She reviewed the acronym VITAMIN C, which stands for:

Vascular
Infectious/Inflammatory
Traumatic
Autoimmune
Metabolic (endocrine)
Iatrogenic
Neoplastic
Congenital

Inflammatory Pathology of the (Luminal) GI Tract

APPROVED

Shannon J. McCall, M.D.

Assistant Professor of Pathology

shannon.mccall@duke.edu

Esophagus

Patients with this present with these two symptoms. Similar to presentation of esophageal neoplasms.

Esophagitis

- Pain when swallowing

aka odynophagia

- Difficulty swallowing

aka dysphagia

Esophagitis

- Reflux
- Infectious
- Inflammatory

Reflux is one of the main causes of esophagitis

Reflux Esophagitis

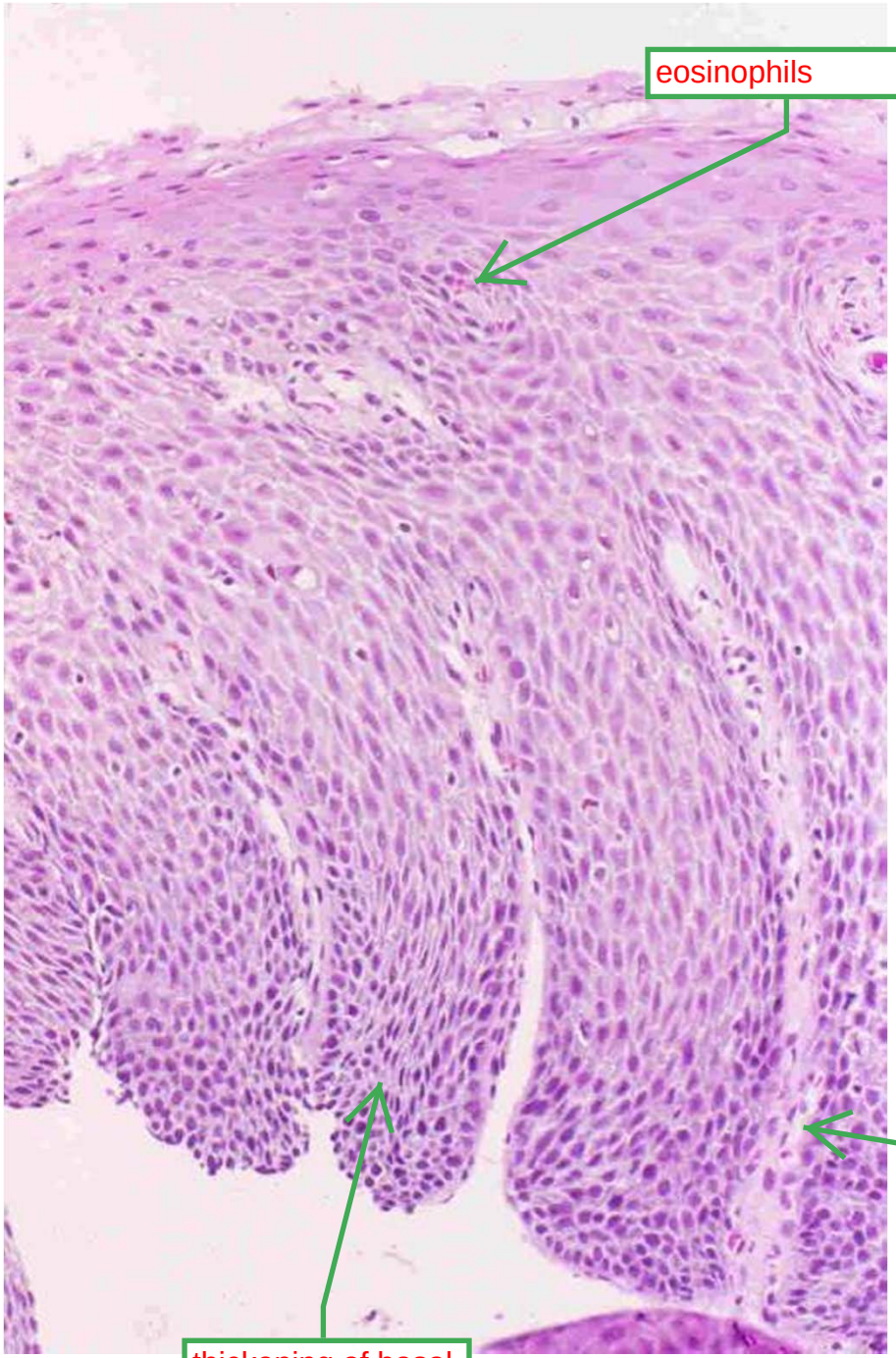
- Commonly associated with hiatal hernia
- Reflux of stomach contents
  - **acid**
  - **pepsin**
  - **possibly bile**

Dont confuse reflux with hiatal hernia. HH is an anatomic problem. Pts with reflux have stomach contents coming up into esophagus (could be acid, enzymes, bile, etc.).

Reflux Esophagitis

- Heartburn
- Sensation of regurgitation
- Worse when the patient lies down
- Worse after a large meal

Pts have a sensation of heart burn --> very uncomfortable. Worse when they lie down or after a large meal (due to physics).

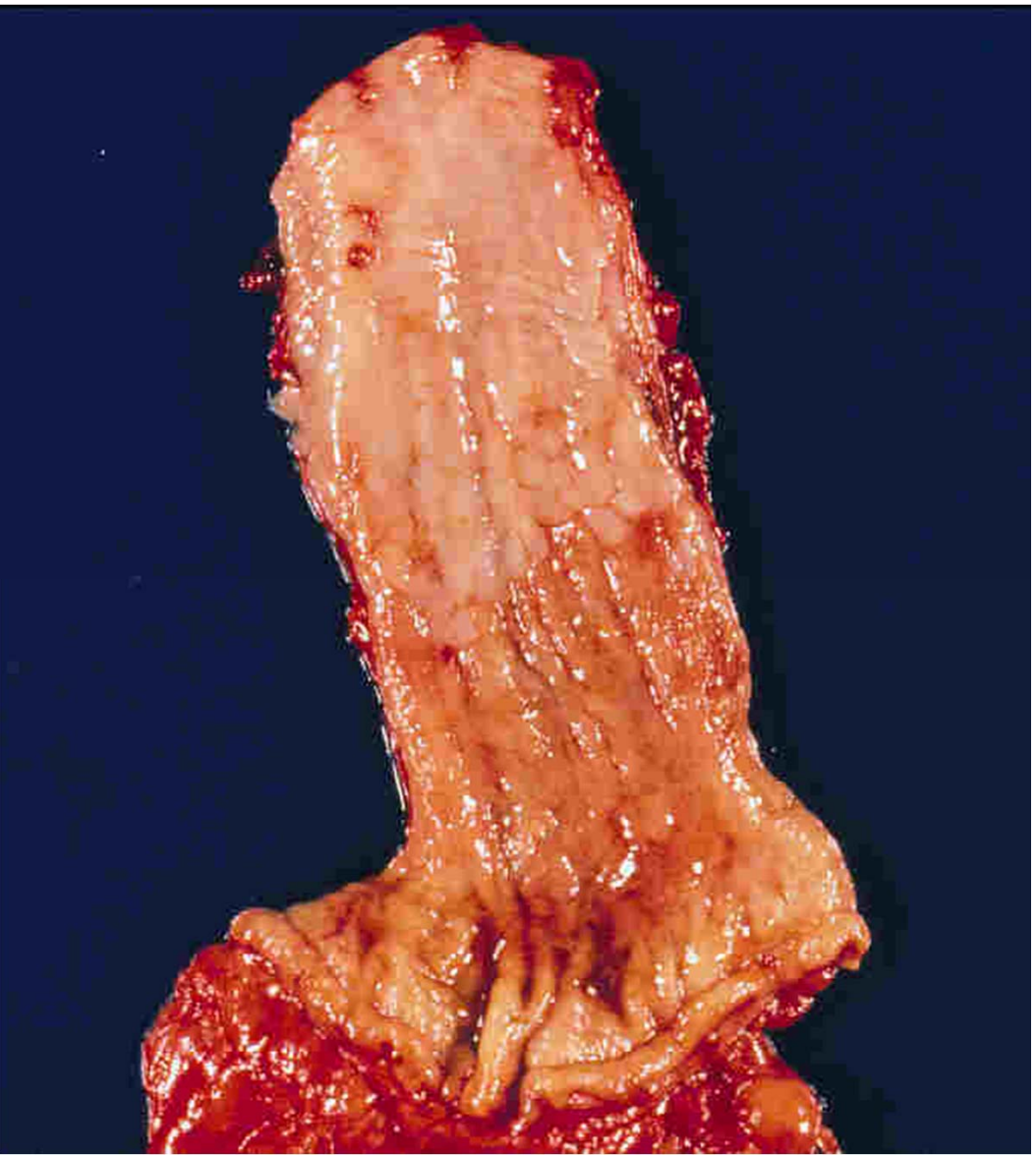


Reflux Esophagitis

- Thickening of the basal portion of the epithelium
- Elongation of rete ridges
- Scattered intraepithelial eosinophils

Esophagus is lined by squamous epithelial with a thin basal layer. Sq. epithelium gradually matures on its way to the top. In pts with chronic reflux the sq epithelium looks different.

3 main complications to be aware of.



Complications

- Ulceration
- Stricture
- Important! Barrett's esophagus = "columnar metaplasia with goblet cells", aka, "goblet cell intestinal metaplasia"

Long standing caustic irritation to the esophogus leads to metaplasia. If you see goblet cells then pt has Barrett's.

Esophagitis

- Reflux
- Infectious
- Inflammatory

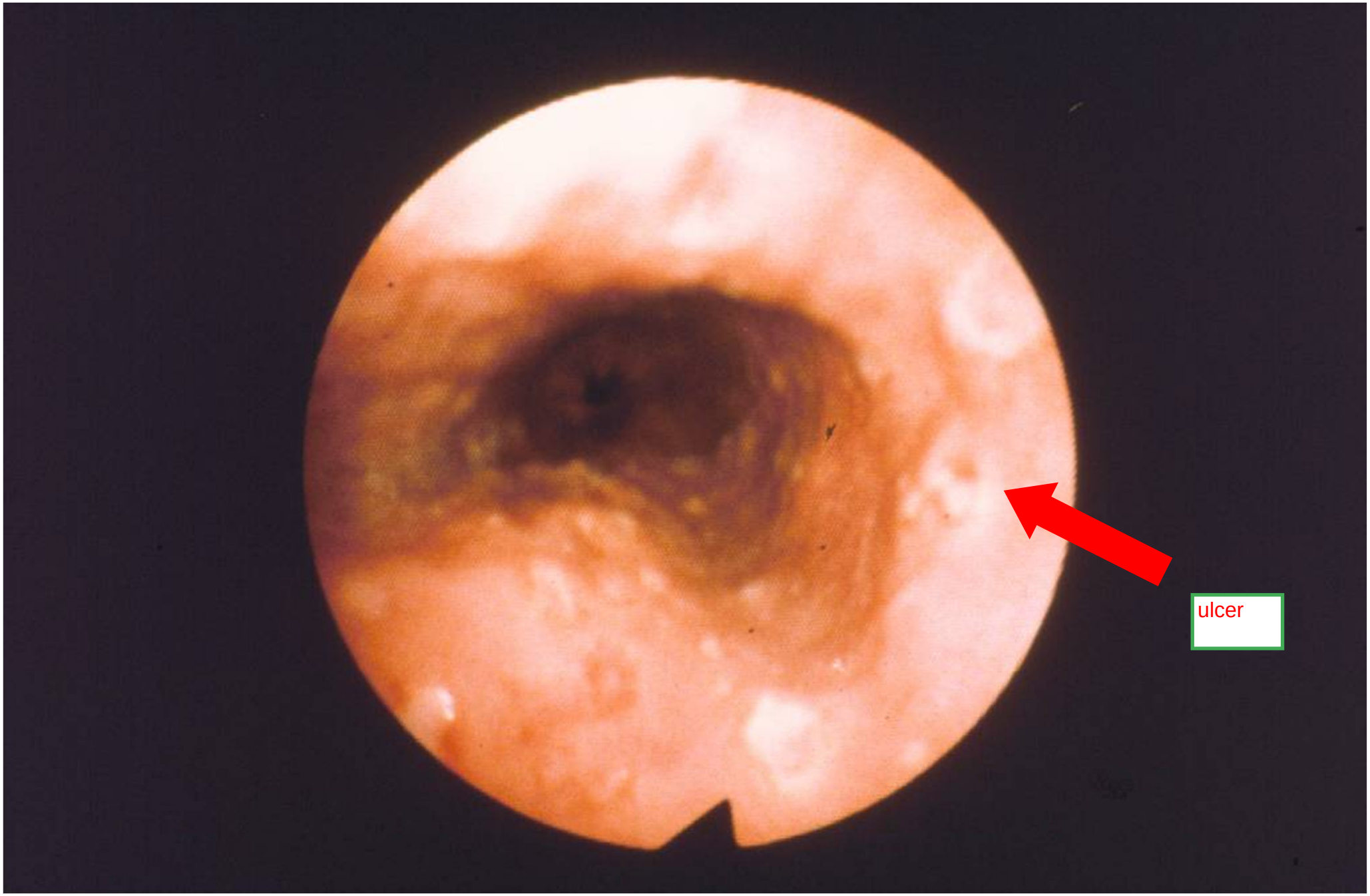
Reflux does not always lead to Barrett's. Can be treated by reducing acid in stomach. Pts usually on protein pump inhibitors.

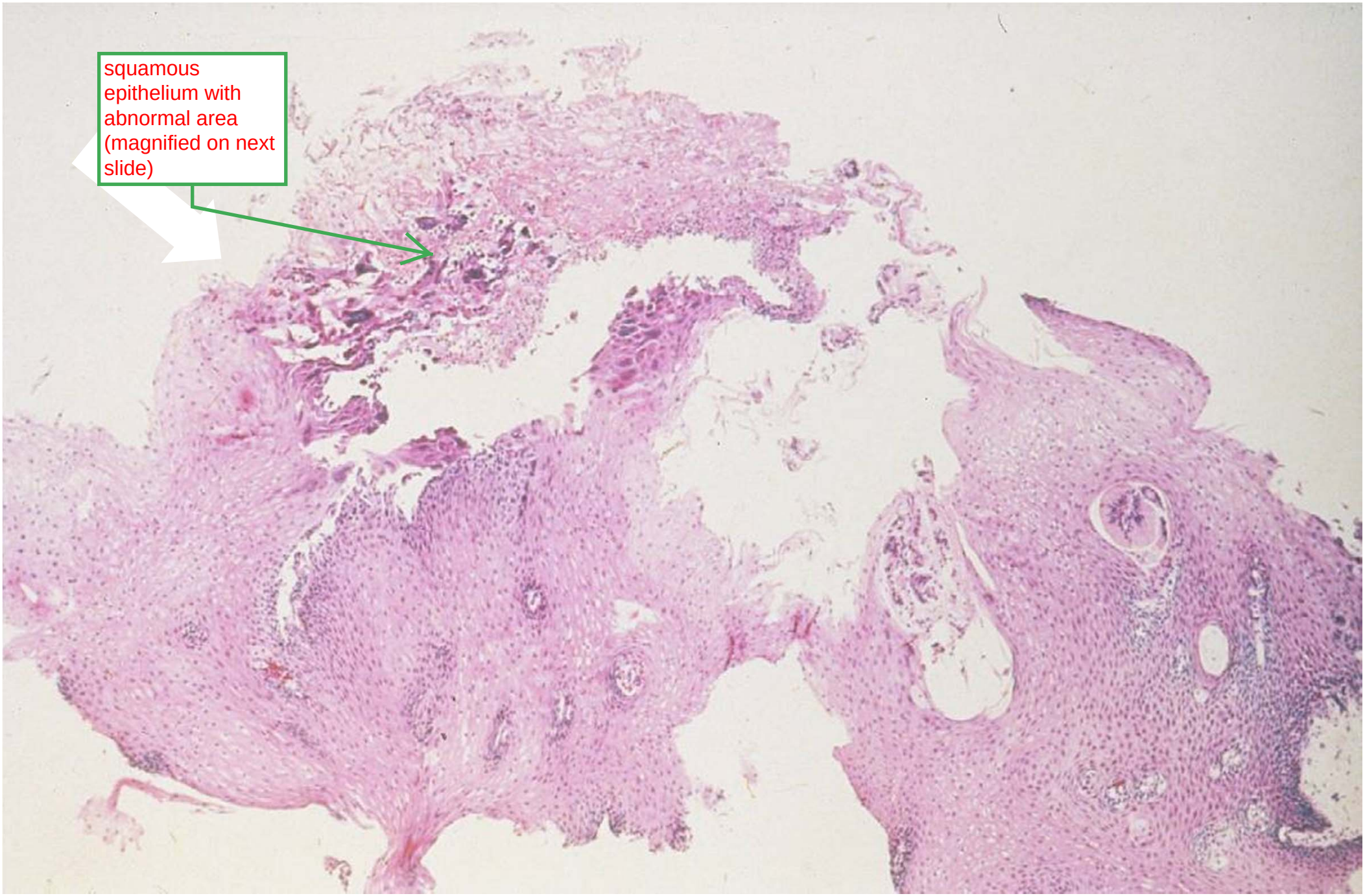
Think about infections in three categories: 1) healthy people 2) people who are slightly immunocompromised (old people, diabetics, etc.) 3) the severely immunocompromised

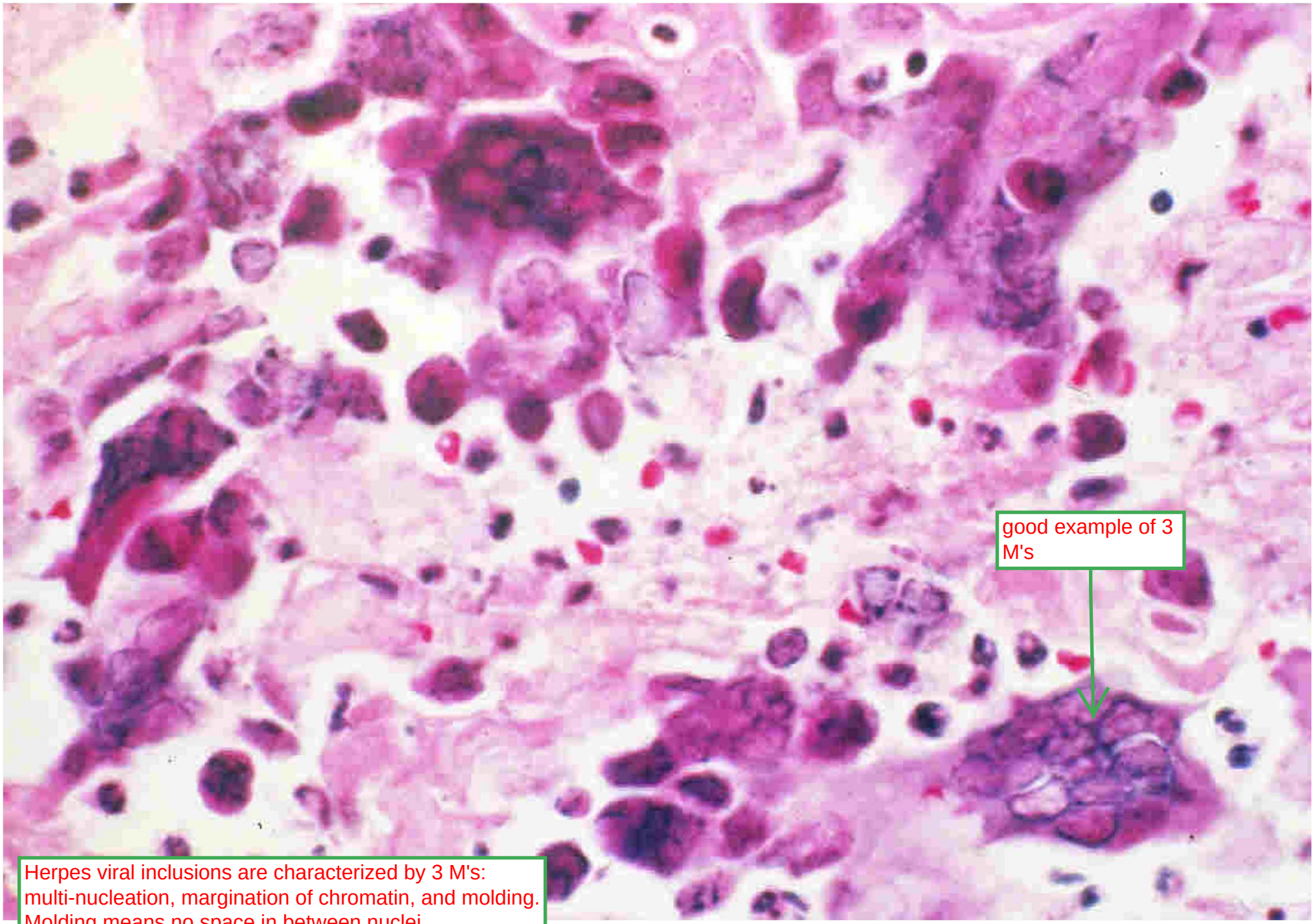
Herpes Esophagitis

- Both immunosuppressed and immunocompetent patients (especially during first outbreak)
- Blister forms early, but usually seen as an ulcer
- Herpetic nuclear changes seen at the edge of the ulcer, *in the squamous epithelial cells*.

Herpes esophagitis can happen to anybody. To a normal person getting it for the first time it can be severe in oral cavity and involve the esophogus. blister form but by the time you get to doc the blisters break open and herpetic ulcers form.


ulcer

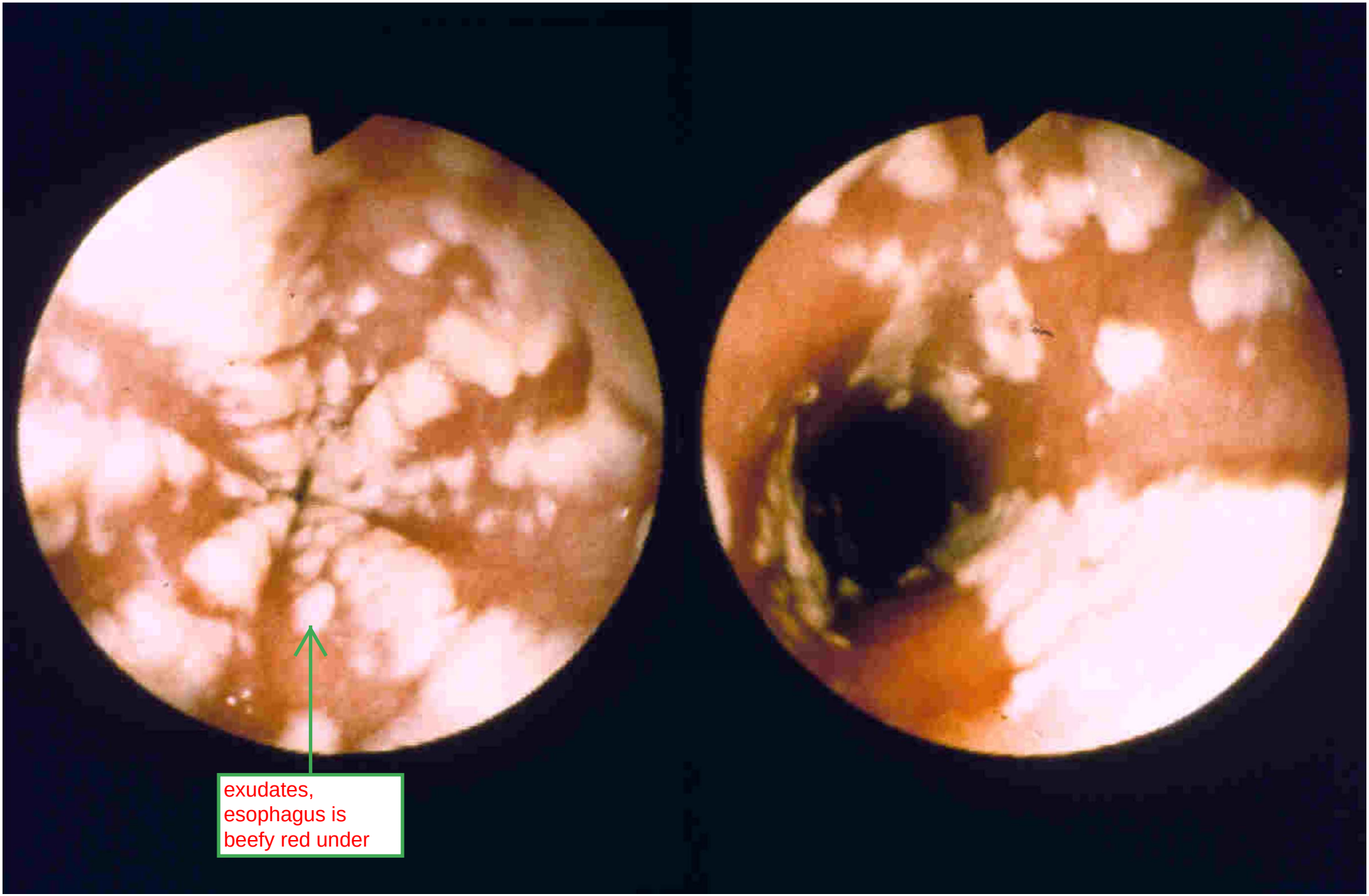

squamous epithelium with abnormal area (magnified on next slide)

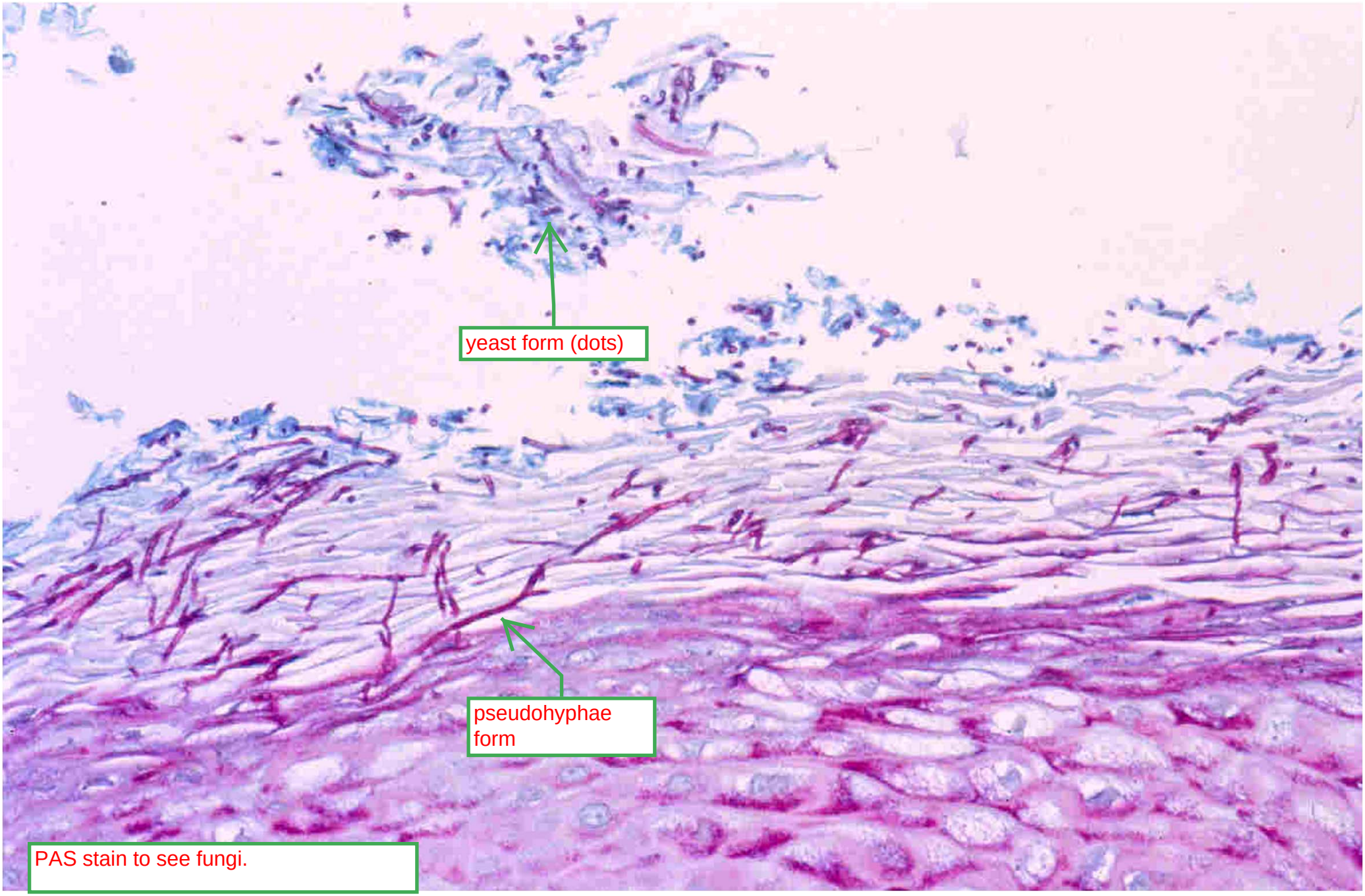


Herpes viral inclusions are characterized by 3 M's: multi-nucleation, margination of chromatin, and molding. Molding means no space in between nuclei.

Candida Esophagitis

- Immunosuppressed patients and others
  - **"Relatively immunosuppressed"**
    - **elderly or sick**
    - **diabetes**
- Exudate forms a 'pseudomembrane' on the mucosal surface. white colored (see next slide)
- Usually <u>not</u> an invasive infection.


exudates,
esophagus is
beefy red under

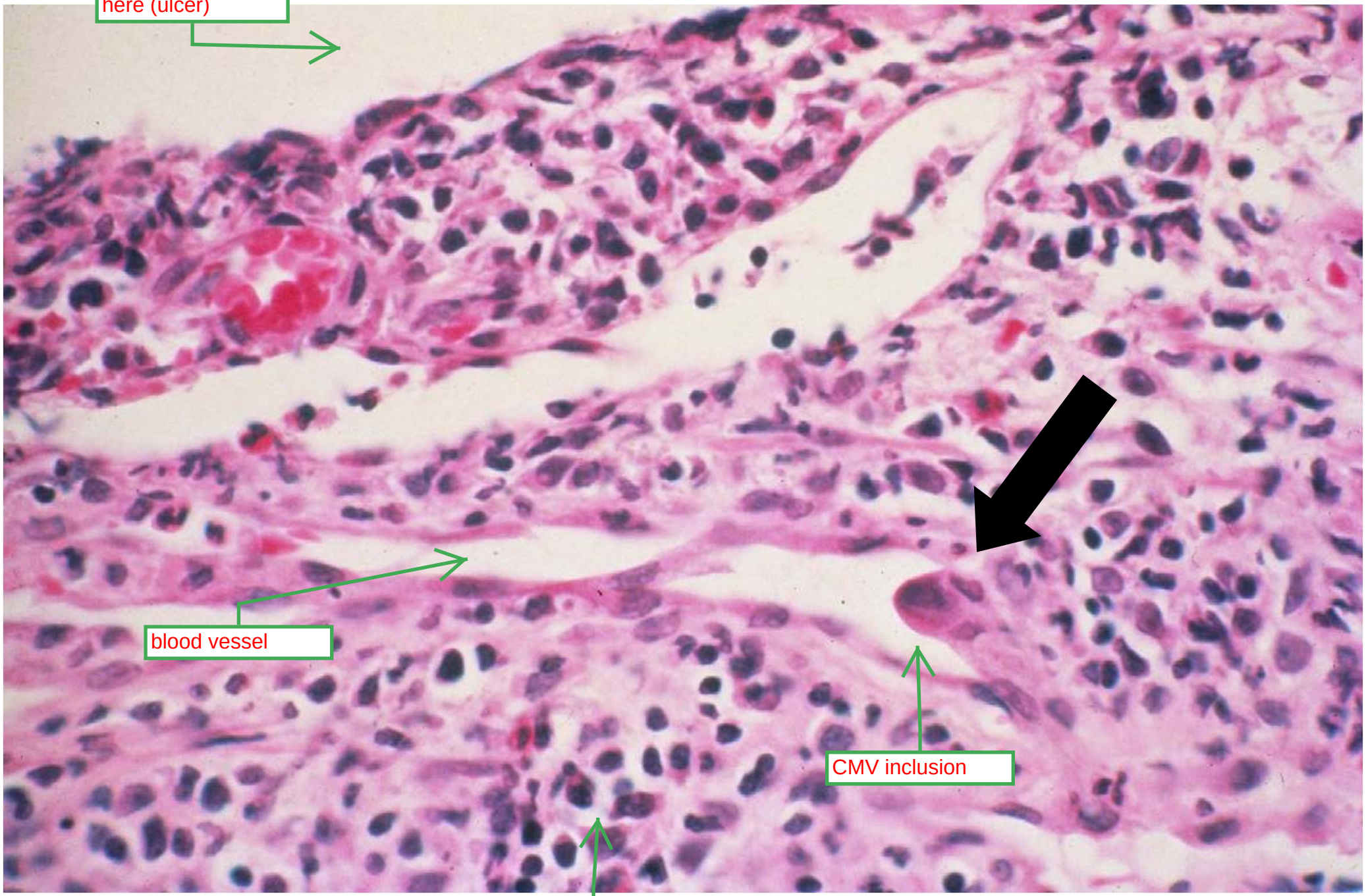

yeast form (dots)
pseudohyphae form
PAS stain to see fungi.

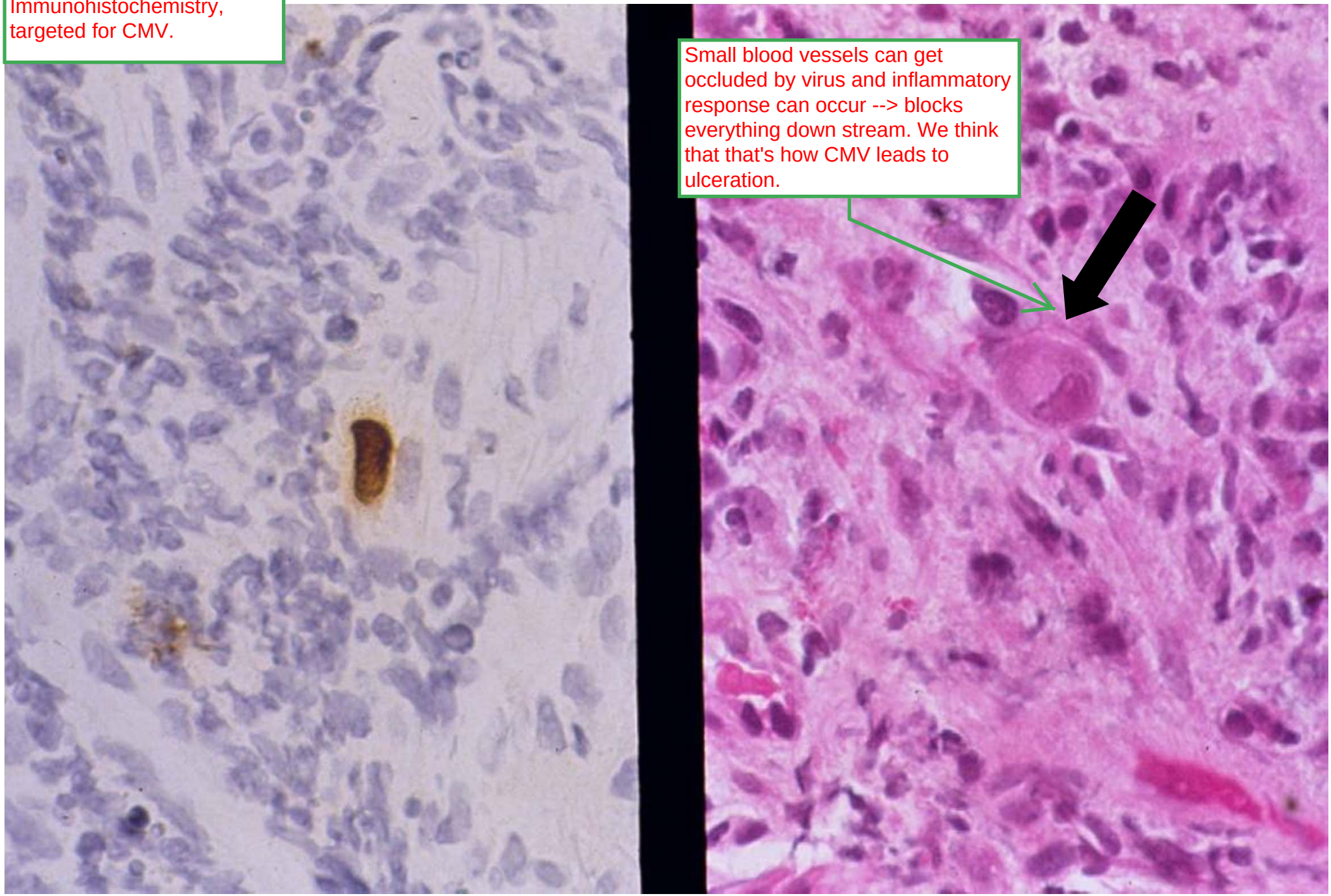
Cytomegalovirus (CMV)

- Immunosuppressed patients
  - Bone marrow transplant
  - Organ transplant
  - Chemotherapy
  - HIV/AIDS
- Endothelialitis
  - Ulceration
  - CMV viral inclusions, *most commonly in endothelial cells*

As opposed to herpes, this infects endothelial cells.

CMV ulcer (arrow). We still get same gross impression.


squmous epithelial supposed to be here (ulcer)
blood vessel
CMV inclusion
granulation tissue


On Left:
Immunohistochemistry, targeted for CMV.
Small blood vessels can get occluded by virus and inflammatory response can occur --> blocks everything down stream. We think that that's how CMV leads to ulceration.

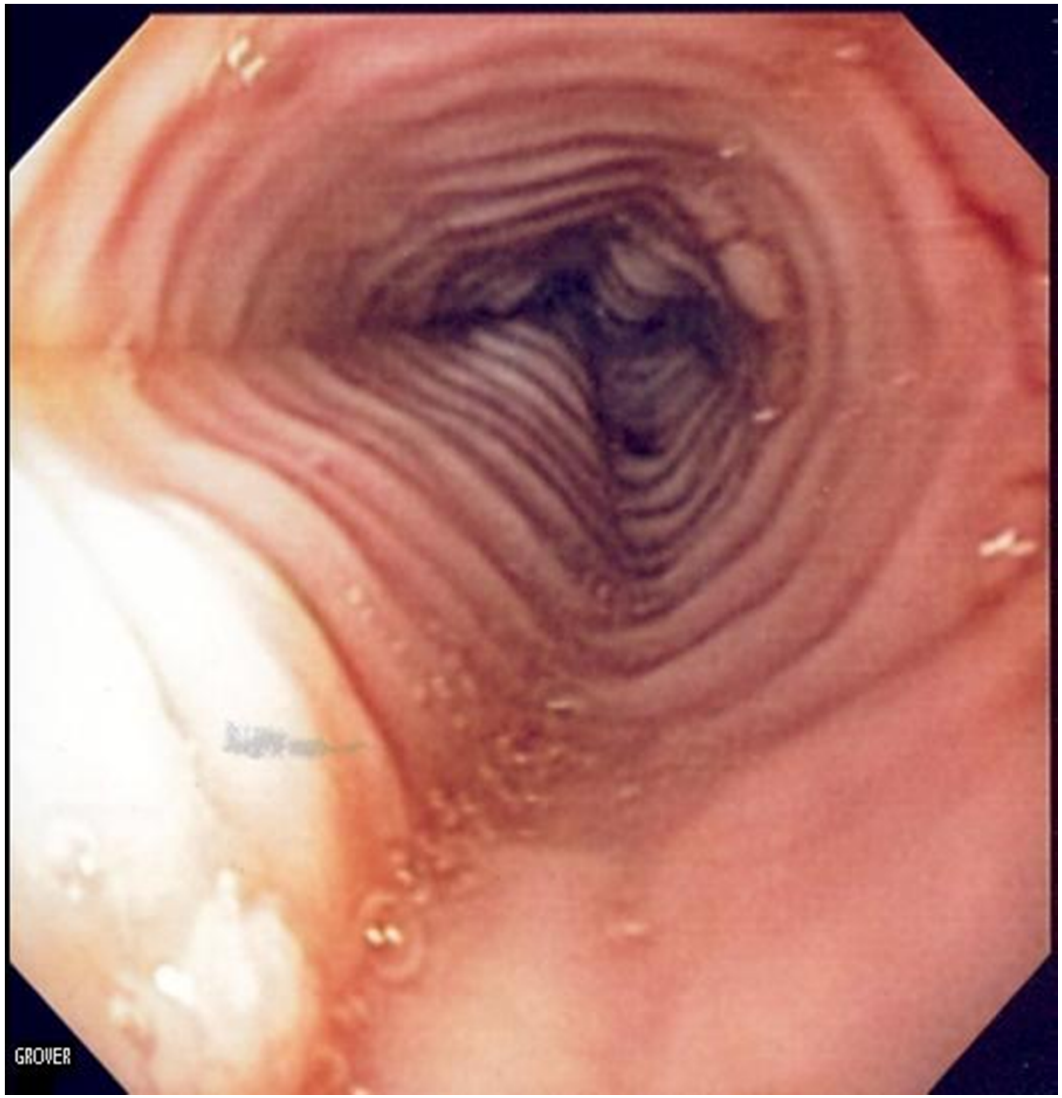
Esophagitis

- Reflux
- Infectious
- Inflammatory

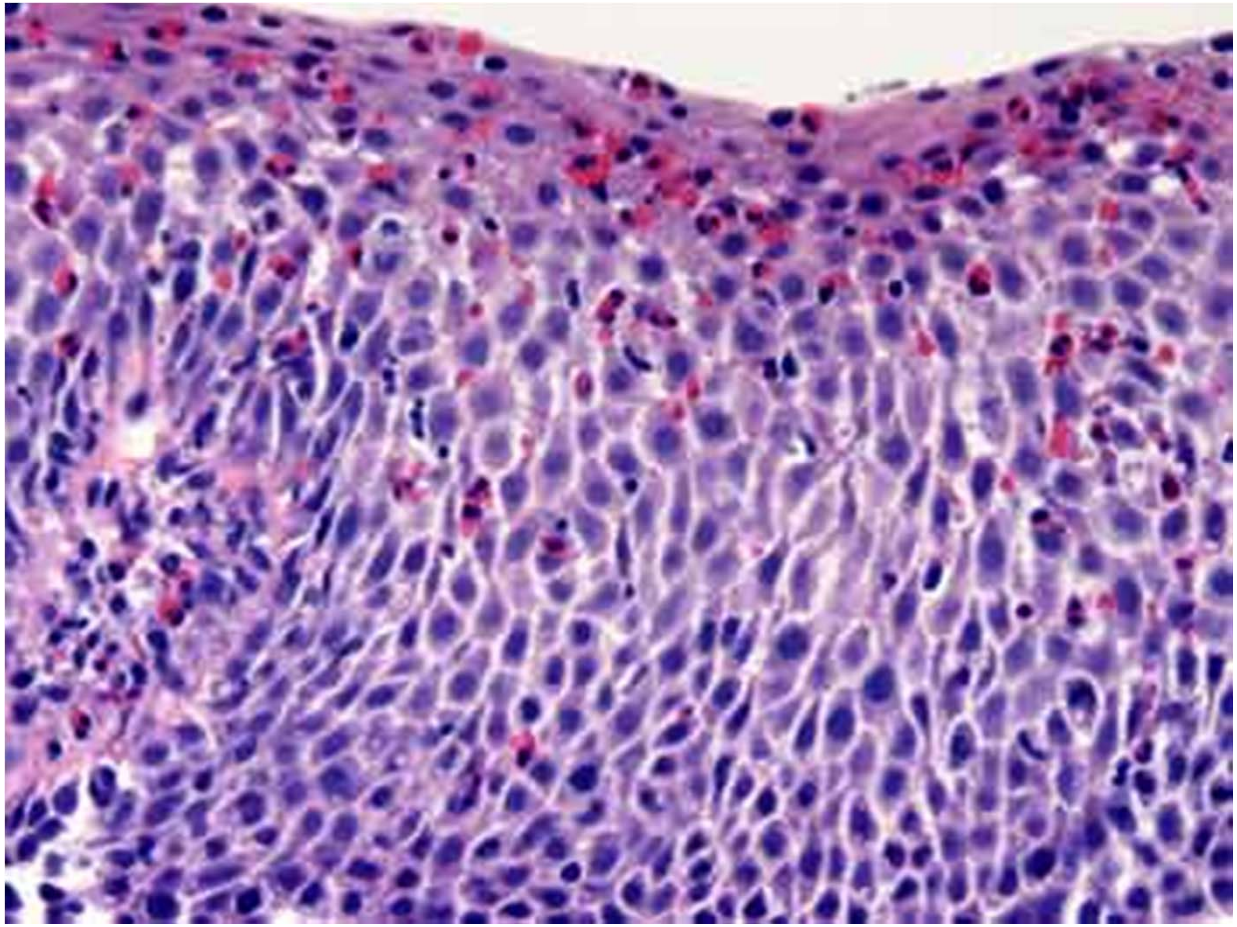
Primary Eosinophilic Esophagitis

- Younger patients, male predominance
- Associated with allergy and asthma
- Causes dysphagia
- Significantly more eosinophils are present than in reflux esophagitis tons of them

Trachealization of the esophagus. Looks like trachea. Some call it felinization.



Diagnosis made by seeing >20 eosinophils in the high power field. Usually at the surface. Can be treated with steroids via inhalation and then swallowing.



Esophagitis

- Reflux
- Infectious
- Inflammatory
- Traumatic: Pill esophagitis, Corrosive esophagitis, Mallory-Weiss tears from repeated vomiting, Radiation esophagitis
- Congenital: malformations
- Vascular: Varices and bleeding associated with portal hypertension

Lots of other ways to get esophagitis.

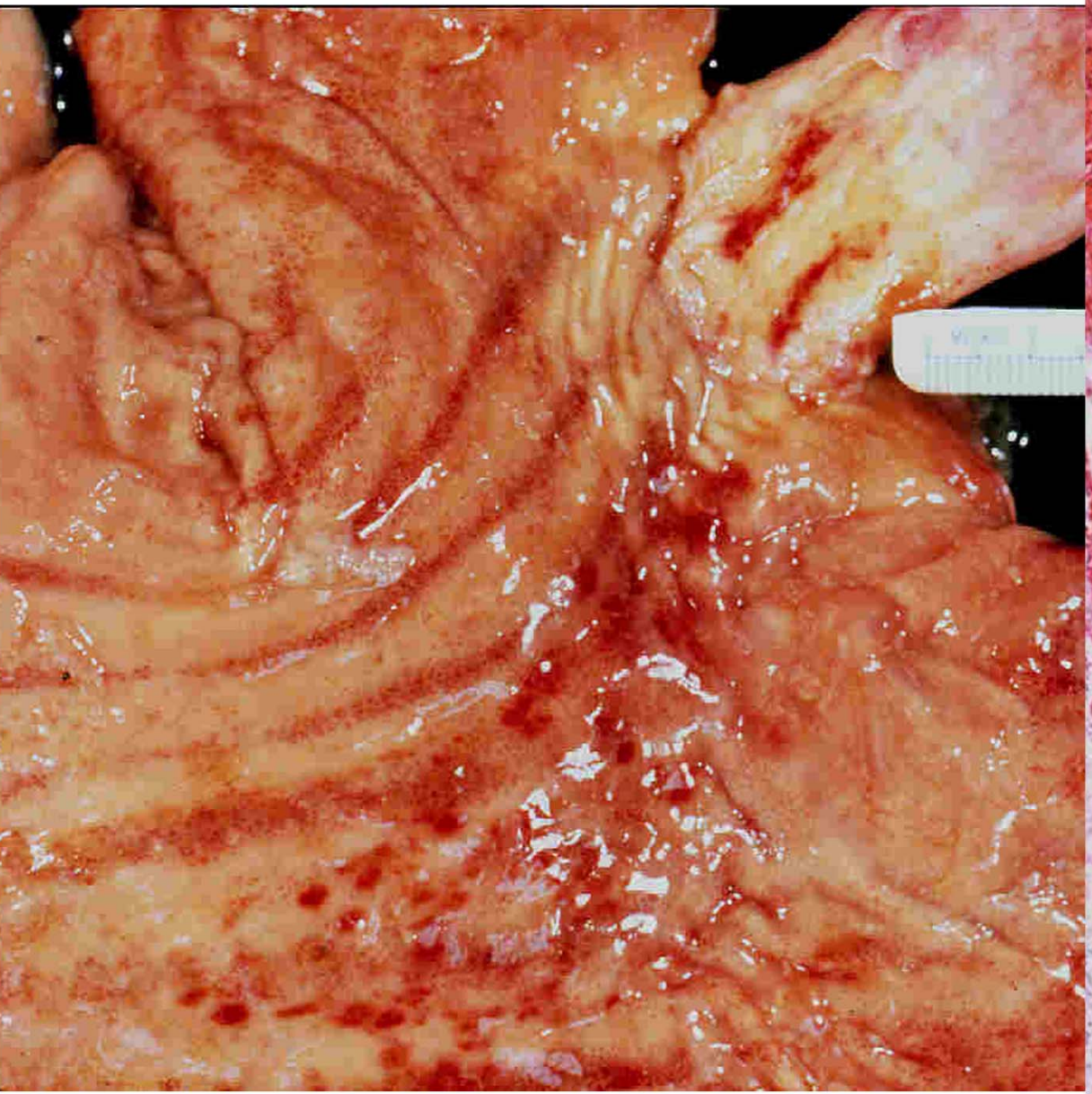
Stomach

Acute Erosive Gastritis

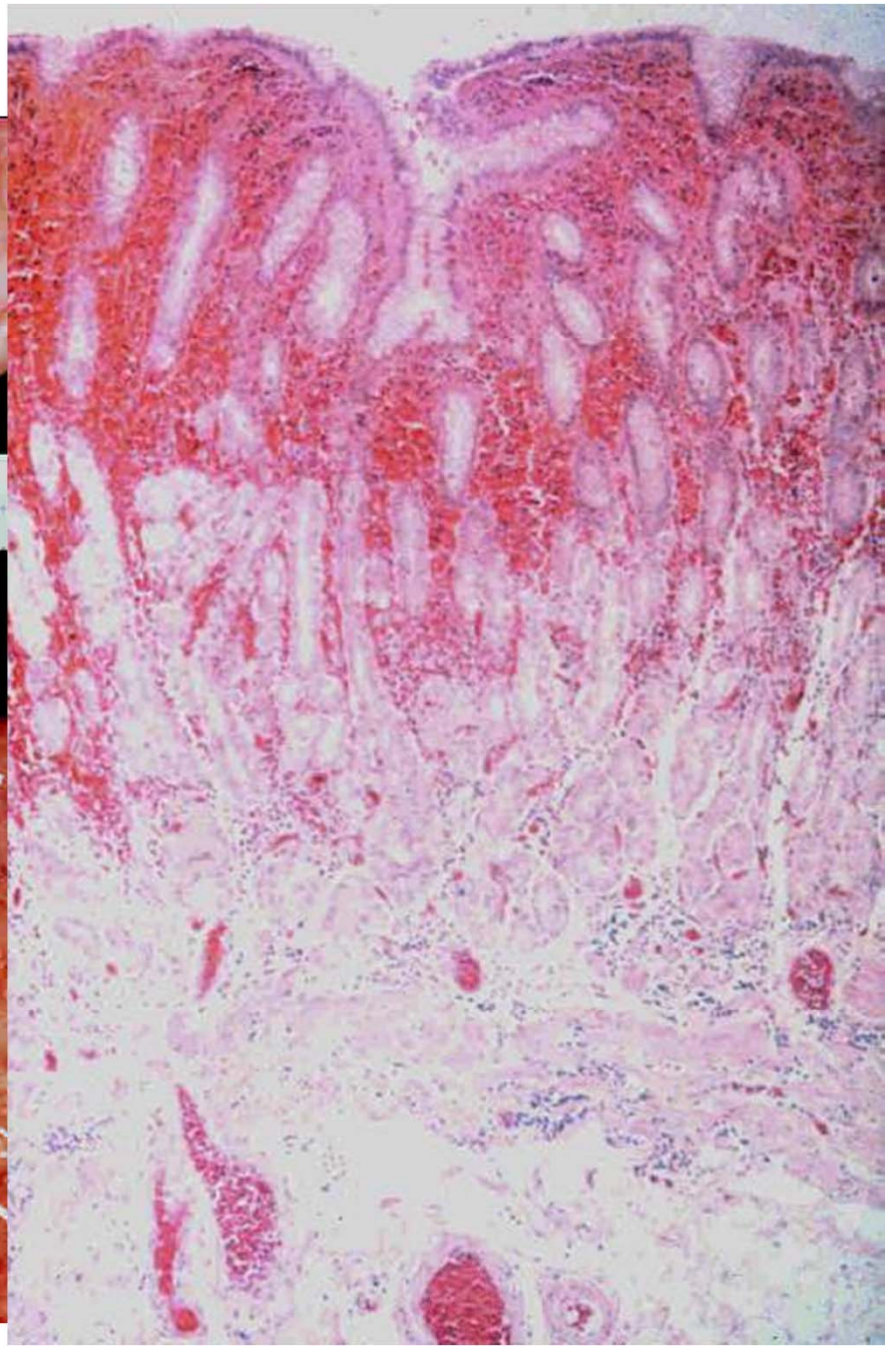
- Alcohol
- Aspirin, NSAIDs
- Smoking
- Uremia
- Steroids
- Stress (MICU patients, burn patients)

Happens in mostly healthy people.

this pt died of severe burns in MICU



erosion and hemorrhage



Chronic Gastritis +/- Activity

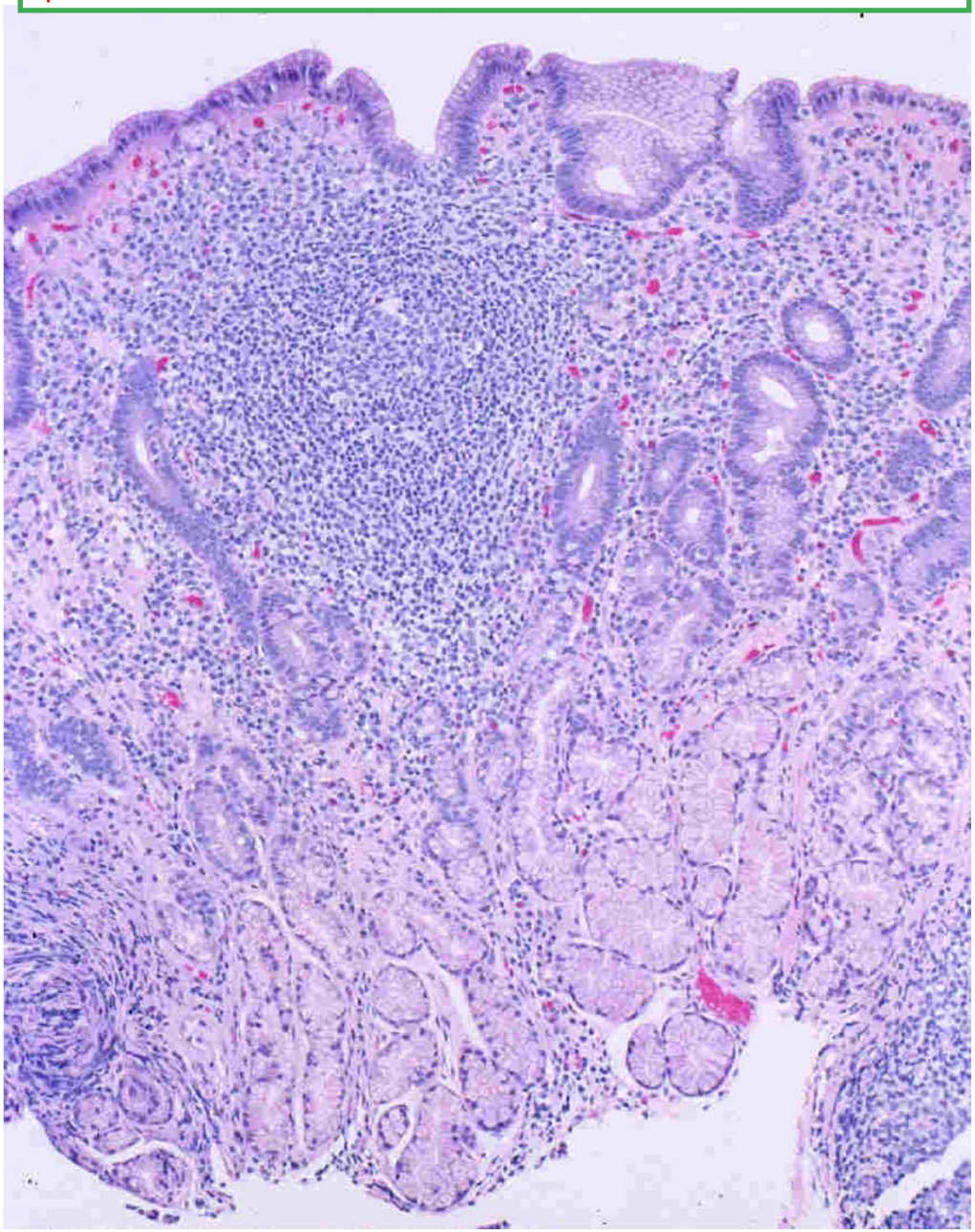
- Antral-predominant gastritis (COMMON)
  - **Infectious, with acute inflammation (*Helicobacter pylori*)**
  - **Involves the entire stomach when severe**

will see one of these two causes

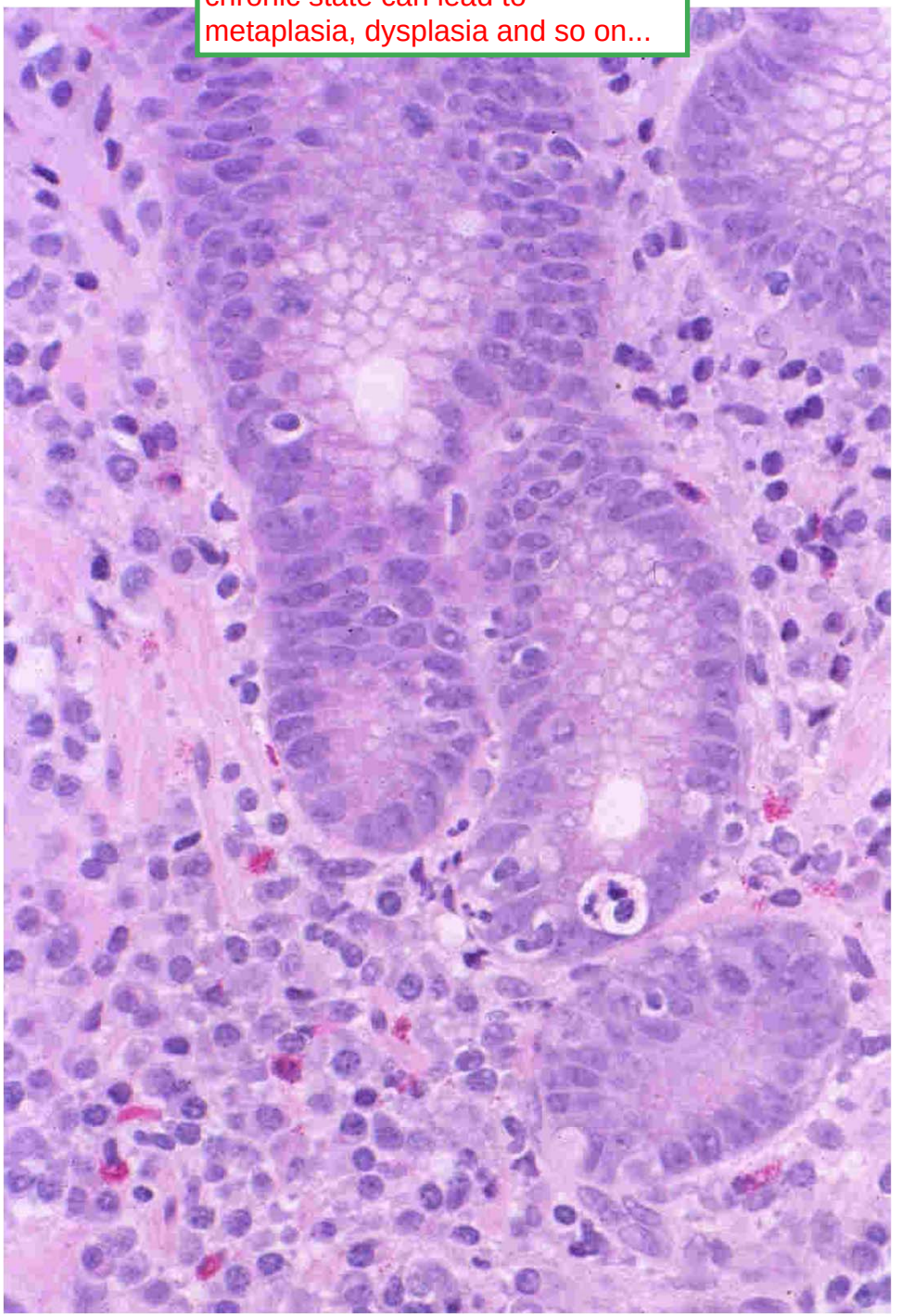
- Body-predominant (less common)
  - **Autoimmune**
  - **Anti-parietal cell and anti-intrinsic factor antibodies**
  - **Dramatic decrease in acid production**

This is more commonly seen.

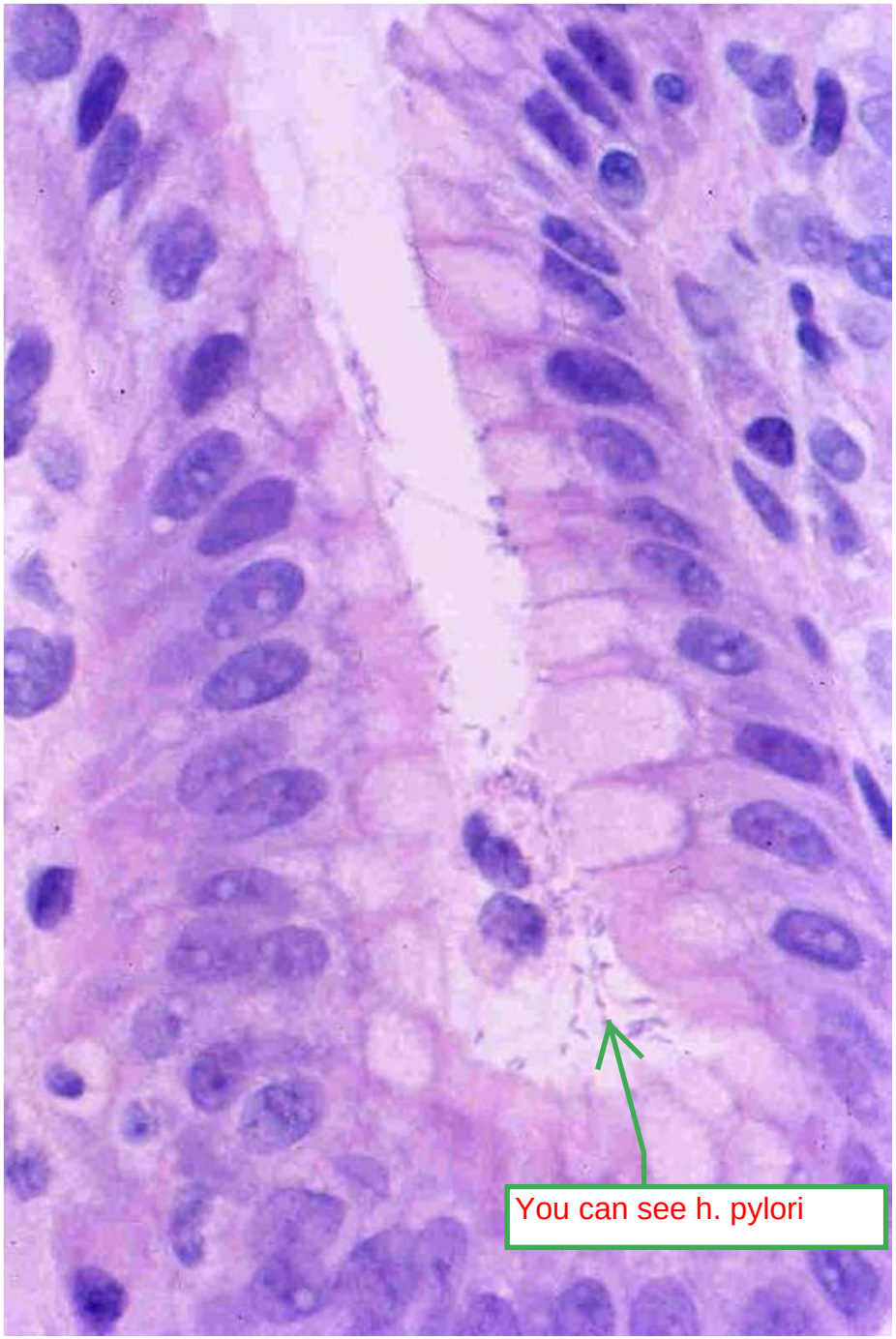
5% of pt population has biopsy that shows chronic active gastritis associated with h. pylori. chracterized by lymphoid follicles in gastric mucosa. increase in plasma cells in lamina propria and neutrophils in epithelium.

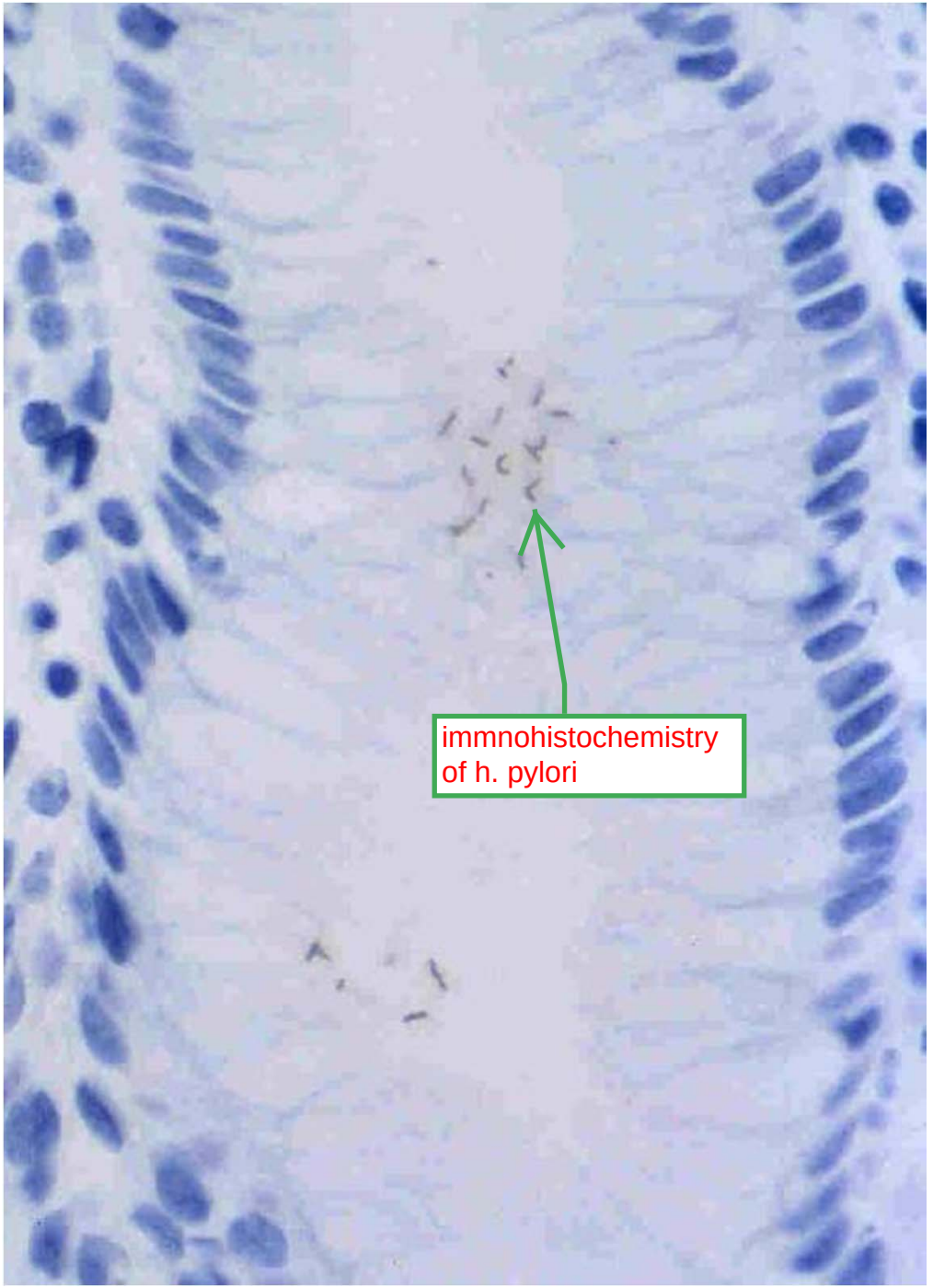


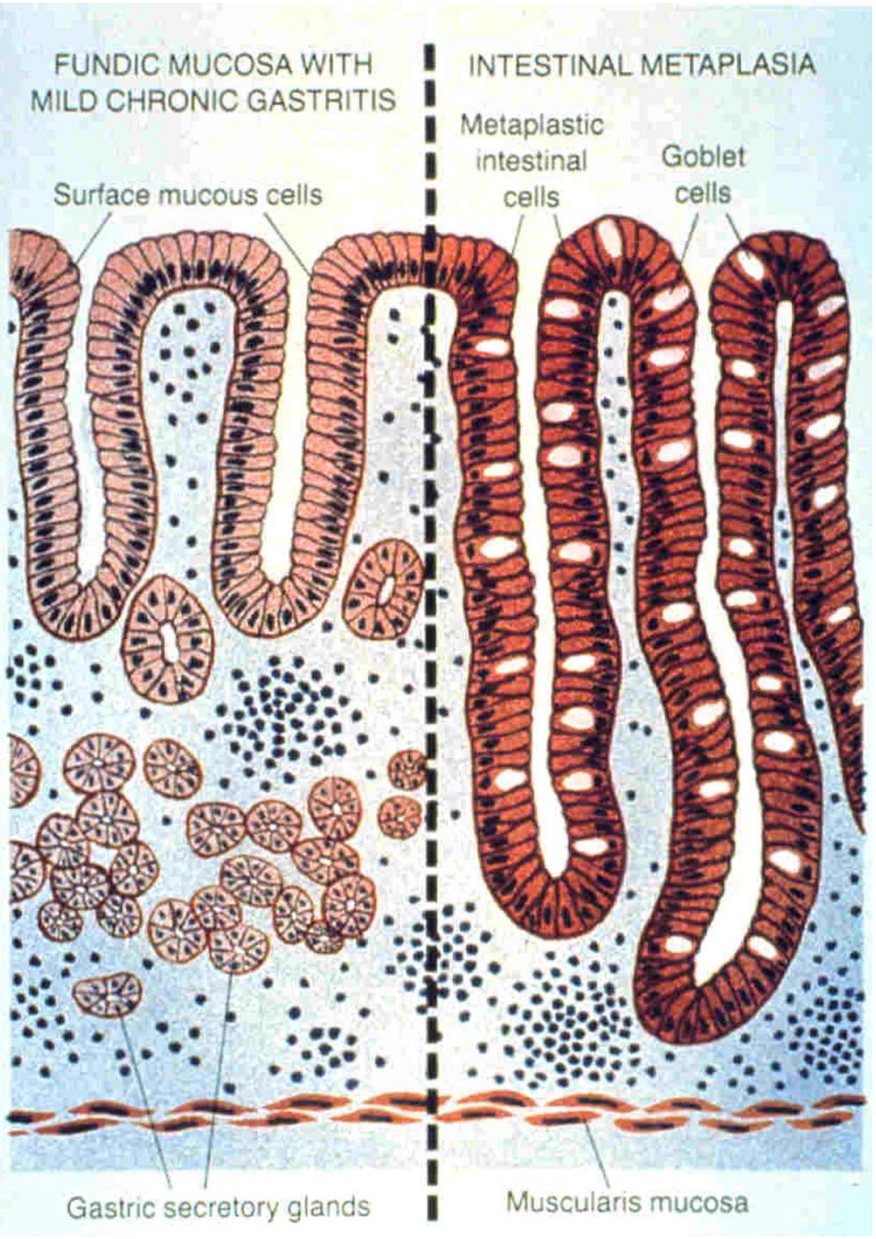
h pylori is a class 1 carcinogen so chronic state can lead to metaplasia, dysplasia and so on...



magnification of pic on left


You can see h. pylori

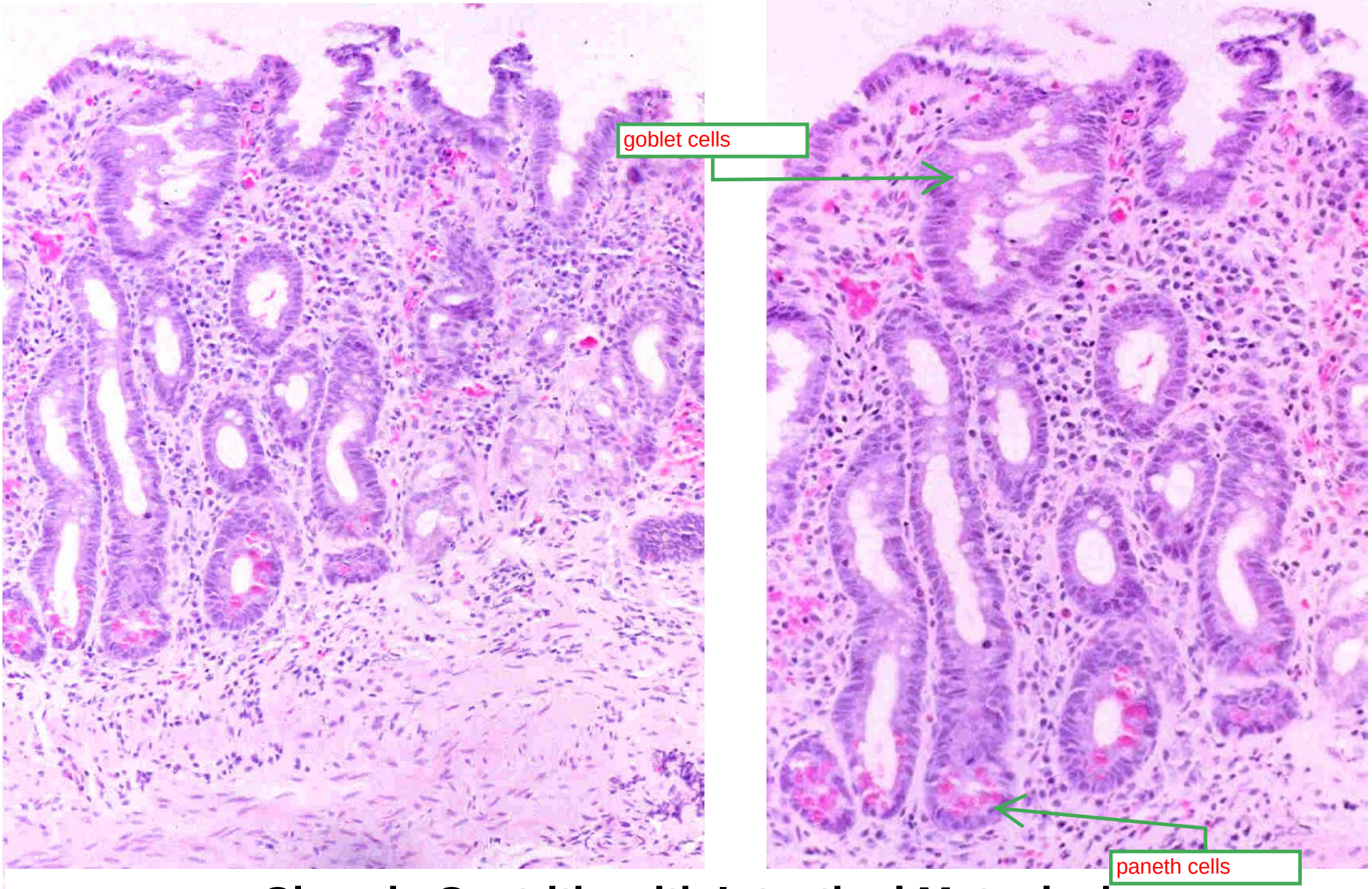

immnohistochemistry
of h. pylori



chronic gastritis leads to intestinal metaplasia

Intestinal Metaplasia of the Stomach

- Response to chronic injury
- Intestinal type mucin (goblet cells)
- Paneth cells
- Brush border
- Villous architecture



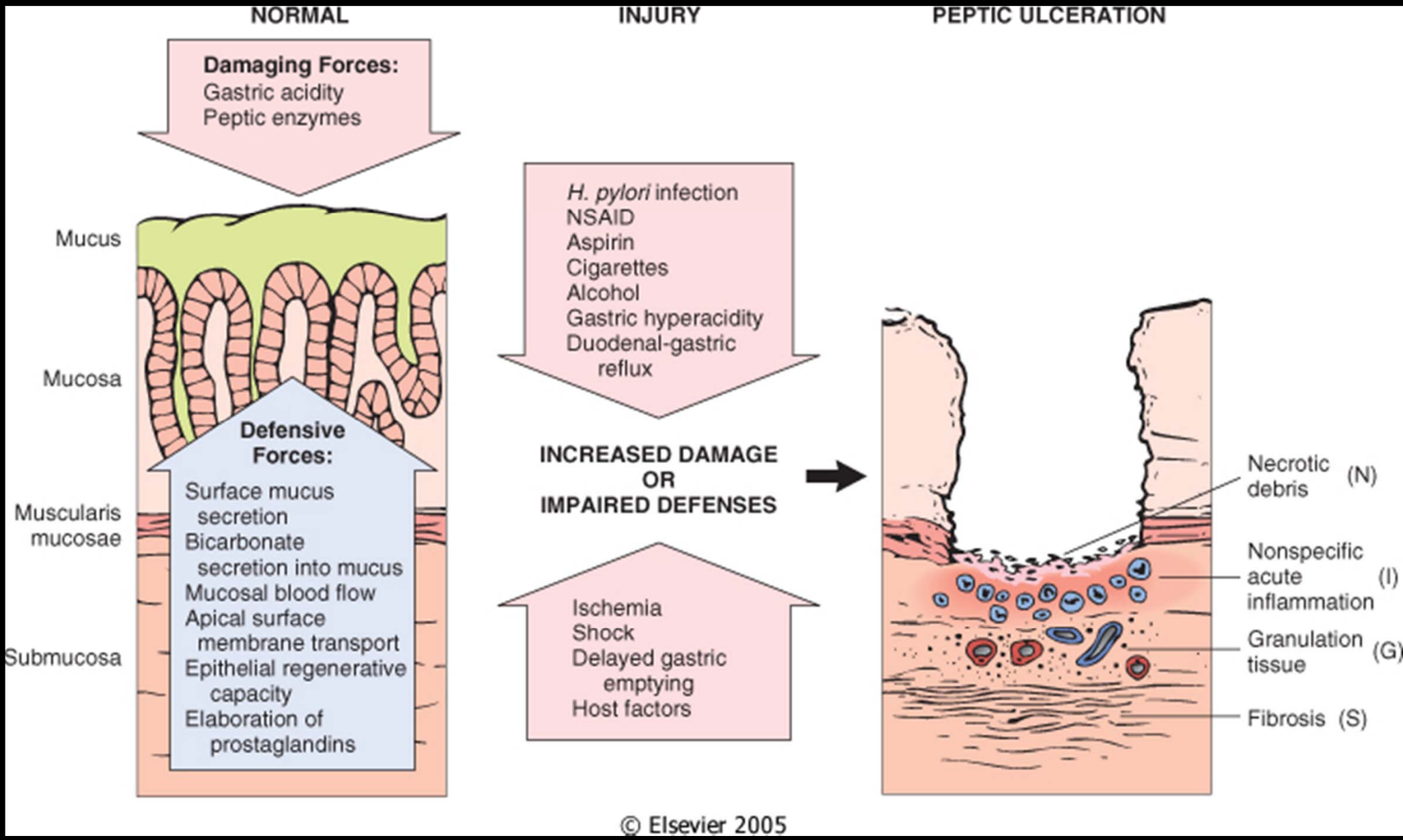
Chronic Gastritis with Intestinal Metaplasia

well developed
intestinal metaplasia

Peptic Ulcer Disease

(PUD)

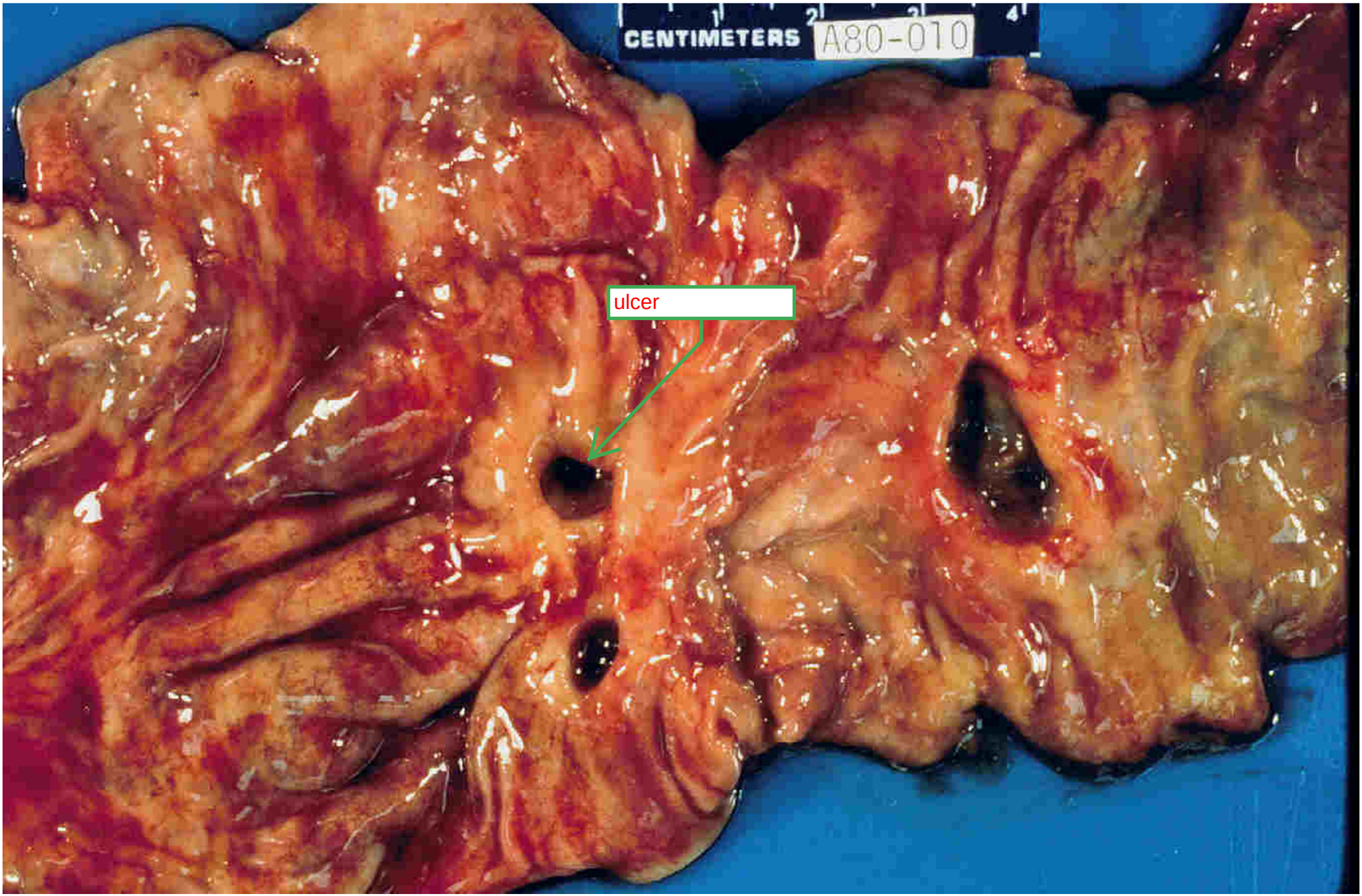
ulcers in duodenum also fall under PUD category



how ulcers form. balance between damaging and defensive forces.

Peptic Ulcer Disease - Defined

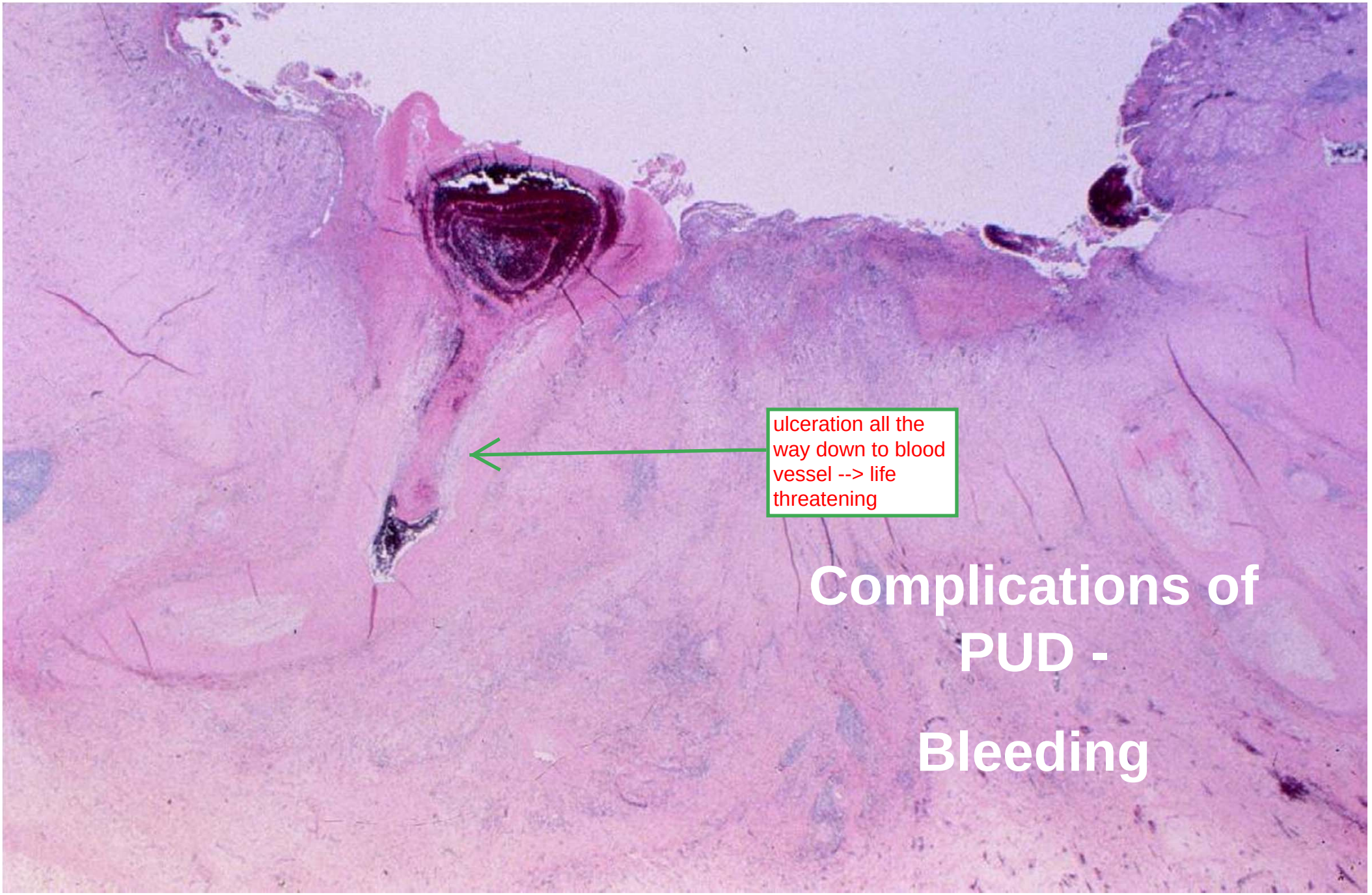
- Usually involves distal stomach or proximal duodenum
- H. pylori-associated vs. Other


CENTIMETERS
A80-010
ulcer

Complications of PUD

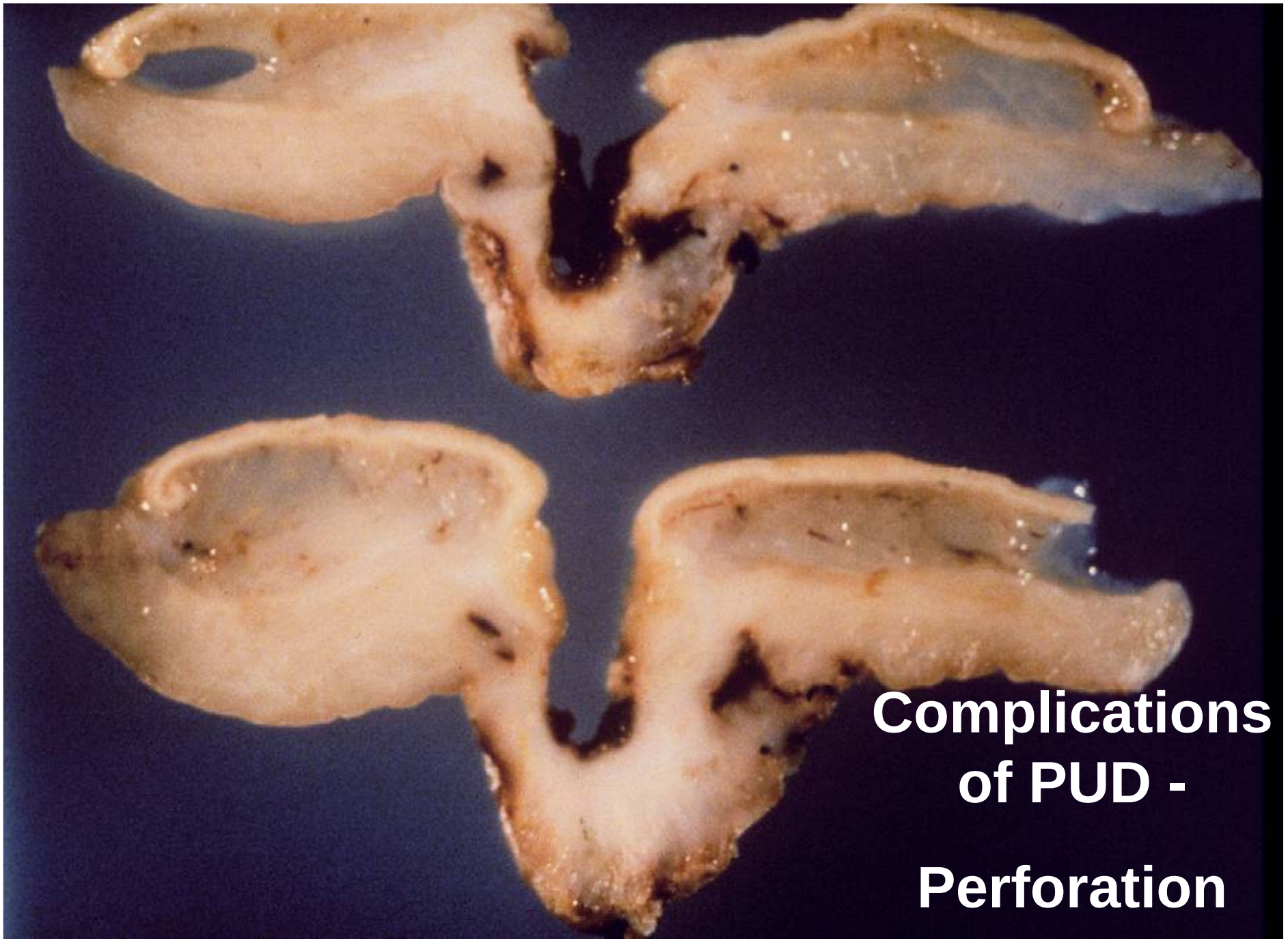
two main complications

- Bleeding
- Perforation



Complications of PUD -

Bleeding

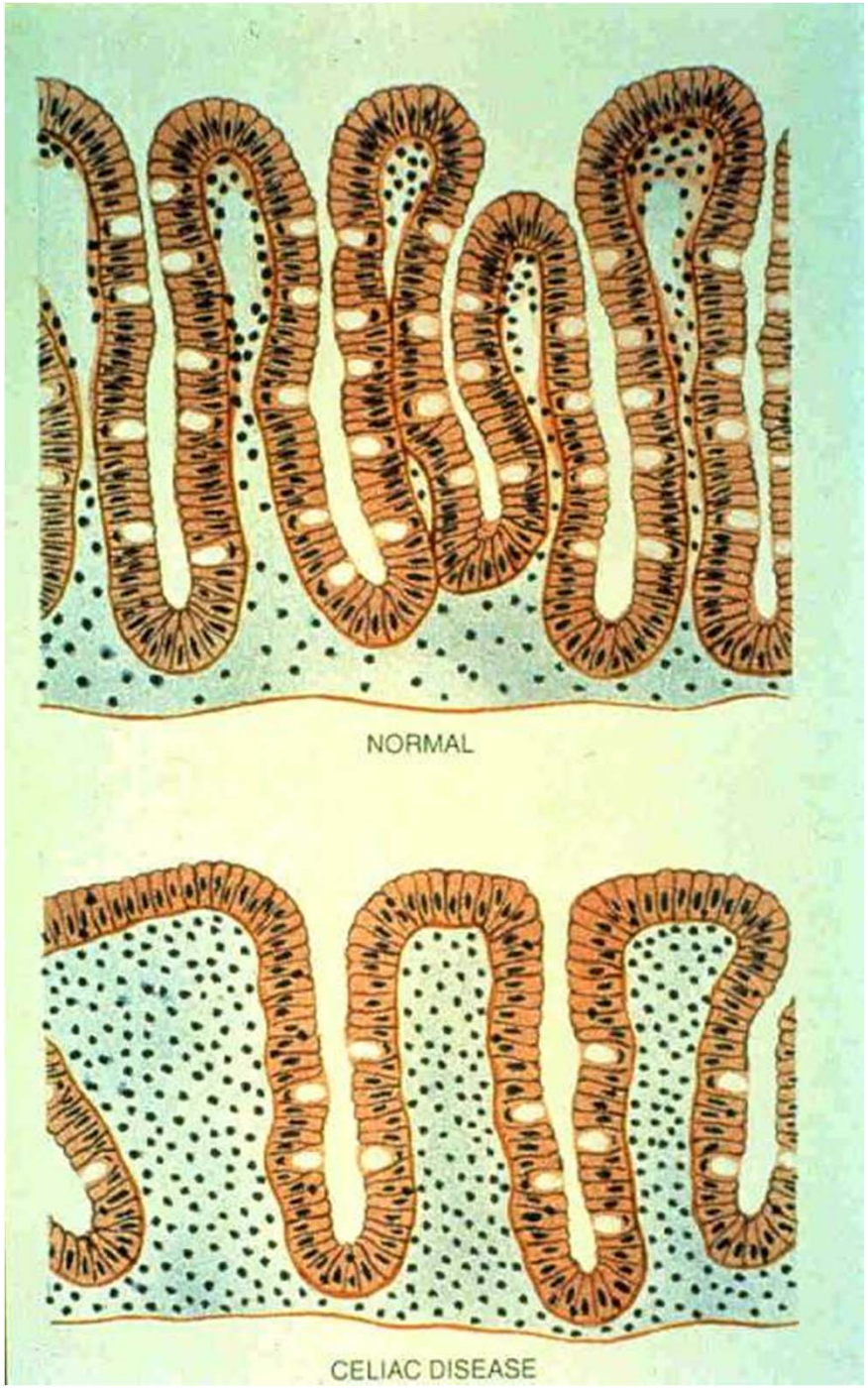


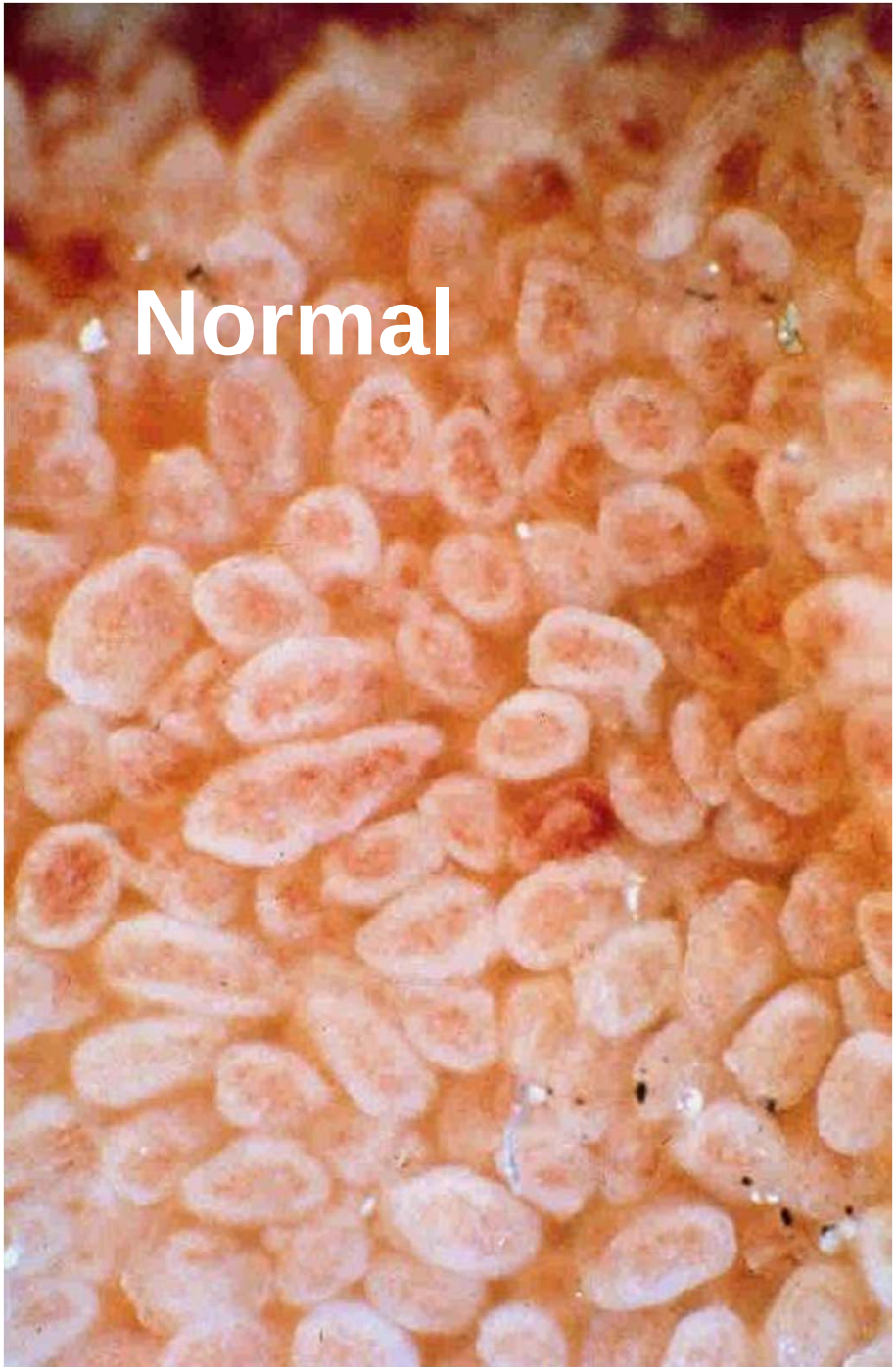
ulcer penetrates entire wall of stomach.
acid enters peritoneal cavity --> bad.

Small Bowel

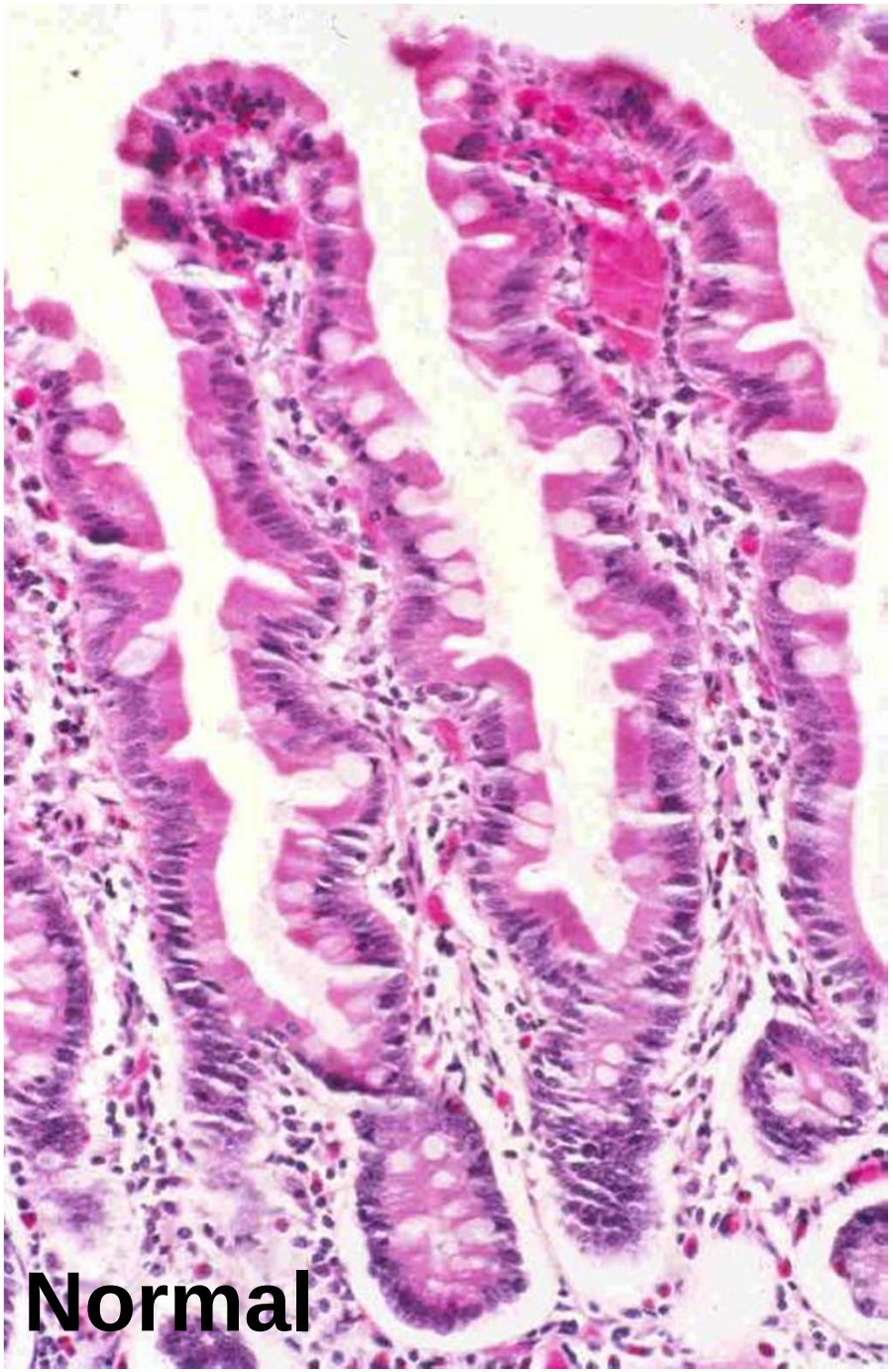
Celiac Sprue
(gluten-sensitive enteropathy)

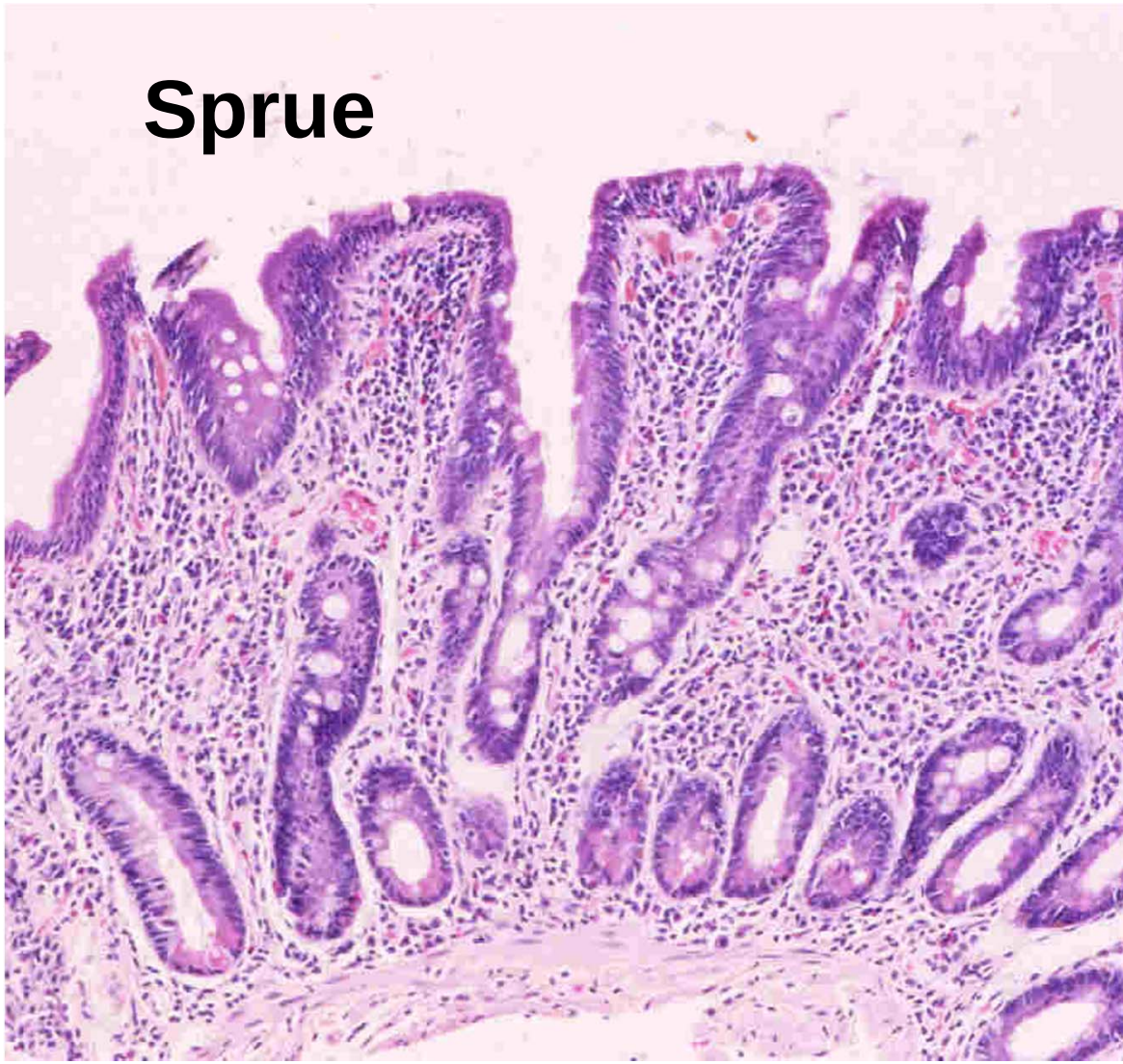
increased T lymphocytes over time --> increased inflammation --> villi begin to appear blunted



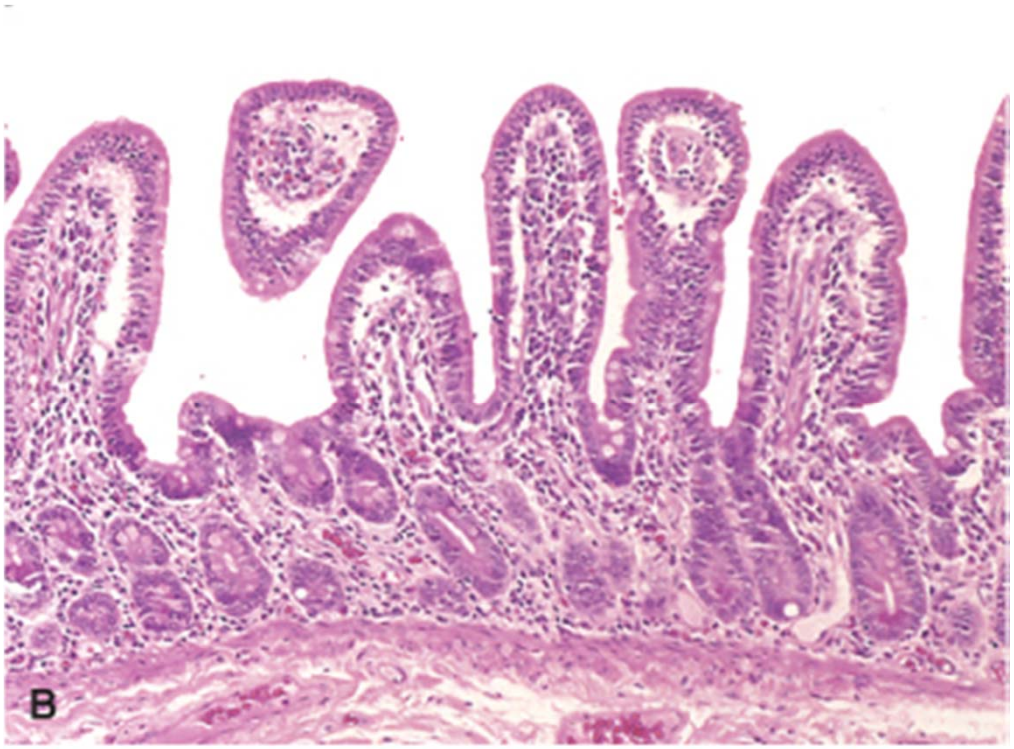


normally villi look like fingers (left). in celiac's you see a more flattened look (right).

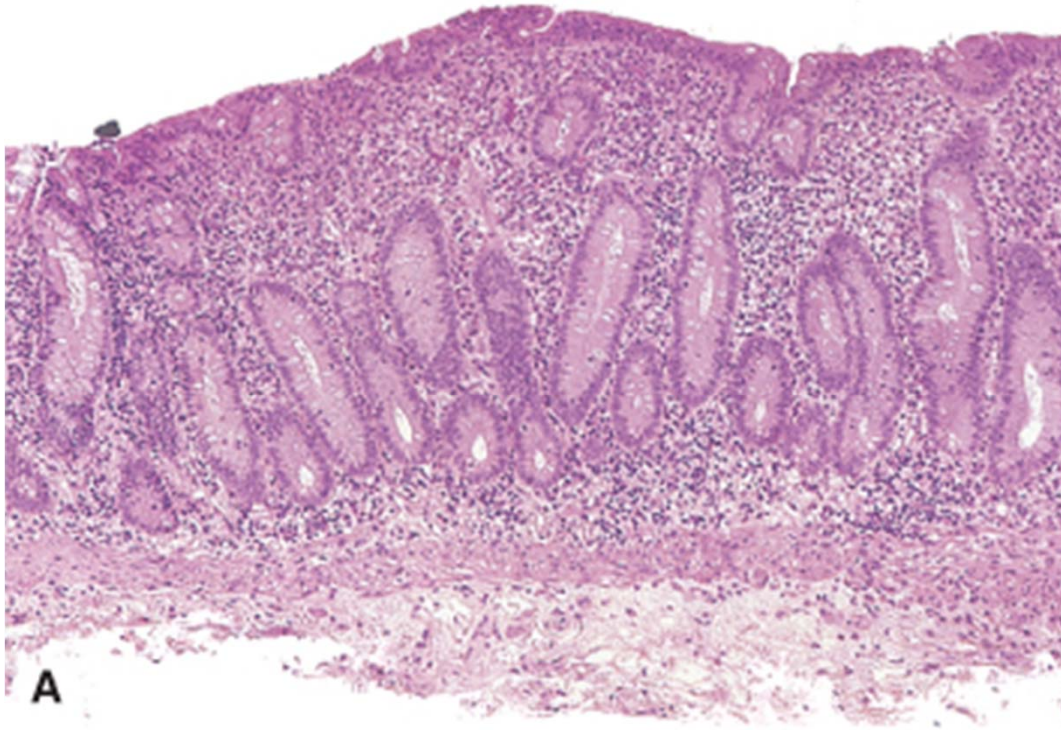




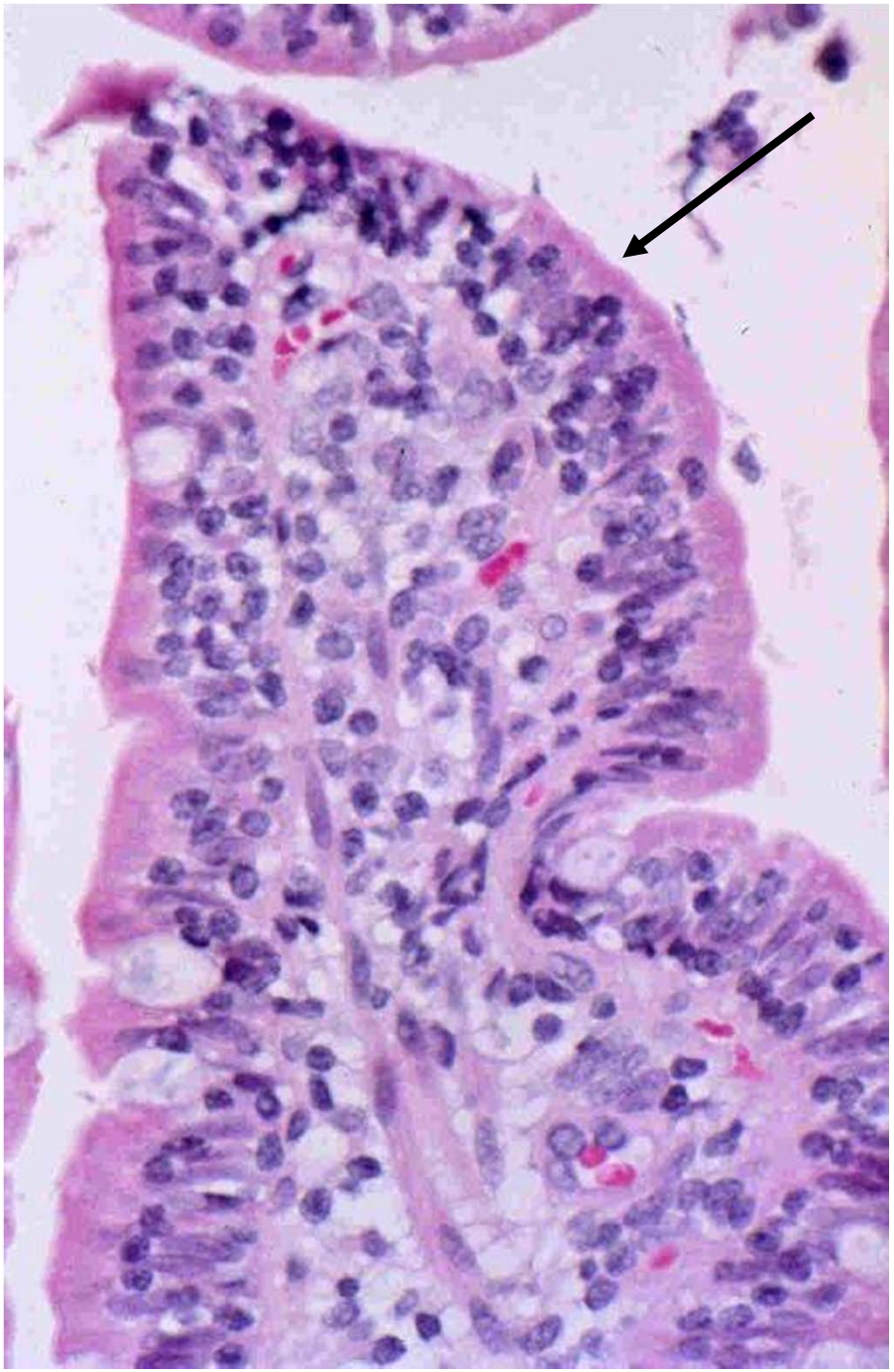
same thing again on histological level



complete flattening can occur



CELIAC SPRUE: Villous atrophy and Increased Intraepithelial Lymphocytes (Normal small bowel on left, celiac sprue on right)



- Increased numbers of lymphocytes in surface epithelium
- Injury of surface epithelium
- Varying degrees of villous atrophy depending on ?chronicity?

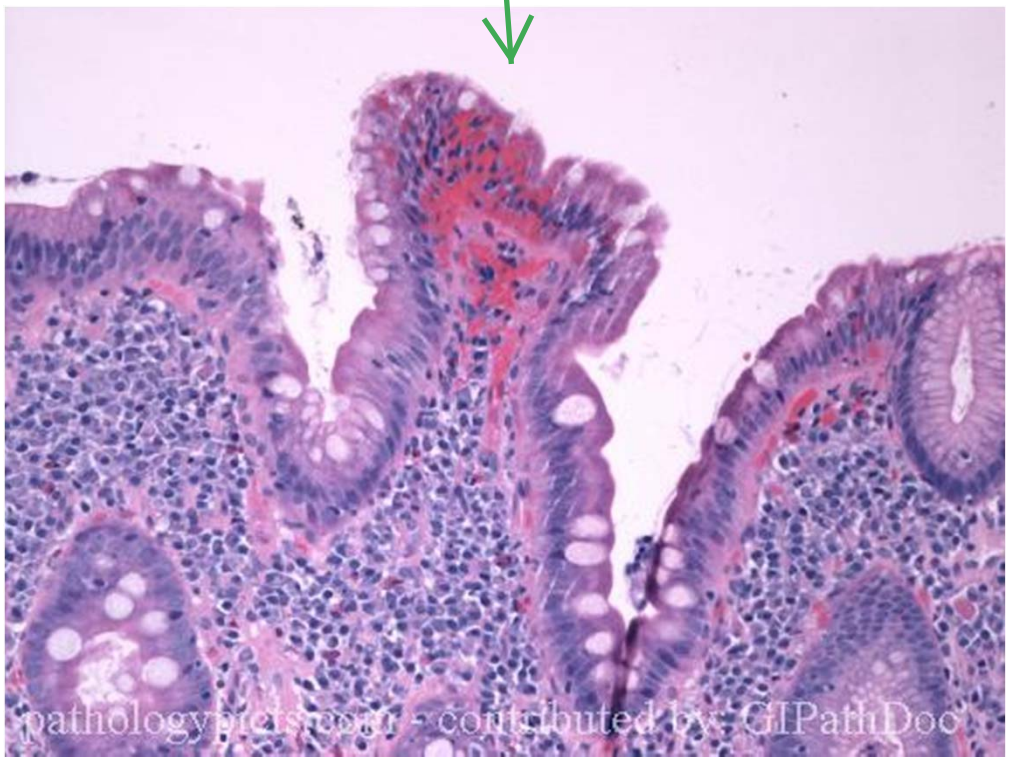
villi become more flattened over time

Peptic Duodenitis

- Proximal duodenal inflammation
- Hyperacidity of gastric contents
- Acute inflammation
- Gastric-type metaplasia (foveolar metaplasia)

basically too much acid in stomach.

some acute inflammation, villus blunting, gastric metaplasia (to protect it from acid)

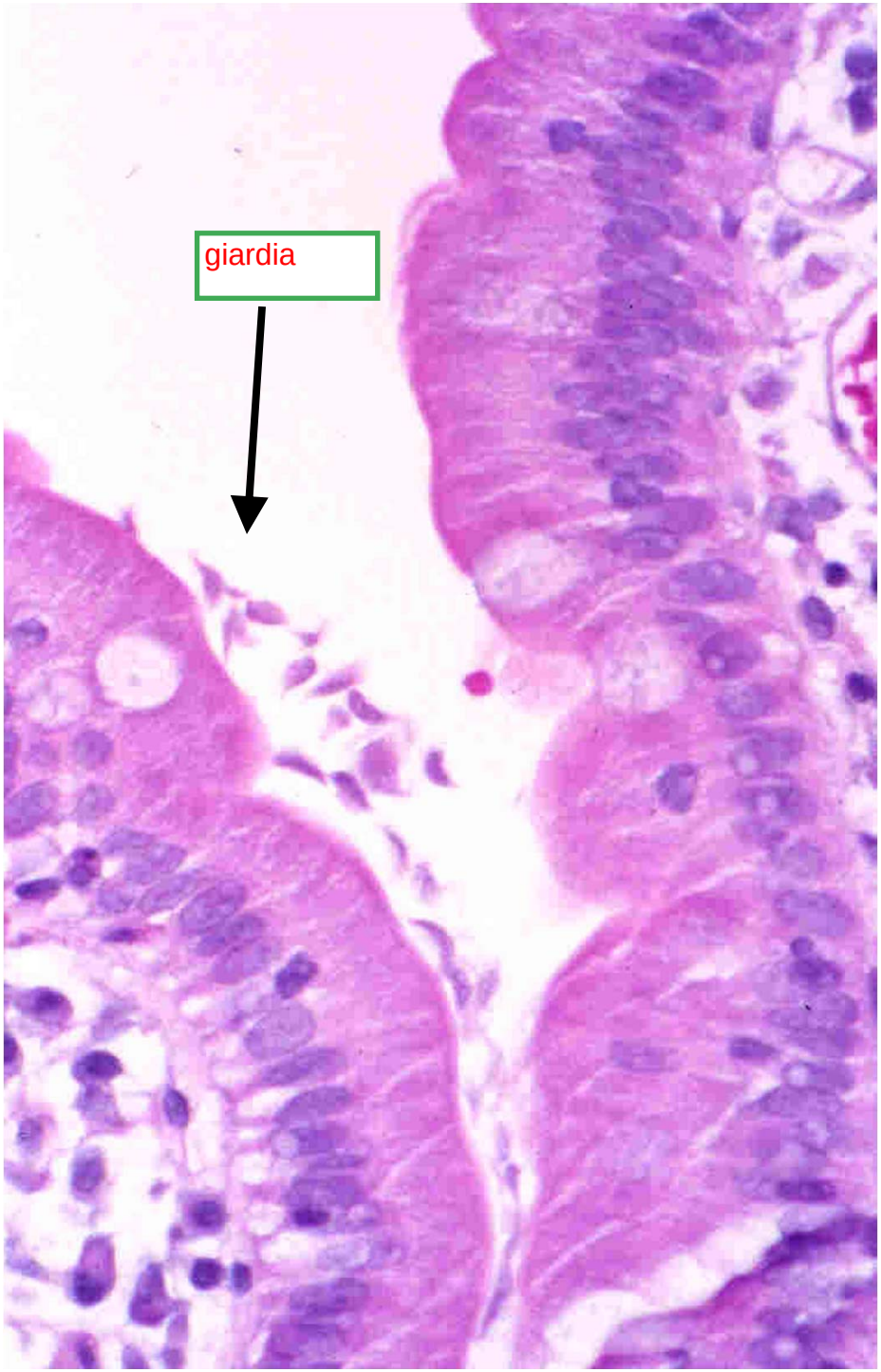


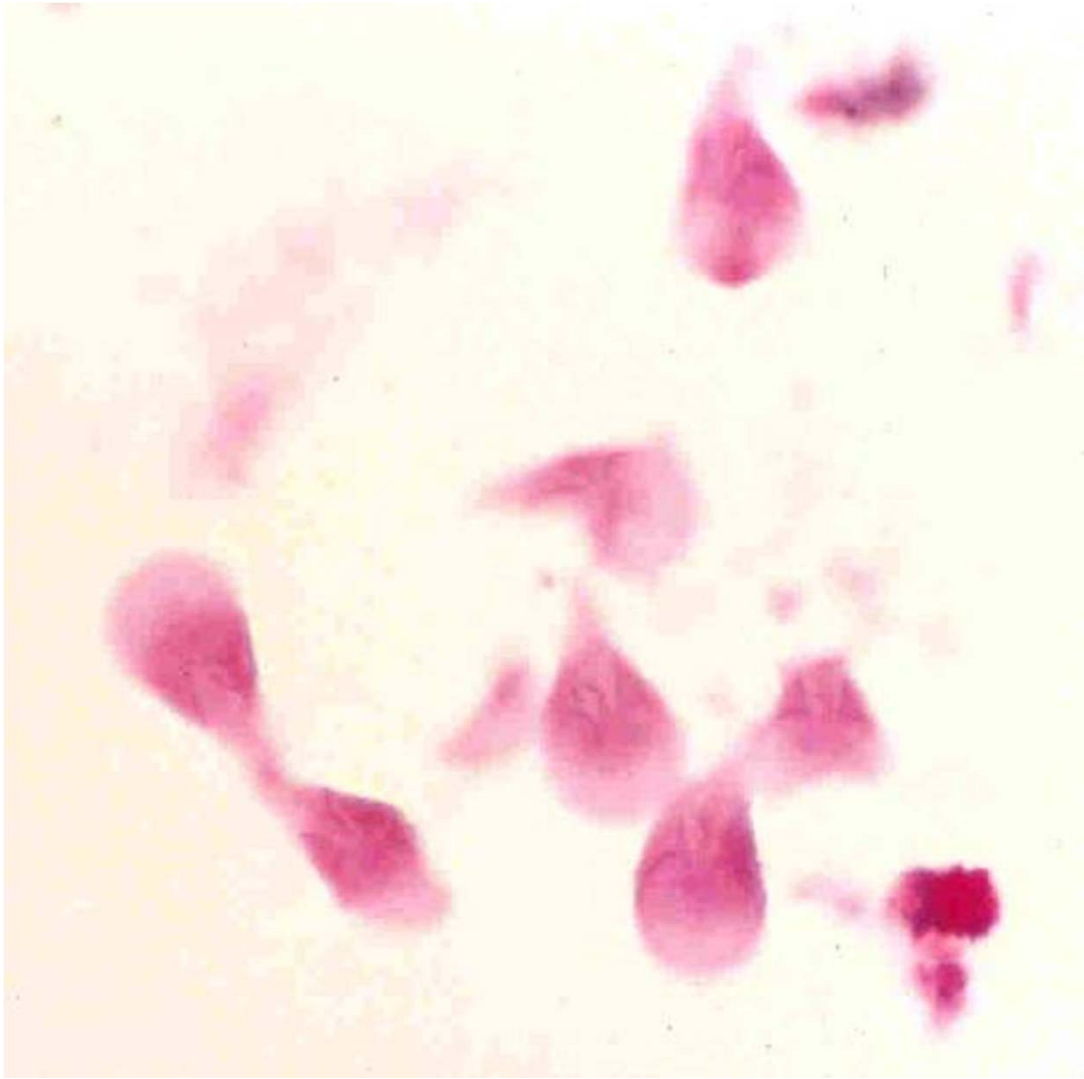
Giardia

- Protozoan gut pathogen
- Trophozoites and cysts (which are shed)
- Usually acquired from drinking water contaminated with cysts
- Poor sanitation and crowded living conditions predispose to infection
- Immunosuppression increases risk

giardia infects the small intestines. can affect anyone.

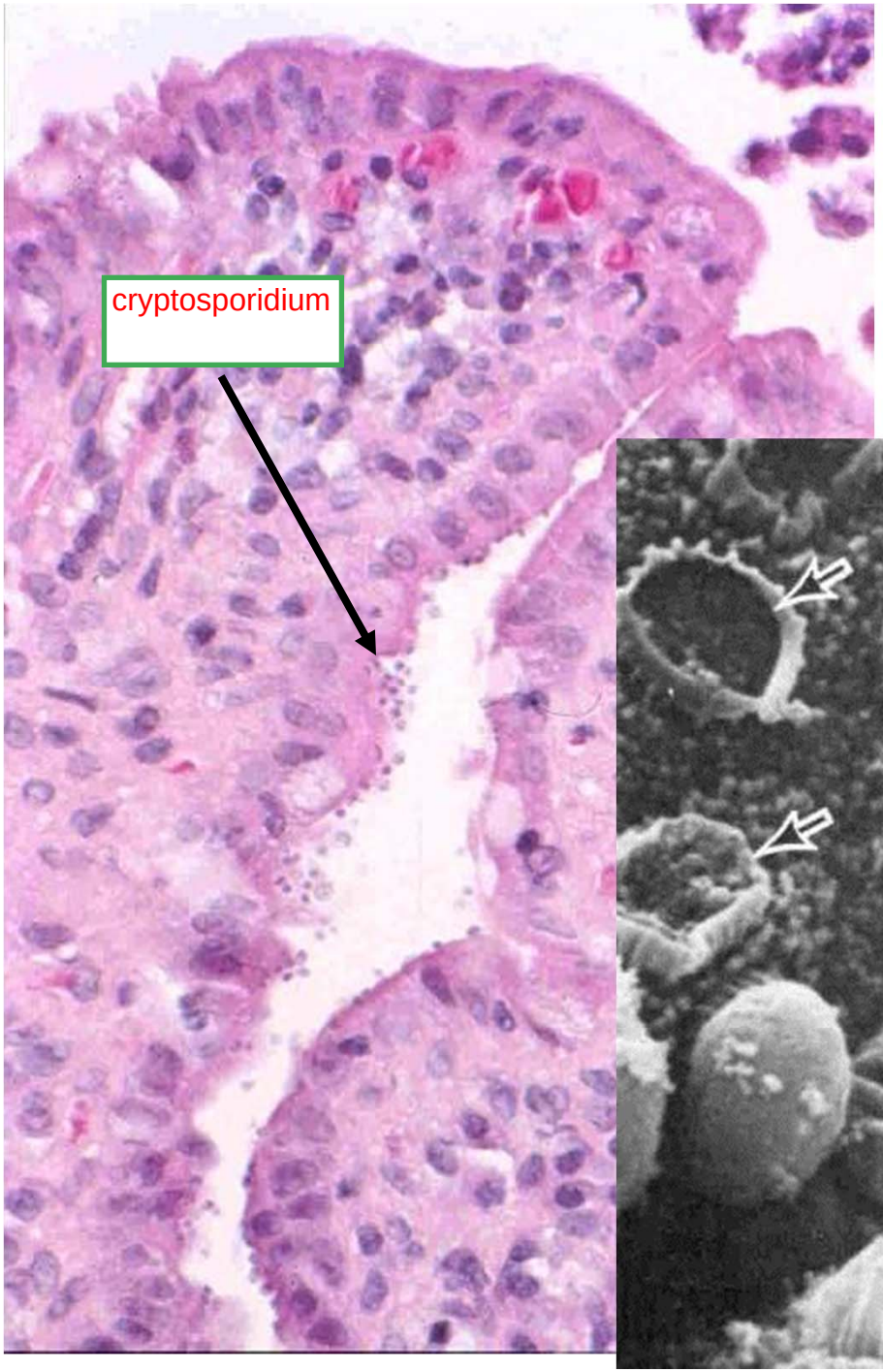
Giardia

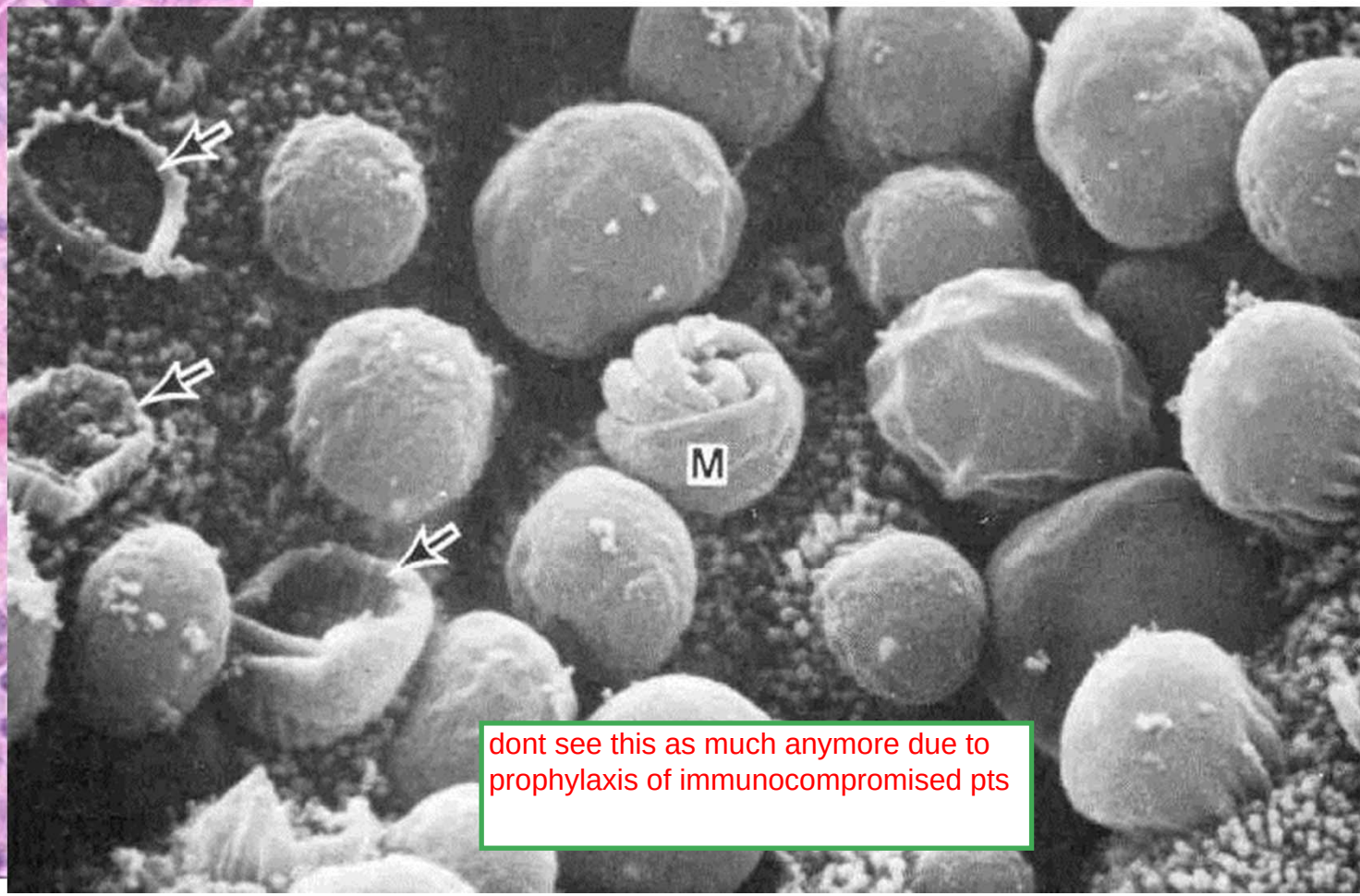




better way to make diagnosis is to look at stool for ova and parasites instead

Cryptosporidium





dont see this as much anymore due to prophylaxis of immunocompromised pts

Bacterial Enterocolitis

- Will be discussed in a different lecture
- Diagnosed by Clinical Pathology (ie, stool studies/microbiology lab), not by Anatomic Pathology (endoscopic biopsies)
  - Toxin-mediated disease
  - Invasive infections
  - (Salmonella, Shigella, Campylobacter, Yersinia, etc.)

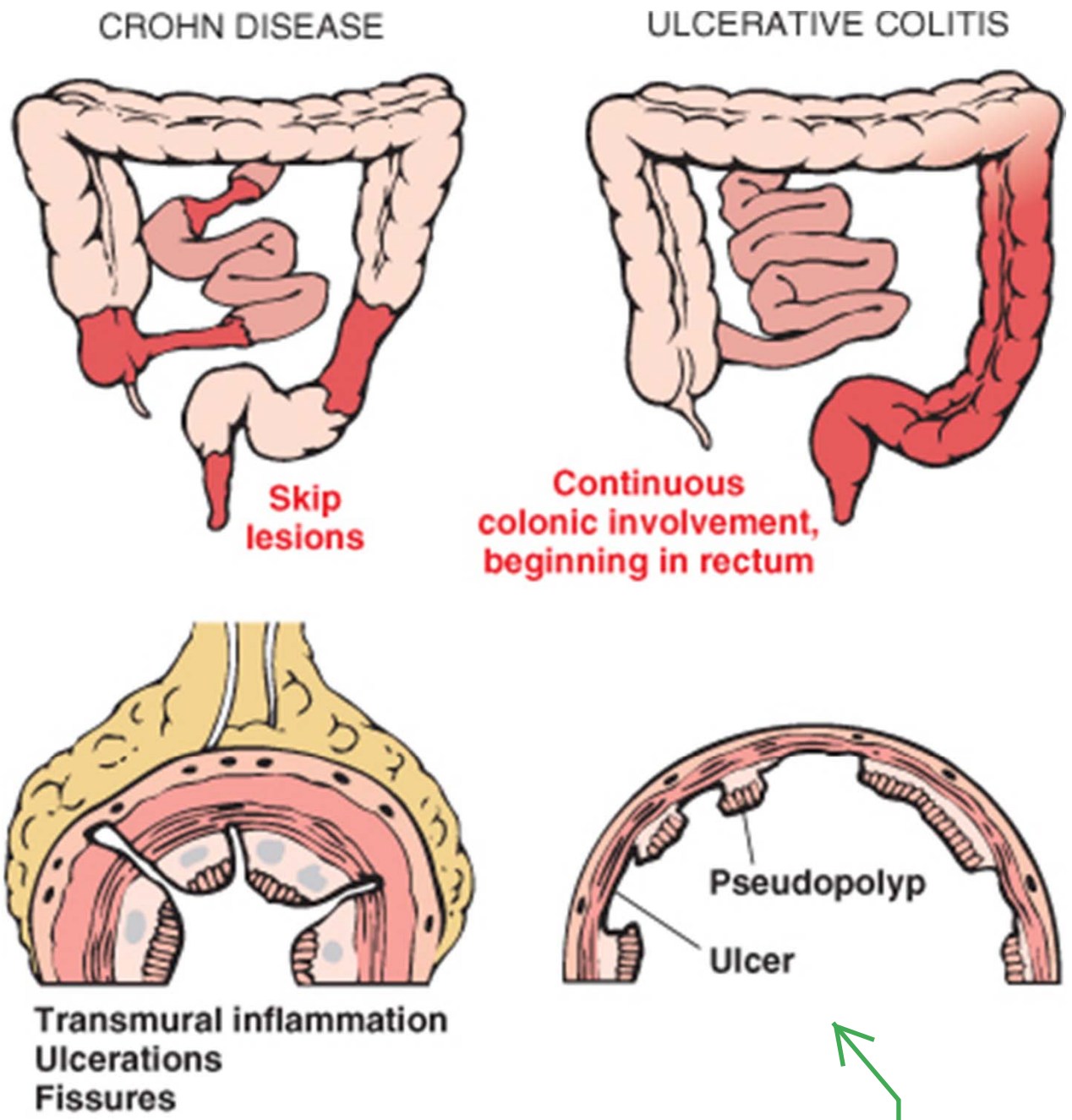
Colon

Inflammatory Bowel Disease

- Crohn’s Disease
- Ulcerative Colitis

Feature of IBD	Crohn's Disease	Ulcerative Colitis
Location?	***Anywhere* in GI Tract, but especially SI and colon**	**Rectum, colon** starts here and moves elsewhere
Involvement?	**Skip Lesions**	**Contiguous, starting in rectum**
Depth of Inflammation?	**Transmural, with fistulas common**	**Limited to Mucosa**
Granulomas?	**Yes**	**No**
Increased risk of CA?	**Yes, if colonic involvement**	**Yes**
Response to surgery?	**Poor**	**Good**

you should know the difference between these two because you will be tested on this on the wards and elsewhere



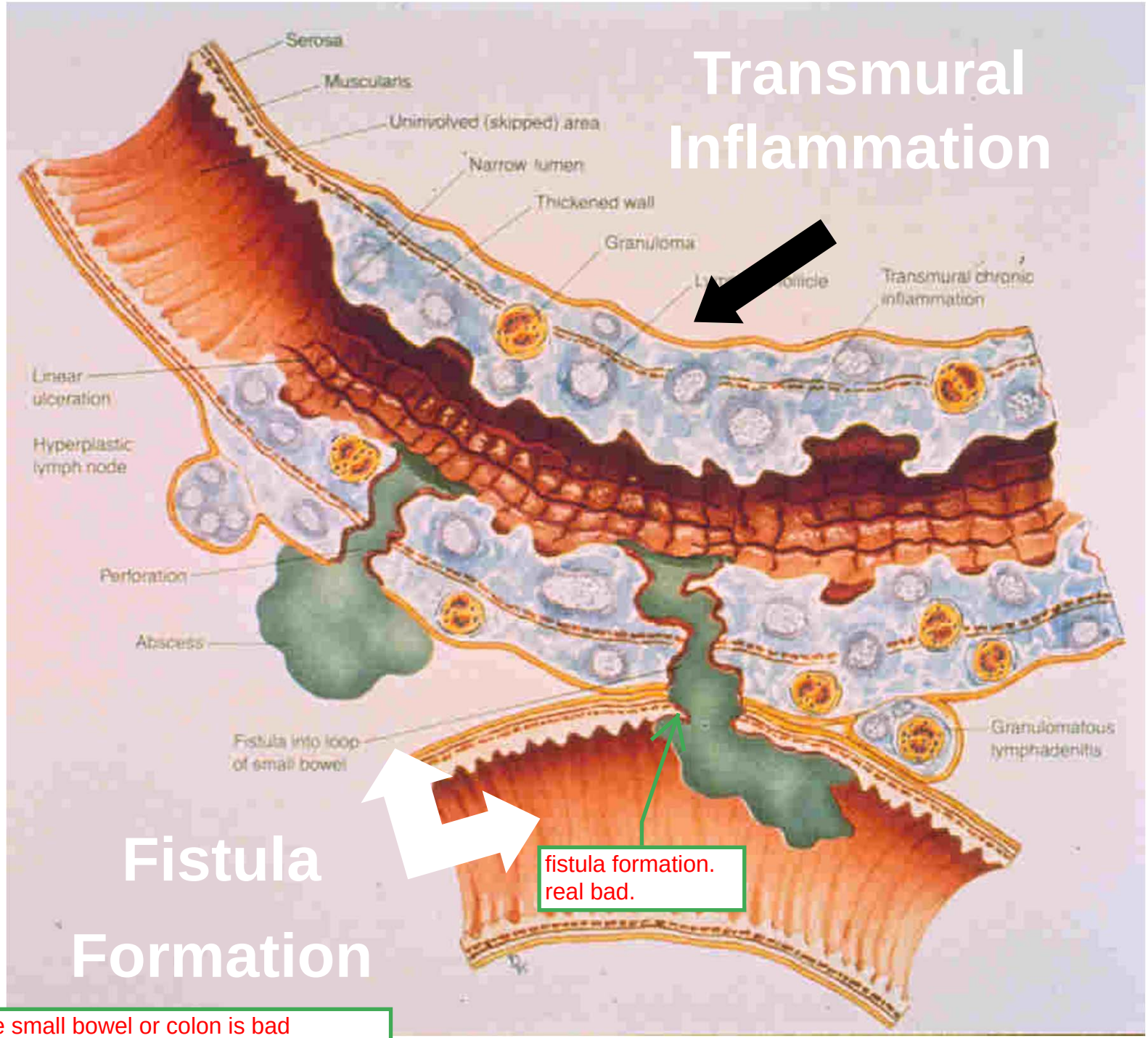
ulcers penetrate entire wall

inflammation limited to mucosa

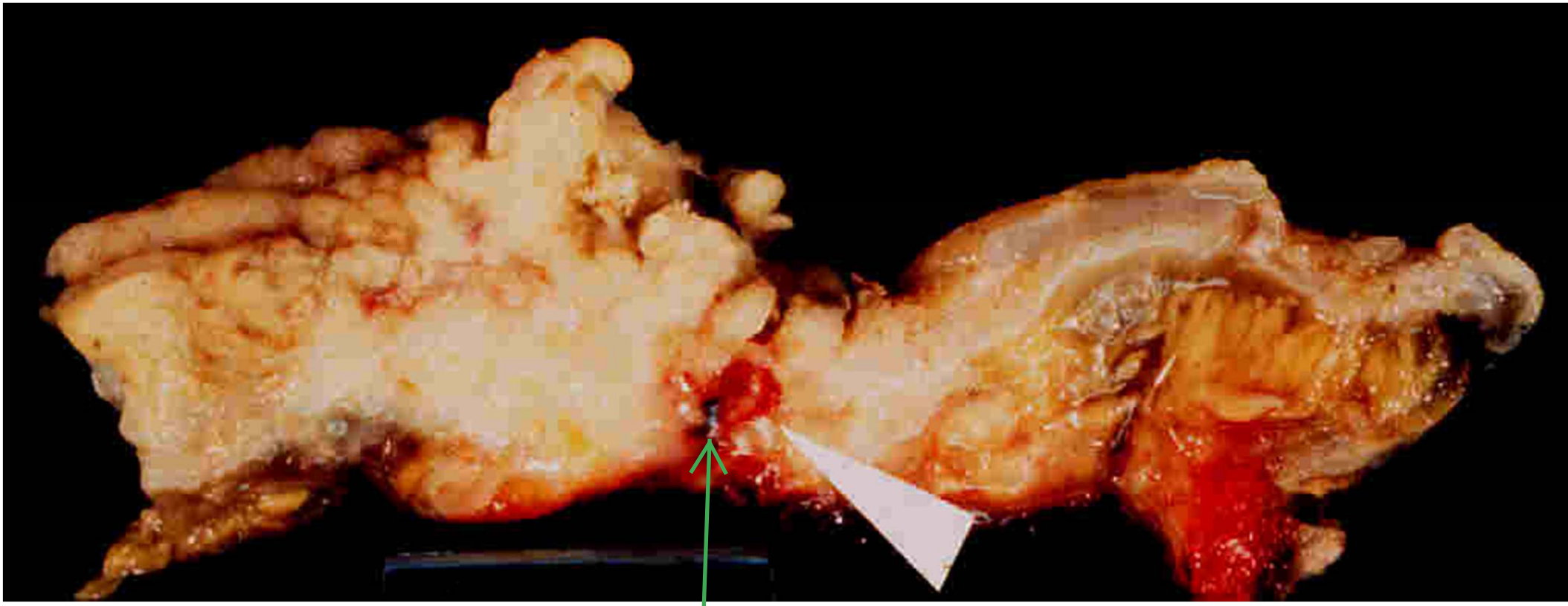
Nice visualization comparing the two

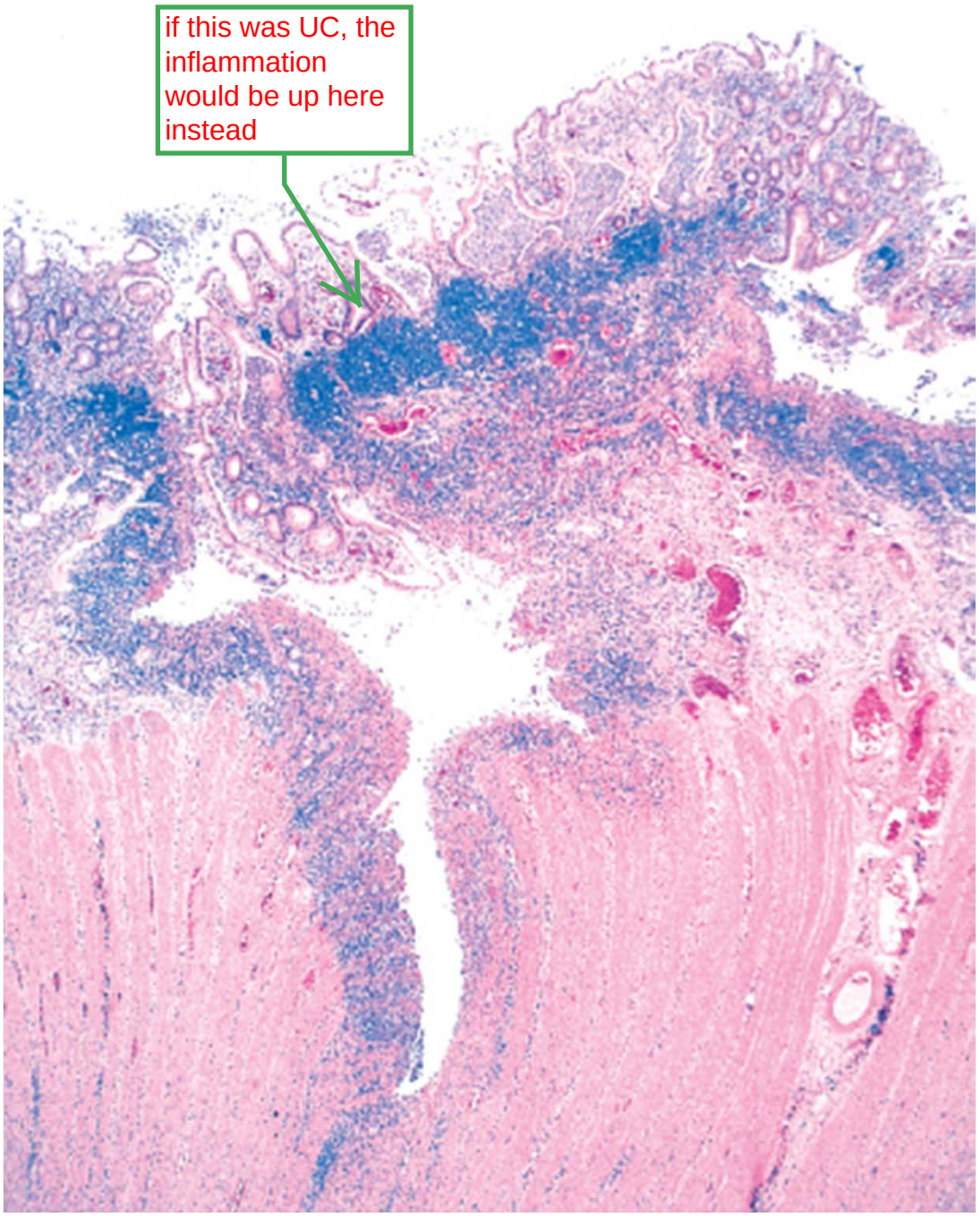
Crohn’s Disease

- Small Bowel only 30%
- Colon Only 20%
- Both 50%



crohn's in the small bowel or colon is bad


fistula

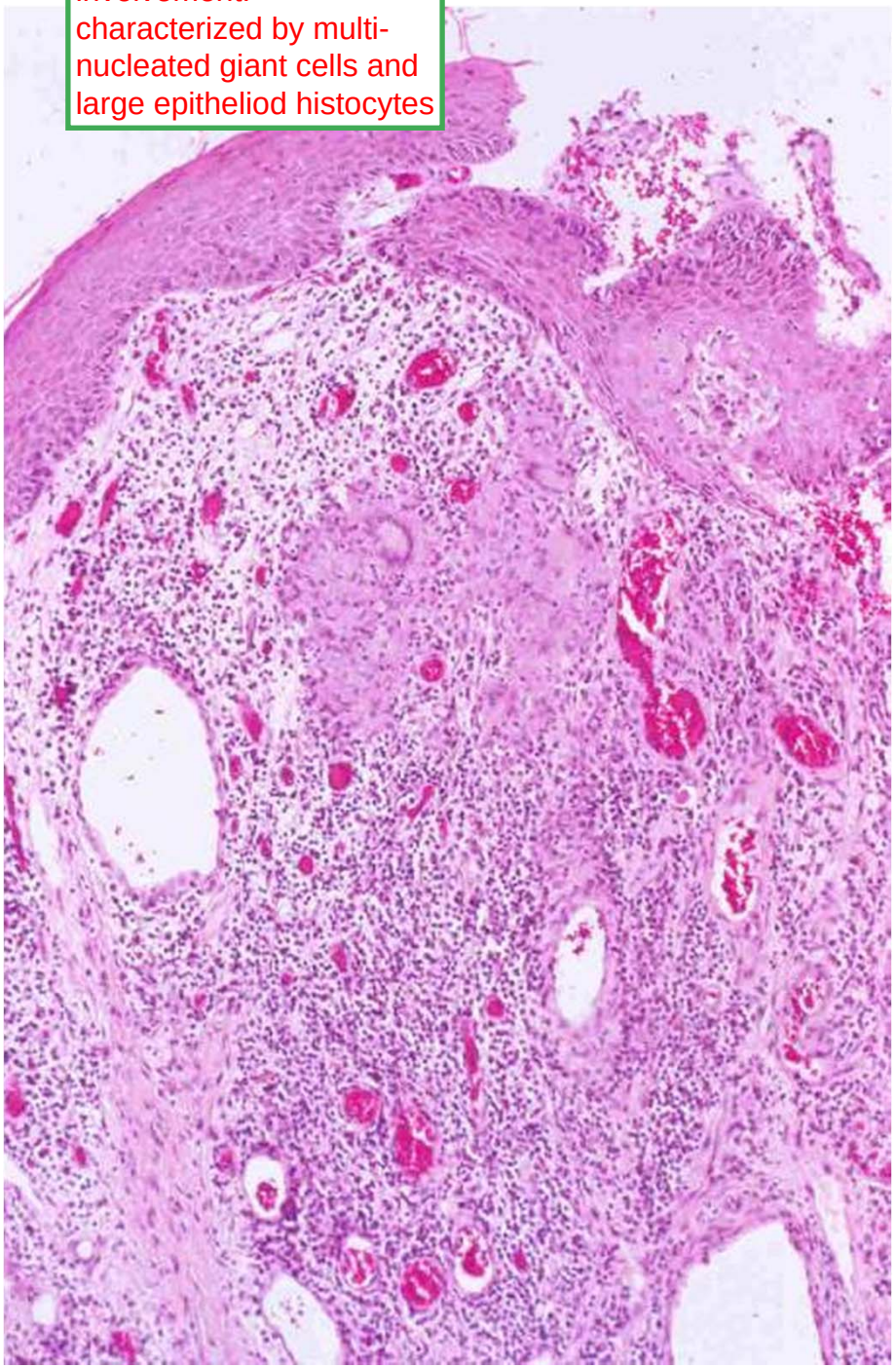


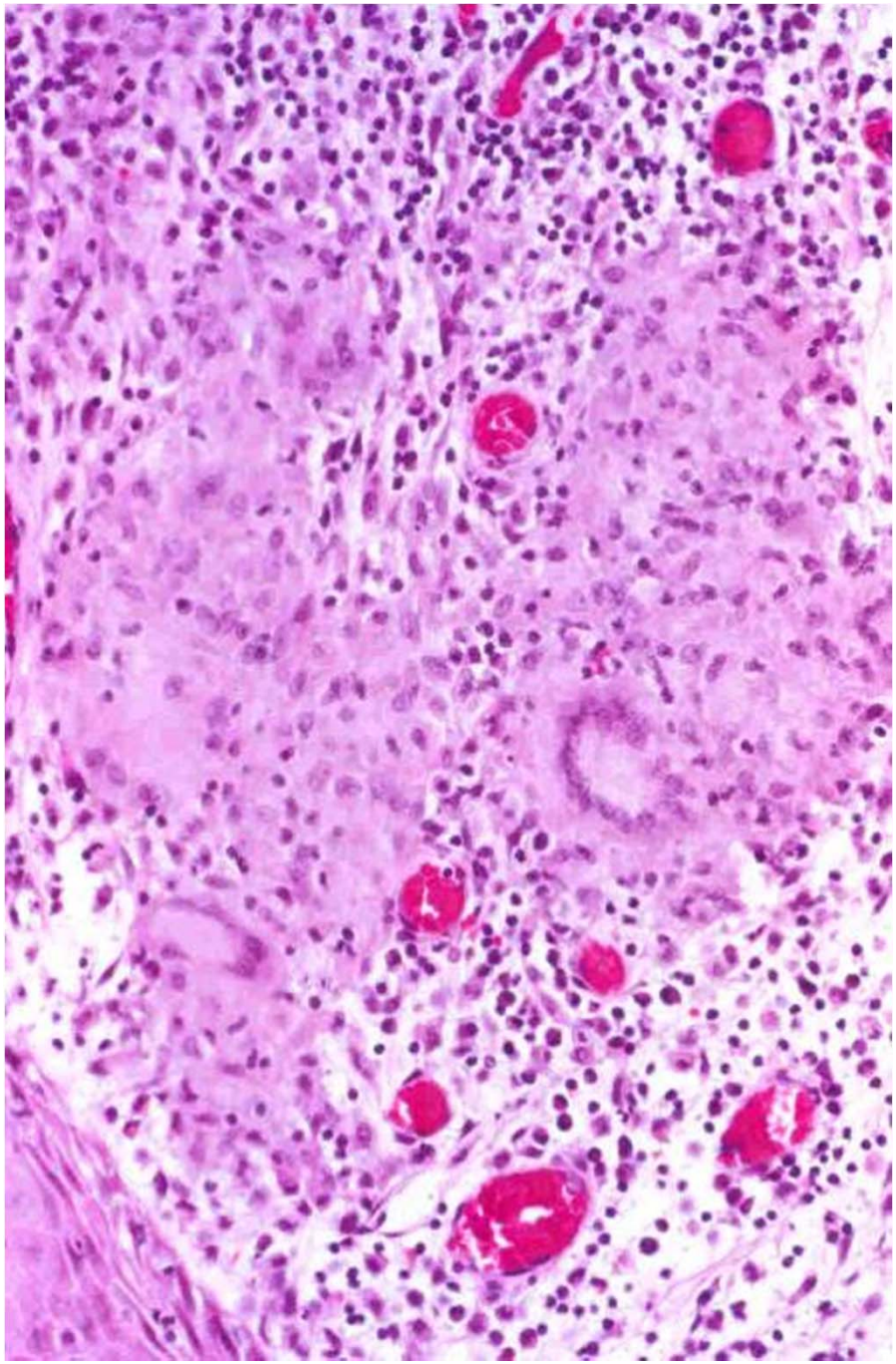
Transmural Inflammation of Crohn's Disease

- Fistulous necrosis
- Lymphocytic infiltrate
- Fibrosis

histo section of small bowel with ulcer penetrating down to muscularis propria

crohn's with esophogeal involvement.
characterized by multi-nucleated giant cells and large epitheliod histocytes

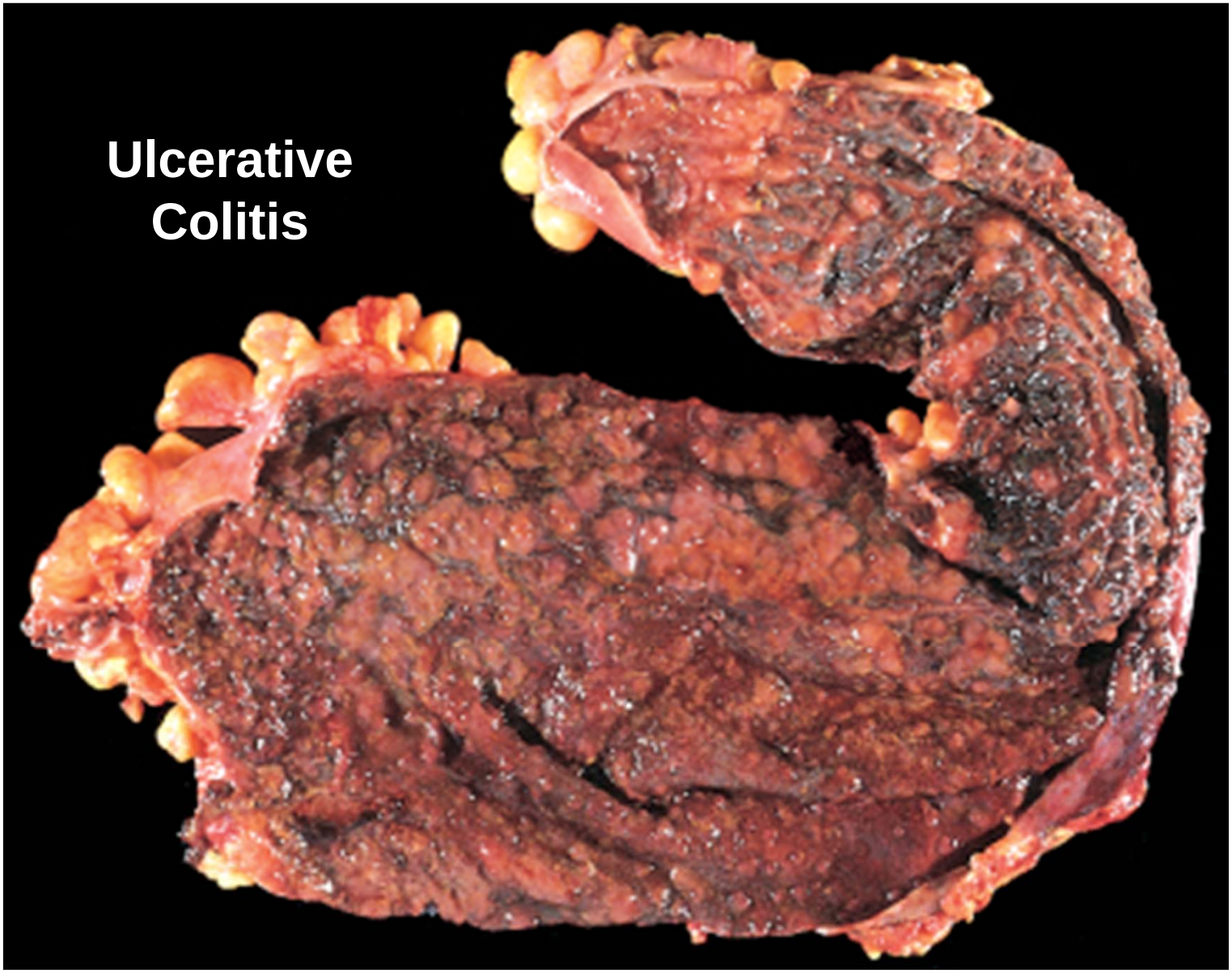




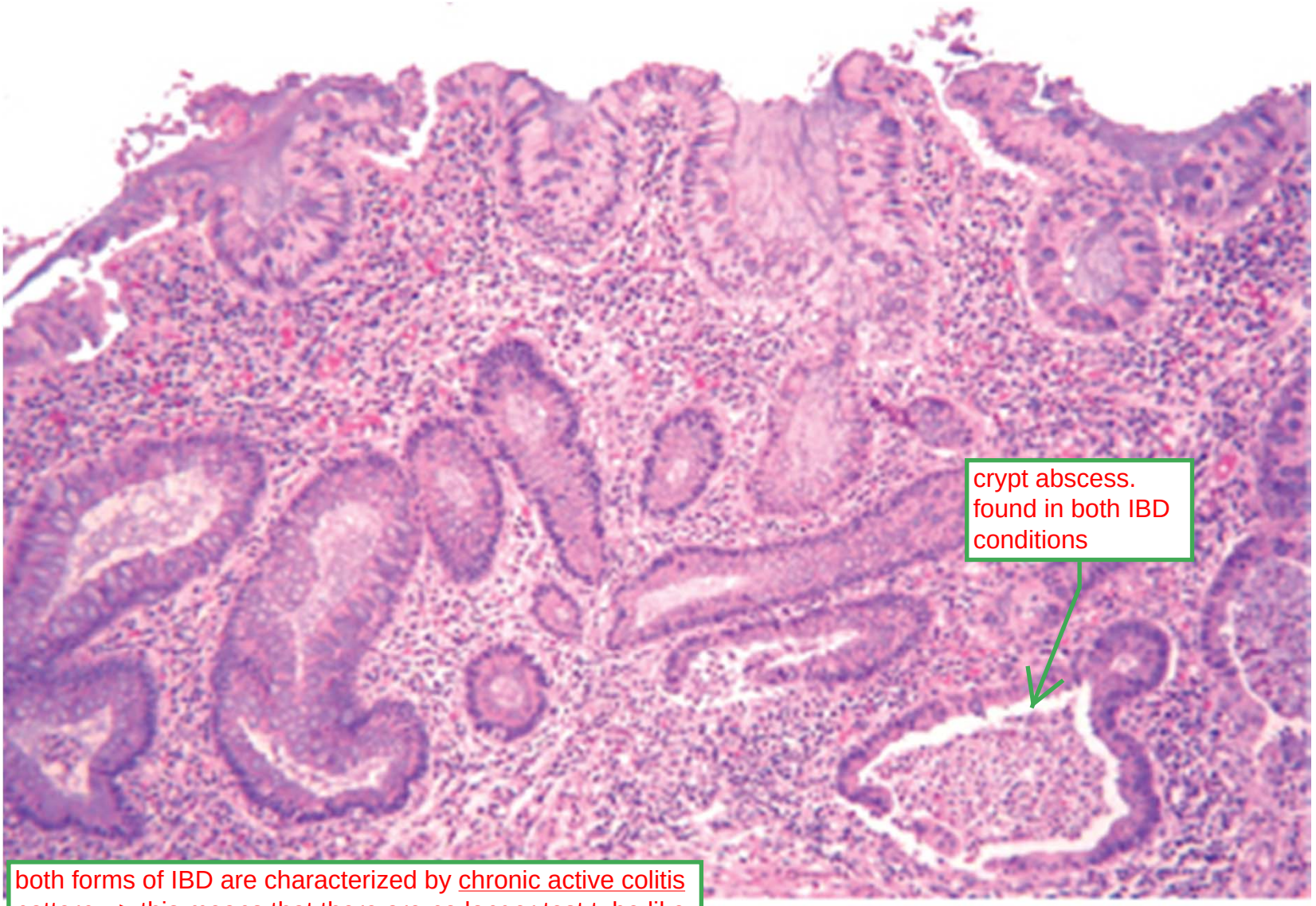
Ulcerative Colitis

- Can involve rectum only
- Can extend continuously and stop anywhere in the colon
- No skip lesions
- No small intestinal involvement

Normal Colon



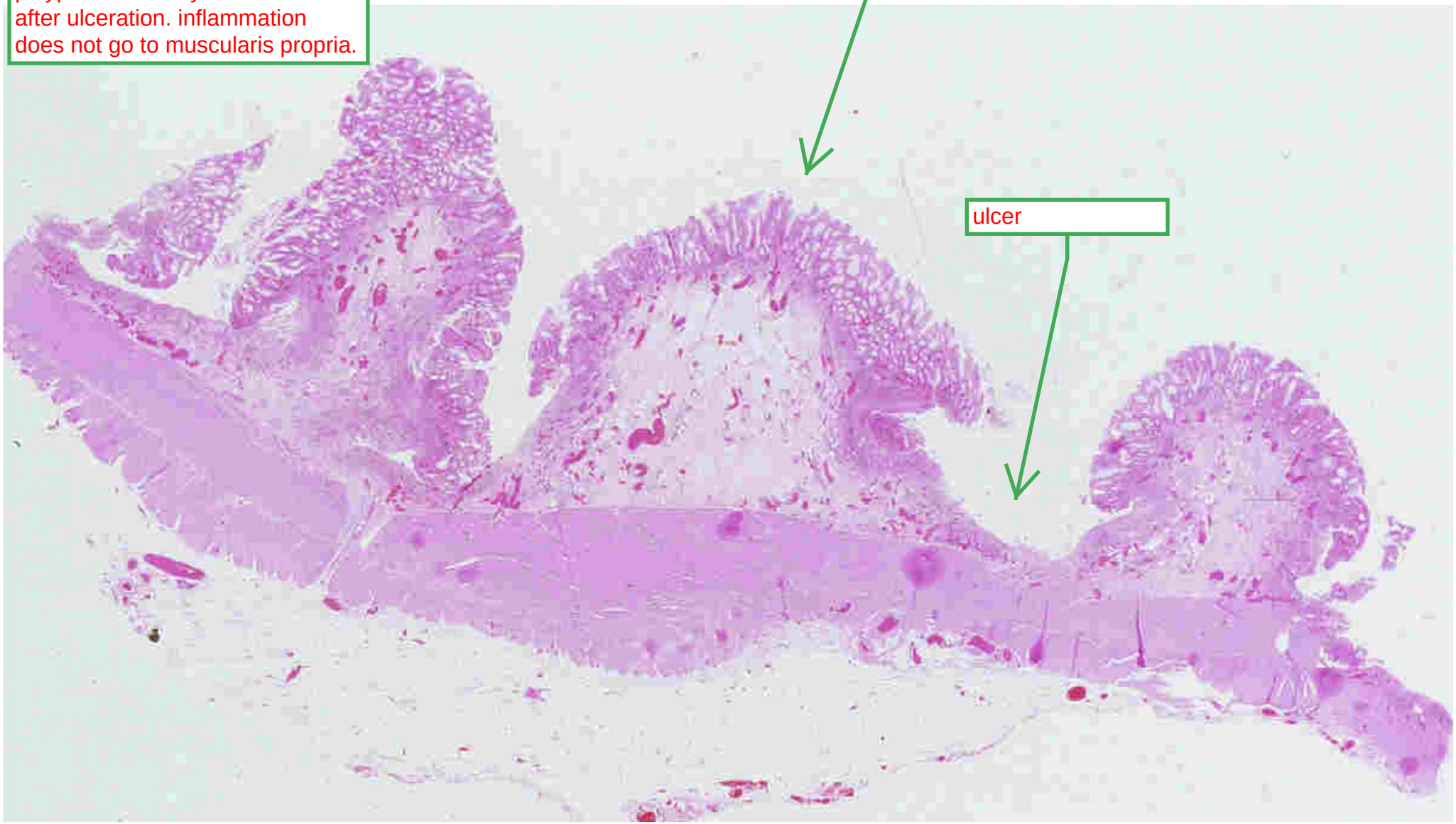
no skip lesions. usually area of inflammation is well demarcated.



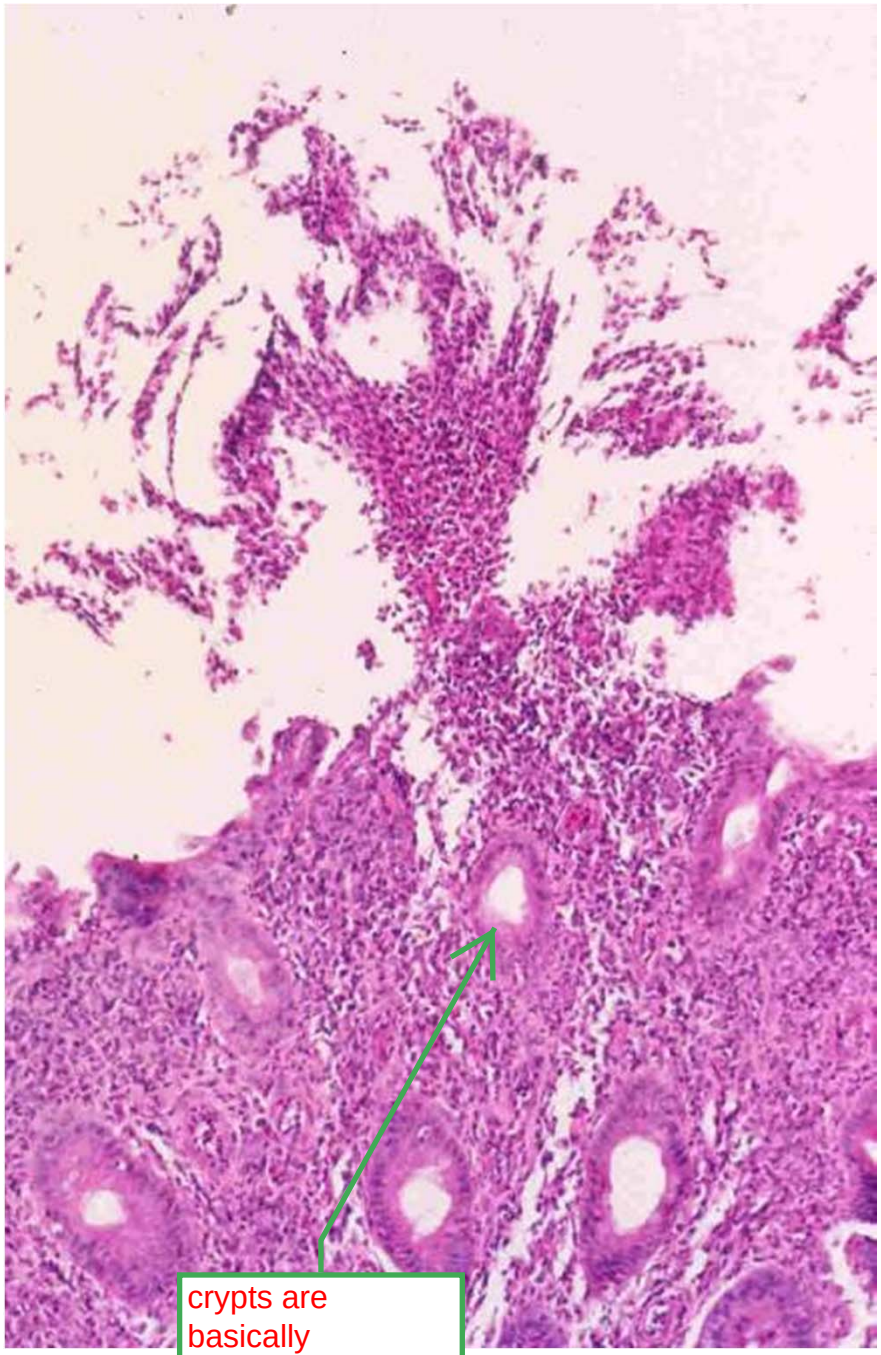
2005

both forms of IBD are characterized by chronic active colitis pattern --> this means that there are no longer test tube like gland anymore because architecture has messed up due to ulceration. "chornic" in the name stands for the architectural disarray and "active" stands for neutrophils eating up epithelial glands. you can't tell difference between the two conditions by this slide. can be either.

surgical resection specimen. this is UC because we see inflammatory pseudopolyps between areas of ulceration. the polyp are basically what remains after ulceration. inflammation does not go to muscularis propria.



Inflammatory Pseudopolyps



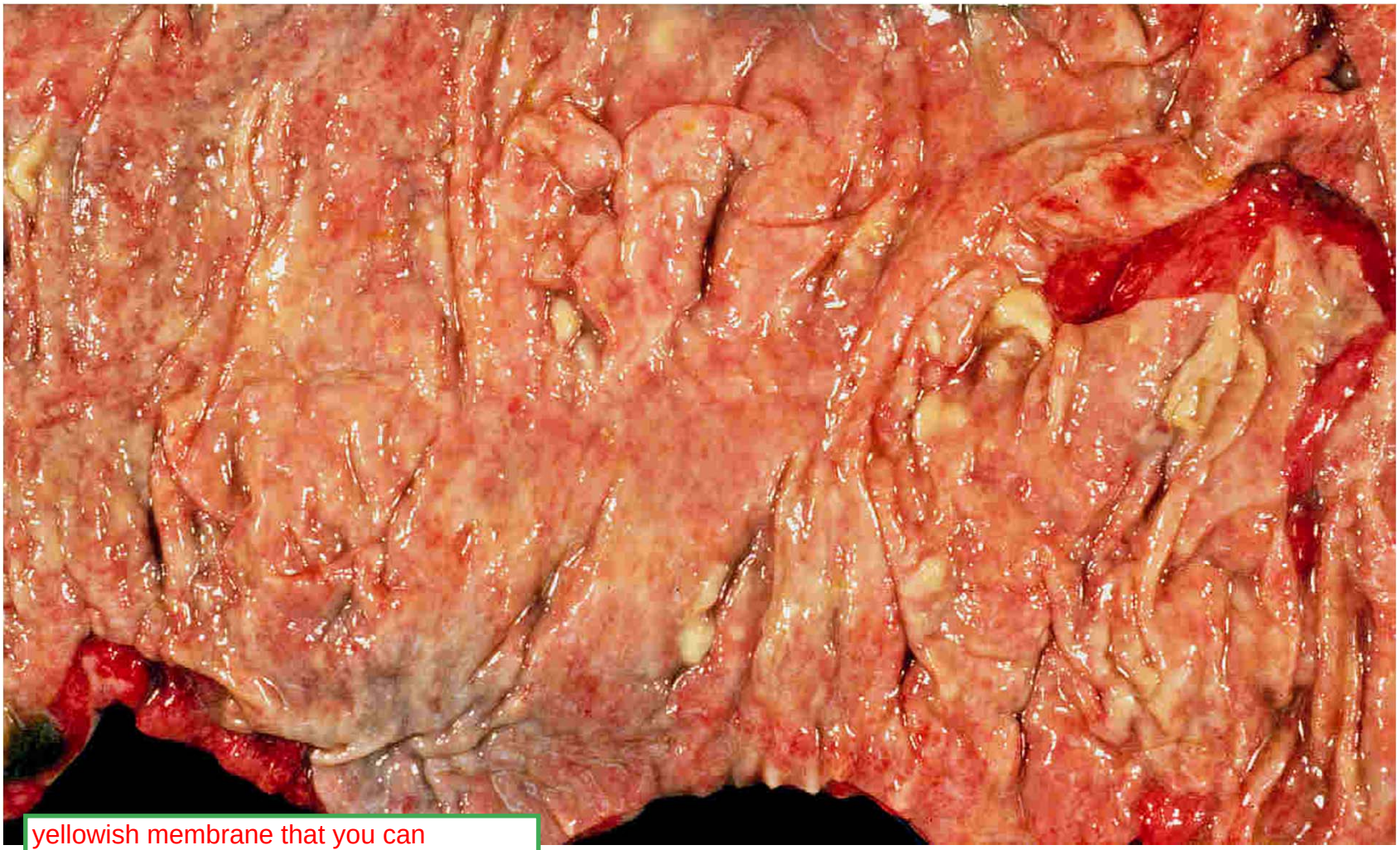
crypts are basically volcanoes that erupt and release neutrophils

Pseudomembranous Colitis

- Superficial Mucosal necrosis
- A membrane of neutrophils and fibrin
- Associated with previous antibiotic treatment and overgrowth of Clostridium difficile

this is iatrogenic. clindamycin is a big cause of this. kills good bacteria and clostridium difficile takes over.

Clostridium Difficile-Associated Pseudomembranous Colitis



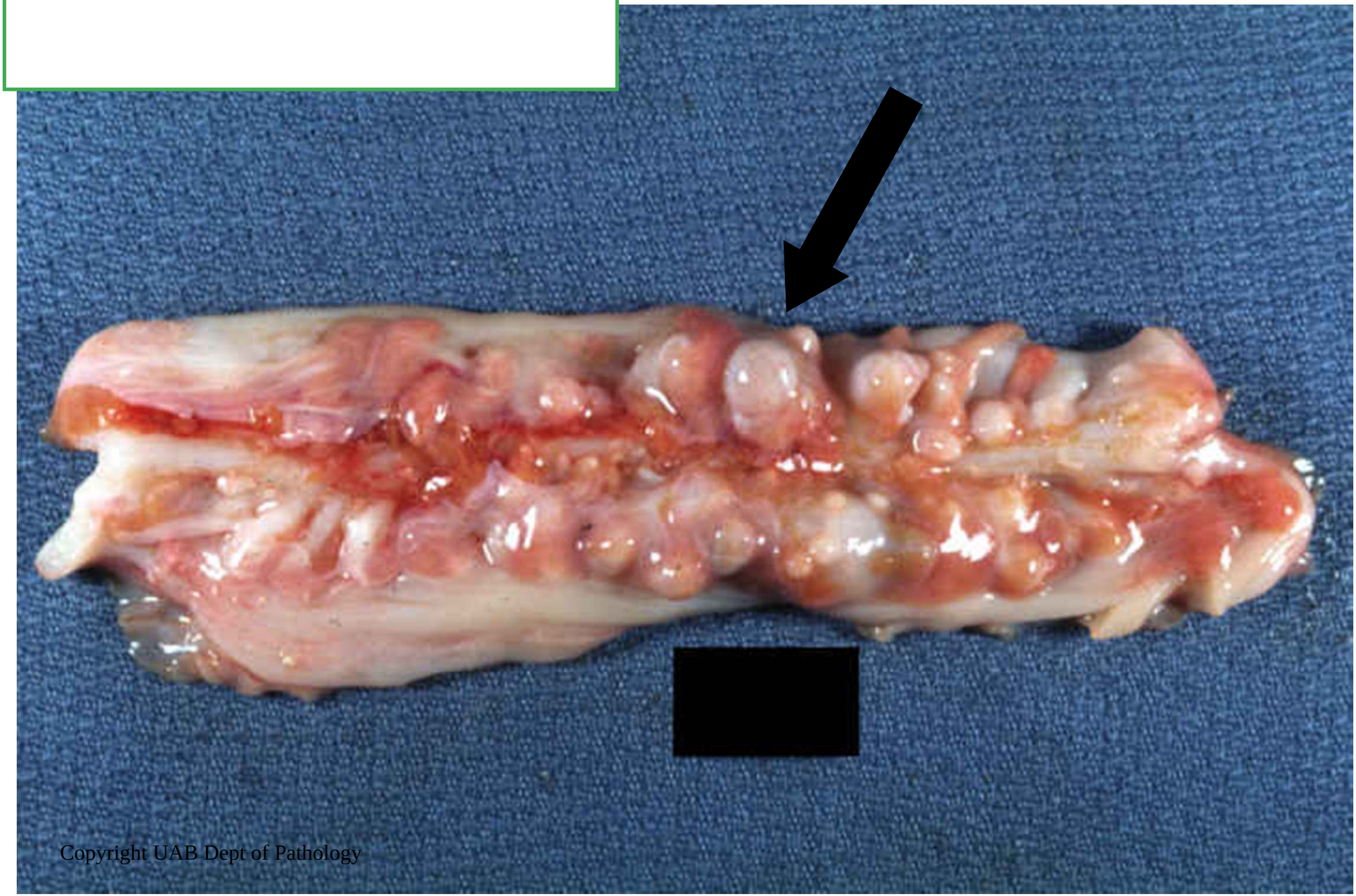
yellowish membrane that you can basically peel off. pus form pseudomembrane

Diverticular Disease

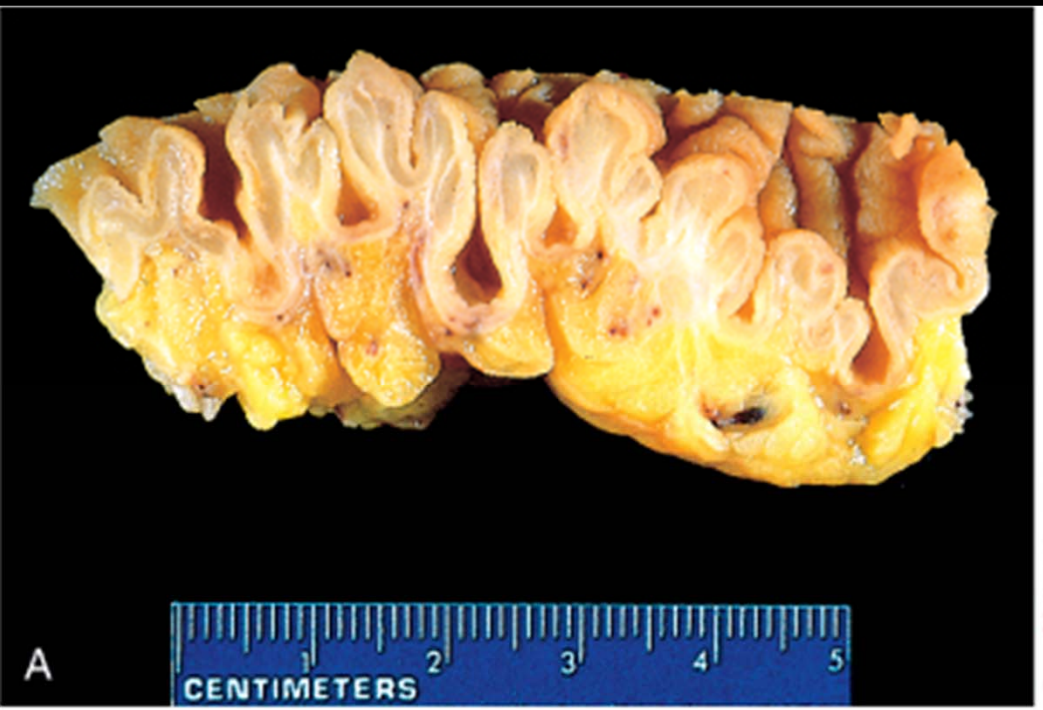
- Uncommon before age 40-50, but seen in more than 50% of patients 70-80
- Associated with Western diet, low in fiber and high in refined carbohydrates and meat
- 95% of disease is seen in the sigmoid colon

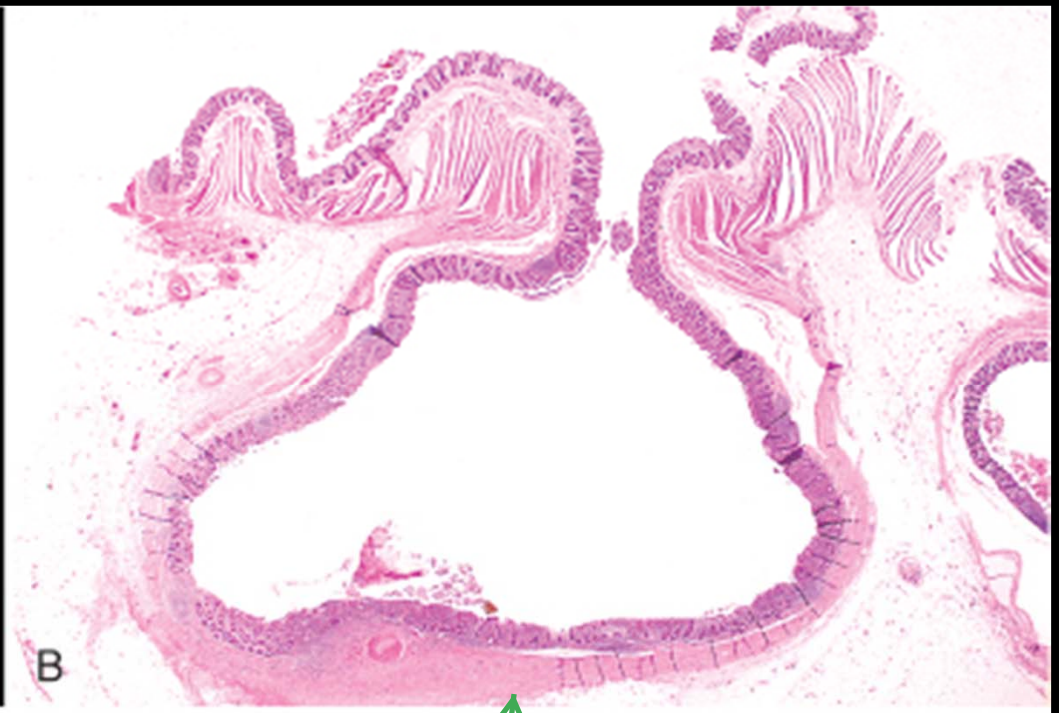
increases intralumenal pressure in colon and causes diverticulum to form

showing outside of colon. normally we should see taenia coli and smooth serosa but instead we see little balloons popping out.



in X-section





diverticulum

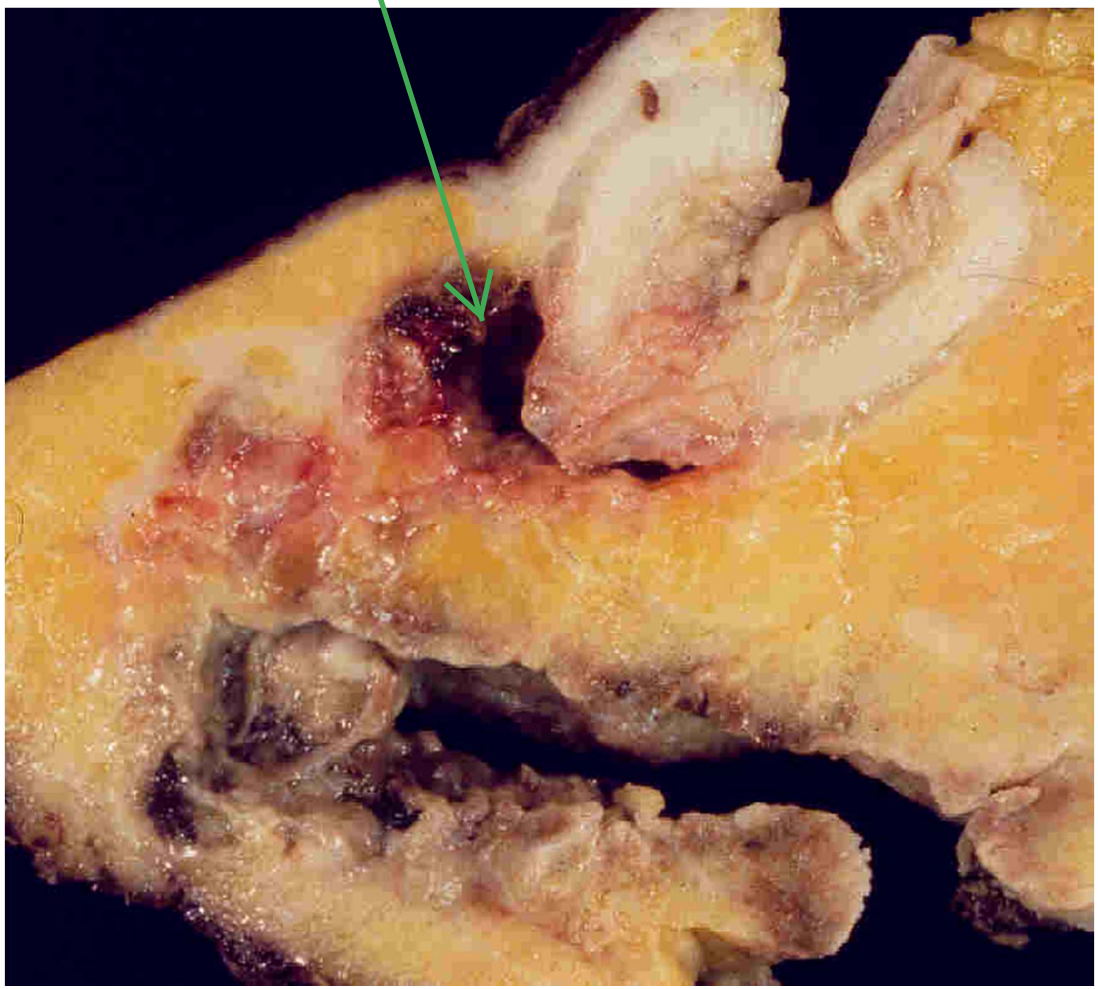
each diverticlum is like a miniature appendix.
obstruction can cause it to become inflamed.
leads to diverticulitis.

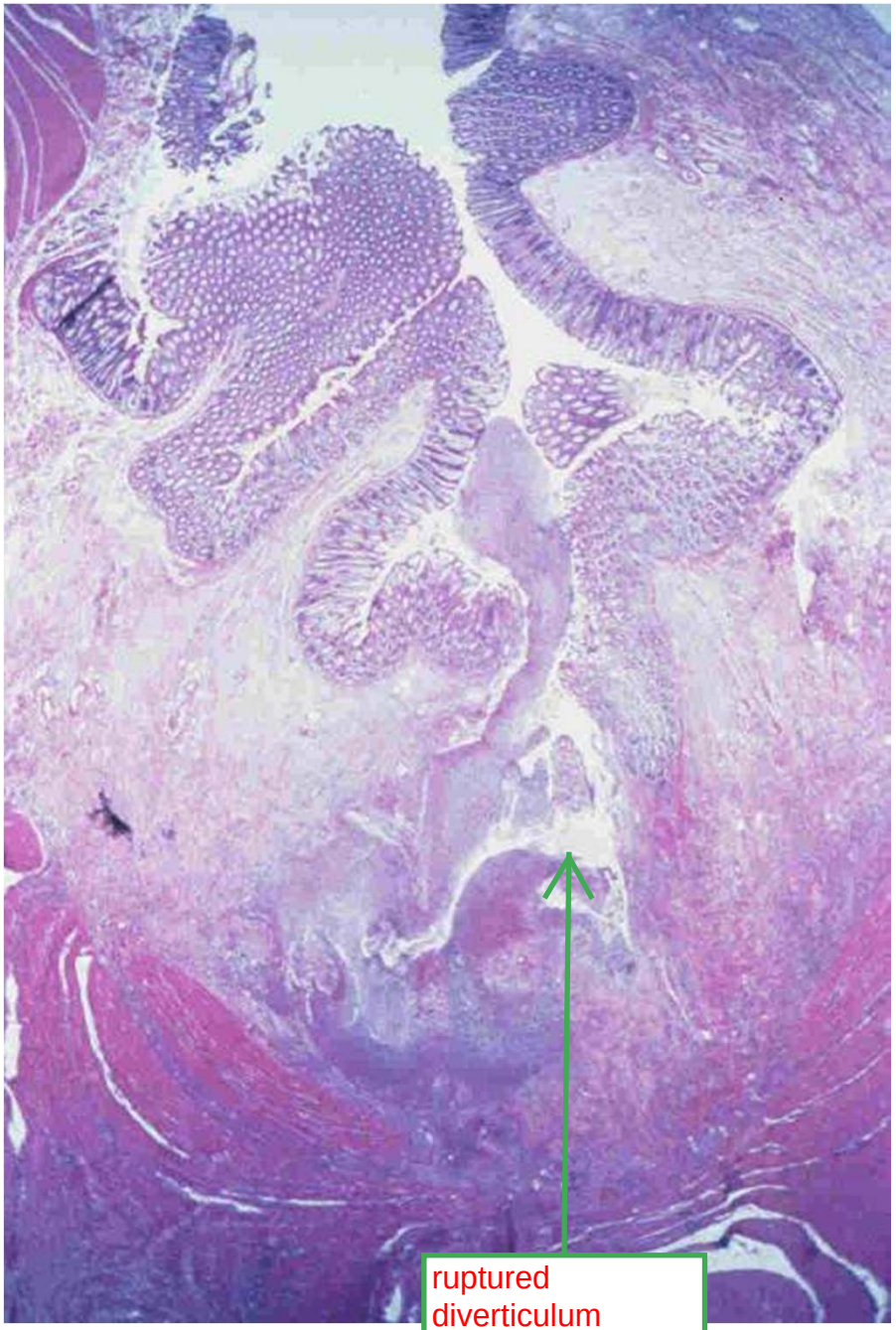
Complications of Diverticular Disease

- Bleeding

not as common as inflammation

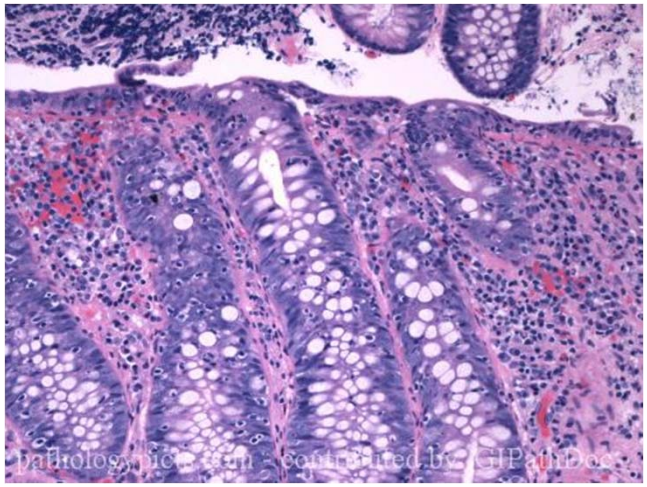
- Inflammation
  - **Diverticulitis**
  - **Perforation**
  - **Abscess, adhesions, fistula**
  - **Stricture**

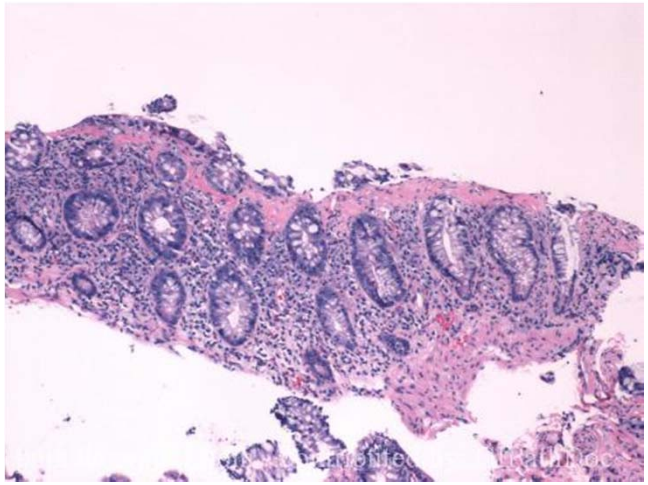

diverticulum


ruptured
diverticulum

“Microscopic” Colitis

- Lymphocytic Colitis or Collagenous Colitis
- Endoscopically Normal
- Watery Diarrhea
- Elderly patients

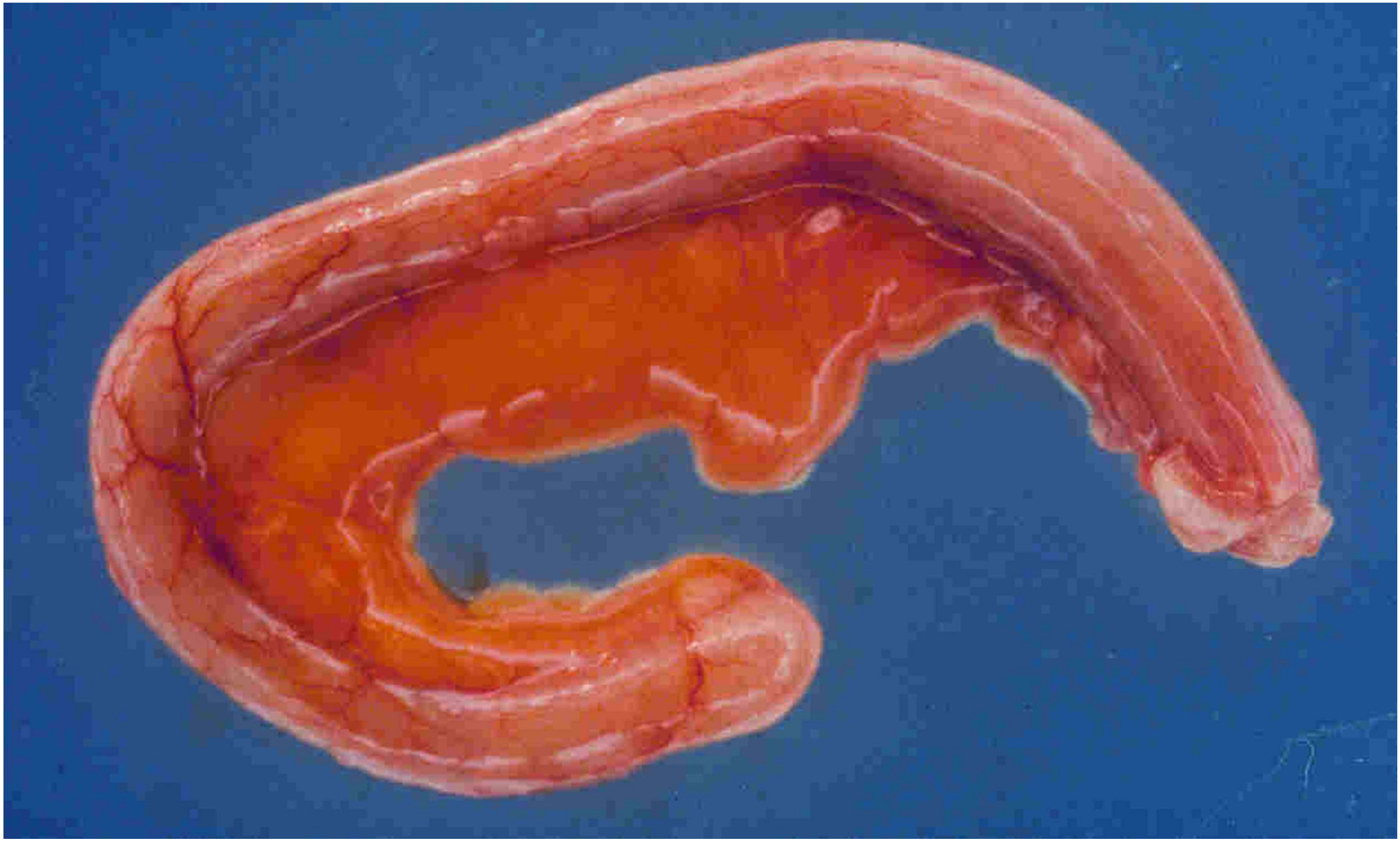




watery diarrhea in elderly folks. we don't know stimulus but pts get increased T cells in their epithelium, increased inflammaiton --> leads to watery diarrhea. if given enough time it can progress from lymphocytic appreance (top) to collagenous appearance (bottom). pts streated with steroids.

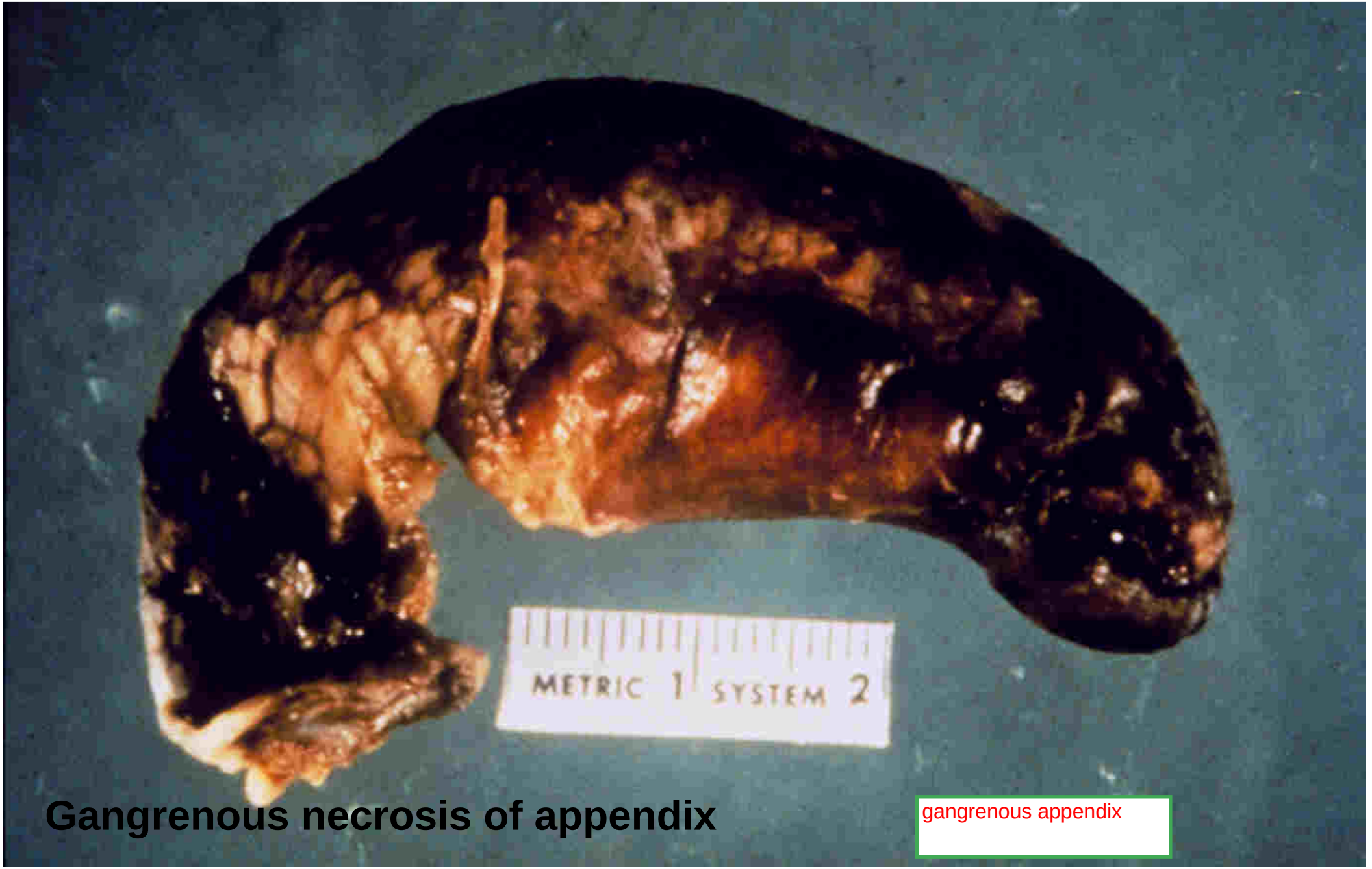
Colon - Other

- Vascular: Ischemic injury
- Traumatic: Prolapse, Radiation, Obstruction (such as appendicitis)
- Infections in immunosuppressed patients (such as CMV)
- Iatrogenic: NSAID colitis, Graft-versus-host-disease



Normal Appendix

normal appendix



Gangrenous necrosis of appendix

gangrenous appendix