An Overview of Colitis and Problems in the Diagnosis of Inflammatory Bowel Disease

Kamal Ishak Memorial Lecture

Aleppo December 7 2007

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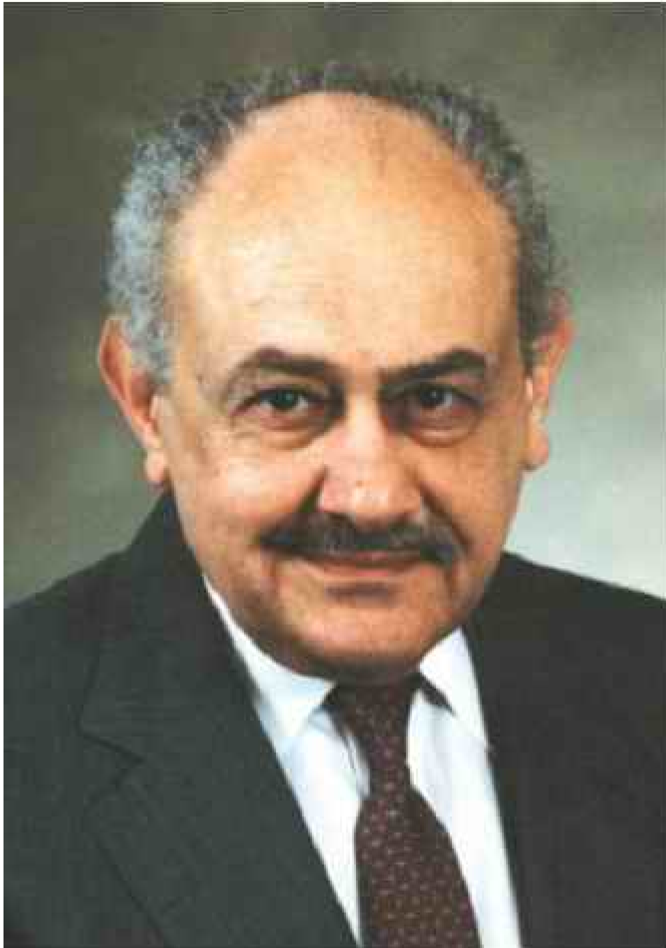
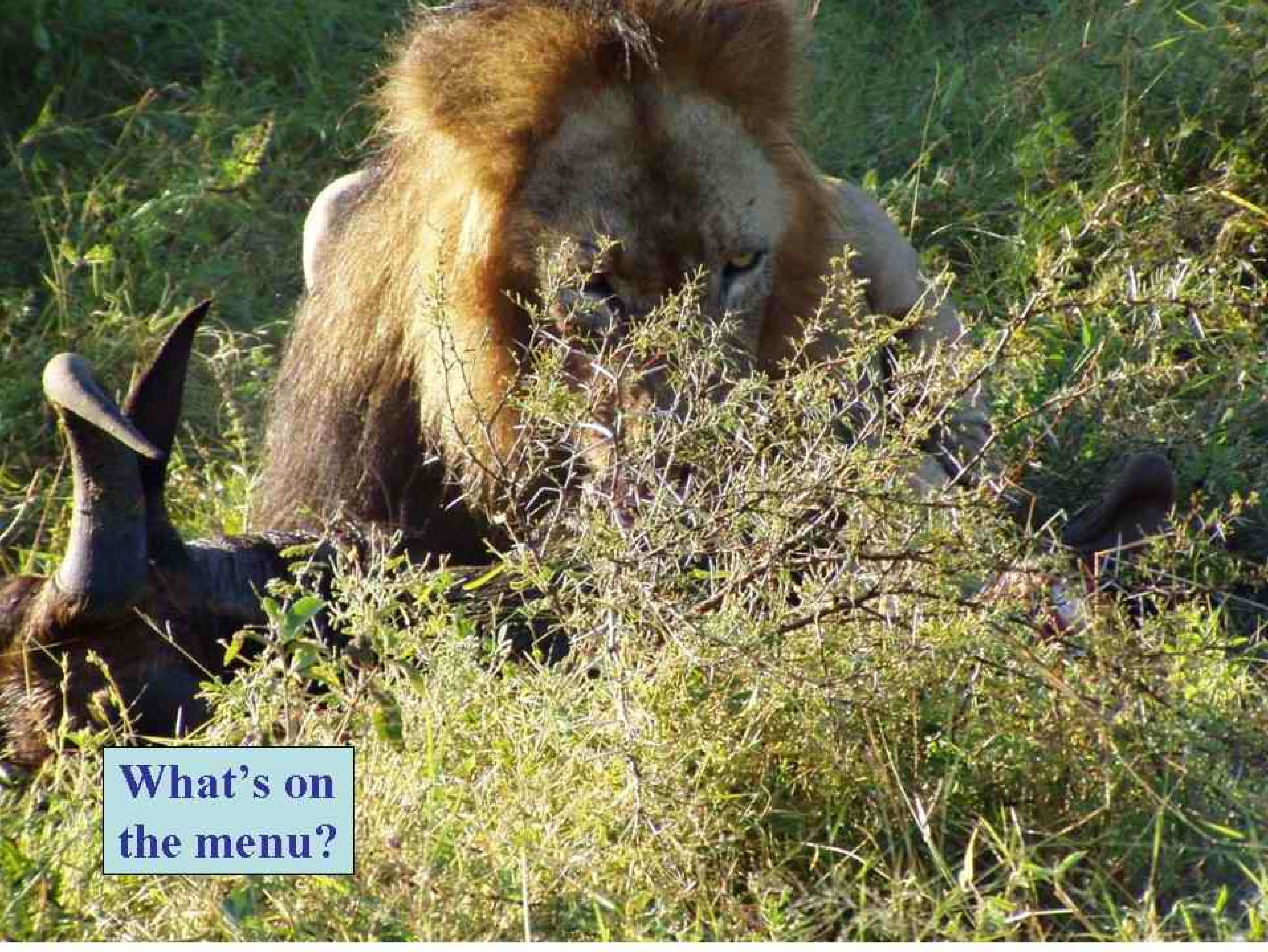
Dr Kamal G Ishak (1928-2004)



- b. Atbara Sudan to Syrian and Turkish parents.
- English Mission College Cairo
- Cairo Univ – MB BCh 1951
- Fullbright Scholar to US Naval Base – Schisto & Brucellosis
- To USA 1957 San Antonio, Baylor Dallas,
- AFIP 1963, Chief Hepatic branch in 1965
- 1967 DD Hepatoblastoma HCC
- DID disease, Knodell score with the "Gnomes" – Ishak score
- Co-editor MacSween – endless book chapters

- Wife Betty 2 daughters (Leila and Magenta)
- Cook
- Photographer
- Tennis fan

- The humble facilitator
- The small giant


What's on
the menu?

Problems in Colitis

- Is it IBD?
  - (Usual DD is ac inf colitis (ASLC)
- Pitfalls in the diagnosis of ulcerative colitis
- Pitfalls in the diagnosis of Crohn's disease
- Mimics of Crohn's disease
- When pathology *can't* help (so don't try)
- Microscopic colitis

Typical infectious colitis

- No architectural changes during active phase
- No (minimal) basal plasmacytosis
- Neutrophils in lamina propria
  - If scant - consider preparation effect
  - If purulent think AIC/ASLC
- If pseudomembranes consider
  - PMC, Verotoxin E.coli, culturable infections
- If crypt destruction can resolve with architectural distortion

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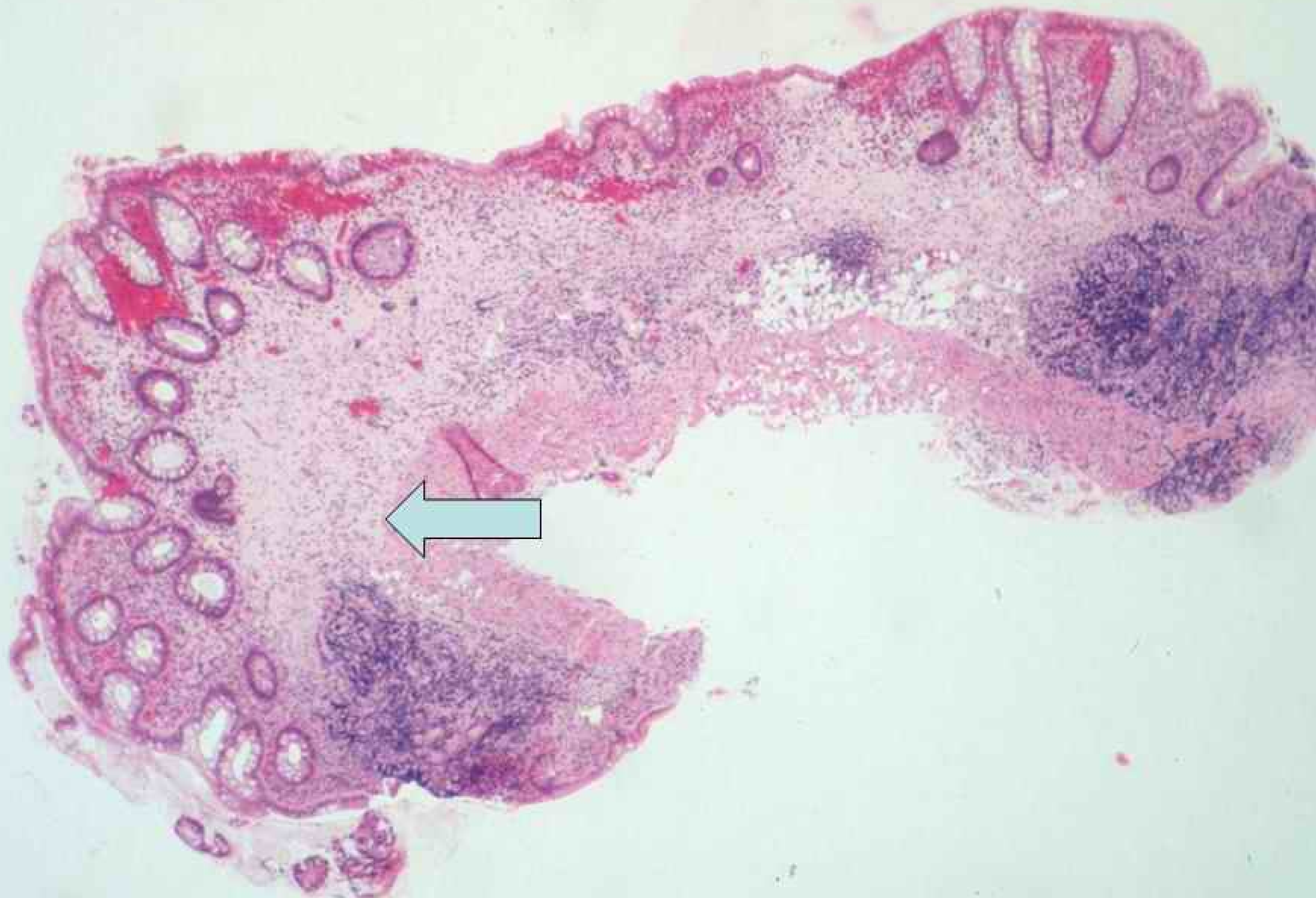
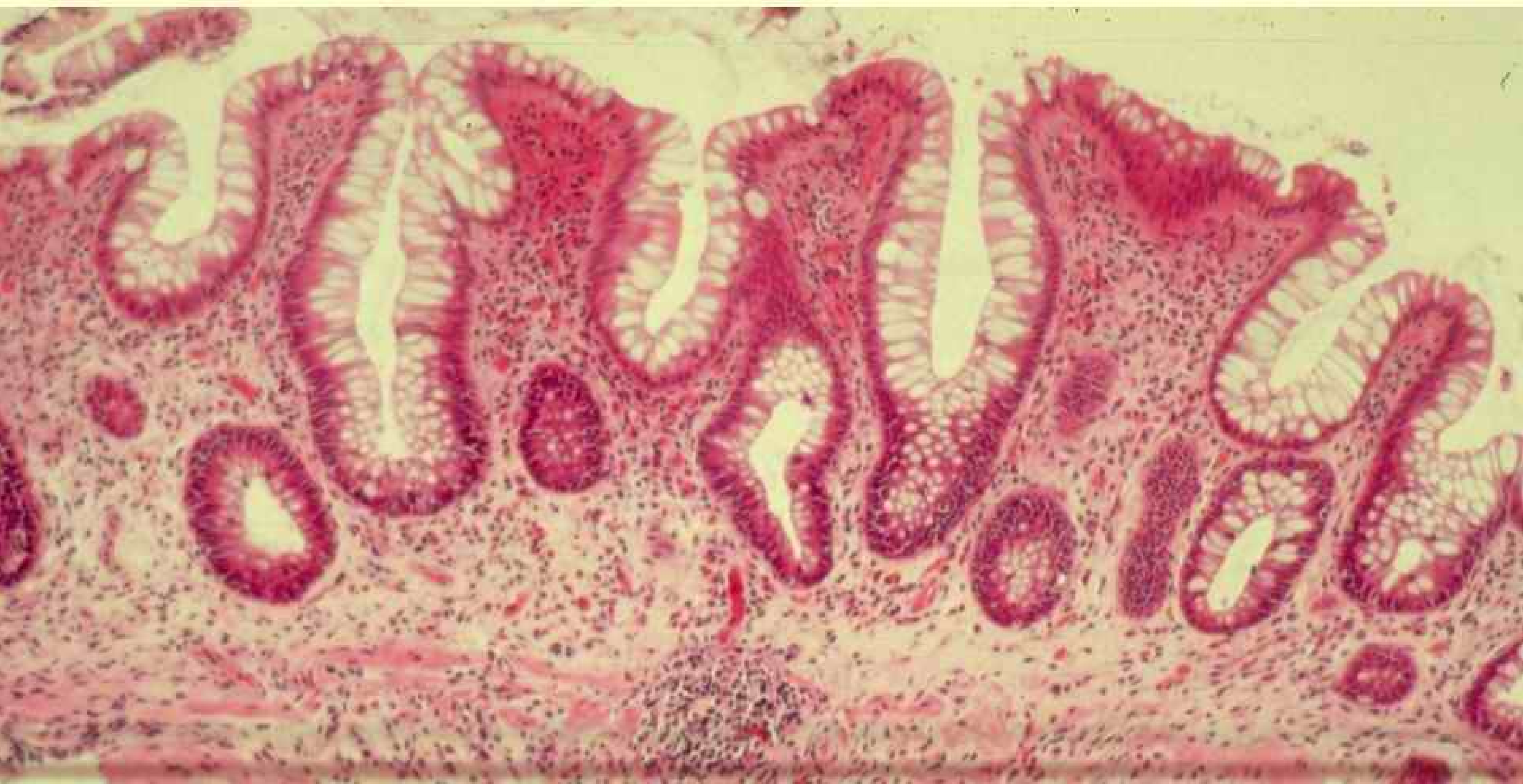
Supposition

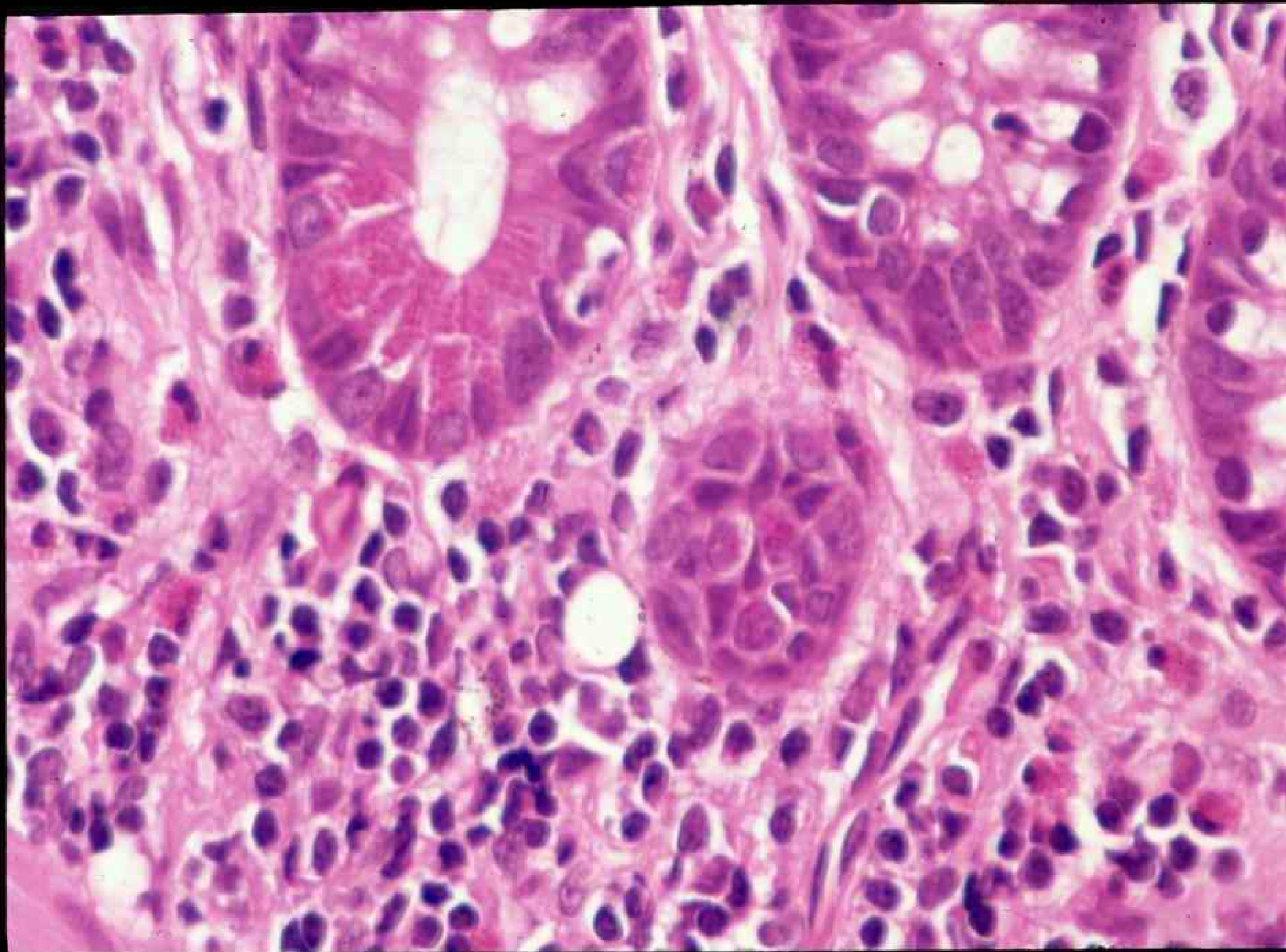
- Ulcerative colitis typically
  - involves the rectum
  - extends proximally for a variable extend
  - often is a transition to a normal mucosa - abrupt or gradual.
- Crohn's colitis
  - can involve the ano-rectal region
  - is usually discontinuous grossly & histologically
  - apthoid ulcers typical
  - can involve SB (TI, more proximal SB, UGI)
- In biopsies – need to demonstrate extent /focality
- So what are the pitfalls?

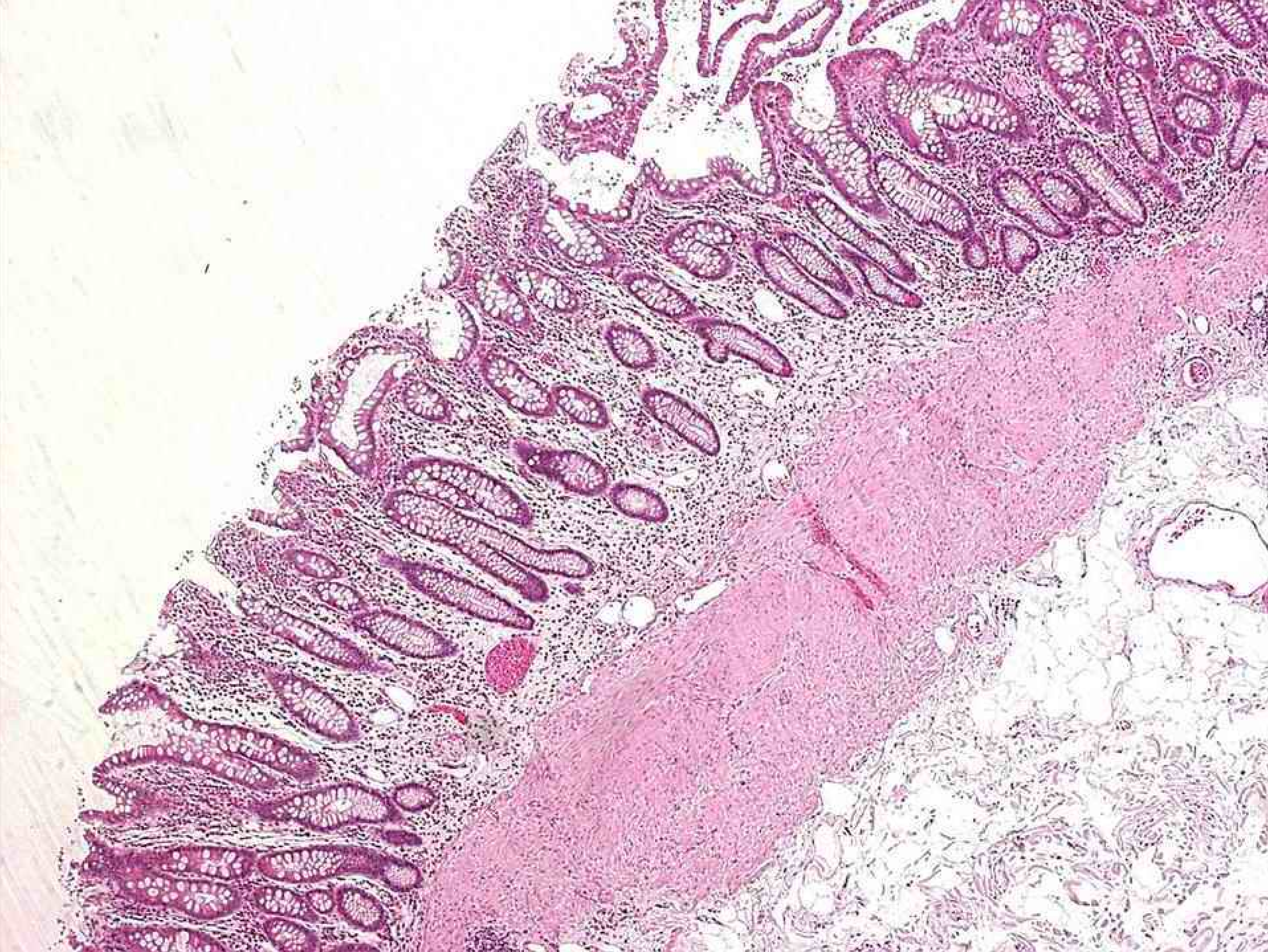


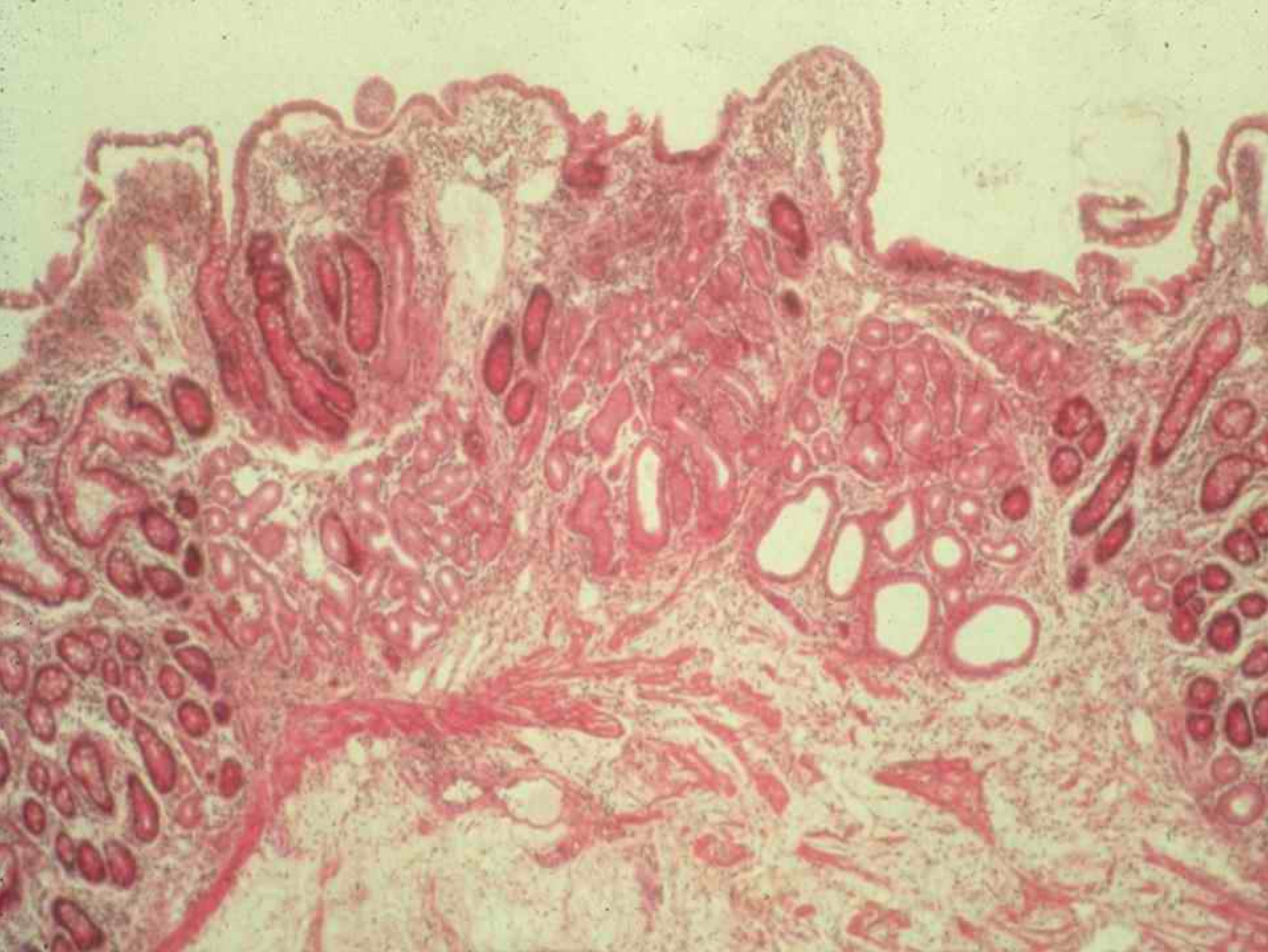


Issues - Is it IBD?

- 1. Architectural distortion
- 2. Paneth cell metaplasia distal to HF (CI) - CC
- 3. Deep plasma cells excluding ICV region (CI)
  - Chronic infection (amoebiasis, resistant PMC), CC/LC
- 4. Duplication of muscularis mucosae (Ulceration) – useful in areas where architecture has reverted to normal







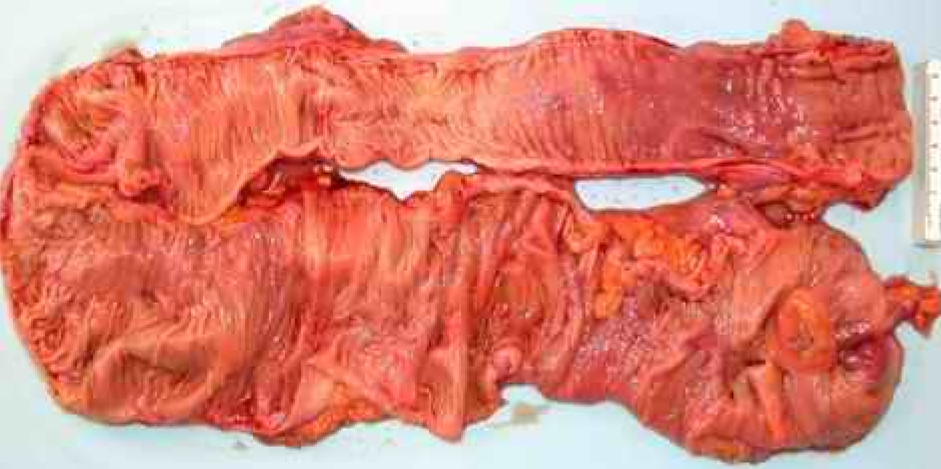
Issues

- Is it IBD?
- Pitfalls in the diagnosis of ulcerative colitis
- Pitfalls in the diagnosis of Crohn's disease
- Mimics of Crohn's disease
- "Hot" colitis
- When pathology *can't* help
- Microscopic colitis

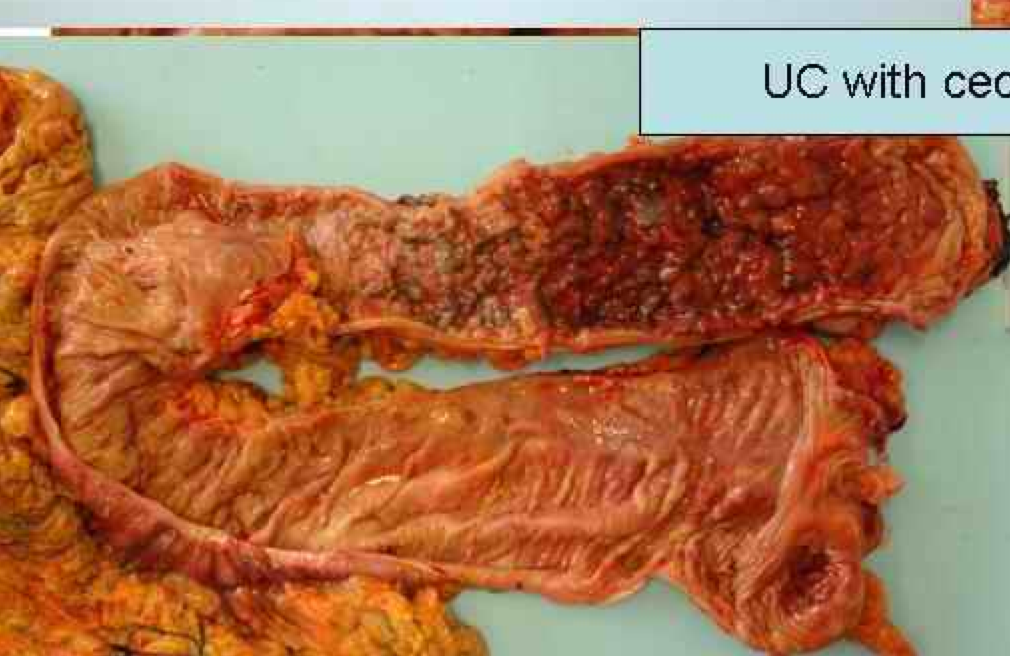
Pitfalls in the diagnosis of UC - Atypical distribution of disease.

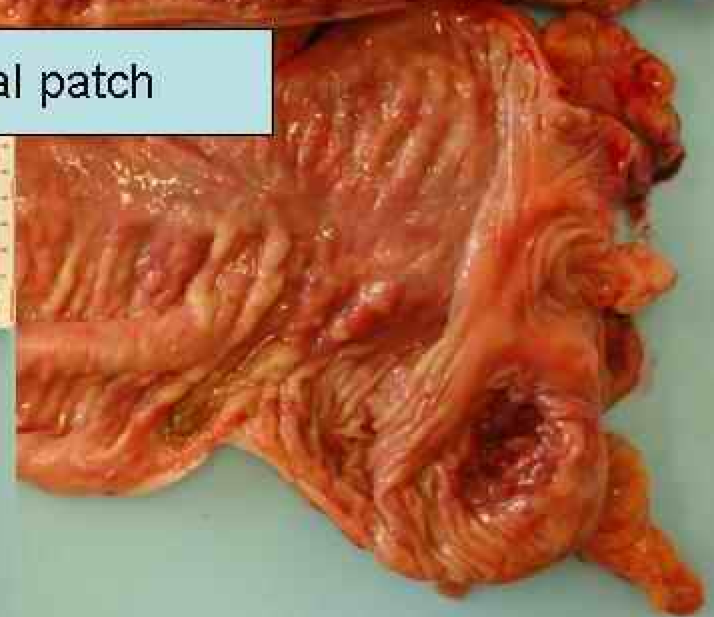
- *Presence of a cecal or periappendiceal patch.*
- *Real rectal sparing*
  - Ab initio (think diverticular colitis as well as CD)
- *Apparent rectal sparing*
  - Longterm reversion to normal
    - Implication – is it ever possible to exclude IBD?
  - Normal grossly but abnormal histologically
- *Bowel preparation effect* – Oral Fleets-associated changes

UC with periappendiceal patch



UC with cecal patch



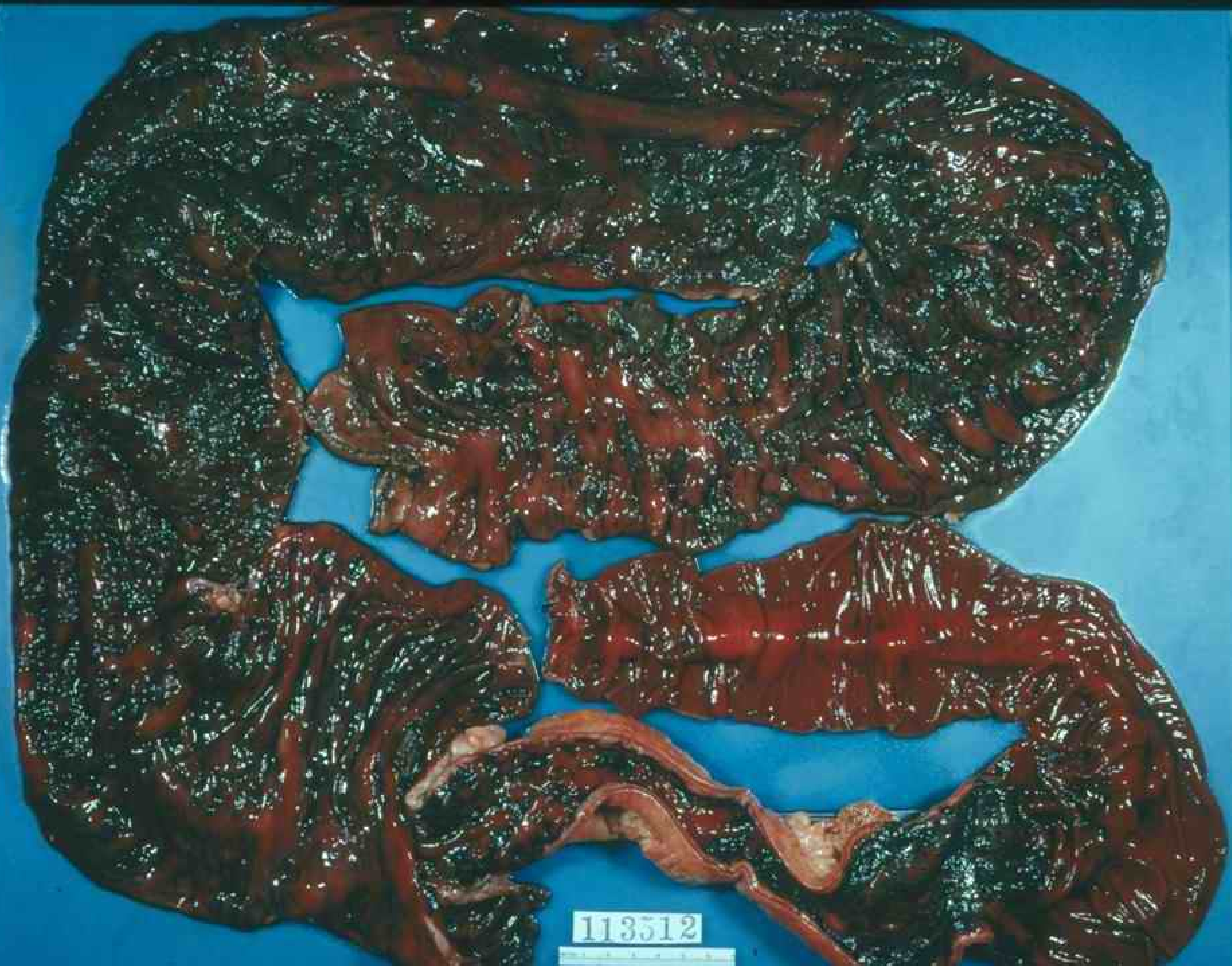


Pathology 201

- Recognize that a cecal patch is part of UC with distal disease and NOT call it CD

Pathology 301

- Recognize that a cecal patch can be part of CD – but needs other evidence of CD – e.g.
  - Focal inflammation / architectural distortion within & between Bx
  - Typical Bx of aphthoid ulcers
  - Granulomata (not mucin)
  - Terminal ileal (or other proximal) disease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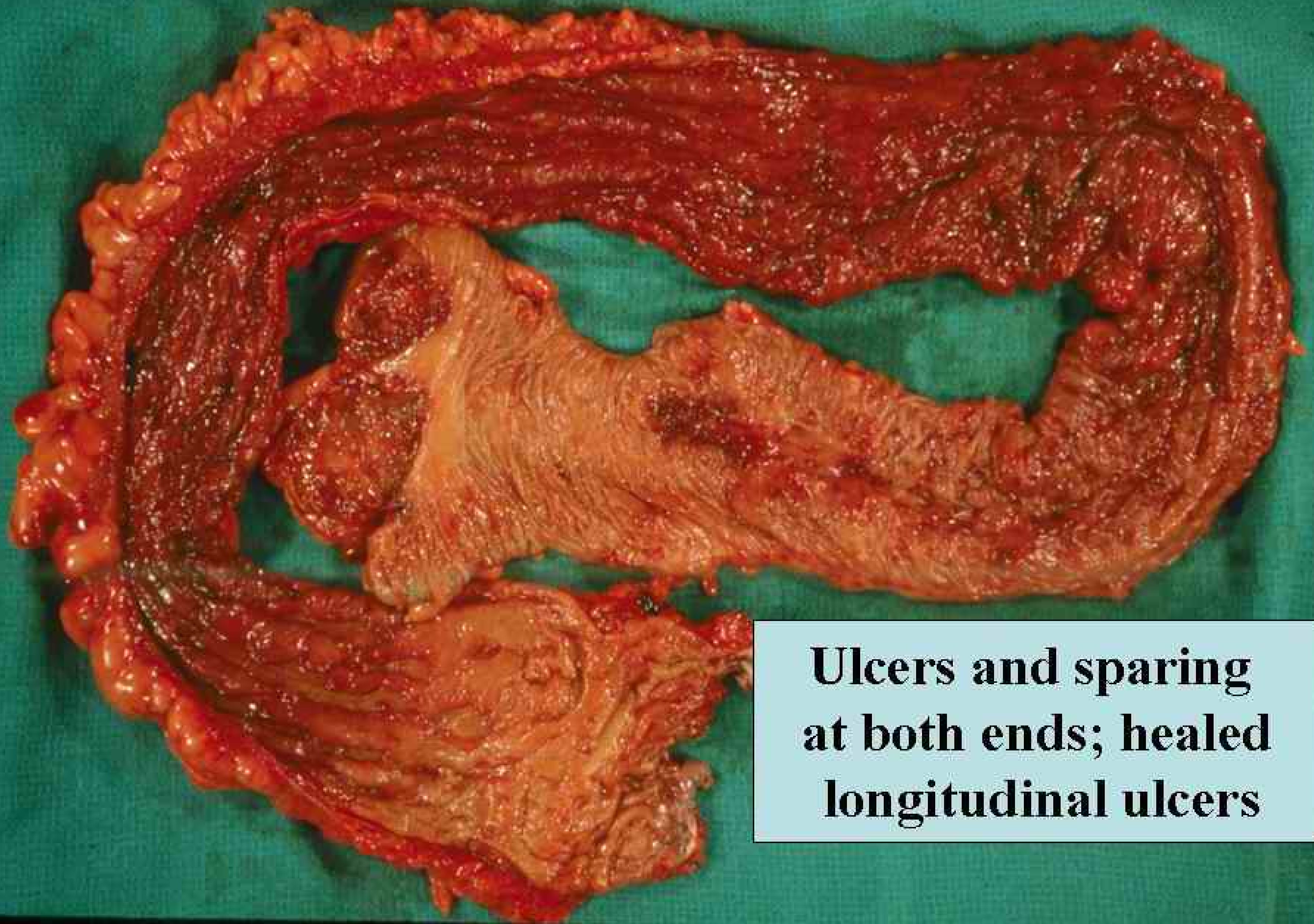
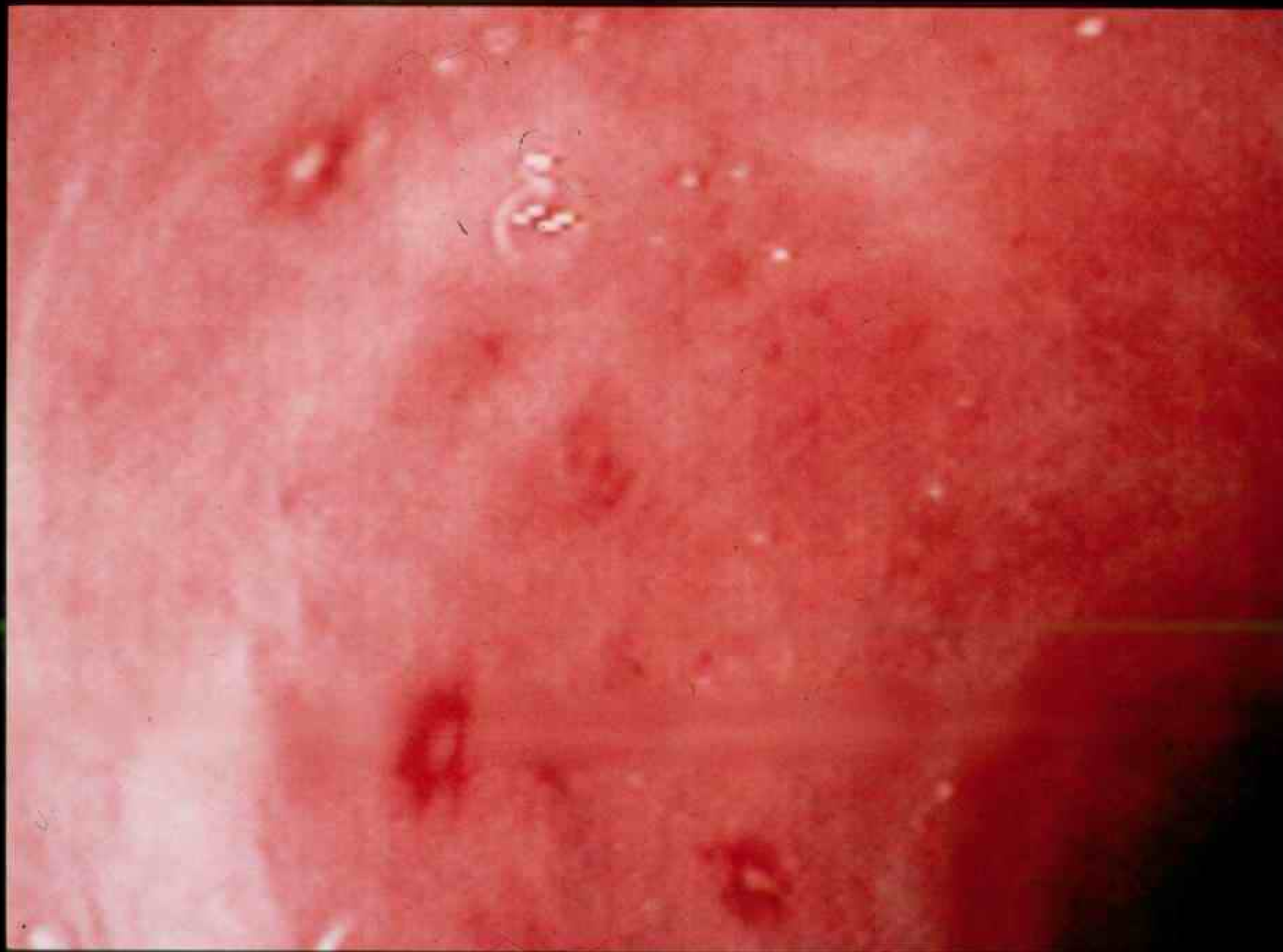

Ulcers and sparing
at both ends; healed
longitudinal ulcers



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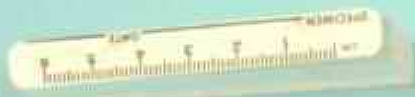
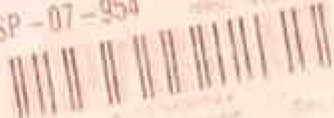
  - Mimics of Crohn's disease
  - "Hot" colitis
- When pathology *can't* help
- Microscopic colitis



Pathology Co[...]n[...]y



Lab number: S
Date: 07/01/17
Room: 1411
Referring Physician: Dr MacRae

[...] at MSH?

[...] History and Current Treatment:

UC Crohn's.

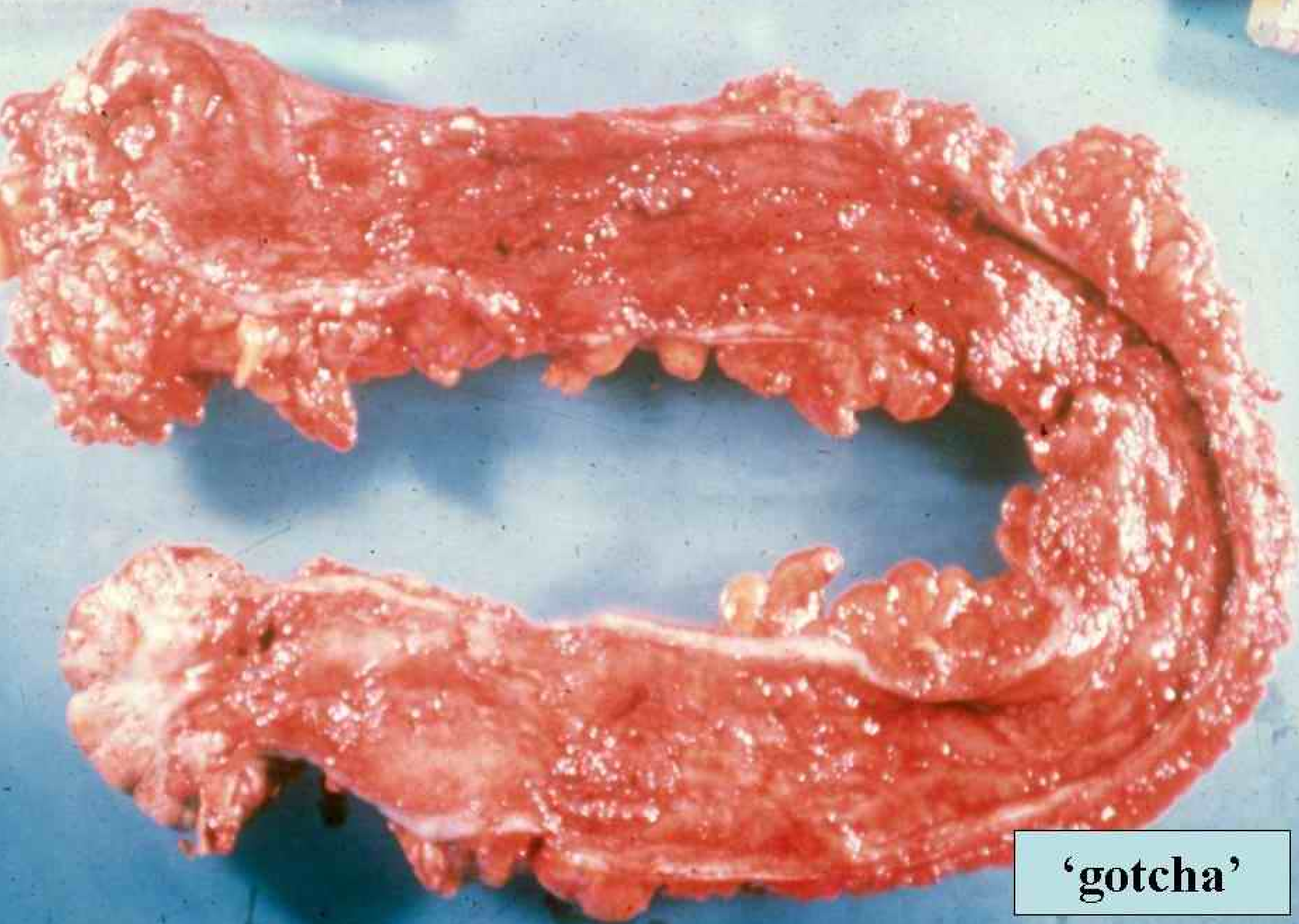
☐ Electron Microscopy ☐ Receptors ☐ Frozen Tissue ☐ Photographs ☐ Specimen Radiographs ☐ Other ______

Nature and Site of Specimen:

① Colon, rectum, anus.

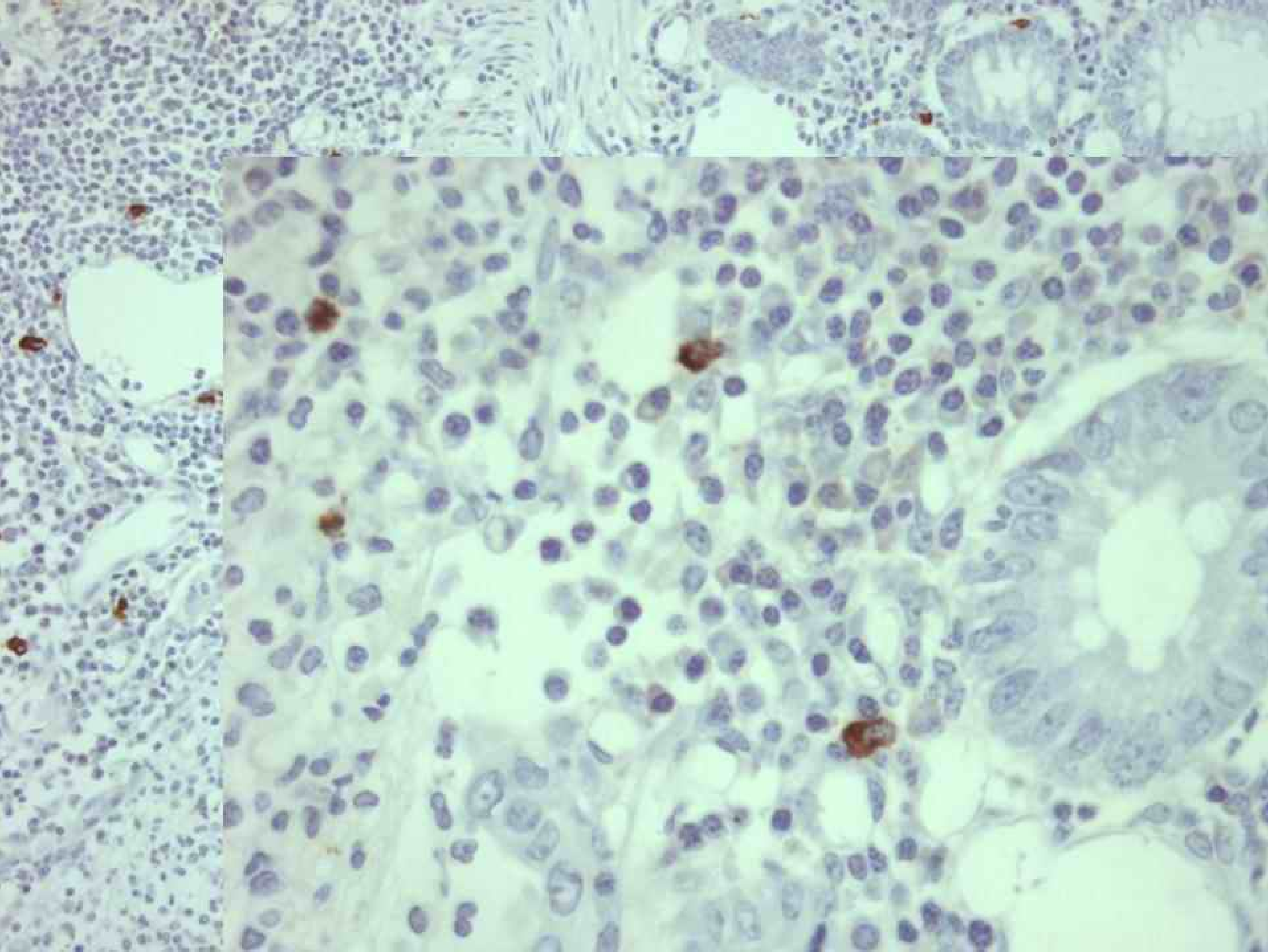
Operative Consultation: (Do not write in this space)

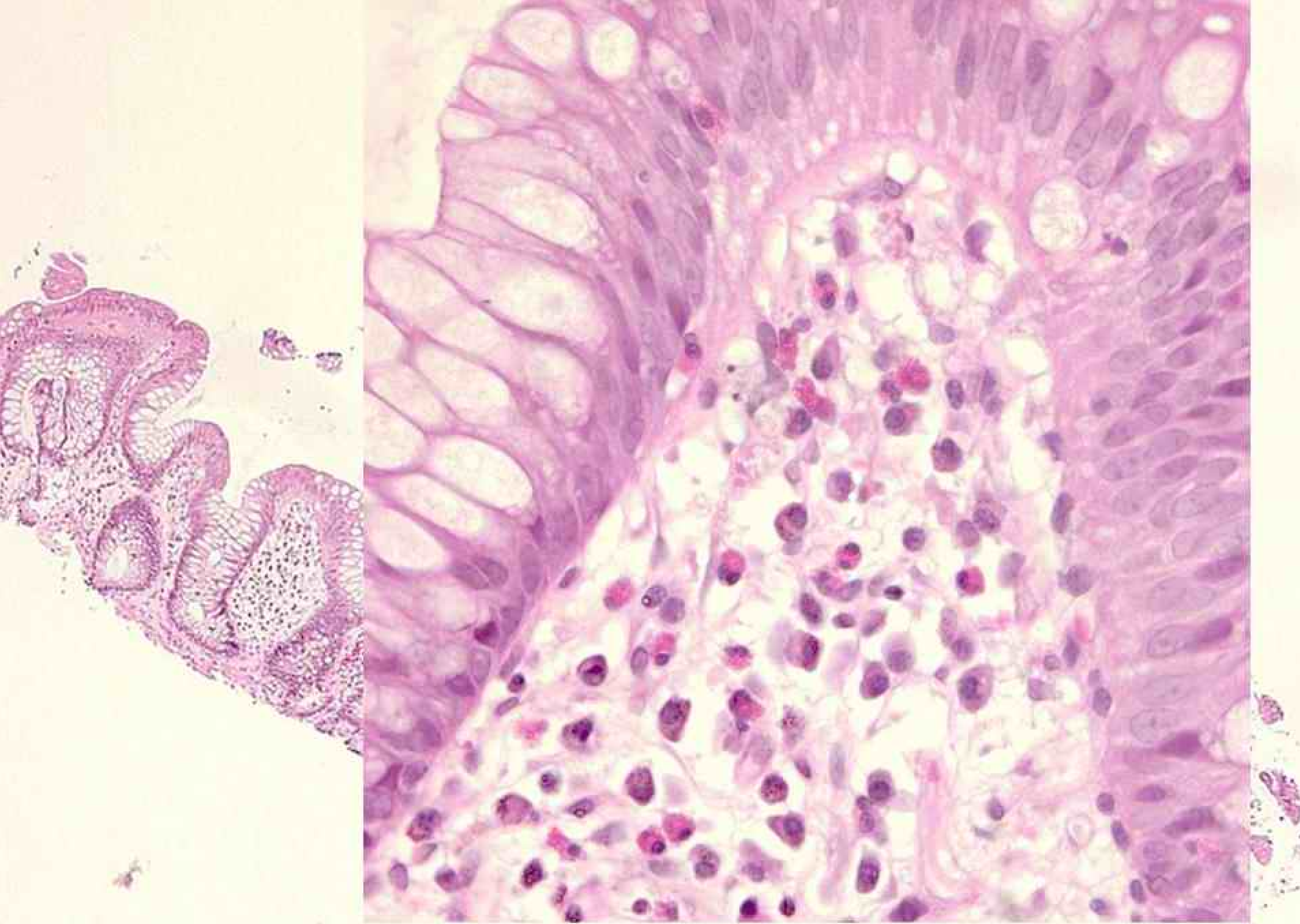
Pathologist: ______________________ M.D.

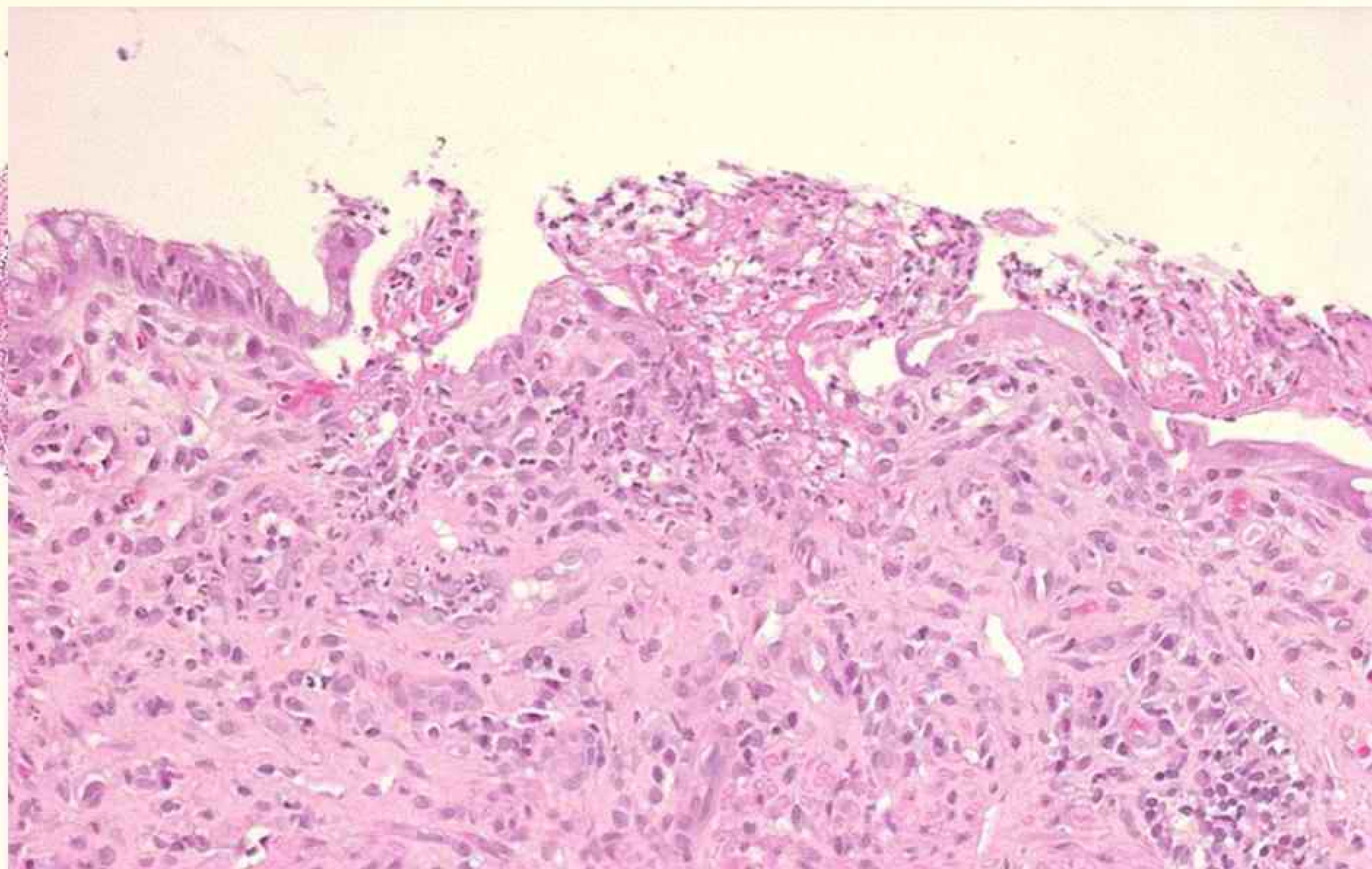

‘gotcha’

Pitfalls - other diseases (mimics or exacerbaters)

- Superimposed infection in IBD
  - Bacterial
  - Viral CMV
- Drugs / medications
  - NSAIDs
  - Rx causing marked focality
- Pediatric disease
  - Chronic eosinophilic infiltrates (kids)
    - Churg-Straus
    - Chronic allergic colitis
  - Atypical CD-like (young +/- severe UGI disease)
- Diversion
- Pouchitis







Upper GI disease

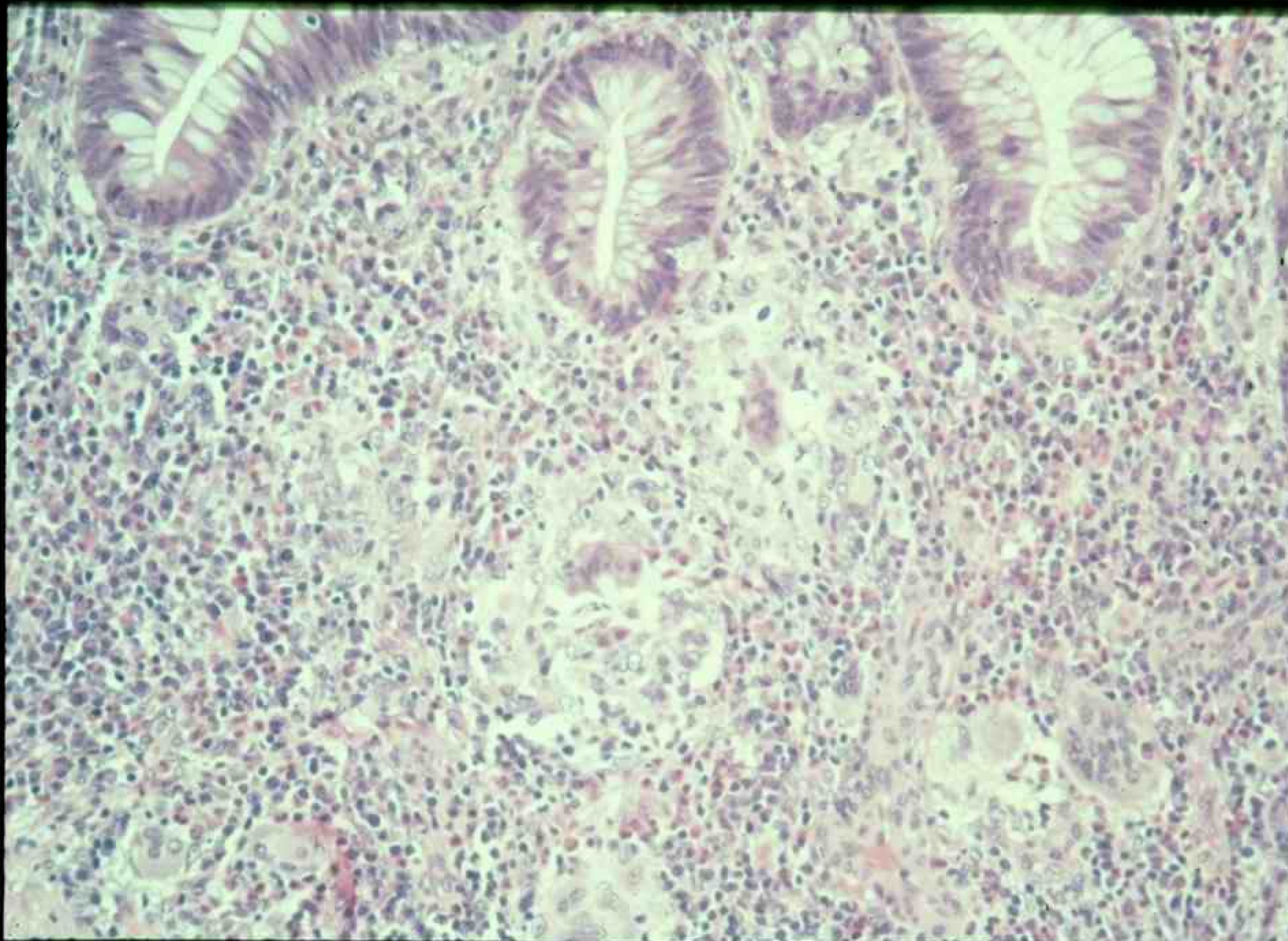
Established in CD

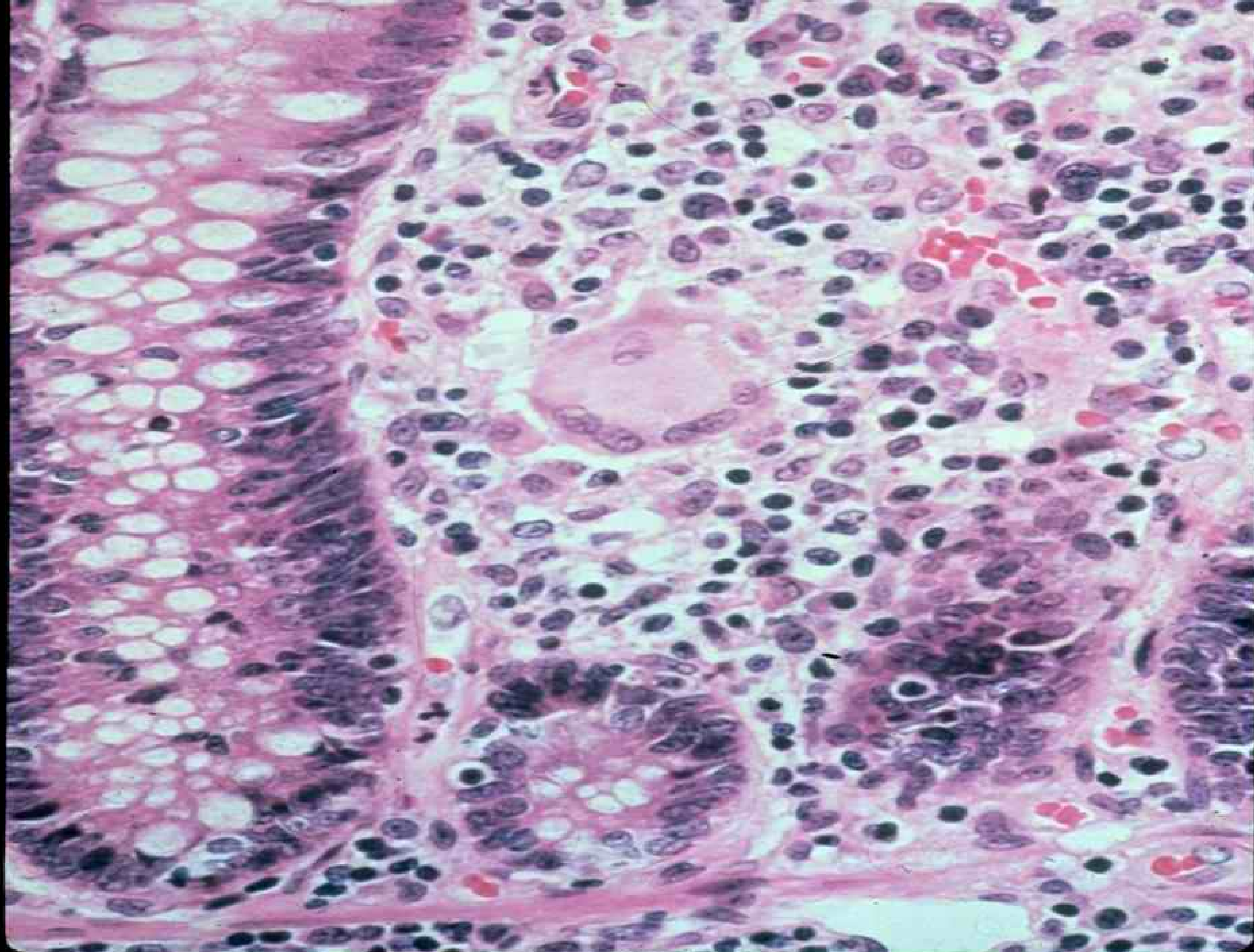
- Focal chronic active Hp neg gastritis
- Hp neg erosions
- Granulomas
- ? Mild superficial chronic gastritis

- Severe UC - esp children (??adults)
  - Active duodenitis (bulb)
  - ? Chronic (active) Hp neg gastritis
  - Resolves post Rx / Colectomy

Why are there problems?

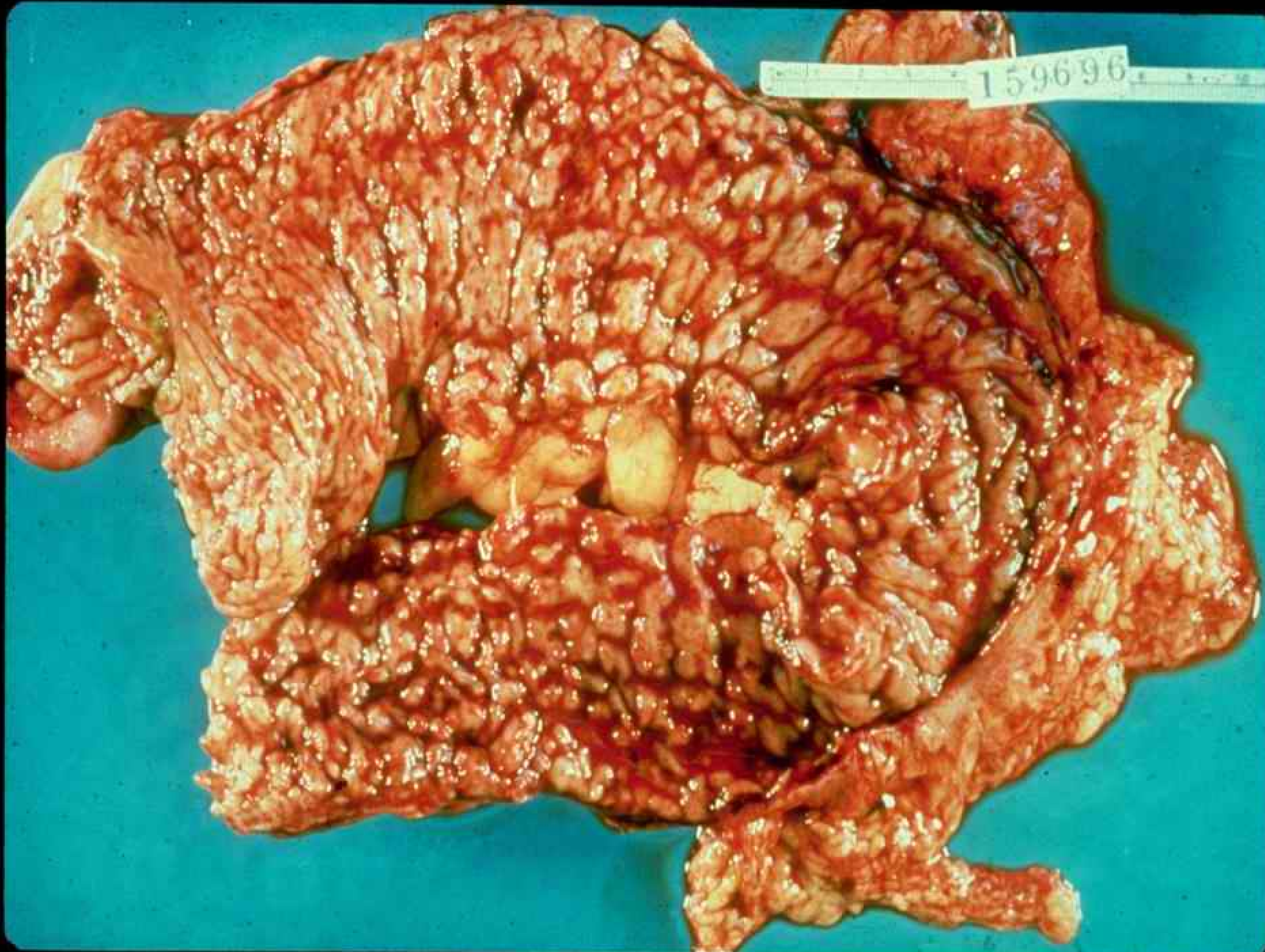
- The pathologist does not know or understanding the reasons why the biopsies were taken
  - question or reason biopsies taken not stated. (Can't answer a question if there isn't one)
- Pathologist is unaware of criteria ("NSp inflammation")
  - CME courses,web, call a friend
- The endoscopist is unaware of what biopsies are needed to answer the questions that has been specifically asked
  - know the criteria used to make the diagnoses
  - take the appropriate biopsies to answer the Qu
- The question being asked cannot be answered at all using biopsies
  - know when pathology *cannot* answer the question





Abnormal endo – Looks like CD. Is it?

- Have to demonstrate the *distribution* and *focality*
- Erosions / Aphthoid ulcers / Edges of ulcers
  - Usually on background of
    - focal inflammation
    - Crypt sparing
    - <5% CD is really diffuse
    - Rare in UC (highly asymmetric healing)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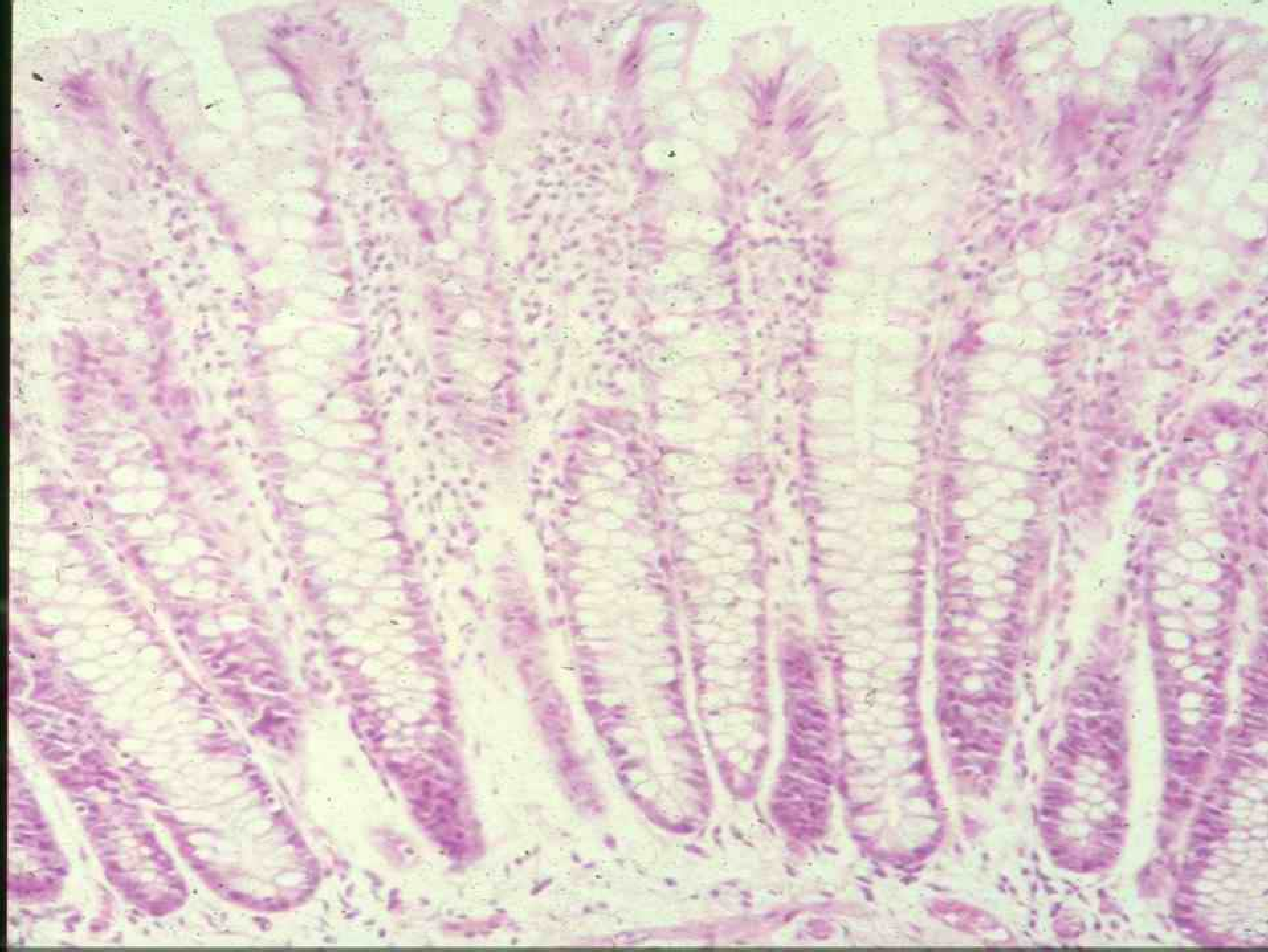
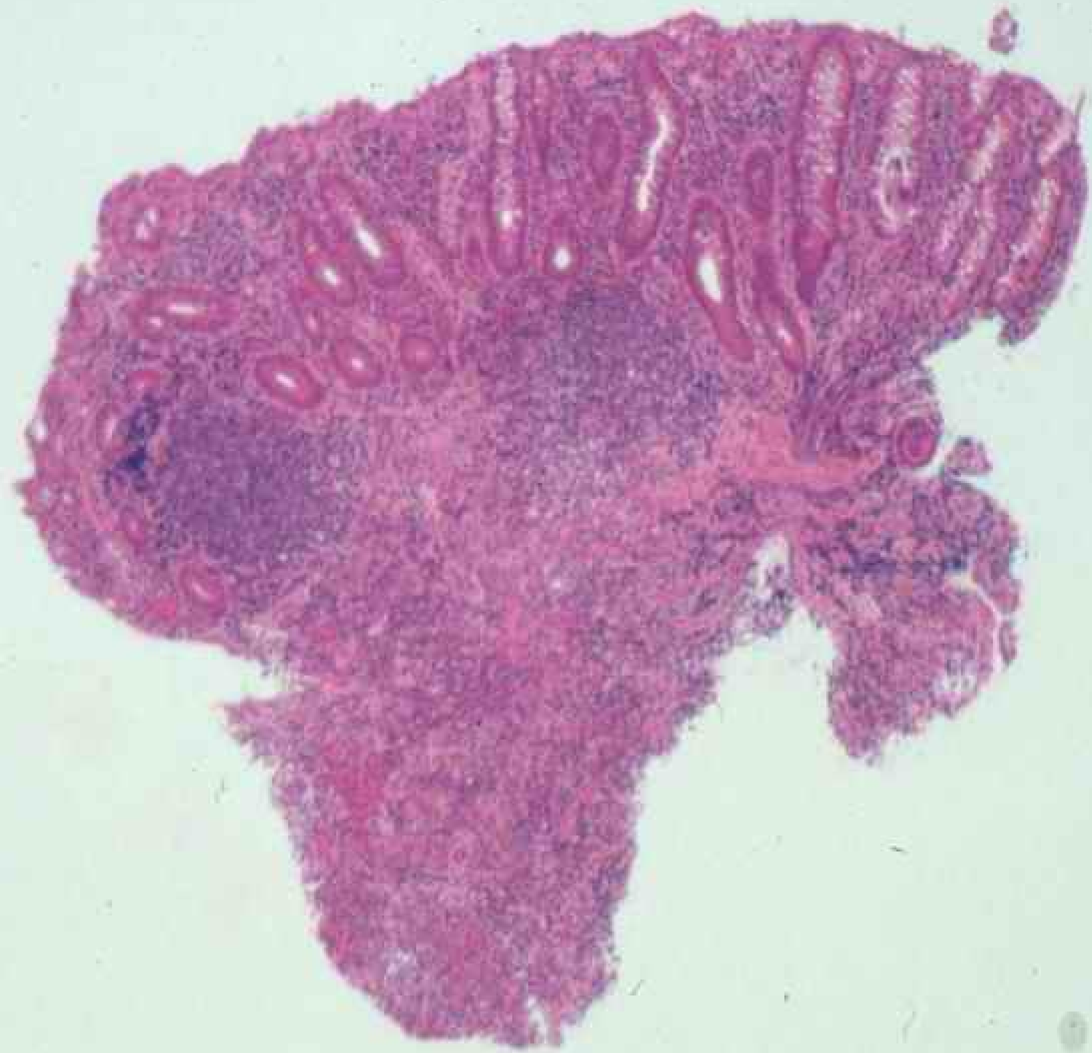
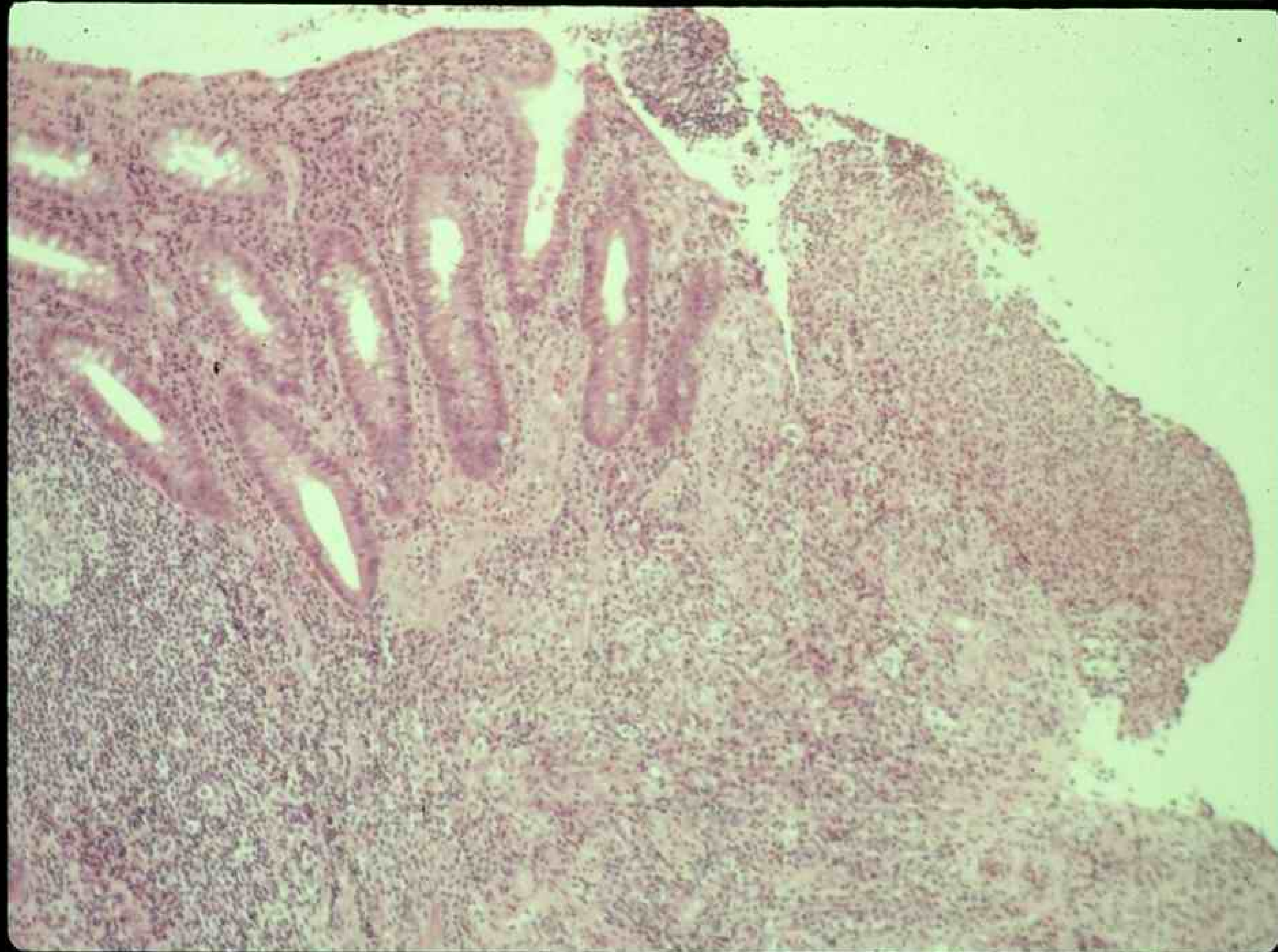
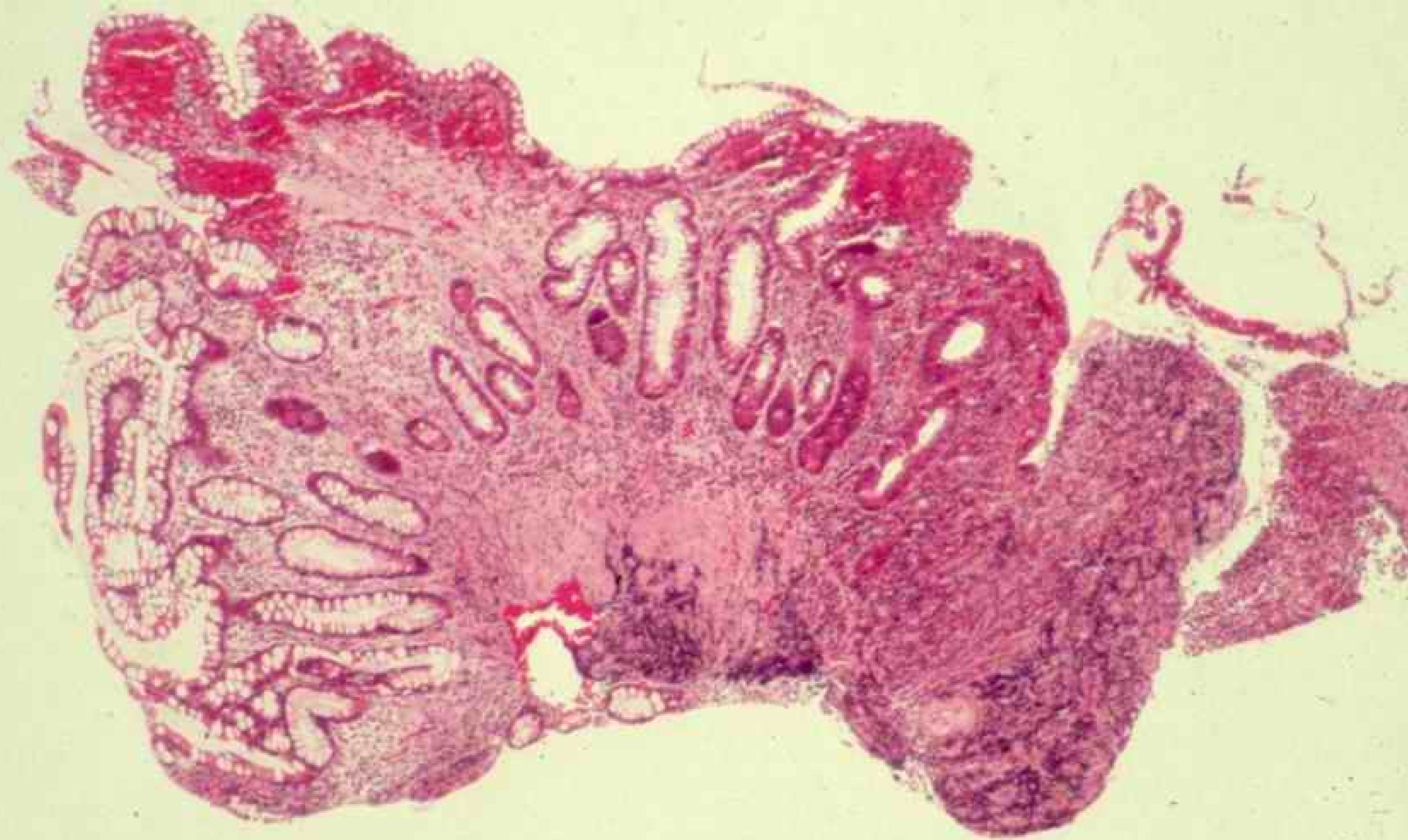


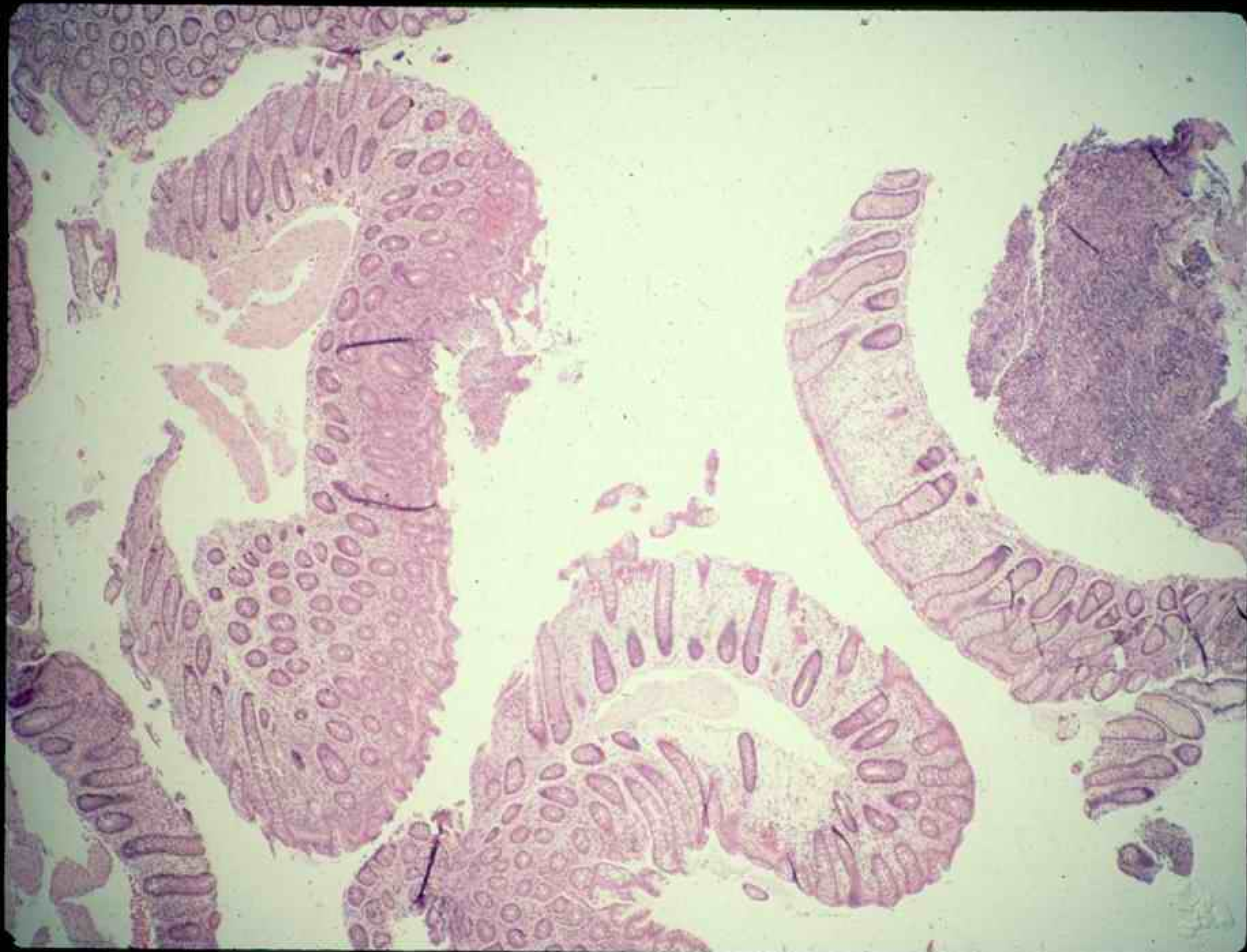


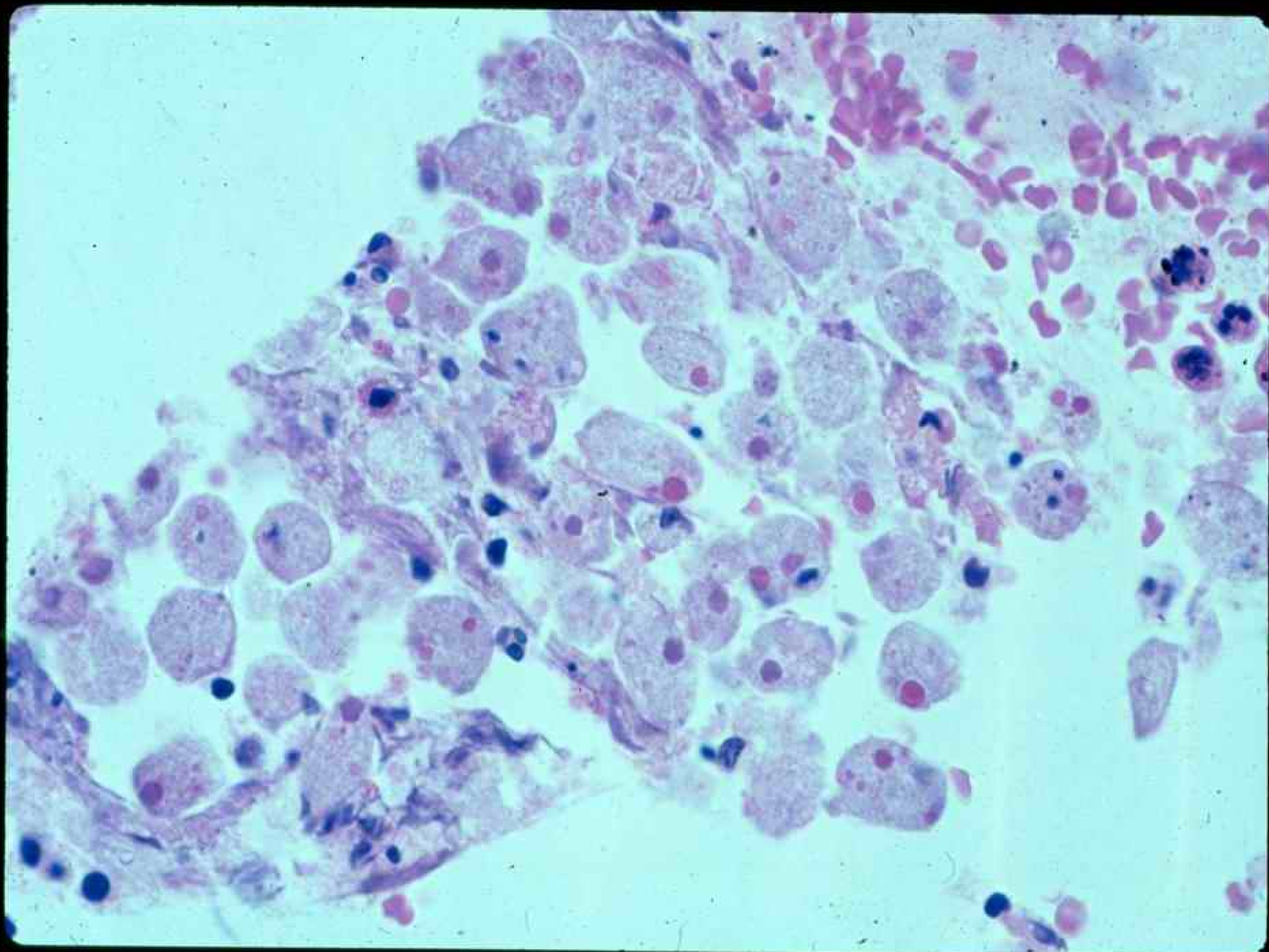




Crohn's disease - pitfalls

- Other causes of focal disease:
  - Biopsy of inflammatory polyps
  - Biopsy of granulation tissue at anastomotic lines
  - Cecal patch (normal, UC as well as CD)
  - Overcalling normal terminal ileal lymphoid aggregates as inflamed
  - Fulminant colitis of any cause - including UC (aphthoid ulcers, rectal sparing)
- Diffuse disease





Differential Diagnosis of CD

- Other cause of endoscopic aphthoid ulcers
  - Diversion proctitis / colitis, Pouchitis, Ischemia
  - Drugs / medications - NSAIDs, BCPs, isotretanoin
  - Fulminant colitis of any cause including UC
  - Oral Fleet's (phosphasoda) preparation
  - Diverticular-associated colitis
  - Reactive arthropathy / Behcets (?subclinical/clinical CD)
- Infections including
  - Yersinia, TB, Salmonella, Herpes
- Immunosuppression / AIDS (including lymphomas &KS)
- Immunological mimicry
  - Behcets , GVHD, Chronic granulomatous disease, Immunodeficiency, Glycogen Storage Disease 1b

Pitfalls

- Is it IBD?
- Pitfalls in the diagnosis of ulcerative colitis
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- Mimics of Crohn's disease
- When pathology *can't* help (so don't try)
- Microscopic colitis

Rectal stump post colectomy

Is it Crohn's?

- Diversion disease / diversion proctitis
  - Classically mucosal lymphoid hyperplasia BUT
  - Can look focal with aphthoid ulcers or diffuse
  - Can have granulomas
  - Can be diffuse with crypt abscesses
  - If resected can have Crohn's like transmural lymphoid hyperplasia
- *Therefore* Can mimic CD or UC

Pouchitis + Fistula. Is it CD?

- Pouchitis
  - Classically is Crohn's-like
  - Can look focal with aphthoid ulcers
  - Can have granulomas
  - If resected can have Crohn's like transmural lymphoid hyperplasia
- *Therefore* Can mimic UC or CD
- *Therefore* DON'T ASK!!! We can't tell you.
  - *It is always Pouchitis*
- Possible exception – pre-pouch ileitis with skip
  - Can mimic CD and may respond to Remicade
  - Does that make it CD?

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Descriptive colitides

Can be based on endoscopic or morphologic descriptors

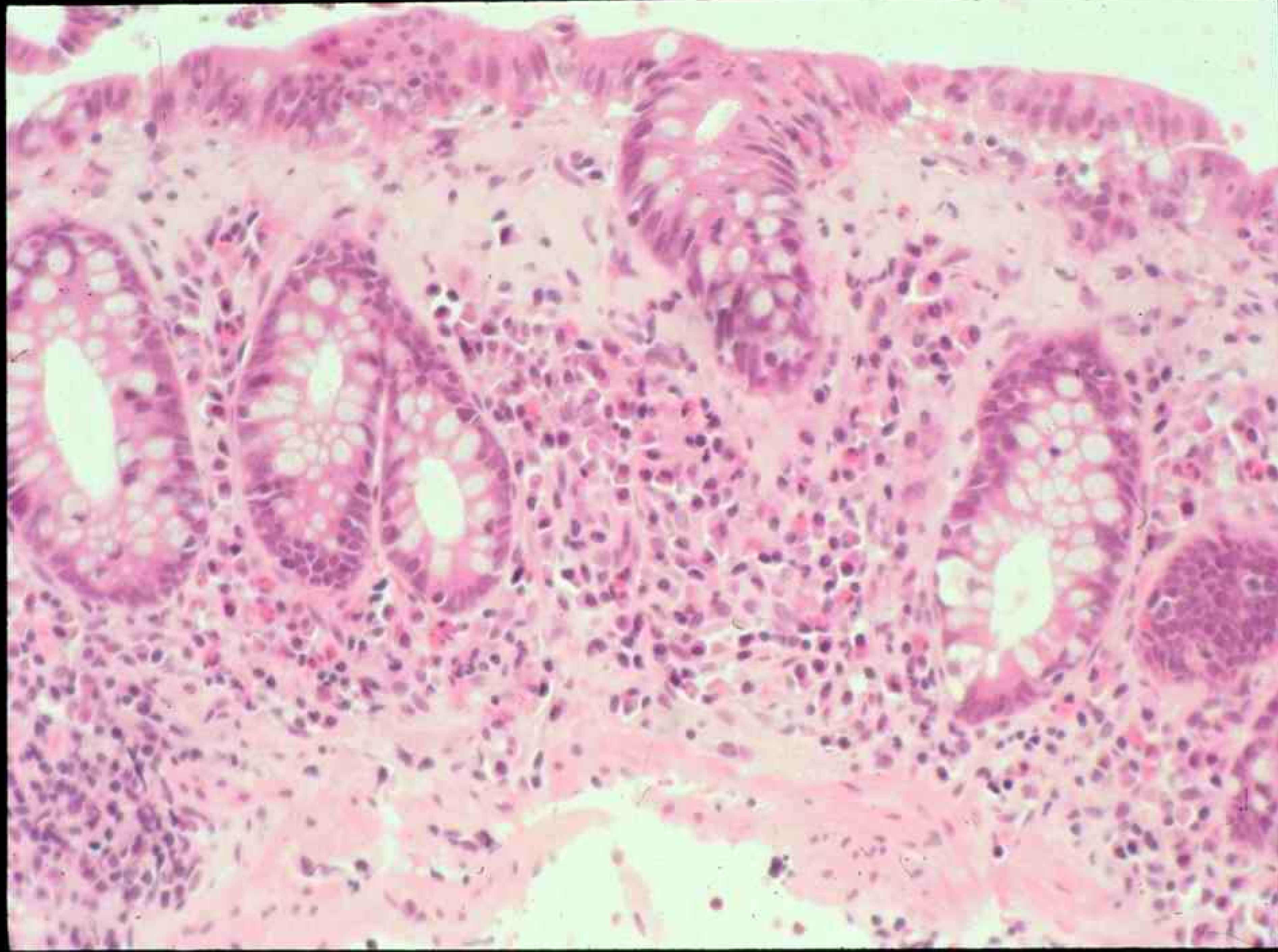
- **Pseudomembranous** — Cl.difficile, Ischemia, Heavy metals –Hg
- **Hemorrhagic** — Verotoxin-producing bugs, Ischemia
- **Collagenous** — NSAIDs, ? ischemia, ? Inf, IBD-related , with Pseudo membranes
- **Microscopic lymphocytic/CC** — ? Infections, CD, ? Bile salts, Celiac, drugs ? NSAIDs, Cyclofort3, Zantac, ticlopidine
- **Granulomatous** — CD, Infections, foreign antigens, drugs
- **Eosinophilic** — Allergies, parasites, occ IBD
- **Follicular** — Diversion, UC, CD, Chlamydia (LGV)

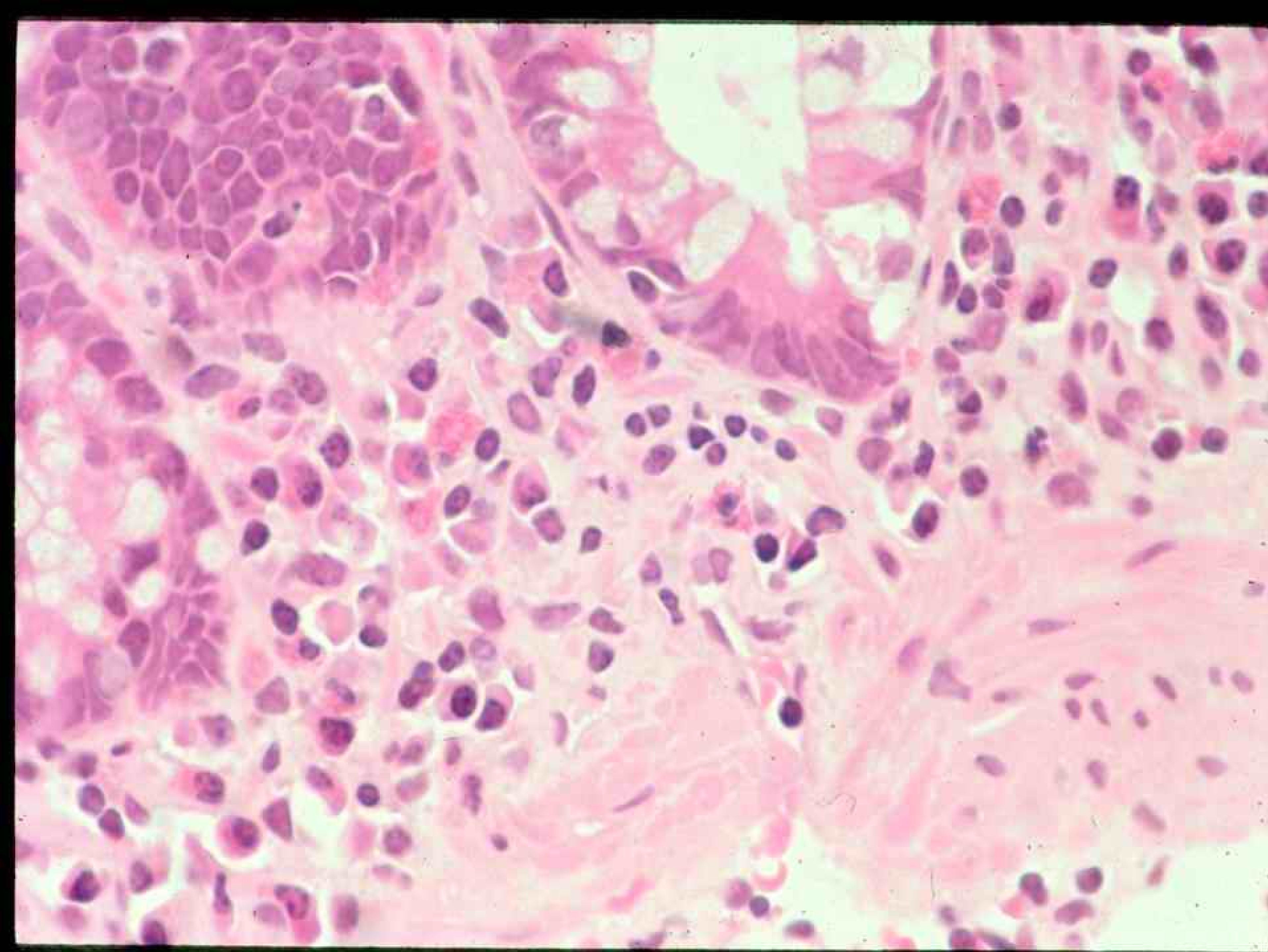
Diarrhea with normal endoscopy, but abnormal biopsy

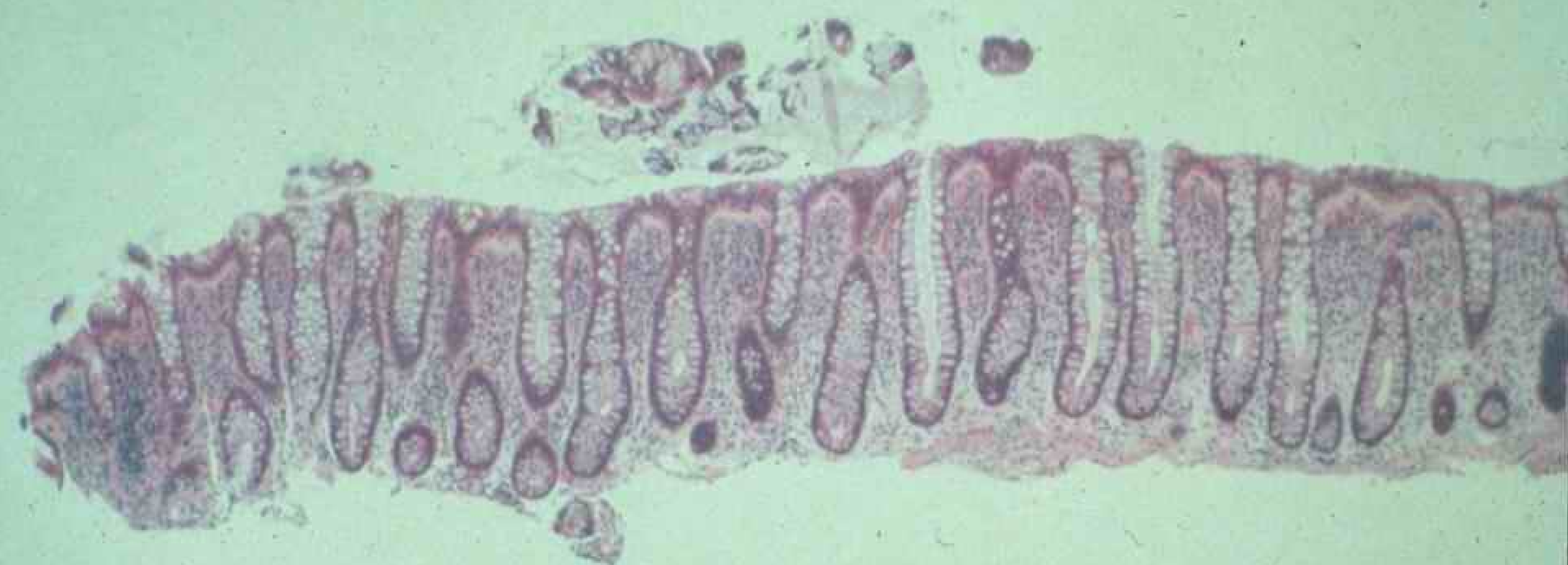
- Microscopic colitides
  - Collagenous colitis, Lymphocytic colitis
  - Granulomas (Crohn's esp.)
  - Microscopic colitis NOS variants
- Drugs / medications (apoptotic colopathy)
  - Laxatives, NSAIDs
- Infections (any may be endoscopically normal)
  - MAI, Cryptosporidia, ? Spirochetosis, Post-inf IBS
  - Eosinophilic infiltration – allergy, mast cell disease
- Amyloid
- Quiescent IBD
- Diabetic changes (E.M.)

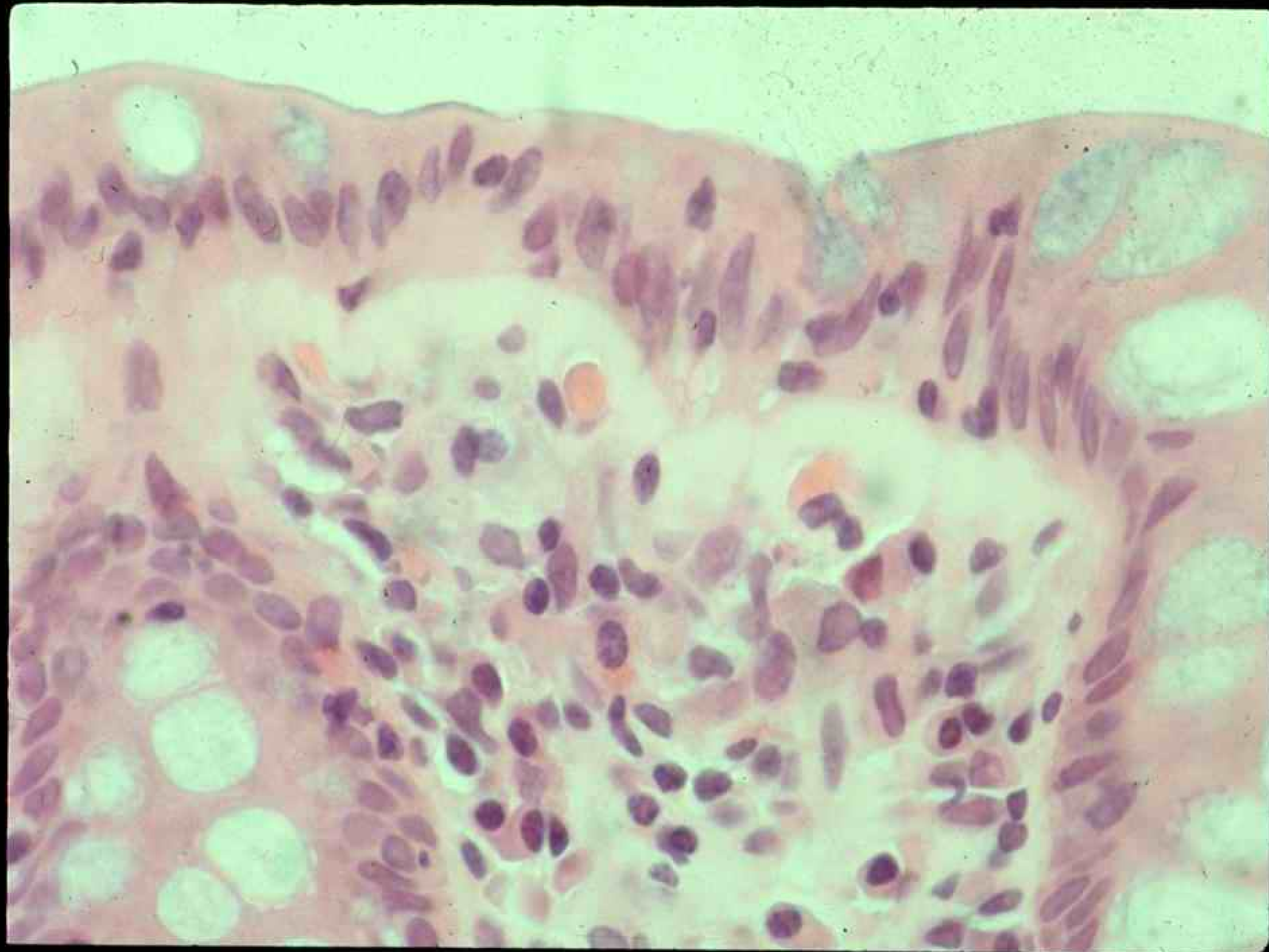
The Microscopic Colitides, Collagenous and Lymphocytic Colitis

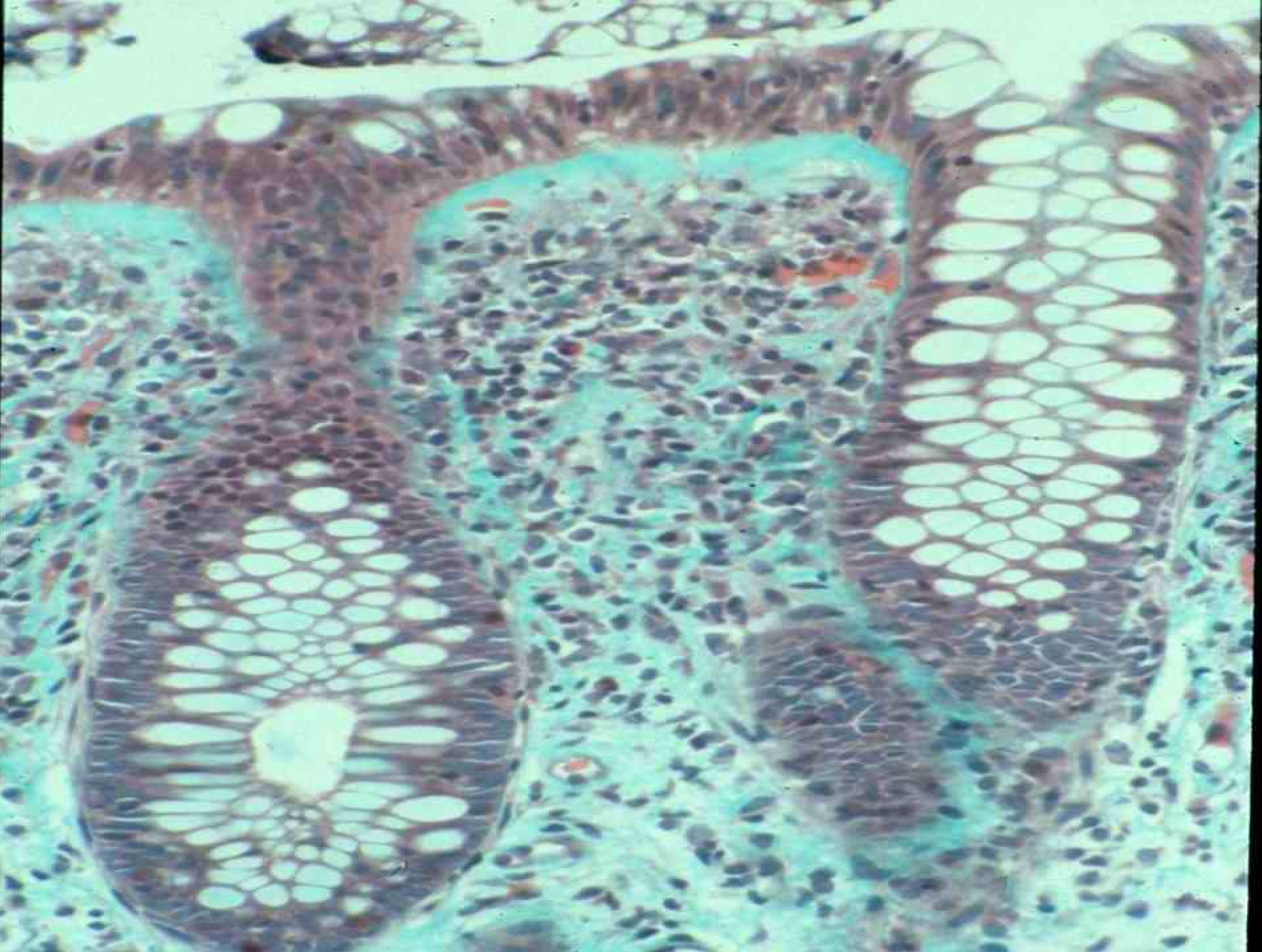
- A group of syndromes characterized by
- Clinically – MC often used to encompass LC and CC
  - Watery diarrhea
  - Often middle-aged to elderly females
- Endoscopically by a normal appearance
- Histologically by
  - An unequivocal colitis – MUST be present – microscopic
  - With increased intraepithelial lymphocytes – lymphocytic
  - With increased PMNs and /or eosinophils - collagenous
  - With a thickened subepithelial collagen band – collagenous
- Must distinguish between non-inflammatory but microscopic causes of diarrhea – e.g. cryptosporidia, ? spirochetosis, amyloid, melanosis





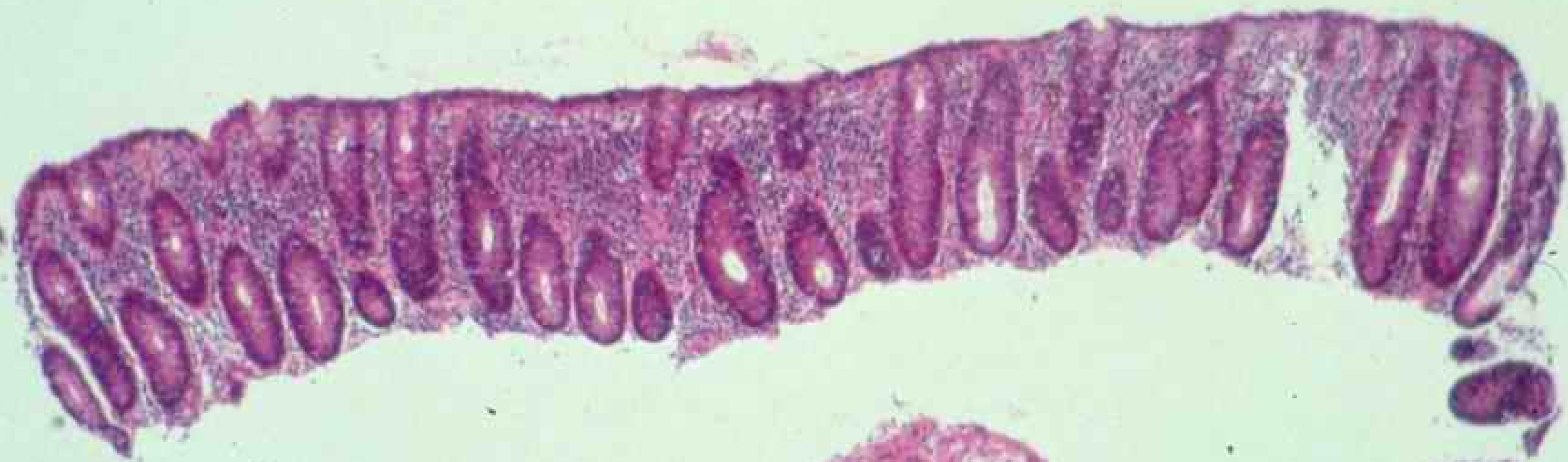
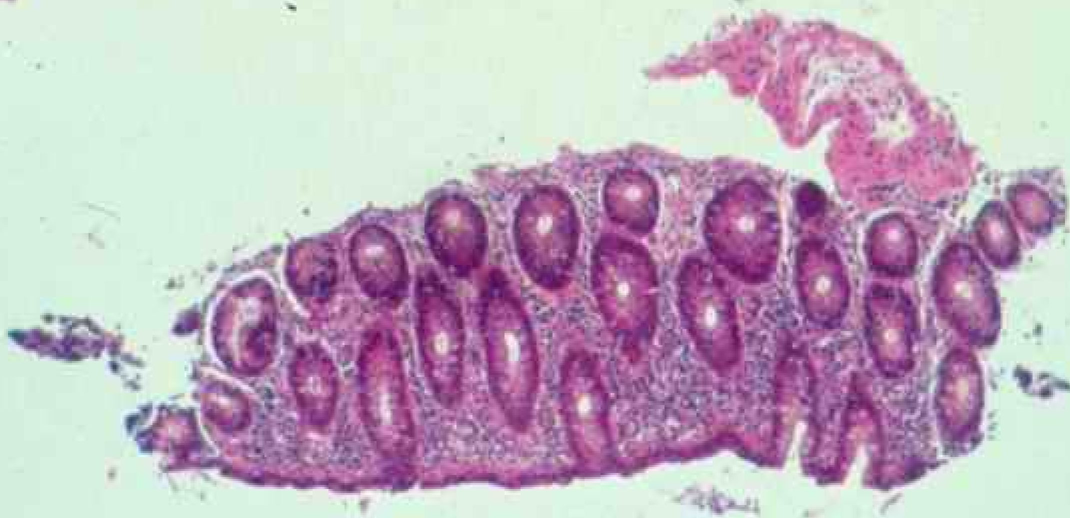


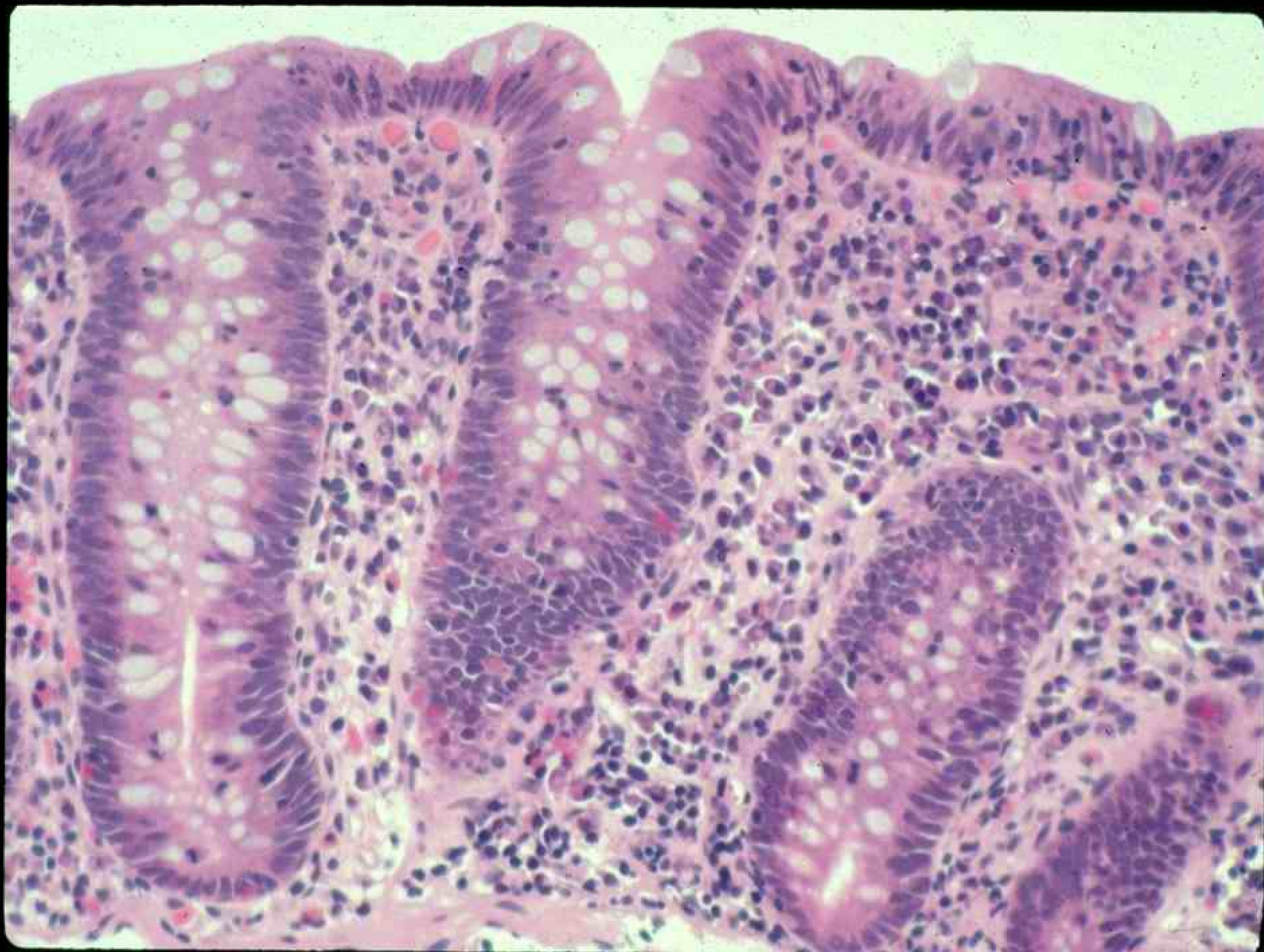


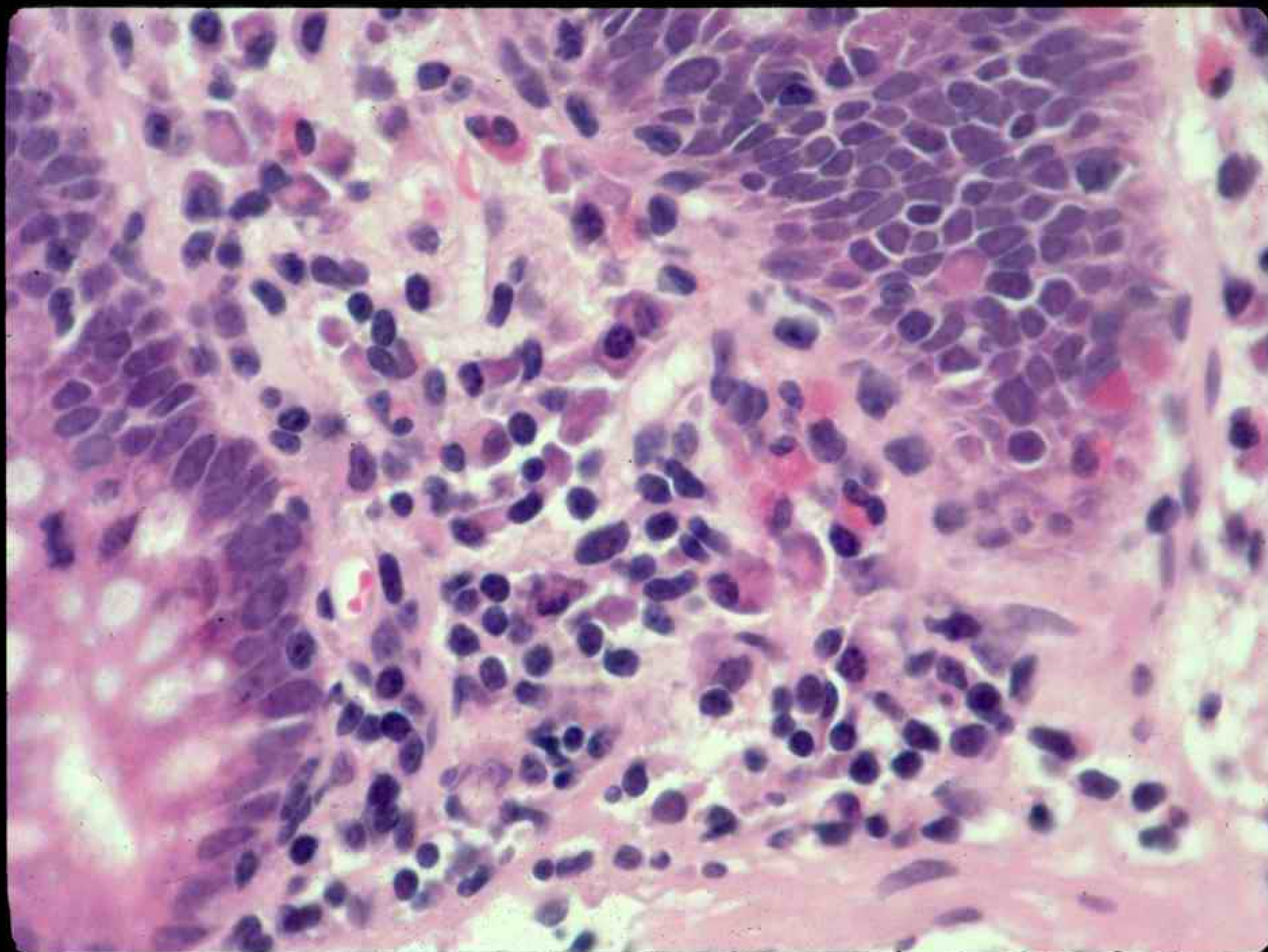


Criteria for microscopic colitis

- There are no agreed upon histological criteria for "MC"
  - Most fit into lymphocytic or collagenous colitis
  - Therefore largely institutionally driven
  - "Mild NSp CI" IS MC - Good communication essential
- Suggested criteria
  - Normal crypt architecture (may be pushed apart)
  - Excess plasma cells – must be a colitis (often to musc. muc)
    - Normal in cecum in some individuals
    - Multiple Bx preferable - ↑ confidence
- Look for IELs, - from c.5 / 10 (N) epithelial cells to 15-25+ in LC
- Collagen band (may be very focal) - > 10μ abnormal
  - Use lympho/plasma cell nucleus – well oriented



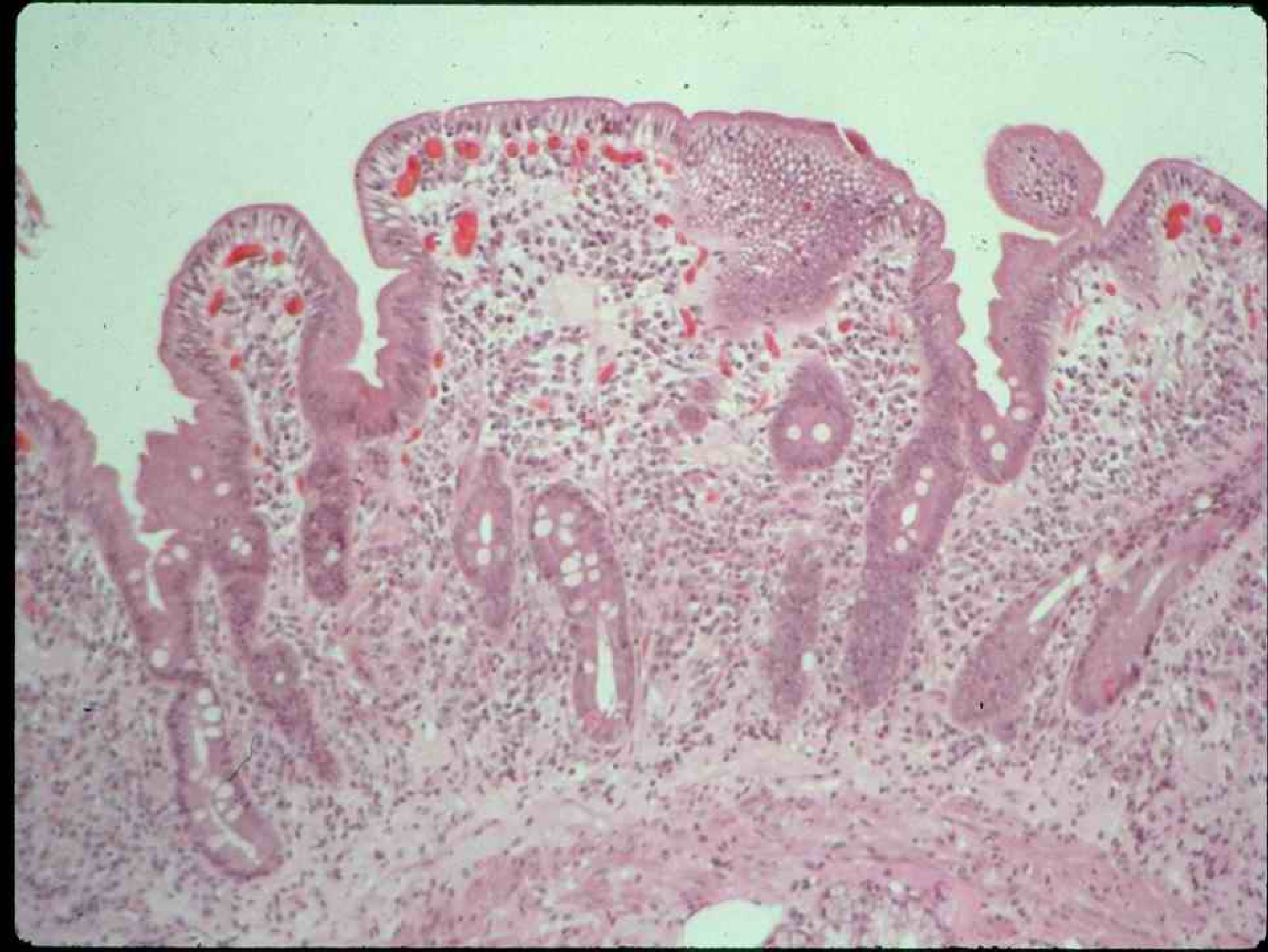


Lymphocytic colitis

- Drug-related
  - NSAIDs, ticlopidine, zantac, cyclofor, PPIs
- Celiac disease-related
- Microscopic colitis with giant cells (behave as LC)
- Microscopic colitis with granulomas (behave as LC)
- Pauci-IEL lymphocytic colitis
- Colonic epithelial lymphocytosis associated with an epidemic diarrhea (Brainerd-type)
- Idiopathic

Associations of MC/LC/CC

- In the GI tract
  - Small bowel disease – celiac disease / PVA (note – celiac disease also associated with intraepithelial lymphocytosis [IELs] in the stomach and proximal large bowel)
  - Collagenous "itides" in other organs
- Extra-intestinal – upregulated immune system
  - Thyroid disease
  - ? Seronegative spondyloarthropathy



Algorithm fo

+ cryptophilic - UC
+ crypt sparing - CD
eration - CD

nt IBD
a - esp fibrosis
use of crypt damage

Yes — Dee

Architectural abn

No Su

ous Colitis

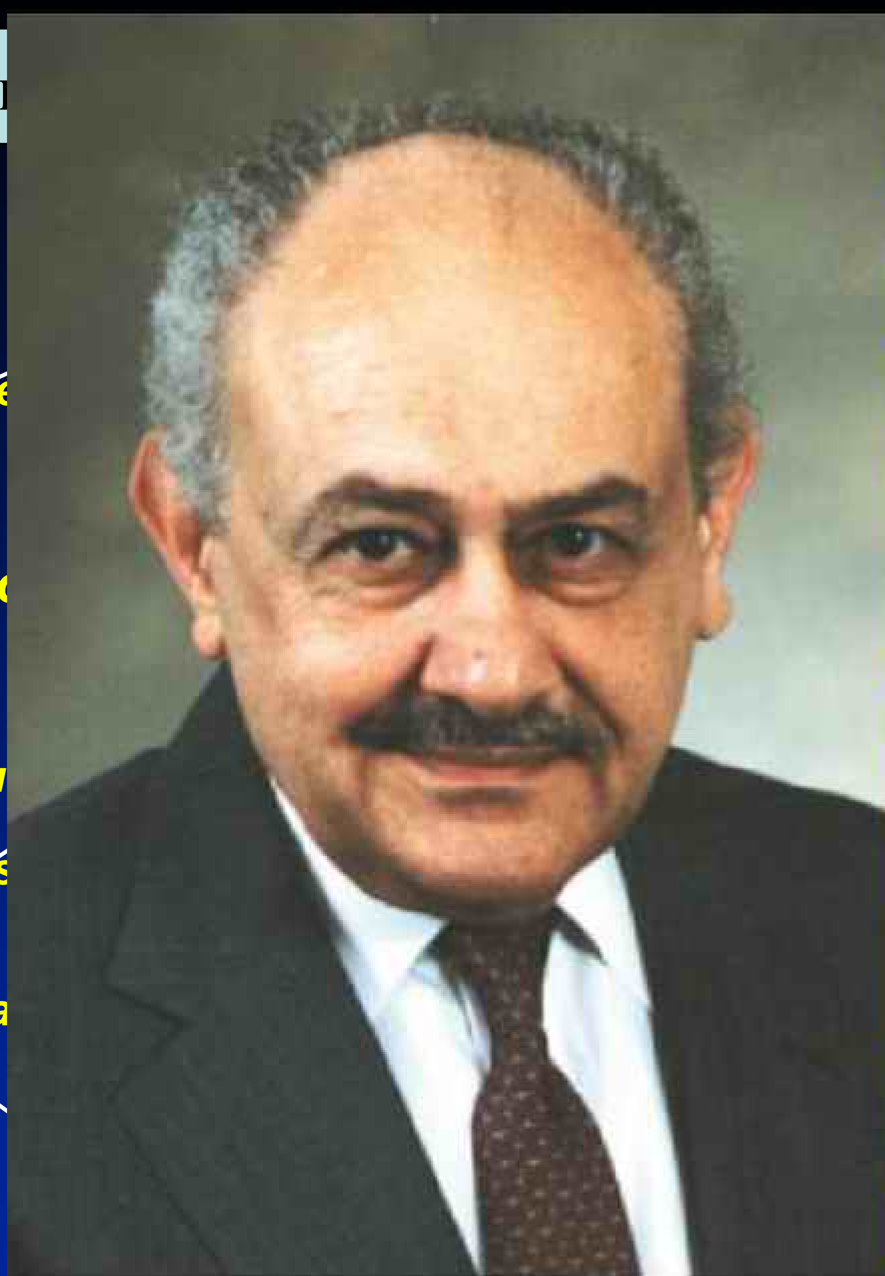
Yes

Yes - LC(CD)
No - MC (IBD)

Deep plasma

s type colitis
nia, ?CD, ?MC)
ion

ficial chronic inflam
nal biopsy



Dr. Kamal G. Ishak