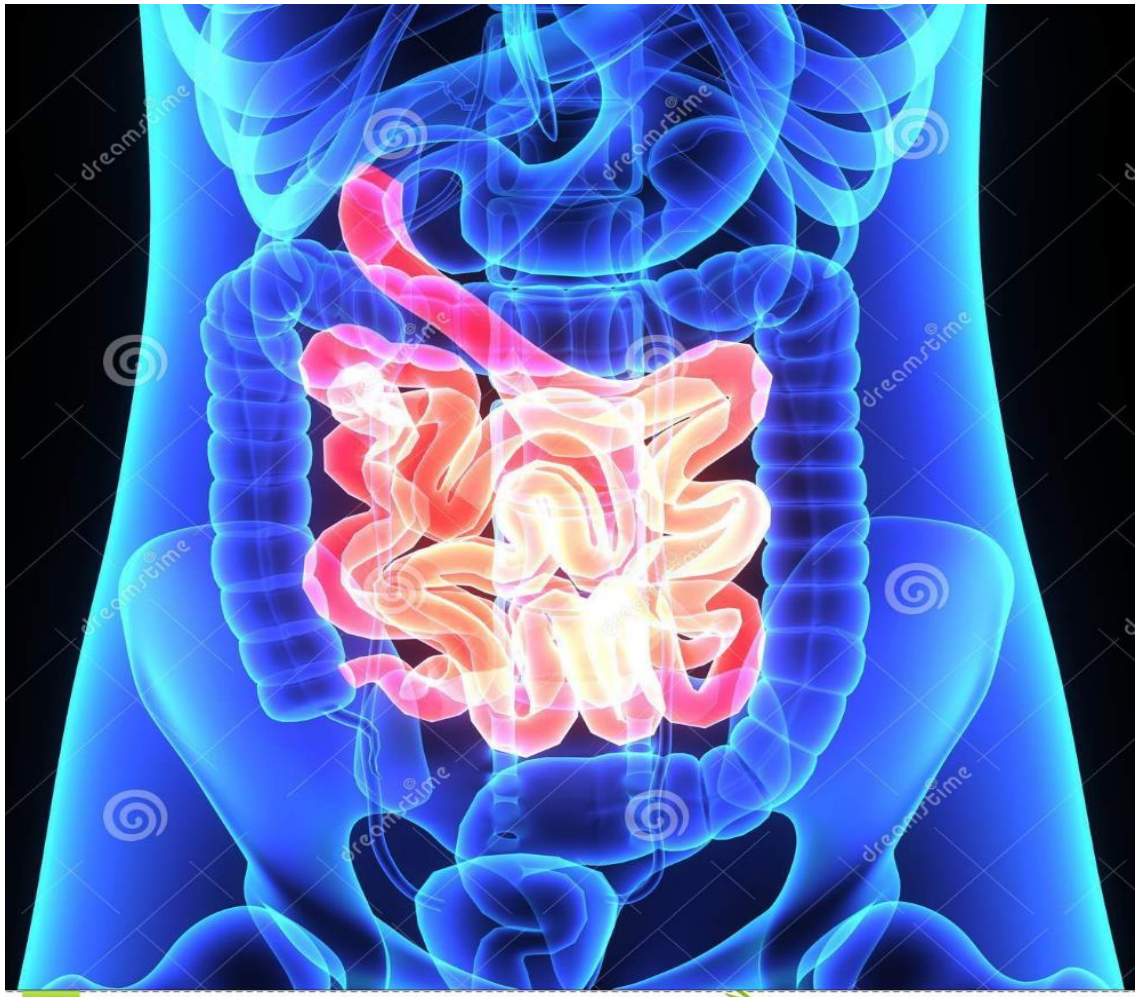
GIT PATHOLOGY

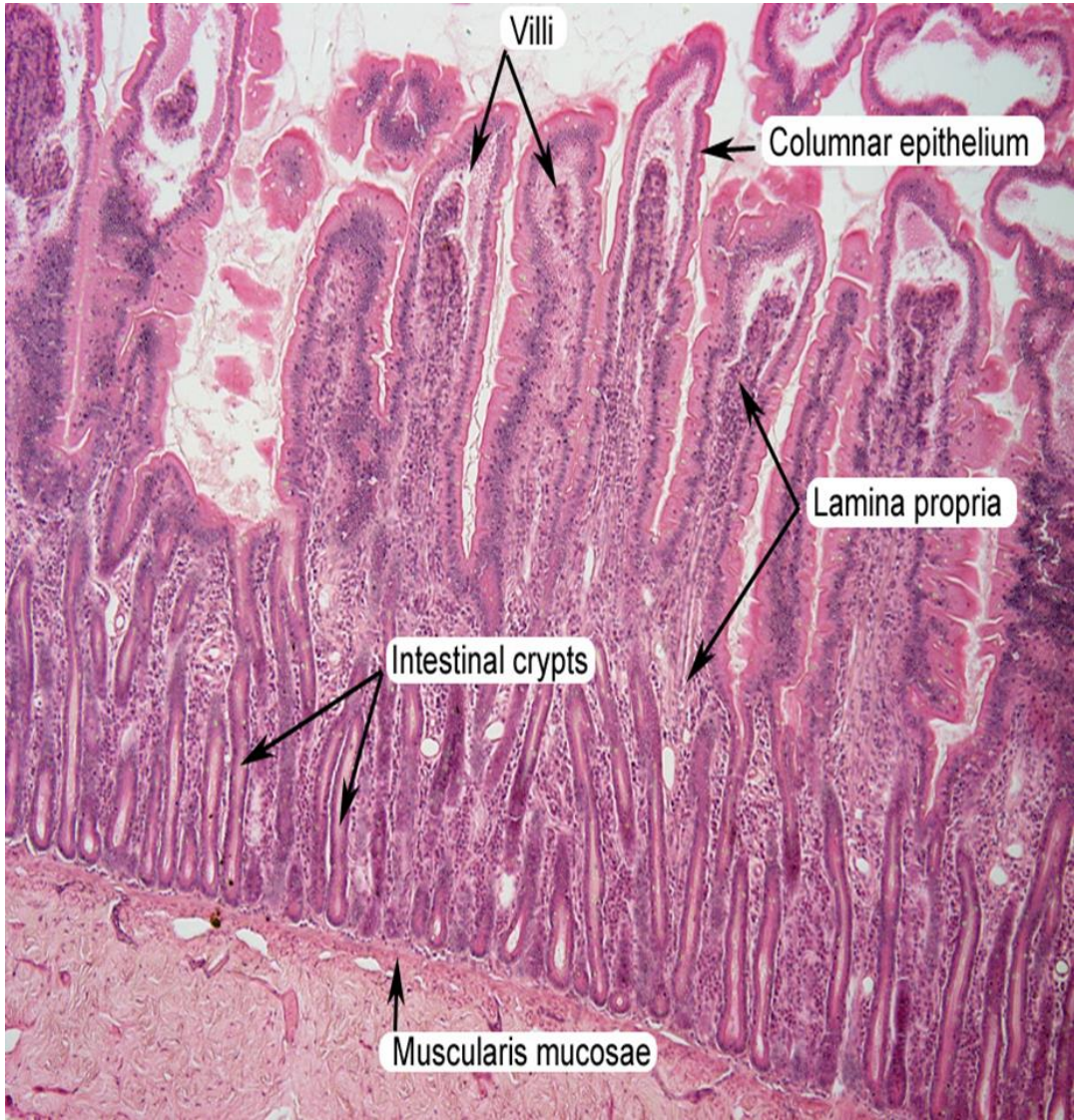
Lec. 4

Dr. Methaq Mueen

The intestine

small intestine: Histologically:The mucosa usually have a mucosal villi and crypts, lined by columnar cells with goblet cell .





- **Malabsorbtion**
- Is characterized by decrease absorption of fat, fat soluble and other vitamins, proteins, carbohydrates, electrolyte and minerals and water .
- It results from disturbance of one of the following normal digestive functions:

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.

- **Clinical features:**

1- There is a wide range of presentations

2- Chronic diarrhea (steatorrhea): is the passage of abnormally, bulky, frothy, greasy yellow stool.

3-Anorexia (loss of appetite) and Weight loss

4- Anemia (iron deficiency or megaloblastic)

5- Edema and ascites

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

Classification:

Defective Intraluminal Digestion

- **Digestion of fats and proteins**

* Pancreatic insufficiency, owing to pancreatitis or cystic fibrosis

- Zollinger-Ellison syndrome, with inactivation of pancreatic enzymes by excess gastric acid secretion
- **Solubilization of fat, owing to defective bile secretion**

* Ileal dysfunction or resection, with decreased bile salt uptake

* Cessation of bile flow from obstruction, hepatic dysfunction

- ***Primary Mucosal Cell Abnormalities***
- **Defective terminal digestion**,

* **Bacterial overgrowth, with brush border damage**

- **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.

- **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 T.G from the epithelium to the circulation, the fat will appear as vacuoles inside the epithelial cells.

- ***Reduced Small Intestinal Surface Area***
- ***short gut syndrome following surgical resection***
- ***Crohn's disease***

- ***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:

- Glutean 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, Ig A antiendomysial autoantibodies and Ig A anti tissue transglutaminase antibodies which is diagnostic.
- There is strong genetic susceptibility :95%of patients HLA-DQ2, HLA-DQ8
- Early exposure of the immature immune system of the infant to high level of gliadin is a prominent cofactor for development of celiac disease later in life.

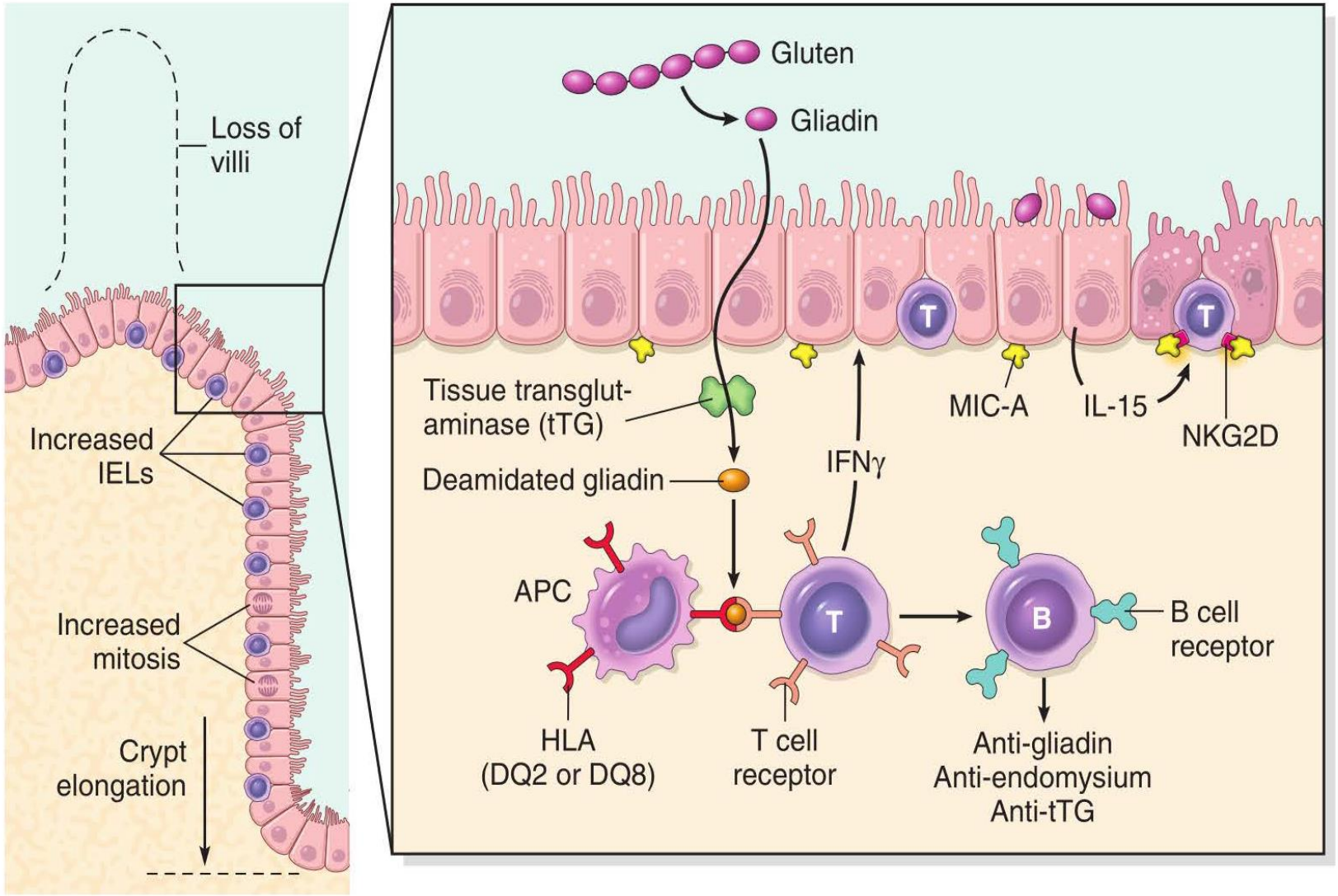


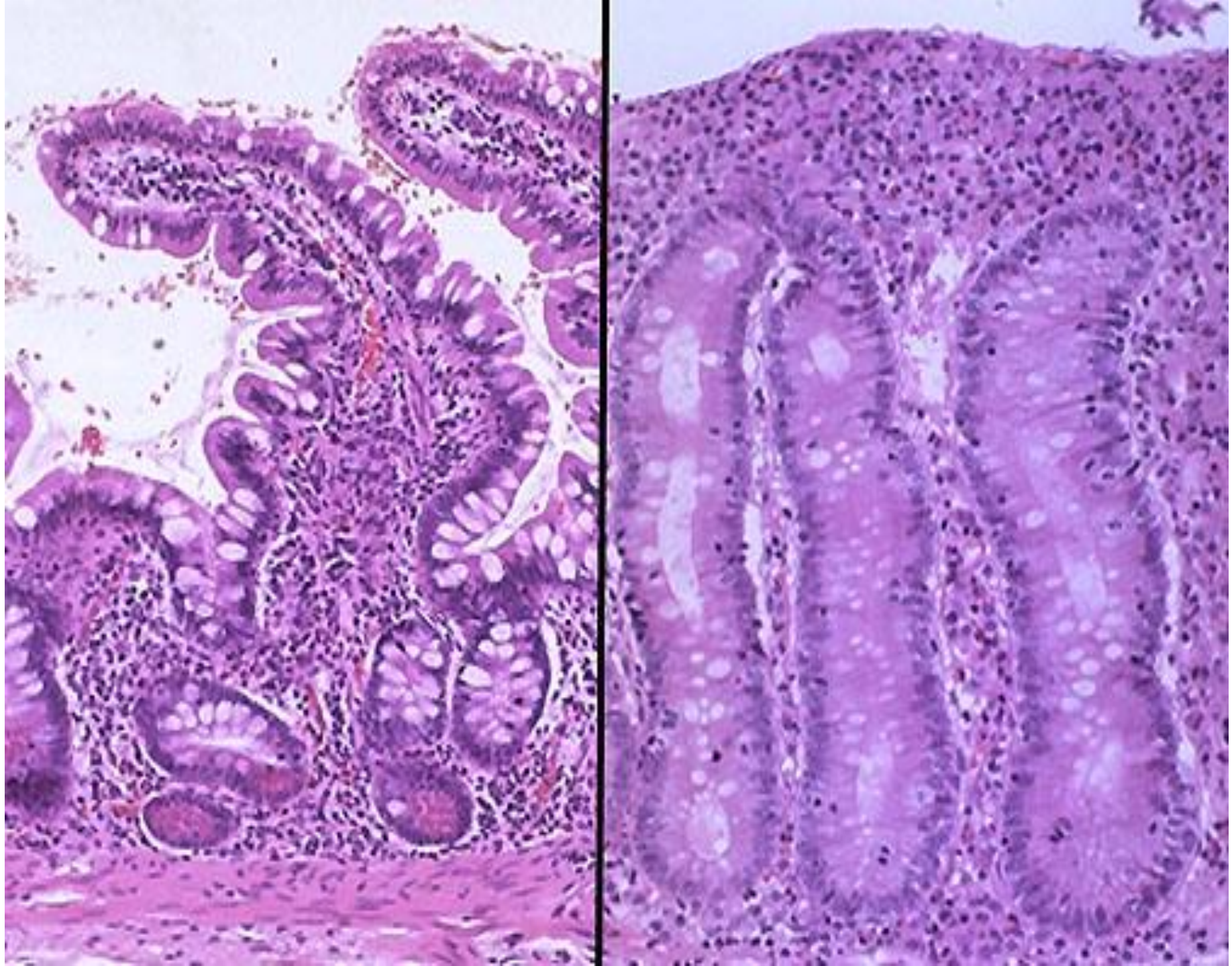
Figure 17-25 The left panel illustrates the morphologic alterations that may be present celiac disease, including villous atrophy, increased numbers of intraepithelial lymphocytes (IELs), and epithelial proliferation with crypt elongation (compare to Fig. 17-26). The right panel depicts a model for the pathogenesis of celiac disease. Note that both innate (CD8+ intraepithelial T cells, activated by IL 15) and adaptive (CD4+ T cells, and B cells sensitization to gliadin) immune mechanisms are involved in the tissue responses to gliadin.

- ***Microscopically:***

1-increase intraepithelial lymphocytes and lymphocyte and plasma cell infiltration of the lamina propria.

2-Normal villi---then decrease in villous height …subtotal villous atrophy---total villous atrophy.

3- Crypt hyperplasia



Celiac disease : Microscopically:

1-increase intraepithelial lymphocytes (IEL) and lymphocyte and plasma cell infiltration of the lamina propria.
2-Normal villi---then decrease in villous height …subtotal villous atrophy---total villous atrophy.
3- Crypt hyperplasia

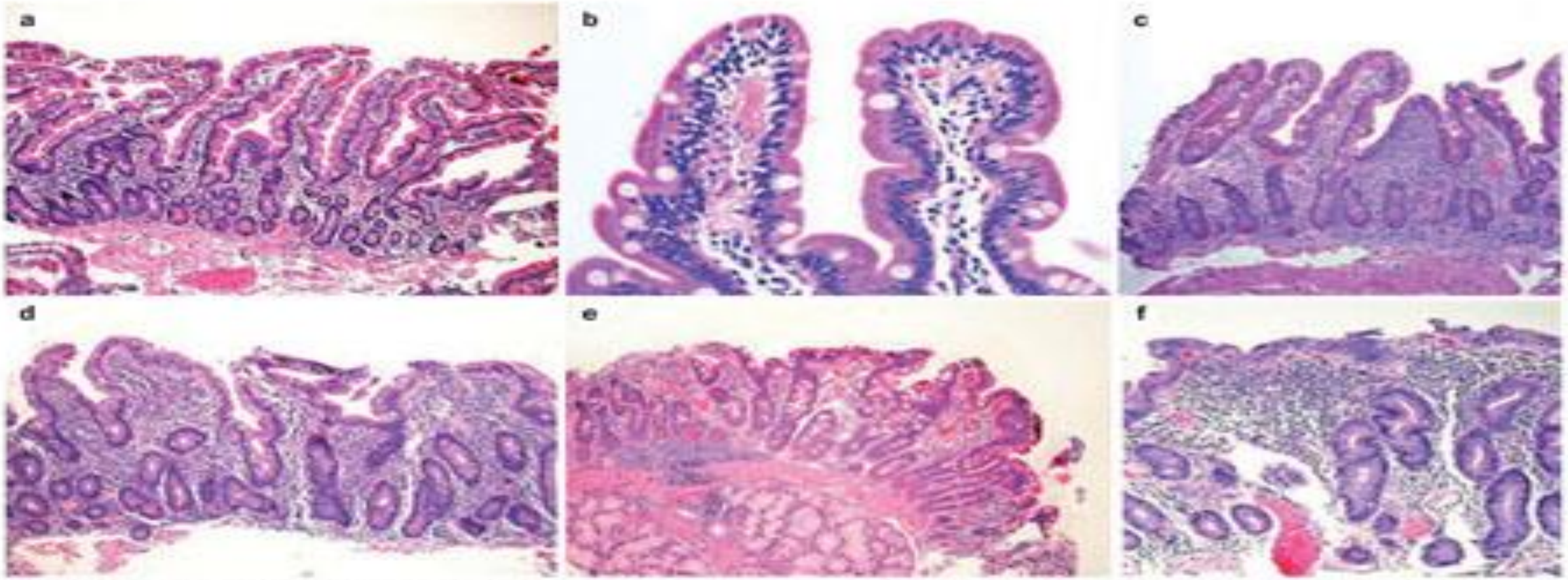


Figure 2 | Histological features of coeliac disease. Coeliac disease enteropathy has a wide spectrum of severity that can vary from **a** | and **b** | the mildest infiltration of the epithelium with lymphocytes and preserved villous architecture, to **c** | crypt hyperplasia alone and progressive degrees in villous atrophy from **d** | mild blunting, **e** | moderate villous atrophy and **f** | total villous atrophy. © Mayo Clinic.

Clinical features:

the patient presented with:

- diarrhea
- weight loss
- anemia
- growth retardation in children
- - ***Complication:***

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

- ***Tropical sprue***
- 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

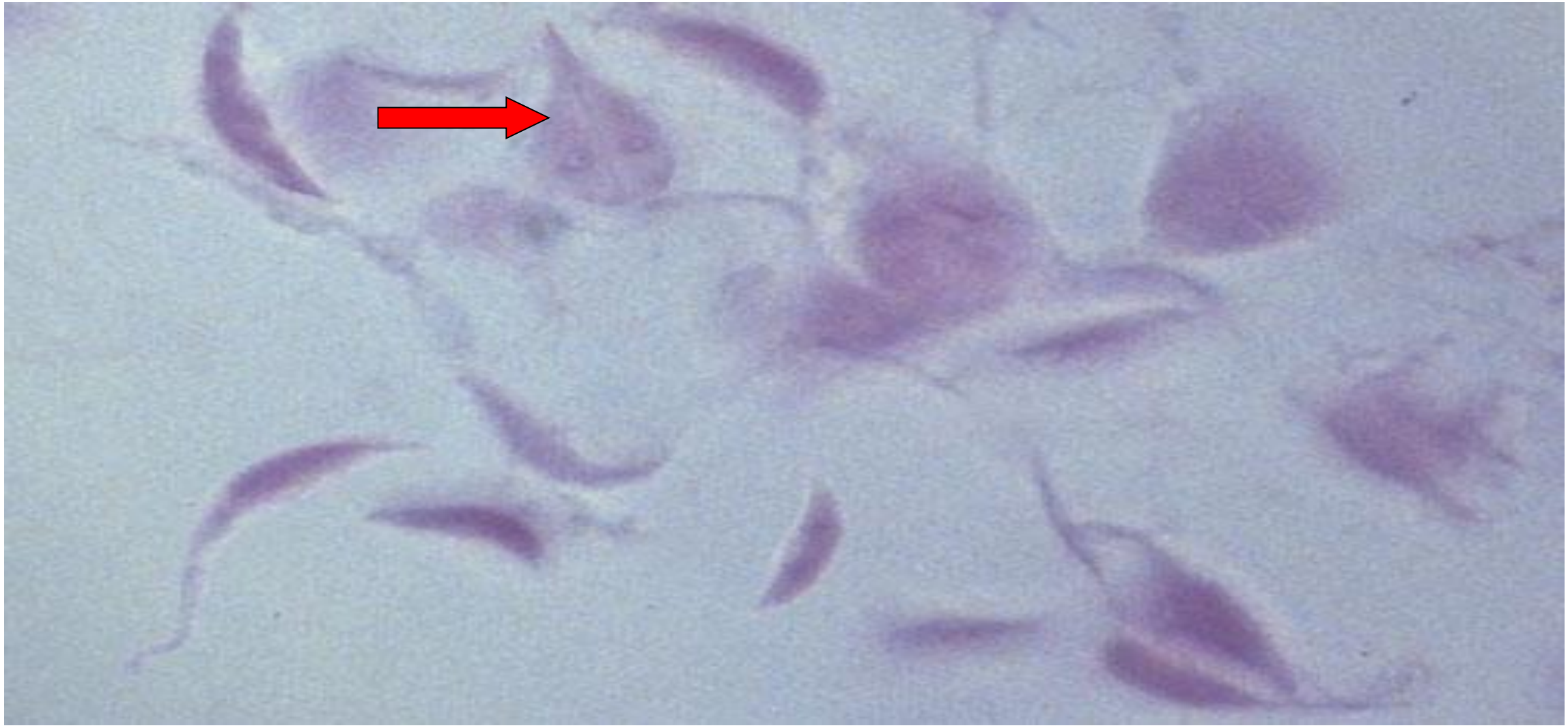
Lymphatic Obstruction

- Lymphoma
- Tuberculosis and tuberculous lymphadenitis

Infection

- ***Acute infectious enteritis***
- ***Parasitic infestation(giardiasis)***

Infection by Giardia



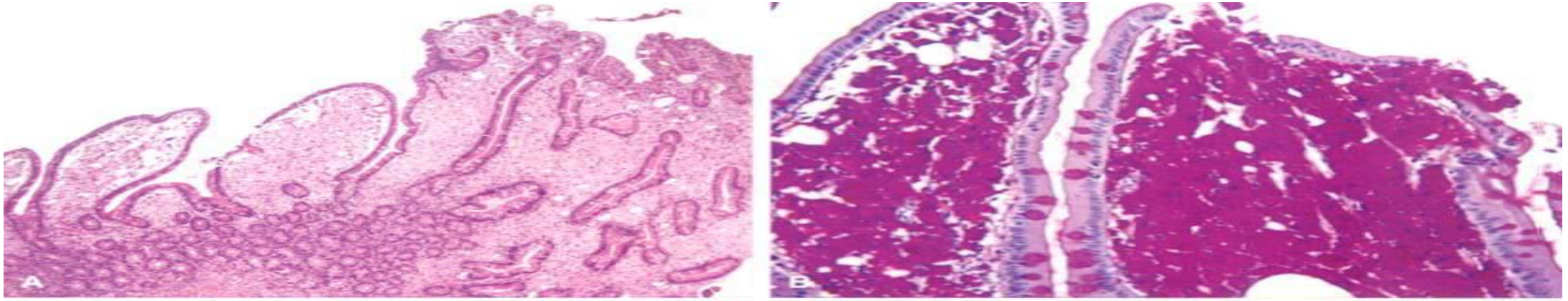
- ***Whipple disease*** A rare systemic disease, may involve any organ in the body
- ***Causative agent*:** Gram +ve actinomycete (rod shape bacilli) ***(Tropheryma whippelii)***
- ***Clinical features:***

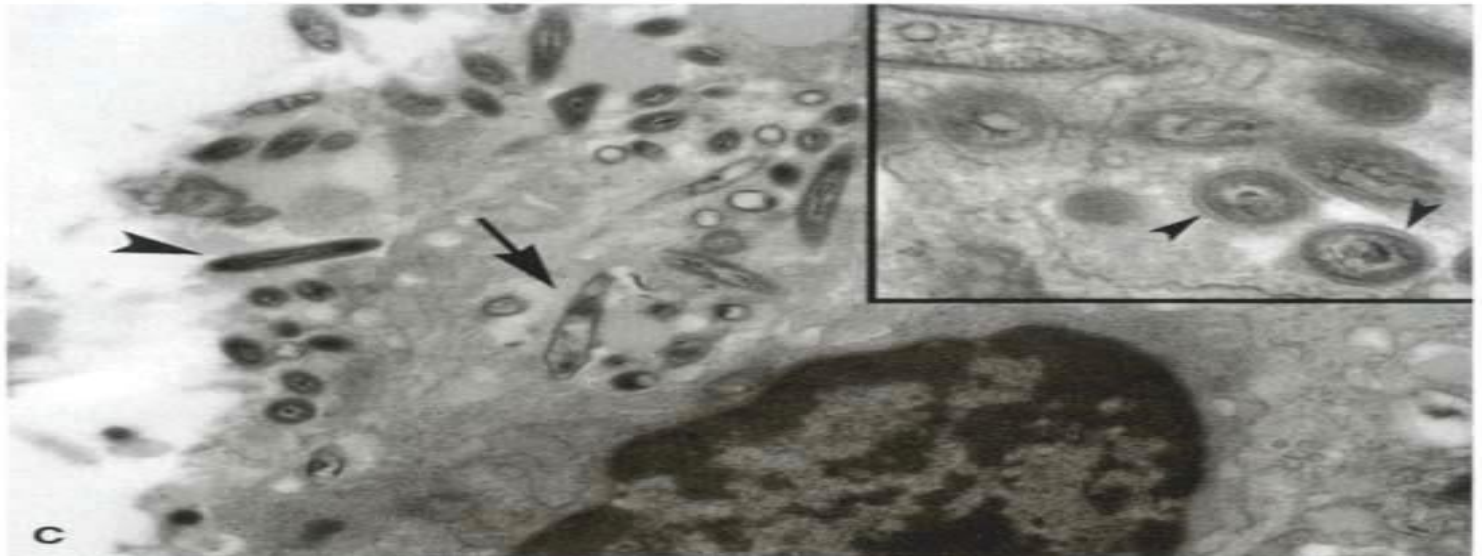
Diarrhea with other organ involvement like CNS and joints.

- ***Microscopically:***

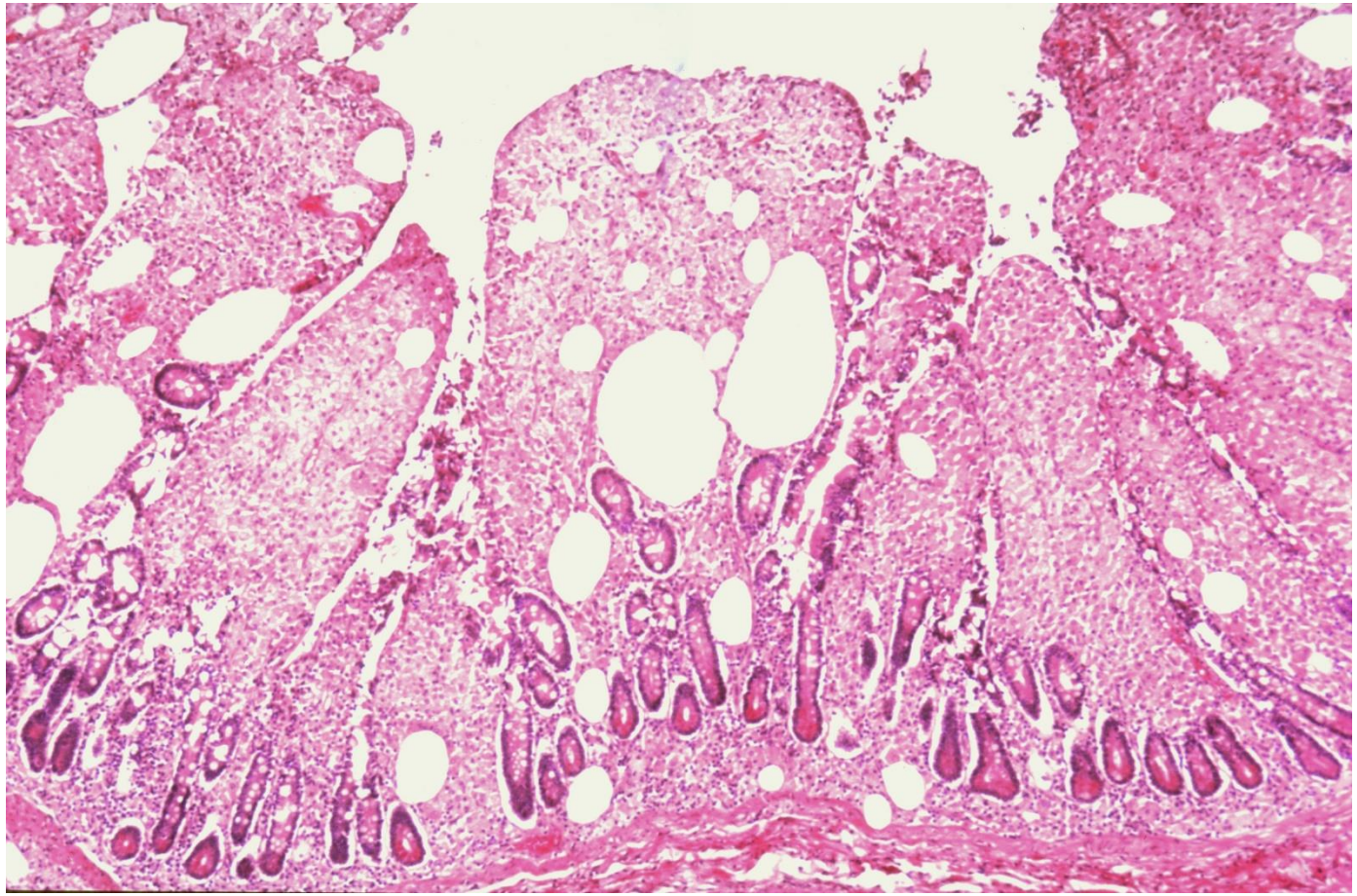
The villi of the small intestine are filled with macrophages containing PAS +ve granules and rod shape bacilli under electron mic.

Whipple disease. *A,* Note 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 crosssectional profiles of bacilli and their cell walls (small *arrows*).

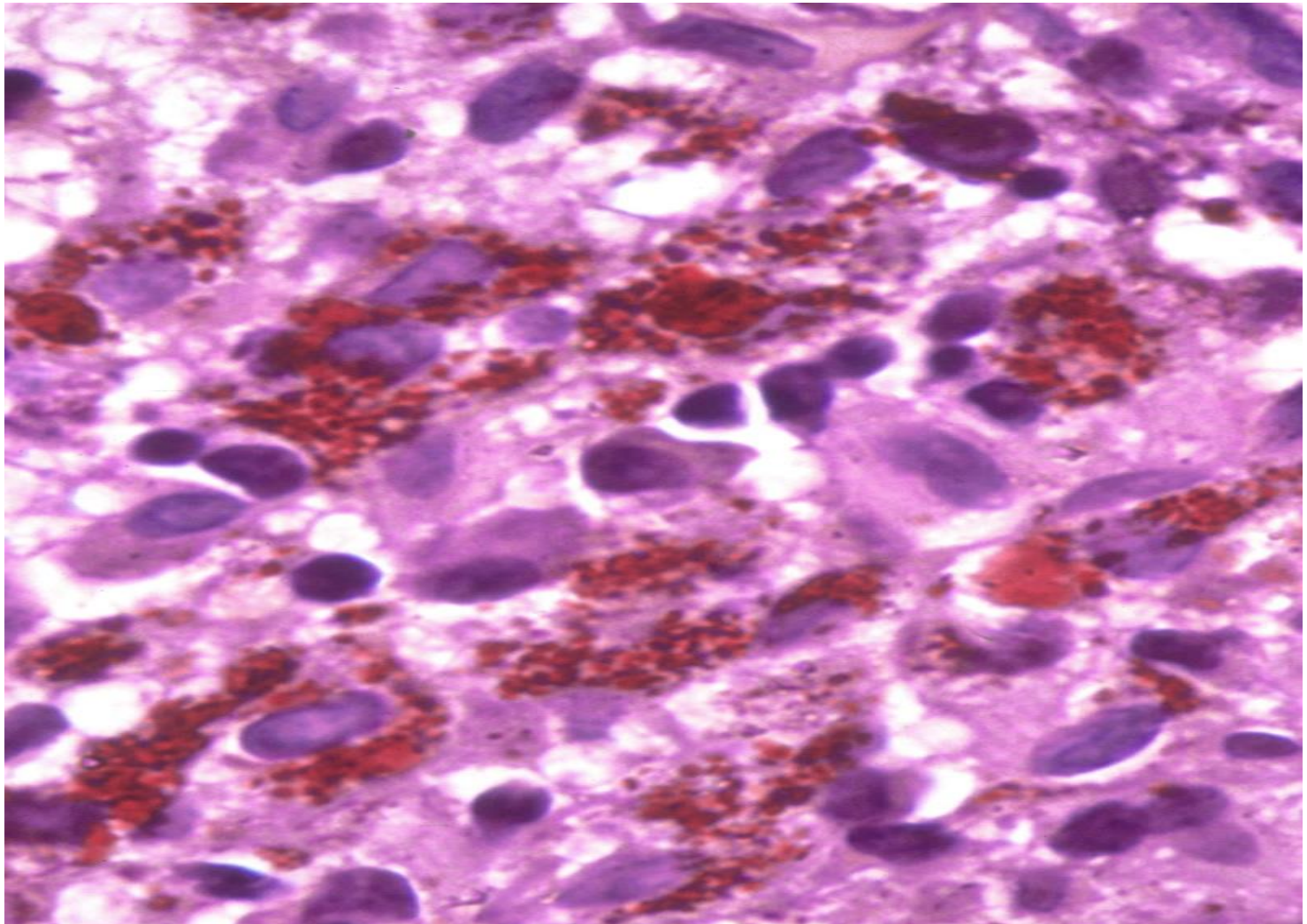




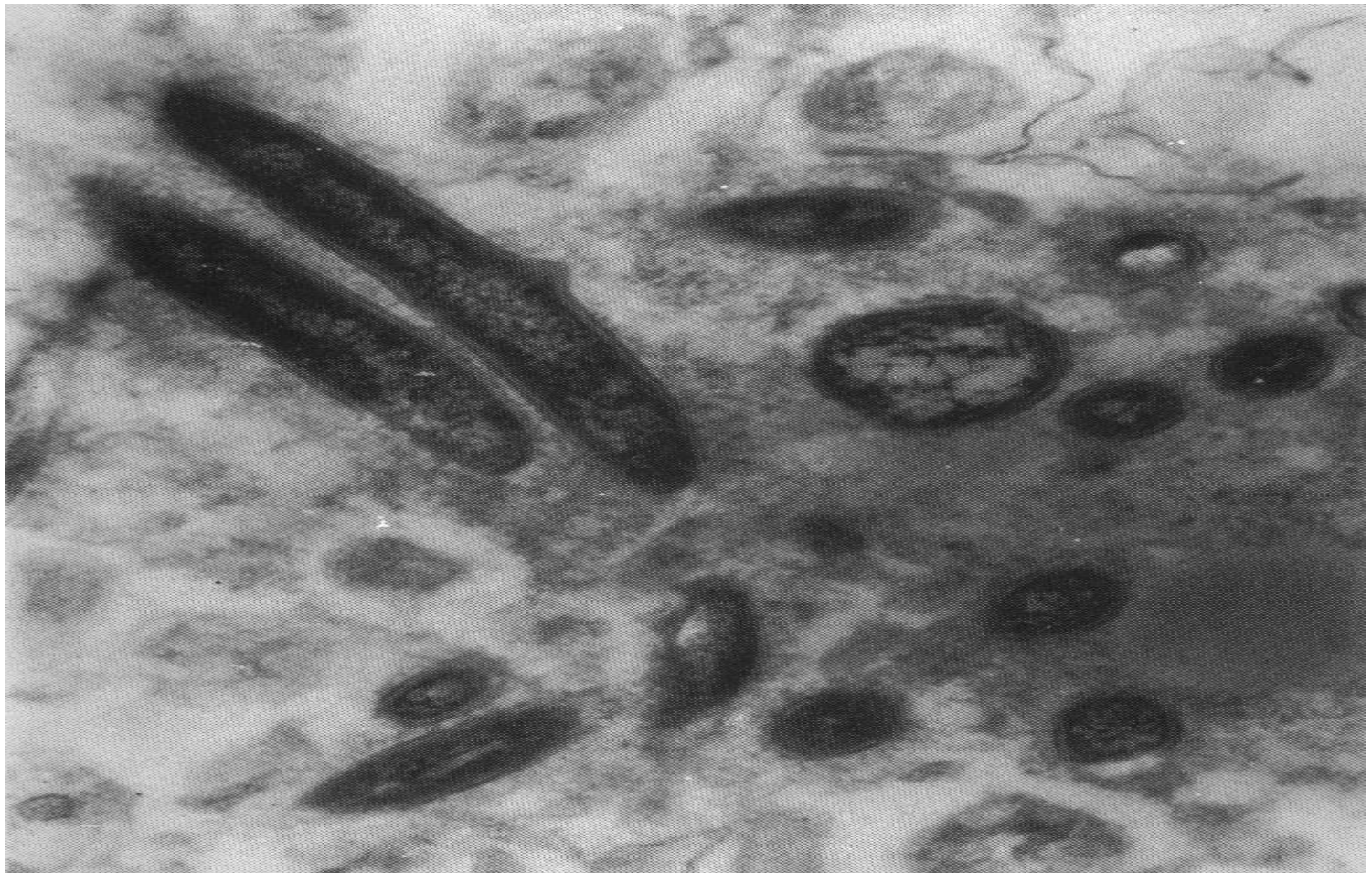
jejunal mucosaThe lamina propria is packed with large, pale-staining macrophages. Dilated mucosal lymphatics are prominent.



Macrophage with cytoplasm that is filled with large glycoprotein granules that stain strongly with periodic acid Schiff. These granules correspond to lysosomes engorged with bacilli in various stages of degeneration



electron micrograph shows small bacilli in a macrophage.

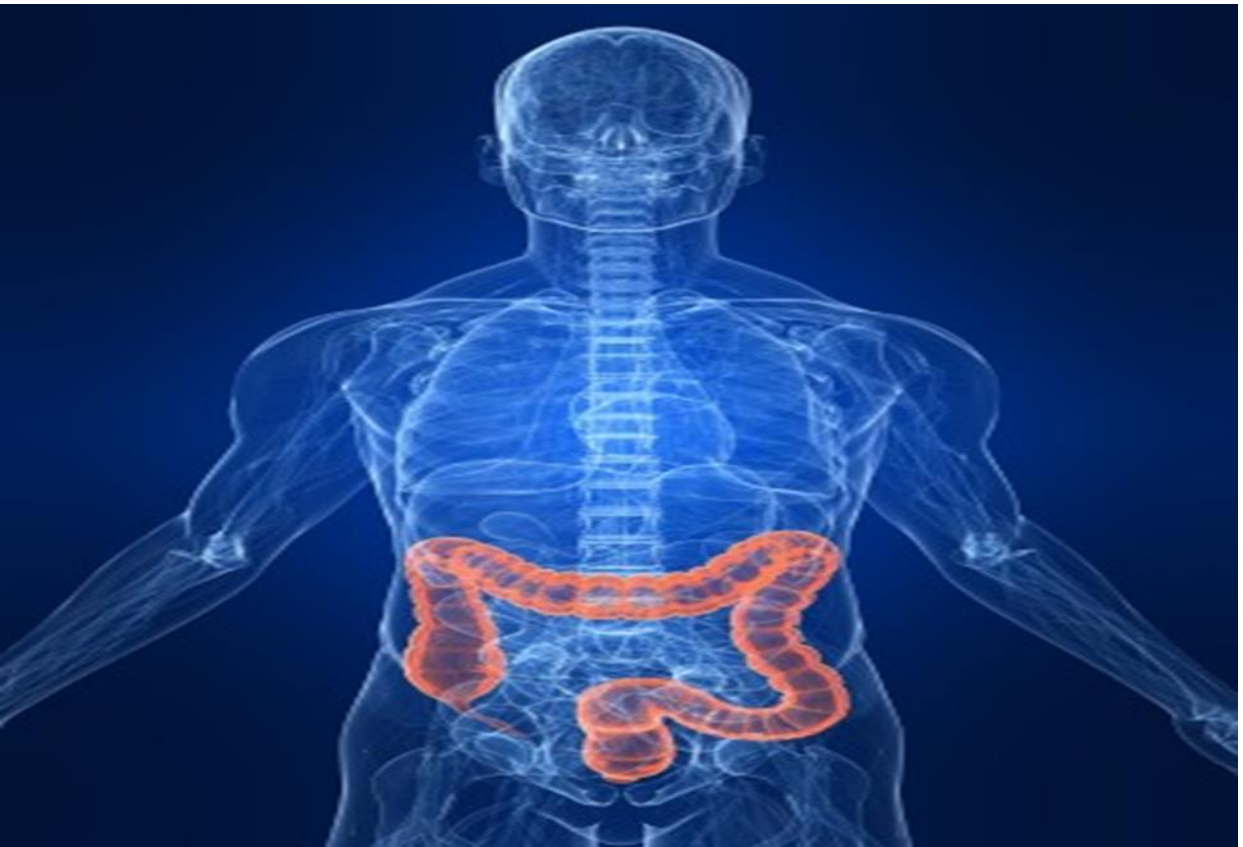


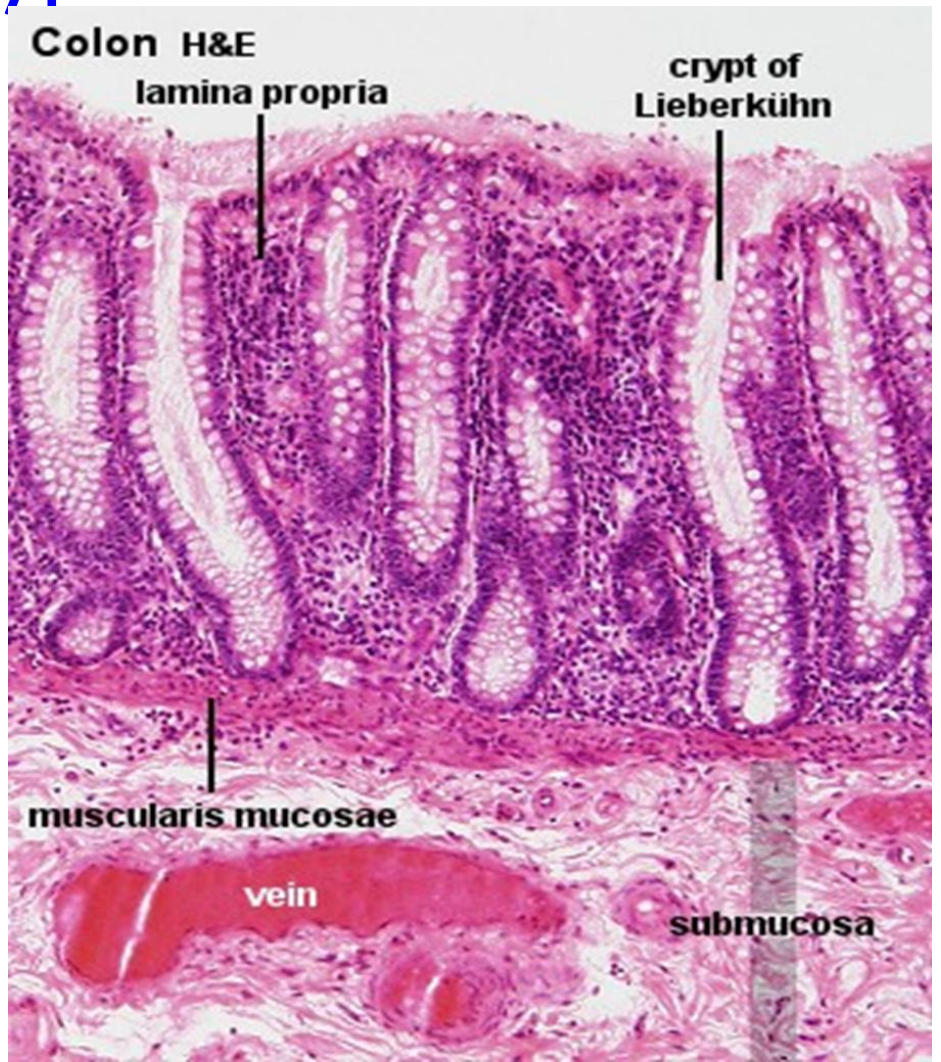
Iatrogenic cause for malabsorption

- Subtotal or total gastrectomy
- Short-gut syndrome, following extensive surgical resection
- Distal ileal resection

Large intestine

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





Idiopathic Inflammatory Bowel Diseases

Two inflammatory disorders of unknown cause affect the GIT, namely, **Crohn** 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 20s)

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

7- Mic:

* There is transmural infiltration by lymphocyte, plasma cells and histiocyte.
* **Non caseating granuloma** presents in 50% of cases at any site from the mucosa to the surrounding structure and even lymph nodes.

- **Clinical features:**

1- Abdominal pain.

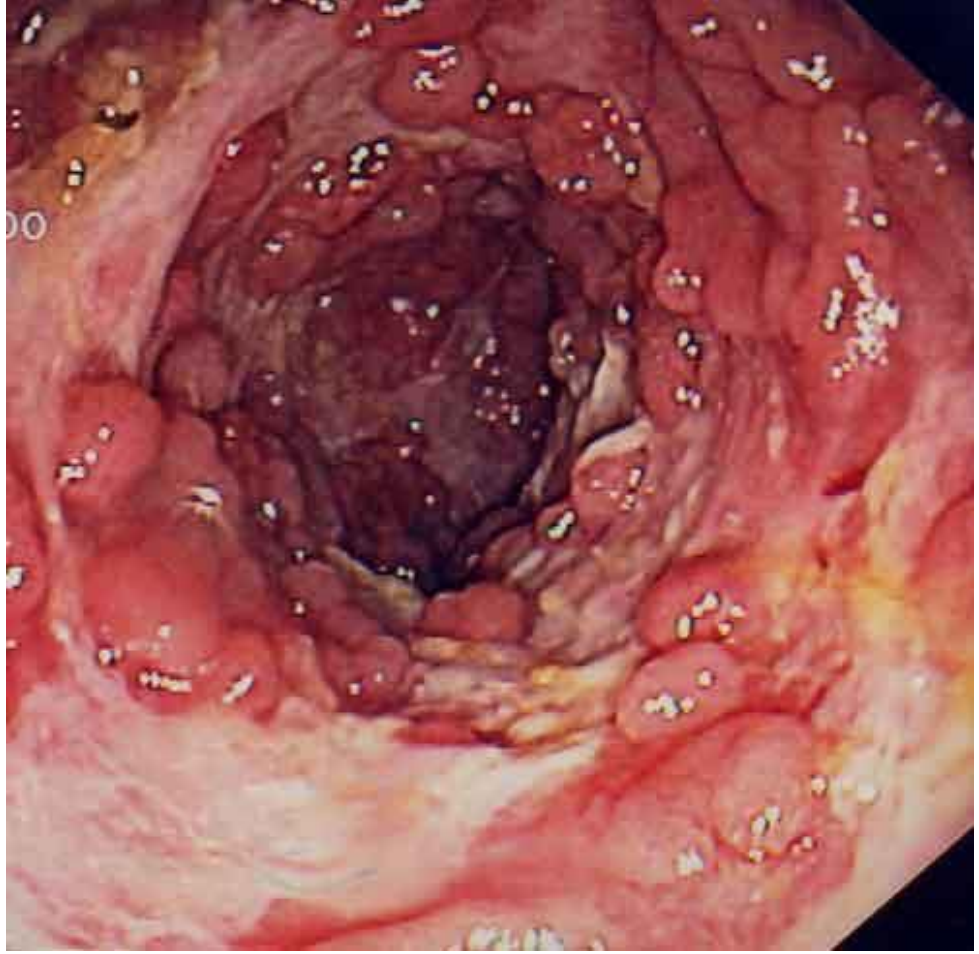
2- Recurrent diarrhea.

3- Generalized malabsorption

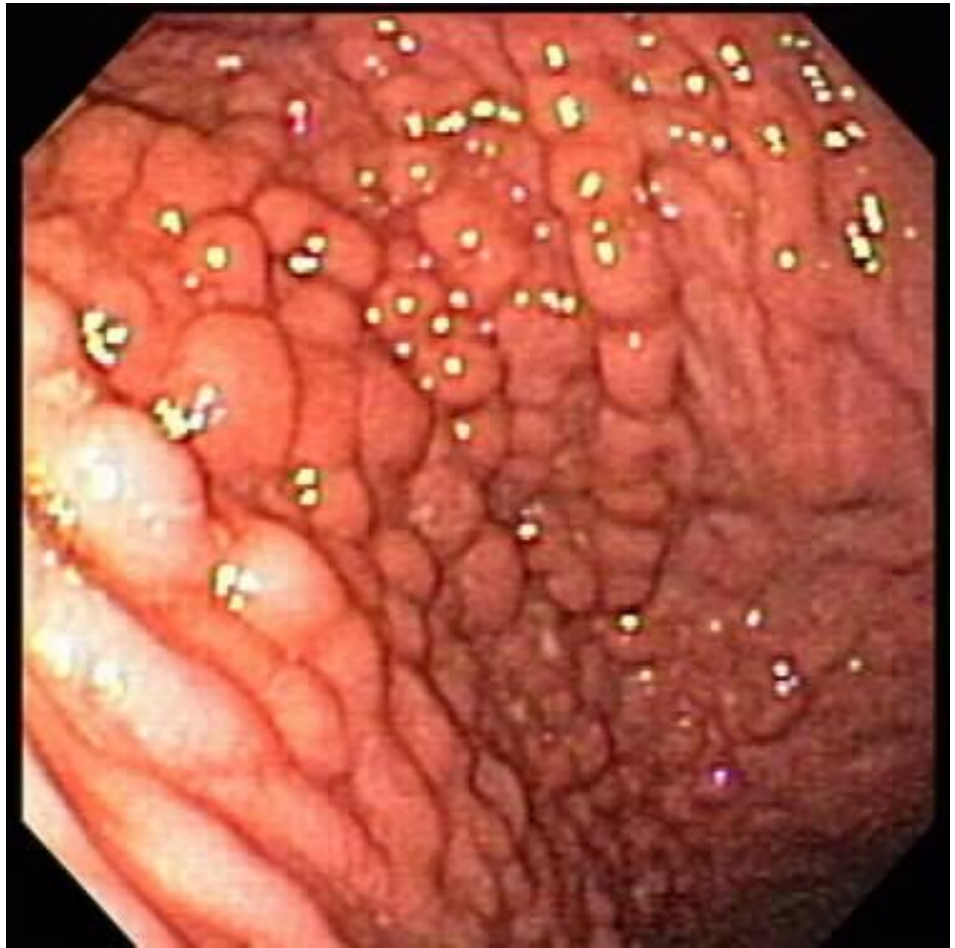
4- Extraintestinal manifestations e.g clubbing of the fingers, sacroiliitis, ankylosing spondylitis

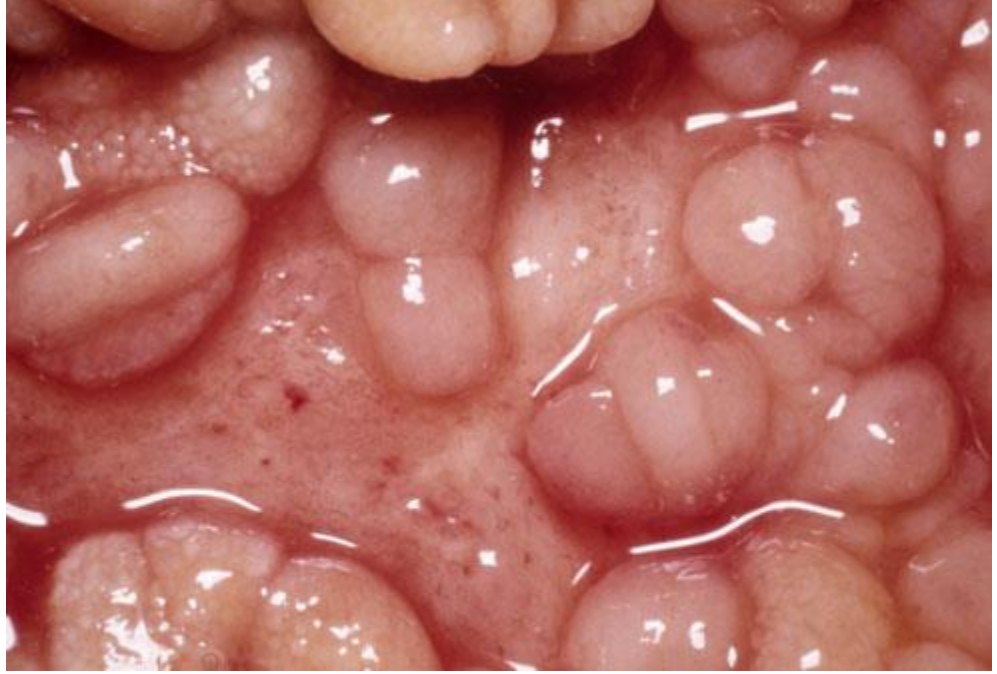
5- Complications which are:

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



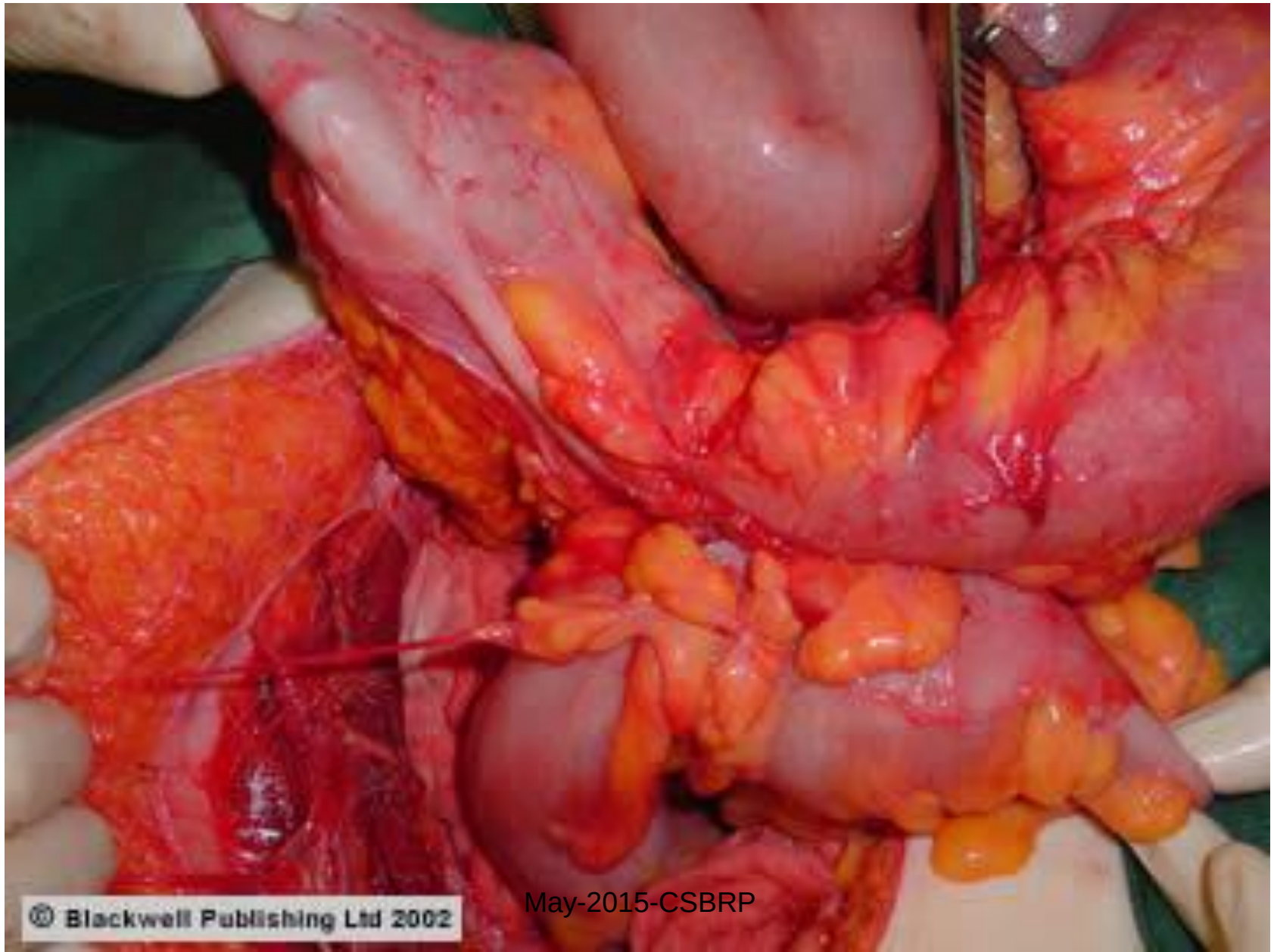
‘Cobble stone’ appearance

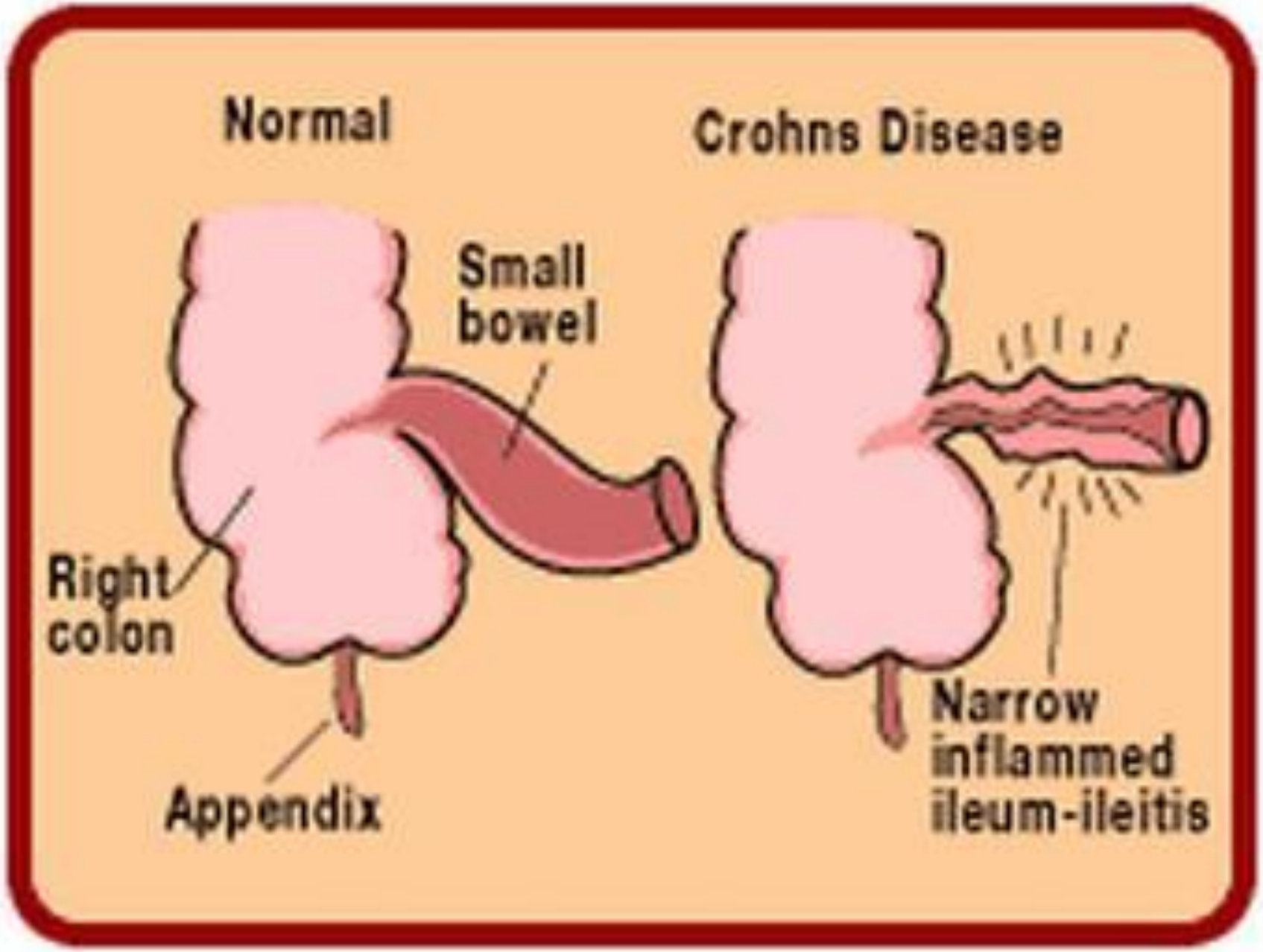


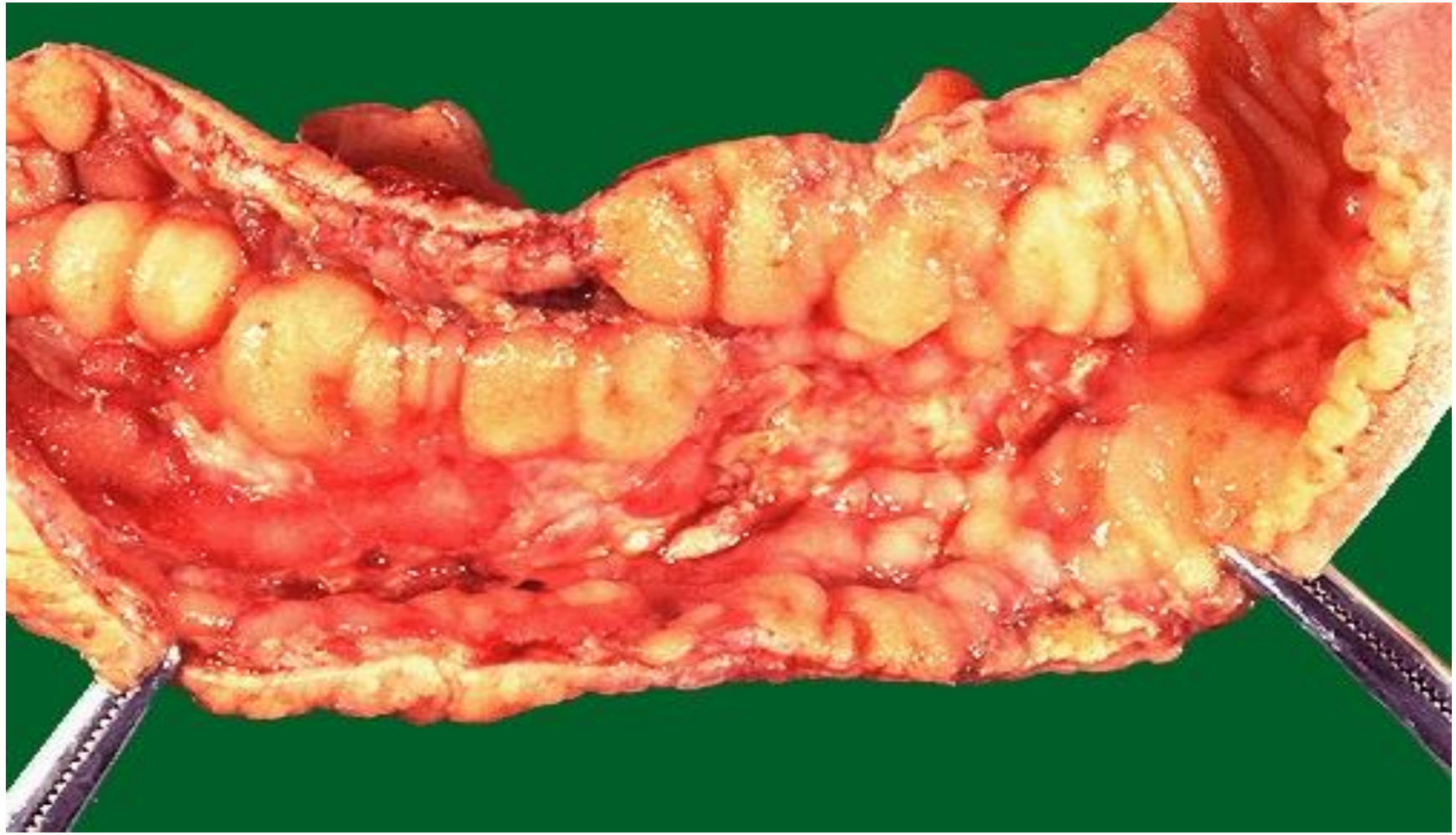


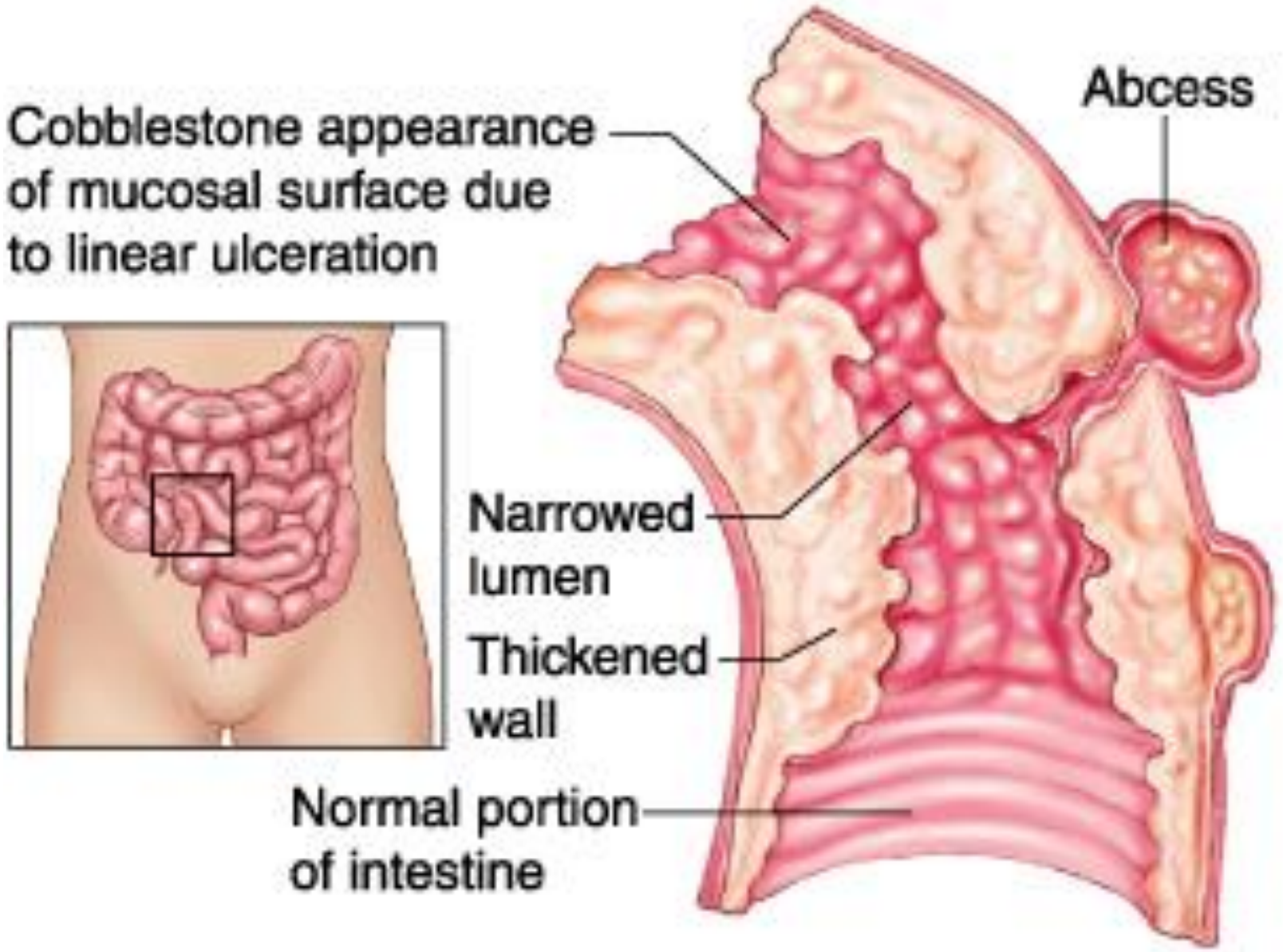
‘Cobble stone’ appearance

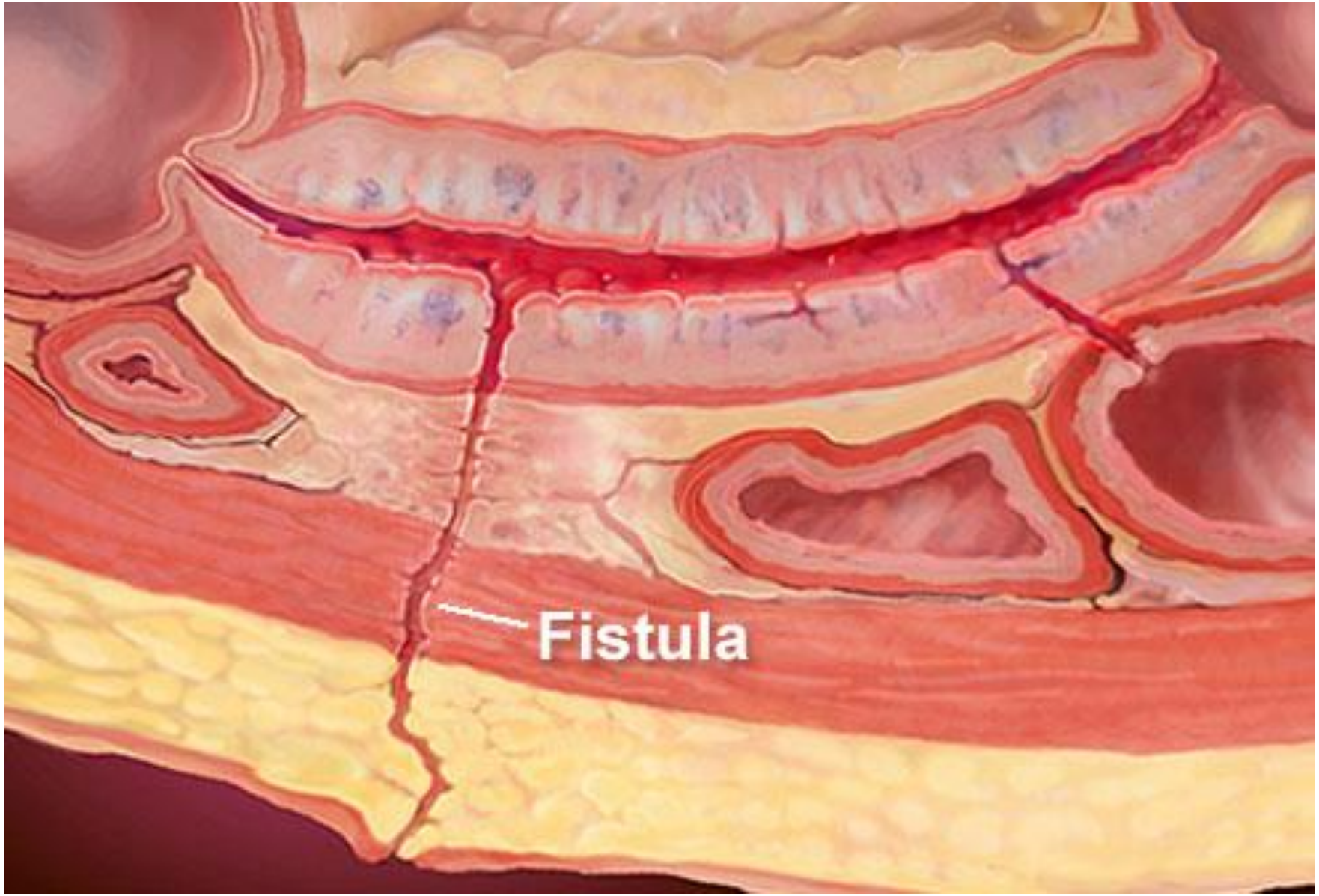
Creeping fat



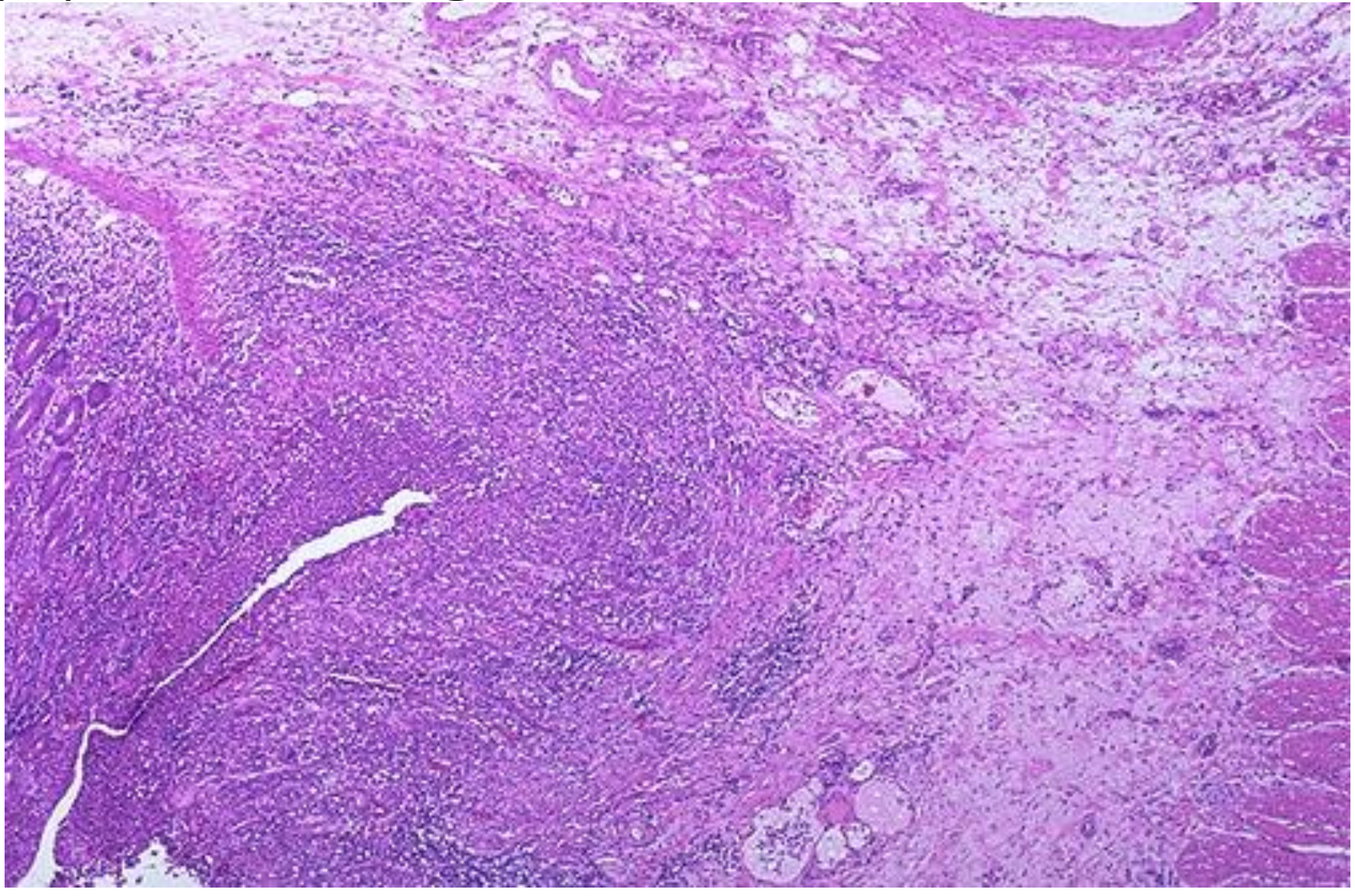

Normal
Crohns Disease
Small bowel
Right colon
Appendix
Narrow inflammed ileum-ileitis



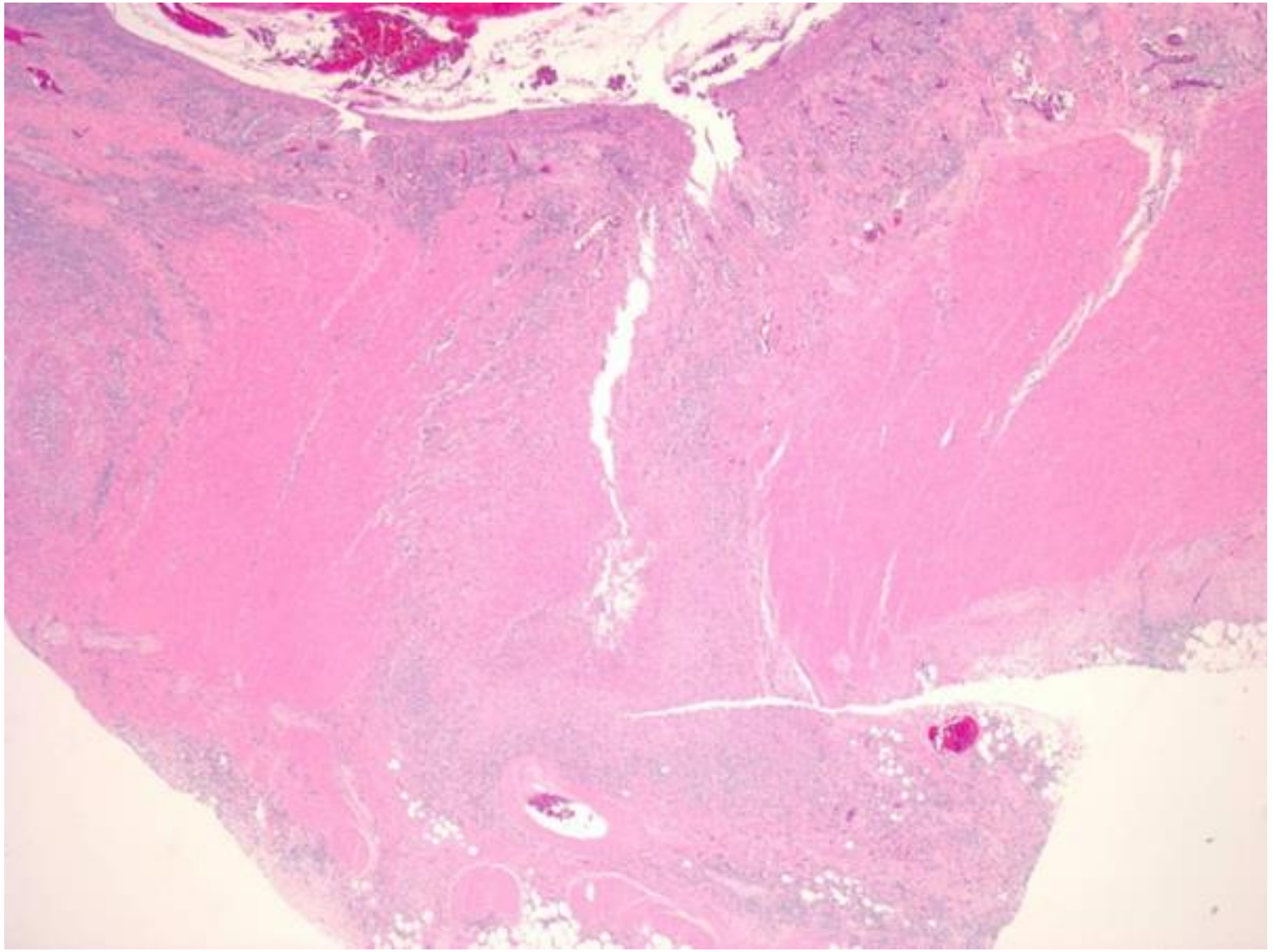

Cobblestone appearance of mucosal surface due to linear ulceration
Abcess
Narrowed lumen
Thickened wall
Normal portion of intestine


Fistula

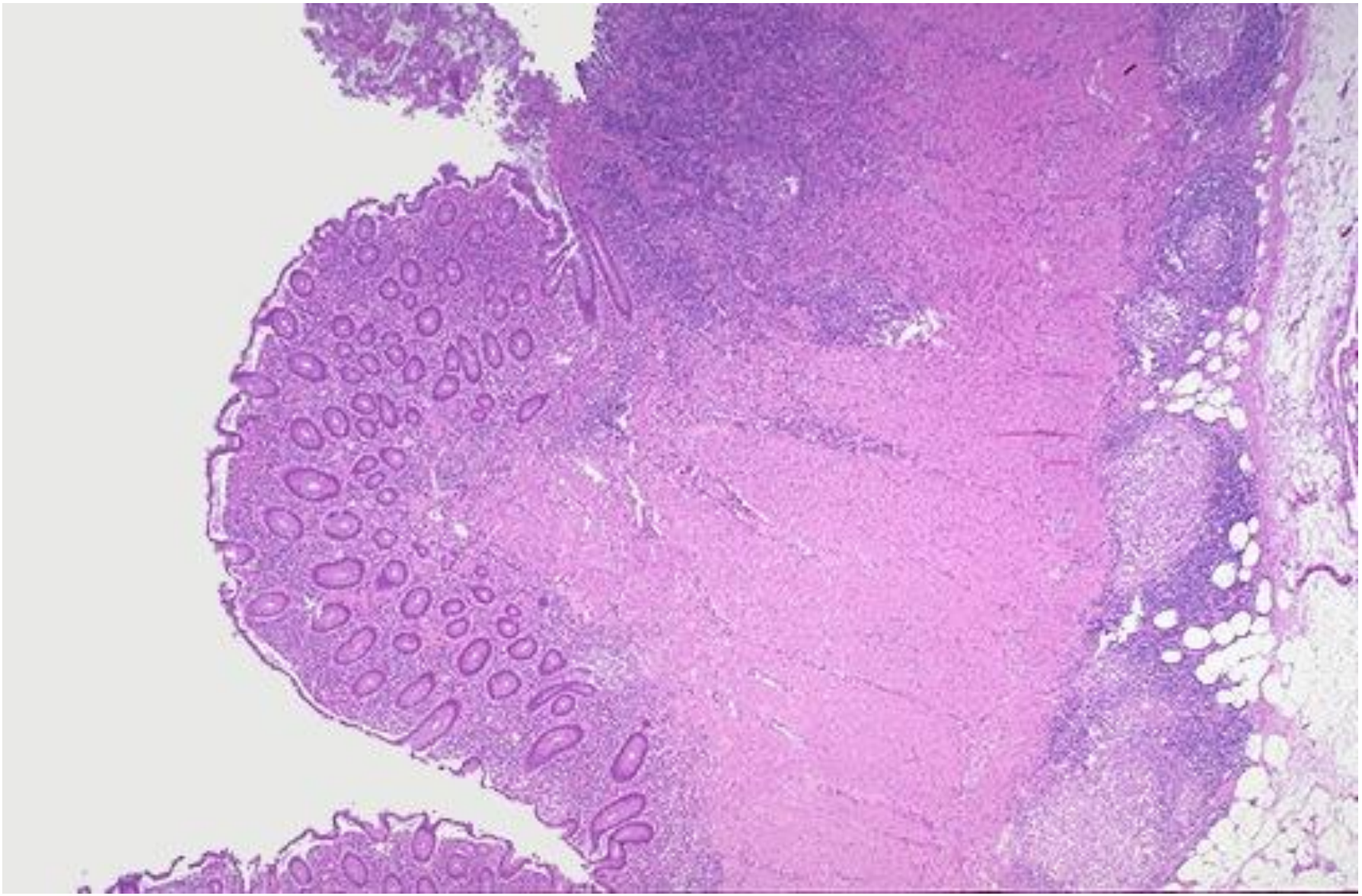
Deep penetrating ulcers



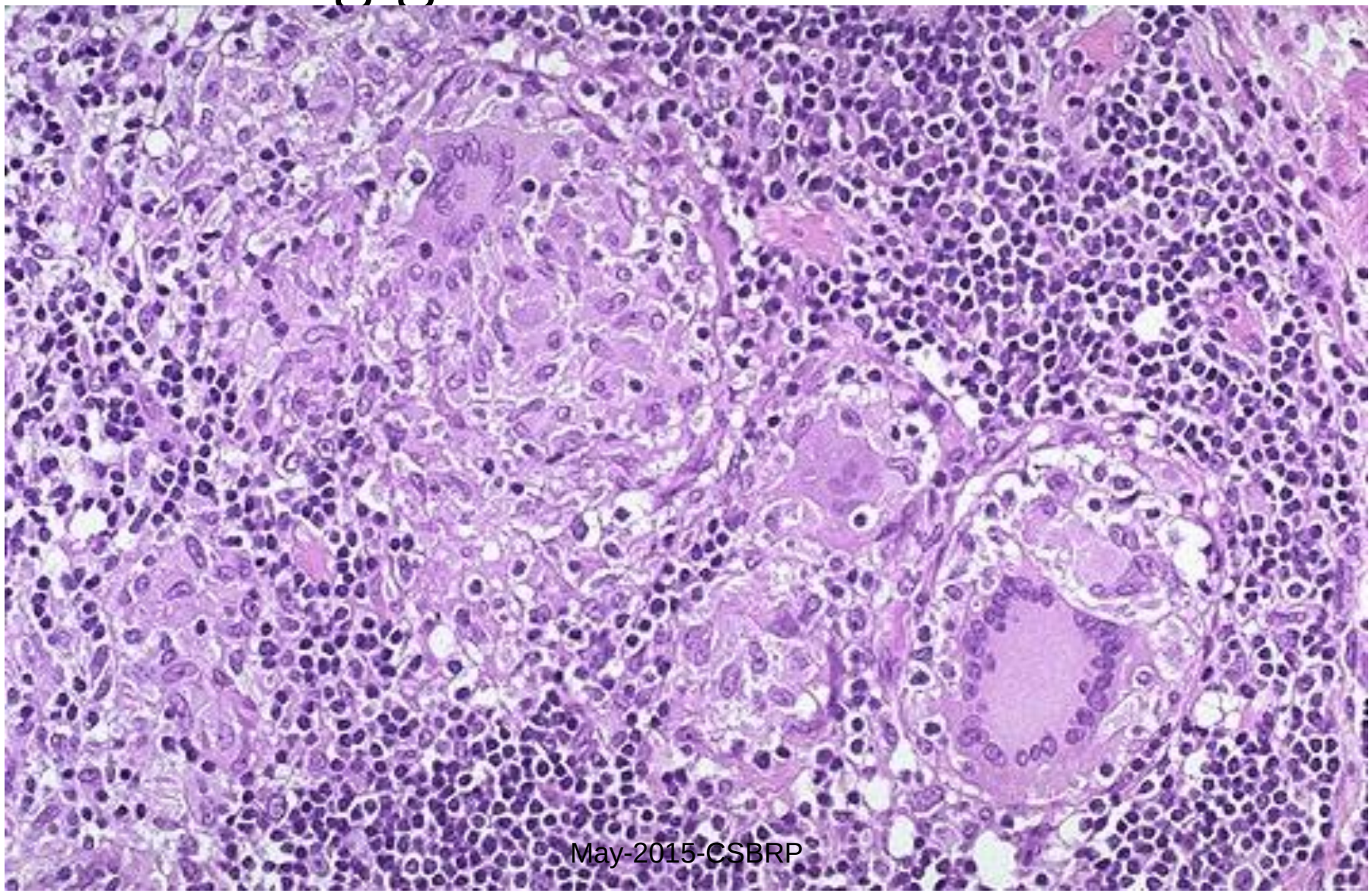
Deep knifelike, fissuring, transmural ulcer in Crohn disease



Transmural inflammation



Non-caseating granulomas



- **Ulcerative colitis**

* Is a chronic disease with remission and relapse presented with bloody diarrhea with 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

.

* The 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**

* Mic:
* 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:**

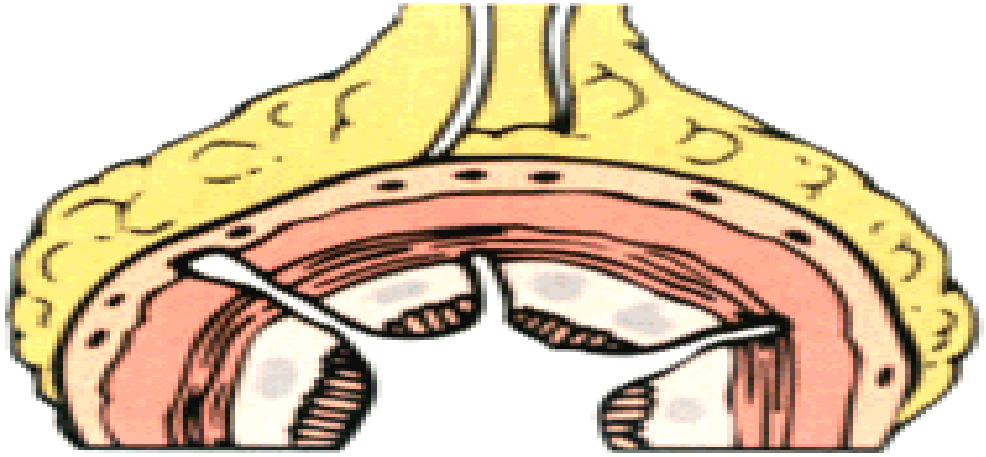
1- massive hemorrhage (bleeding per rectum)

2- perianal and ischiorectal abcesses

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

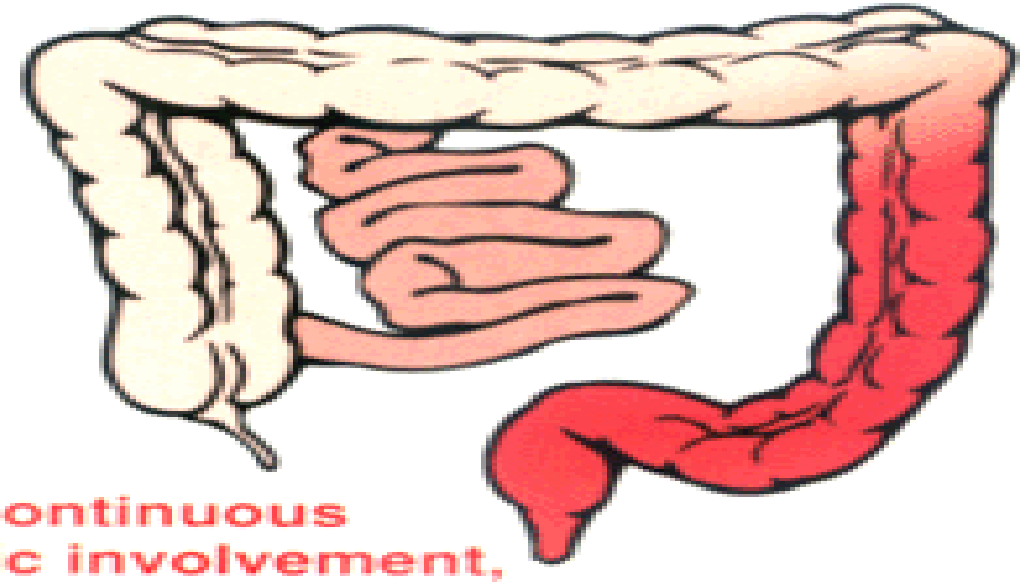
CROHN DISEASE

Skip lesions

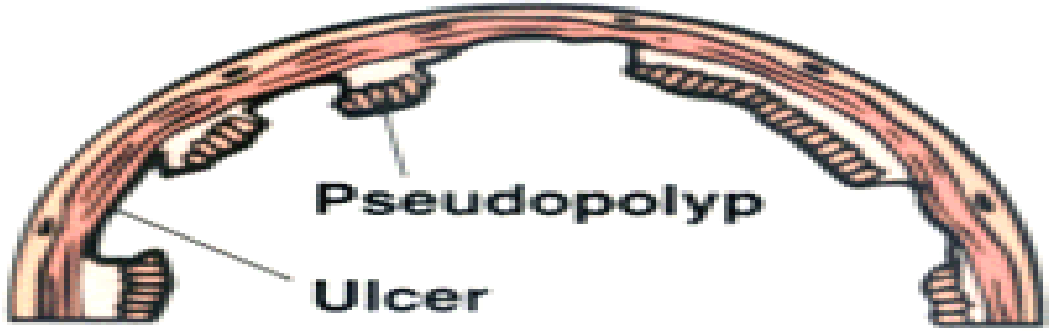


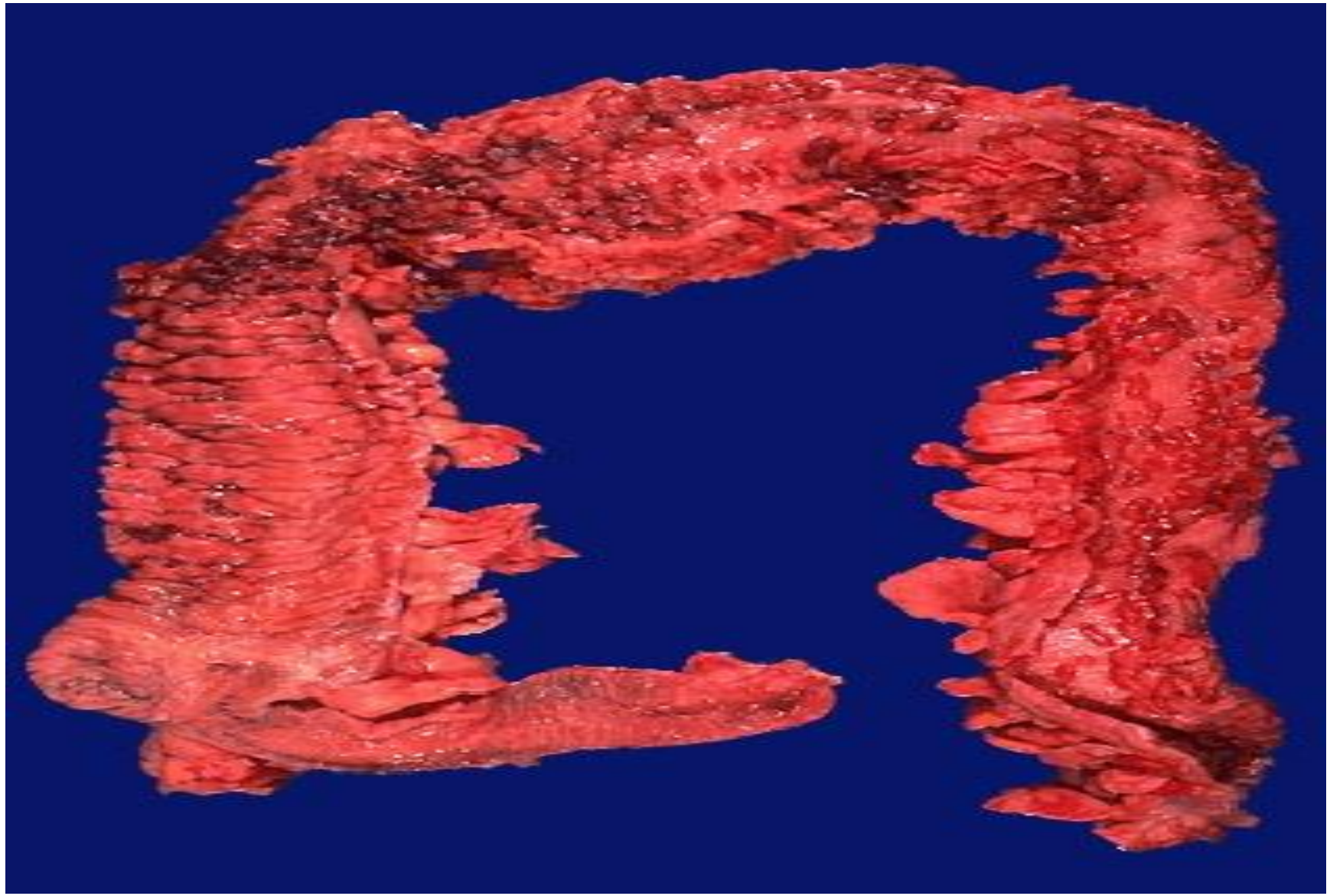
Transmural inflammation
Ulcerations
Fissures

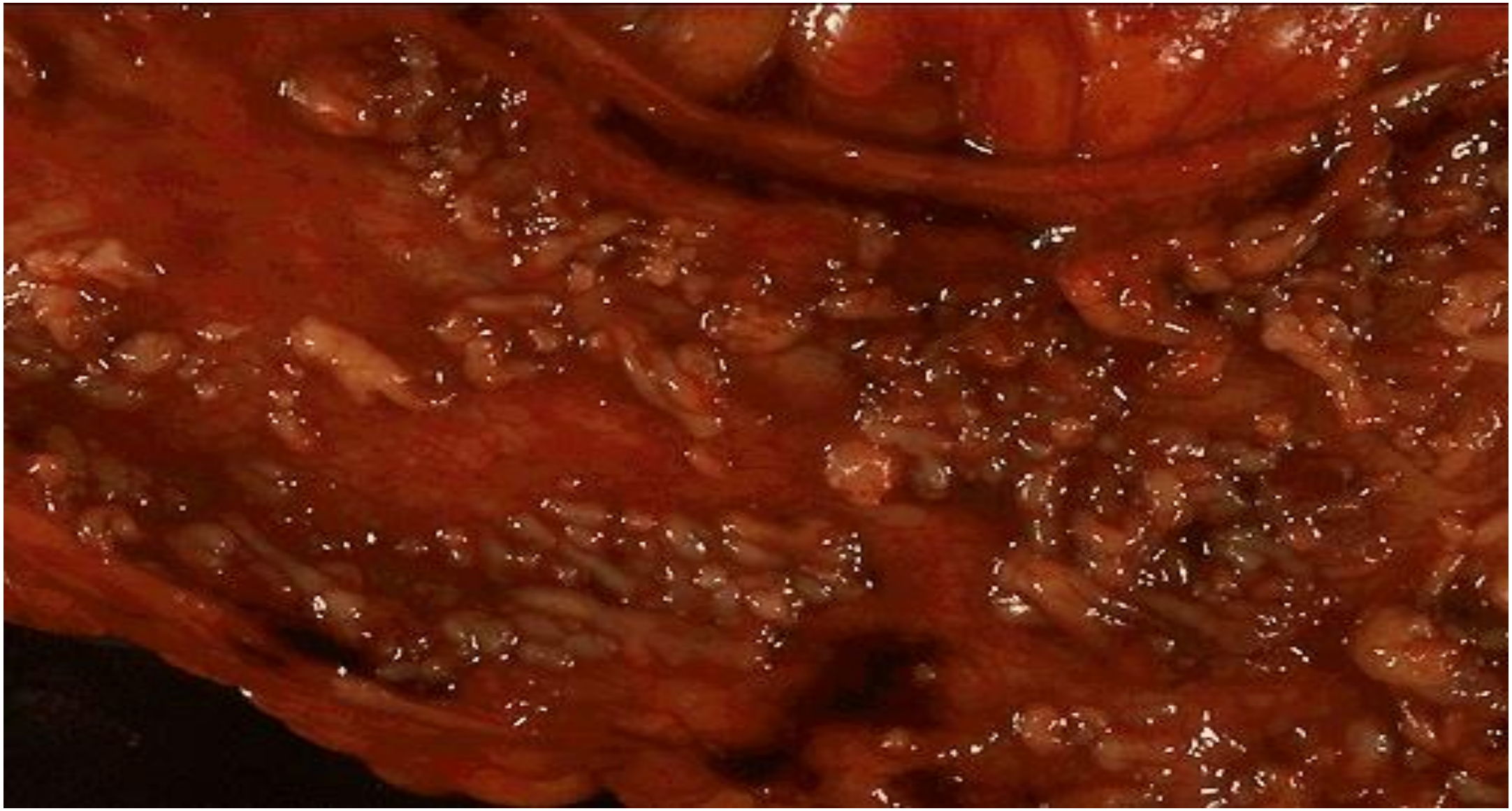
ULCERATIVE COLITIS



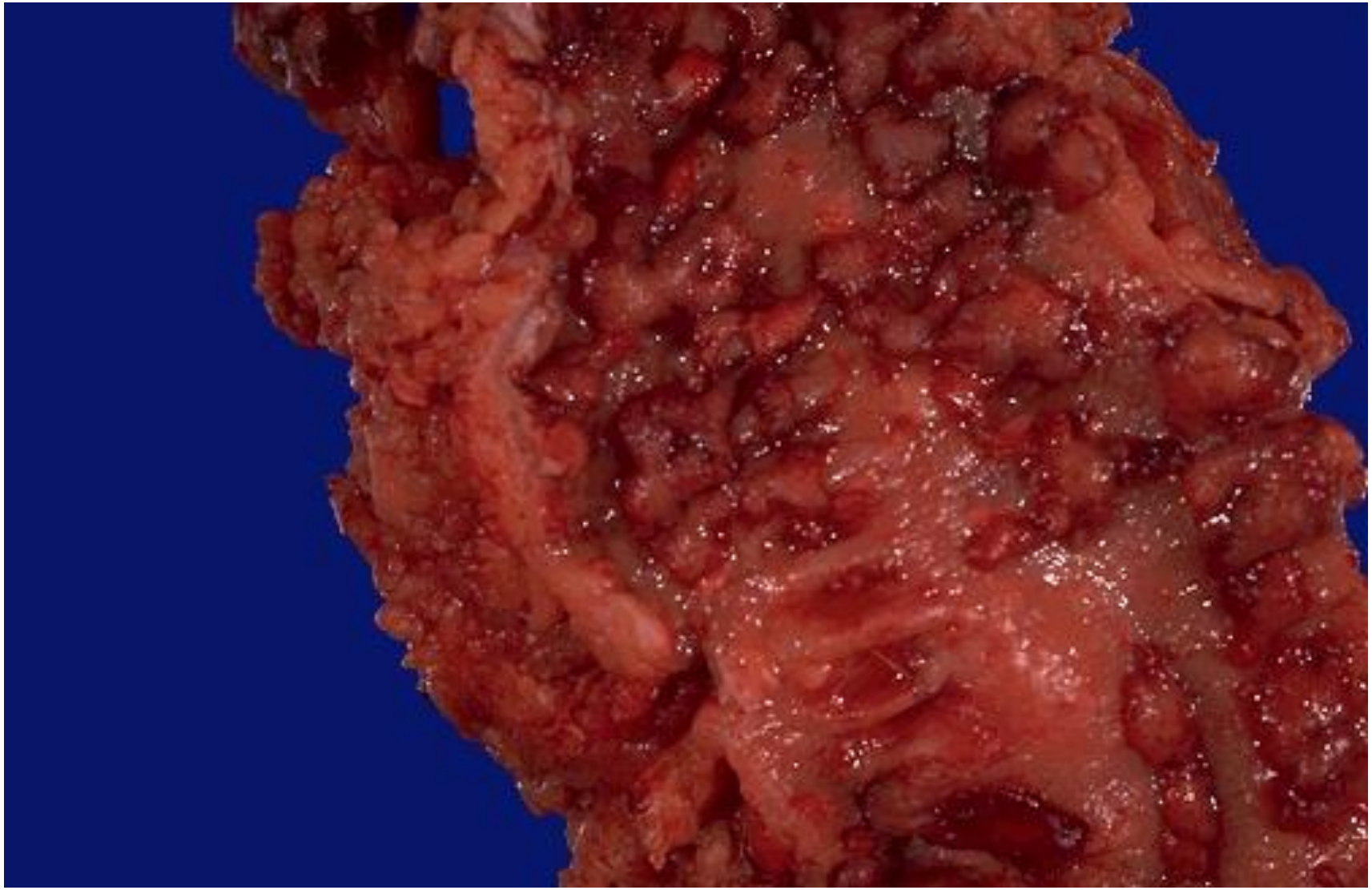
Continuous colonic involvement, beginning in rectum





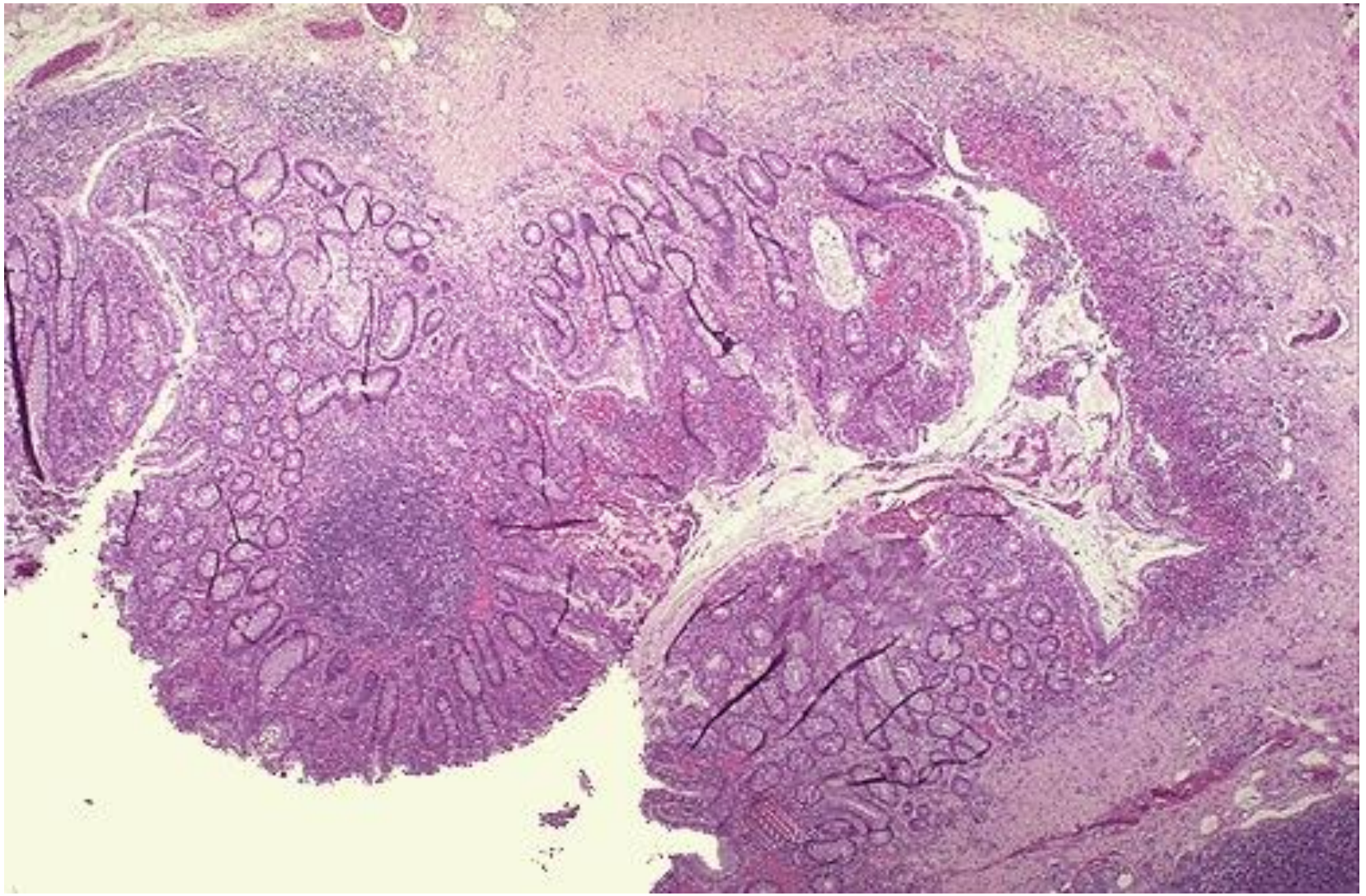


Serpigenous ulcers, mucosal bridges and pseudopolyps

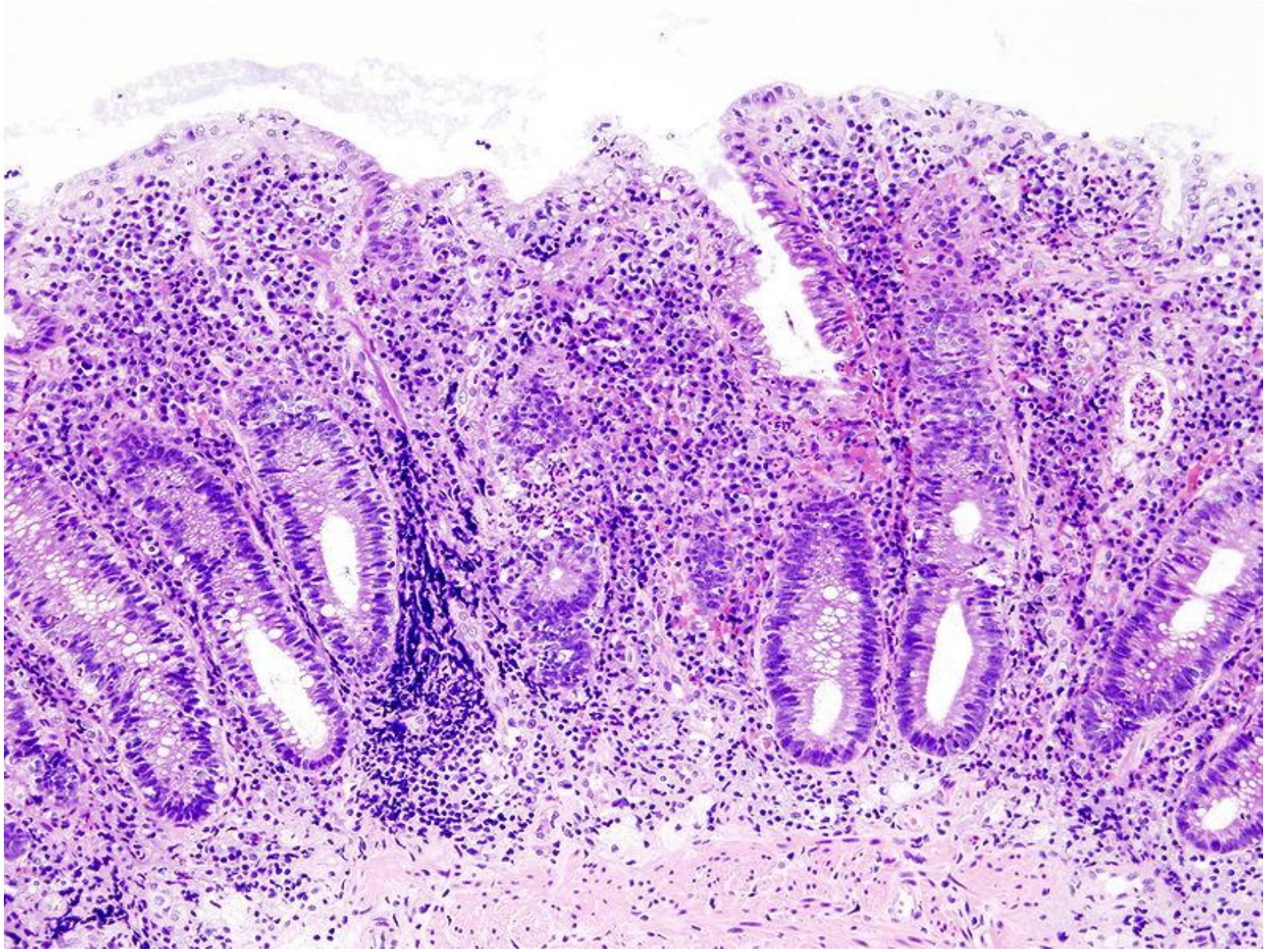


UC - pseudopolyps

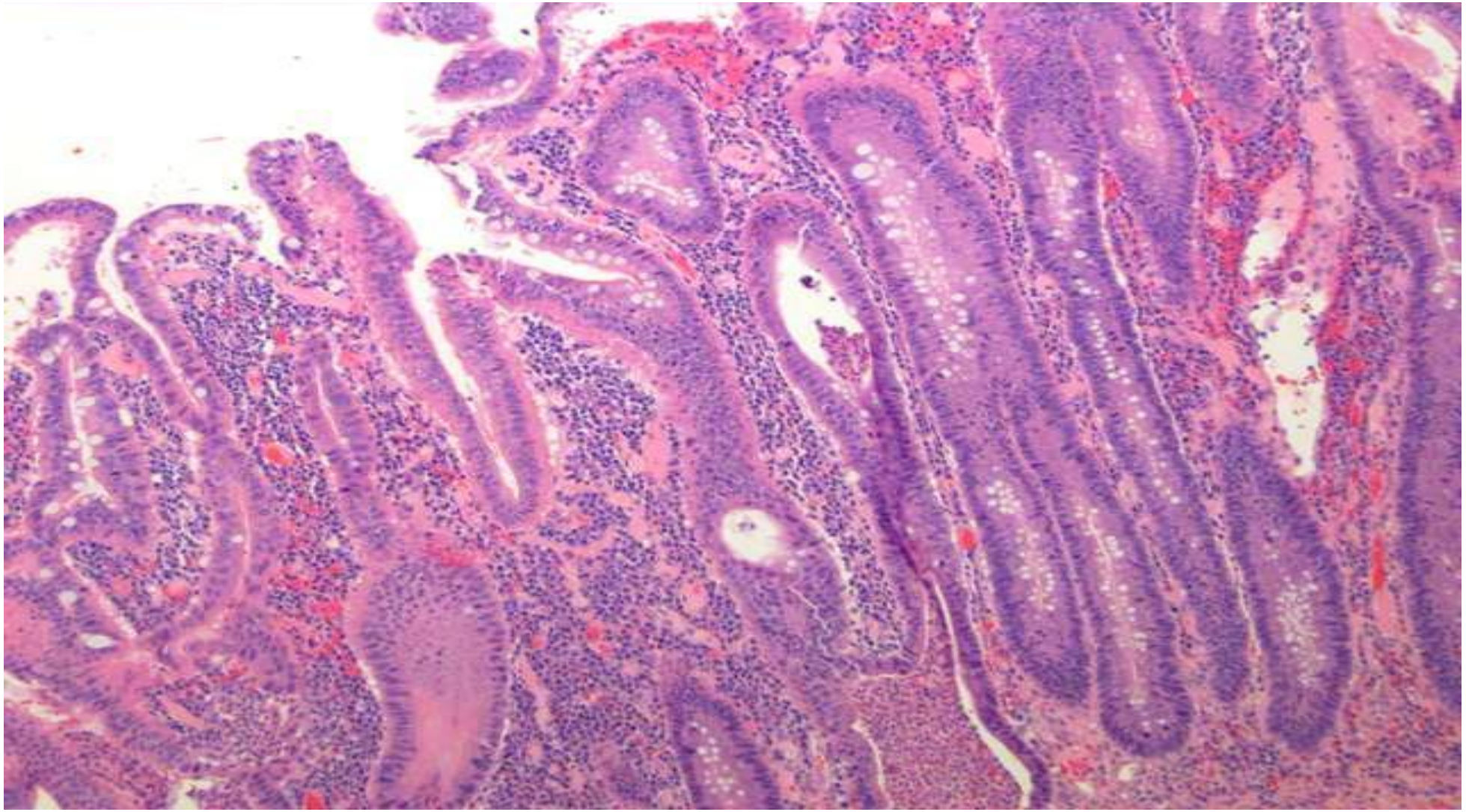
Ulcers confined to mucosa



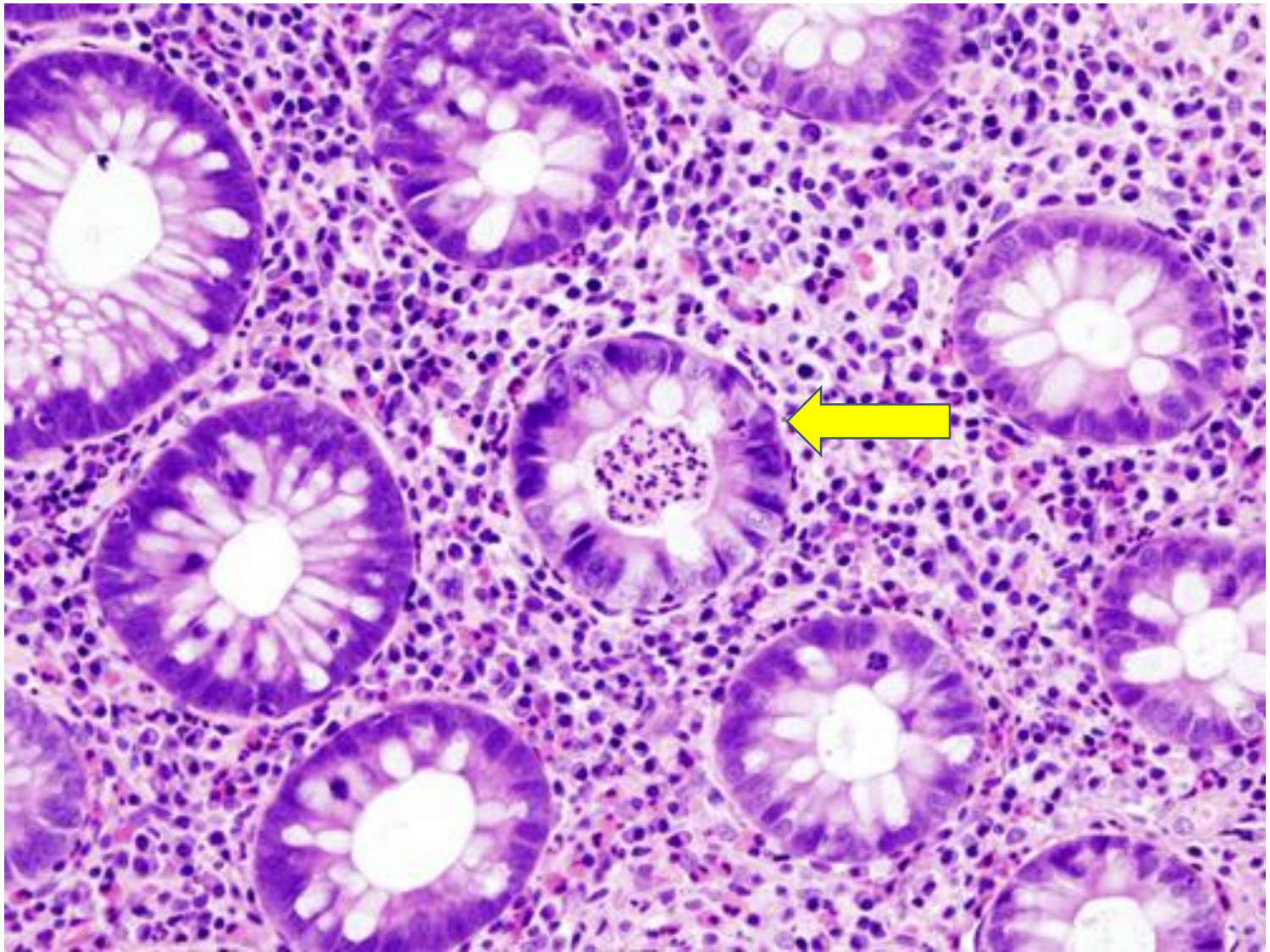
Marked lymphocytic infiltration of the intestinal mucosa and architectural distortion of the crypts



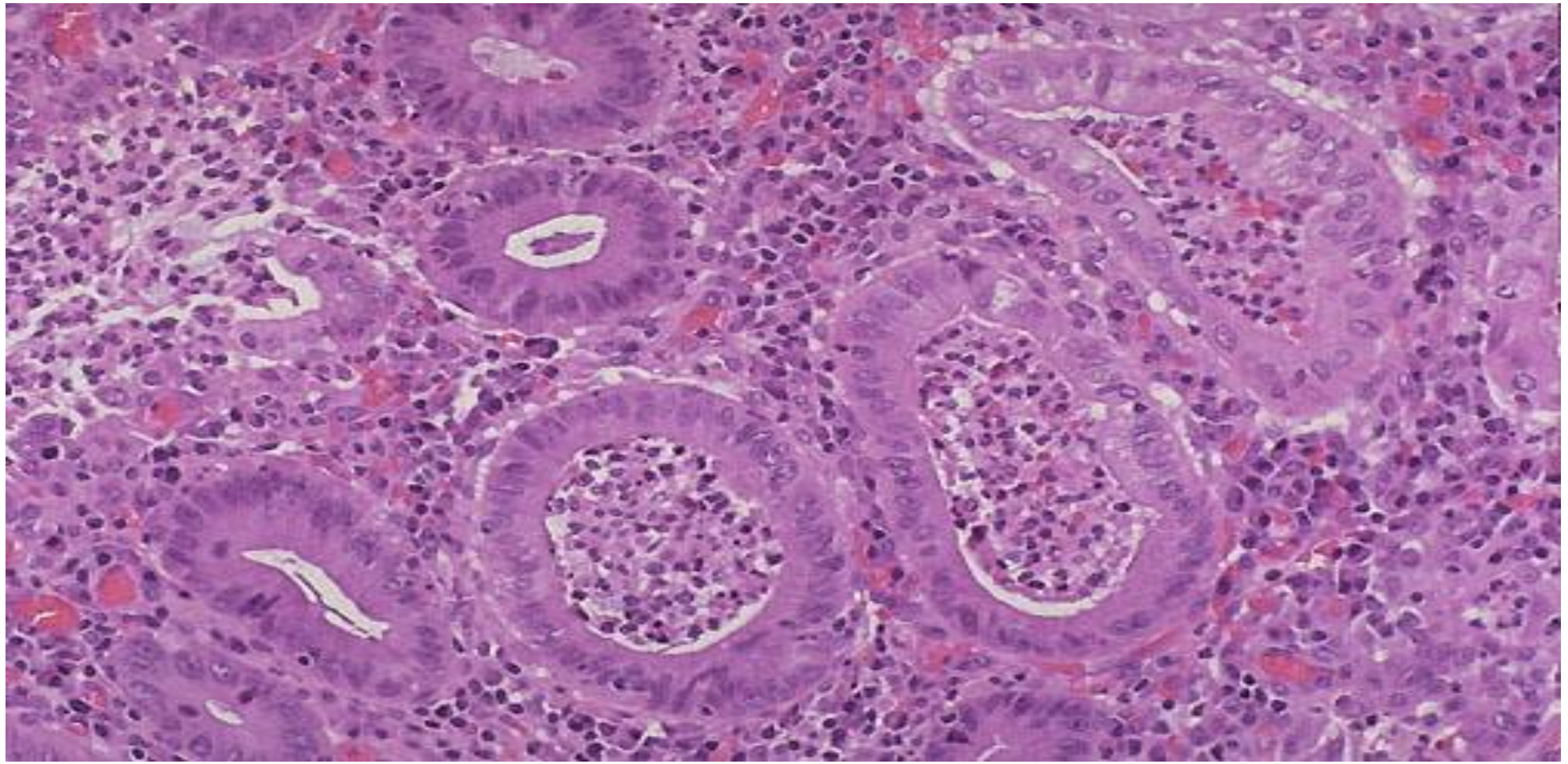
Chronic architectural changes in ulcerative colitis. Note the crypt branching and irregularity of size and shape, with an increase in chronic inflammatory cells in the lamina propria



Cryptitis and Crypt abscess



U.C mic.



Feture	Crohn's disease	Ulcerative colitis
Macroscopic		
Site	Ileum +/- colon	Colon only
Distribution	Skip lesions	Diffuse
Strictures	Early	Late
Wall appearance	Thickened	Thin
Dilatation	No	Yes
Microscopic		
Pseudopolyps	No	Marked
Ulcers	Deep linear	Superficial
Lymphoid reaction	Marked	Mild
Granulomas	Present	Absent
Fibrosis	Marked	Mild
Fistulae/sinuses	Present	Absent
Clinical		
Malabsorptions	Yes	No
Malignant potential	Yes	Yes
Response to surgery	Poor	Good