GI

Pathology

LEC no.

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Celiac Disease

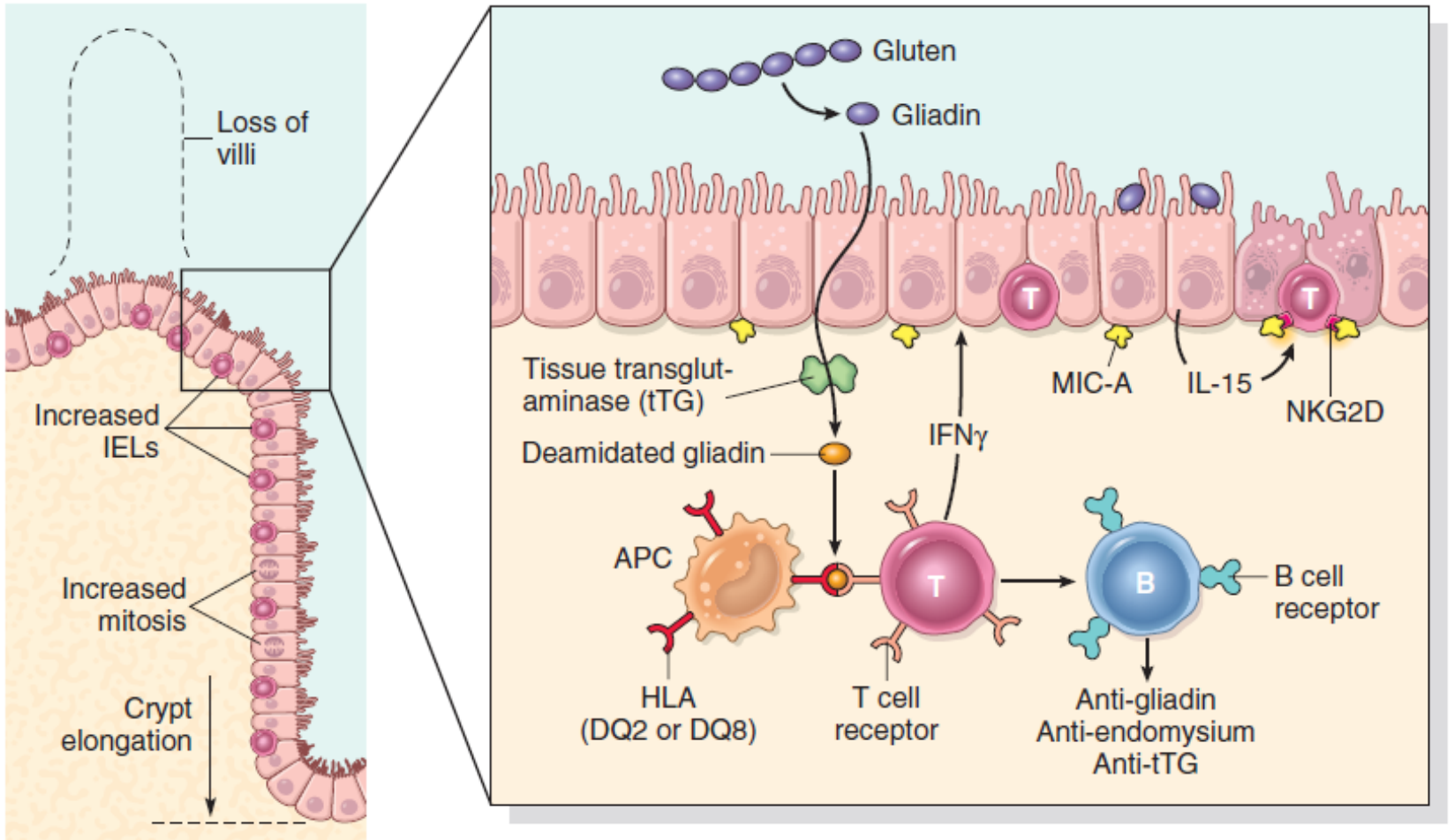
- *Gluten sensitive enteropathy*
- Immune mediated enteropathy (allergic disease)
- Wheat(mainly), rye or barley.
- Genetically predisposition, HLA-DQ2 or HLA-DQ8.
- Treatment: gluten free diet.
- Association with: type 1 diabetes, thyroiditis, and Sjogren syndrome

Sjögren's syndrome, also known as Sjögren's and Sjögren's disease, is a chronic (long-lasting) autoimmune disorder that happens when the immune system attacks the glands that make moisture in the eyes, mouth, and other parts of the body(from google).

Pathogenesis

- The main problem is by exposure to gluten.
- 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



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- Gliadin enter between intestinal type epithelial cells to lamina propria and submucosa and if the patient genetically predisposed, he will have DQ2 and DQ8 that recognize gladin and make activation for T cells which make activation for B cells which transform to plasma cells and produce antibodies which have 3 types (anti-tissue transglutaminase, anti-gliadin and anti-endomysial)
- The antibodies present to help in diagnosis and there level decrease in gluten free diet
- Normally, the small intestines are in vili shape which increase surface area for absorption very huge
- In celiac disease, with damage and inflammation and cytokines release, it is shortening until the mucosa becomes flat ,so when the biopsy come, we can see in early features only lymphocytes and shortening of the bowel and flattening with antibodies.

MORPHOLOGY

Why we do endoscopy in the second part of duodenum?

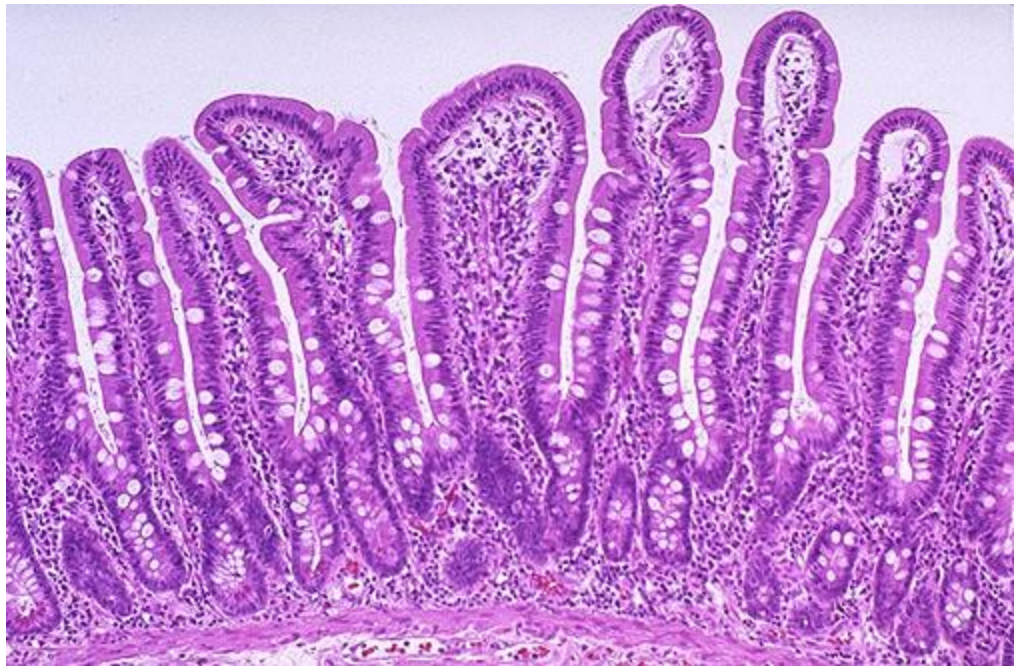
Because the first part usually affected by gastric acidity

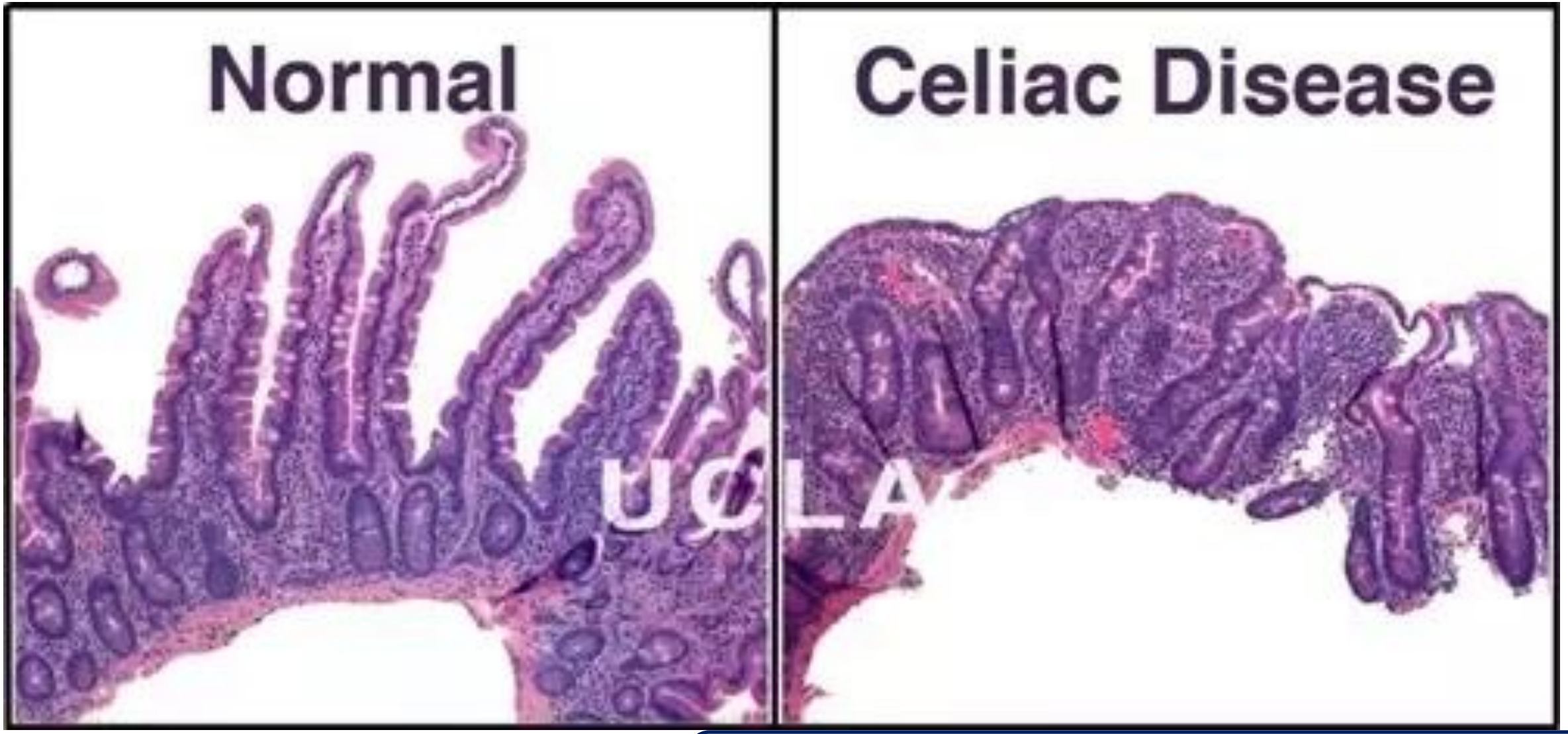
- As a microscopic features, when the doctor enters to do endoscopy, he will see fissuring and loss of folds in Second portion of the duodenum or proximal jejunum.
- **Triad**: increase in intraepithelial lymphocytosis (CD8+ T cells)(earliest manifestation, then crypt hyperplasia, and villous atrophy(the last manifestation).
- Lamina propria: lymphocytes, plasma cells, eosinophils…….(because it's chronic inflammation)
- IEL (intraepithelial lymphocytes) & villous atrophy are not pathognomonic, seen in viral enteritis(inflammation in small intestines).

- Diagnosis: Clinical, histologic and serologic correlation.
- To diagnose, we need clinicopatgoloic, serologic correlation, so it isn't an easy diagnosis.
- The disease rest in all life, so any glutin eaten will make manifestations

- # Normal intestine

Finger like projections





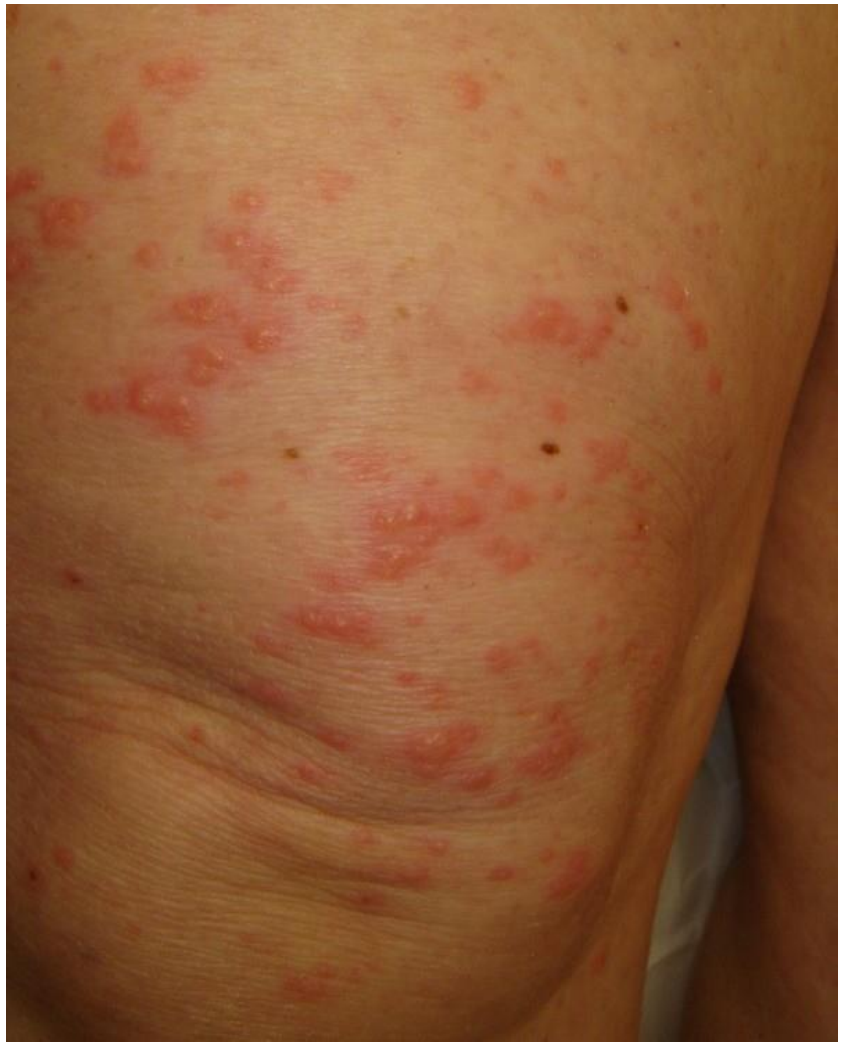
It transferred to a flat lined mucosa with infiltration of epithelium by lymphocytes(villous atrophy)

Clinical Features

- **It can be affected at any age, but it doesn't come before 6 months because there isn't exposure for food, so when child starts to eat, the symptoms start appear if he has celiac disease.**
- **Children 6-24 months : classical or non classical symptoms**
- **Classica**l: Irritability, abdominal distention, anorexia(loss of appetite), diarrhea, failure to thrive, weight loss, or muscle wasting(malabsorptive symptoms)
- **Non-classical: (we should know them to diagnose)**abdominal pain, nausea, vomiting, bloating, or constipation.(if we see them in a children 6-24 months, it couldbe celiac disease)
- Blistering skin lesion, **dermatitis herpetiformis**, in 10% of Pnts.

Dermatitis herpetiformis.

It’s name due to it’s similar to herpes bacillus.



- Adults (30-60 years)
- We see clinical manifestations like distension, diarrhea, weight loss and anemia.
- Anemia: iron deficiency (because the iron mainly absorbed in the duodenum)
- B12 and folate deficiency: less common.(because it absorbed in the terminal ileum of the intestines which isn't affected by celiac disease).
- Diarrhea , bloating, and fatigue.
- Missed diagnosis: Silent celiac (positive serology and biopsy but asymptomatic).
- The patient has positive serologic and the biopsy is positive in family history, so we make screening for the family for celiac, but it is asymptomatic and at any time the patient could has symptoms (they treated by gluten free diet), the treatment will reverse serologic antibodies (disappear) and the biopsy will go back to the normal as well as if it isn't treated properly and still with damage and inflammation, this will increase risk for T cells lymphoma (enteropathy-associated T cells lymphoma) and adenocarcinoma.

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

Diagnosis:

- **It is clinicopathologic correlation**
- **We start with Non invasive serologic tests:**
- **Most sensitive:**
- Anti tissue transglutaminase antibody, IgA(the most sensitive, but less specific)(if it presents, it doesn't mean that there is celiac)
- Anti deamidated gliadin antibodies, IgA & IgG

- **Most specific, but less sensitive(if it is positive, it means that there is celiac disease, but we can examine patient and doesn't find celiac (false negative)**
- Antiendomysial antibody.

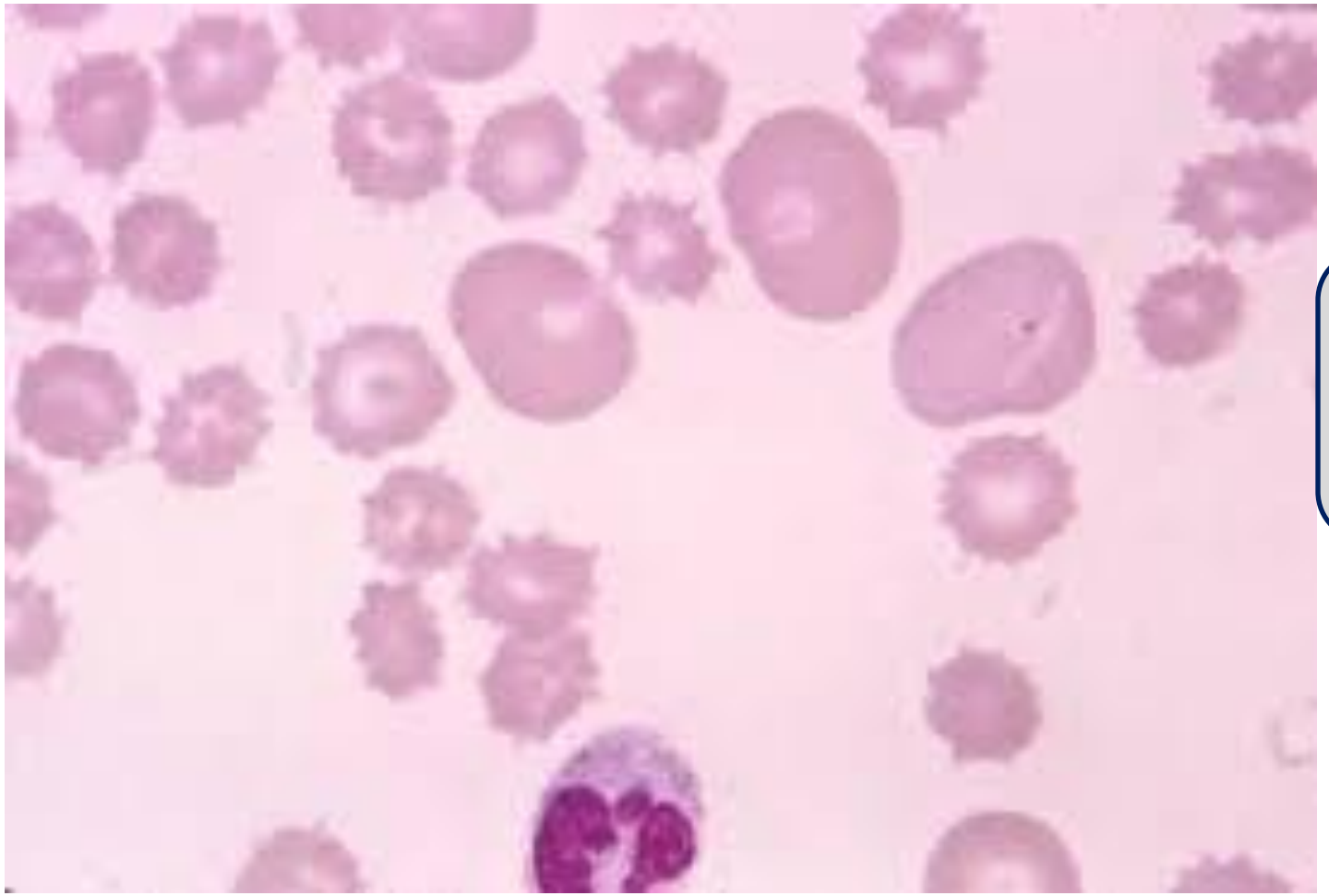
- **Invasive tests: small bowel biopsy.**

Lactase (Disaccharidase) Deficiency

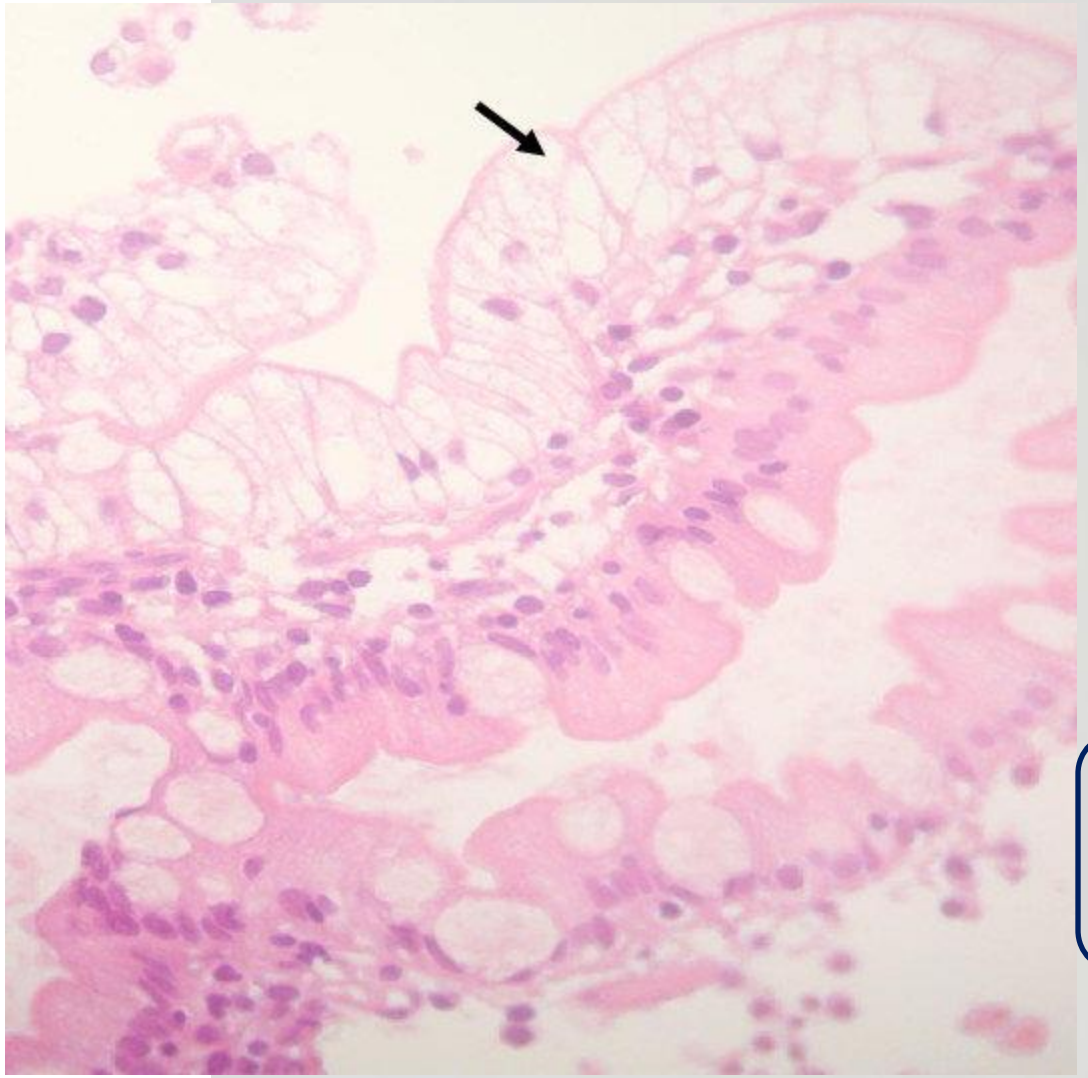
- It is one of malabsorptive conditions
- Lactose is a disaccharides and it exposed to terminal digestion in brush border of vili by lactase enzyme
- If lactase doesn't exist, it will cause osmotic diarrhea(because the sugar stay in gut (not digested), this will lead to pull of water and cause osmotic diarrhea)
- Lactose remains in the gut lumen.
- We can't see it microscopically because it is a biochemical, so we diagnose it clinically.
- Lactase found at apical brush border membrane
- Normal biopsy findings.
- Two types:
- ***Congenital*** *: AR(autosomal recessive), 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 worlds population (50% of USA population).
- The treatment is lactose free milk.
- **Transient**: caused by injury after infectious or inflammatory insults (reversible) (because there is a damage for brush borders and loss of enzymes, but it's transient, so when there is regeneration for the epithelium and after weeks to months, it backs to the normal.

Abetalipoproteinemia

- Autosomal recessive, rare.
- Because of inability of enterocytes to secrete triglyceride-rich chylomicrons.
- Lack of absorption (Transepithelial transport defect of lipoproteins, FAs and fat-soluble vitamins).(because these fatty acids should be carried by proteins (lipoproteins) and if there isn't transport, there isn't absorption)
- Infants' w/ failure to thrive, diarrhea, and steatorrhea
- Vitamin K deficiency, skeletal CNS and retinal abnormalities.
- Spur cells in peripheral blood.
- The epithelial cells due to accumulation of triglycerides, they become under the microscope with white color in H & E stain.
- Monoglycerides and triglycerides accumulate in epithelial cells.
- In children, fats are very important for the developing of CNS, so there is CNS manifestations, retinal abnormality and symptoms of malabsorption especially steatorrhea.



- These are the spur cells
- The membrane has spikes due to defect of plasma membrane because it formed by fatty acids and lipids.



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

- Instead they has a pink color, they have a white color because of accumulation of fats.

Intestinal pathology, part 2

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Diseases of the intestines

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

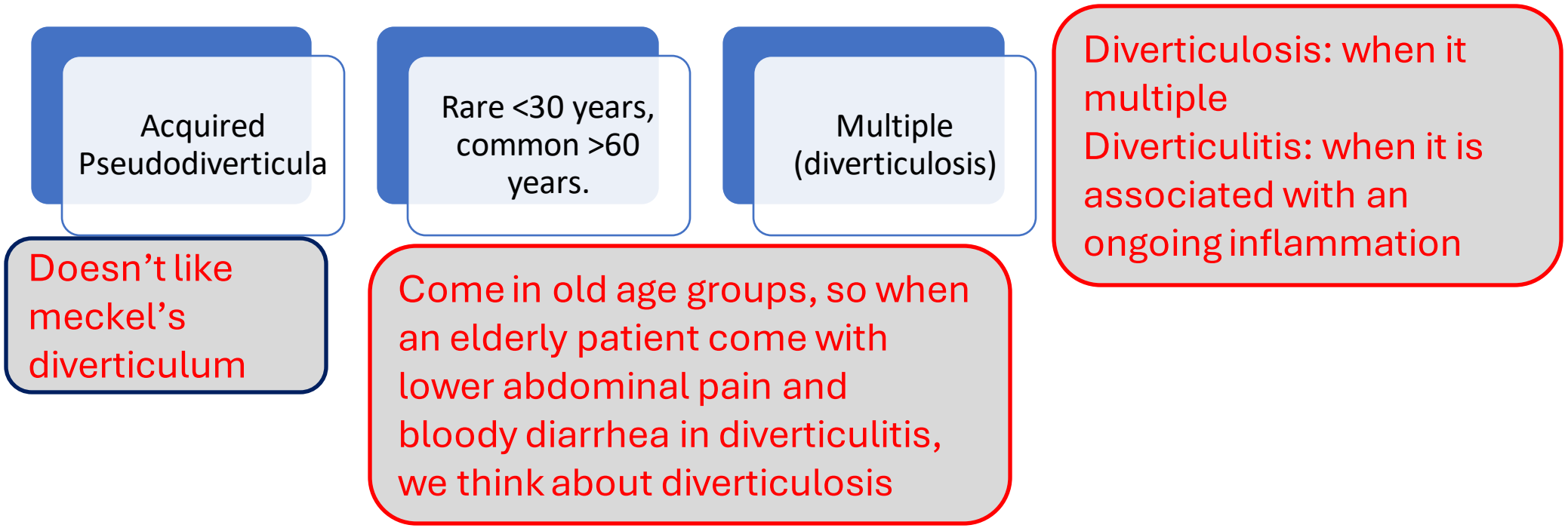
INFLAMMATORY INTESTINAL DISEASE

- **We will divide it into:**
- **Sigmoid Diverticulitis (in segmoid colon)**
- **Chronic Inflammatory bowel diseases (CIBD)**

  Crohn disease

  Ulcerative colitis

Sigmoid Diverticulitis



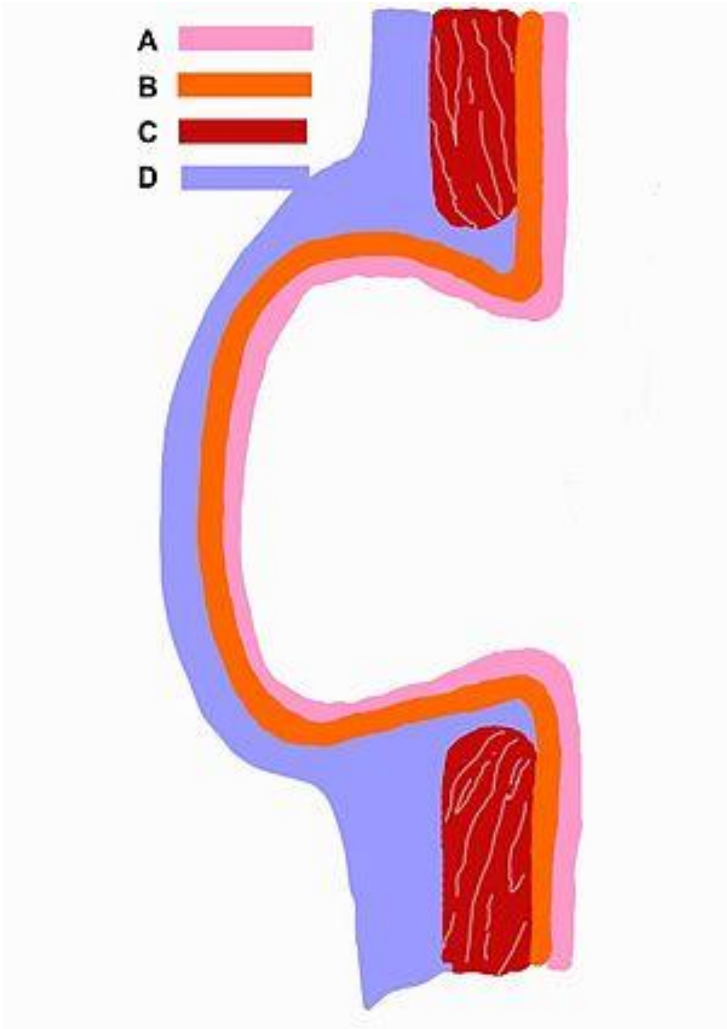
Pathogenesis:

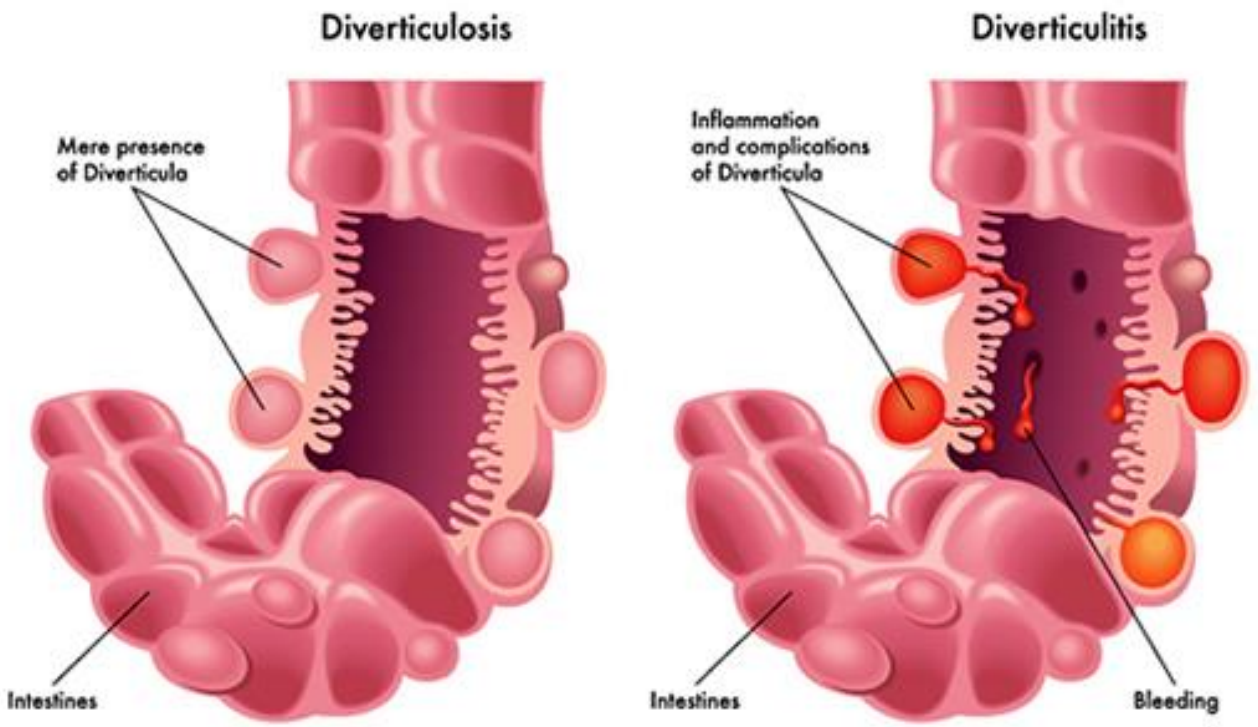
- **Elevated intraluminal pressure inside the gut and colon.**
- **The most affected part in the colon is segmoid because it is the narrowest part**
- Unique location (discontinuos at points of nerve and vessels entry).
- Longitudinal muscle layer is discontinuous in colon (taeniae coli). (So, we could have some part with inner circular layer without outer longitudinal muscle layer).
- Which lead to area of weakness: outward herniation of mucosa and submucosa.(due to the weakness, any increase in intraabdoinal pressure will lead to outpouching of mucosa and submucosa to outside).
- It is called pseudo because it occurs just in mucosa with submucosa without muscle layer, so it is weak, thin and it could cause perforation and rupture if there is an inflammation.
- Most common in sigmoid (narrowest part)
- There is increase exaggerated peristaltic contractions.(increase intraabdominal pressure).
- The main causes: low fiber diet, constipation, sedentary lifestyle, obesity, and smoking.(predisposing factors)

It begins like vicious circle which means the patient start with constipation, low fiber diet and start dicerticule ,then diverticulosis when they increase in number, then there is an inflammation and fibrosis followed by narrowing (stenosis) and more constipation and so

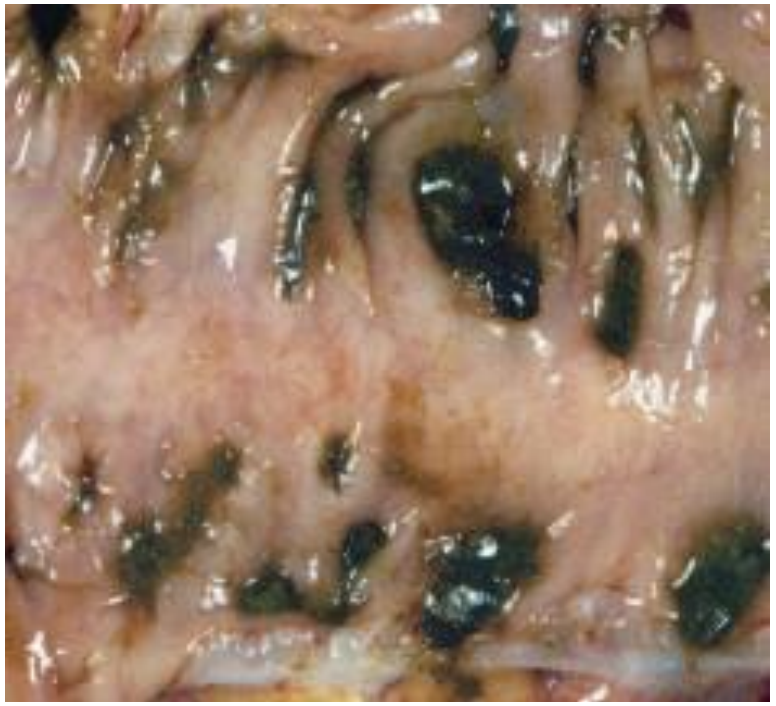
MORPHOLOGY

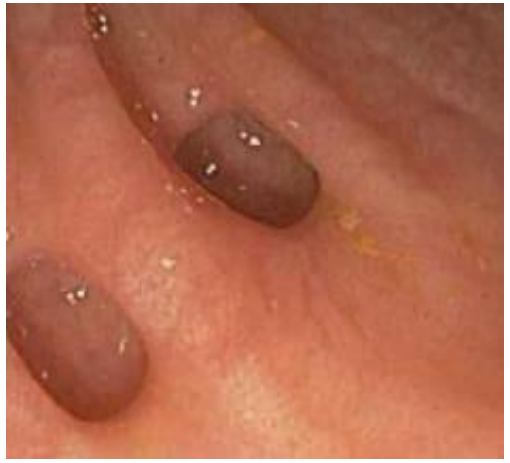
- There is mucosa and submucosa, but the muscle layer is discontinuous (absent or attenuated)
- Flasklike outpouchings
- Between taeniae coli.
- Thin wall (atrophic mucosa, compressed submucosa)
- Attenuated or absent muscularis propria.
- The neck of diverticule when it opens to the colon, if there is an obstruction or impaction of the stool in the neck, it will cause bacterial overgrowth and bacterial diverticulitis and the patient come with acute abdominal pain, fever and bloody diarrhea because of ulceration.
- Obstruction leads to diverticulitis.
- Risk of perforation.
- Recurrent diverticulitis leads to fibrosis (strictures).





They look like outpouching (multiple diverticulosis), when they inflammed, there is bleeding, inflammation and usually pus, mucus and blood



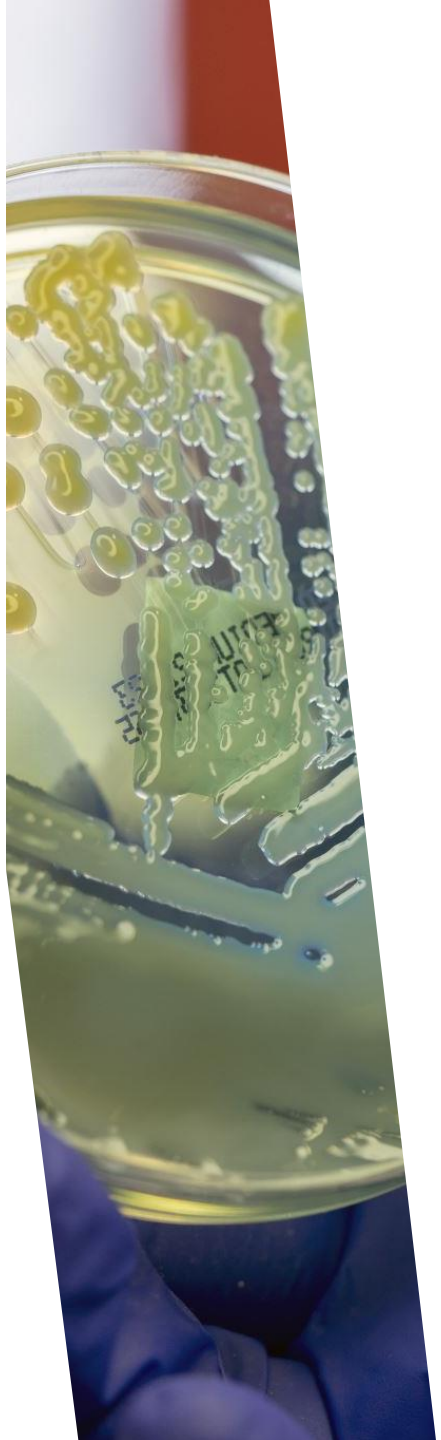


- There is an impaction of the stool at the neck of diverticule
- This is seen by the doctor through colonoscopy
- It has opening through the colon

Clinical Features

- **Mostly asymptomatic.** (Just constipation)
- When it becomes complicated and multiple, the patient complained by **Intermittent lower abdominal pain**, fever or diarrhea in inflammation
- **Constipation or diarrhea.**

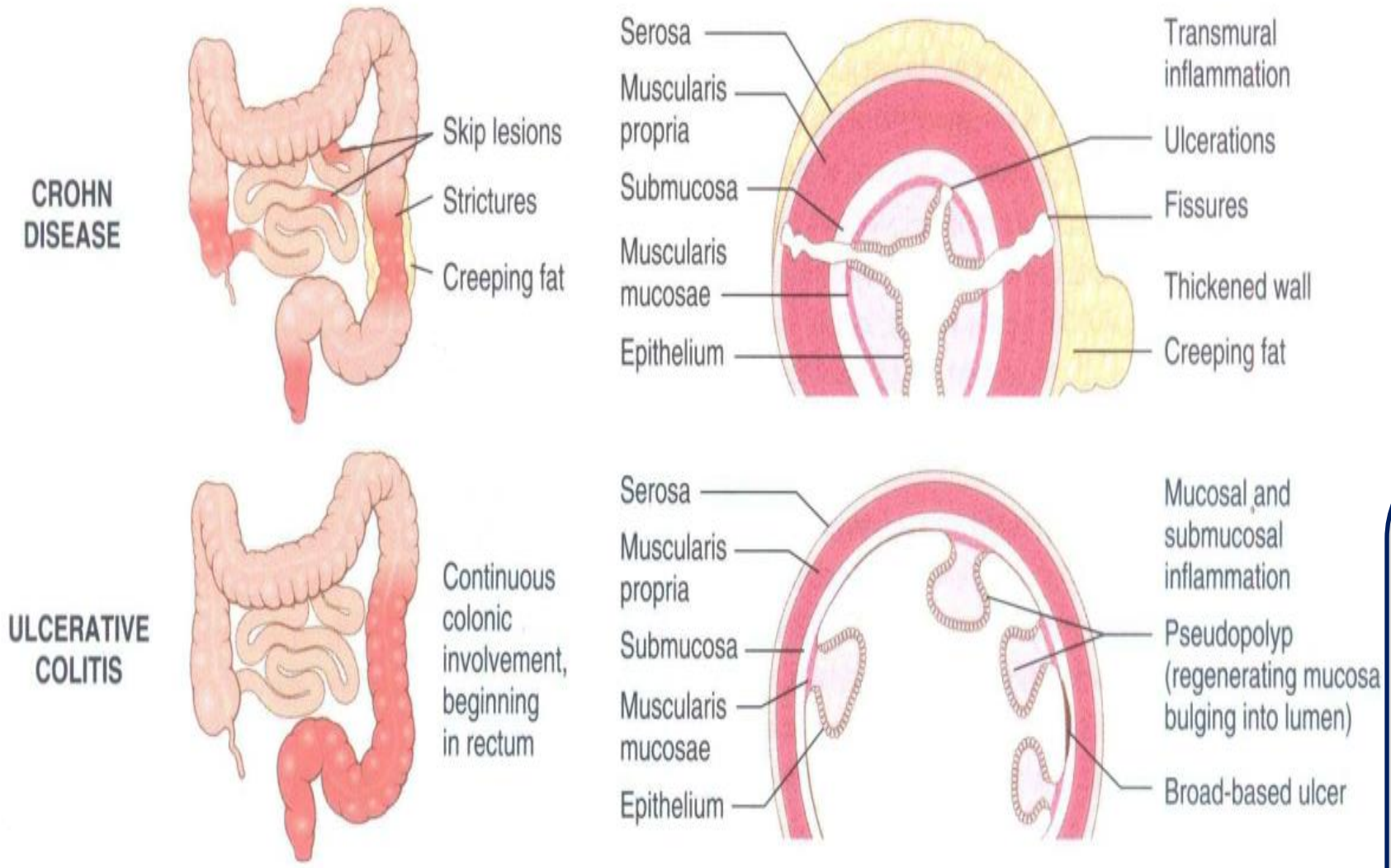
- **Tx** (treatments)
- We need to treat the cause, if it is occurred, it won't go back to the normal, but we try to make prevention (prophylaxis)
- **High fiber diet.**
- **Antibiotics in diverticulitis.**
- **Surgery.** (It is limited in conditions of strictures, fibrosis or perforation)



Chronic Inflammatory Bowel Disease

- This is very important not just for exam also is the real life because it is common.
- **Genetic predisposition**
- Immune response to intestinal microbes.(immune mediated disease)
- It isn't an infection, but infections can provoke or can predisposed the patient to the attack of disease, so they always have immune mediated reactions and exaggerated immune response in the bowel (they could be the starting point that make exaggerated immune response because they are genetically predisposed and then any viral infection or intercurrent infection or stressful event if it is physiological or psychological, the attack of disease occurs.
- Inappropriate mucosal damage.

- **Ulcerative colitis**: limited to the colon and rectum(almost always starts in the rectum), extends only into mucosa and submucosa.(it extention proximally different between patients, some stay in the rectum, some just in segmoid and it's called proctitis or proctosegmoiditis and in some patients in all colon)
- **Crohn disease**: regional enteritis, frequent ileal involvement, affect any area in GIT, frequently transmural(mucosa, submucosa, muscularies and serosa are affected).



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- Ulcers can go deep to the serosa, there is fissures and the wall is thick due to fibrosis
- We can find them in the rectum then descending colon then cecum and small bowel, this is called strip lesions

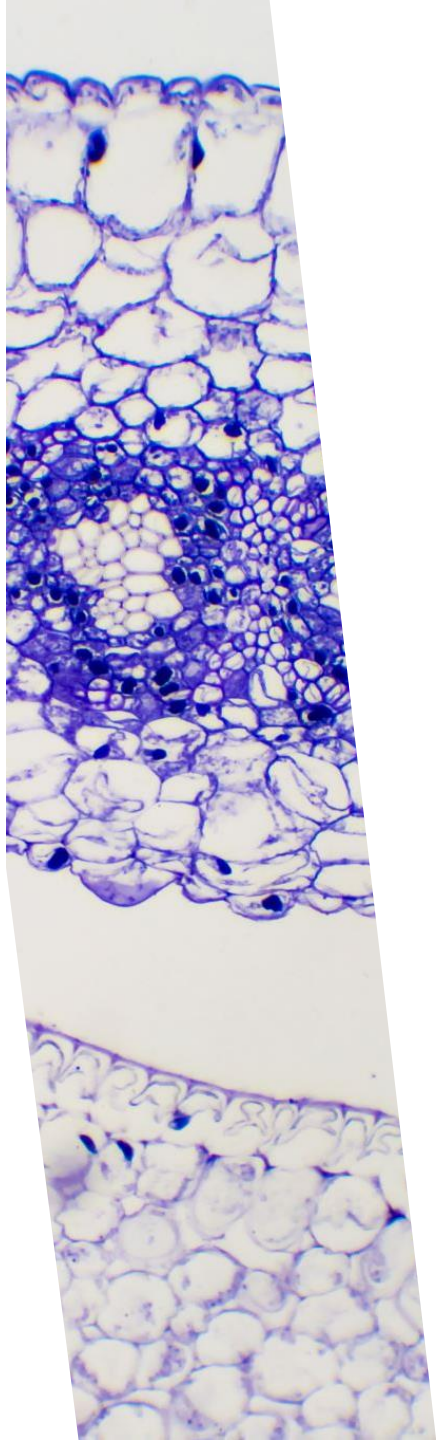
- Ulcers are shallow and they don't go deep, so there is no fissures, deep ulcersand the wall is thin
- The disease starts in the rectum and progresses proximally, continuous and there is nospared

Epidemiology

- Adolescence & young adults
- 2nd peak in fifth decade.
- Geographic variation.(common in developed countries)
- Proposed explanation:
- ***Hygiene hypothesis****: childhood exposure to environmental microbes prevents excessive immune system reactions.(if it is immune mediated disease like ulcerative colitis or chronic disease or in allergic conditions like asthma and eczema) Firm evidence is lacking!!!.*

Pathogenesis:

- Combined effect of:
- The patient should be genetically predisposed.
- Altered host interaction with intestinal microbiota.
- Intestinal Epithelial dysfunction (we loss the protective barrier provided by those epithelial cells).
- Aberrant (abnormal or exaggerated) mucosal immune responses.

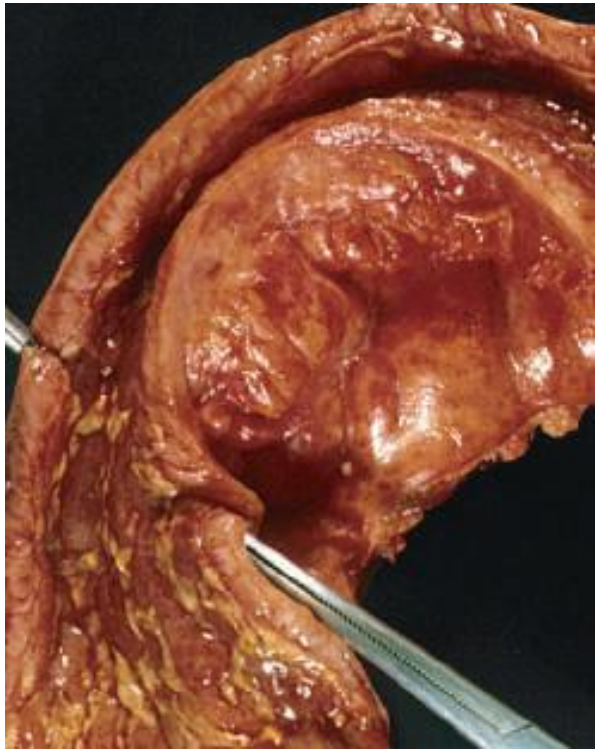


Crohn Disease Morphology

There are differences between crohn disease and ulcerative colitis, but in real life we can't differentiate between them and on biopsy we favor crohn disease
We diagnose them as a chronic inflammatory bowel diseases

- Macroscopic:

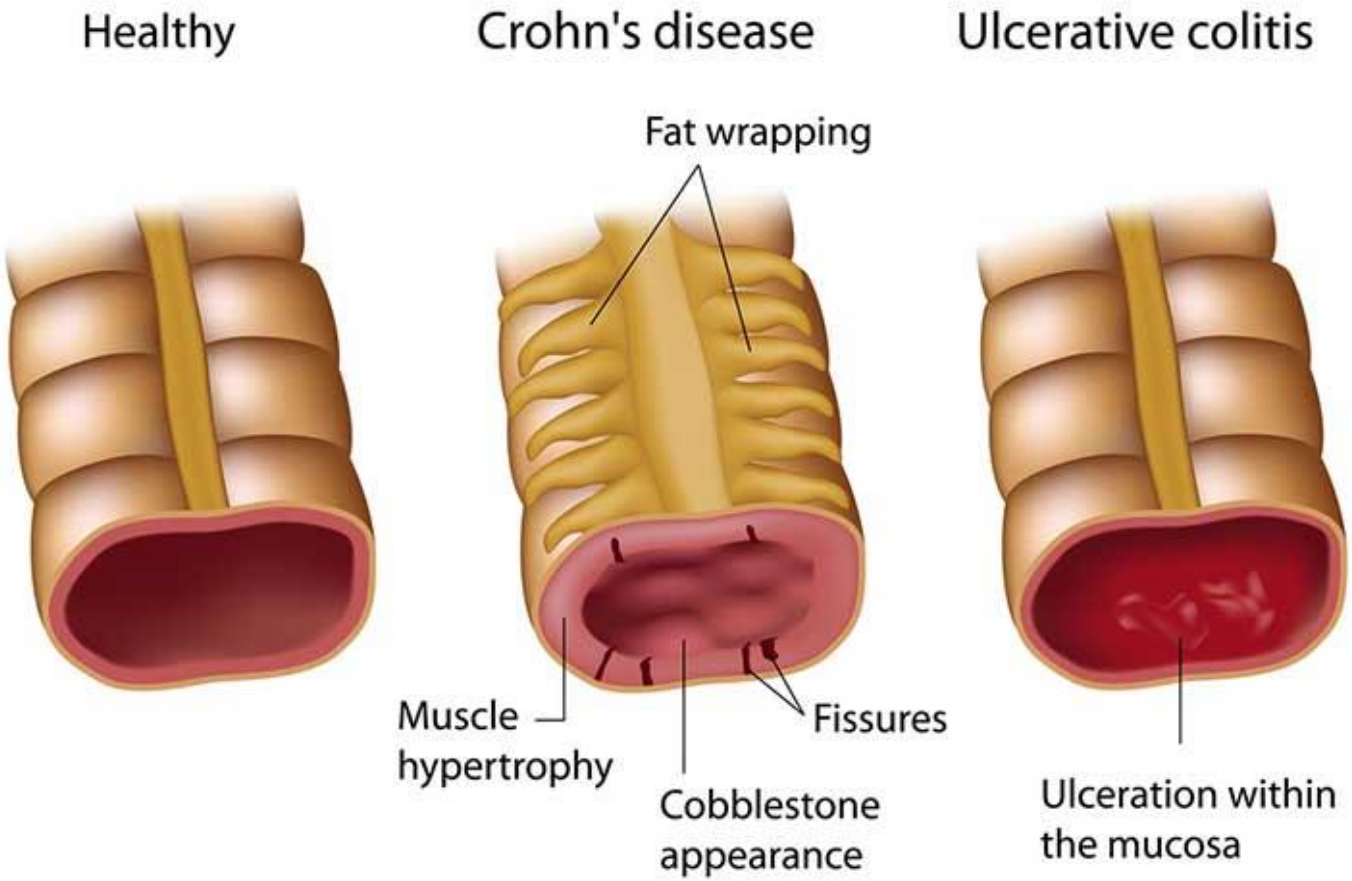
- Regional enteritis. (Strip lesions)
- Any area of GIT.
- Most common sites: terminal ileum, ileocecal valve, and cecum (right side of the colon).(they usually present in a picture similar to acute appendicitis, in some patients, the doctor enter as acute appendicitis and find the appendix normal and terminal ileum, ileocecal valve and cecum inflammed ,so he make resection to them)
- Small intestine alone 40%
- Small intestine and colon 30%
- Colon only 30%
- Skip lesions
- Strictures common because the is thickened due to fibrosis and strictures occur.



Small bowel stricture.

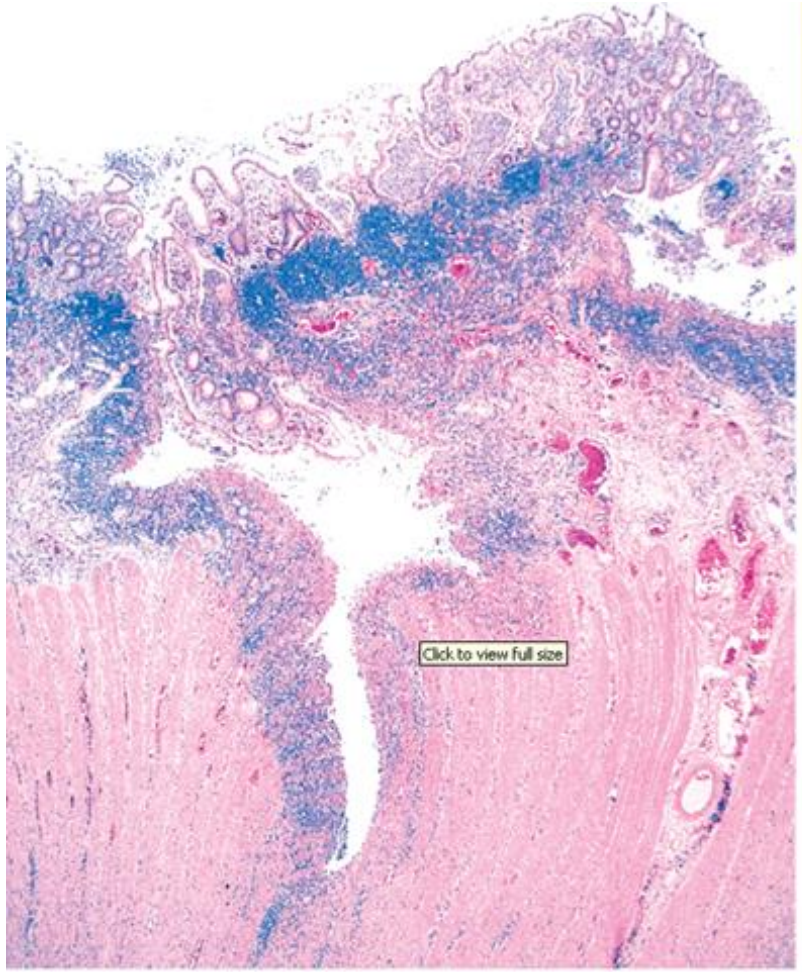
It is a narrowing like stenosis and the patient complains from obstruction

- Earliest lesion: aphthous ulcer
- Elongated, serpentine ulcers.(could cause fissures)
- Edema , loss of bowel folds.
- Cobblestone appearance
- Toxic megacolon(dilation of the colon)(before fibrosis) More to occur with ulcerative colitis
- Fissures (deep ulcer) (fistulas, perforations and it could open to adjacent organs like bladder or in uterus of females or vagina). Any fistula is more to occur with chron disease
- Thick bowel wall (transmural inflammation, edema, fibrosis, hypertrophic MP) >>strictures.
- Creeping fat because of the inflammation reach serosa in crohn disease not like ulcerative colitis which occurs just in mucosa and submucosa.



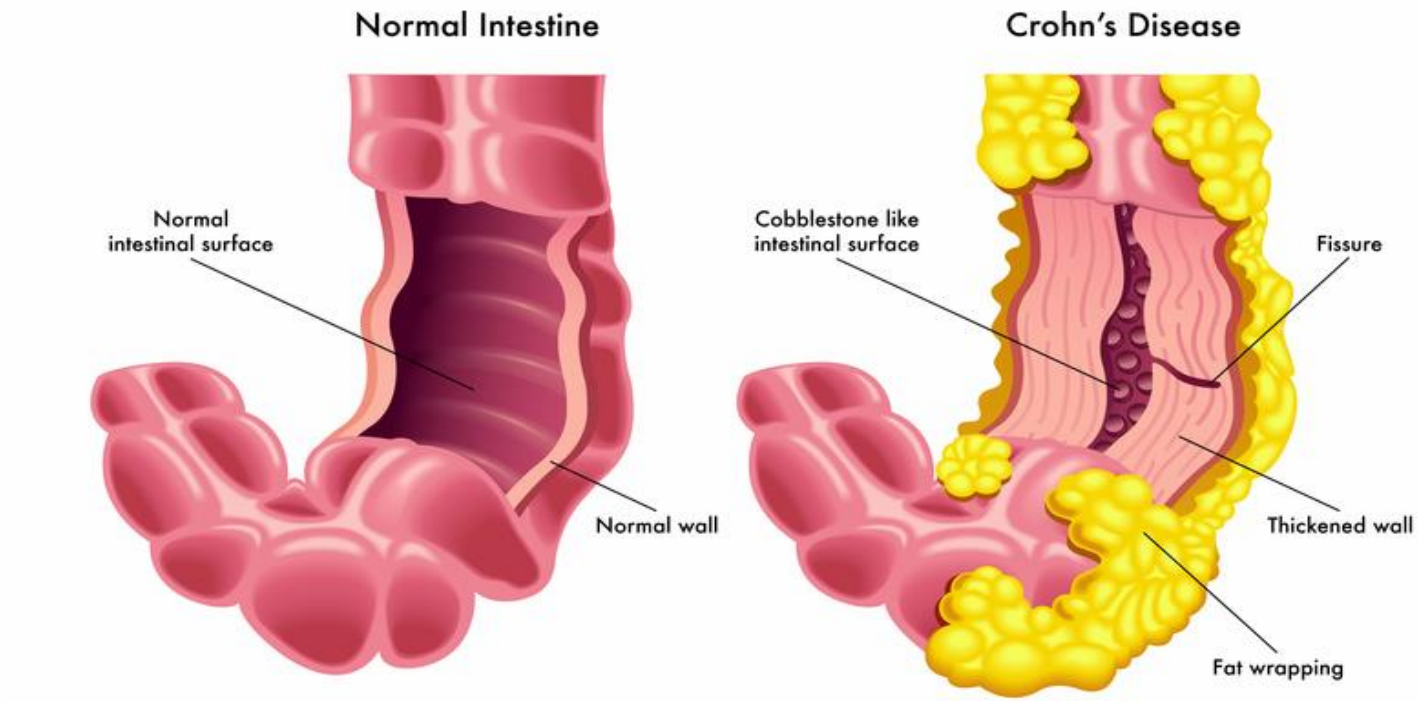
There is deep fissures

fissure



Crohn disease of the colon showing a deep fissure extending into the muscle wall, a second, shallow ulcer (upper right), and relative preservation of the intervening mucosa. Abundant lymphocyte aggregates are present, evident as dense blue patches of cells at the interface between mucosa and submucosa

- If it continues to the outside (to the serosa) ,it make perforation or fistula

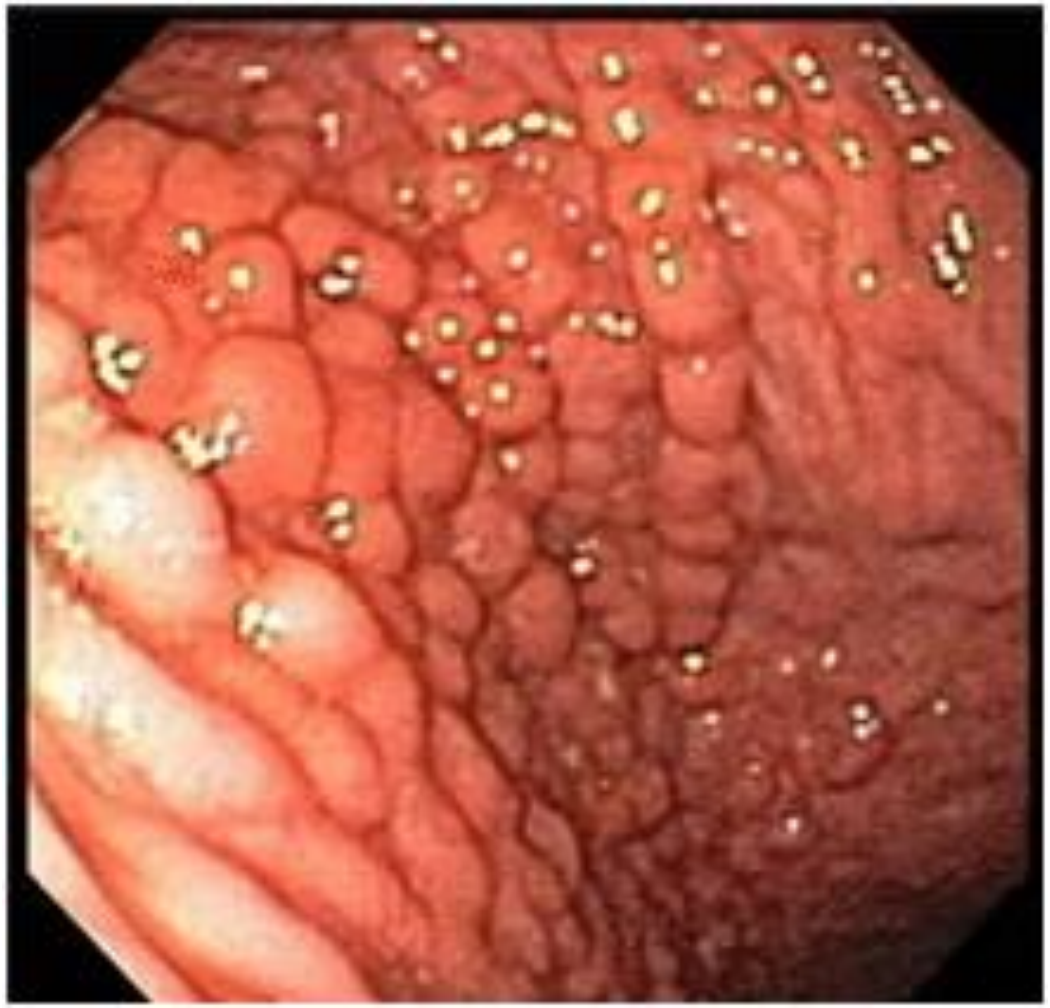


Creeping fat

- The fat is collected
- The bowel wall is thick (fibrotic)
- The mucosa inside has cobblestones appearance

- The areas of inflammation in the trapped area (depressed)
- The normal areas is elevated

Cobblestone appearance

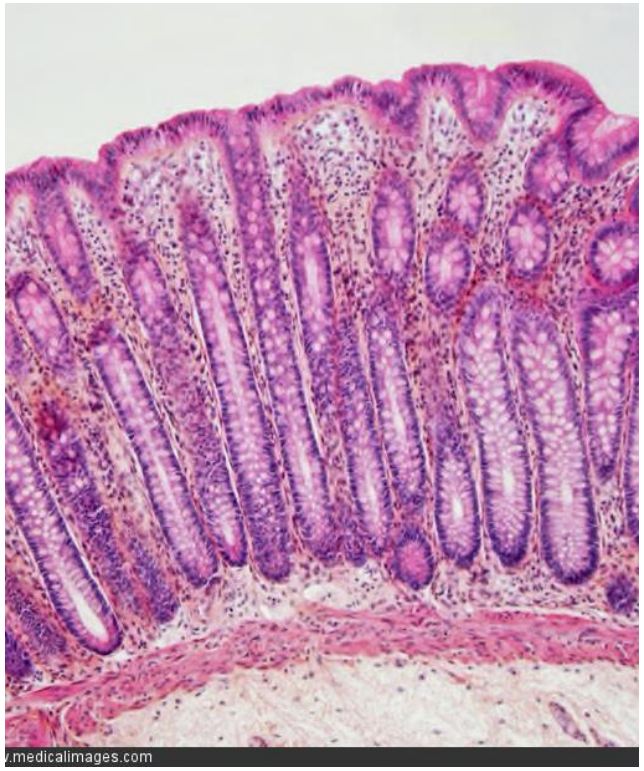


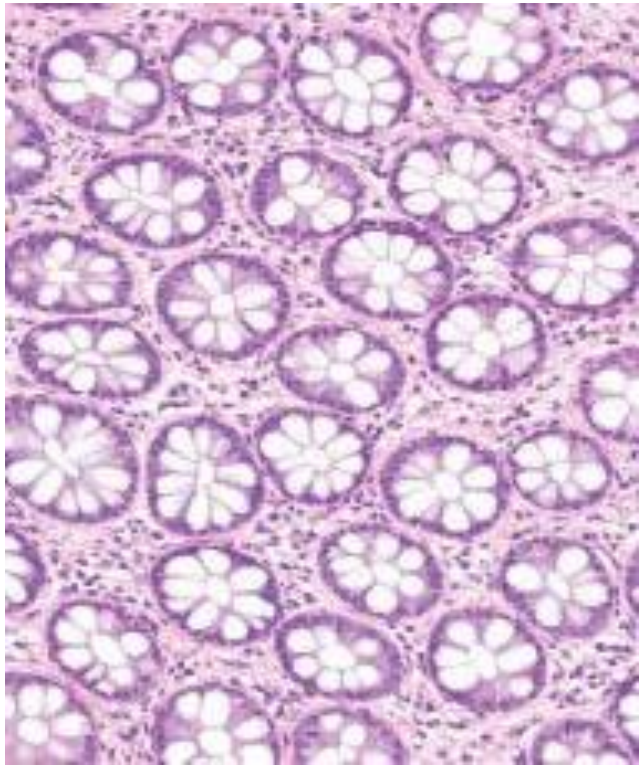
The red areas (depressed) are inflamed and the normal areas in between

- Microscopic:

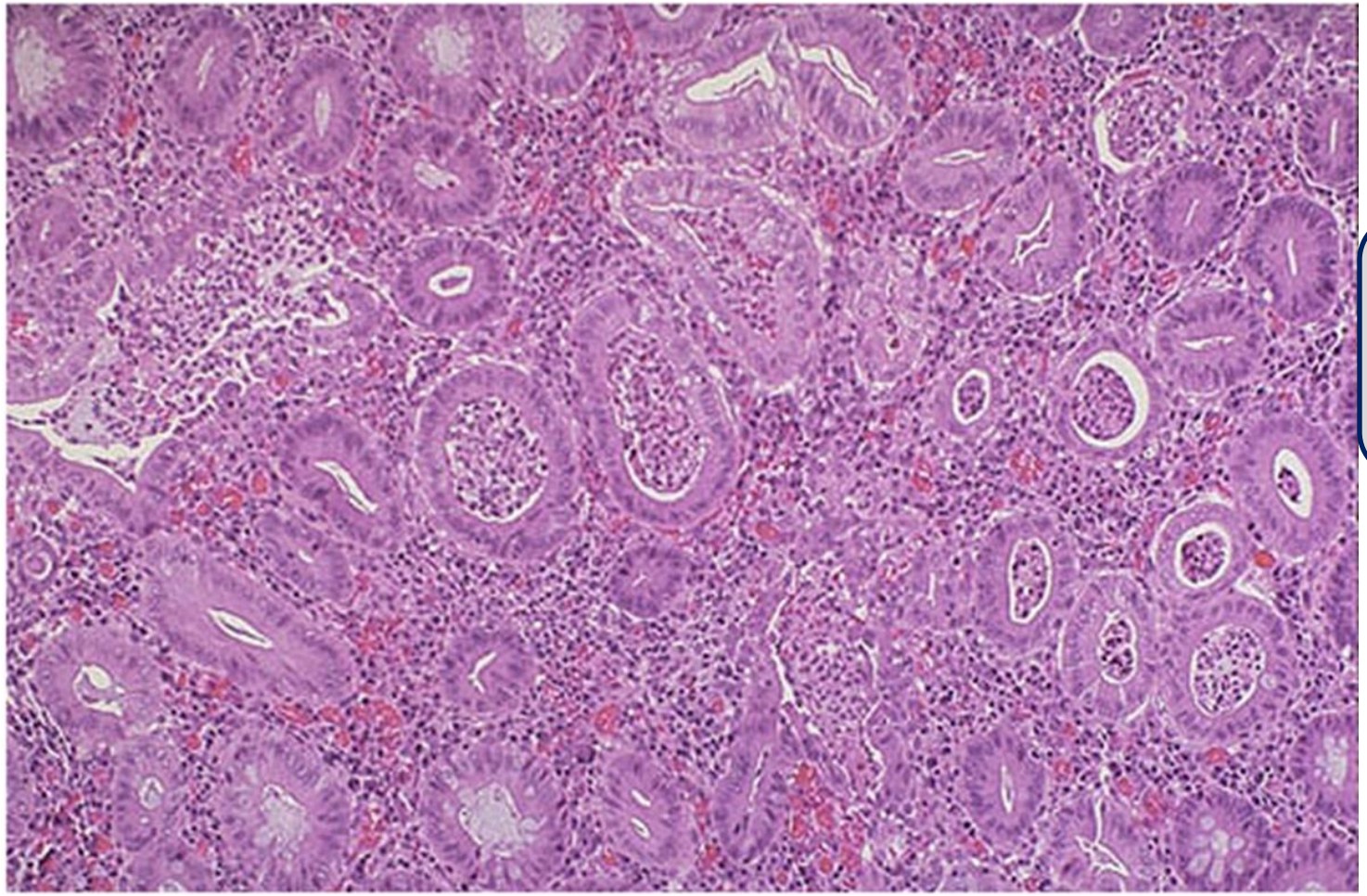
Features of active disease :

- Neutrophils in active disease.
- Crypt abscesses.
- Ulceration.
- We have to have some features to call it a chronic like:
- Distortion of mucosal architecture (repeated cycles)
- Paneth cell metaplasia in left colon
- Mucosal atrophy.
- Noncaseating granulomas (hallmark) only in 35% of cases. Anywhere!!

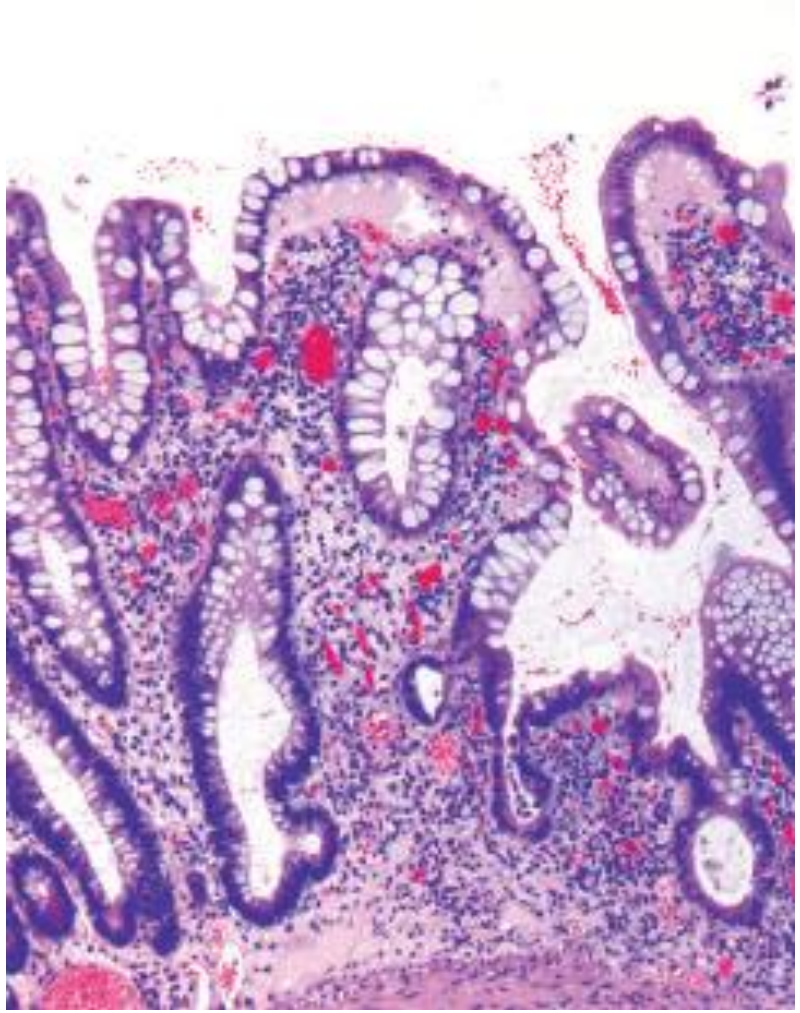




Normal colon

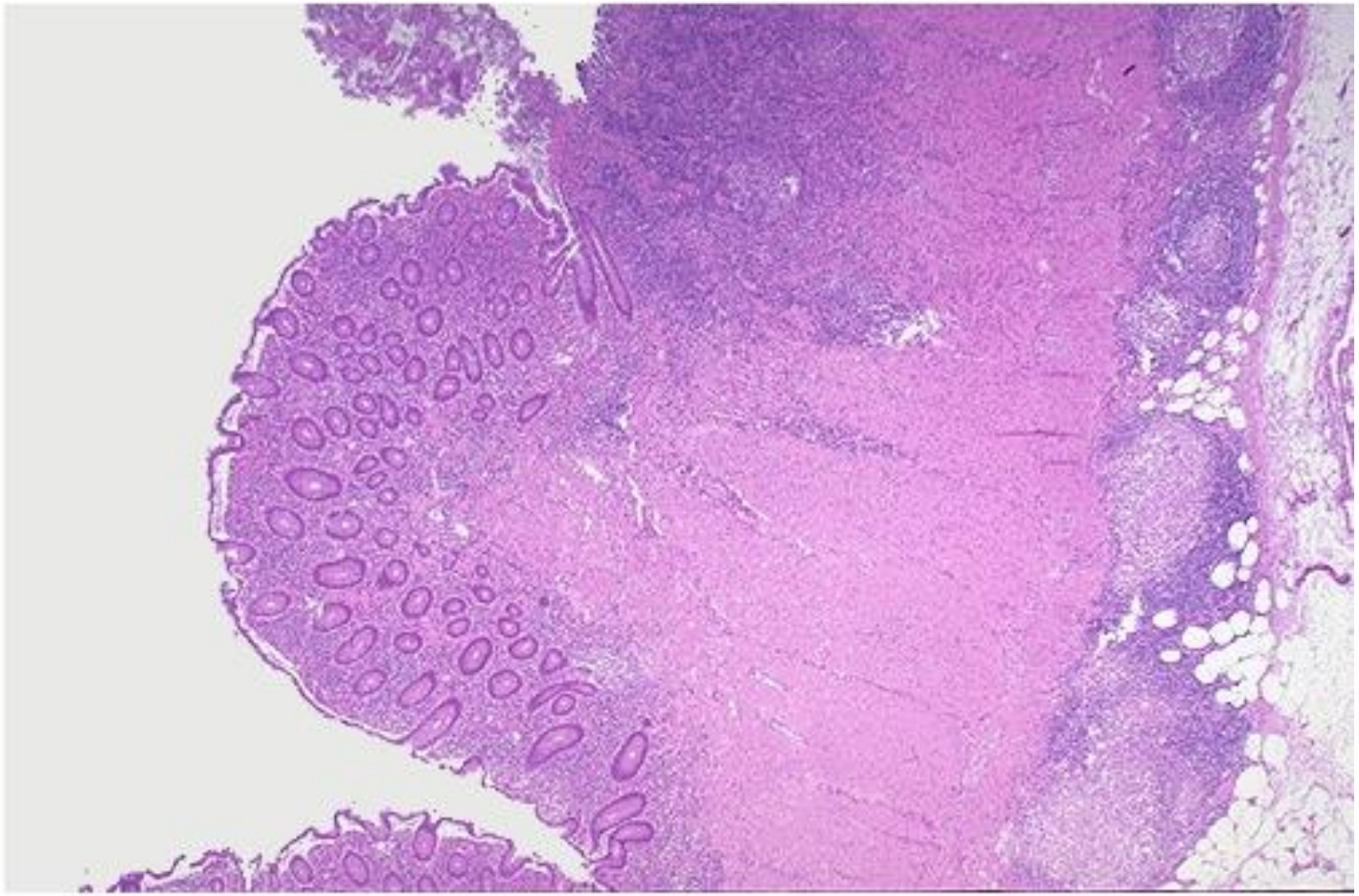


- These are the neutrophils inside the crypts (crypts abcess)



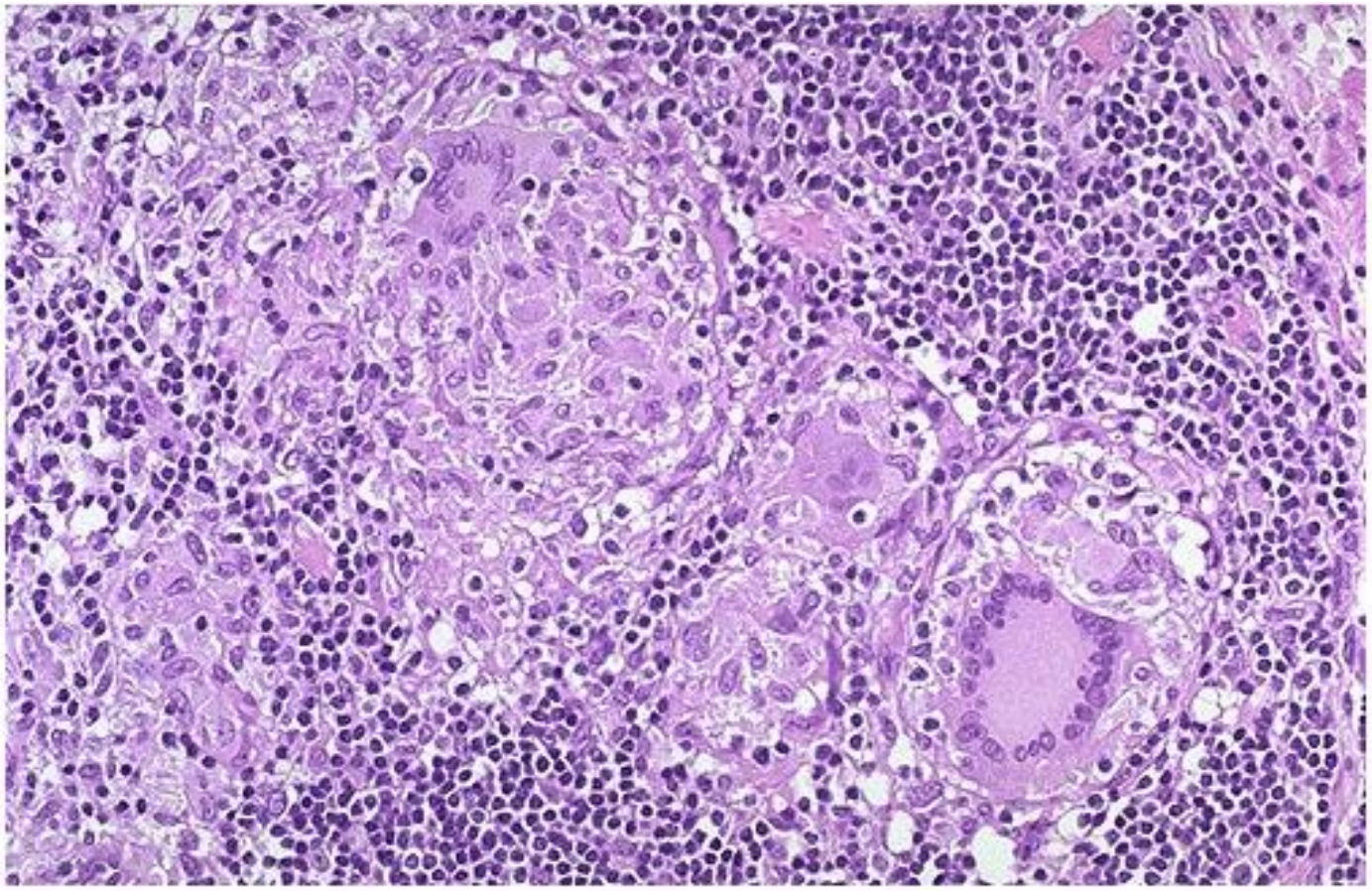
Haphazardly arranged crypts

- It persists even when the patient becomes in the remitting phase, the patient doesn’t has symptoms, but in the biopsy there is ongoing architecture distortion



Transmural inflammation.

It reaches to the serosa



Non-caseating granuloma.

There is macrophages and multinucliated giant cells

Clinical Features

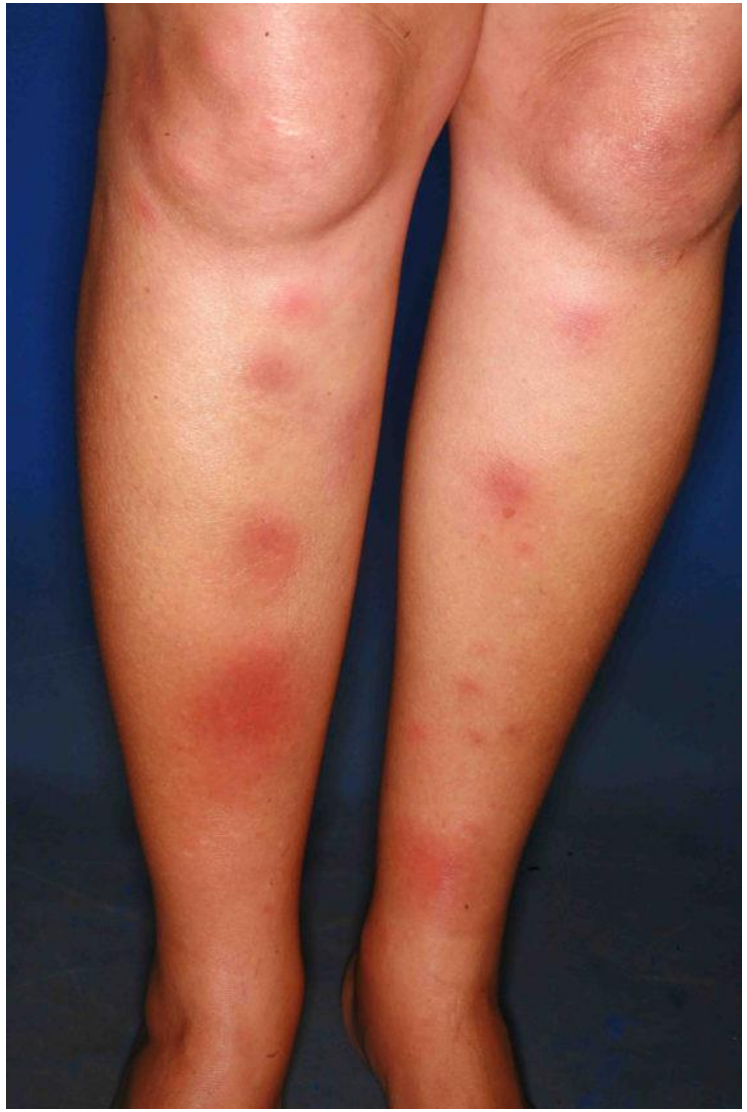
- Intermittent attacks of mild diarrhea(bloody diarrhea because of ulceration and inflammations), fever, and abdominal pain.
- Acute right lower-quadrant pain and fever (20%)(like acute appendicitis)
- Bloody diarrhea and abdominal pain (colonic disease)
- Asymptomatic intervals (weeks to months)(it is on and off, attack then asymptomatic then attack again)
- Triggers: physical or emotional stress, specific dietary items, NSAID use, and cigarette smoking.

- **Complications:**
- Colonic: Iron-deficiency anemia
- Small bowel: Hypoproteinemia and hypoalbuminemia, malabsorption of nutrients, vitamin B12 and bile salts, so the patient come with wasting and weight loss.
- Fistulas, peritoneal abscesses, strictures
- Risk of colonic and small intestinal adenocarcinoma ……
- We should make periodic surveillance in patients every year to see if there is dysplasia which could predisposed patient to carcinoma.

Extra intestinal manifestations

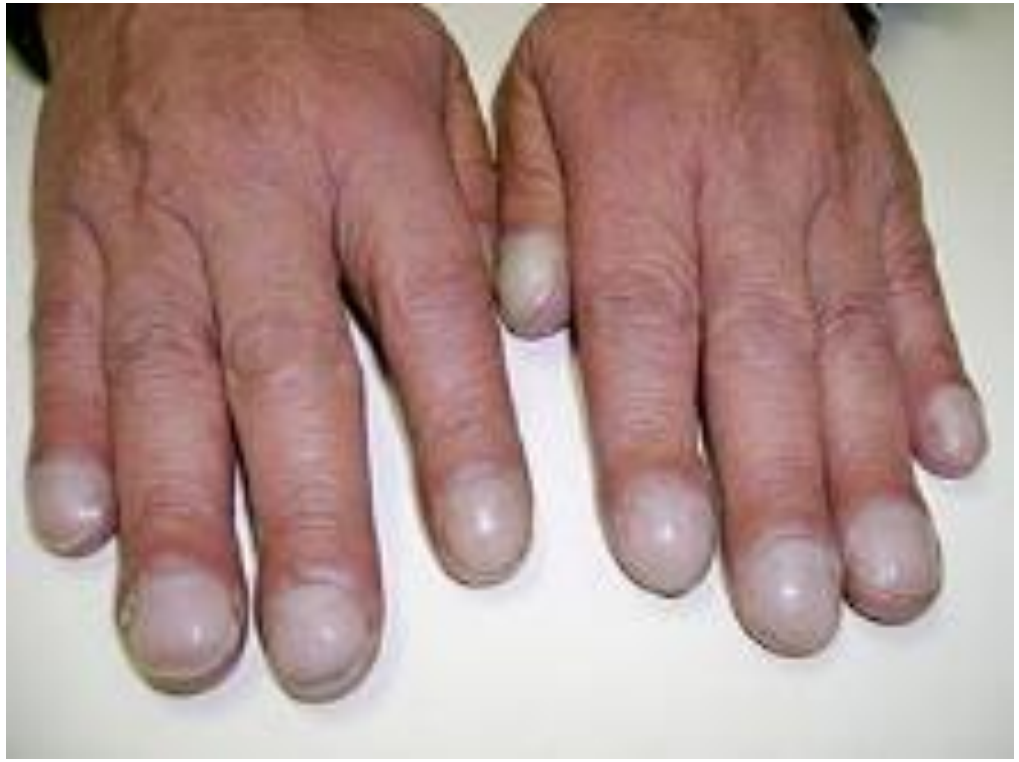
- They are immune mediated.
- Uveitis
- Migratory polyarthritis,
- Sacroiliitis,
- Ankylosing spondylitis,
- Erythema nodosum
- Clubbing of the fingertips
- Primary sclerosing cholangitis(important) (more with UC(ulcerative colitis)(they come with jaundice and hepatic manifestations because the obstruction of bile duct in liver

Erythema nodosum



Neurology Advisor

Clubbing



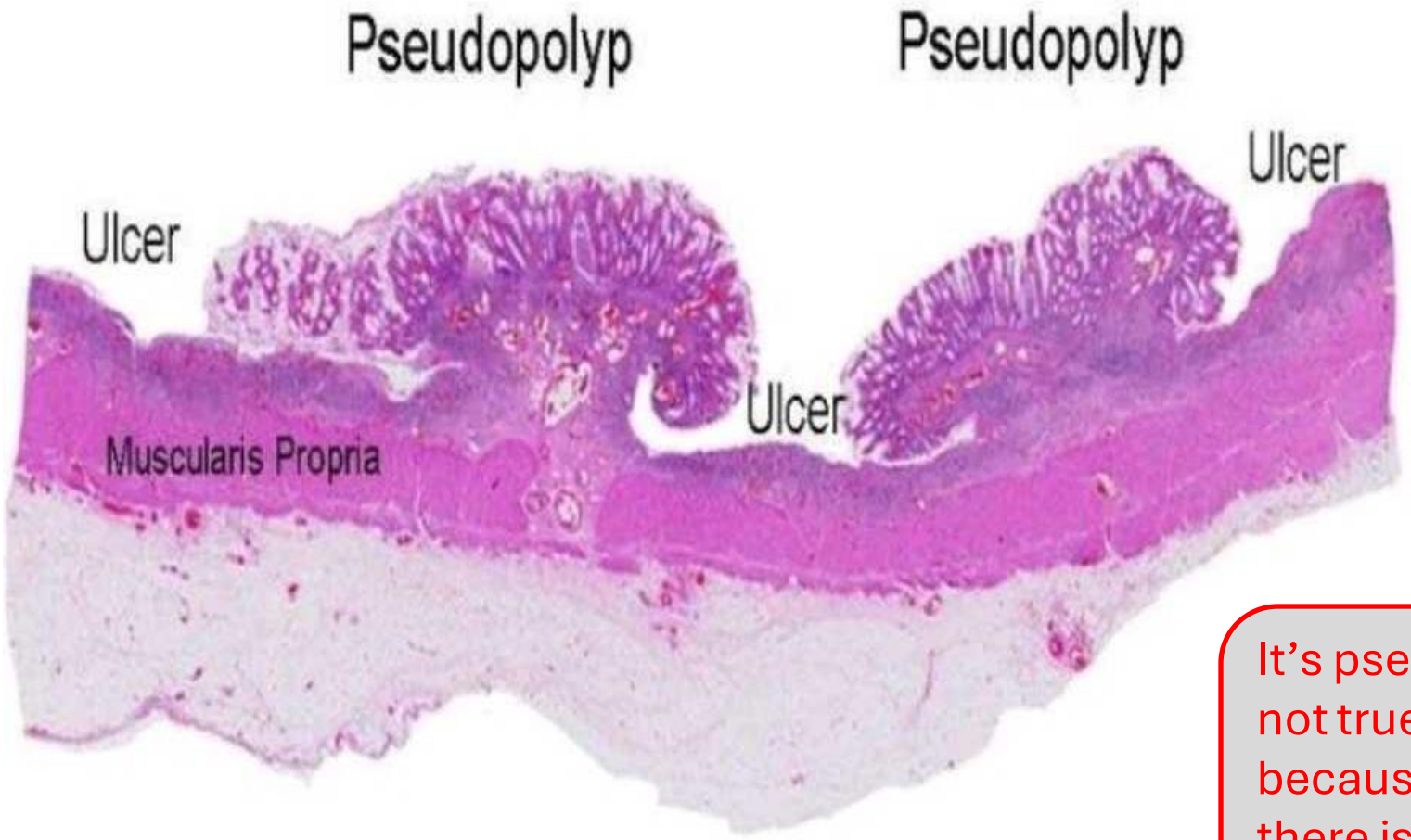
Wikipedia

Ulcerative Colitis Morphology

- Always involves the rectum
- Extends proximally in continuous pattern.
- Pan colitis in the severest form.
- No skip lesions
- Occasionally focal appendiceal or cecal inflammation.
- Limited diseases: Ulcerative proctitis or ulcerative proctosigmoiditis
- Small intestine is normal (except mild backwash ileitis)
- If the patient has pancolitis reach to the cecum, the terminal ileum could has an inflammation.

- Macroscopic:

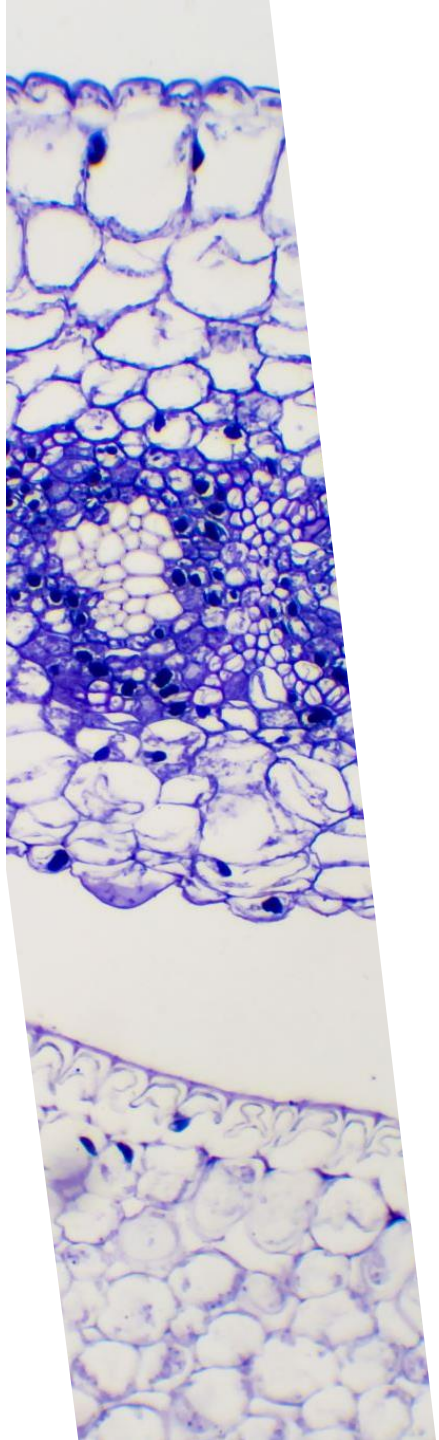
- Shallow.
- No fissures.
- No fibrosis and thickening.
- No creeping fat.
- Broad-based ulcers.
- Pseudo polyps (regenerating mucosa).
- Mucosal atrophy in long standing.
- Mural thickening absent.
- Serosal surface normal.
- No strictures.
- Toxic megacolon (damage of MP(muscularis propria), disturbed neuromuscular function).



It’s pseudo because it’s not true plastic polyps, because of inflammation, there is regeneration, so it look like a polyp

Toxic megacolon

It is more common in ulcerative colitis

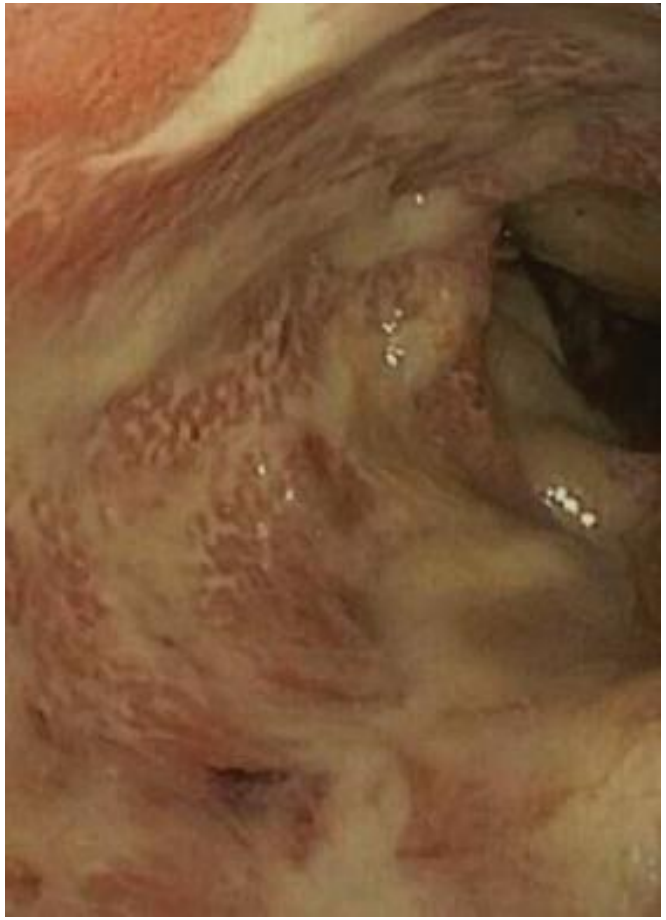


- Microscopic:

- Inflammatory infiltrates
- Crypt abscesses
- Crypt architecture distortion
- Epithelial metaplasia
- Submucosal fibrosis
- Inflammation limited to mucosa and submucosa.
- No skip lesions
- No granulomas.
- No sparing of some areas.
- No serosal inflammation

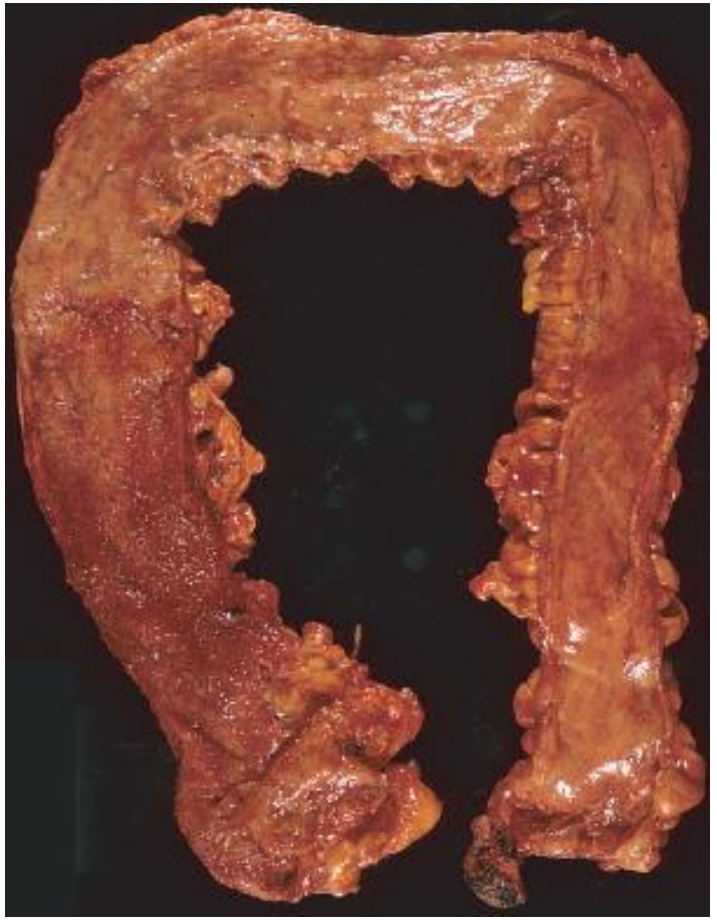
Mucopurulent material and ulcers.

In a patient with active disease



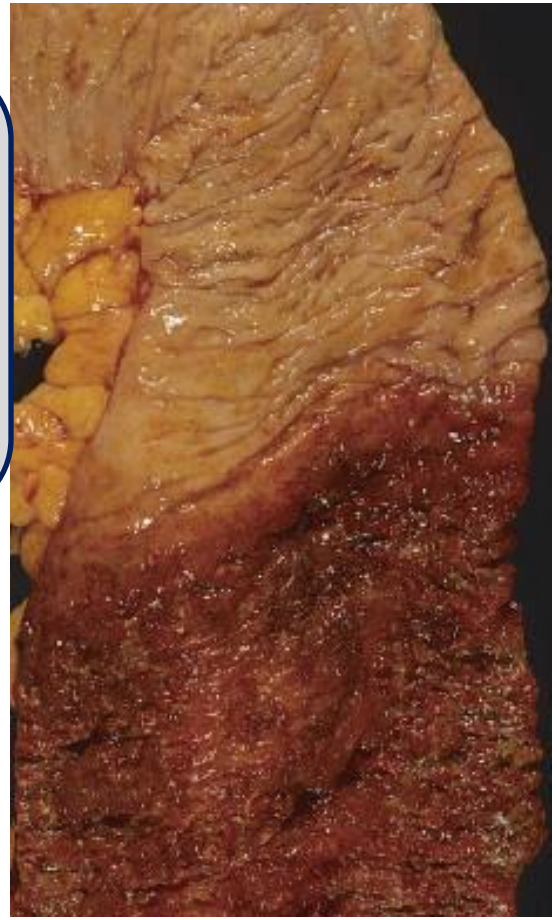
Pancolitis.

All of the colon inflamed



Abrupt transition b/w normal and disease segment.

The doctor during colonoscopy can say that the boundaries clear between inflamed and non-inflamed, no skip areas no cobblestones apperence and we can’t diagnose by just a biopsy



Clinical Features

- It is very similar to crohn disease
- Relapsing remitting disorder
- Attacks of bloody mucoid diarrhea +lower abdominal cramps and iron deficiency anemia
- Temporarily relieved by defecation
- Attacks last for days, weeks, or months. Then it becomes asymptomatic then the attack returns and so in all of his life.
- Asymptomatic intervals.
- Infectious enteritis may trigger disease onset, or cessation of smoking.(the cause in unknown)
- The disease is chronic, so it doesn't has a treatment and cure.
- Usually Colectomy cures intestinal disease only
- Anti-inflammatory (steroids and immune modulating agents) and biologic agents.

Colitis-Associated Neoplasia

- It is the development of disease in a patient with:
- Long standing UC (ulcerative colitis) and CD(crohn disease).
- So, we make periodic surveillance for patients
- Begins as dysplasia >>>> carcinoma.
- Colonoscopy surveillance programs.

- Risk depends on
- **Duration of disease**: increase after 8-10 years.(after it the screening becomes regular)
- **Extent of involvement**: more with pancolitis.
- **Inflammation**: frequency & severity of active disease with neutrophils.