GI
PATHOLOGY

#5

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DIARRHEAL DISEASE

- Diarrhea: increase in stool mass, frequency or fluidity.
- Dysentery: painful , bloody, small volume diarrhea.

Small amount

- **Malabsorptive Diarrhea**
- Pancreatic insuffciency.
- **Celiac disease**
- Crohn disease
- **Cystic Fibrosis**
- **Lactase (Disaccharidase) De**
- **Abetalipoproteinemia**
- **Infectious Enterocolitis**
- **Inflammatory bowel diseases…..**

Malabsorption is caused because of :

- maldigestion no breakdown of nutrients
- malabsorption due to defect in the small bowel microvilli and brush border which increases the surface area and incr. the absorption - **and these brush borders also have certain enzymes for terminal digestion to allow for absorption**

In micro

Chronic illness,inflammation,abdominal pain,diarrhea,patients mainly young adolescents,adults appears with other extra intestinal manifestations sometimes

Even increase in stool frequency only without fluidity can indicate a diarrhea

We have many types of diarrhea with certain features:

* secretory diarrhea : which is not affected by the food intake (even if the patient is fasting diarrhea still there)

*osmotic diarrhea : it is caused by the presence of a highly osmotic content in the bowel -بتصير تسحب معها مية - for ex: patients with lactase deficiency - lactose stuck in the bowel and absorb water which will cause diarrhea

*malabsorptive diarrhea : very important topic we will talk about it today - it is because there is no absorption of nutrients so this nutrients will stay in the lumen of the bowel and causes frequent stool (diarrhea)

*exudative diarrhea : which is mainly caused by infections (bacterial infections) . Contains: exudate,mucous,neutrophils,pus cells

No brush borders = No digestive enzymes = No absorption

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السلايد مكررة don't panic بس عشان في كمان كلام

History is very important :
When child comes to your clinic with fever , mucous in the stool , painful (dysentery)
You will think of infectious causes.

When someone comes to you with long duration of diarrhea (months)
You must think of :Chronic problems

Malabsorptive Diarrhea

- **Chronic.**
- Defective absorption of fats, fat- and water-soluble vitamins, proteins, carbohydrates, electrolytes, minerals and water

Fat soluble vitamins are: A,K,E,D

- **Hallmark is :** steatorrhea.

The stool is greasy, yellowish , sticky, bulky
Due to the presence of high amount of fat

Malabsorptive diarrhea
Defect in one of the following:

- Intraluminal digestion.
- Terminal digestion. For example: in the lactase deficiency
- Transepithelial transport.
- Lymphatic transport. Like if the patient have blockage of lymphatic system congenital or infection related blockage

Manifestations:

It is seen according to the material that is malabsorped

- Weight loss, anorexia,

Malabsorption of proteins will cause weight loss and muscle wasting especially large muscles ex. Gluteus muscles

- Flatus, abdominal distention,

نفخة

The nutrients are not absorbed so the bacteria (normal flora will digest it and cause this abdominal distention

- Borborygmi, Muscle wasting
- Anemia and mucositis (iron, pyridoxine (VB6), folate, or vitamin B12 deficiency)

Inflammation in the mucus membranes especially in the angles of the mouth -associated with iron deficiency

Patient is : Pale شاحب, easy fatigability ,loss of appetite

- Bleeding (vitamin K deficiency)
- Osteopenia and tetany (calcium, magnesium, or vitamin D deficiency)
- Neuropathy (vitamin A or B12 deficiency)
- Skin and endocrine disorders.

Thyroid problems because of malabsorption of iodine

Cystic Fibrosis

- Mutations in cystic fibrosis transmembrane conductance regulator (CFTR)
- Defects in ion transport across intestinal and pancreatic epithelium.
- Thick viscous secretions.
- Mucus plugs in pancreatic ducts >>> pancreatic insufficiency (80% of patients).
- Defect in intraluminal digestion.

Example of ion transport : NA+2 channels
Defect in na+2 channels -> no NA+2 -> no water -> so the secretions will be viscous because of low amounts of water .

Meconium ileus : very thick , difficult to pass , obstruction of bowel in neonates

Cystic fibrosis is multi-system disorder , you will find symptoms in Gi tract & respiratory system for ex. If we're considering maldigestion in our interest ,Patients can be given certain enzymes orally, so they directly reach Gi tract & mimic the function of pancreatic enzymes in digestion.

Celiac Disease

- *Gluten sensitive enteropathy*
- Immune mediated enteropathy
- Wheat, rye (الشعير) or barley (الشعير).
- Genetically predisposition, HLA-DQ2 or HLA-DQ8.
- Treatment: gluten free diet.

- Association with: type 1 diabetes, thyroiditis, and Sjogren syndrome

Entero = small bowel
Pathy = disease

The patient carries these genes

Pathogenesis

Starts with :-

Ingesting of :

Cleaved into

- Gluten >>> gliadin >>> react with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells >>> CD4+ T cells activation >>> cytokines >>> tissue damage.

Activation of immune system

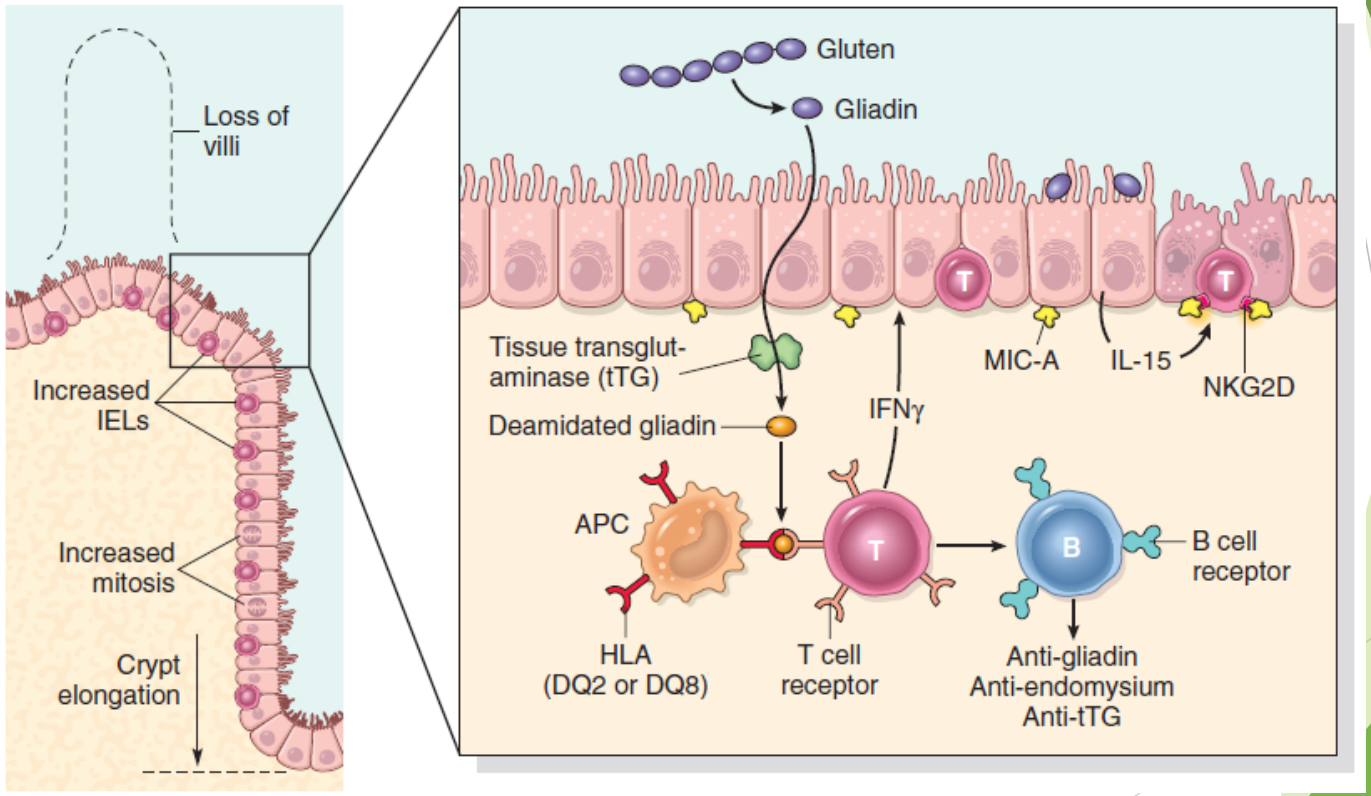
This damage starts with shorting in the villi Until it becomes flat and the surface area will decrease leading to malabsorption

- Serology:
- Anti- tissue transglutaminase antibodies

Highly sensitive but not specific - it the starting step for evaluating celiac

- Anti-gliadin antibodies.
- Anti -endomysial antibodies

Celiac disease is Neither allergy nor completely autoimmune disease it is : **“ Immune-mediated disease “**



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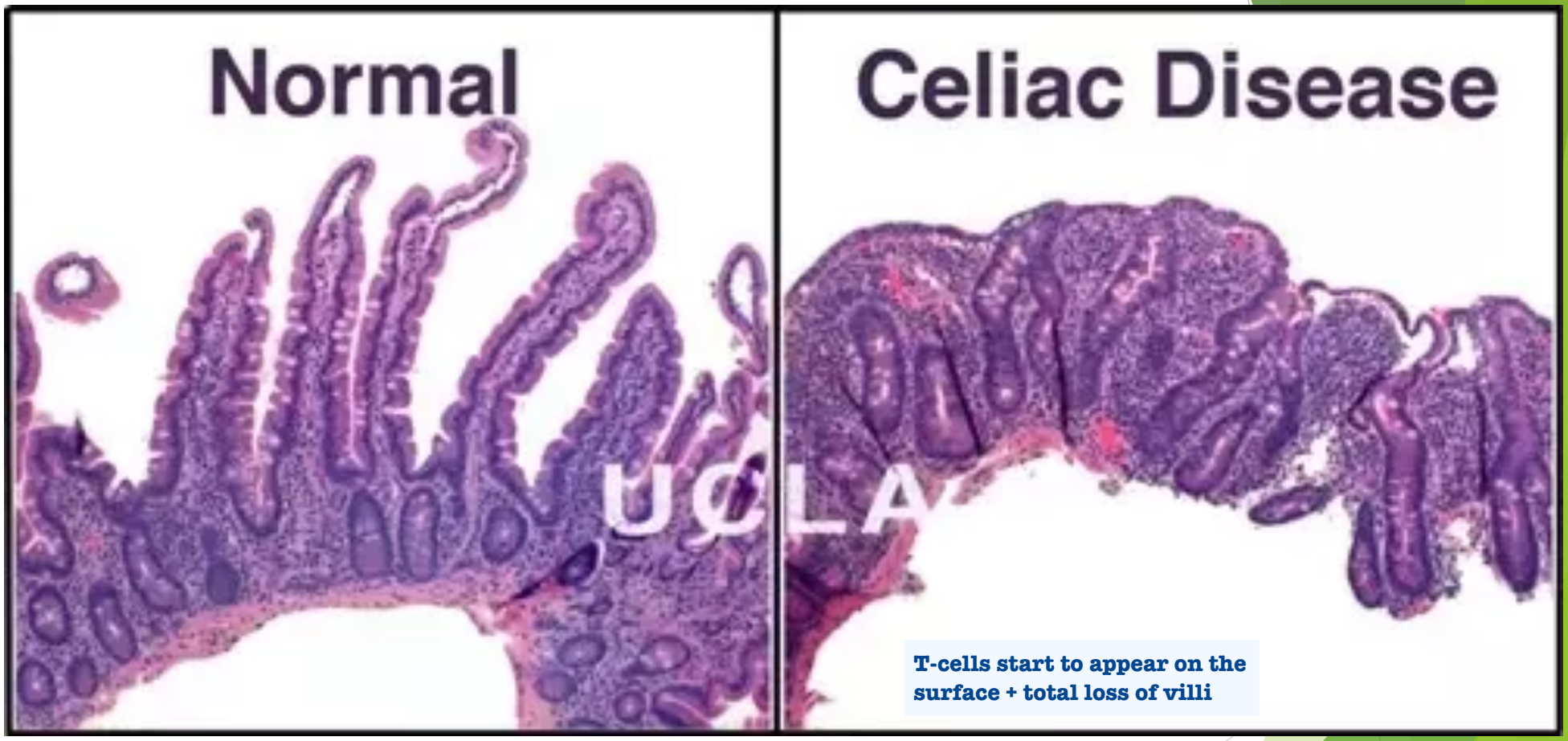
MORPHOLOGY

The first portion of duodenum is NOT the preferred place to take a biopsy to diagnose celiac disease , **WHY** ?? because the first portion is normally inflamed due to the gastric juice.

- Second portion of the duodenum or proximal jejunum.
- **Triad**: intraepithelial lymphocytosis (CD8+ T cells), crypt hyperplasia, and villous atrophy.
- Lamina propria: lymphocytes, plasma cells, eosinophils…….
- IEL & villous atrophy are not pathognomonic, seen in viral enteritis.

Intraepithelial lymphocytes

- Diagnosis: Clinical, histologic and serologic correlation.



NORMALLY: villi are long, cylindrical lined by epithelial cells & some goblet cells on the surface

Clinical Features

- **Children 6-24 months : classical or non classical symptoms**
- **Classical**: Irritability, abdominal distention, anorexia, diarrhea, failure to thrive, weight loss, or muscle wasting
- **Non-classical:** abdominal pain, nausea, vomiting, bloating, or constipation.
- Blistering skin lesion, **dermatitis herpetiformis**, in 10% of Pnts.

Doesn't gain weight

Misdiagnosed with herpes

Dermatitis herpetiformis.

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

Their absorption is in the terminal ileum NOT in duodenum or jejunum .

No symptoms

خامل ورح يظهر في مرحلة معينة

Diagnosis:

- **Non invasive serologic tests:**
- **Most sensitive:**
- Anti tissue transglutaminase antibody, IgA
- Anti deamidated gliadin antibodies, IgA & IgG

We start with the sensitive serology

If positive we ask the patient to do the antiendomysial test (most specific one)

- **Most specific, but less sensitive**
- Antiendomysial antibody.

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

Endoscopy

Lactase (Disaccharidase) Deficiency

Watery diarrhea
NOT steatorrhea

- Osmotic diarrhea

Due to presence of high sugar content in the bowel lumen.

- Lactose remains in the gut lumen.
- Lactase found at apical brush border membrane
- Normal biopsy findings.
- Two types:
- ***Congenital*** *: AR, genetic mutation, rare*, explosive diarrhea, watery, frothy stools & abdominal distention, after milk ingestion

Very early age presentation

- ***Acquired*** *: follow* viral or bacterial enteritis, downregulation of gene, after childhood.

More common

It can present at any age

Abetalipoproteinemia

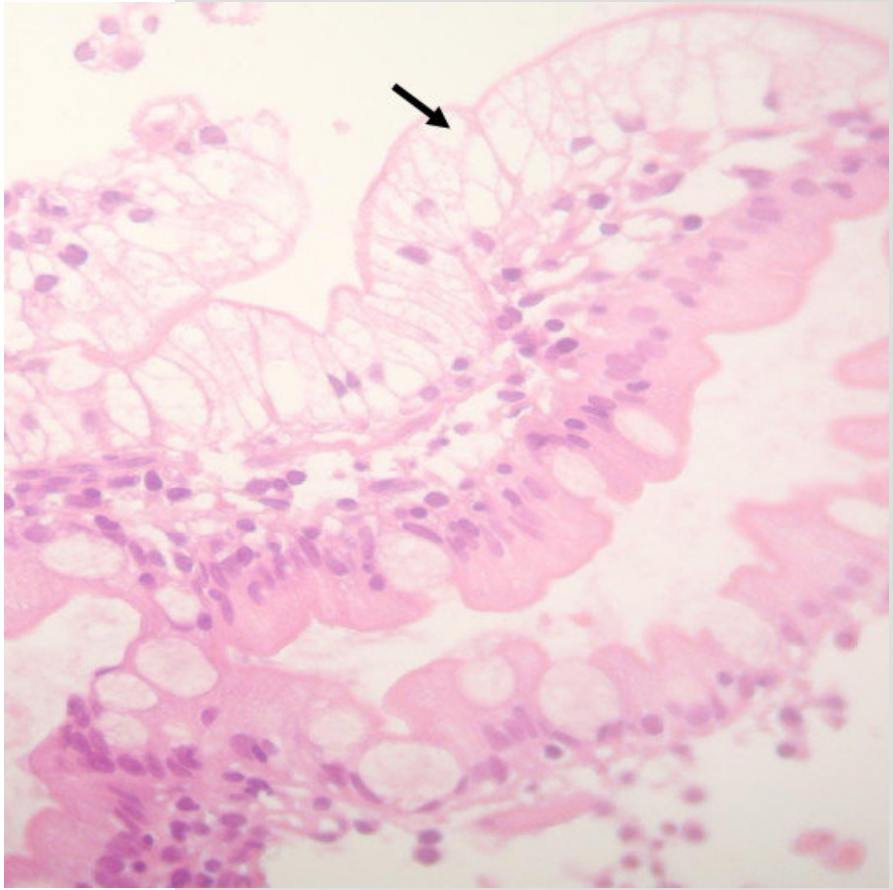
- Autosomal recessive, rare.
- Infants w/ failure to thrive, diarrhea, and steatorrhea
- Lack of absorption of fat and fat soluble vitamins

- Inability to synthesize triglyceride-rich lipoproteins.
- Transepithelial transport defect of TG and FAs.
- Monoglycerides and triglycerides accumulate in epithelial cells.

Because of

Clear cytoplasm appearance under the microscope

Looks like the appearance of fat tissue under the microscope



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

الدكتورة حكت انه اذا في شي مش لازم تنسوه هو ال celiac disease

Diseases of the intestines

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

INFLAMMATORY INTESTINAL DISEASE

- **Sigmoid Diverticulitis**
- **Chronic Inflammatory bowel diseases (CIBD)**

  Crohn disease

  Ulcerative colitis

Chronic .
Genetic predisposition .
Immune mediated conditions (not autoimmune no antibodies present in the serum to diagnose inflammatory bowel diseases).
Diagnosis based on the clinical scenario and histopatholgy findings .
Difficult to diagnose ,it may take months to be diagnosed and start treatment.

Inflammatory Bowel Disease

Affect the intestinal tract from the mouth to the anus .

There is many differences between crohn disease and ulcerative colitis we have to know it because the management will differ

- Chronic IBD.
- Genetic predisposition.
- Inappropriate mucosal damage.

Exact mechanism still unknown

Exaggerated response due to allergen or certain type of food

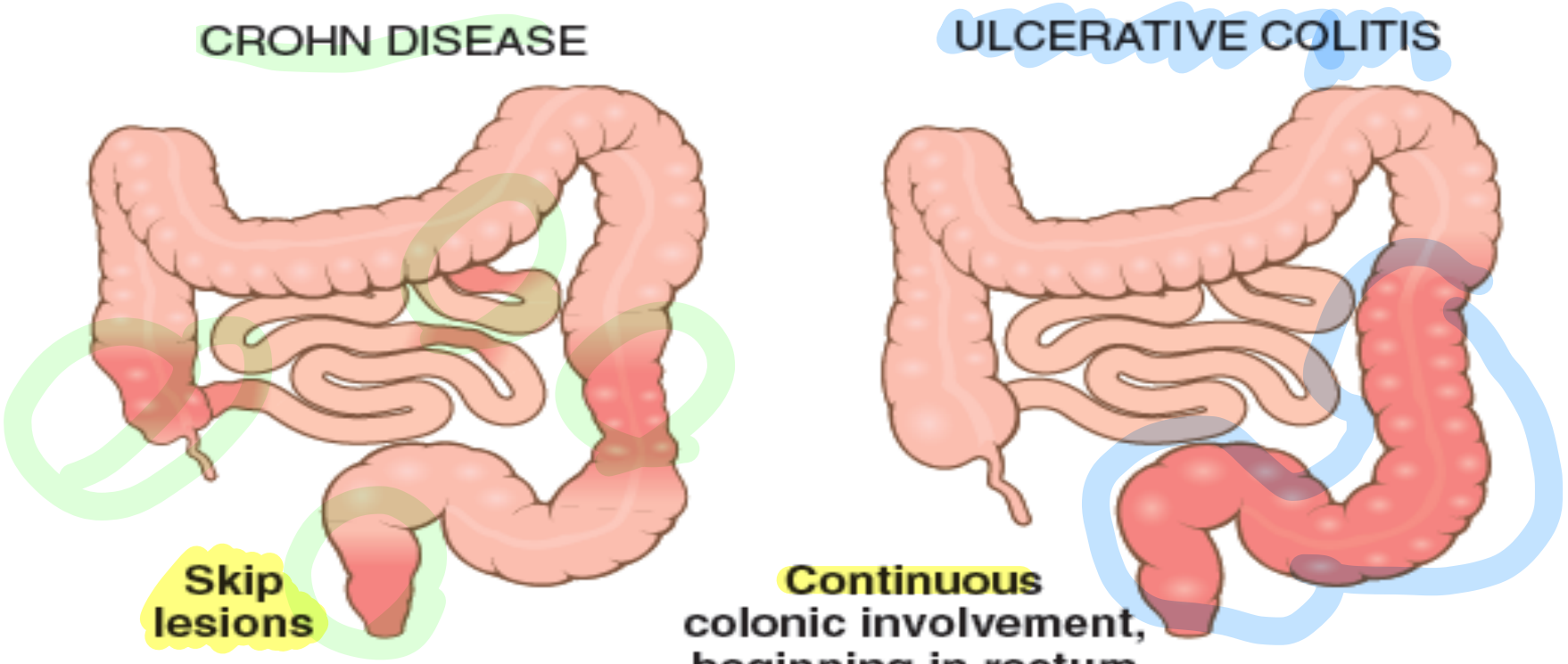
- ***Ulcerative colitis**: limited to the colon and rectum, extends only into mucosa and submucosa.*

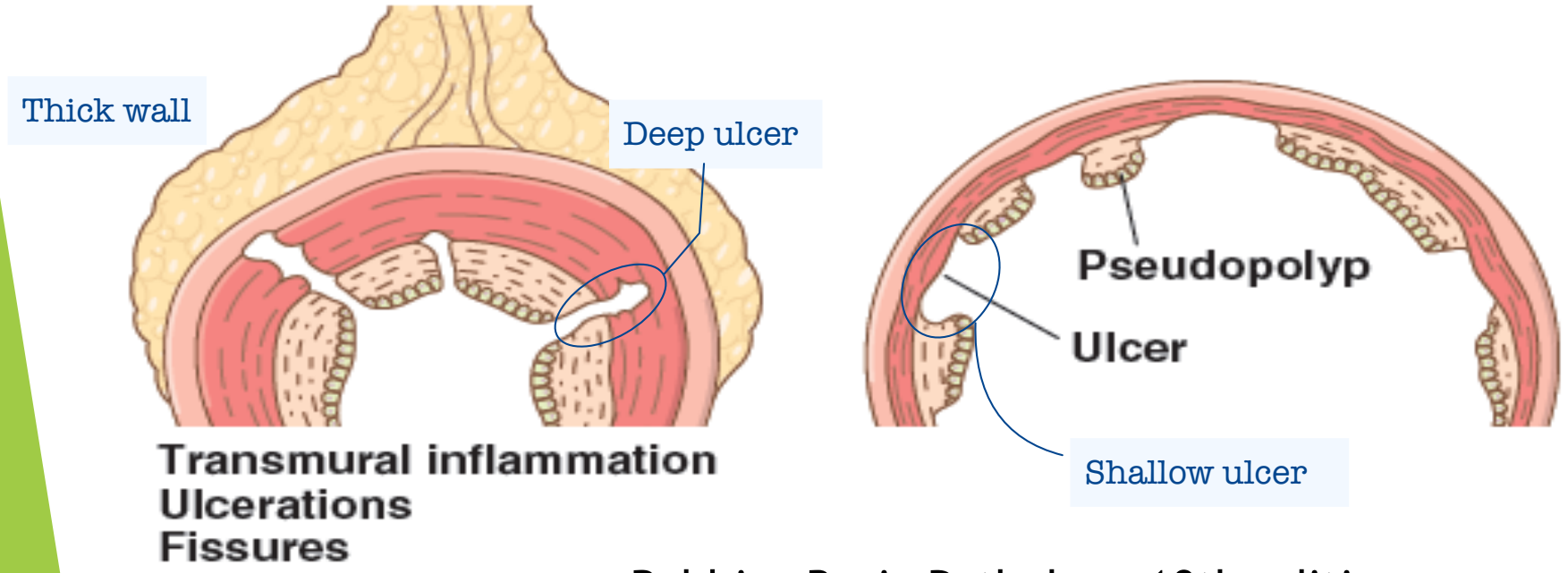
Mainly colon but it can extend to the cecum

Superficial parts of the bowel

- ***Crohn disease**: regional enteritis, frequent ileal involvement, affect any area in GIT, frequently transmural.*

The whole wall is involved





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Epidemiology

- Adolescence & young adults
- 2nd peak in fifth decade.

- Geographic variation.
- ***Hygiene hypothesis***: *childhood exposure to environmental microbes prevents excessive immune system reactions. Firm evidence is lacking!!!.*

مش مؤكدة علميًا اذا صحيحة او خاطئة لكن الدكتورة تؤمن بها

The more you exposed to microbes in your childhood
The more your immunity becomes better

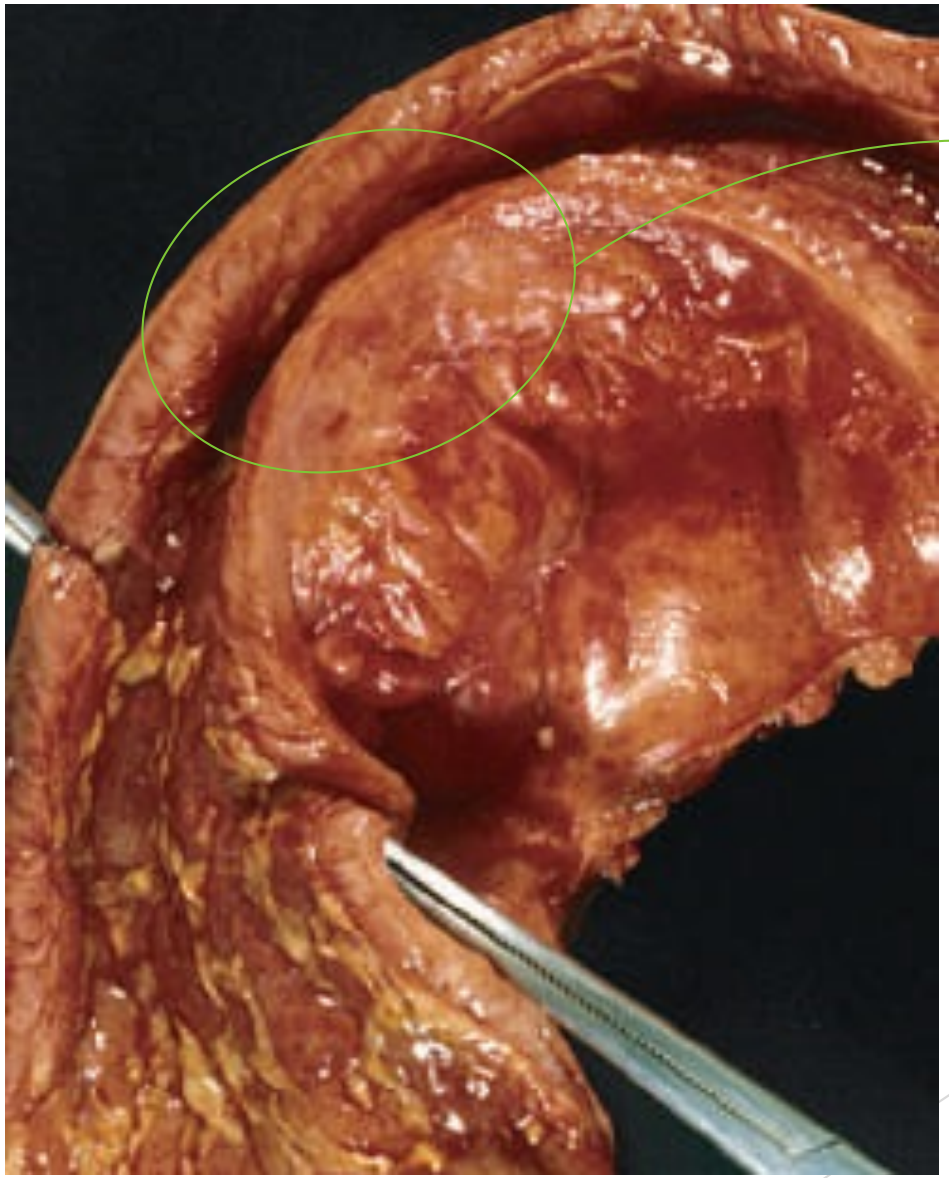
Crohn Disease Morphology

- Macroscopic:

- Regional enteritis. Small parts of the bowel are affected
- Any area of GIT.
- Most common sites: terminal ileum, ileocecal valve, and cecum.
- Small intestine alone 40%
- Small intestine and colon 30%
- Colon only 30% If presented here it is Hard to differentiate between it and ulcerative colitis
- Skip lesions
- Strictures common

Narrowing

Small bowel stricture.



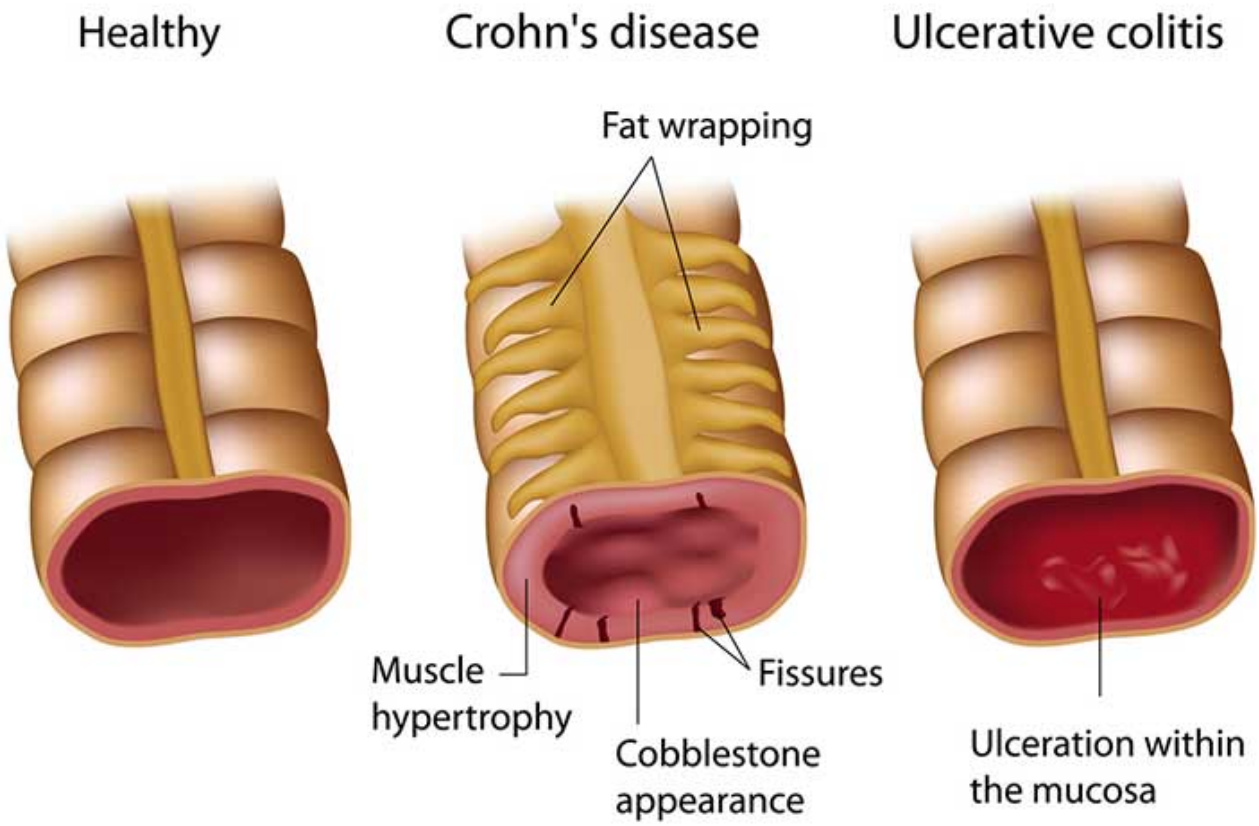
Once the patient is diagnosed with crohn disease or inflammatory bowel disease, this disease will stay for life like diabetes

- Earliest lesion: aphthous ulcer
- Elongated, serpentine ulcers.
- Edema , loss of bowel folds.
- Cobblestone appearance

Characteristics for crohn disease

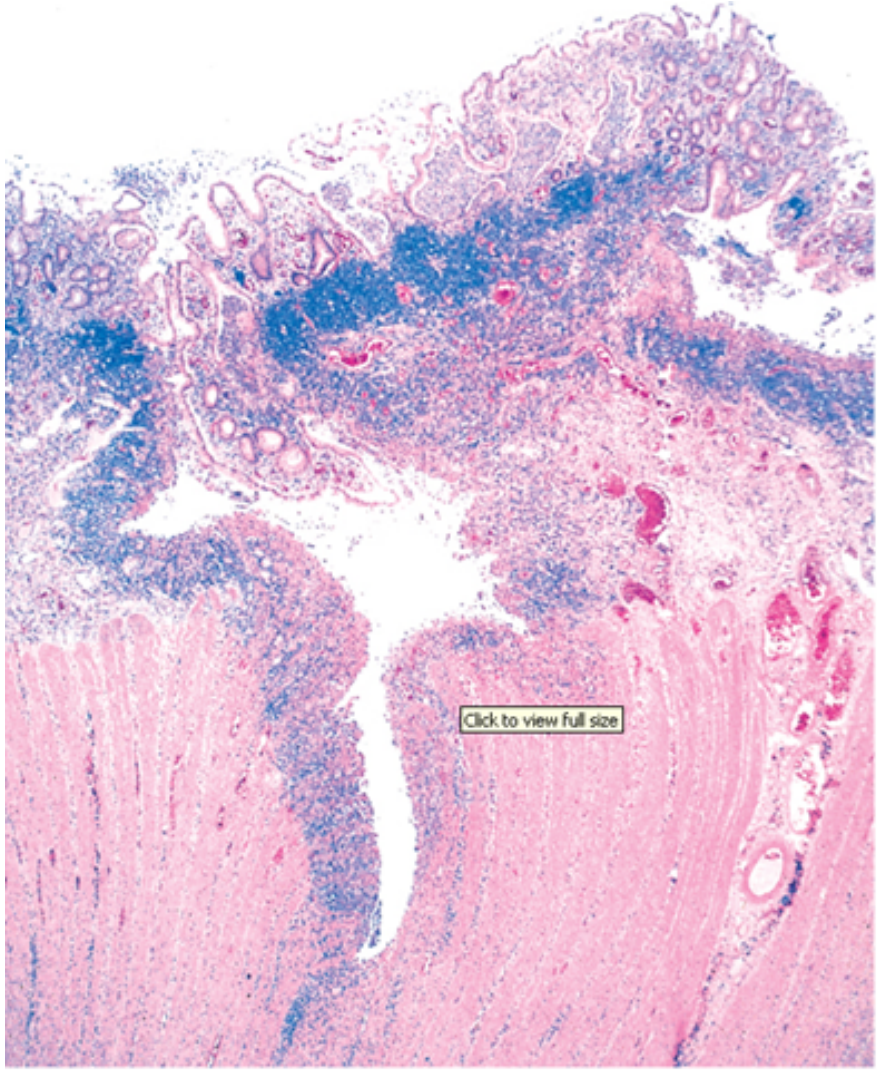
- Fissures, fistulas, perforations.
- Thick bowel wall (transmural inflammation, edema, fibrosis, hypertrophic MP)
- Creeping fat

We don't see fissures in ulcerative colitis it appears only in crohn disease


Healthy
Crohn's disease
Ulcerative colitis
Fat wrapping
Muscle hypertrophy
Cobblestone appearance
Fissures
Ulceration within the mucosa

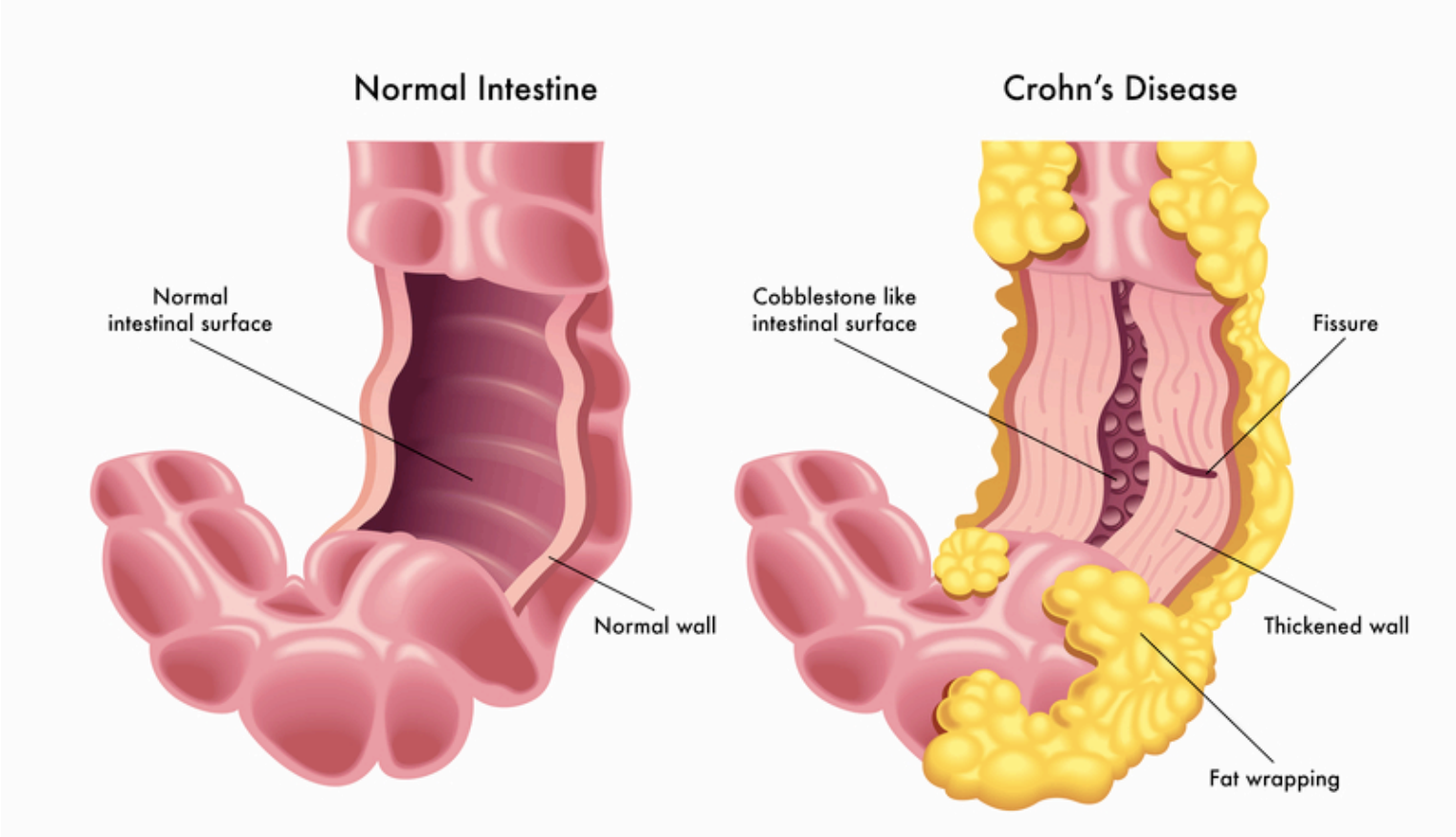
fissure

Deep ulceration



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

Creeping fat



Cobblestone appearance

ResearchGate

- Microscopic:

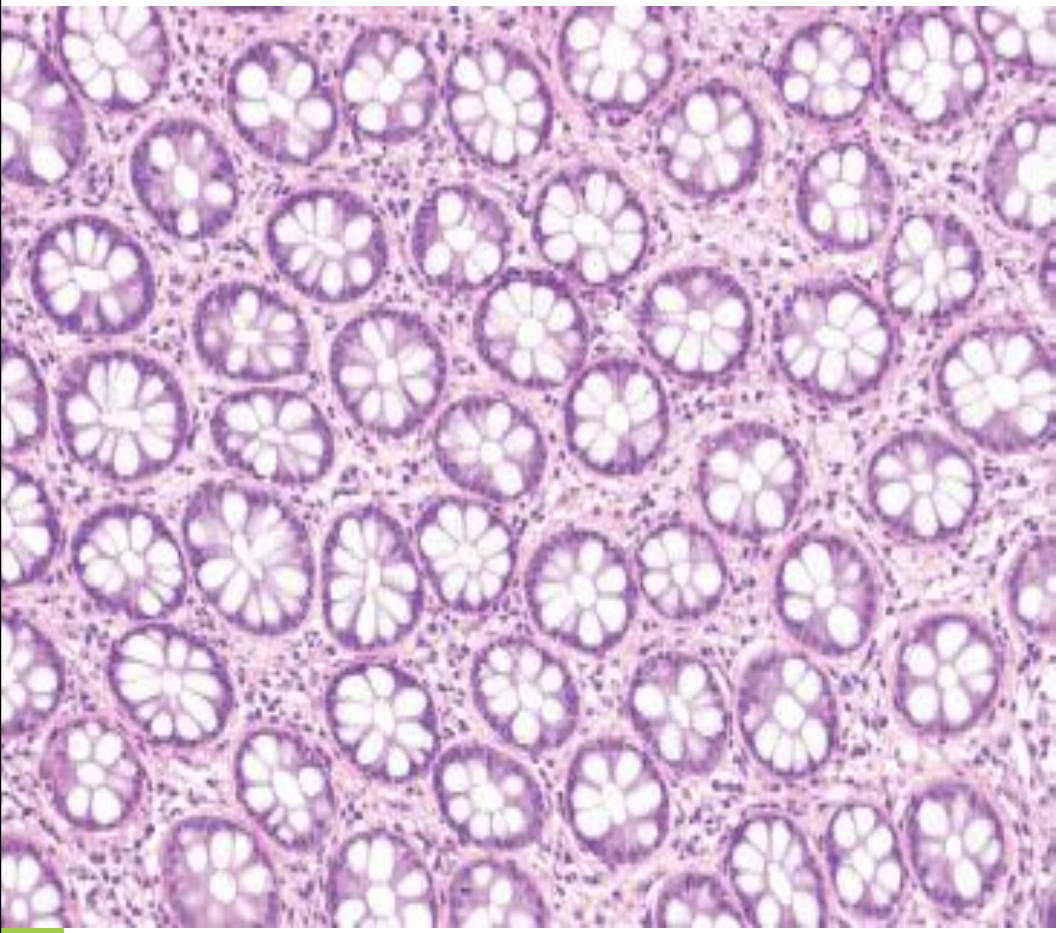
- Neutrophils in active disease.
- Crypt abscesses.
- Ulceration.
- Distortion of mucosal architecture
- Paneth cell metaplasia in left colon
- Mucosal atrophy.

Chronic phase

- Noncaseating granulomas (hallmark) only in 35% of cases. Where??????

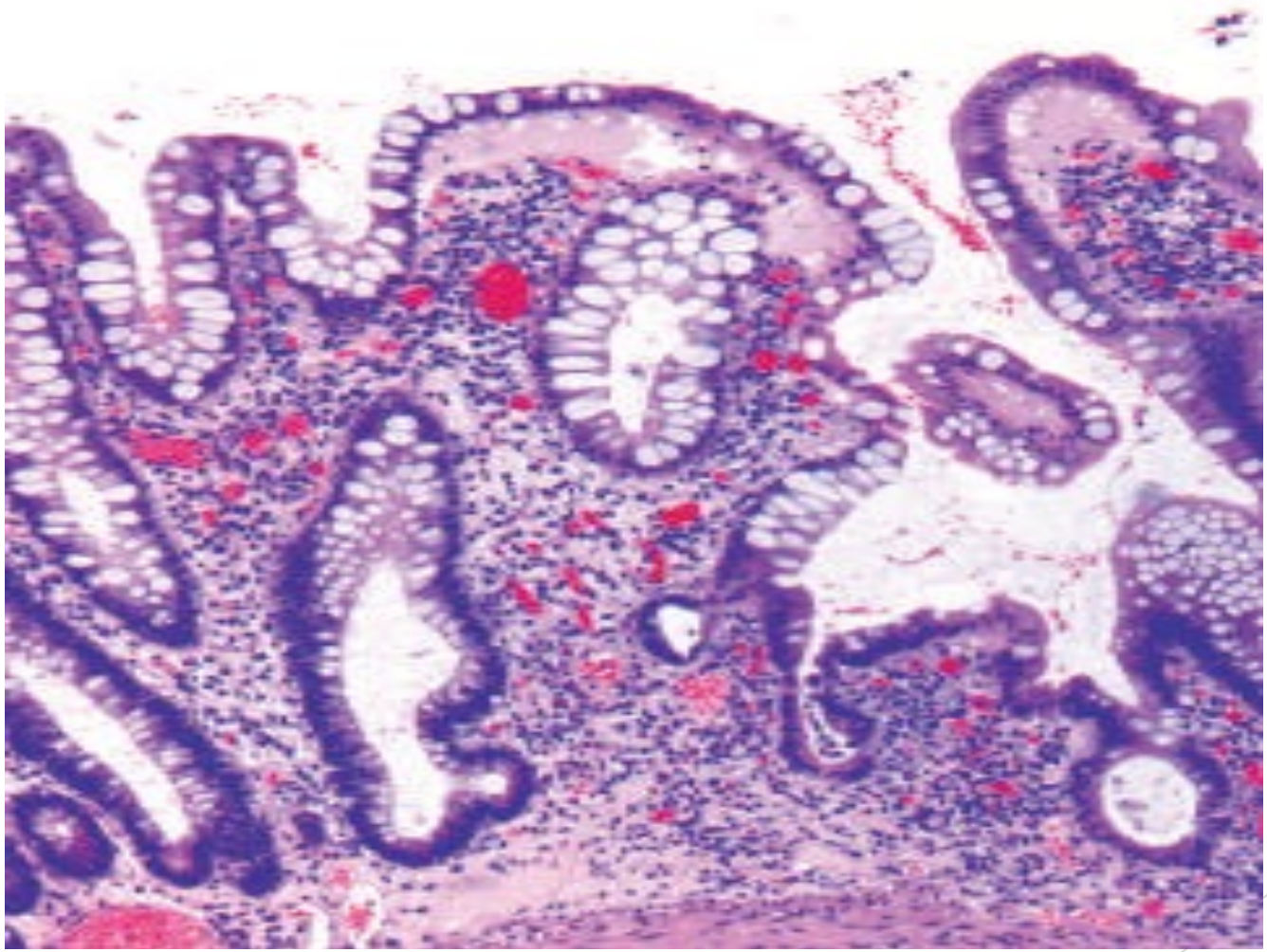
If the pathologist was lucky and find the noncaseating granulomas – firm background to say it is crohn for sure and not ulcerative colitis.

Normal colon

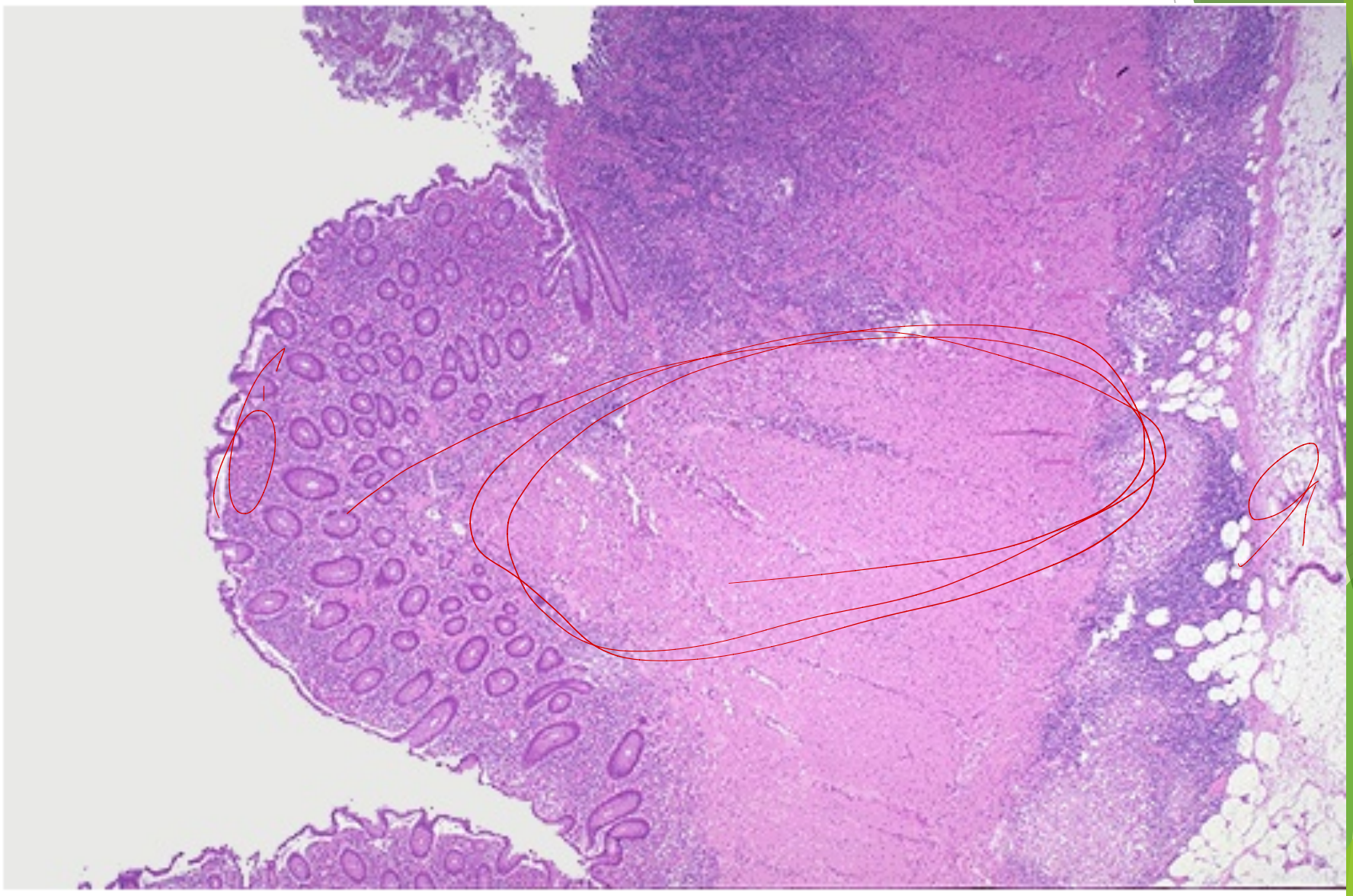


Haphazardly arranged crypts

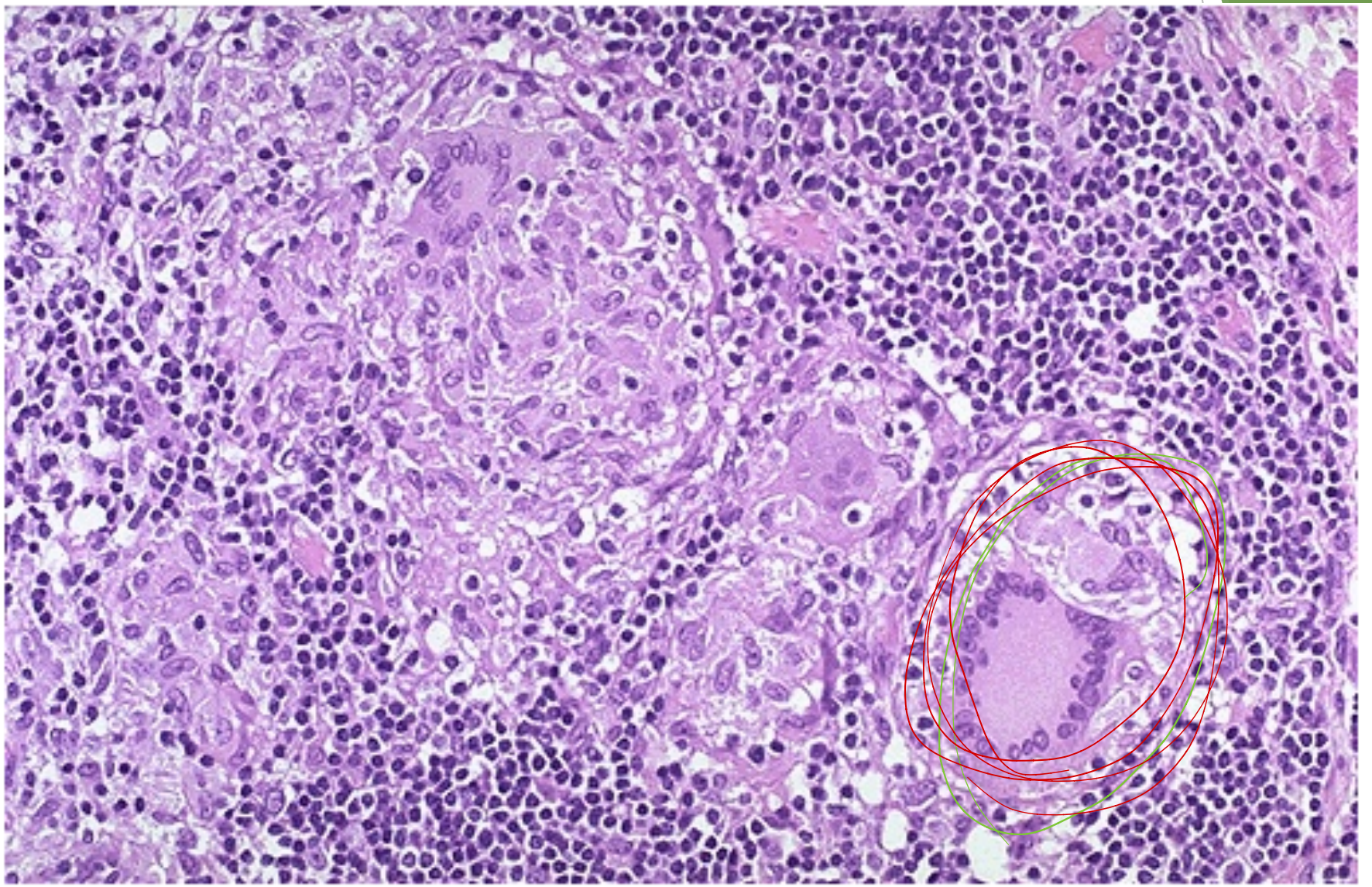
Ugly appearance



Transmural inflammation.



Non-caseating granuloma.



Clinical Features

- Intermittent attacks of mild diarrhea, fever, and abdominal pain.
- Acute right lower-quadrant pain and fever (20%)
- Bloody diarrhea and abdominal pain (colonic disease)
- Asymptomatic intervals (weeks to months)
- Triggers: physical or emotional stress, specific dietary items, NSAID use, and cigarette smoking.

- Complications:
- Iron-deficiency anemia
- Hypoproteinemia and hypoalbuminemia, malabsorption of nutrients, vitamin B12 and bile salts

Because it can attack small bowel

- Fistulas, peritoneal abscesses, strictures

Very important complications

- Risk of colonic adenocarcinoma ……

After 10 yrs of disease the patient can develop risk of getting adenocarcinoma ,so they must undergo periodic surveillance endoscopy & biopsy to see whether there's dysplasia or not .