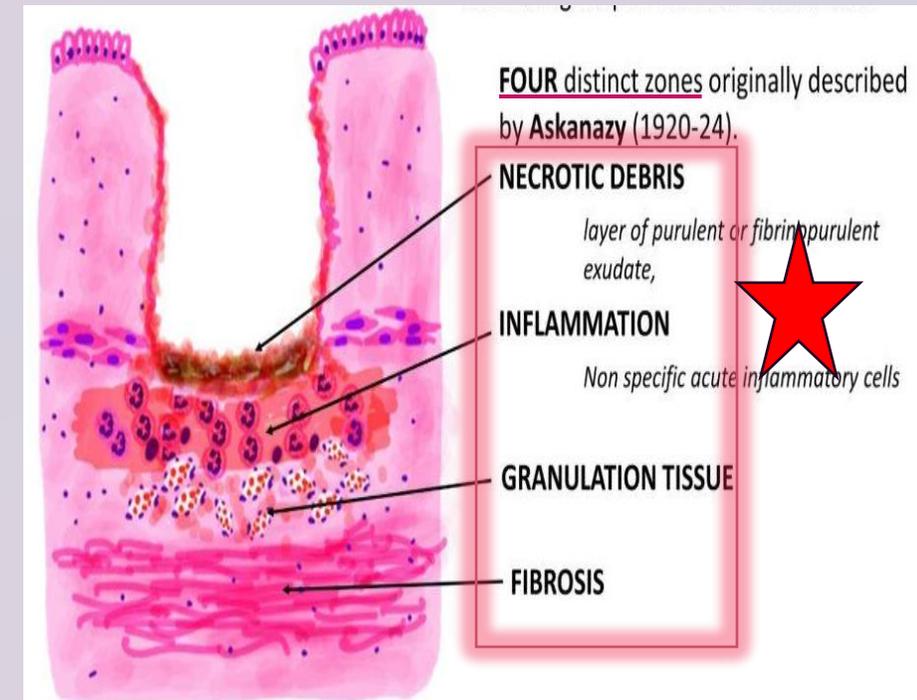
- It's a Gram negative bacteria producing (Urease, Adhesins, and Toxins), destroying the mucosa.
- Located in antrum.
- Morphology: Lymphoid aggregates with or without germinal centers and abundant plasma cells within the superficial lamina propria/ and Intraepithelial neutrophils.
- Investigations:
  - 1) histologic identification of the organism,
  - 2) serology for antibodies to H. pylori,
  - 3) fecal bacterial detection,
  - 4) the urea breath test, which is positive due to ammonia produced by the bacterial urease.
  - 5) polymerase chain reaction (PCR)-based detection of H. pylori DNA.



## # Peptic Ulcer Disease:

- **Definition:** chronic mucosal ulceration (breach in the mucosa), involving submucosa or deeper layers.
- **Site:** Most common in Duodenum (first part)/ then Stomach ( lesser curvature near the junction between body and antrum)
- **Risk factors:** almost always associated with *H. pylori* infection, NSAIDs, or cigarette smoking.
- **Pathogenesis:** imbalance between protective factors and damaging factors.
- **Symptoms:**
  - 1) Epigastric burning
  - 2) Pain worse at night, within 1-3 hours after meals
  - 3) Pain may decrease with food / alkali
  - 4) Perforation associated with pain in back, left upper quadrant, chest
- Heals in 15 years without treatment versus weeks with treatment
- **Complications:** perforation, hemorrhage, obstruction, Malignancy.

Damaging factors	Protective factors
• Gastric acid	• Mucus and bicarbonate secretion
• Pepsin	• Mucosal blood flow
• Smoking, alcohol	• Prostaglandin production
• Drugs like NSAIDs	• Epithelial regenerative capacity
• <i>H. pylori</i>	
• Ischemia and shock	
• Delayed gastric emptying	
• Duodenal gastric reflux or gastric hyperacidity	



## # Gastric polyps:

- Definition: nodules or masses that project above the level of the surrounding mucosa, are identified in up to 5% of upper GI endoscopies.
- Polyps may develop as a result of epithelial or stromal cell hyperplasia, inflammation, ectopia, or neoplasia.

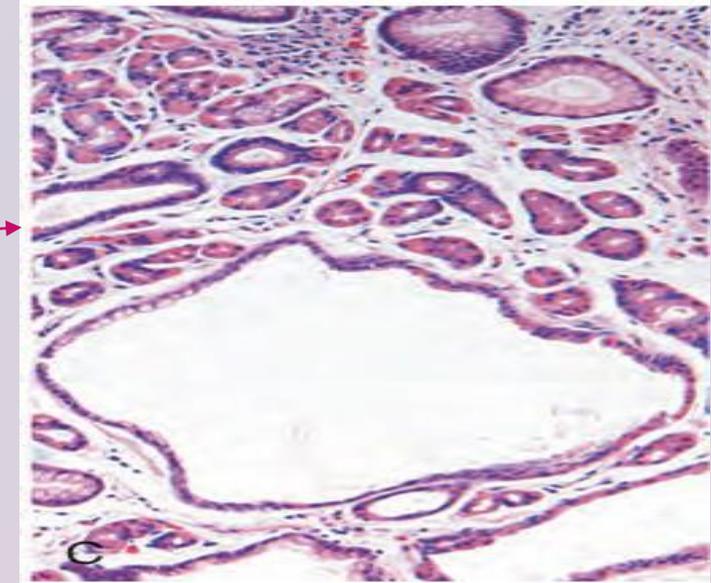
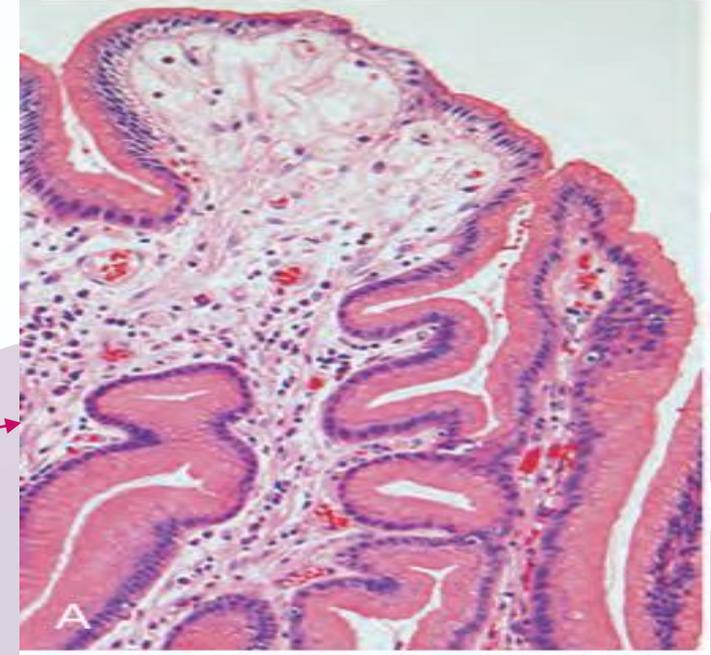
### ❖ The most common types:

#### 1) Inflammatory and hyperplastic polyps:

- **Up to 75% of all gastric polyps**
- between 50 and 60 years of age and usually develop in association with chronic gastritis.
- The risk of dysplasia in inflammatory polyps ranges from 1% to 20% .

#### 2) fundic gland polyps:

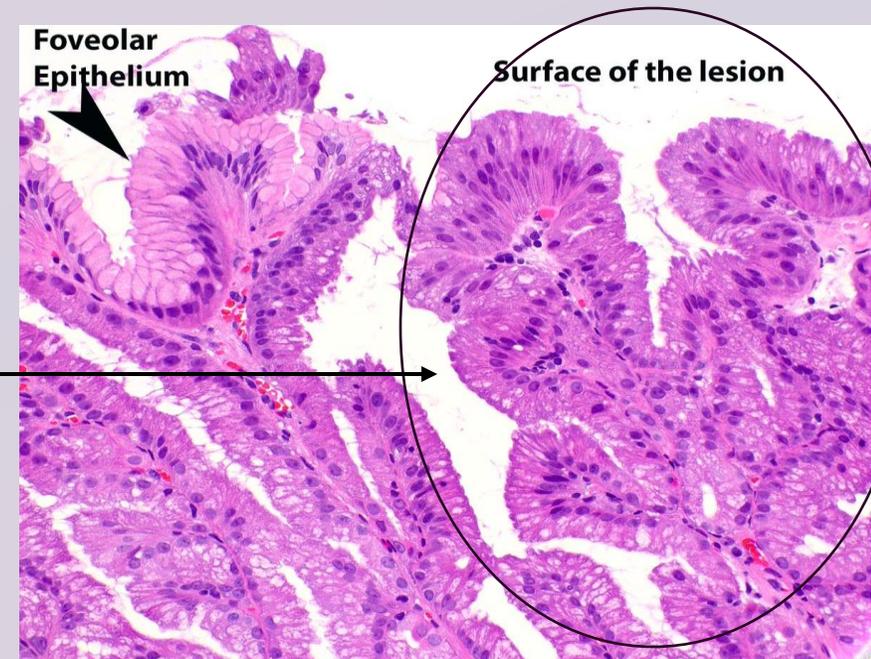
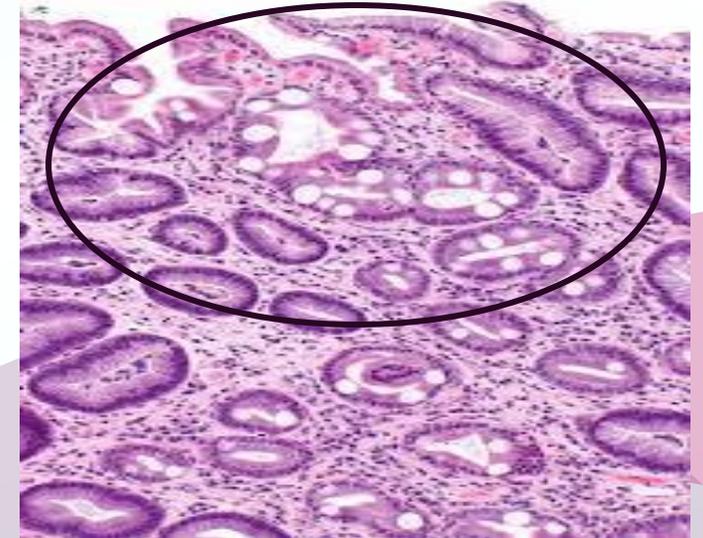
- **germline mutations in the APC gene** (the cause of familial adenomatous polyposis) or the DNA repair gene MUTYH
- **Associated with increased use of proton pump inhibitors**



### 3) Gastric adenoma:

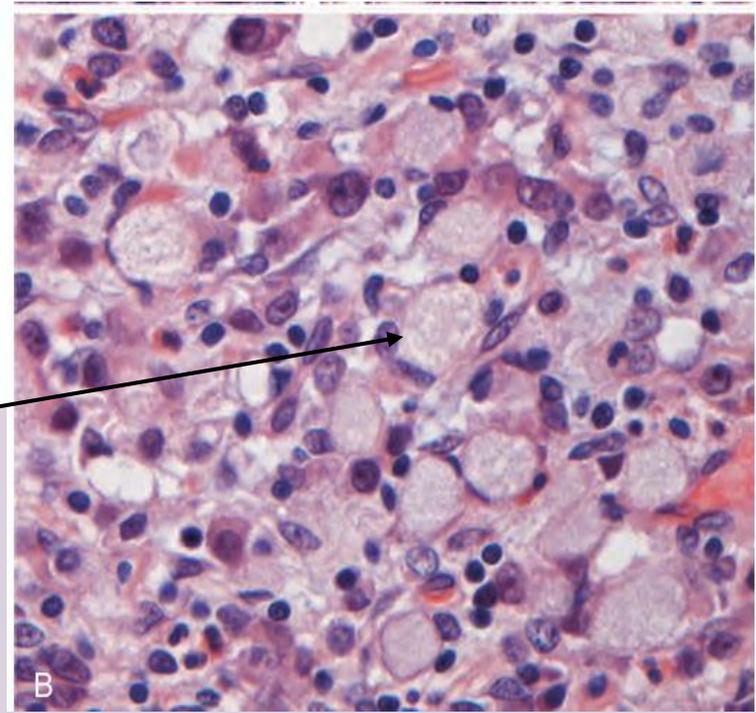
- develop in a background of chronic gastritis with atrophy and intestinal metaplasia.
- Patients are usually between 50 and 60 years of age, and males are affected three times more often than females.
- The risk of adenocarcinoma within gastric adenomas correlates with size and is particularly elevated in lesions greater than 2 cm in diameter.
- Morphology: All adenomas exhibit dysplasia, which is classified as low- or high-grade. Both grades of dysplasia are characterized by nuclear enlargement, elongation, pseudostratification, and hyperchromasia.

**Intestinal metaplasia**



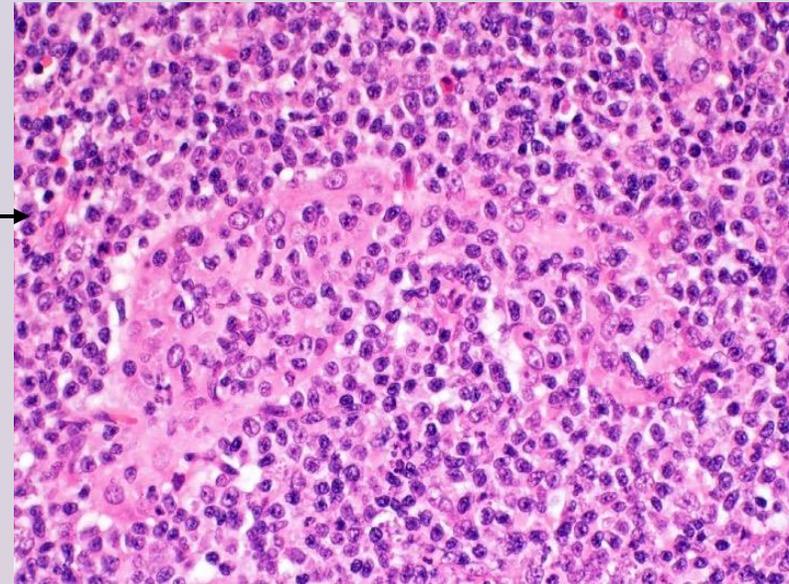
## # Gastric Adenocarcinoma:

- Adenocarcinoma is the most common malignancy of the stomach, comprising more than 90% of all gastric cancers.
- Classification:
  - 1) Intestinal type: form bulky masses, and composed of neoplastic glands (intestinal like glands)
  - 2) diffuse type: infiltrates and thickens the gastric wall, typically composed of signet-ring cells
- Early symptoms of both types of gastric adenocarcinoma resemble those of chronic gastritis and peptic ulcer disease, including dyspepsia, dysphagia, and nausea. As a result, these tumors are often discovered at advanced stages, when symptoms such as weight loss, anorexia, early satiety (primarily in diffuse cancers), anemia, and hemorrhage appear



## # Gastric Lymphoma:

- The most common site of extranodal lymphoma is the GI tract particularly the stomach.
- The most common type is Extranodal marginal zone B-cell lymphomas (referred to as lymphomas of MALT, or MALToma's)
- MALT (Mucosa Associated Lymphoid Tissue) is not present in the normal stomach but can be induced, typically as a result of chronic gastritis. H. pylori infection is the most common inducer of gastric MALT and therefore is found in association with most gastric MALToma's.



# Intestine

## # Infectious Diseases:

- Enterocolitis can present with a broad range of symptoms including diarrhea, abdominal pain, urgency, perianal discomfort, incontinence, and hemorrhage
- Bacterial infections, such as enterotoxigenic E. coli and Salmonella spp., are frequently responsible for acute diarrheal illnesses.
- Rotavirus and adenovirus are common causes of death in children under 5 years of age.

## The most important types:

### 1) Cholera:

- Vibrio cholerae are comma-shaped, gram-negative bacteria.
- **It is primarily transmitted by drinking contaminated water** and may cause epidemics in areas where disasters such as earthquakes or war have destroyed sewage systems with resultant fecal contamination of drinking water supplies.
- Pathogenesis: Severe diarrhea is caused by the toxin released by the bacteria.
- **The rate of diarrhea may reach 1 L per hour, leading to dehydration, hypotension,** muscular cramping, shock, loss of consciousness, and death.

### 2) Campylobacter Enterocolitis

- Campylobacter jejuni is the most common bacterial enteric pathogen in high income countries and is an important **cause of traveler's diarrhea** and food poisoning.
- Infections are most often **associated with ingestion of improperly cooked chicken, unpasteurized milk and contaminated water**
- **Watery diarrhea is the primary symptom,** but dysentery develops in 15% of adults and more than 50% of children

### 3) Salmonella:

- the causative agent *Salmonella enteritidis*.
- The latter are the most common cause of salmonellosis,
- **Salmonella is transmitted via contaminated food, particularly raw or undercooked meat, poultry, eggs, and milk**
- Symptoms range from loose stools to cholera-like profuse diarrhea to dysentery. Fever often resolves within 2 days, but diarrhea can persist for a week, and organisms can be shed in the stool for several weeks after resolution.
- **Antibiotic therapy is not generally recommended** because it can prolong the carrier state or even cause relapse and does not typically shorten the duration of diarrhea.

### 4) Viral Gastroenteritis:

- ❖ Rotavirus: This encapsulated virus with a segmented, is highly prevalent and a significant cause of diarrheal deaths worldwide.
- Children between 6 and 24 months of age are most vulnerable, probably because antibodies in breast milk confer protection during the first 6 months of life.
- **Rotavirus outbreaks in hospitals and daycare centers are common,**
- ❖ Adenovirus. A common cause of pediatric diarrhea, adeno virus also affects immunocompromised patients

## # Irritable Bowel syndrome:

- Characterized by chronic, relapsing abdominal pain, bloating, and changes in bowel habits.
- Despite very real symptoms, **the endoscopic and microscopic evaluations are normal in IBS patients.**
- **IBS is currently divided into diarrhea-predominant, constipation-predominant, and mixed subtypes.**
- The peak prevalence of IBS is between 20 and 40 years of age, and **there is a significant female predominance**
- IBS is presently diagnosed using clinical criteria that require **the occurrence of abdominal pain or discomfort at least 3 days per month over 3 months with improvement following defecation and a change in stool frequency or form.**
- Other causes, such as enteric infection or inflammatory bowel disease, must be excluded.

### IRRITABLE BOWEL SYNDROME (IBS)

#### Symptoms



Abdominal Pain



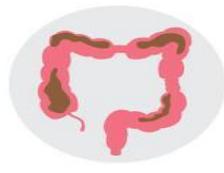
Diarrhea



Cramping



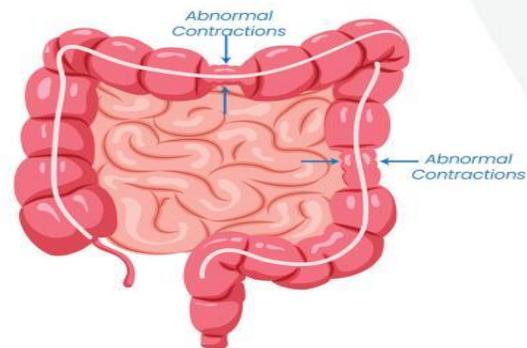
Mucus In Poop



Constipation



Bloating And Gas



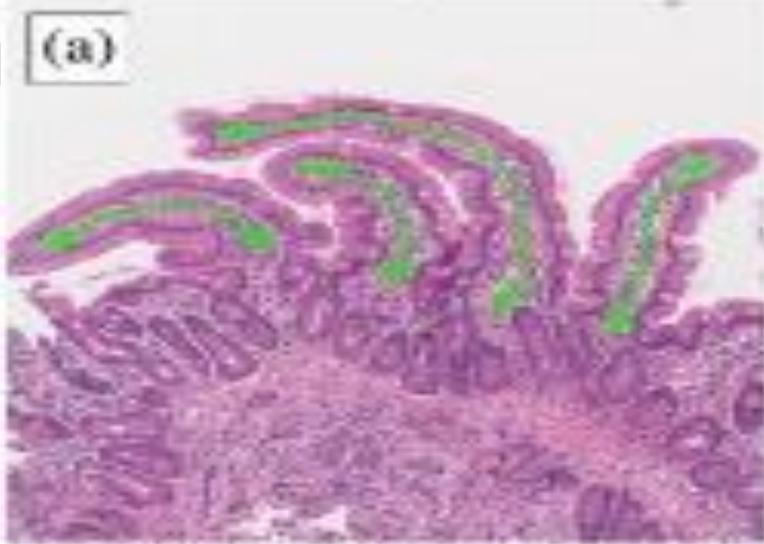
LARGE INTESTINE



## # Celiac disease:

- known as celiac sprue or gluten sensitive enteropathy
- **An immune-mediated disorder triggered by the ingestion of gluten-containing foods such as wheat, rye, or barley in genetically predisposed individuals.**
- **Biopsy specimens from the second portion of the duodenum or proximal jejunum, which are exposed to the highest concentrations of dietary gluten, are generally diagnostic in celiac disease.**
- **The histopathology is characterized by increased numbers of intraepithelial CD8+ T lymphocytes (intraepithelial lymphocytosis), crypt hyperplasia, and villous atrophy**
- Symptoms in adult: chronic diarrhea, bloating, or chronic fatigue, but can also be asymptomatic/ may present with anemia due to chronic iron and vitamin malabsorption./ Dermatitis herpetiformis (itchy, blistering skin lesion),
- Symptoms in children: typically begins after introduction of gluten to the diet, between 6 and 24 months of age, and manifests as irritability, abdominal distention, anorexia, chronic diarrhea, failure to thrive, weight loss, or muscle wasting
- Investigations other than biopsy:
  - 1) measurement of IgA antibodies against tissue transglutaminase.
  - 2) IgA anti endomysial antibodies.
  - 3) IgG anti-tissue transglutaminase antibodies may be detected in patients with IgA deficiency
- **The only treatment currently available for celiac disease is a gluten-free diet.**

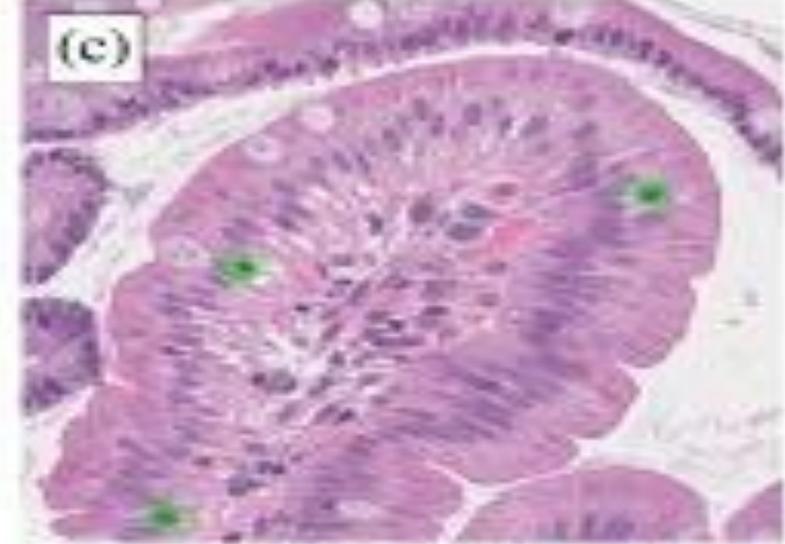
**Healthy villi**



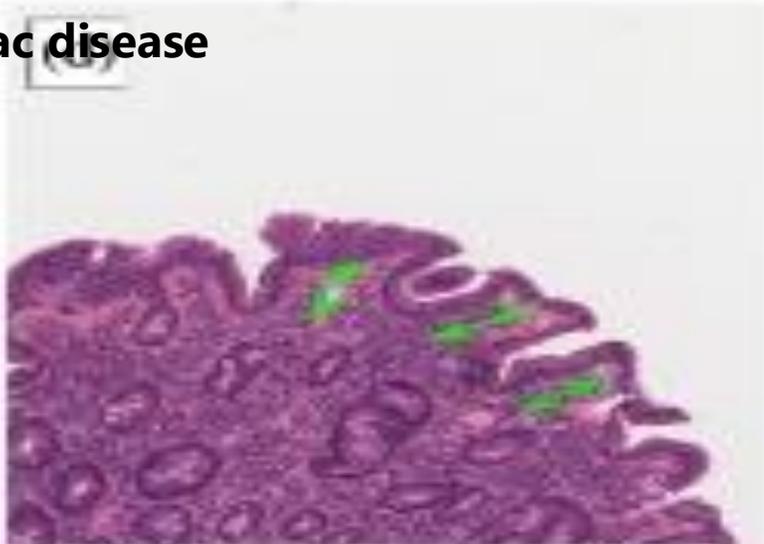
**Healthy crypts**



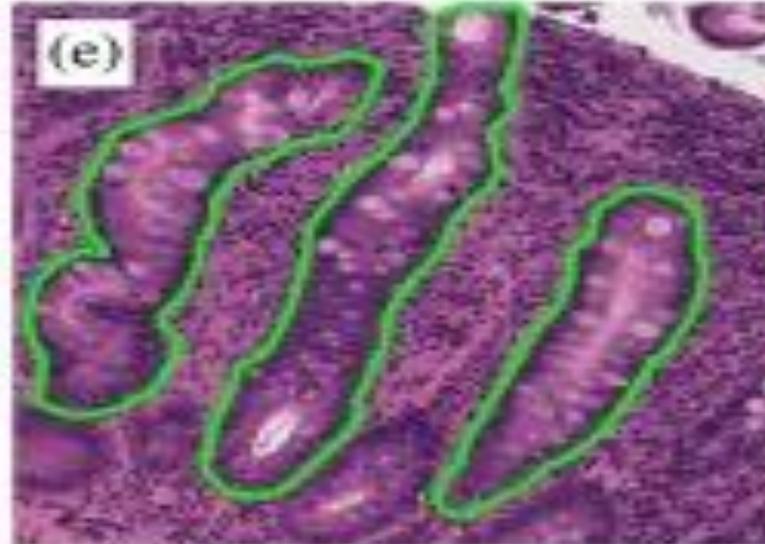
**Few IELs**



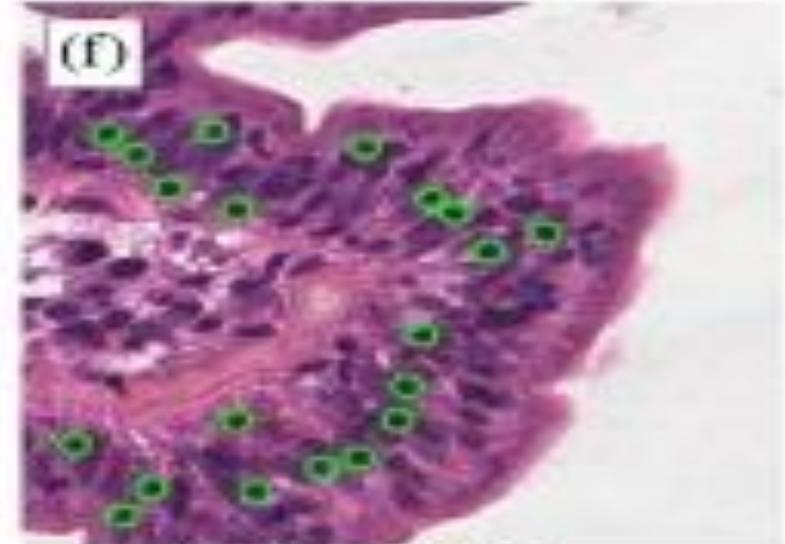
**Celiac disease**



**Villous atrophy**



**Crypt hyperplasia**



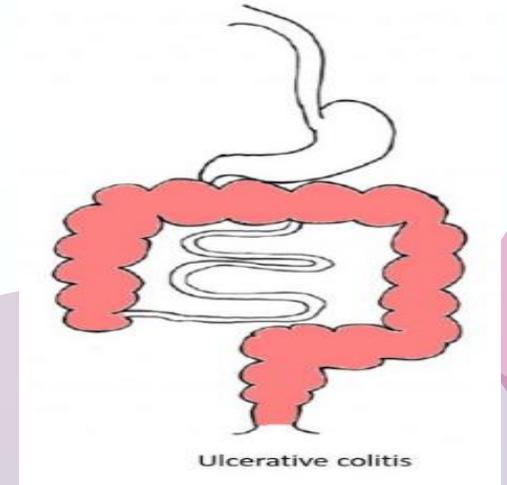
**Raised IELs**

## # Inflammatory Bowel Disease:

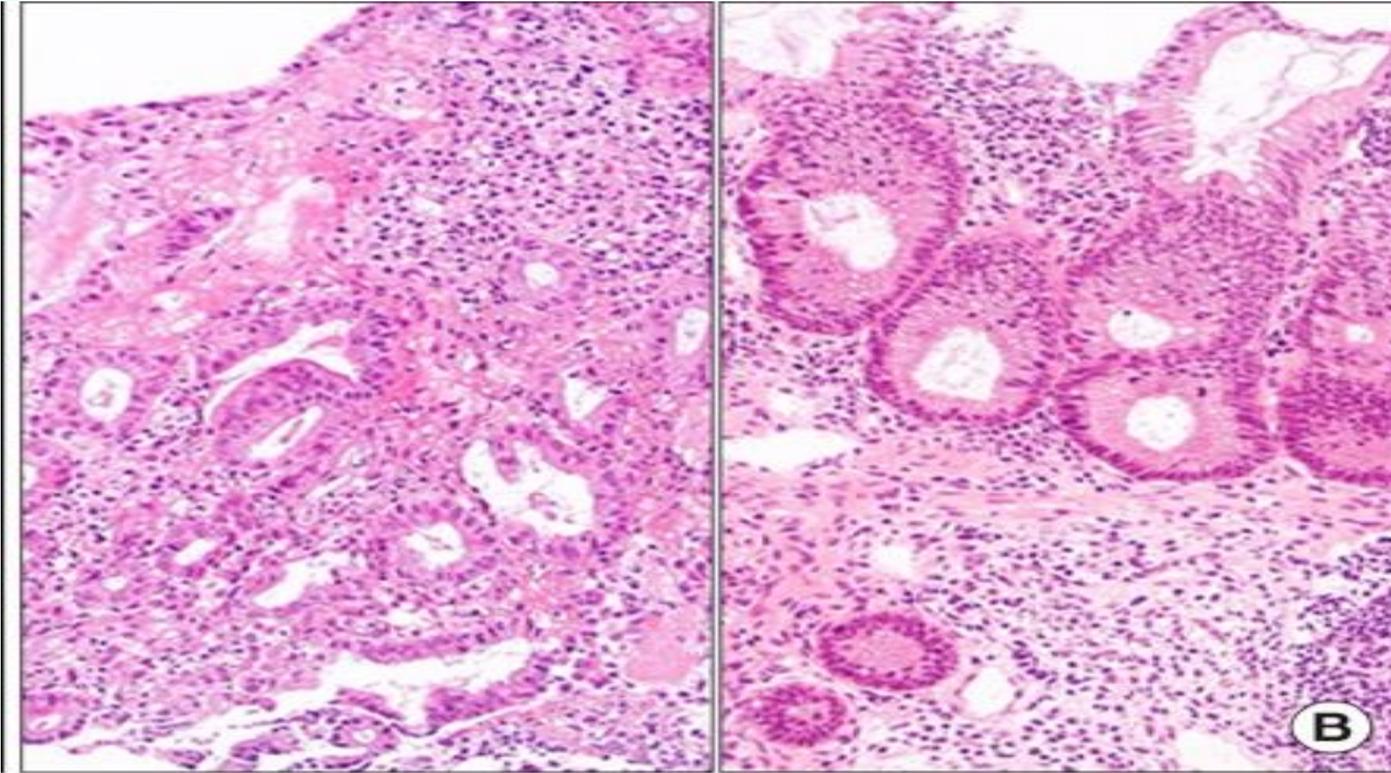
- chronic condition resulting from unregulated and persistent activation of the immune system in genetically susceptible individuals.
- Two types:

### 1) Ulcerative colitis:

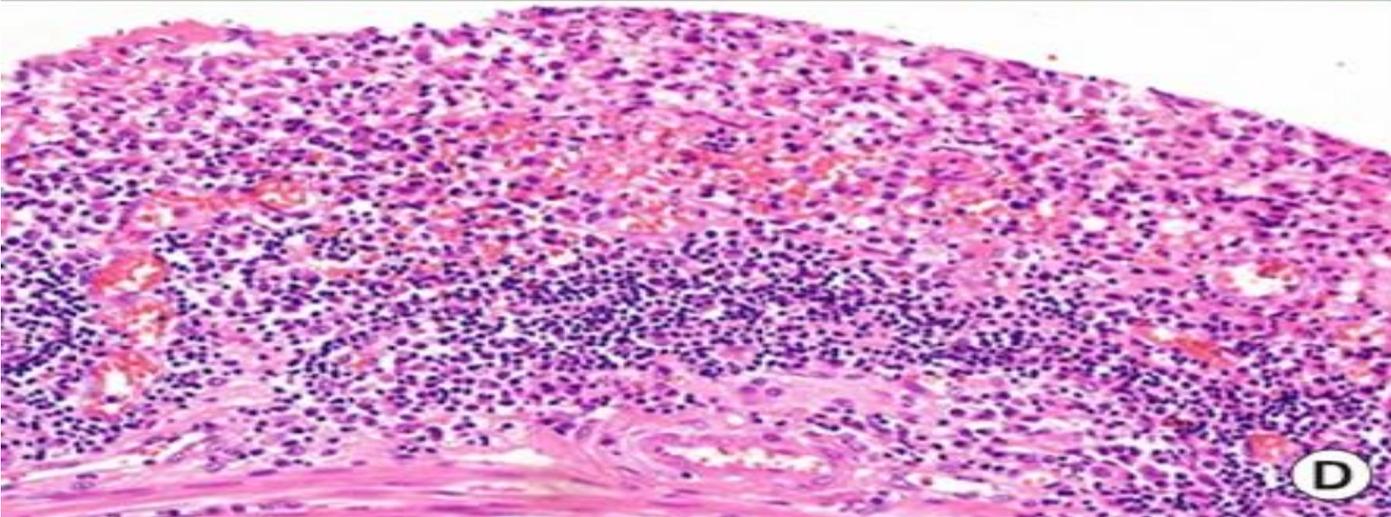
- **Site of inflammation:** It most commonly start from the rectum involving the entire colon (pancolitis). May extend to ileum causing Backwash ileitis.
- **Layers affected:** the superficial layers (mucosa and submucosa)
- **Morphology grossly:** Presence of regenerating mucosa which project in the lumen called Pseudopolyps.
- **Morphology microscopically:** Ulceration, cryptitis and crypt abscess ,  
**Absence of granuloma and fissuring**
- Increased risk of progression to cancer.
- **Clinically:** intermittent attacks of abdominal pain, bloody mucoid stool and fever.
- **Serology:** p-ANCA antibody.



pseudopolyps



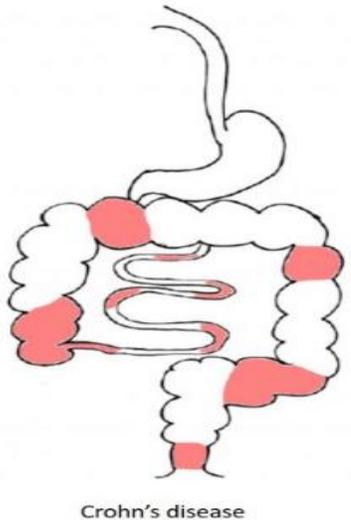
B) Low-power view of histological features in the colonic biopsy specimen compatible with ulcerative colitis, including active inflammation with cryptitis



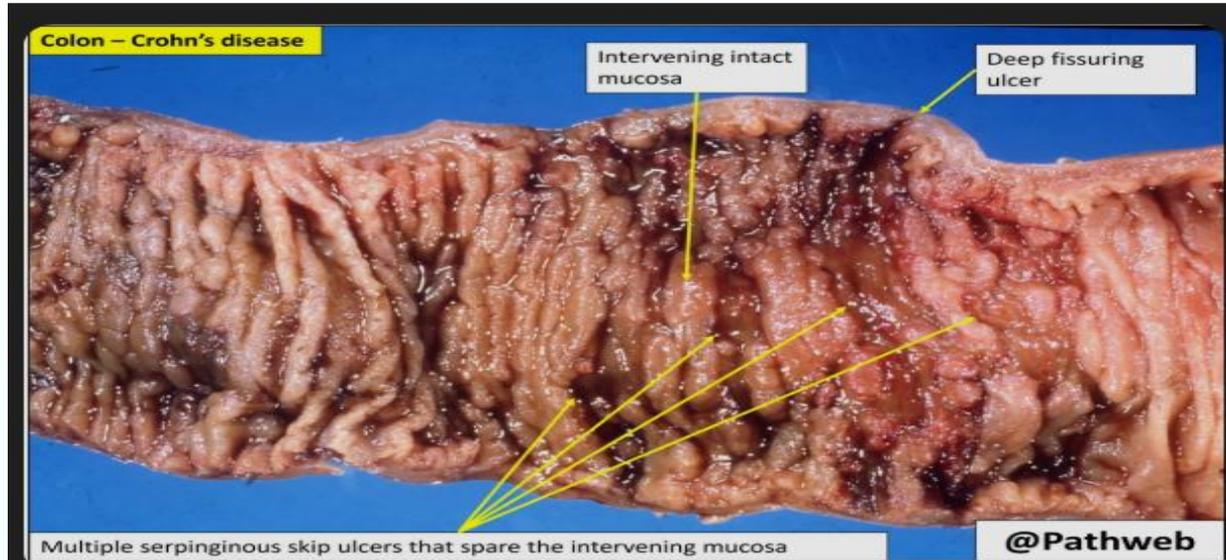
D) Medium-power view of a section of the colon, demonstrating severe active inflammation with loss of crypts and epithelium

## 2) Crohn's disease:

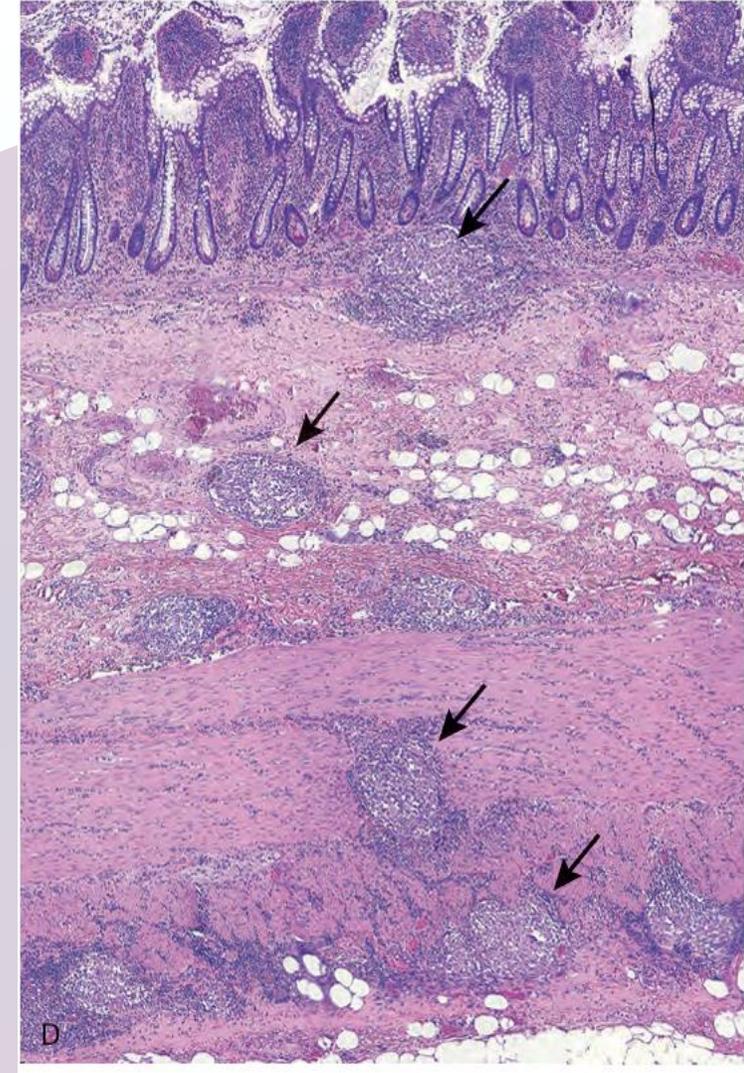
- **Site of inflammation:** can affect any part of the GIT from the esophagus to the large intestine.
- **Layers affected:** full thickness (transmural inflammation)
- **Patchy involvement of the GIT known as "Skip lesions"** , the intervening area between the two areas affected is completely normal.
- **Morphology grossly:** Fissure and Fistula mostly perianal, the involved part of intestine appears rigid with creeping of fat.
- **Morphology microscopically:** non-caseating granuloma
- **Serology:** ASCA antibody



Crohn's disease



## granulomas



## # Intestinal Obstruction:

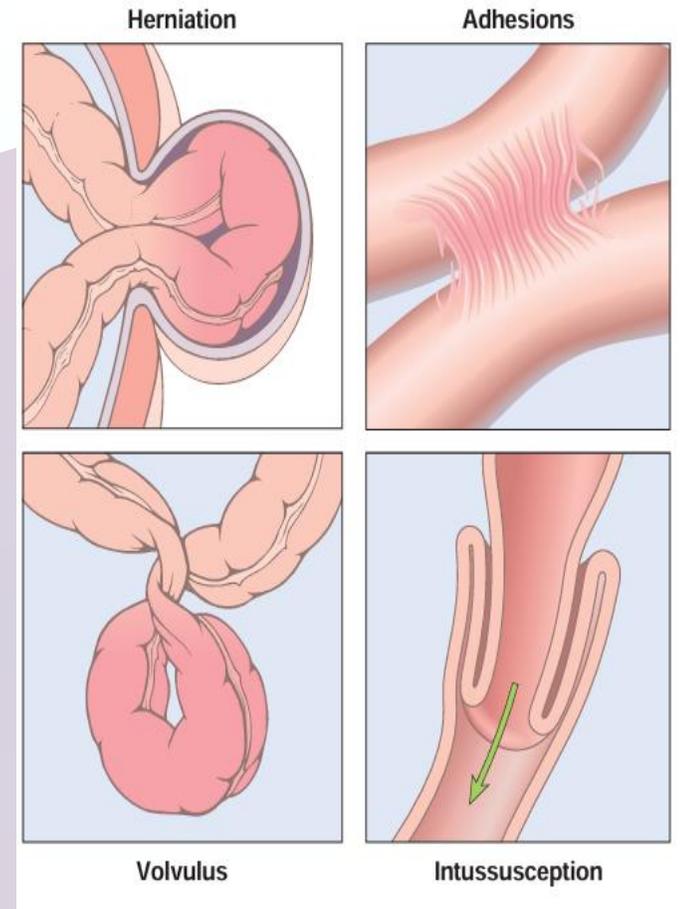
- Site: may occur at any level, but the small intestine is most often involved because of its relatively narrow lumen.
- Causes: mechanical obstruction 80% (hernias, intestinal adhesions, intussusception, and volvulus)/ Tumors, infarction, and other causes of strictures, for example, Crohn disease, make up the remainder.

### ❖ Hernia:

- Any weakness or defect in the abdominal wall may permit protrusion of a serosa-lined pouch of peritoneum called a hernia sac. Acquired hernias typically occur anteriorly, via the inguinal and femoral canals, via the umbilicus, or at sites of surgical defects

### ❖ Adhesions:

- Surgical procedures, infection, or other causes of peritoneal inflammation, such as endometriosis, may lead to development of adhesions between bowel segments, the abdominal wall, or operative sites.
- These fibrous bridges can create closed loops through which other viscera may slide and become entrapped, resulting in internal herniation



### ❖ **Volvulus:**

- Volvulus occurs when a loop of bowel twists about its mesenteric point of attachment and results in both luminal and vascular compromise.
- **It occurs most often in sigmoid colon.**

### ❖ **Intussusception:**

- occurs when a segment of the intestine, constricted by a wave of peristalsis, telescopes into the immediately distal segment. Once trapped, the invaginated segment is propelled by peristalsis and pulls the mesentery along.
- **Intussusception is the most common cause of intestinal obstruction in children younger than 2 years of age**
- Children: Associated with viral infections due to reactive hyperplasia of Peyer patches and other mucosa-associated lymphoid tissues that can act as the leading edge.
- Adult: intraluminal mass or tumor that serves as the initiating point of traction

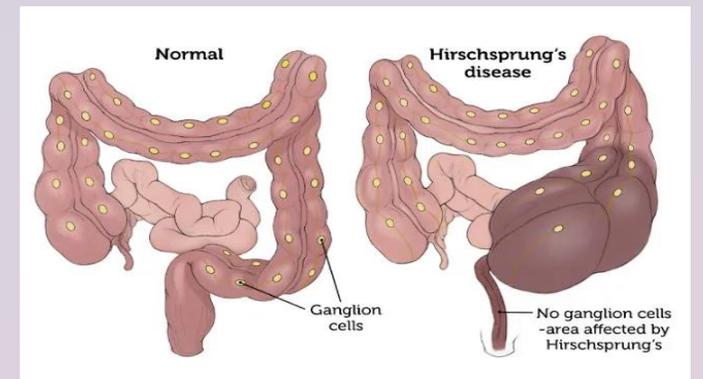
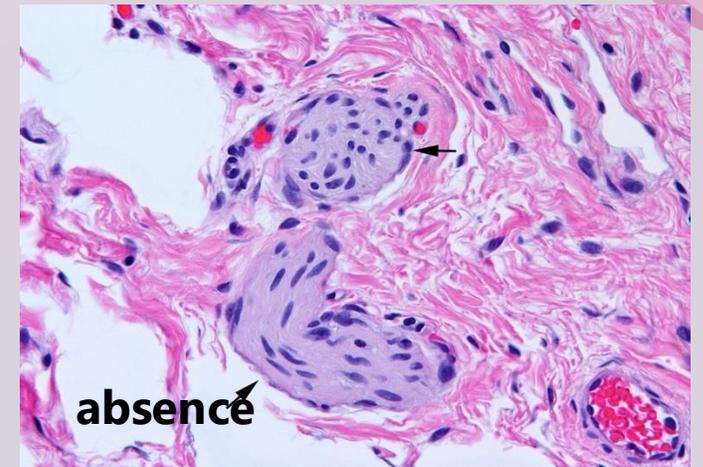
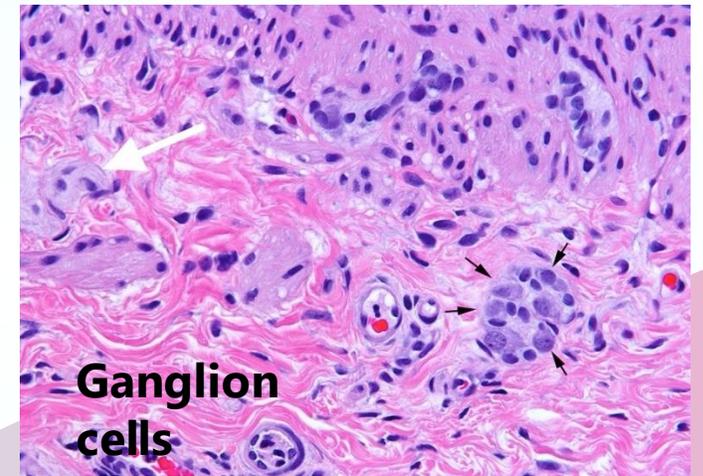
## # Meckel Diverticulum:

- Definition: A true diverticulum is a blind outpouching of the GI tract that communicates with the lumen and includes all three layers of the bowel wall.
- **The most common true diverticulum, and the most common congenital anomaly of the GI tract, is Meckel diverticulum.**
- The “rule of 2’s” is often used to help remember characteristics of Meckel diverticula, which:
  - Occur in approximately 2% of the population
  - Are generally present within 2 feet (60 cm) of the ileocecal valve
  - Are approximately 2 inches (5 cm) long
  - Are twice as common in males
  - Are most often symptomatic by age 2 (only approximately 4% are ever symptomatic)



## # Hirschsprung disease:

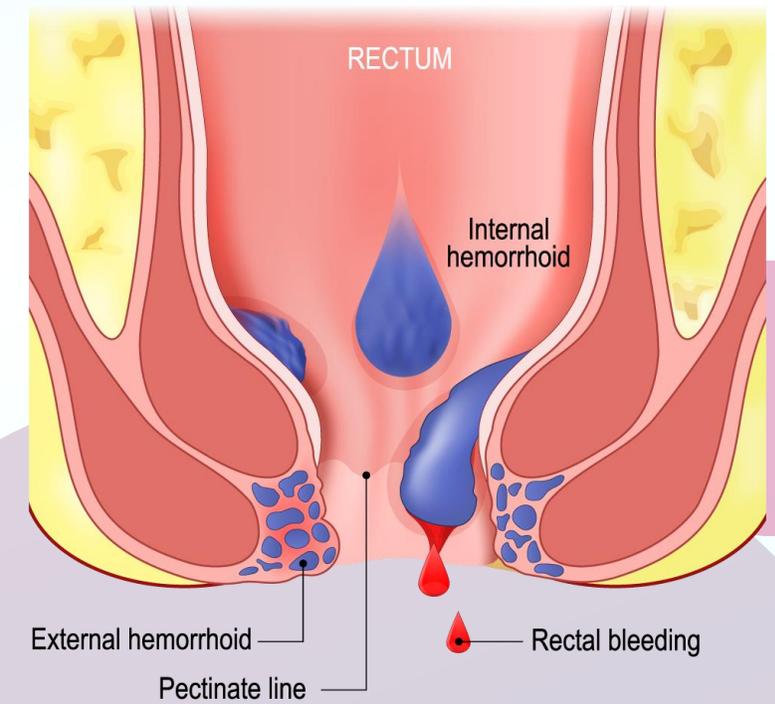
- Failure of ganglion cells to migrate to the wall of the colon, resulting from a mutation in the receptor tyrosine kinase.
- occurs in approximately 1 in 5000 live births
- **Pathogenesis:** distal intestinal segment that lacks both the Meissner submucosal plexus and the Auerbach myenteric plexus, termed aganglionosis. Result in absence of coordinated peristaltic contractions, and functional obstruction occurs, resulting in dilation proximal to the affected segment.
- **Diagnosed by absent of ganglion cells on biopsy.**
- **Clinically:** typically presents with a failure to pass meconium in the immediate postnatal period. constipation follows, often with visible but ineffective peristalsis, abdominal distention and vomiting.
- **Complication:** perforation and enterocolitis
- Treatment consists of surgical resection of the aganglionic segment and anastomosis of the normal proximal colon to the rectum.



# Anus

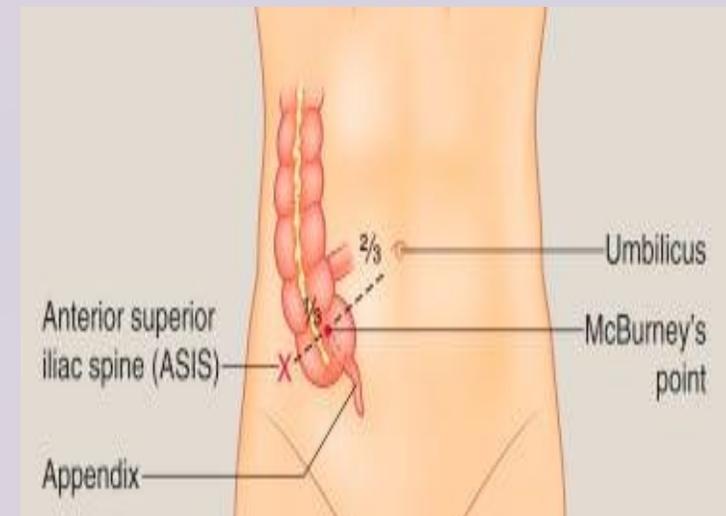
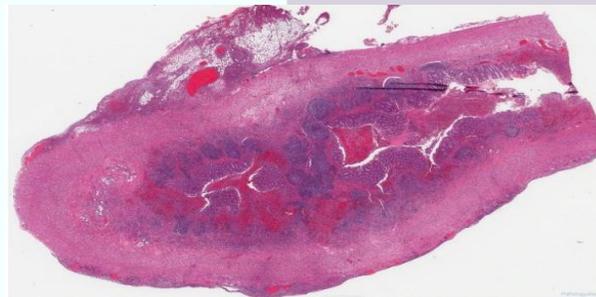
## # Hemorrhoids:

- develop secondary to persistently elevated venous pressure within the hemorrhoidal plexus. The most frequent predisposing influences are straining at defecation, e.g., in constipation, and venous stasis of pregnancy.
- Clinically: Hemorrhoids often present with pain and rectal bleeding.
- Except for pregnant women, hemorrhoids are rarely encountered in persons younger than age 30.
- treated by sclerotherapy, rubber band ligation, or infrared coagulation.
- Extensive or severe internal or external hemorrhoids may be removed surgically by hemorrhoidectomy



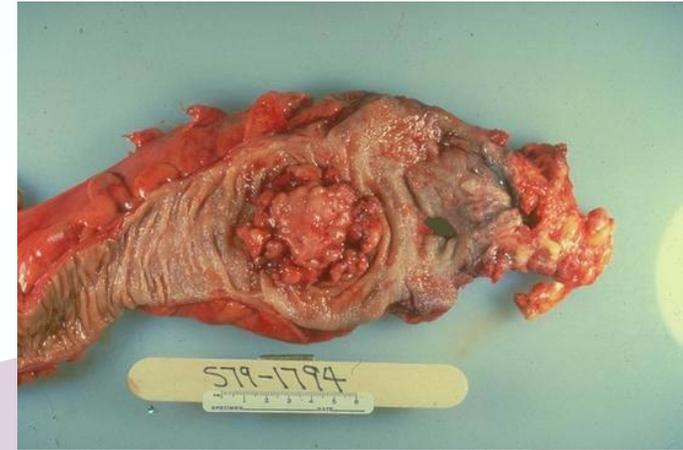
# Appendix

- The appendix is a normal true diverticulum of the cecum that is prone to acute and chronic inflammation
- Appendicitis is most common in adolescents and young adults, with a lifetime risk of 7%. Males are affected slightly more often than females
- Acute appendicitis is associated with overt luminal obstruction, usually caused by a small stone-like mass of stool, or, less commonly, tumor, or mass of worms (vermicularis)
- **Microscopically: neutrophilic infiltration of the muscularis propria**
- **Clinically: Typically, early acute appendicitis produces periumbilical pain that ultimately localizes to the right lower quadrant, followed by nausea, vomiting, low-grade fever, and a mildly elevated peripheral white cell count.**
- A classic physical finding is the McBurney sign, deep tenderness located two thirds of the distance from the umbilicus to the right anterior superior iliac spine (McBurney point).

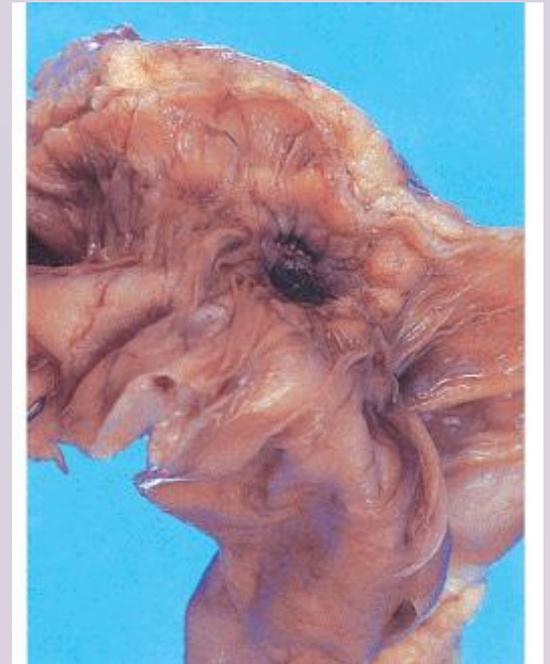


## # Adenocarcinoma of intestine:

- **Epidemiology:** Adenocarcinoma of the colon is the most common malignancy of the GI tract and is a major cause of morbidity and mortality worldwide
- In contrast, the small intestine which accounts for 75% of the overall length of the GI tract, is an uncommon site for benign and malignant tumors
- Colorectal adenocarcinoma is responsible for nearly 10% of all cancer deaths worldwide
- The dietary factors most closely associated with increased risk of colorectal cancer are low intake of unabsorbable vegetable fiber and high intake of refined carbohydrates and fat
- **Morphology:**
- Grossly: Tumors in the proximal colon often grow as polypoid, exophytic masses , In contrast, carcinomas in the distal colon tend to be annular lesions that produce constrictions and luminal narrowing

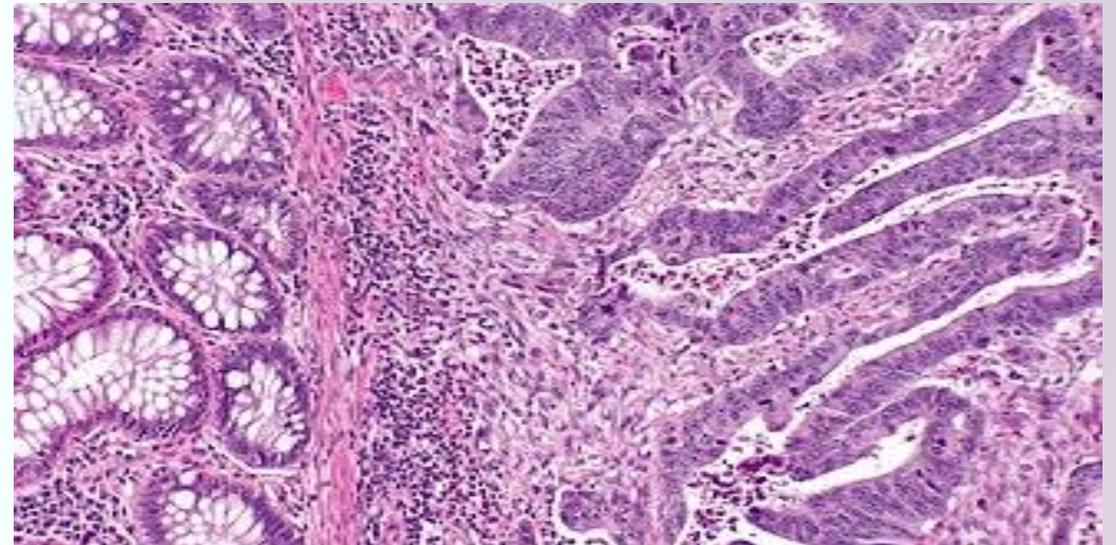


**Exophytic**



**Ulcerated**

- **Clinically: Unfortunately, colorectal cancers develop insidiously and may go undetected for long periods.**
- Cecal and other right sided colon cancers are most often called to clinical attention by the appearance of fatigue and weakness due to iron deficiency anemia.
- Left-sided colorectal adenocarcinomas may produce occult bleeding, changes in bowel habits, or cramping and left lower quadrant discomfort.
- **The two most important prognostic factors are depth of invasion and the presence or absence of lymph node metastases.**



# Gallbladder

## # Gallstones (Cholelithiasis):

- More than 95% of biliary tract disease is attributable to gallstones.
- There are two general classes of gallstones:
- 1) Cholesterol stones, containing more than 50% of crystalline cholesterol mono hydrate. the liver excretes more cholesterol than bile salts and phospholipids can dissolve. So Excess cholesterol forms crystals, which clump together and harden into stones (appears yellow)
- 2) Pigment stones composed predominantly of bilirubin calcium salt.
- Form from too much bilirubin (from red blood cell breakdown) or bacterial infection, .



Table 18.11 Risk Factors for Gallstones

### Cholesterol Stones

Demography: northern Europeans, North and South Americans, Native Americans, Mexican Americans

Advancing age

Female sex hormones

Female gender

Oral contraceptives

Pregnancy

Obesity and metabolic syndrome

Rapid weight reduction

Gallbladder stasis

Inborn disorders of bile acid metabolism

Hyperlipidemia syndromes

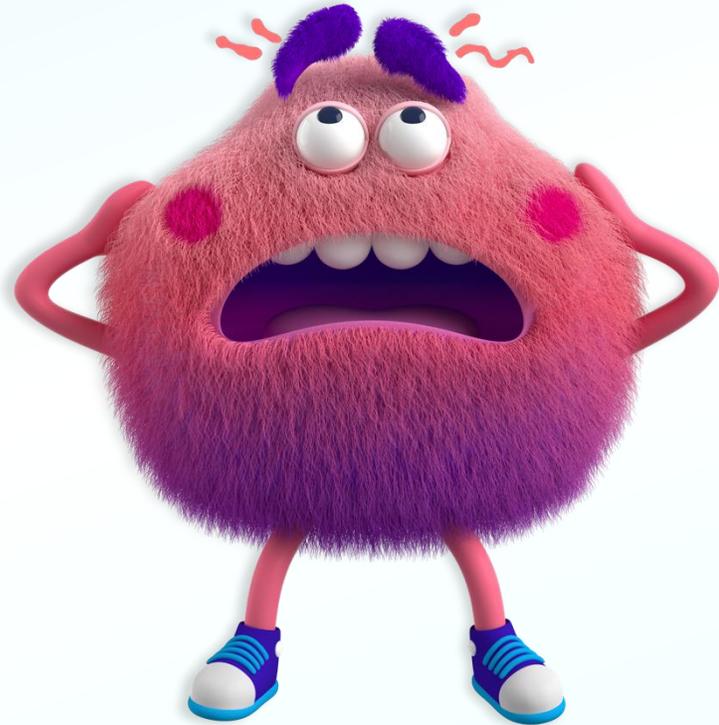
### Pigment Stones

Demography: Asians more than Westerners, rural more than urban

Chronic hemolytic anemias

Biliary infection

Gastrointestinal disorders: ileal disease (e.g., Crohn disease), ileal resection or bypass, cystic fibrosis with pancreatic insufficiency



**ANY QUESTIONS ?**