Small and Large Intestinal pathology, part 2

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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

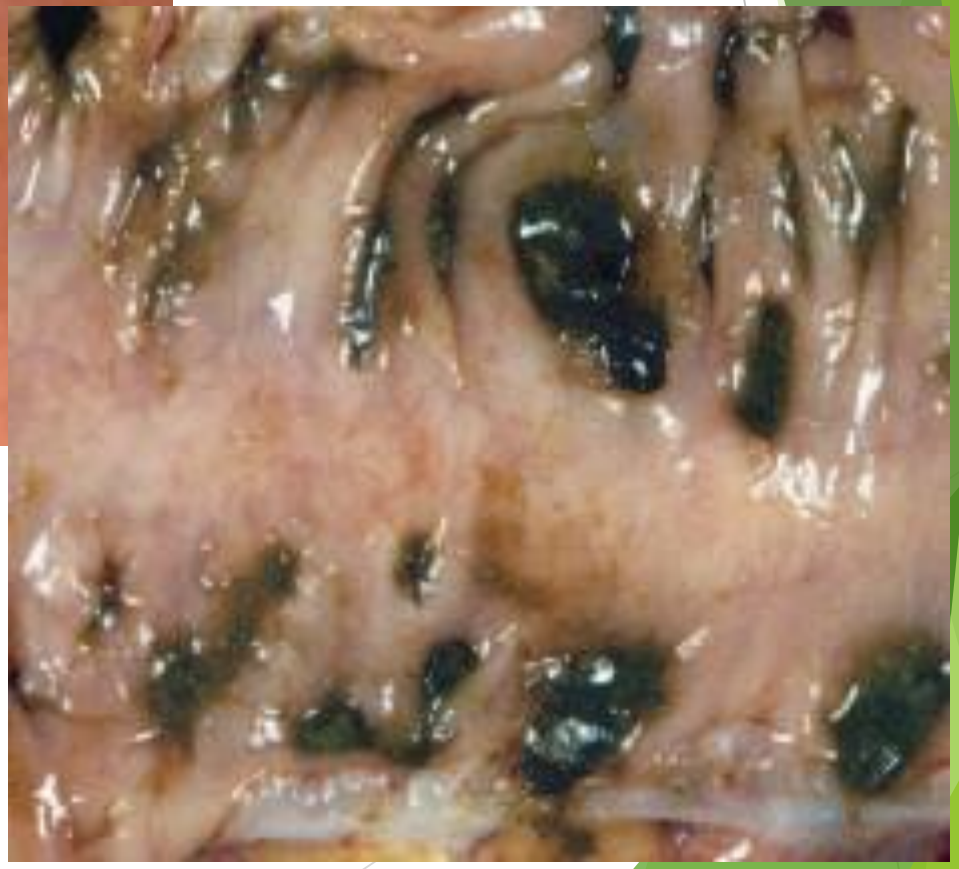
  Ulcerative colitis

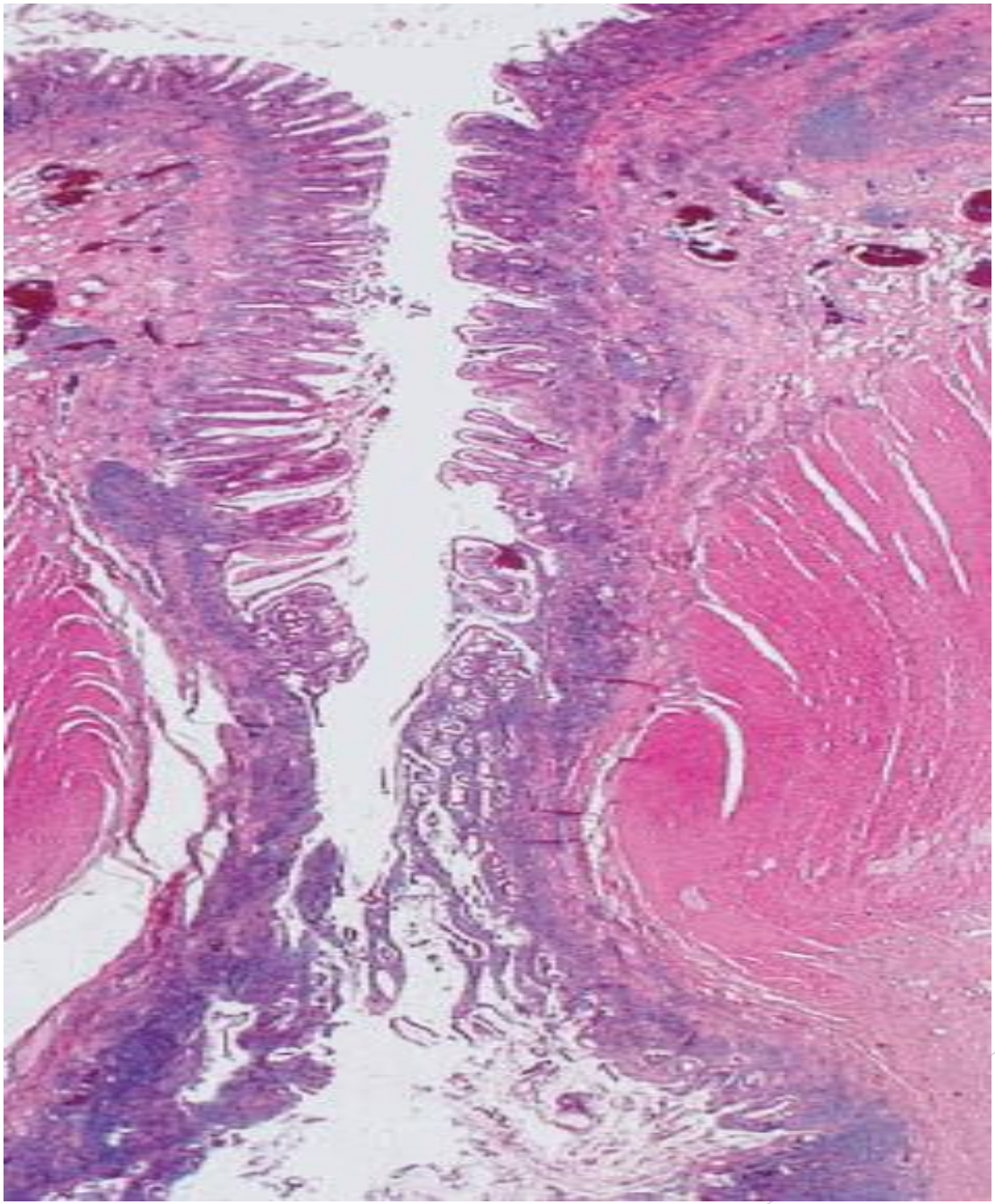
Sigmoid Diverticulitis

- Pseudodiverticulae.
- Outpouchings of colonic mucosa and submucosa.
- Acquired.
- Elevated intraluminal pressure in the sigmoid colon
- Exaggerated peristaltic contractions,
- Low fiber diet.

MORPHOLOGY

- Flasklike outpouchings
- Mostly in sigmoid colon.
- Thin wall (atrophic mucosa, compressed submucosa)
- Attenuated or absent muscularis.
- Obstruction leads to diverticulitis.
- Risk of perforation.
- Recurrent diverticulitis leads to strictures.





Clinical Features

- Mostly asymptomatic.
- Intermittent lower abdominal pain
- Constipation or diarrhea.

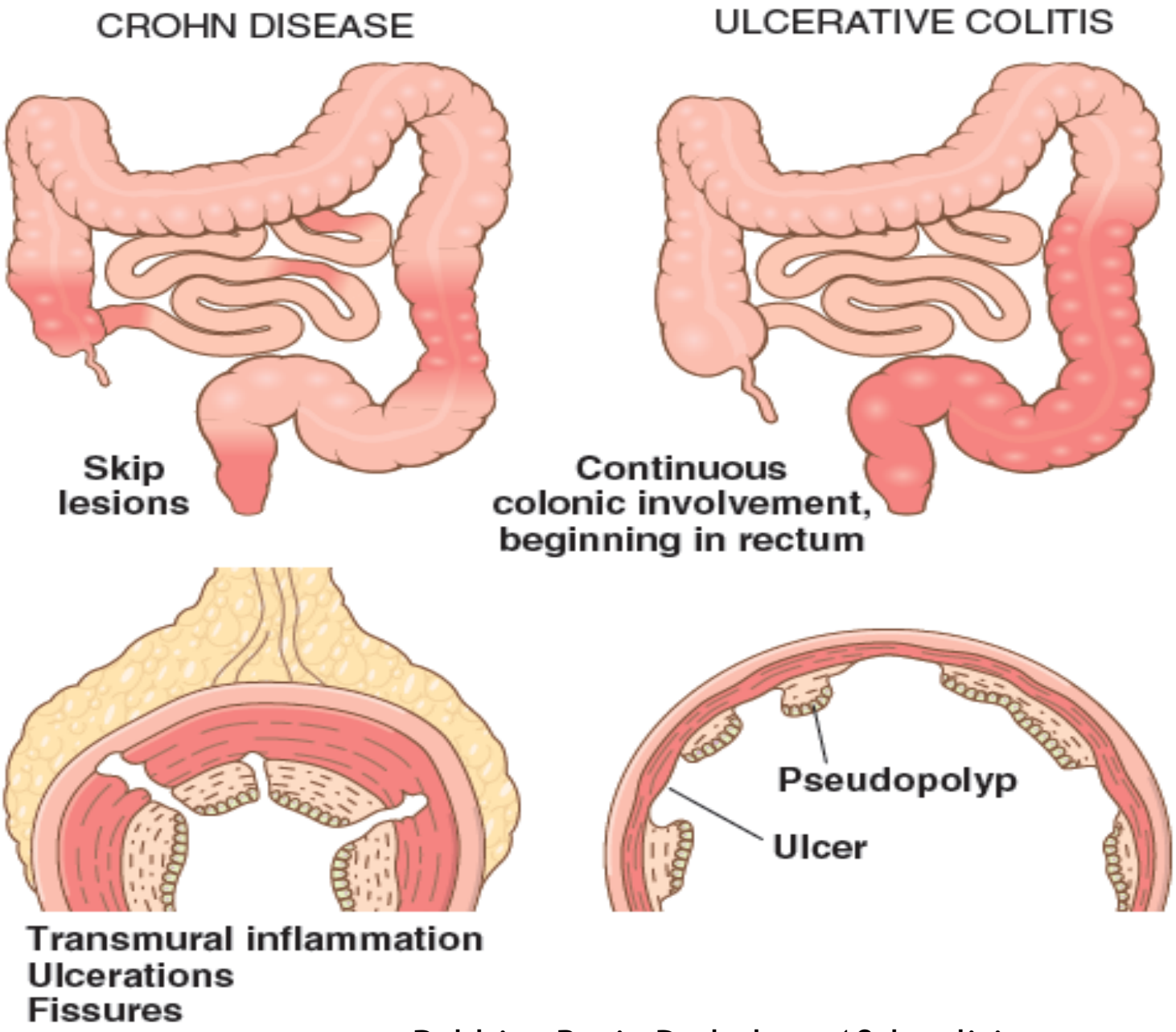
- Tx
- High fiber diet.
- Antibiotics in diverticulitis.
- Surgery.

Inflammatory Bowel Disease

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

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

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



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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!!!.*

Pathogenesis:

- Combined effects.

- Genetic factors.
- Alterations in host interactions with intestinal microbiota
- Intestinal epithelial dysfunction.
- Aberrant mucosal immune responses
- Altered composition of the gut microbiome.

Genetics:

- *Family history.*
- *Concordance rate for monozygotic twins :20% for CD, 16% for UC.*
- > 200 genes associated with IBD, all with CD.
- *NOD2*(nucleotide oligomerization binding domain 2): susceptibility gene in Crohn disease.
- Disease-associated NOD-2: ineffective at defending intestinal bacteria.
- Bacteria enters through epithelium & trigger inflammatory reactions.
- Autophagy genes

Mucosal immune responses

- Immunosuppressive and immunomodulatory agents are mainstays of IBD therapy.

- Excessive immune activation by intestinal microbes.
- Defective immune regulation of T cell
- TH1 (mainly in CD) and TH2 (mainly in UC)

Epithelial defects

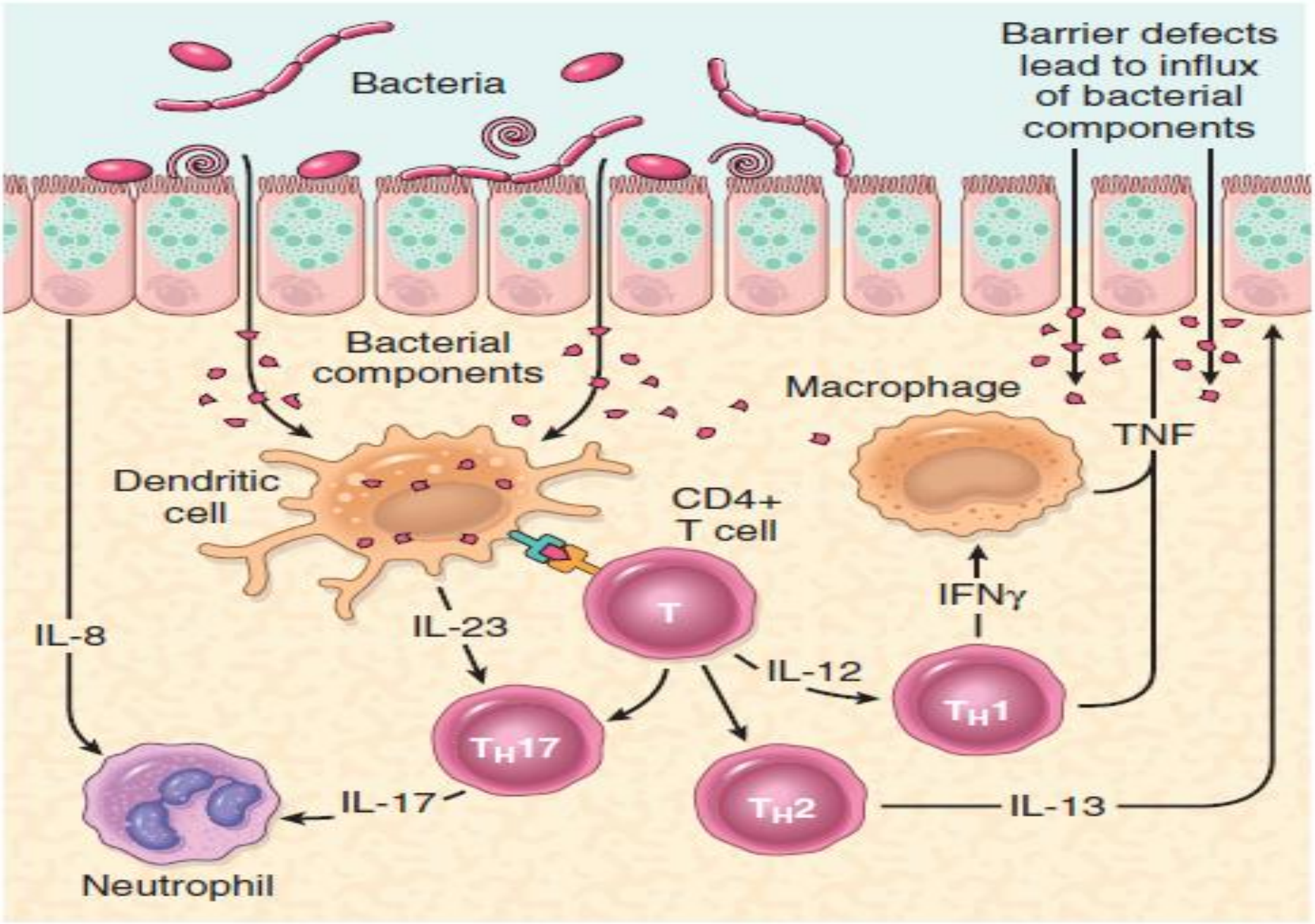
- Defects in intestinal epithelial tight junction barrier function >>>> in Crohn disease
- Barrier dysfunction >>> activate innate and adaptive mucosal immunity >>> sensitize subjects to disease.
- Defects in Paneth cell (anti microbial) granules.

Microbiota

- Quantity of microbes in gastrointestinal lumen is enormous (50% of stool mass)
- **Inter-individual variation in microbial composition.**
- Probiotic (or beneficial) bacteria may benefit IBD patients.

Disease model

- Trans epithelial flux of bacteria.
- Activation of innate and adaptive immune responses (genetically susceptible host)
- Release of TNF and immune signals
- Increase tight junction permeability
- More flux of luminal bacteria.
- Self amplifying cycle: stimulus at any site is sufficient to initiate IBD.



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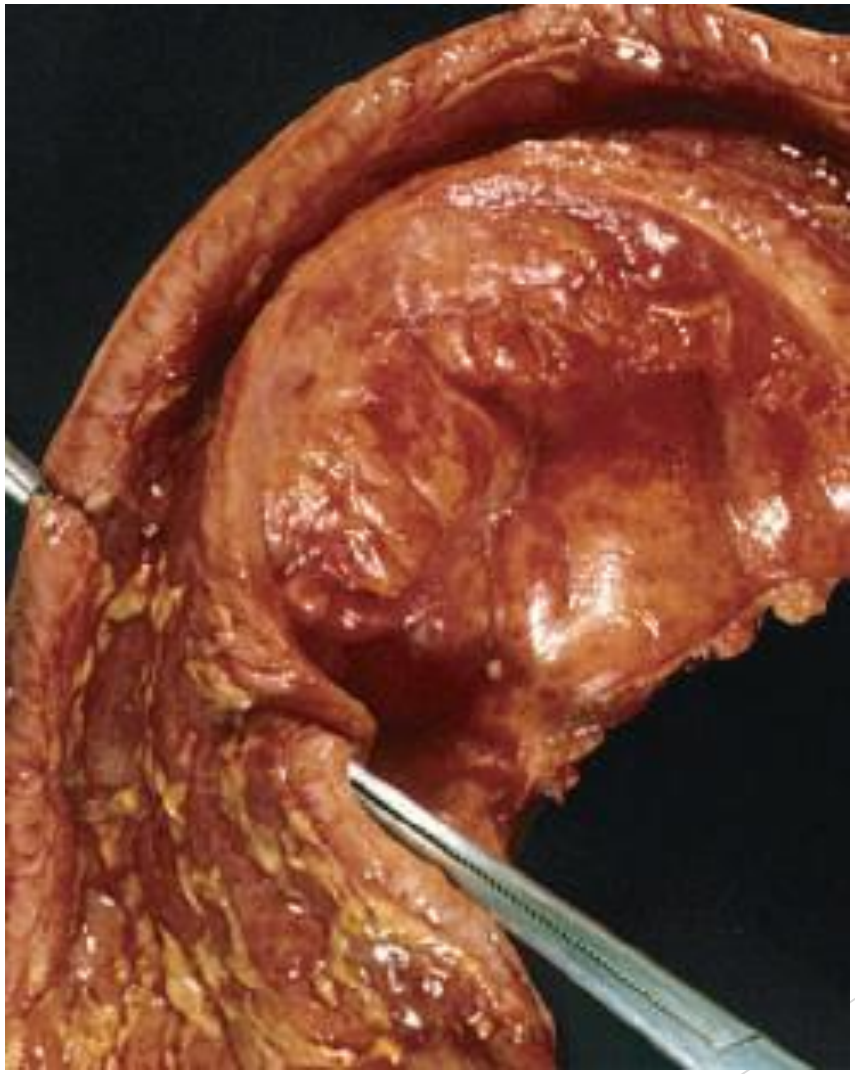
Crohn Disease Morphology

- Macroscopic:

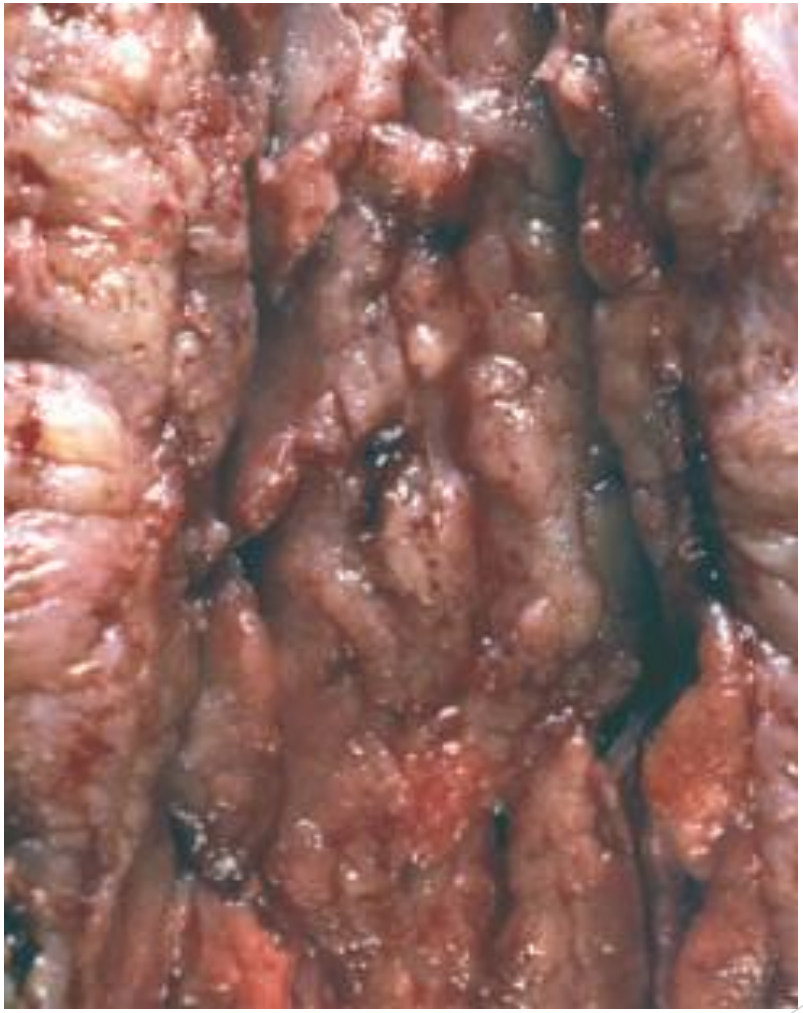
- Regional enteritis.
- Any area of GIT.
- Most common sites: terminal ileum, ileocecal valve, and cecum.
- Small intestine alone 40%
- Small intestine and colon 30%
- Colon only 30%
- Skip lesions
- Strictures common

Small bowel stricture.



- Earliest lesion: aphthous ulcer
- Elongated, serpentine ulcers.
- Edema , loss of bowel folds.
- Cobblestone appearance
- Fissures, fistulas, perforations.
- Thick bowel wall (transmural inflammation, edema, fibrosis, hypertrophic MP)
- Creeping fat

Linear ulcers.



Creeping fat

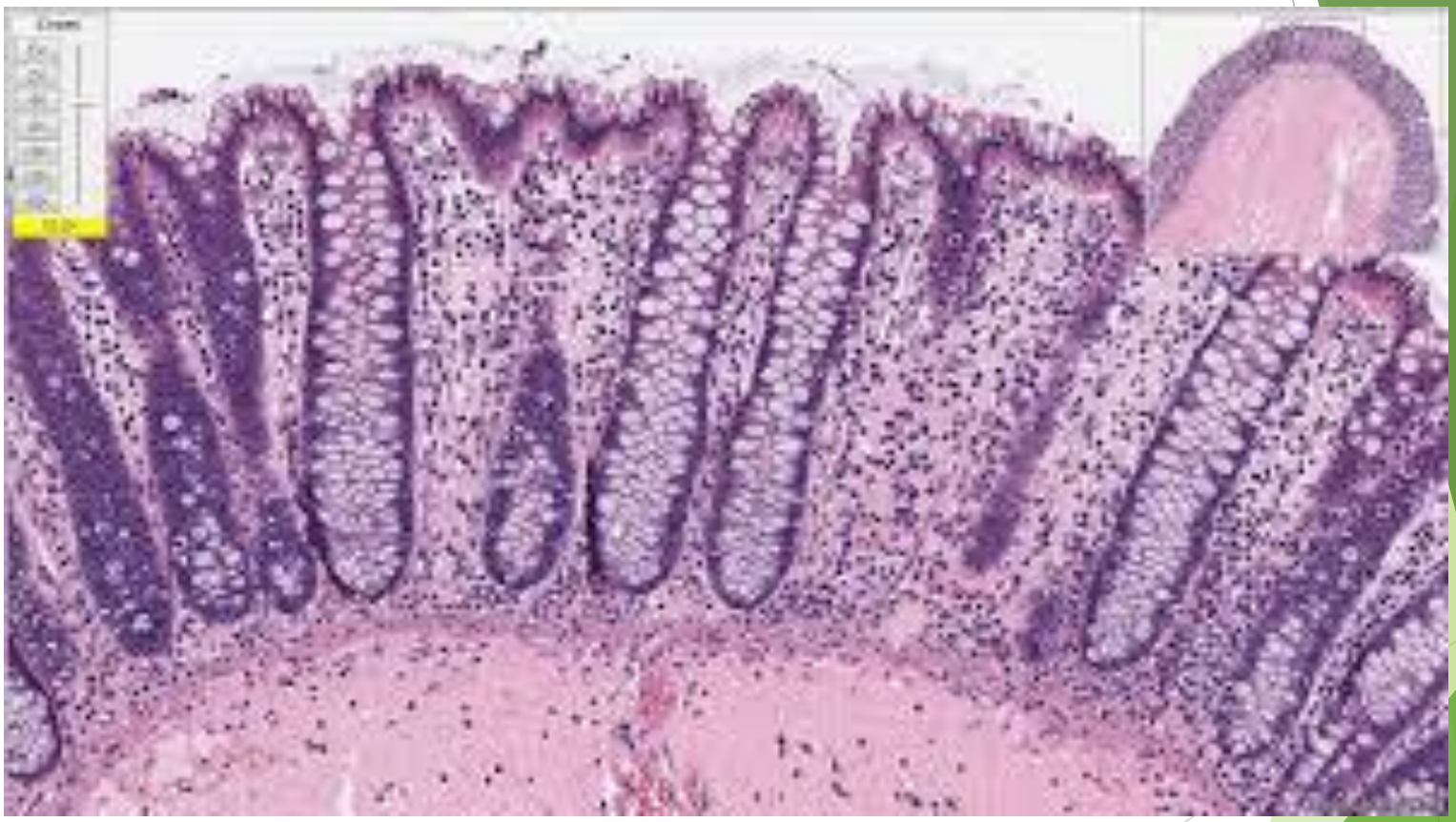
Cobblestone appearance

ResearchGate

- Microscopic:

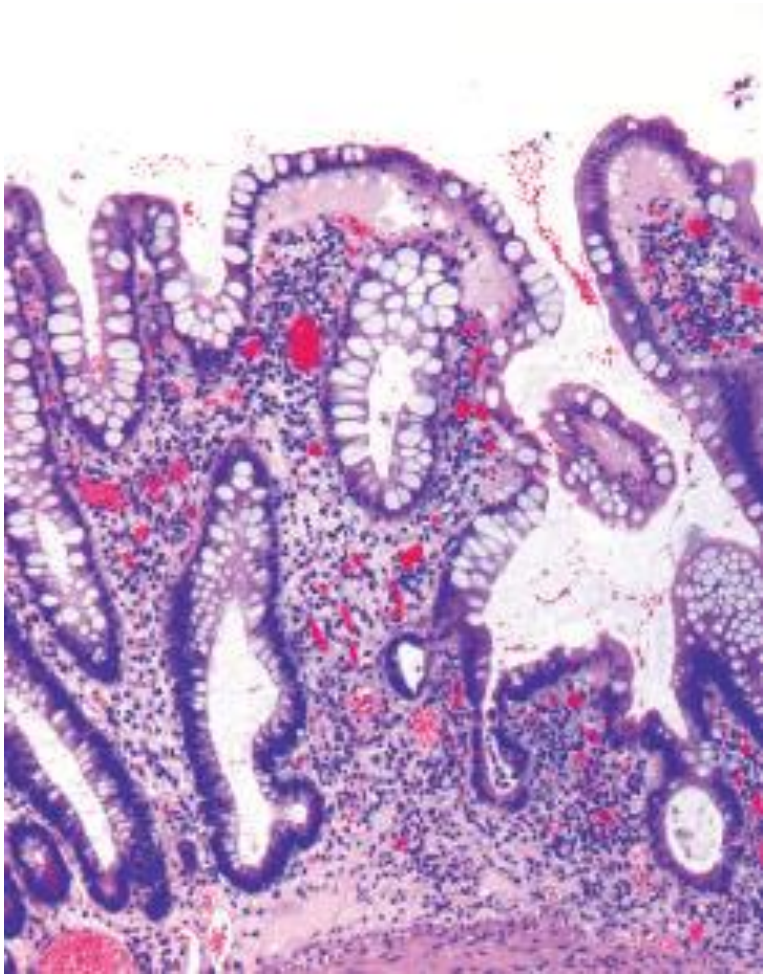
- Neutrophils in active disease.
- Crypt abscesses.
- Ulceration.
- Distortion of mucosal architecture
- Paneth cell metaplasia in left colon
- Mucosal atrophy.
- Noncaseating granulomas (hallmark) only in 35% of cases. Where??????

Normal colon

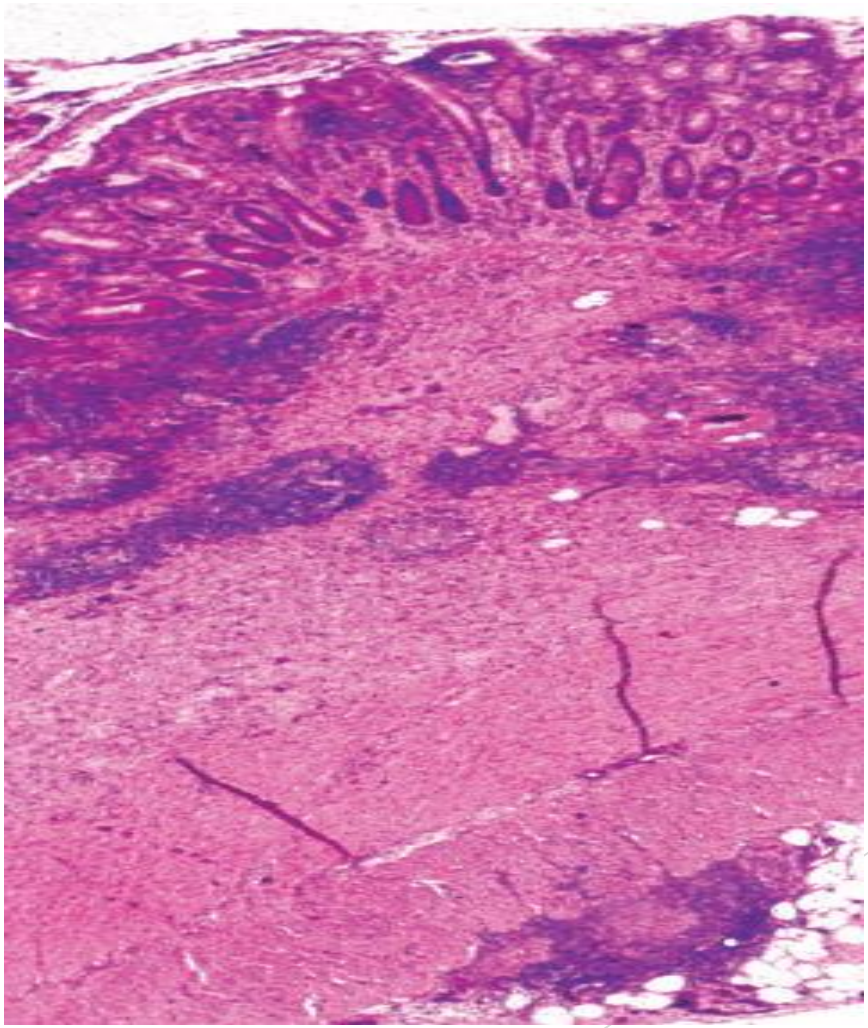


Khan Academy

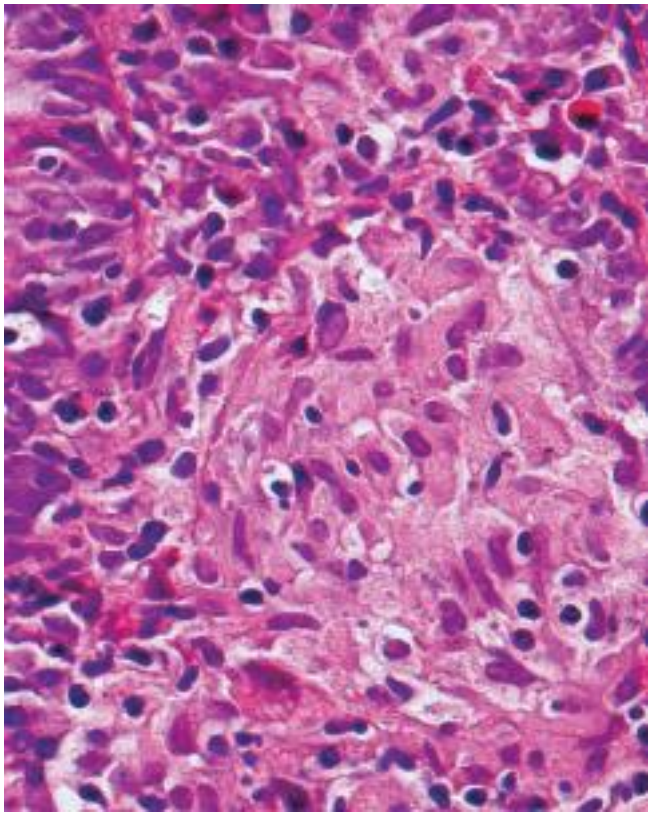
Haphazardly arranged crypts



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
- Fistulas, peritoneal abscesses, strictures

Extra intestinal manifestations

- Uveitis
- Migratory polyarthritis,
- Sacroiliitis,
- Ankylosing spondylitis,
- Erythema nodosum
- Clubbing of the fingertips
- Primary sclerosing cholangitis (more with UC)
- Risk of colonic adenocarcinoma ……

Erythema nodosum

Neurology Advisor

Clubbing

Wikipedia

Ulcerative Colitis Morphology

- Always involves the rectum
- Extends proximally in continuous pattern.
- Pan colitis.
- Occasionally focal appendiceal or cecal inflammation.
- Ulcerative proctitis or ulcerative proctosigmoiditis
- Small intestine is normal (except in backwash ileitis)

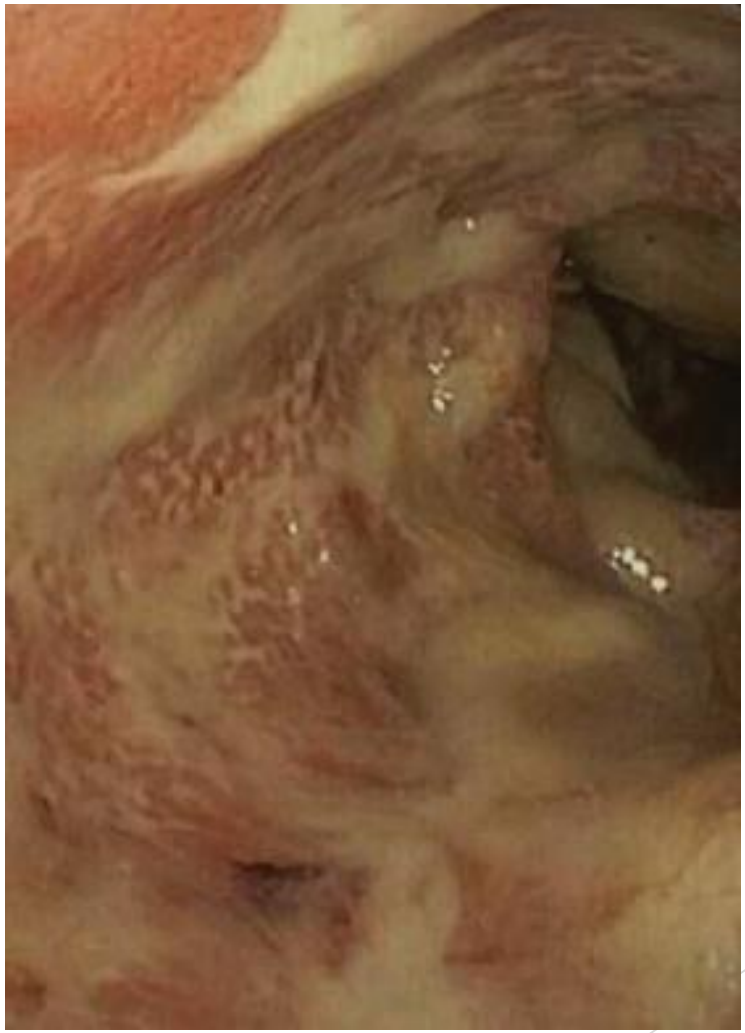
- Macroscopic:

- Broad-based ulcers.
- Pseudopolyps
- Mucosal atrophy in long standing
- Mural thickening absent
- Serosal surface normal
- No strictures
- Toxic megacolon

- Microscopic:

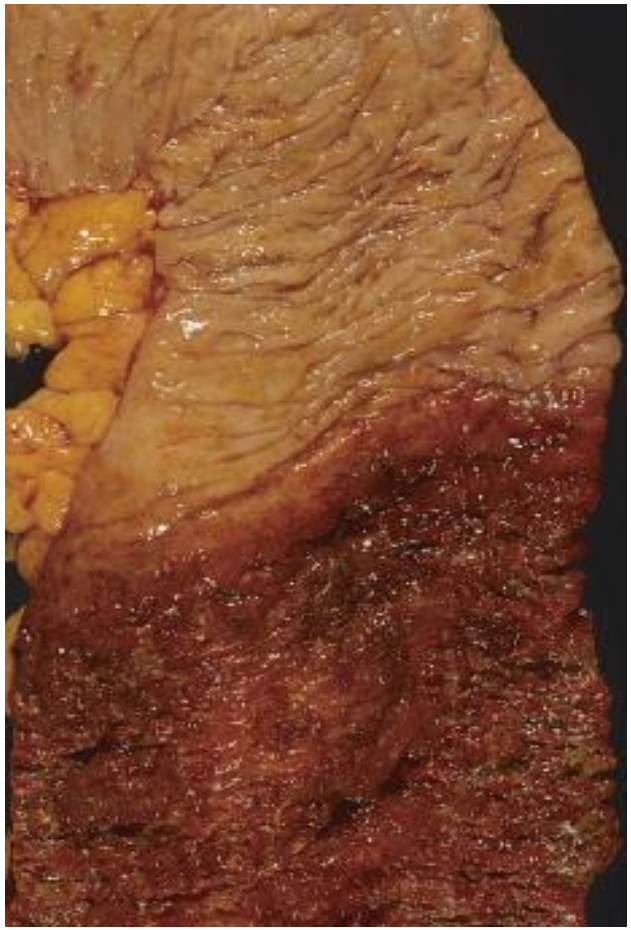
- Inflammatory infiltrates
- Crypt abscesses
- Crypt distortion
- Epithelial metaplasia
- Submucosal fibrosis
- Inflammation limited to mucosa and submucosa.
- No skip lesions
- No granulomas.

Mucopurulent material and ulcers.

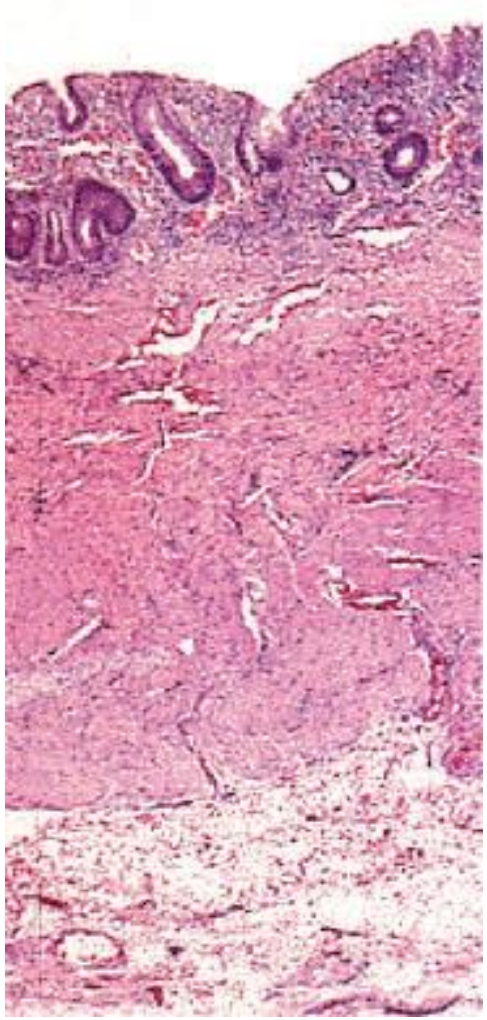


Pancolitis.

Abrupt transition b/w normal and disease segment.



Limited to mucosa



Clinical Features

- Relapsing remitting disorder
- Attacks of bloody mucoid diarrhea +lower abdominal cramps
- Temporarily relieved by defecation
- Attacks last for days, weeks, or months.
- Asymptomatic intervals.
- Infectious enteritis may trigger disease onset, or cessation of smoking.

- Colectomy cures intestinal disease only

Feature	Crohn Disease	Ulcerative Colitis
Macroscopic		
Bowel region affected	Ileum ± colon	Colon only
Rectal involvement	Sometimes	Always
Distribution	Skip lesions	Diffuse
Stricture	Yes	Rare
Bowel wall appearance	Thick	Thin
Inflammation	Transmural	Limited to mucosa and submucosa
Pseudopolyps	Moderate	Marked
Ulcers	Deep, knifelike	Superficial, broad-based
Lymphoid reaction	Marked	Moderate
Fibrosis	Marked	Mild to none
Serositis	Marked	No
Granulomas	Yes (~35%)	No
Fistulas/sinuses	Yes	No

Feature	Crohn Disease	Ulcerative Colitis
Clinical		
Perianal fistula	Yes (in colonic disease)	No
Fat/vitamin malabsorption	Yes	No
Malignant potential	With colonic involvement	Yes
Recurrence after surgery	Common	No
Toxic megacolon	No	Yes

NOTE: Not all features may be present in a single case.

Colitis-Associated Neoplasia

- Long standing UC and CD.
- Begins as dysplasia >>>> carcinoma.

- Risk depends on
- **Duration of disease**: increase after 8-10 years .
- **Extent of involvement**: more with pancolitis.
- **Inflammation**: frequency & severity of active disease with neutrophils.

- Early detection needs surveillance programs approximately 8 years after diagnosis
- Exception is with PSC patients, screening at diagnosis