GIT Pathology
LEC 4

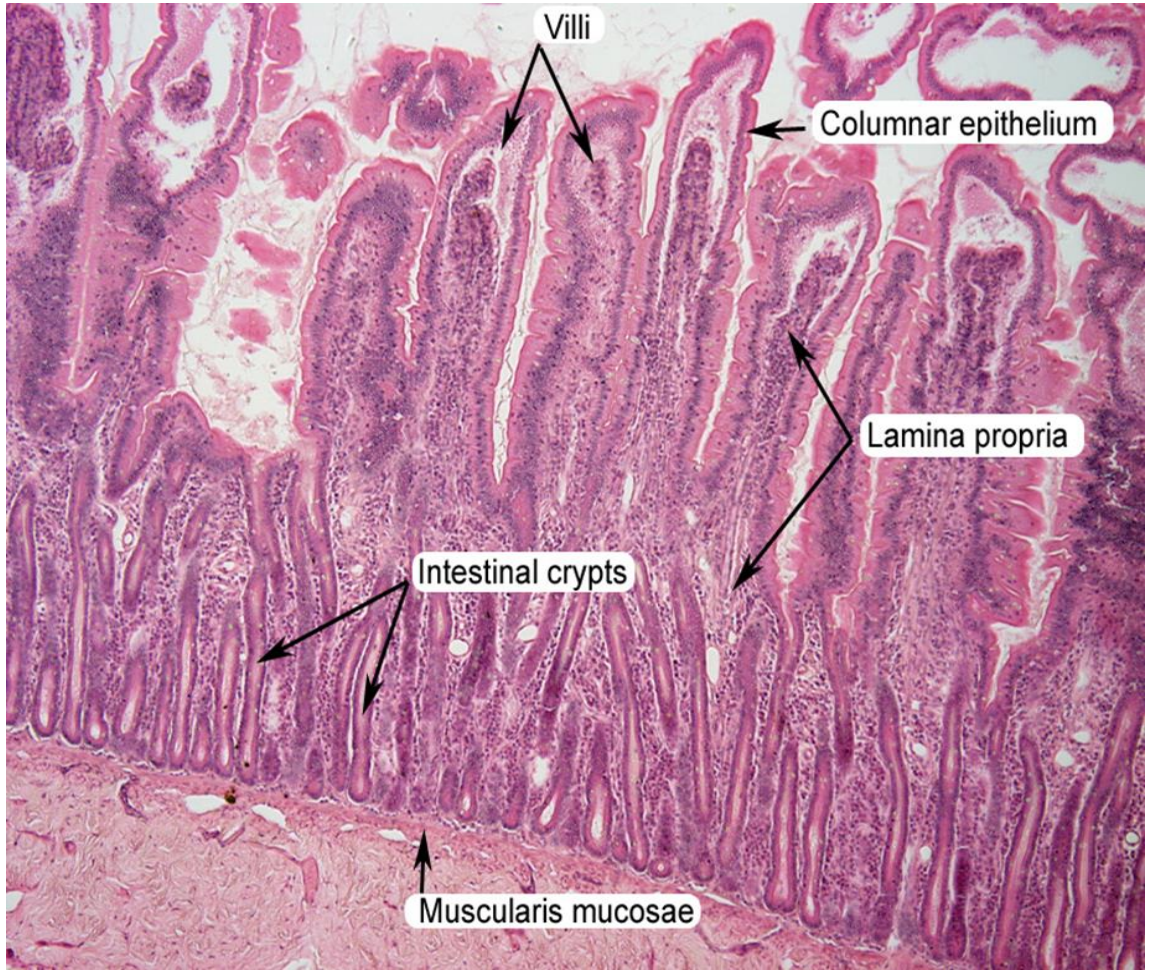
Dr. Raghad Hanoon

The intestine

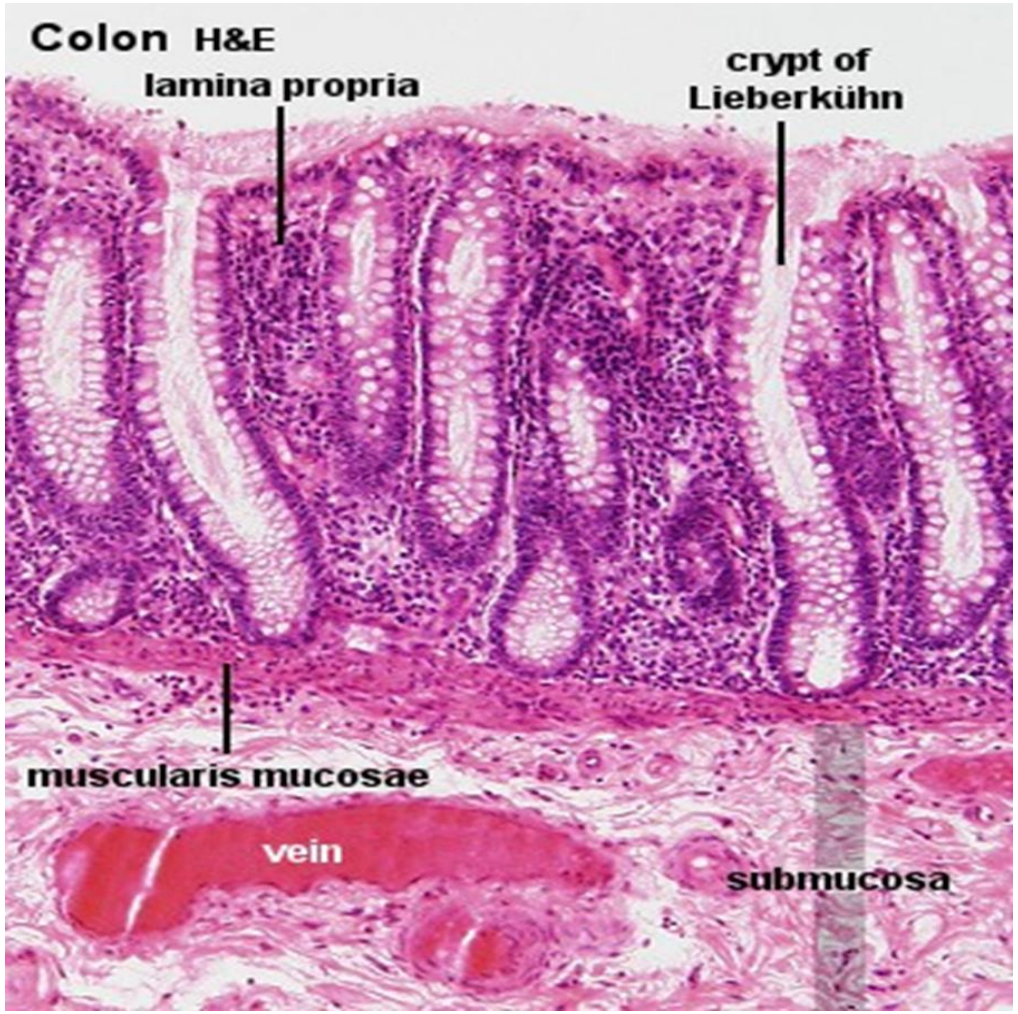
- It is composed of the small and large intestine.

Histologically:

- The small intestinal mucosa usually have a mucosal villi and crypts, lined by columnar cells .



The large intestine has a flat mucosa with numerous vertically oriented crypts covered with columnar cells with goblet cell.



CONGENITAL ANOMALIES

❖Anomalies of the intestine are rarely encountered; these include:

- *Duplication* of the small intestine or colon;
- *Malrotation* of the entire bowel;
- *Omphalocele* (birth of an infant with herniation of abdominal contents into a ventral membranous sac related to umbilicus);
- *Heterotopia* of pancreatic tissue or gastric mucosa;
- *Atresia and stenosis*
- *Imperforate anus* (due to failure of the cloacal diaphragm to rupture).

➢ Meckel diverticulum

- Occur in **2%** of normal population
- It lies **2 feet** (85cm) from the ileocecal valve
- It measures about **2 inches**
- It results from failure of obliteration of the vitelline duct (which connects the lumen of the gut to the yolk sac), this will leave a solitary tubular diverticulum
- It is considered as a true diverticulum since it contains the three layers of normal bowel mucosa.
- Sometimes there is **heterotopic** gastric mucosa that functions as the stomach, so peptic ulcer might develop in the adjacent intestinal mucosa which may cause complications.

- **Complications:**

1- Diverticulitis

2- Intestinal obstruction

3- Complication of peptic ulcer (bleeding, perforation, peritonitis)

➢ Congenital aganglionic megacolon (Hirschsprung disease)

- This disorder characterized by absence of ganglionic cells in a segment of large bowel that become constricted leading to functional obstruction and progressive colonic dilation proximal to the affected segment.
- **Morphologically:**

1- Absence of ganglion cells in the muscle wall (Auerbach plexus) and from the submucosa (Meissner plexus) in the affected segment.

2- Progressive dilation and hypertrophy of the colon proximal to that segment.

• Clinical features:

1- It is noticed in the immediate neonatal period by failure to initially pass meconium.

2- Constipation

3- Abdominal distension

• Complications:

* Enterocolitis with water and electrolyte imbalance

* Perforation of the colon with superadded peritonitis

INTESTINAL OBSTRUCTION

- The small intestine is most often involved due to its narrow lumen. **Tumors** and **infarction,** although the most serious, account for only up to 20% of small-bowel obstructions. The remaining 80% are due to:
- Hernias
- Intestinal adhesion
- Intussusception
- Volvulus
- The clinical manifestations include abdominal pain and distention, vomiting, constipation, and in complete obstruction failure to pass flatus.

Hernias

Any weakness or defect in the wall of the peritoneal cavity may permit protrusion of a serosa -lined pouch of peritoneum (hernial sac).

Adhesions

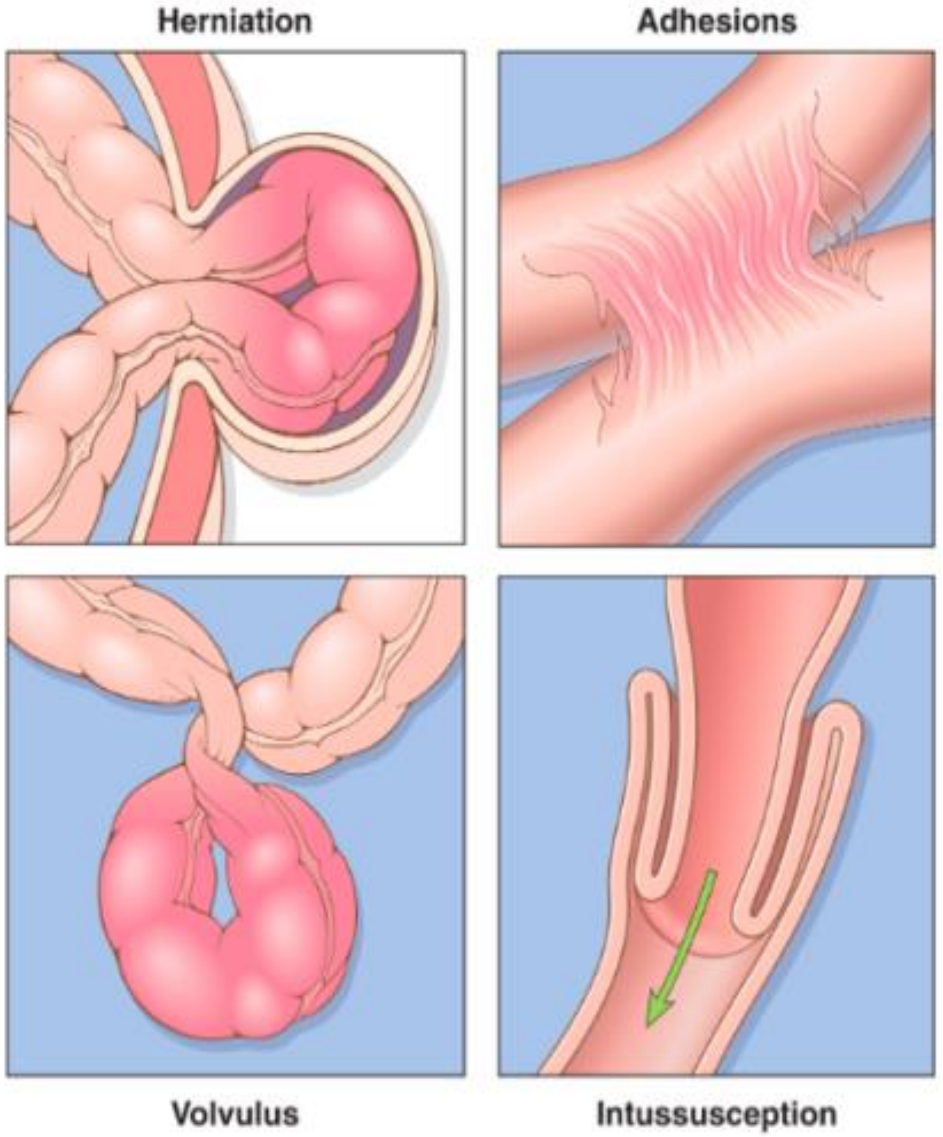
Surgical procedures, infection, or other causes of peritoneal inflammation, such as endometriosis, may result in development of fibrous bridges.

Volvulus

Complete twisting of a loop of bowel about its mesenteric base of attachment.

Intussusception

A segment of the intestine, constricted by a wave of peristalsis, telescopes into the immediately distal segment.



Malabsorbtion

- Is characterized by decrease absorption of fat, fat soluble and other vitamins, proteins, carbohydrates, electrolyte and minerals and water .

- Malabsorption results from disturbance in at least one of the four phases of nutrient absorption:

1- Intraluminal digestion: assisted by enzymes present in saliva, gastric juice , bile acids (salts) and pancreatic enzymes.

2- Terminal digestion: by the presence of special enzymes on the small intestinal brush boarder.

3- Transepithelial transport (absorption): where the nutrients cross the epithelium of the small intestine to reach the vascular element of the small intestine.

4- Lymphatic transport of absorbed lipids

• Clinical features:

1- Hallmark of malabsorption is steatorrhea, characterized by excessive fecal fat and bulky, frothy, greasy, yellow or clay-colored stools.

2-Anorexia (loss of appetite) and Weight loss

3- Anemia (iron deficiency or megaloblastic)

4- Edema and ascites

5- Signs of vit. deficiency e.g hypocalcemia (def. of vit D)

Classification:

1. Defective intraluminal digestion

Pancreatic insufficiency Primarily from chronic pancreatitis or cystic fibrosis, is a major cause of defective intraluminal digestion that leads to diarrhea and steatorrhea.

2. Defective terminal digestion

Disaccharidase deficiency (lactose intolerance) In which there is a deficiency of the enzyme lactase which is normally present on the apical cells of the villous epithelium. This deficiency is usually acquired. This will lead **to inability to break down the lactose into simple monosaccharides** (glucose and galactose); this will lead to osmotic diarrhea and malabsorption.

3. Defective transepithelial transport

Abetalipoproteinemia

It is a rare A.R inborn error of metabolism characterized by absence of apoprotein B. This will lead to accumulation of triglyceride in the epithelial cell, since this lipoprotein is essential for mobilization of triglyceride from the epithelium to the circulation, the fat will appear as vacuoles inside the epithelial cells.

Gluten-sensitive enteropathy (celiac disease)

- Is an autoimmune enteropathy
- Triggered by the **ingestion of gluten-containing foods,** such as wheat, rye, or barley, in genetically predisposed individuals.
- Characterized by mucosal lesion of the small intestine with impaired absorption that usually **improves on withdrawal** of gliadin which is a component of gluten.

Pathogenesis:

- Gluten that contain Gliadin (in wheat, barley and rye) act as a foreign substance in those individuals which lead to accumulation of CD8+ (cytotoxic T cells) on the surface of the small intestinal mucosa, this will cause an inflammatory reaction that damages the intestinal epithelium leading to villous atrophy…malabsorption.

- The patients have antigliadin Ab (antibodies against tissue transglutaminase and endomysium) which is diagnostic.
- There is strong genetic association exists between celiac disease and HLA haplotypes DQ2 and DQ8.

Microscopically:

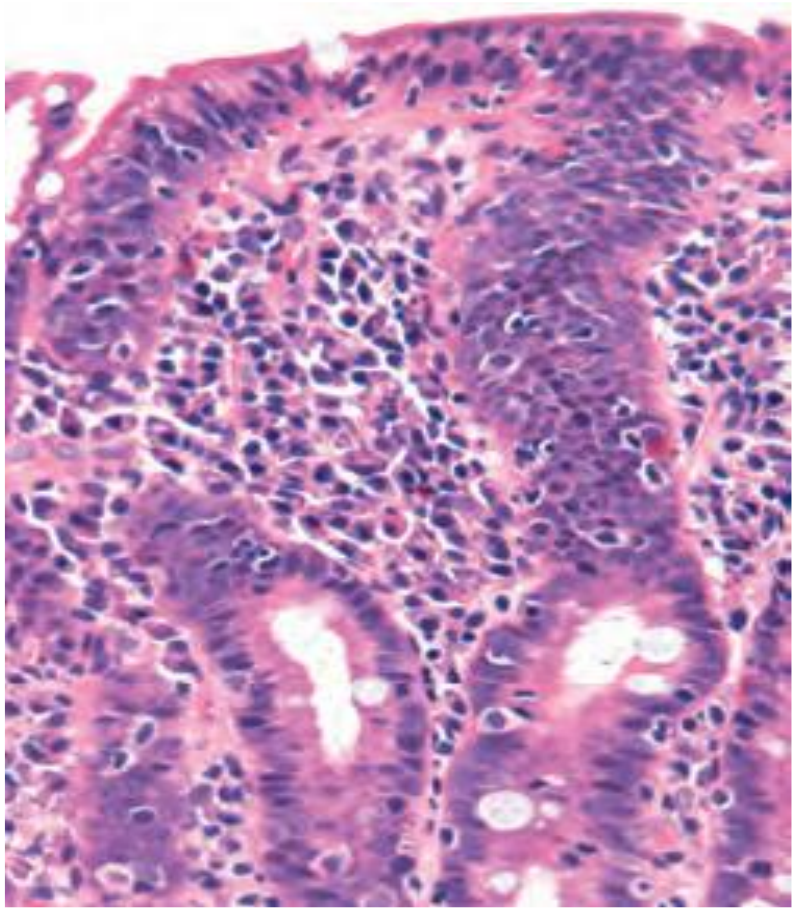
- Biopsy specimens from the second portion of the duodenum or proximal jejunum, which are exposed to the highest concentrations

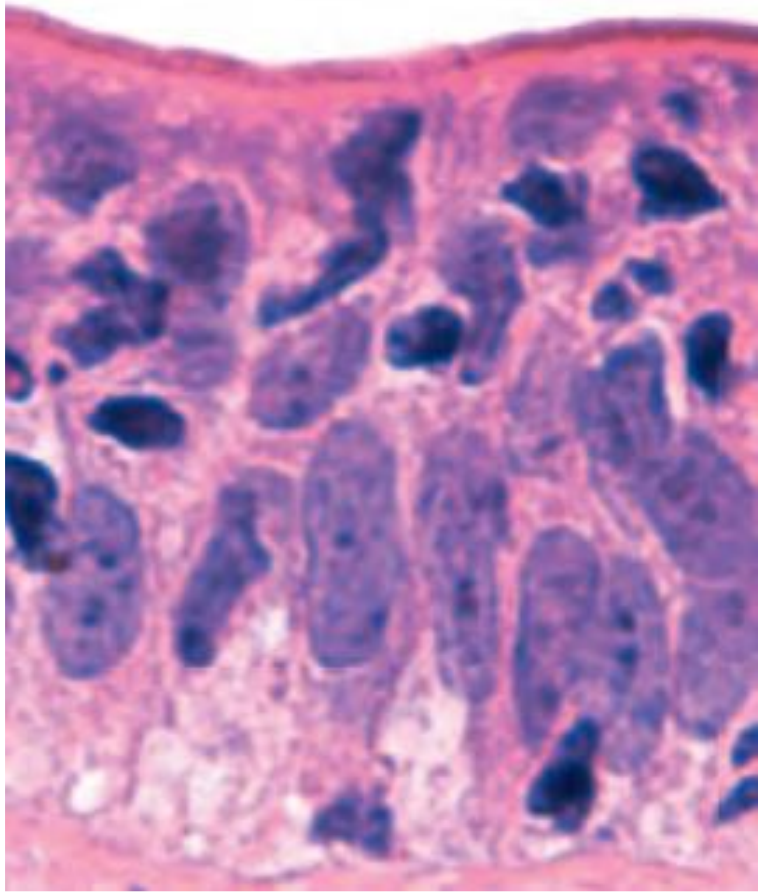
of dietary gluten, are generally diagnostic in celiac disease.

1-Partial or complete villous atrophy.

2-Increase intraepithelial lymphocytes and lymphocyte and plasma cell infiltration of the lamina propria.

3- Crypt hyperplasia





Celiac disease:

Complete loss of villi, or total villous atrophy, dense plasma cell infiltrates in the lamina propria.

Infiltration of the surface epithelium by T lymphocytes, which can be recognized by their small, densely stained nuclei relative to larger, pale-staining epithelial nuclei.

Clinical features:

➢At childhood, the patient presented with:

- diarrhea
- weight loss
- growth retardation
- anemia

Complication:

- Malignant transformation in 10-15%, the most common is **lymphoma, adenocarcinoma**

Tropical sprue (Environmental Enteropathy)

- Is a celiac like disease, it is malabsorption due to intestinal infection but no causative agent identified. It has a certain world distribution (Caribbean), South Africa….etc.

***Microscopically*:**

- Partial villous atrophy

Clinical features:

- The patient presented with acute diarrhea following a visit to those areas

Treatment:

- Broad spectrum antibiotic supporting the infectious nature

4. Defective lymphatic transport of absorbed lipids:

Lymphatic Obstruction

- Lymphoma
- Tuberculosis and tuberculous lymphadenitis
- ***Whipple disease***

- A rare systemic disease, may involve any organ in the body

Causative agent: Gram +ve actinomycete (rod shape bacilli) ***(Tropheryma whippelii)***

Clinical features:

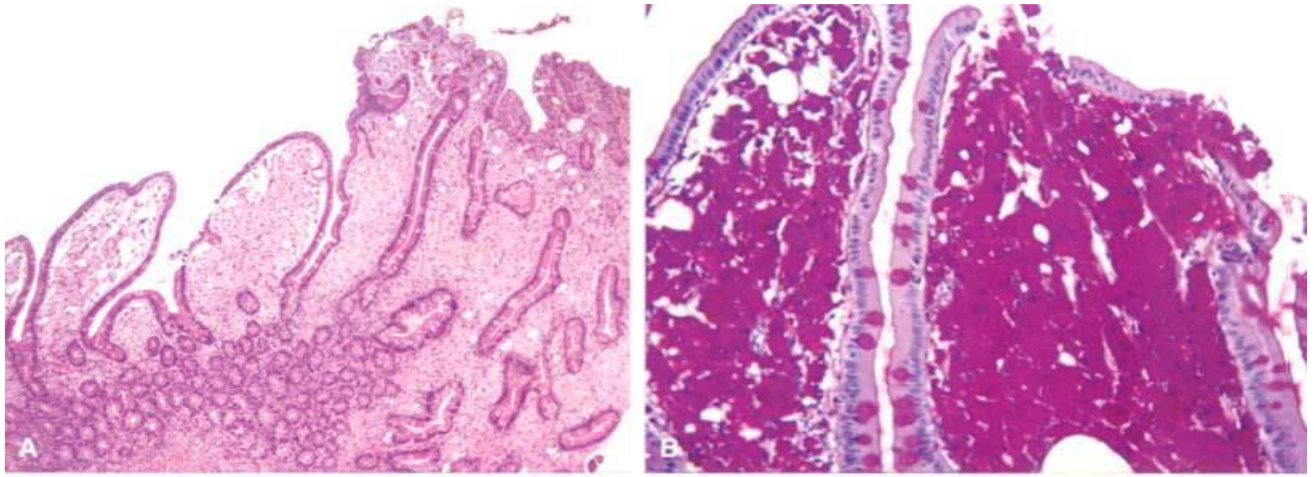
Diarrhea with other organ involvement like CNS and joints.

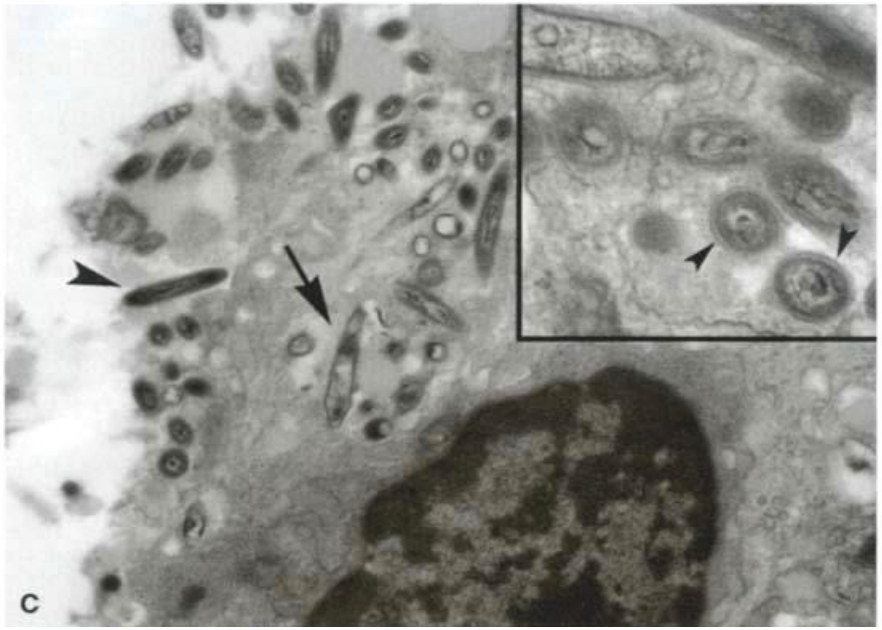
Microscopically:

The villi of the small intestine are filled with macrophages containing PAS +ve granules and rod shape bacilli under electron mic.

Whipple disease.

A. Foamy macrophages in the lamina propria.
B. PAS stain showing the positive granules in the foamy macrophages.
C. Electron micrograph of a lamina propria macrophage showing many bacilli within the cell (arrow) and in the extracellular space (arrowhead). Inset, Higher magnification of macrophage cytoplasm showing cross-sectional profiles of bacilli and their cell walls (small arrows).





INFECTIOUS ENTEROCOLITIS

- Enterocolitis can present with a broad range of symptoms including:

Diarrhea, abdominal pain, urgency, perianal discomfort, incontinence, and hemorrhage.

❖Viral enterocolitis

- The lesions caused by enteric viruses in the intestinal tract are similar. The small intestinal mucosa shows partial villous atrophy (shortening of the villi) with infiltration of the lamina propria by lymphocytes. However, in infants, rotavirus and adenoviruses can produce total villous atrophy (flat mucosa), thus resembling celiac disease.

❖Bacterial enterocolitis

- Salmonellosis and Typhoid Fever
- Campylobacter Enterocolitis
- Cholera
- Antibiotic-Associated Colitis (Pseudomembranous Colitis)
- Tuberculous enteritis

❖Parasitic enterocolitis:

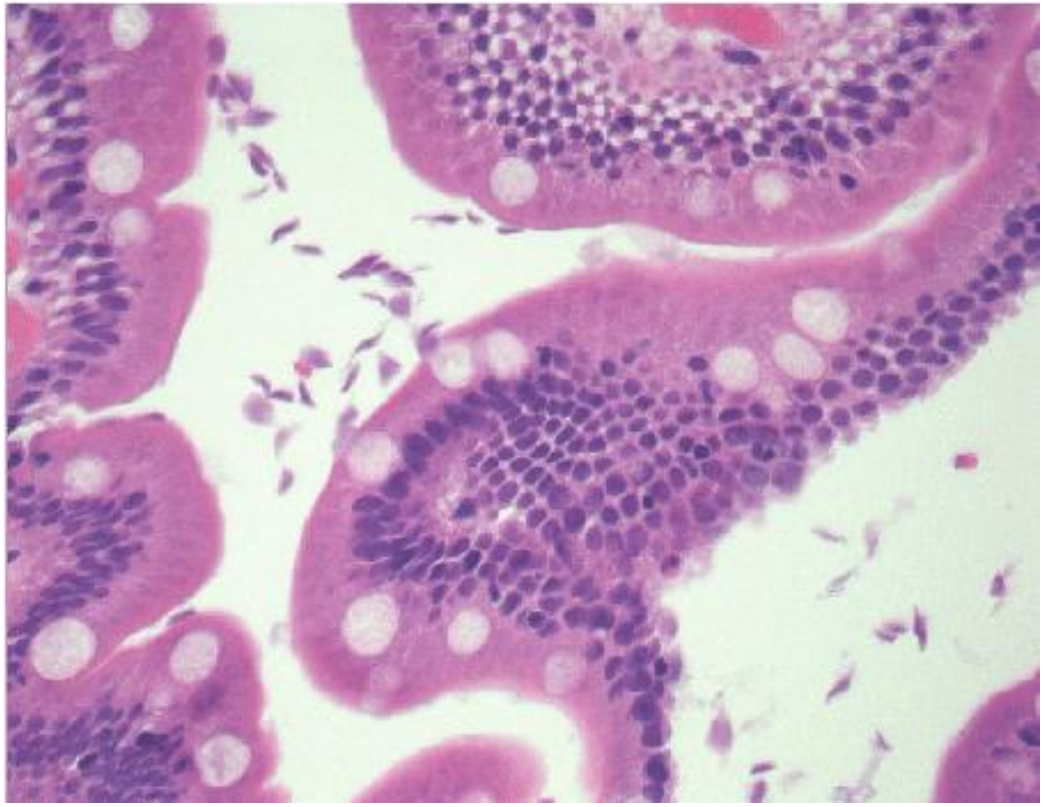
- Ascaris lumbricoides
- Strongyloides
- Hookworm (*Necator duodenale* and *Ancylostoma duodenale*) infection
- Enterobius vermicularis (pinworms)
- Amebiasis
- Giardiasis

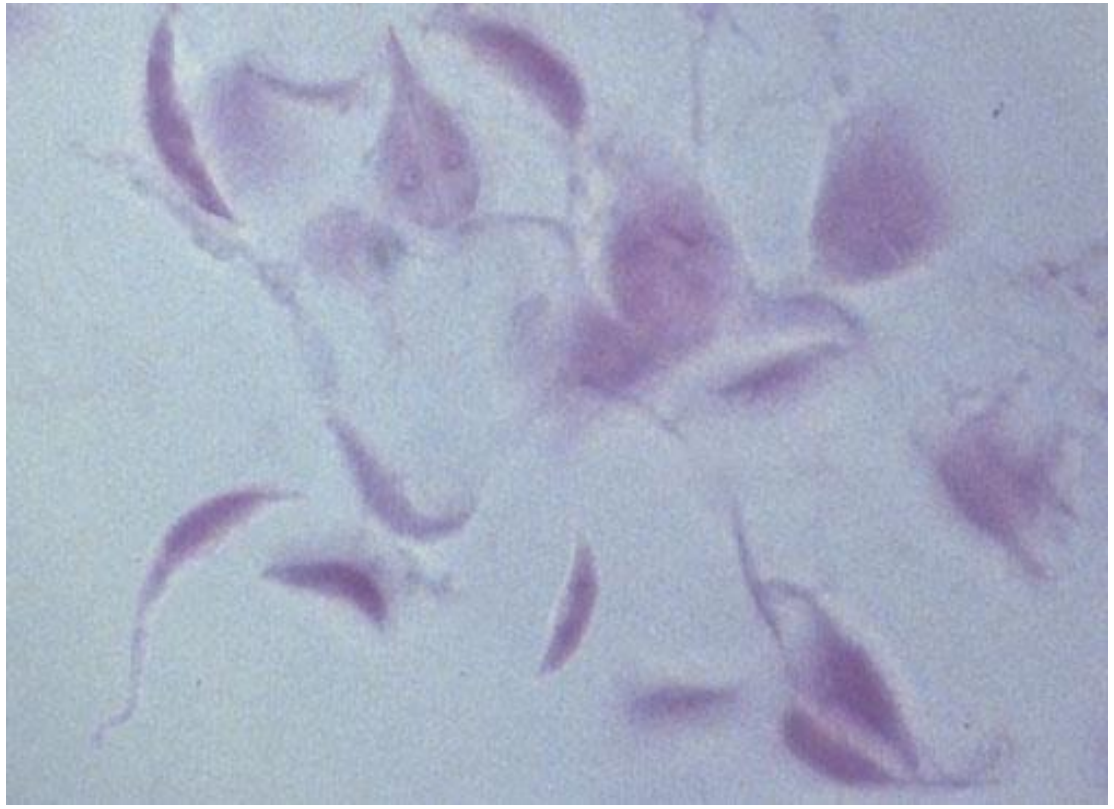
Giardiasis

- Caused by Giardia Lamblia.
- Route of infection: Contaminated food and water by giardia cyst.
- Site: Duodenum & small intestine.
- The cyst will hatch into a trophozoite that adheres to the mucosal surface without penetrating it.

➢**Mic.:**

- Villous atrophy
- Chronic inflammatory cells infiltrating the area (lymphocytes and plasma cells)
- Trophozoite can be detected near the mucosal surface.





Giardia lamblia, which are present in the luminal space

Idiopathic Inflammatory Bowel Diseases

- Two inflammatory disorders of unknown cause affect the GIT, namely, **Crohn's** disease and **ulcerative colitis.**
- They share many common features and are collectively known as **chronic idiopathic inflammatory bowel disease.**
- And since the actual, real cause remains unexplained thus they are termed idiopathic.

Pathogenesis:

These two diseases share partly or totally the same pathogenesis. many theories shared in this explanation.

1- Genetic predisposition:

- High incidence in first degree relatives (3-20 times).
- Associated with HLA –class II gene located on chromosome (6).
- Other gene association e.g. mutated NOD2 which is important in host response to bacteria

2-Infectious cause:

- Specially unidentified m.o. e.g viruses, Chlamydia, atypical bacteria.

3- Abnormal host immunoreactivity:

- Inappropriate exposure to luminal antigens ---the mucosal immunity is stimulated and then--- fail to down-regulate. Also the presence of plasma cells indicates the immune mediated mechanism.
- The fact that immunosuppressive drugs, e.g. corticosteroids improve the symptoms supports the immune mediated nature.

4- Inflammation

Activation of inflammatory cells which cause non specific tissue injury.

Crohn’s disease

- Is a chronic relapsing inflammatory disease
- It is common in the western countries
- Can occur at any age (peak in the 20 years)
- Affect the whites more than black
- Females more than males.
- Smoking was found to be a strong risk factor.

It is characterized by the followings:

1- It can involve **any part of the GIT** (mouth, esophagus, duodenum,……anus). But most commonly it affect the small intestine 40% specially the terminal ileum hence the term (terminal ileitis), colon 30%.

2- It affects the whole wall thickness of the affected part **(transmural involvement)** with its surrounding mesentery and s.t lymph nodes. Thus, the wall will get thick and rubbery

3- 25% of patients have **extra intestinal manifestations**

4- The mucosa first show an aphthous like superficial ulcer, when it unite it will form a serpentine linear ulcer, and if it extend deep it will form **fissures** which are a longitudinal ulcers , that if extend through the wall it will lead to fistula formation

5- It is characterized by **skip lesions** which mean there is a sharp demarcation between the normal unaffected areas and those with diseased mucosa.

6- **Cobblestone** appearance is the result of fissures surrounding an edematous mucosa

Crohn’s disease

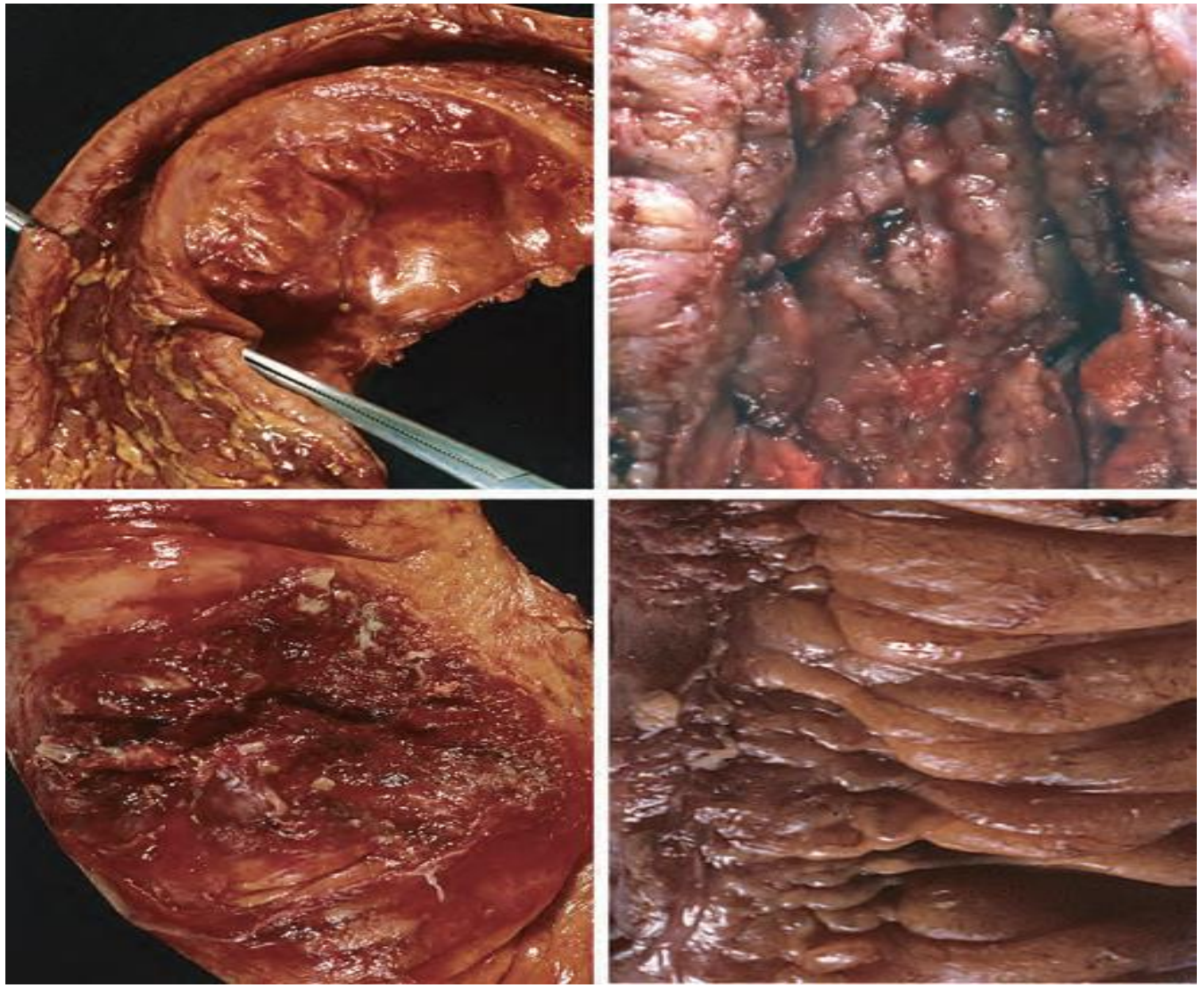
Gross:

(A) Small intestinal stricture.

(B) Linear mucosal ulcers, which impart a cobblestone appearance to the mucosa, and thickened intestinal wall.

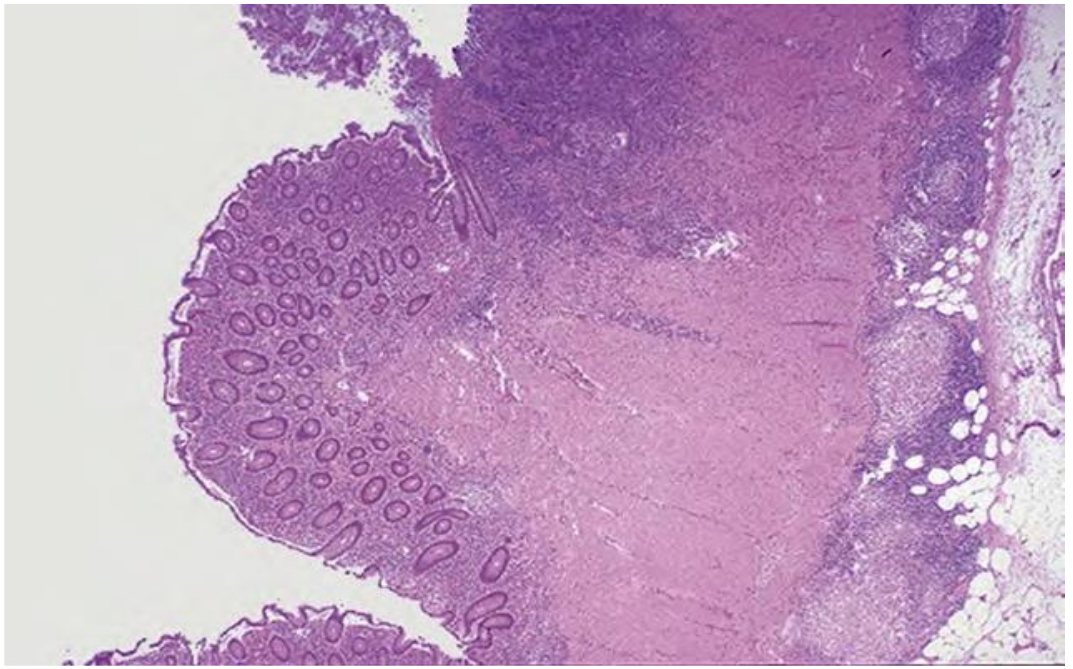
(C) Perforation and associated serositis.

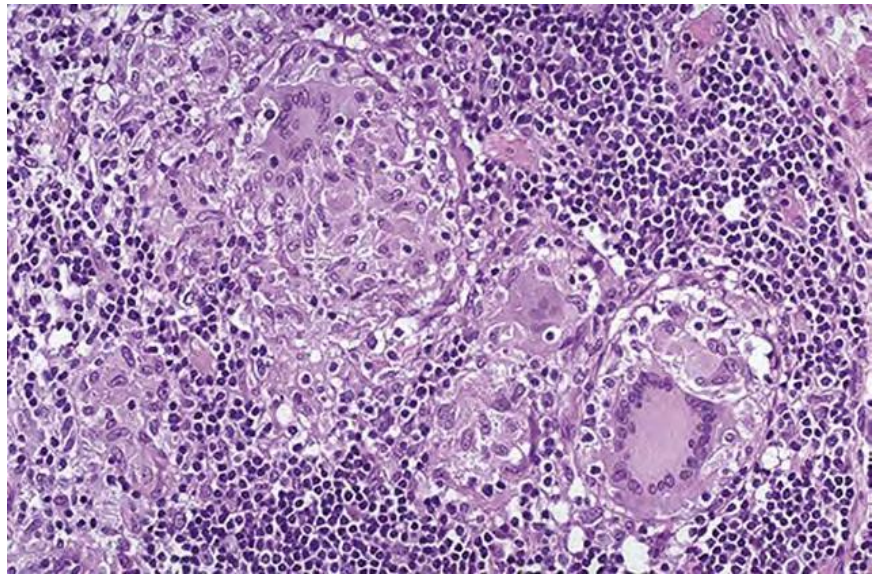
(D) Creeping fat.



7- Microscopically:

* There is transmural infiltration by lymphocyte, plasma cells.
* **Non caseating granuloma** presents in 35% of cases at any site from the mucosa to the surrounding structure and even lymph nodes.





Clinical features:

1- Abdominal pain.

2- Recurrent diarrhea.

3- Generalized malabsorption

4- Extraintestinal manifestations e.g. clubbing of the fingers, sacroiliitis and ankylosing spondylitis

Complications:

1. Intestinal obstruction
2. Perforation of deep fissures
3. Fistula with the bladder, colon, abdominal wall
4. Carcinoma but less frequent than ulcerative colitis.

Ulcerative colitis

- Is a chronic disease with remission and relapse presented with bloody diarrhea, abdominal cramps s.t fever and weight loss
- More in whites than blacks.
- No sex predilection
- The onset of the disease is usually at 2nd -3rd decades
- Pathogenesis is still unknown as with Crohn's dis. but it results from many **environmental** factors that lead to **loss of tolerance** of the mucosa for normal flora in genetically susceptible individuals.

➢ It is characterized by:

1- It involves **only the colon** hence the name “colitis”

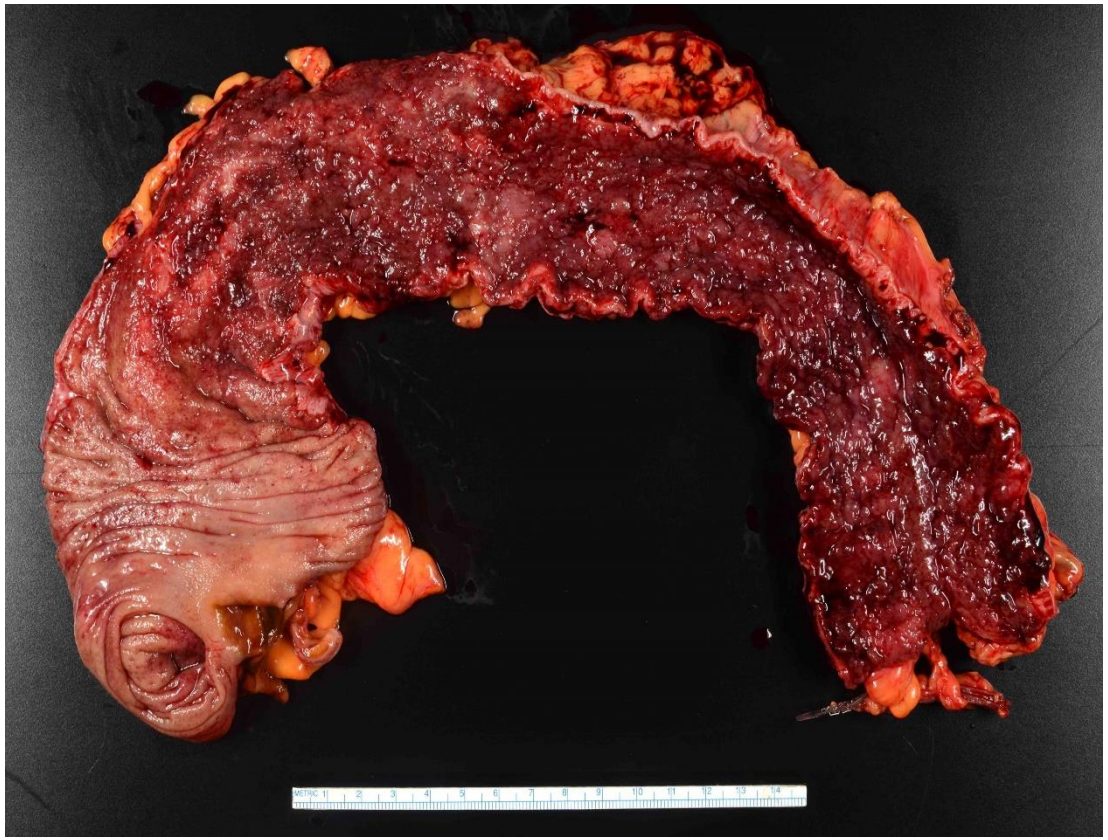
2- The involvement is **continuous** (not skip) starting from the rectum and ascend upwards in a continuous way till it reach the ileum (s.t. it involves the distal ileum where it is called backwash ileitis)

3- It involves the **mucosa and submucosa** only (not trasmural)

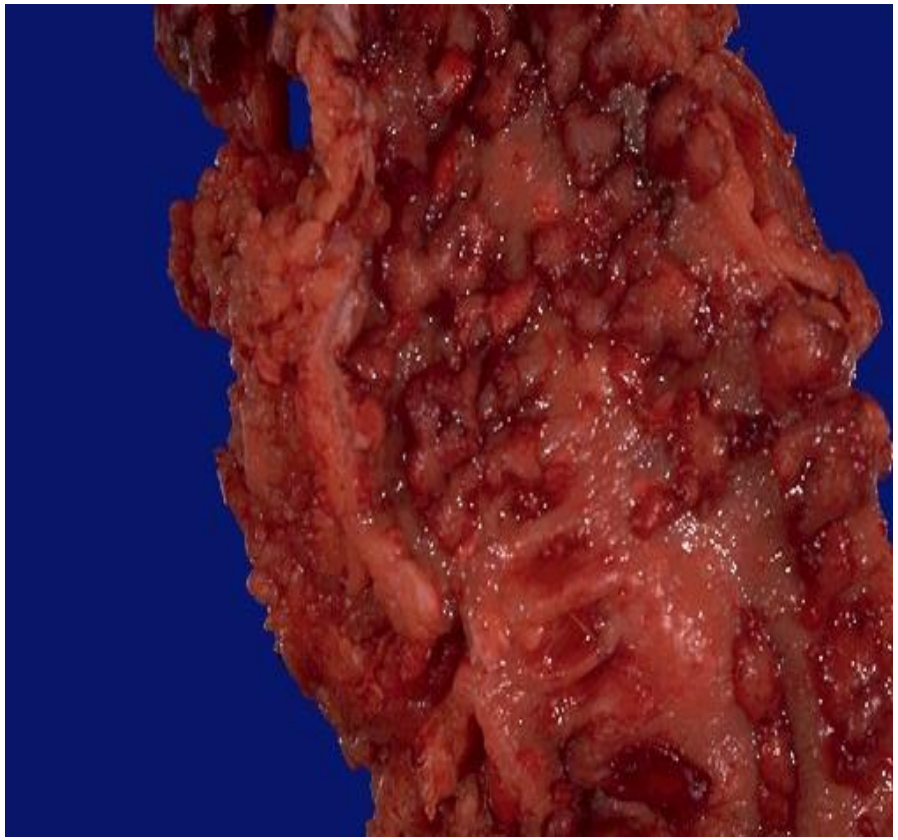
4- The ulcer is **superficial** and never forms (fissures)

5- There is no cobblestone appearance instead there is inflamed hyperemic mucosa with islands of regenerating mucosal cells forming the **pseudopolyps**

Grossly:



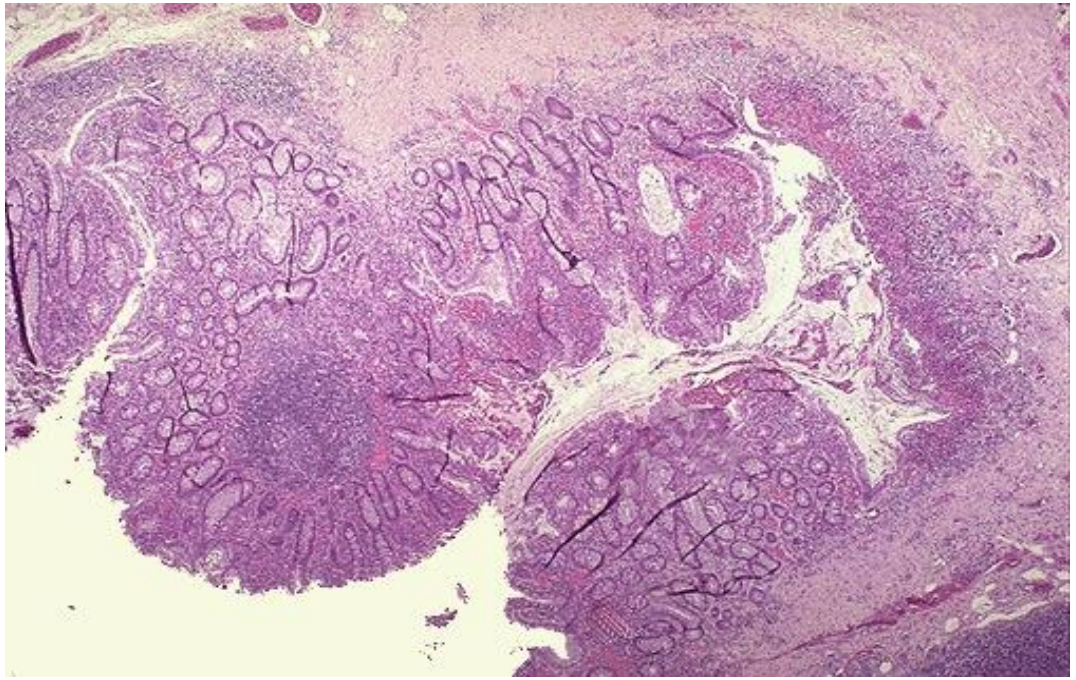
Diffuse, continuous involvement of the distal colon with mucosal erythema and granularity.

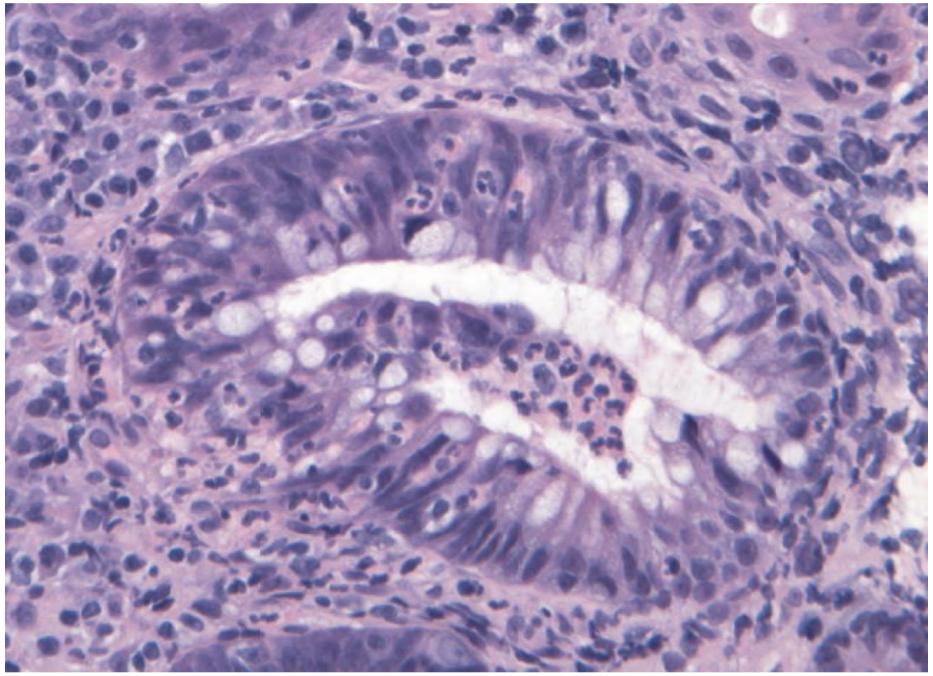


pseudopolyps

➢Microscopically:

* Congested mucosa
* Acute and chronic inflammatory cell infiltration of the lamina propria.
* Crypt abscess (collection of neutrophils in the glandular lumen)
* There is goblet cell depletion
* No granuloma





➢Complications:

1- Massive hemorrhage (bleeding per rectum)

2- Perianal and ischiorectal abcesses

3- Colorectal carcinoma cause by continuous regeneration--- dysplasia---carcinoma

Thank you