What Is New & Worth Discussing in Chronic Colitis & Associated Dysplastic Lesions

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Outline

Non-IBD Chronic Colitis

- Microscopic Colitis
  - *Lymphocytic colitis*
  - *Collagenous colitis*
- Ischemic colitis
- Granulomatous colitis
- NSAIDs colitis

IBD Chronic Colitis

- Grading
- Managemant
- 'Novel' subtypes

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Non-IBD Colitis

Global perspective

- *IBD is major health and economic issue*:
  - Annual incidence: CD [5] and UC [8-12] cases per 100,000 patient-yrs
  - Prevalence: 1.2 million pts; annual direct economic burden of ~ $6.3 billion [US data]

- ***HOWEVER, OTHER LOWER GI CONDITIONS ARE IMPORTANT IN TERM OF INCIDENCE, MORBIDTY, MORTALITY & COST***

- Annual incidence of *microscopic colitis*: 8.6/100 000 person-yrs.
  - *3.1/100 000 for collagenous colitis; 5.5/100 000 for lymphocytic colitis*
  - significant secular trend with increasing incidence.

- Annual incidence of lower GI ***ischemia***: 15.6/100,000 patient-yrs (F>M)
  - w/ a marked age-related increase

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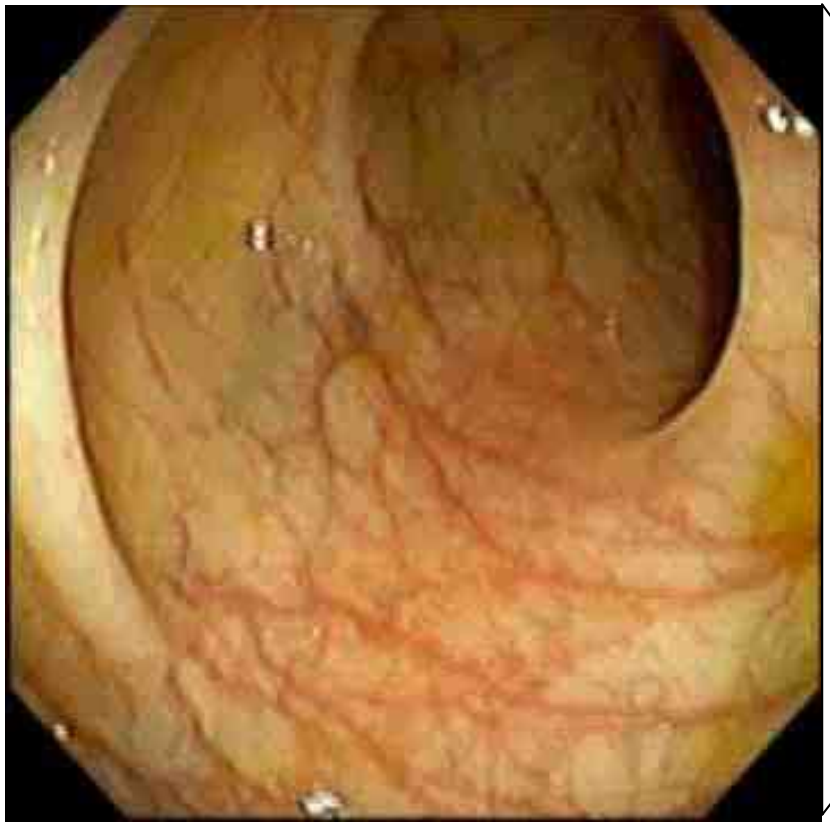
Microscopic Colitis



Collagenous colitis
Lymphocytic colitis
Focal active colitis

- ***Microscopic Colitis*** used for microscopically evident colitides w/ normal endoscopy.
- Initial cases were lymphocytic colitis however the spectrum of 'microscopic colitis' has broadened to include collagenous colitis*

(Gastroenterology. 1980;78)

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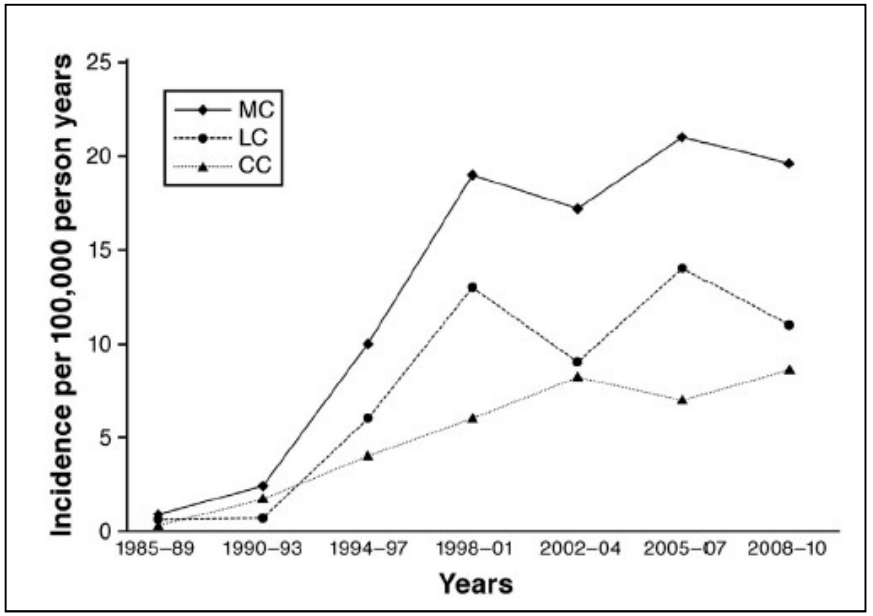
Clinical Features of Microscopic Colitis

- 10-20% of cases of chronic watery diarrhea, highest >70yo
- Chronic non-bloody diarrhea associated with:
  - Urgency [70%], Incontinence [40%]
  - Nocturnal diarrhea; Abd, cramps [50%]
  - Mild wt. loss [40%]
  - Dehydration, electrolyte disturbances – uncommon



- Female predominance, esp. Collagenous colitis (~8:1)
- Sx of LC more likely to be mild and to disappear
- 80% response to budesonide but 60-80% relapse if discontinued; rarely some need chronic immunosuppresion

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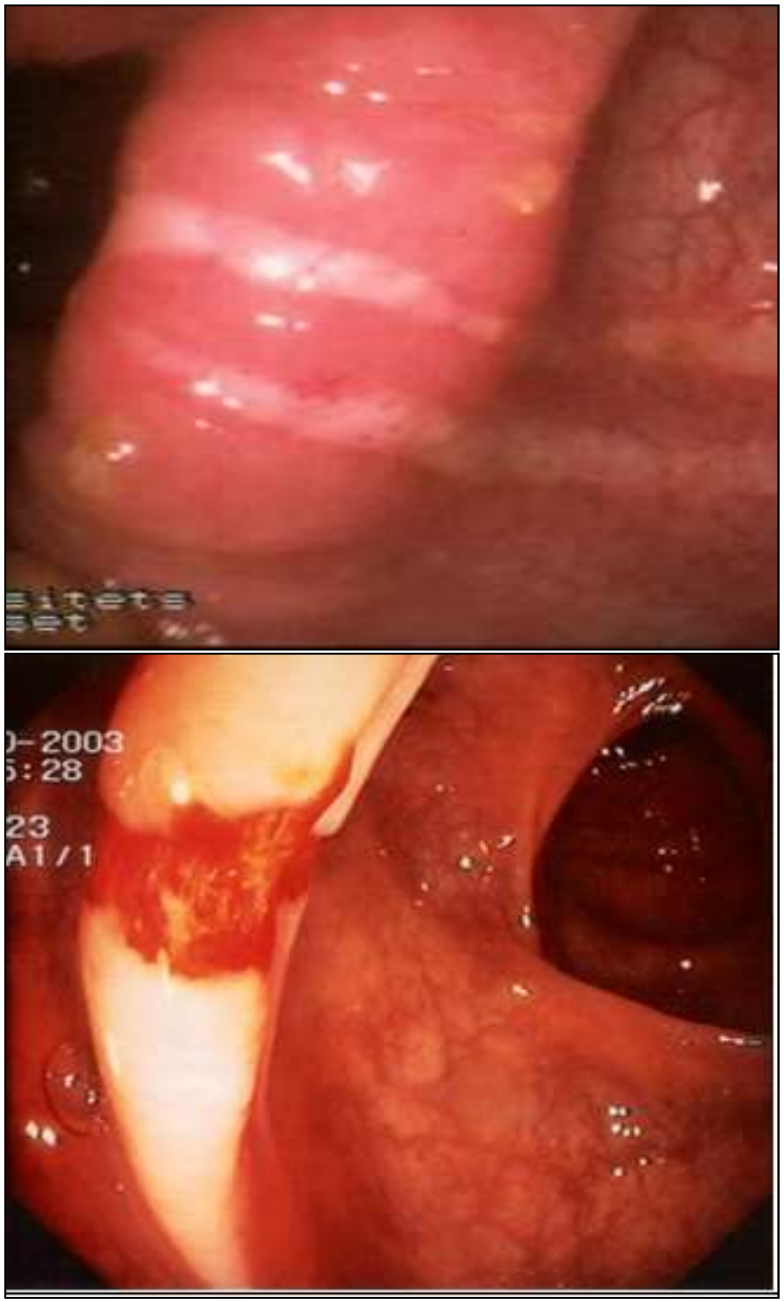
Microscopic colitis with *near normal* endoscopy…..



Patchy abnormalities [30%]

- **Erythema, edema**
- **Vascular, pruning**
- **Minor erosions**
- **Red spots**
- **Mucosal tears**
- **Ulcerations rare**
  (associated with NSAIDs?)

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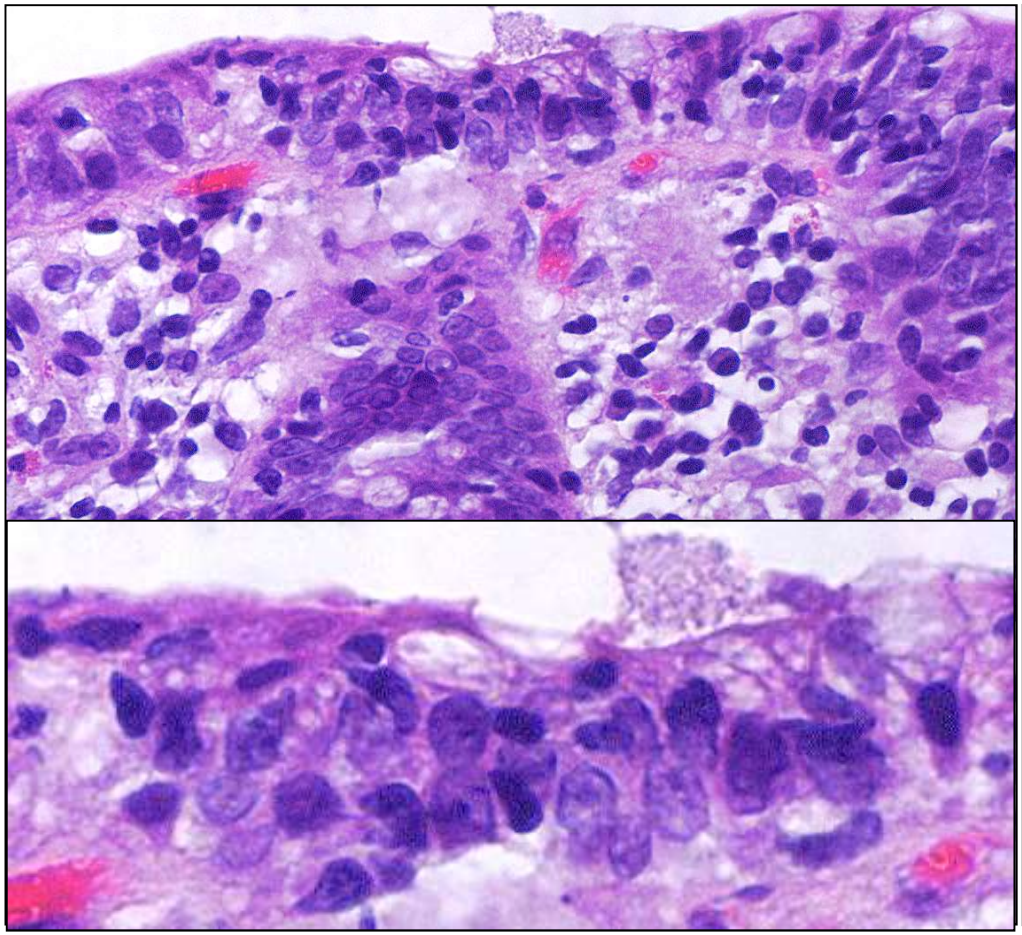
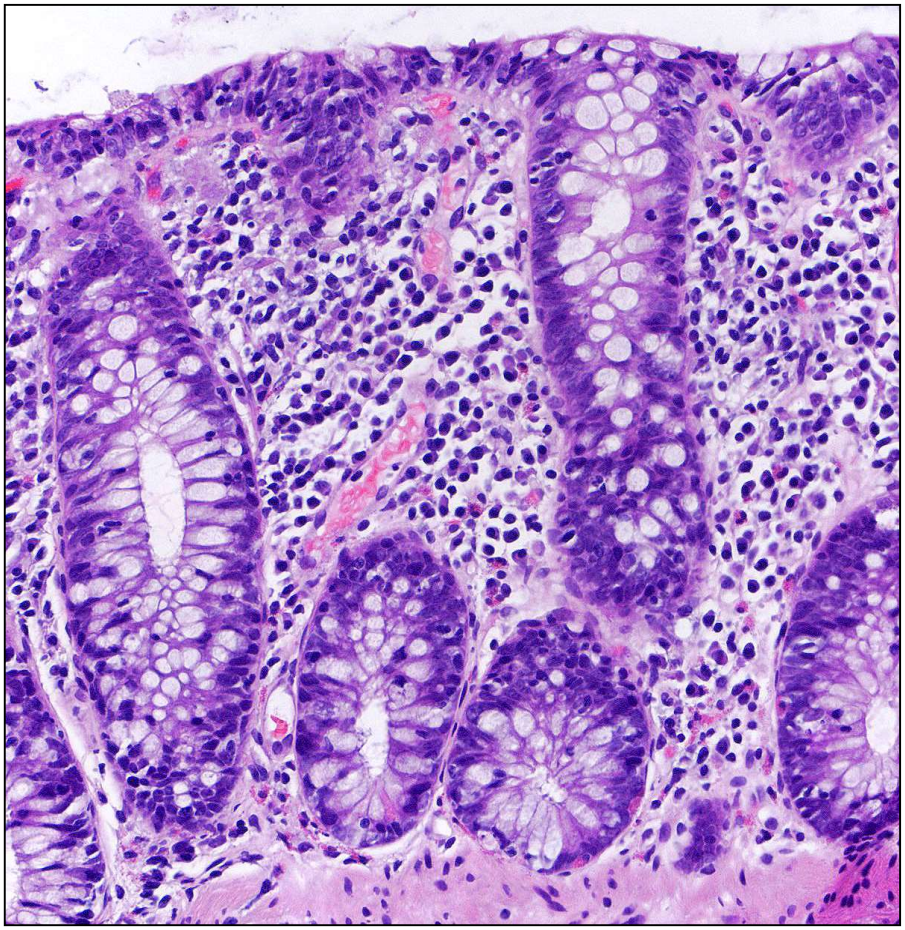
Lymphocytic colitis





- CD3+/CD8+ intraepithelial lymphocytes >15 /100 epithelial cells; crypt and surface
- Normal thickness collagen band

- Usually inflammation in LP – lymphocytes and plasma cell; may include eosinophils and neutrophils

Lymphocytic colitis
etiologies

- Idiopathic (~ 75%)
- Celiac disease – 9-20%; (5-31% of usual celiac and 67% of diet refractory celiac patients have a LC pattern)
- Drugs – (~ 10%) most common classes include NSAID's, PPIs, SSRIs and statins; also ipilimumab, herbal remedies, ticlopidine, carbamazepine
- Autoimmune disease – 20-50% of cases
  - Thyroiditis: 9-20%;
  - Diabetes M: 5-10%,
  - Celiac disease 9-12%

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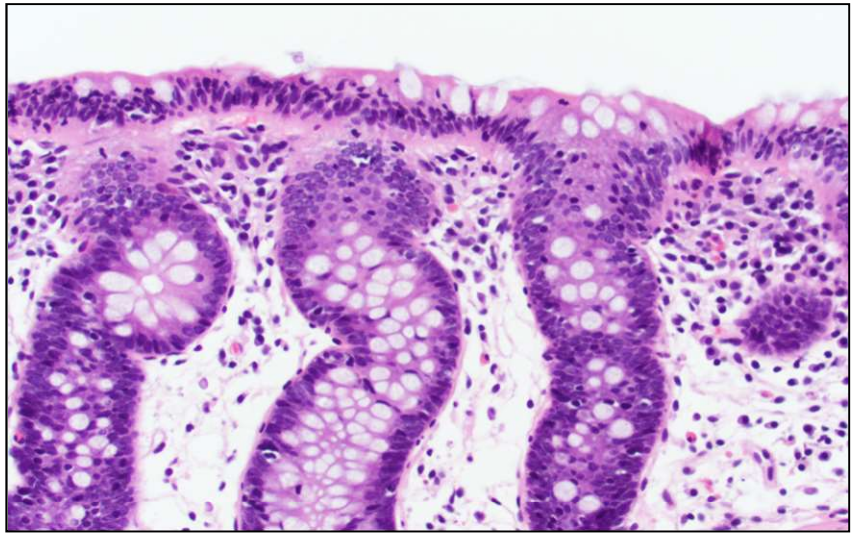
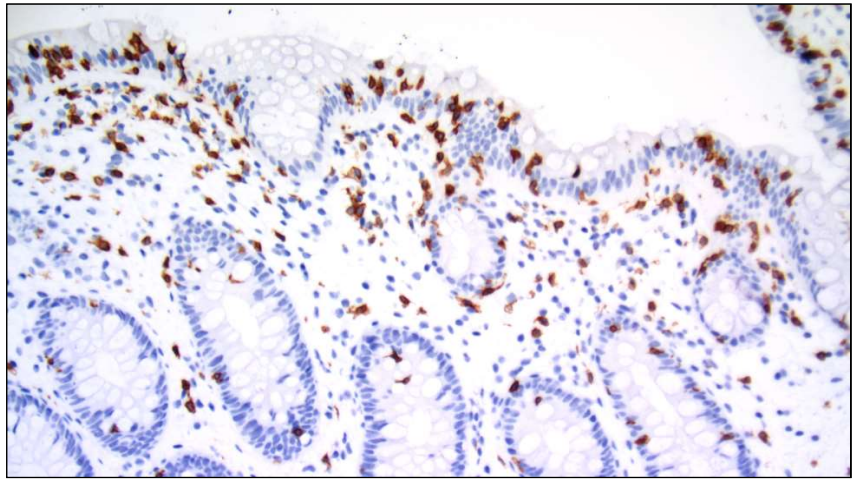
Differential Diagnosis: Colonic lymphocytosis



- Increased IELs (7-20/100 EC) but no appreciable lamina propria inflammation.
- Sometimes reported as *'pauci-cellular lymphocytic colitis*.
- Be careful in the cecum



- **Brainerd diarrhea**
  - Outbreaks of watery diarrhea of presumed viral etiology
- **Resolving Infectious Colitis**
- **Crohn disease, CVID**
- **Allergy, drugs, IBS**

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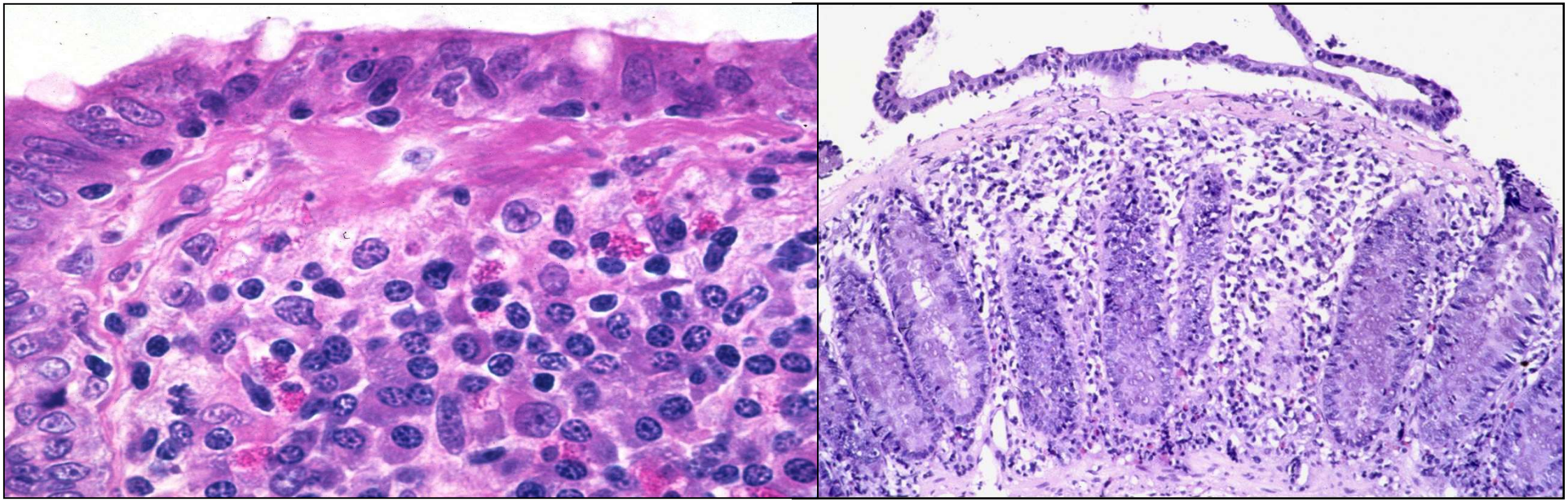
Collagenous Colitis



- Irregular thickening of the subepithelial collagen layer >10µm – collagen types 1 and 3
- Increased IELs
- Inflammation in LP – lymphocytes and plasma cell but may include eosinophils and neutrophils
- Rarely - collagen in ileum and elsewhere in GIT

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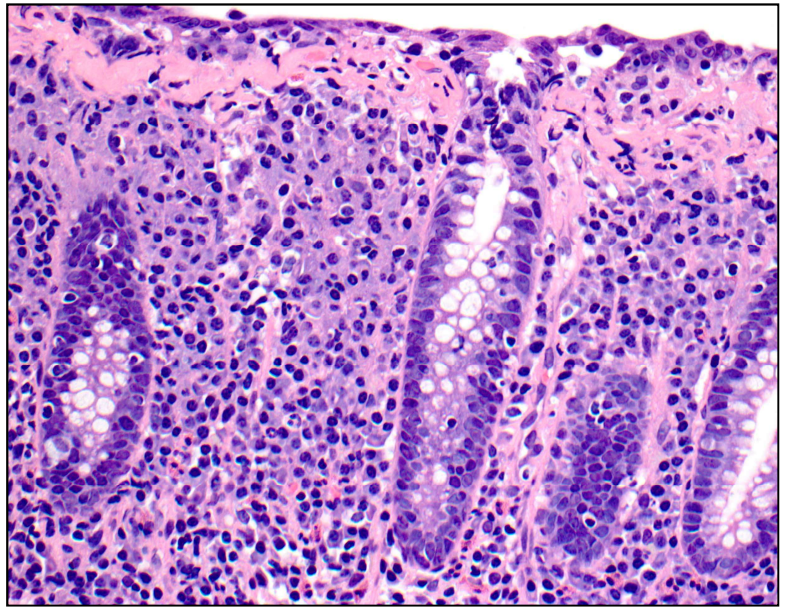
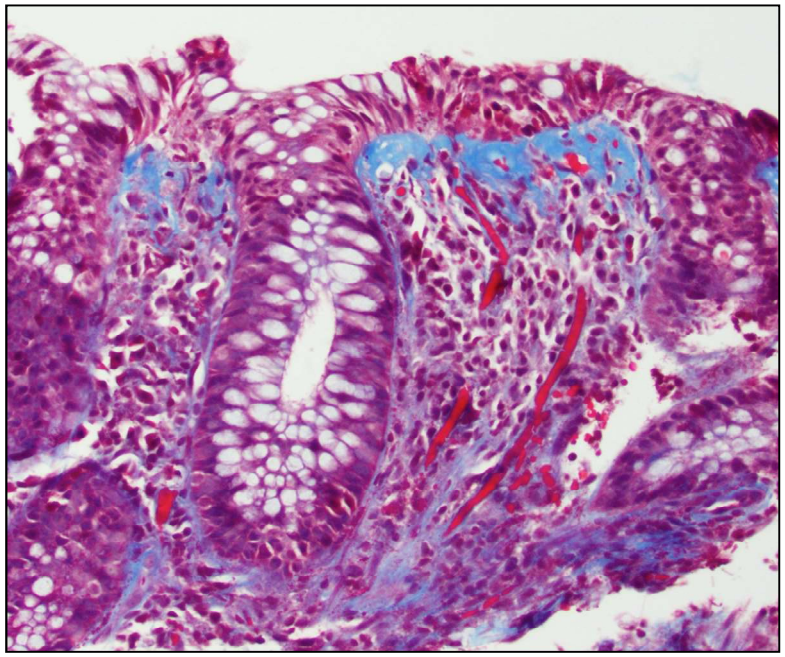
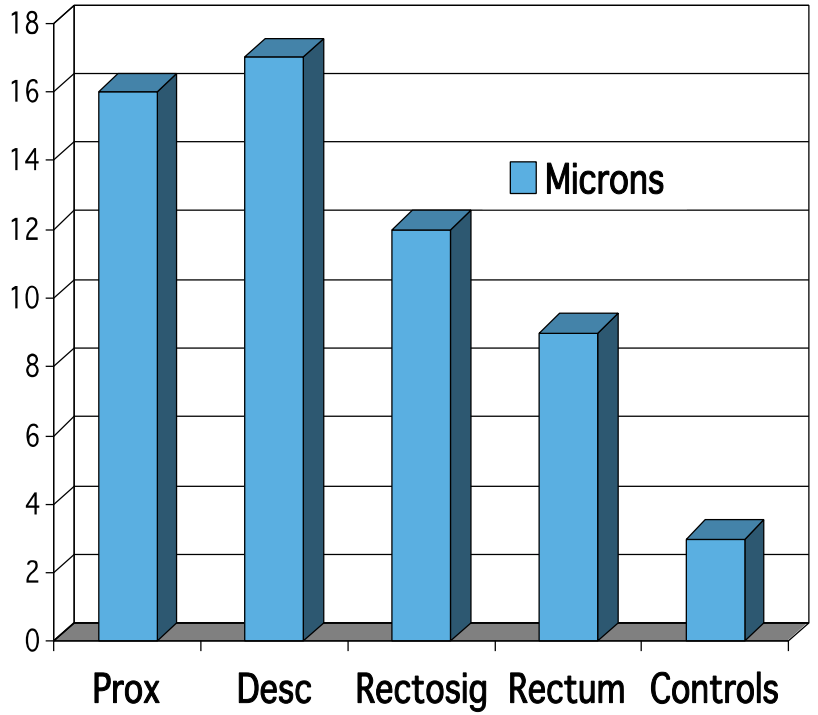
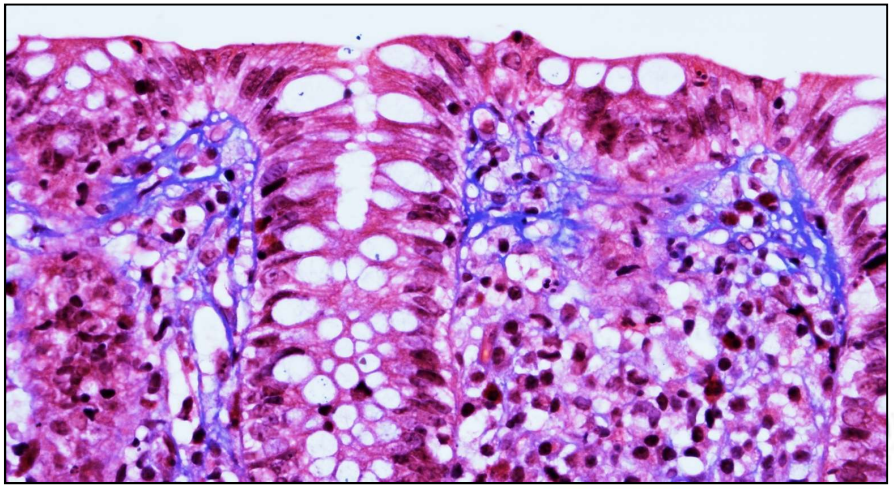
Thickness of Collagen by Site







(Human Pathol 18:839-848, 1987)



Collagenous Colitis

etiologies

- Idiopathic (most cases)
  - ✓ "Luminal content" important since disappearance of collagen on diversion of fecal stream
- Drugs
  - ✓ NSAID's, others
- Autoimmune disease
  - ✓ Association with many autoimmune diseases (autoimmune thyroid disease & rheumatoid arthritis)
- Celiac disease (reported in up to 25%)

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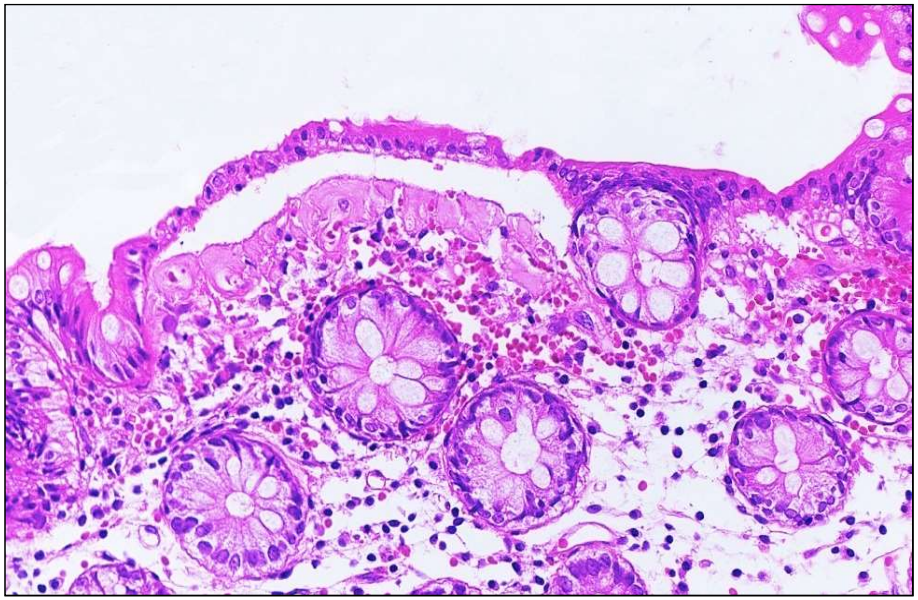
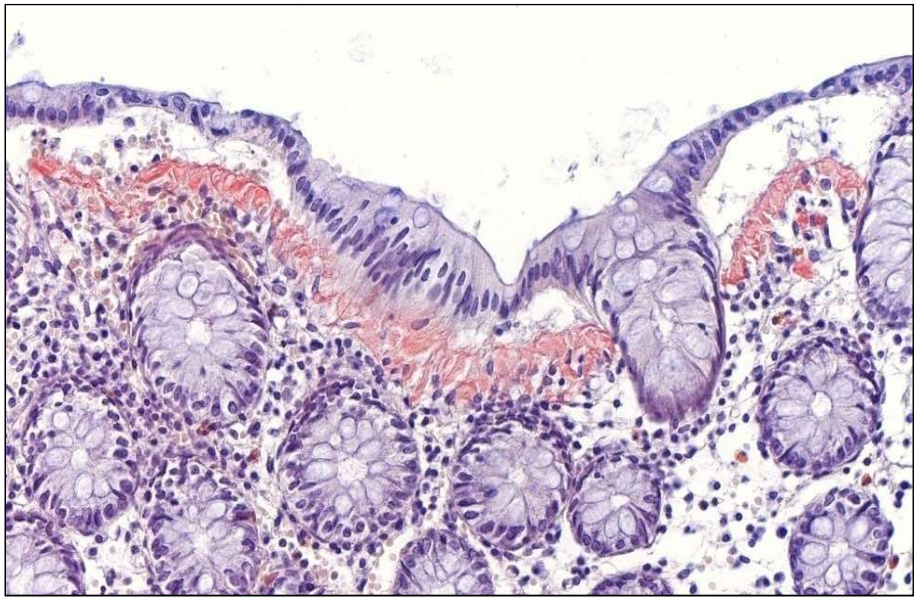
Diff. diagnosis of Collagenous colitis

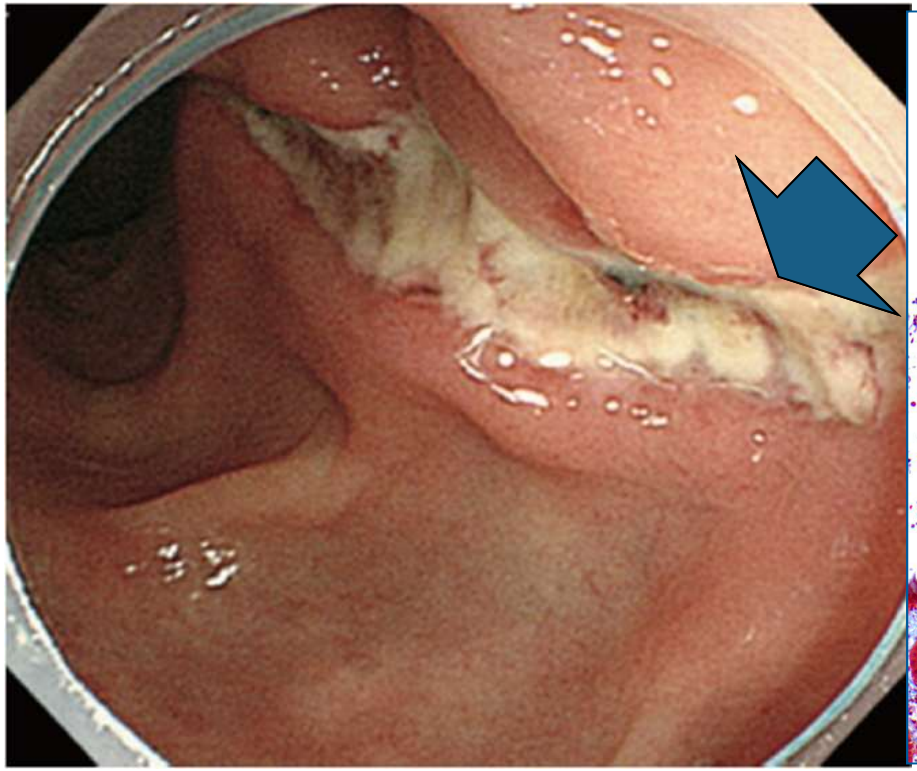
- Lymphocytic colitis – pb=patchy minimal subepithelial collagen thickening.
  (Personal approach – diagnose as CC if irregular thickened collagen in >10% of submitted bx and mixed infl. Infiltrate with eosinophils)
- Ischemic colitis
- BM thickening in diabetes
- Solitary Rectal Ulcer Syndrome
- Diverticular disease
- Amyloidosis

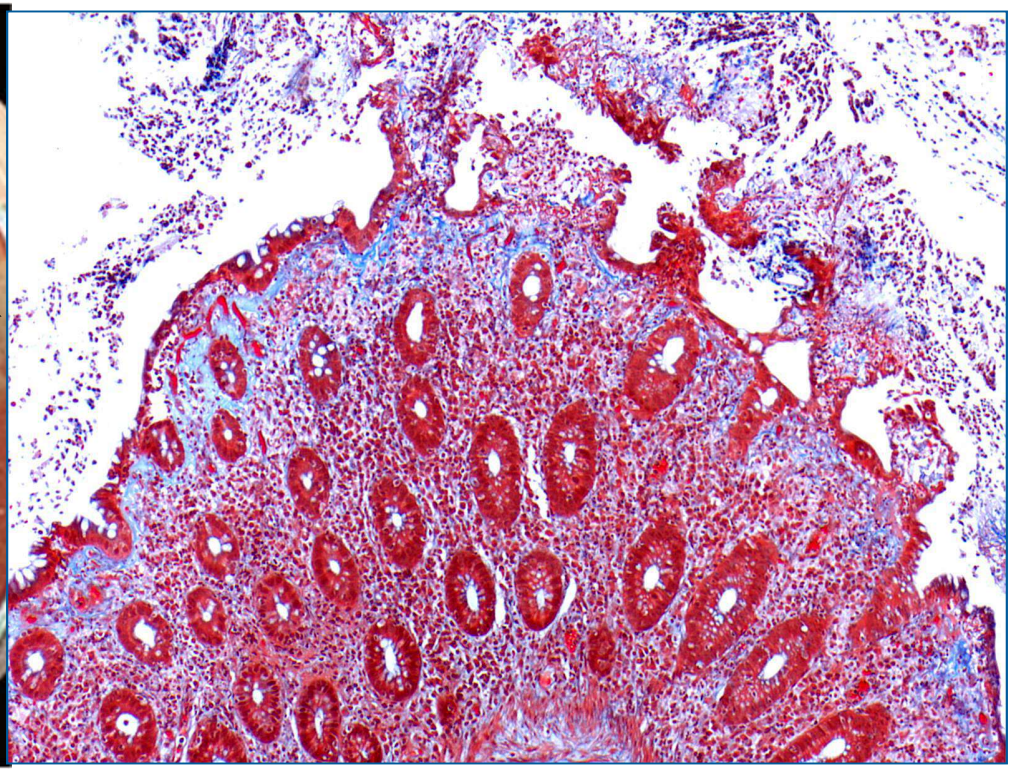




Variants of microscopic colitis

- Pseudomembranous collagenous colitis
  - Usually not associated with C.difficile
  - Superimposed ischemia ?





Mucosal (linear) tear

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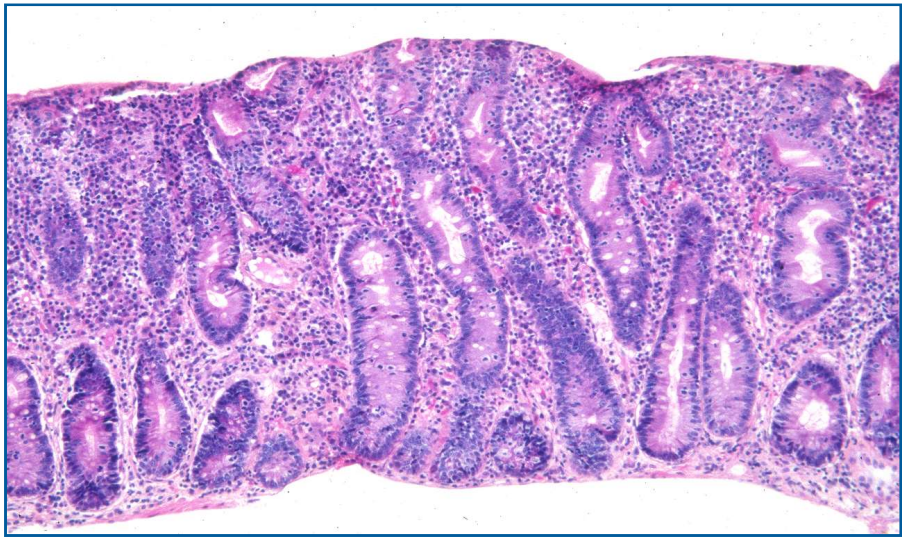
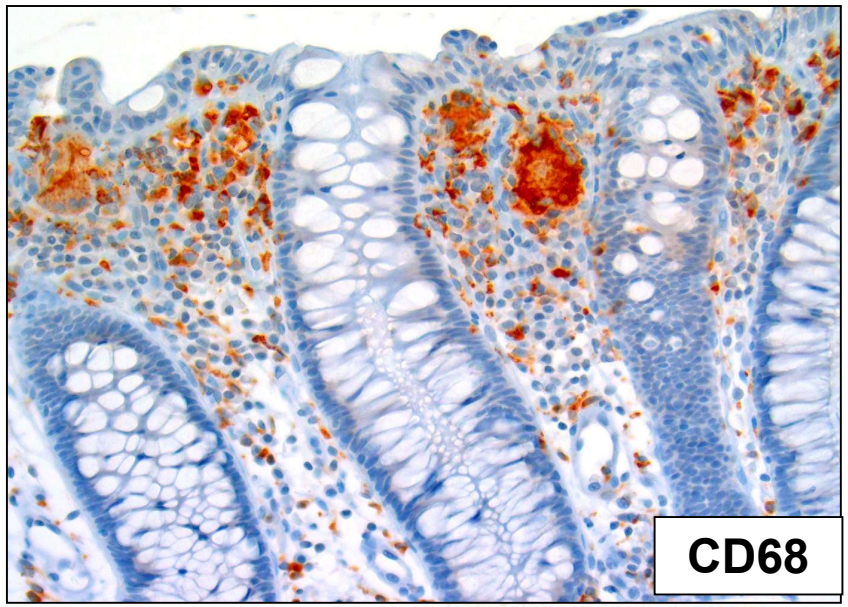


- **IBD-Like Morphology in MC**
  - Rare
  - Crypt atrophy / disarray <10%
  - Active inflammation ~35%
  - Paneth cell metaplasia: 14%-44% (CC)
  - Lymphoid nodules ~65%

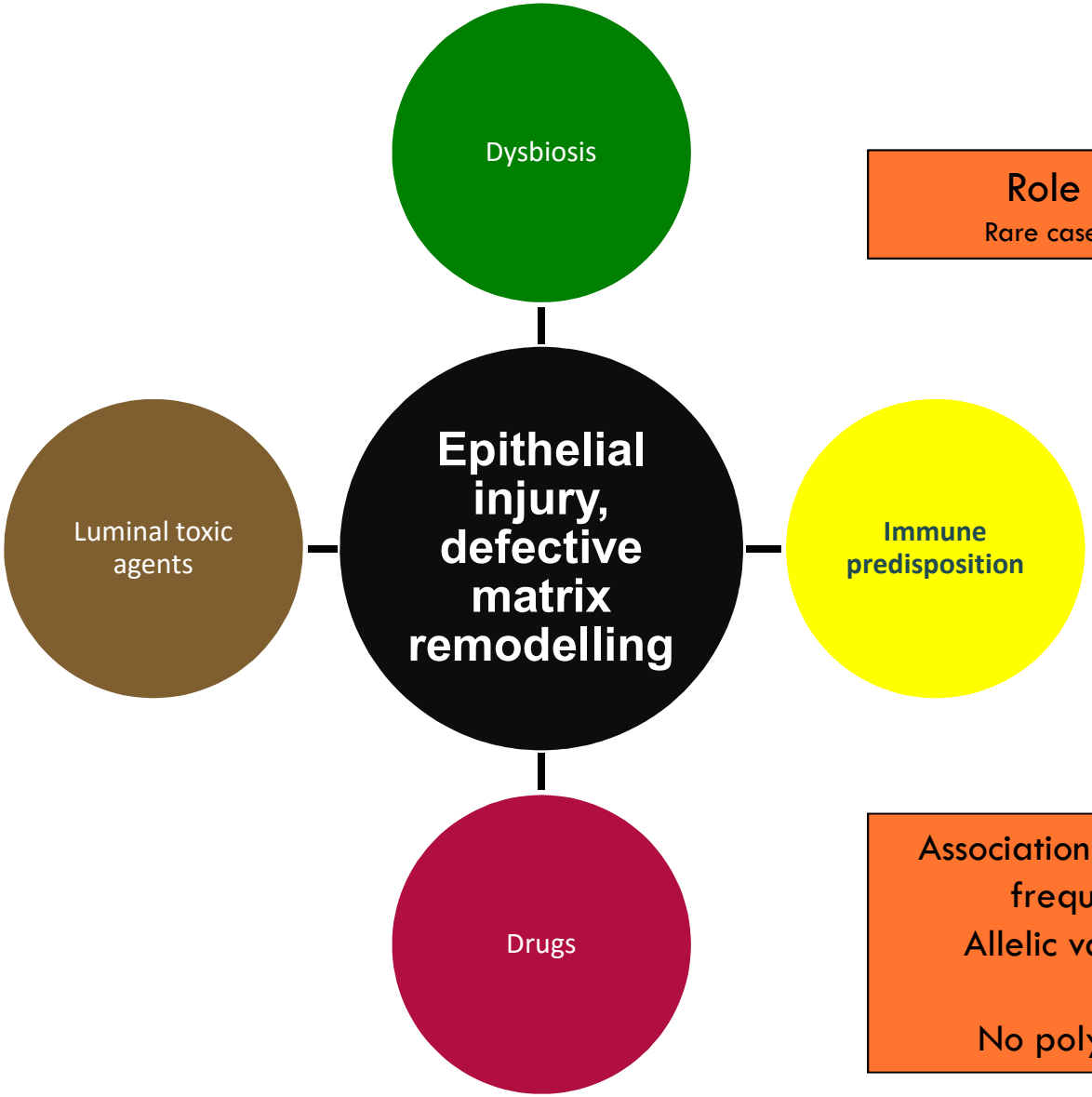
- **Granulomas in MC**

- Subepithelial macrophages & giant cells can be observed in typical collagenous (and lymphocytic) colitis
- No clinical consequence

- **Granulomatous microscopic colitis (?)**
  - Epithelioid granulomata; often a history of chronic diarrhea
  - ?drugs (Histopathology 2004;45:82)



Pathogenesis of microscopic colitis



Role of genetic factors unclear

Rare cases of familial microsocpic colitis reported

Association with HLA-DQ2 or DQ1/3 and high frequency of hladr2dq2 haplotype

Allelic variations of *MMP9* associated w/ collagenous colitis

No polymorphism in *NOD2* or *CARD15*.

Ischemic colitis

etiologies

- Low Blood Flow (shock / cardiac failure)
- Thromboses & Emboli
- Mechanical (volvulus,hernia,adhesions, tumors)
- Vasculitis, Diabetes mellitus,
- Trauma, Surgery, Radiation injury
- Hematologic disorders
  - sickle cell disease , distance runner , Protein C/S antithrombin III deficiencies
- Iatrogenic
  - Oral contraceptives, vasopressin, digitalis, Kayexalate
- Infectious
  - E. coli O157:H7 (Shiga-like Toxins); CMV

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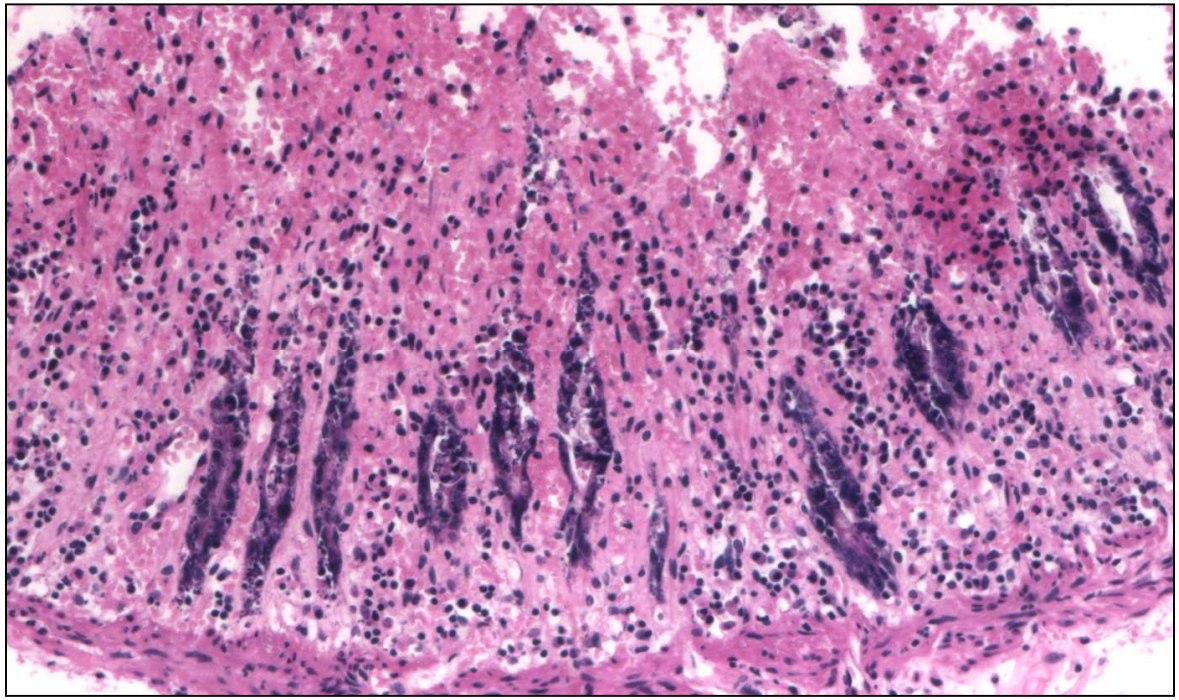

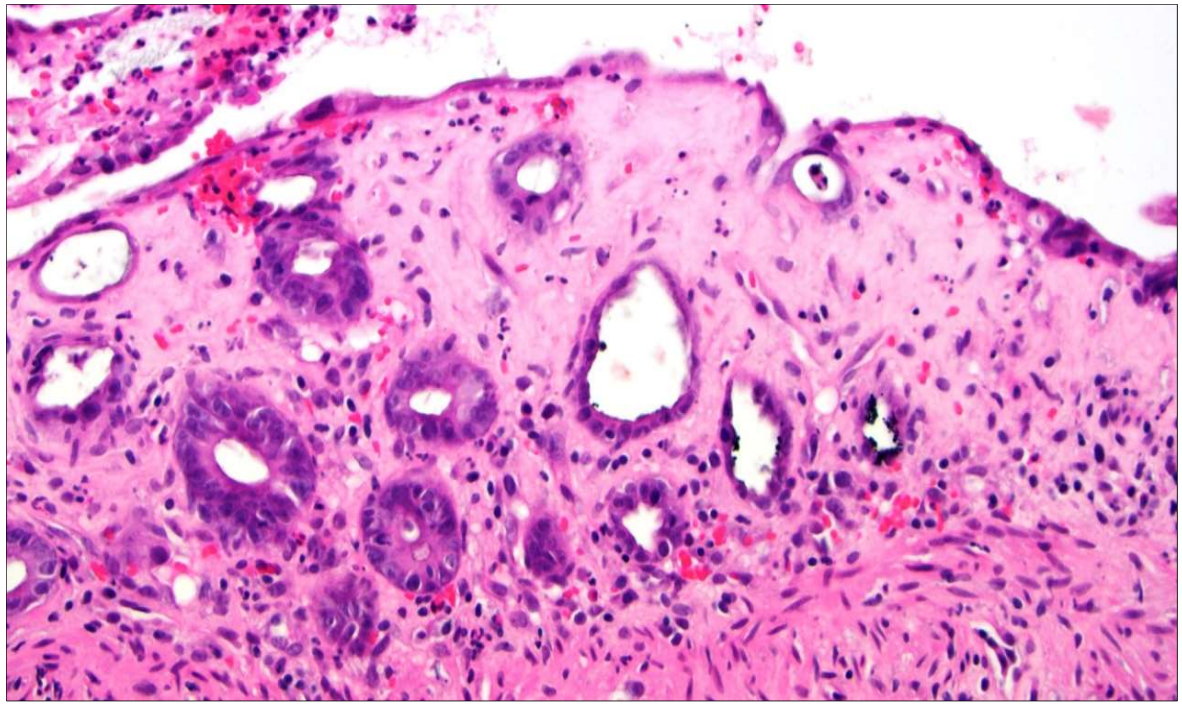

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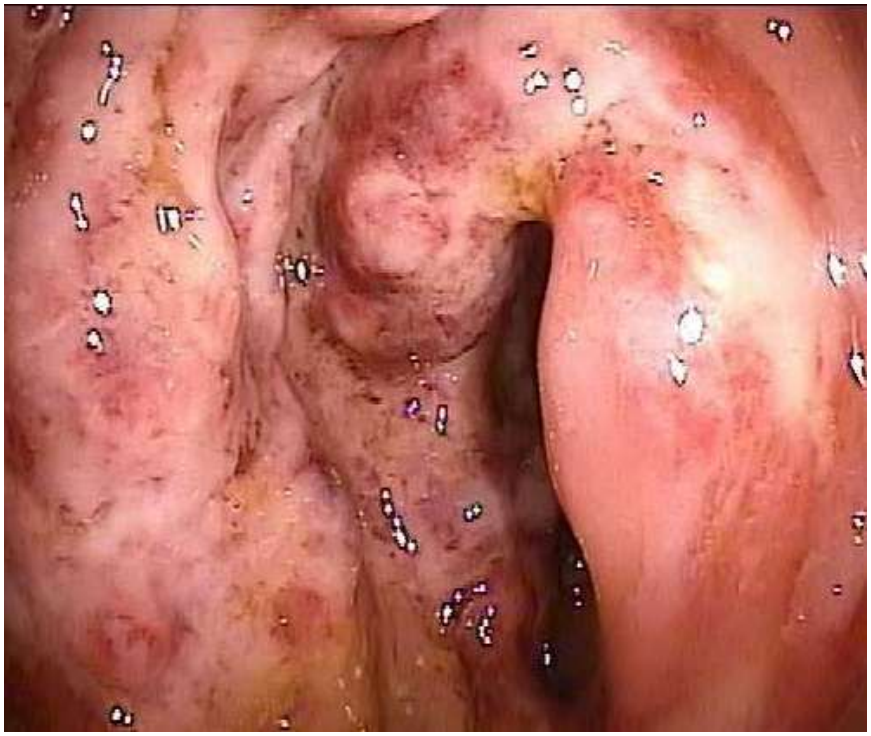
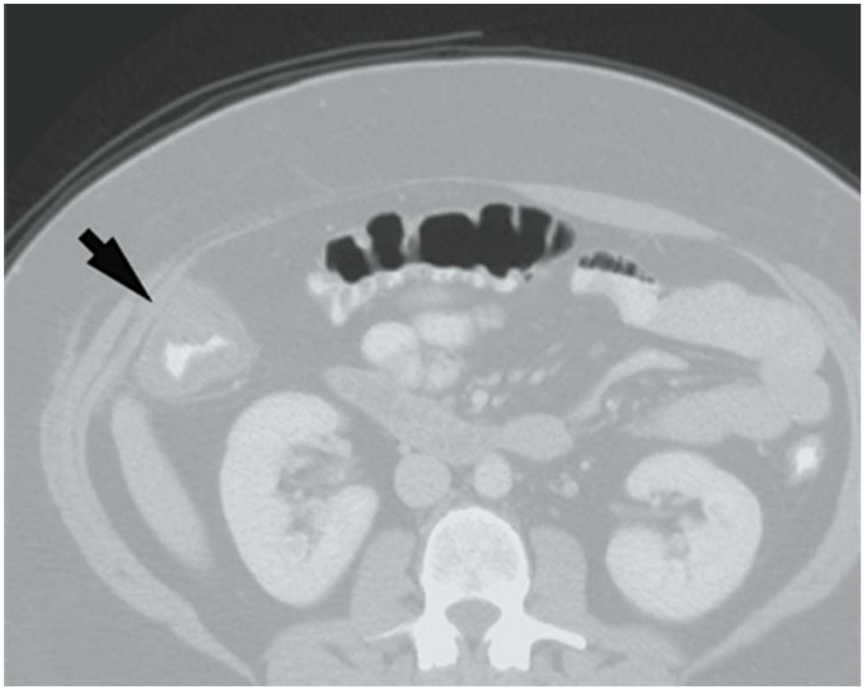
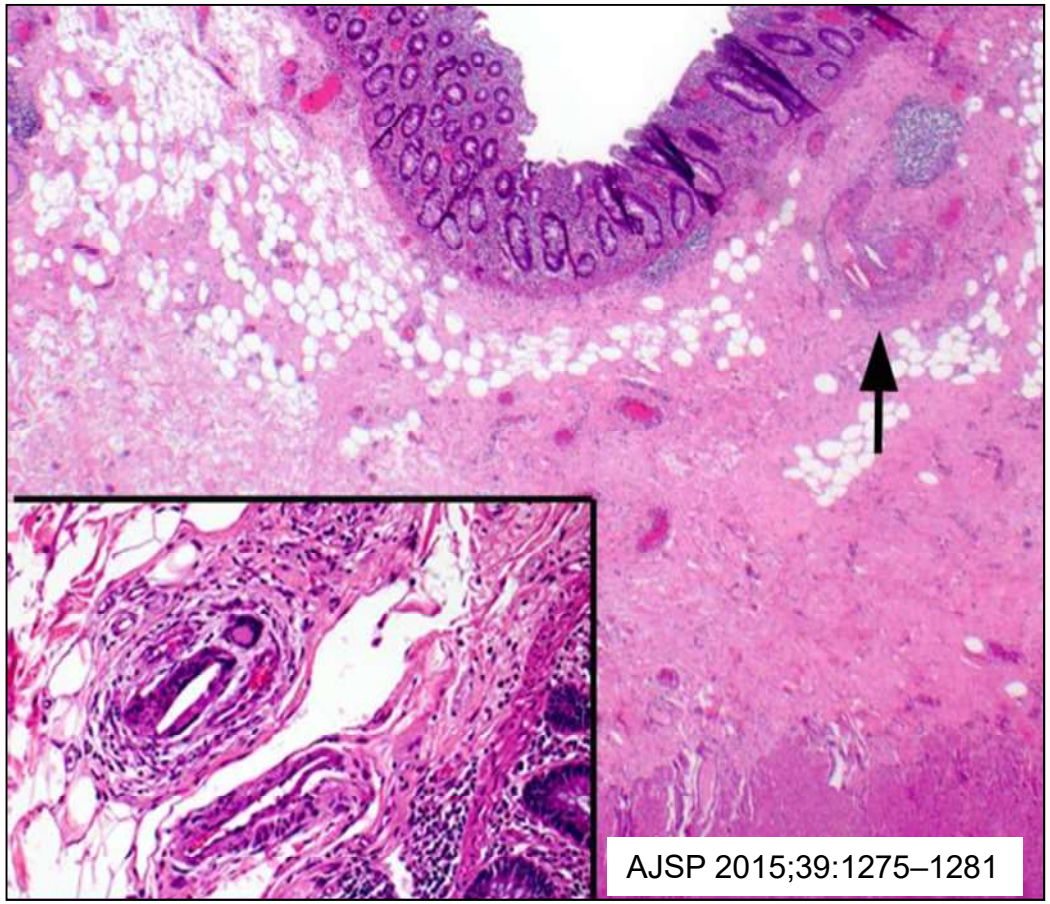


"Mass-forming" variant of ischemic colitis

Elderly (mean age 71.8 y) women (63.2%)
Right colon (13/19) & cecum (n = 6).
CT scan: segmental thickening suspicious for malignancy in 6/8 pts.
Exophytic / stricturing mass (mean size: 4.6 cm)

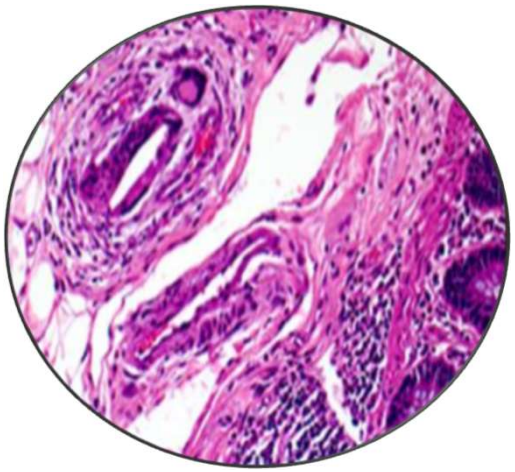




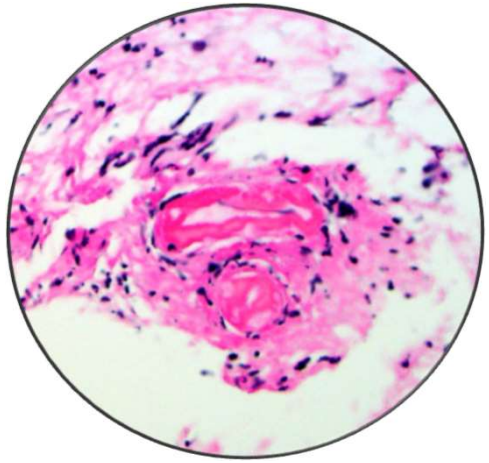
AJSP 2015;39:1275–1281

Etiologic clues of ischemic colitis

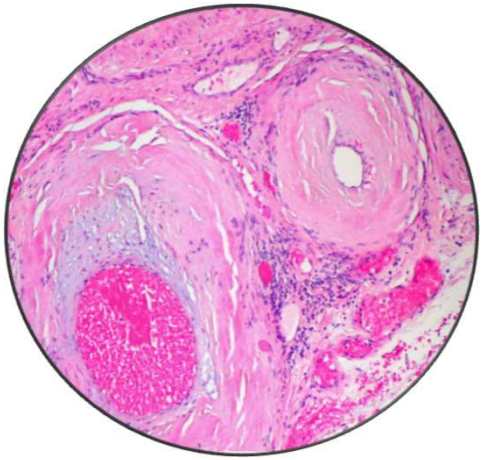
- Check the vessels!



– **Thrombi /emboli**



Vasculitis



Amyloid

- Mucosa/superficial submucosal eosinophils may suggests cholesterol embolus
- Left colon (& distal transv.) in young females: ?OCP?
- Right colon: NSAIDs, thrombotic microangiopathies, Behcet's disease & severe cardiovascular disease

Am J Surg Path 1991:15(11);1078-82
Am J Surg Pathol 1995:19;454-63

Granulomatous colitis

etiologies

- IBD: Crohn disease & U.C. *[mucin granuloma]*
- Sarcoidosis
- Inherited *[CGD, Hermansky-Pudlak syndrome]*
- Systemic Infection *[TB, histoplasmosis]*
- GI infections *[salmonella,yersinia,campylobacter]*
- Venereal infections *(syphilis, LGV)*
- Drugs *[e.g.,diclofenac]*
- Foreign Body *[talc, starch, barium]*
- Others – Diverticular Disease associated Colitis, pneumatosis

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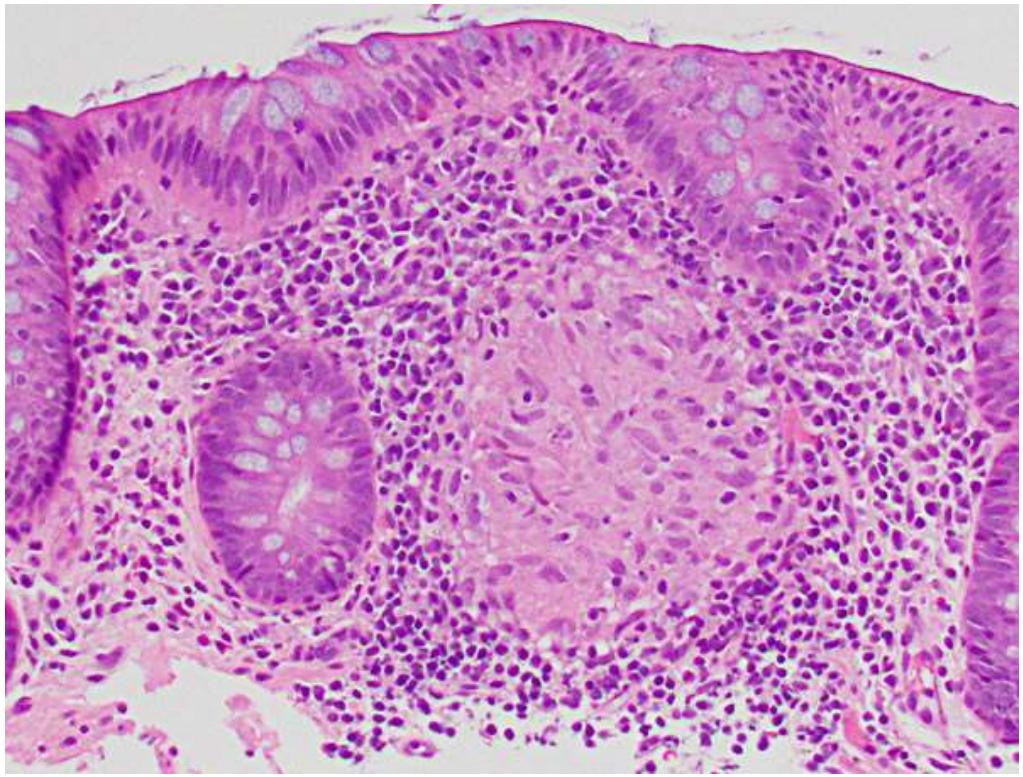
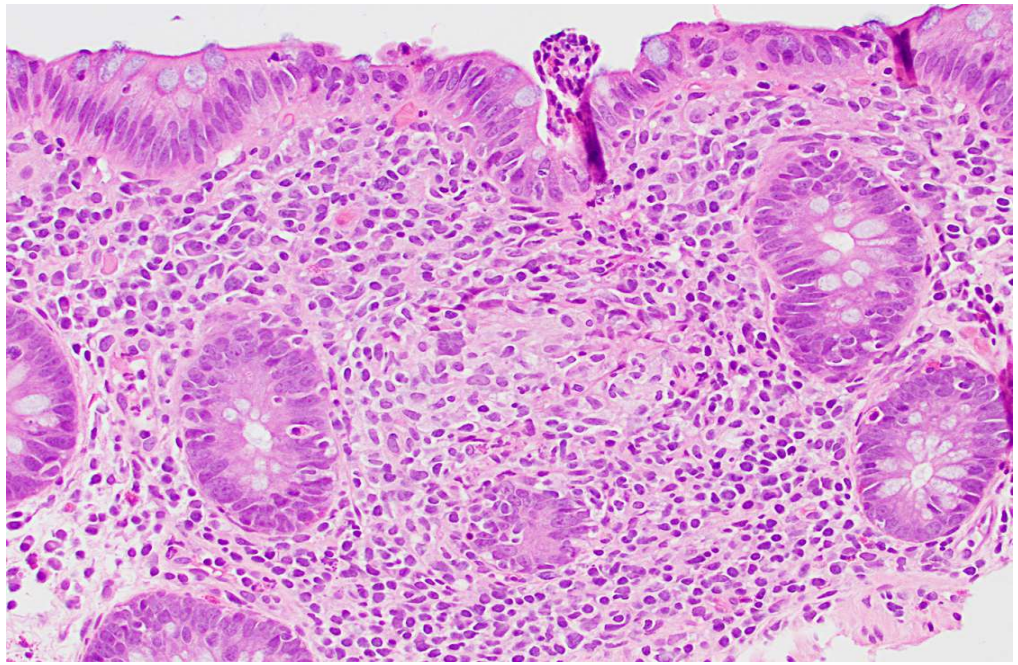
How to approach to colonic granulomata?

- What is the clinical setting?
  - Endoscopic appearance
  - UGIT/extraintestinal disease
  - Immunocompetence
  - Recent medication/travel
  - Response to treatment
- What is the histology?

Likely Crohn disease
OR
possibly
something else

Look for foreign material/parasites/pigments
Organism stains (Gram, PAS, ZN, Fite) ± proceed to PCR (TB, ?fungi, ?Yersinia) from paraffin material





Crohn's disease
- Granulomas -

- Noted in 15%-65% of bx
- Infrequent (< 5),
- small (< 200 µm in size)
- Discrete or poorly organized or histiocytic aggregates
- Crypt-centered inflammation, i.e., pericryptal granulomas & focally enhanced colitis

Makhariah G *m J Gastroenterol* 2010; 105:642–651;
Pulimood AB *World J Gastroenterol* 2011; 17: 433-443
Pulimood AB(*Gut* 1999;**45**:537–541

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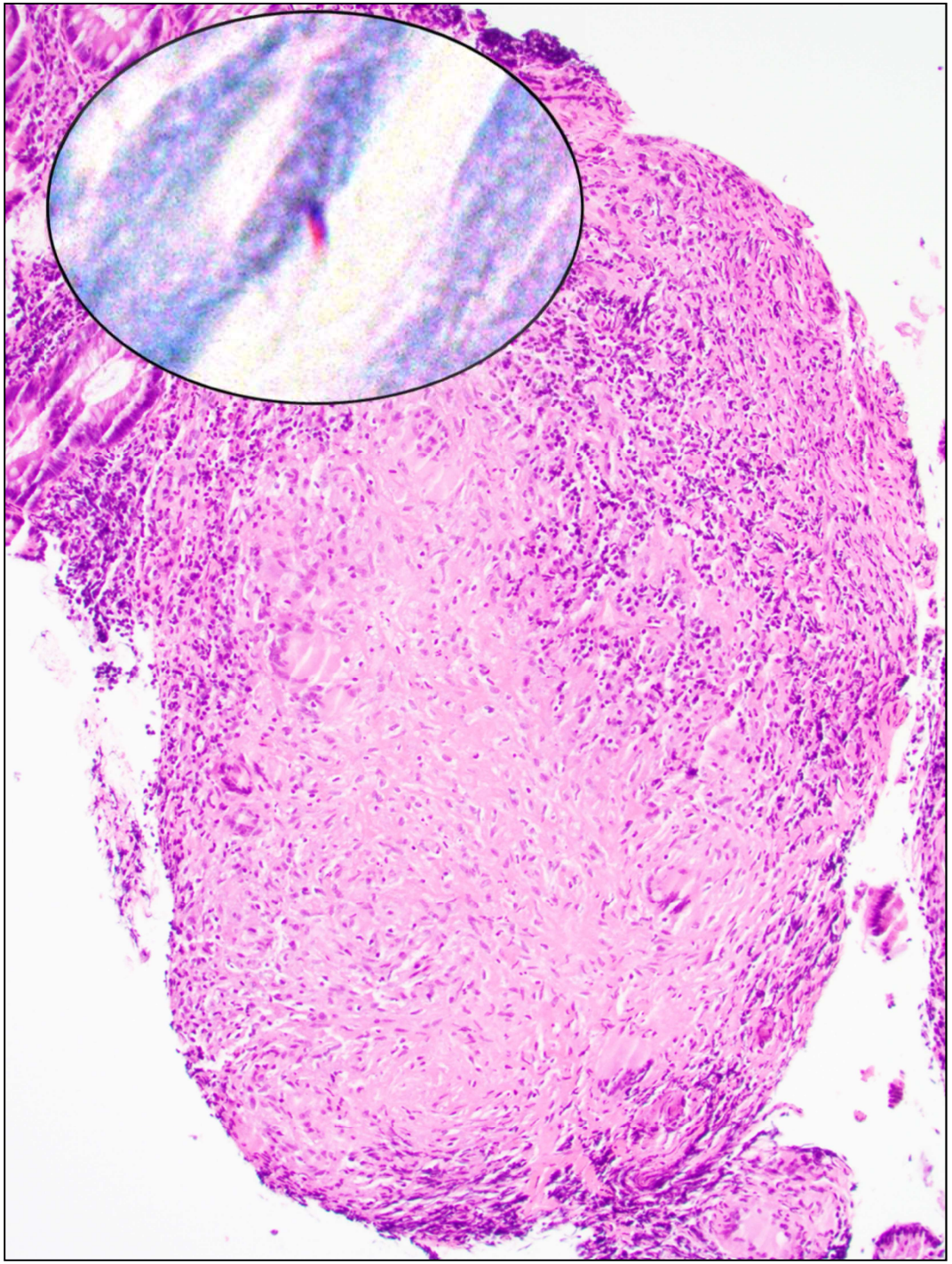
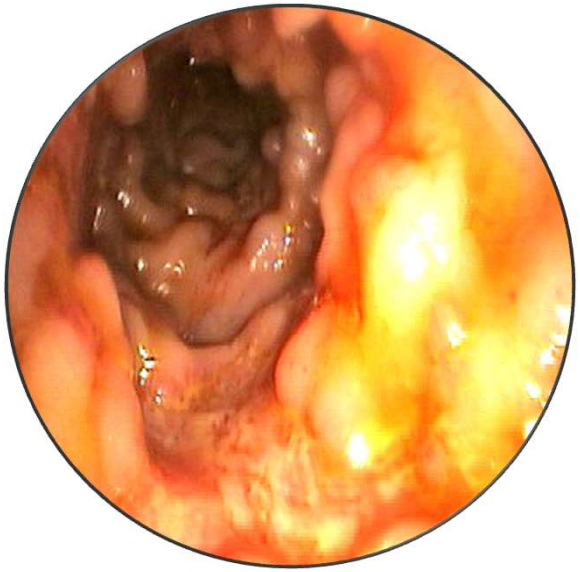


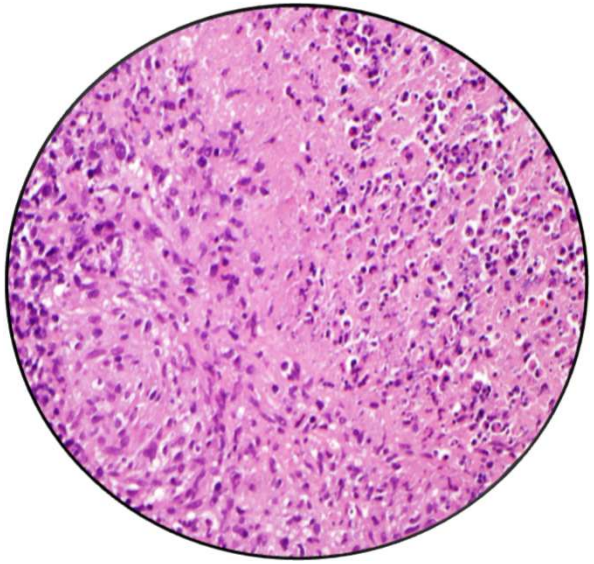
Tuberculosis
- Granulomas -

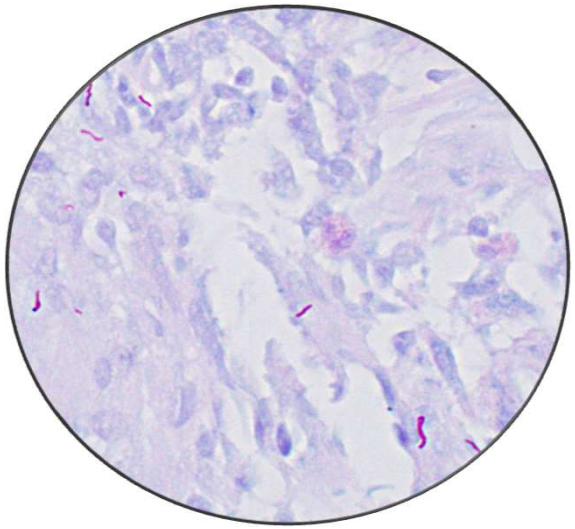
- In 50%-80% of bx.
- Caseation & AFB (+) 18%-33% (as low as 5%)
- Confluent granulomas (up to 50%) , lymphoid cuff, > 400 µm, > 5 granulomas in bx from 1 segment (up to 10 in one series)
- Palisaded epithelioid histiocytes in granulation tissue & disproportionate submucosal inflammation

Makhariah G *m J Gastroenterol* 2010; 105:642–651;
Pulimood AB *World J Gastroenterol* 2011; 17: 433-443
Pulimood AB(*Gut* 1999;**45**:537–541

Features favoring Tuberculosis over CD







Partial intestinal obstruction

Constipation, presence of nodular lesions

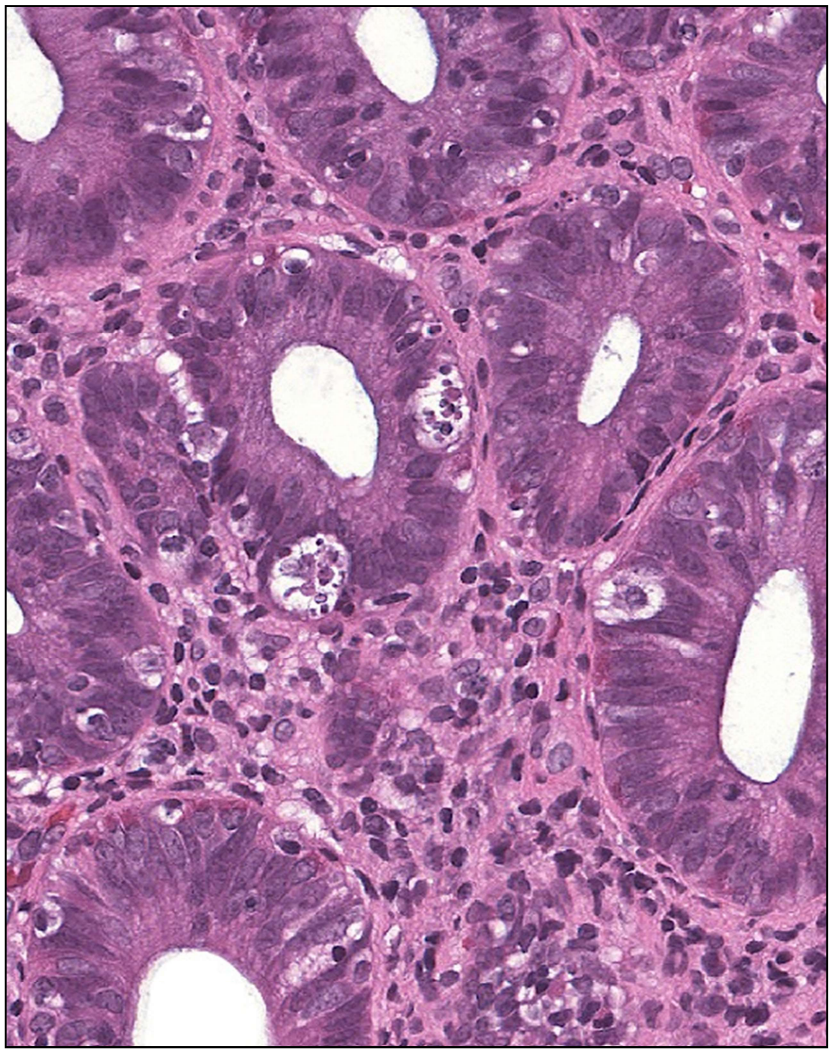
J Clin Pathol 2006;59:840-44
Am J Gastroenterol 2010;105:642-51

Confluent granulomata (50% vs 0%)
≥10 granulomata/biopsy site (33% vs 0%)
Caseous necrosis (22% vs 0%)
Absence of focally enhanced colitis (64% vs 32%)
No involvement of Sigmoid colon (89% vs 33%)

In favor of Crohn: longer duration of disease ; Chronic diarrhea / blood in stool; Perianal disease; Extra-intestinal manifestations

Skip lesions ; Aphthous ulcers ; Cobblestoning; Longitudinal ulcers.

Colitis with increased apoptosis



etiologies

- Bowel Prep
- Drugs (Chemotherapy,Mycophenolate)
- GVHD
- Infection (CMV, HIV)
- Radiation
- Autoimmune enteropathy

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Autoimmune enteropathy

- Immune-mediated clinicopathologic condition characterized by:
    1. Intractable diarrhea
    2. *Severe small bowel villous atrophy* not responding to any dietary restriction (malabsorption)
    3. Circulating gut autoantibodies and/or associated autoimmune conditions
    4. Lack of severe immunodeficiency

Unsworth DJ. Walker-Smith A. J Ped Gastroenterol Nutr 1985;4:375-380
Catassi C. J Ped Gastroenterol Nutr 1999;29:63-68
Goulet OJ. J Ped Gastroenterol Nutr 1998;26:151-161

Autoimmune Enteropathy with Severe Atrophic Gastritis and Colitis in an Adult: Proposal of a Generalized Autoimmune Disorder of the Alimentary Tract

H. MITOMI, S. TANABE, M. IGARASHI, T. KATSUMATA, N. ARAI, S. KIKUCHI, A. KIYOHASHI & I. OKAYASU
Depts. of Pathology, Internal Medicine, and Surgery, School of Medicine, Kitasato University, and Dept. of Gastroenterology Section, Kanagawa Cancer Center, Kanagawa, Japan

Scan J Gastroenterol 1998;33:716-720

Adult Autoimmune Enteropathy: Mayo Clinic Rochester Experience

SALMA AKRAM,* JOSEPH A. MURRAY,* DARRELL S. PARDI,* GLENN L. ALEXANDER,* JOHN A. SCHAFFNER,* PIERRE A. RUSSO,‡ and SUSAN C. ABRAHAM§

*Division of Gastroenterology and Hepatology, Department of Internal Medicine, Mayo Clinic and §Division of Anatomic Pathology, Department of Pathology, Mayo Clinic College of Medicine, Rochester, Minnesota; and ‡Department of Pathology and Laboratory Medicine, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

Clin Gastroenterol Hepatol 2007;5:1282-1290

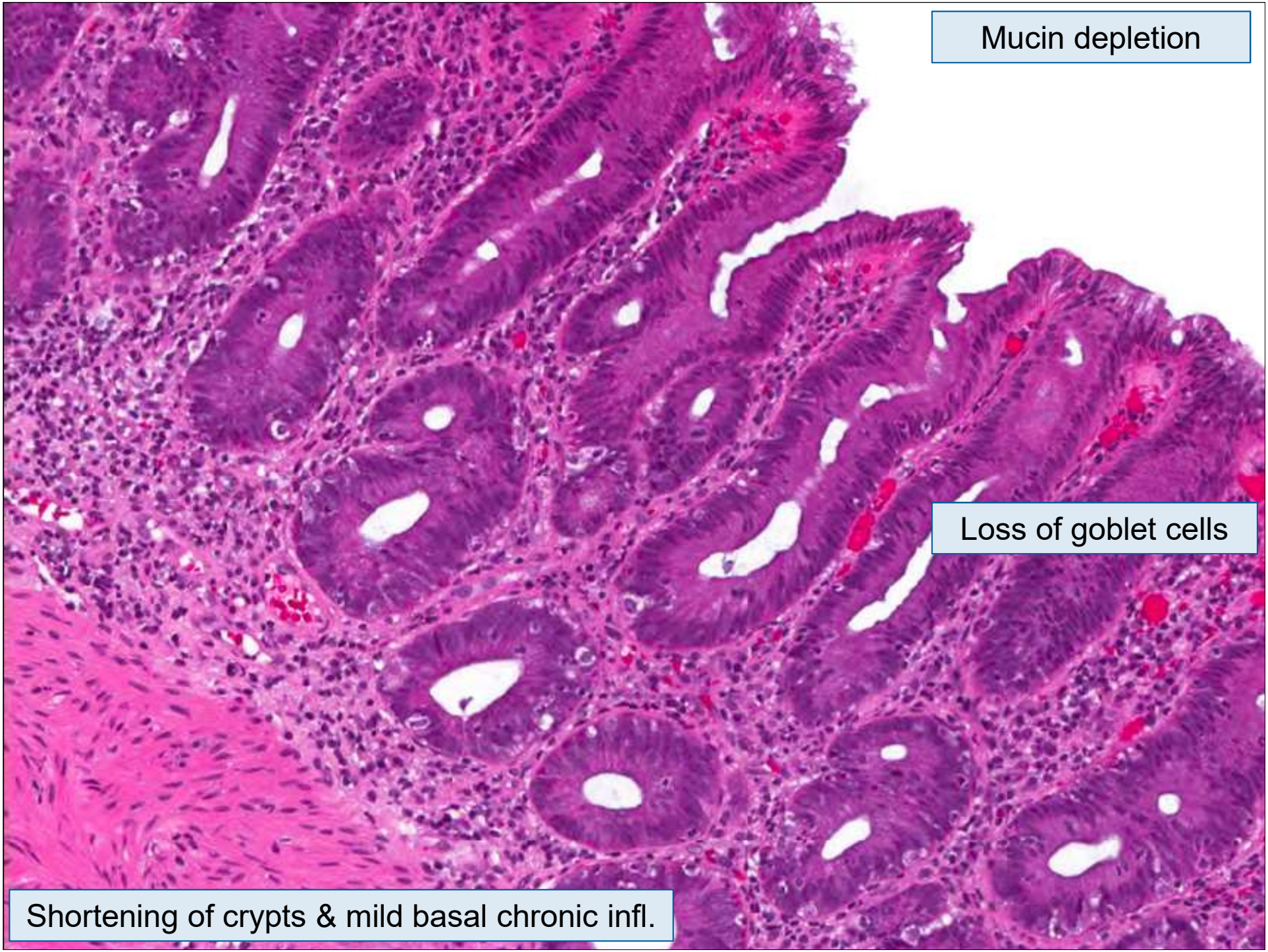
Gastrointestinal Biopsy Findings of Autoimmune Enteropathy

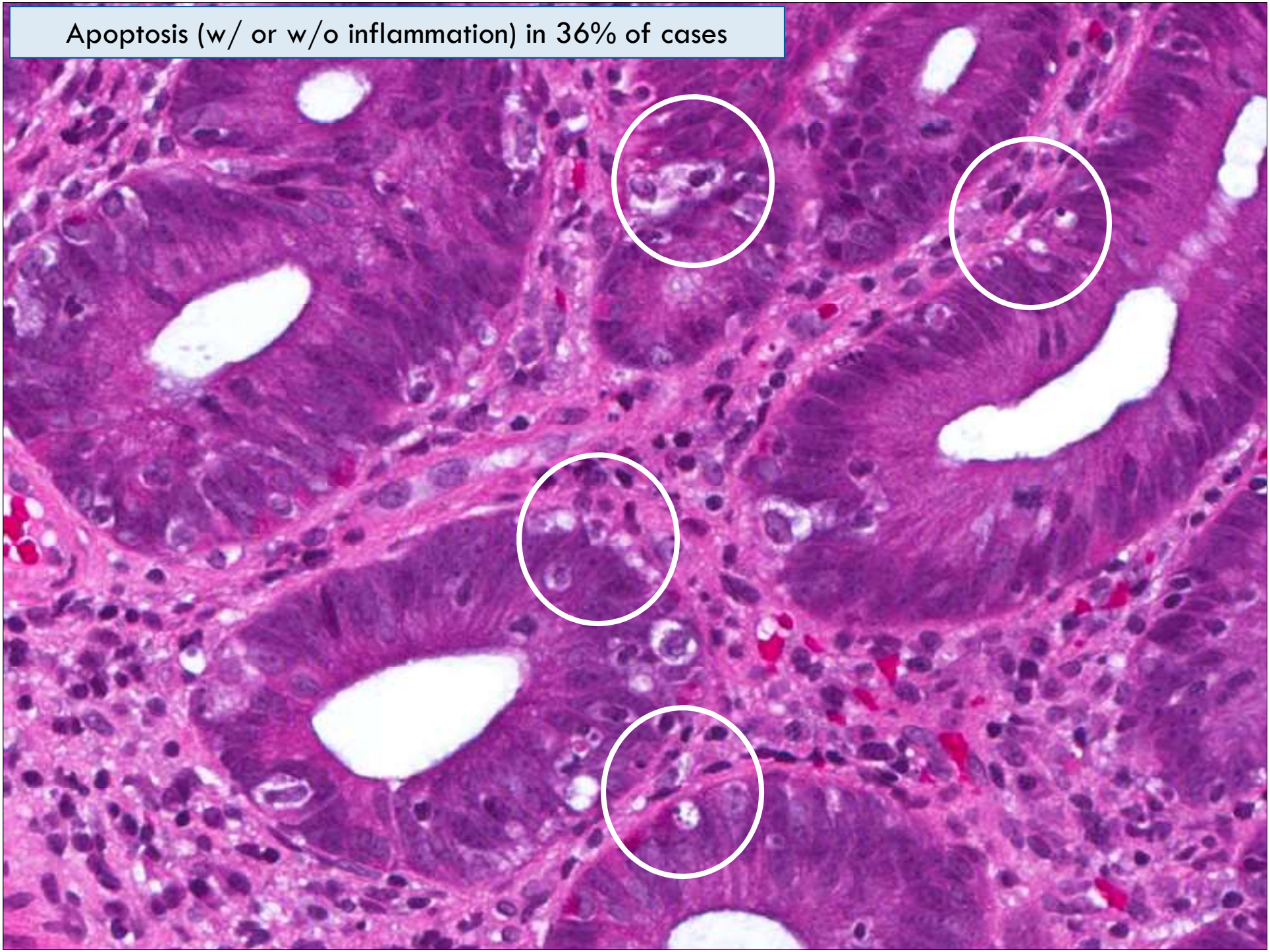
A Review of 25 Cases

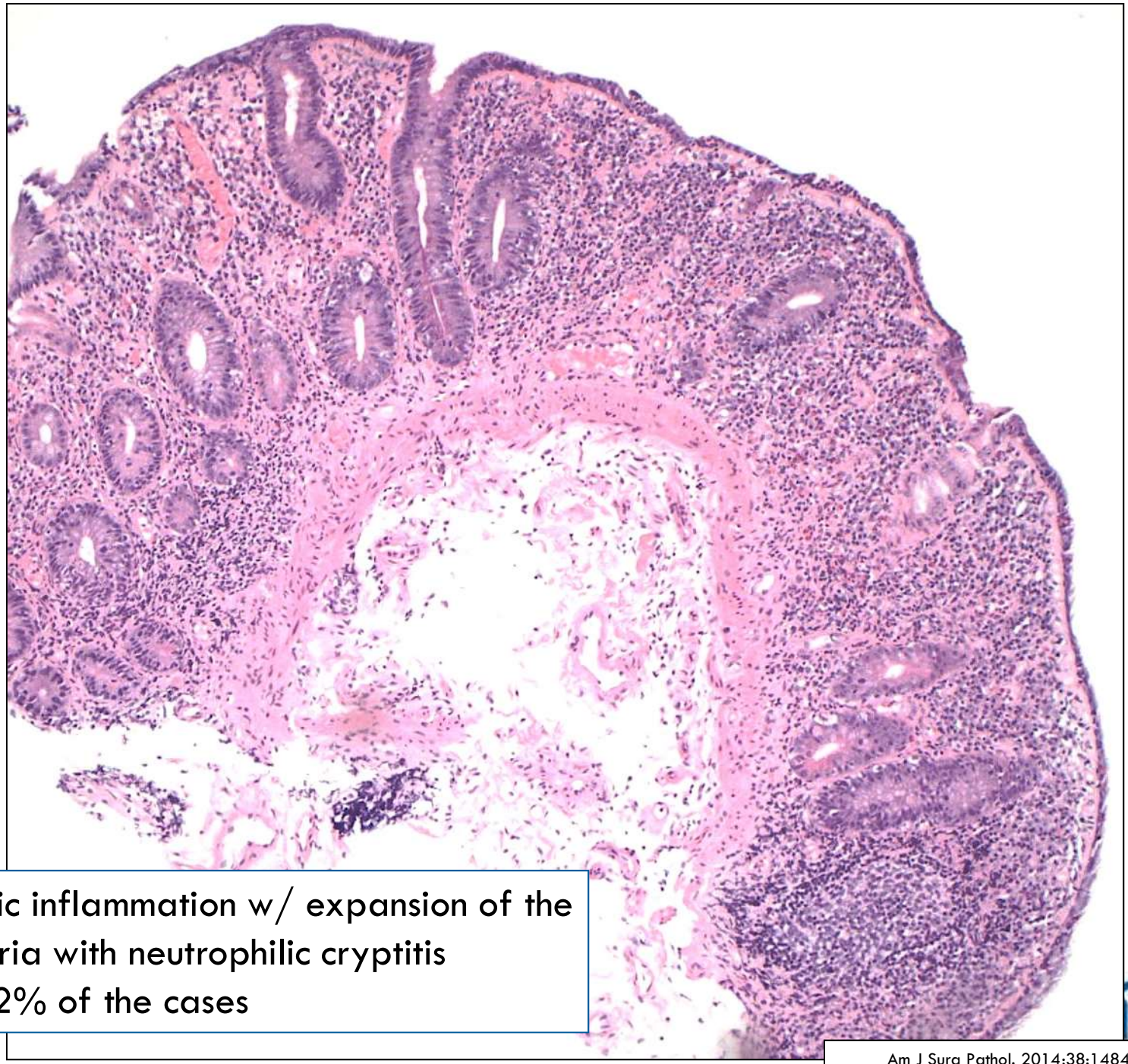
Ricard Masia, MD, PhD, Stephen Peyton, MBBS,† Gregory Y. Lauwers, MD,* and Ian Brown, MBBS, FRCPA†‡*

- Abnormal findings in non–small intestinal biopsies were present in 100% of patients.
  - Stomach: most common non–small intestinal site to exhibit abnormalities (86% of the cases),
  - Colon: abnormal in 65% of cases w/ biopsies

Am J Surg Pathol. 2014;38:1484-93


Mucin depletion
Loss of goblet cells
Shortening of crypts & mild basal chronic infl.

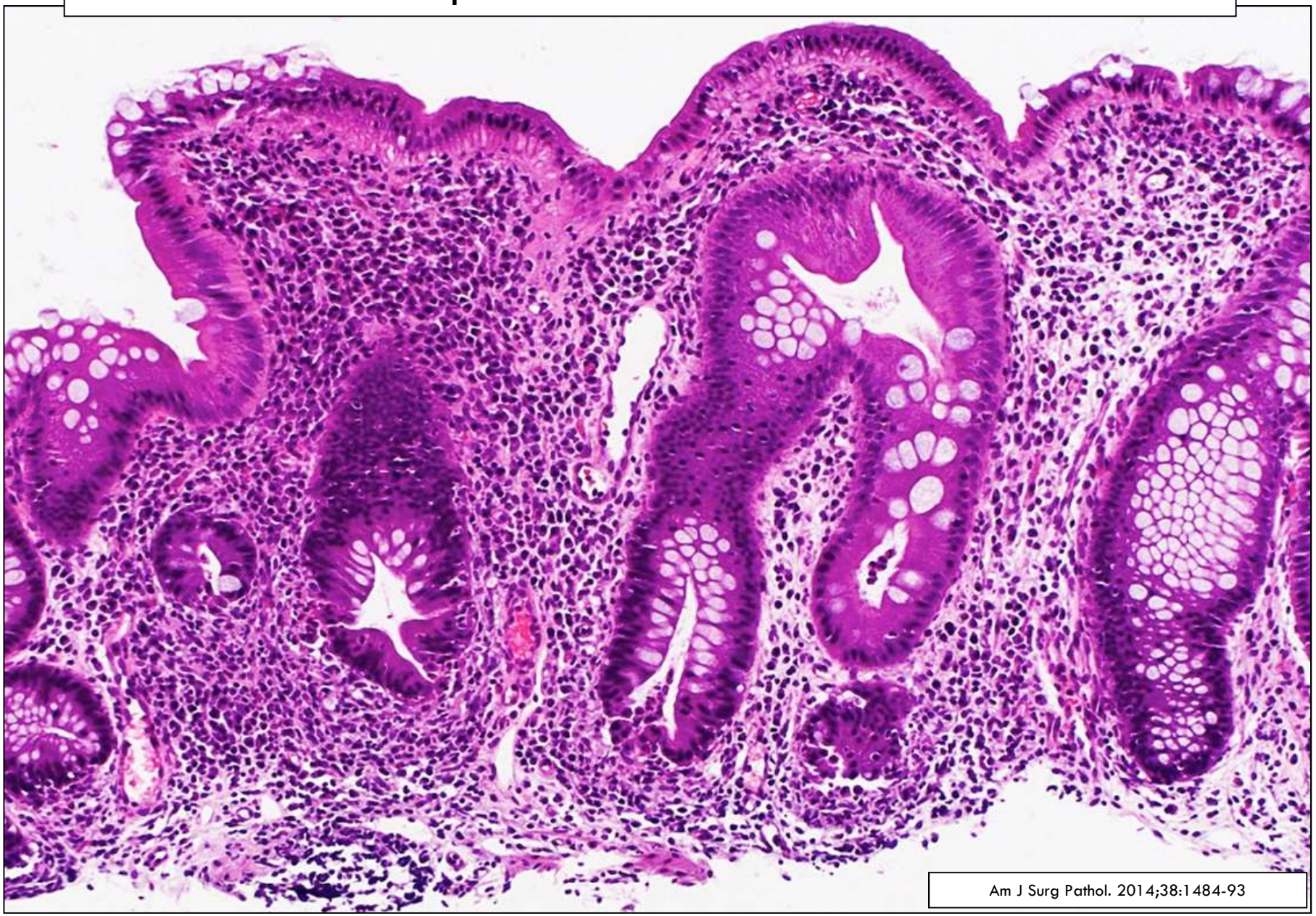

Apoptosis (w/ or w/o inflammation) in 36% of cases



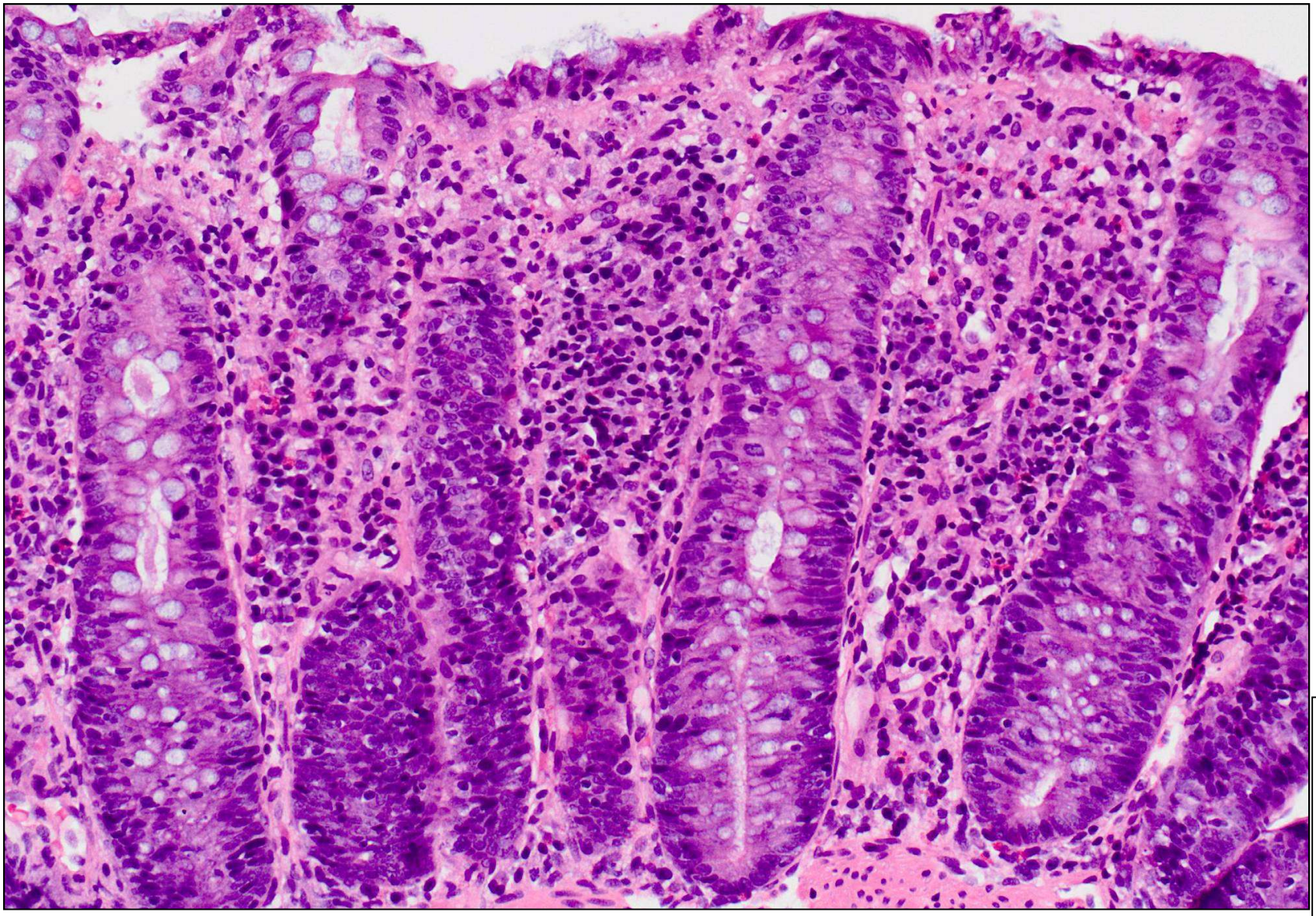
Active chronic inflammation w/ expansion of the lamina propria with neutrophilic cryptitis present in 32% of the cases

Am J Surg Pathol. 2014;38:1484-93

- Crypt architectural distortion in 9% of cases
- Paneth cell metaplasia in 9% of cases



Am J Surg Pathol. 2014;38:1484-93



Intraepithelial lymphocytosis w or w/o expansion of the lamina propria, reminiscent of lymphocytic colitis in 14% of the cases

Active inflammation alone seen in 9% of cases

Am J Surg Pathol. 2014;38:1484-93

Iatrogenic gut damages are common:
2-8% of pts receiving drugs experience an adverse reaction.

- Various (but limited) GI side-effect: diarrhea, constipation, nausea and vomiting.
- Entire gut is variably affected.
- Various mechanisms & patterns of injury:
  - Erosions/ulcerations/necrosis/fibrosis & stenosis
  - Hyperplastic/reactive changes
  - Inflammatory infiltrate (lymphocytes/eosinophils)
  - Crystals deposition
  - Apoptosis / Mitotic arrest / abnormal mitoses

Generic injury patterns	Specific injury patterns	Drugs
Inflammation	FAC	NSAIDs, NaPO4
	Chronic colitis	NSAIDs
	Microscopic colitis	NSAIDs, lansoprazole, ranitidine, PPI, ticlopidine, simvastatin, paroxetine carbamazepine, penicillin, flutamide, cyclo 3 Fort, sertraline
	Hypereosinophilia	NSAIDs, Estroprogestatifs, Plavix?
	Malakoplakia	Corticosteroids
	Pseudomembranous colitis	Antibiotics, PPI
Fibrosis	Diaphragms	NSAIDs
		sumatriptan,dopamine, methysergide, amphetamines, estrogens, ergotamine, alostron, digitalis, pseudoephedrin, vasopresin, interferon
	Pseudomembranous colitis	
Apoptosis / IELs	'Apoptotic ileitis / colitis'	Mycophenolate, Ipilimubab NSAIDs, NaPO4, 5-FU
	Melanosis coli	NSAIDs; Laxatives
Increased / abnormal mitosis	Increased number	Colchicine/ Taxane
	Mitotic arrest	
Erosion / perforation		NSAIDs, KCL, Iron, Kayexalate, Cochicine, Yttrium 90,corticosteroids
Epithelial atypia		IV cyclosporin

Dx methodology: temporal relationship / improvement with withdrawal & test w/ rechallenge is 'unpractical'.
….in most cases: index of suspicion / clinicopathologic exercise

NSAIDs and colonic damage: a long tale

- Possibly increasing due to use of enteric coated or sustained (slow) release formulation (higher concentrations in the prox. colon)
- Various types of Colitis
  - Focal active colitis and chronic colitis.
  - Collagenous colitis and Lymphocytic colitis
  - Pseudomembranous colitis (*Diclofenac*®)
  - Eosinophilic colitis (*Naproxen*®)
  - Ulcers (Rt colon)
  - Diaphragm disease
  - Exacerbation of pre-existing IBD or diverticular disease (or perforation)

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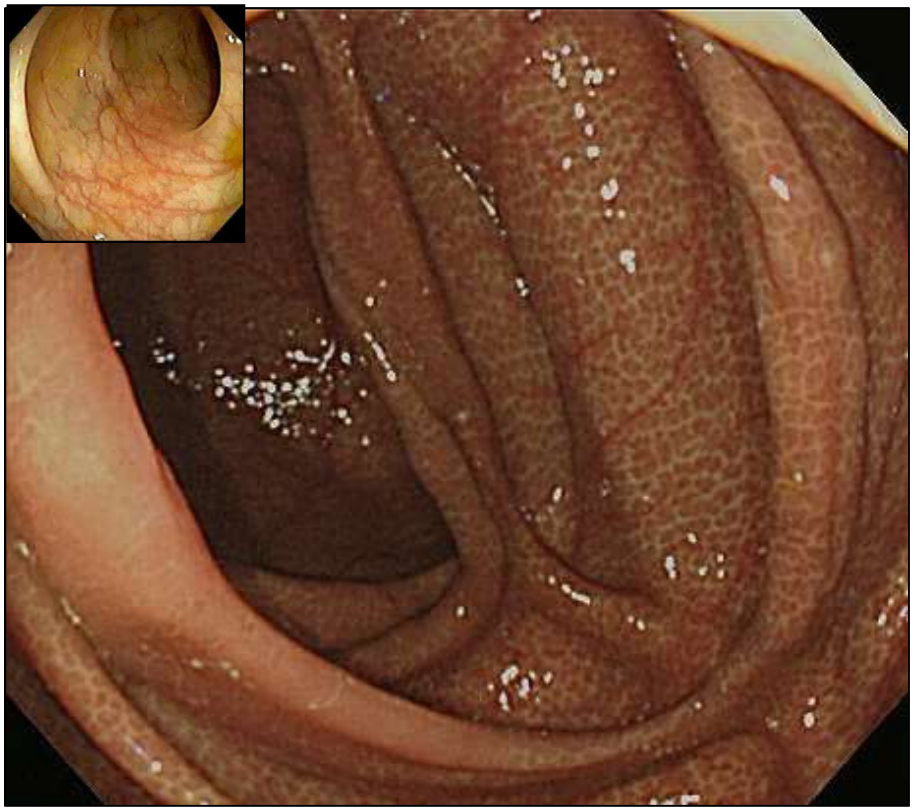
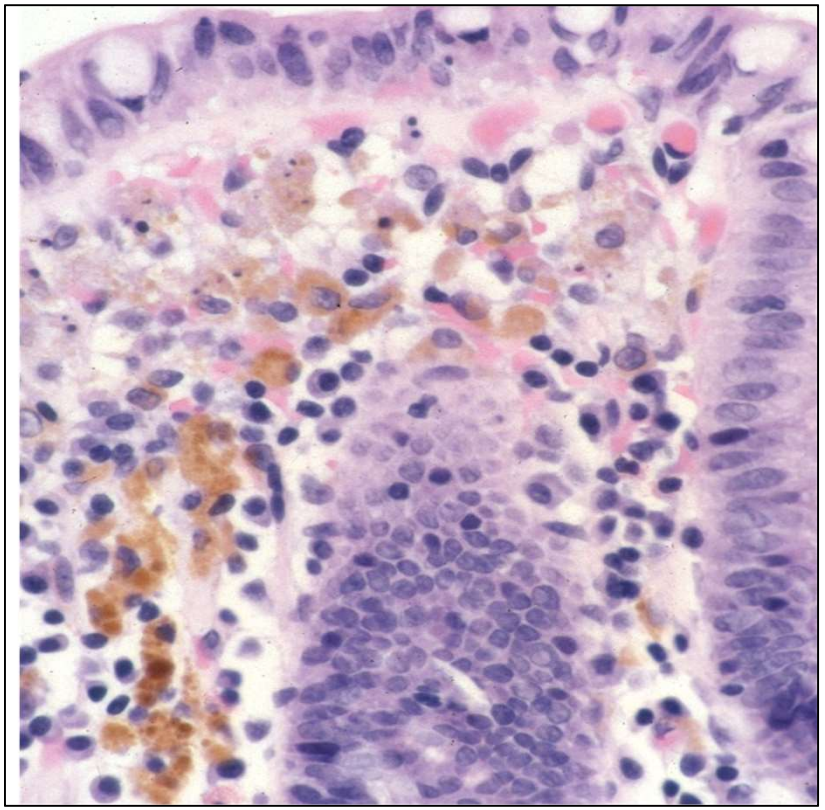
Melanosis coli





- Lipofuscin is formed from the breakdown of apoptotic epithelial cells
- NSAIDs and other drugs (e.g., 5-FU) can lead to significant apoptosis and thus melanosis coli.

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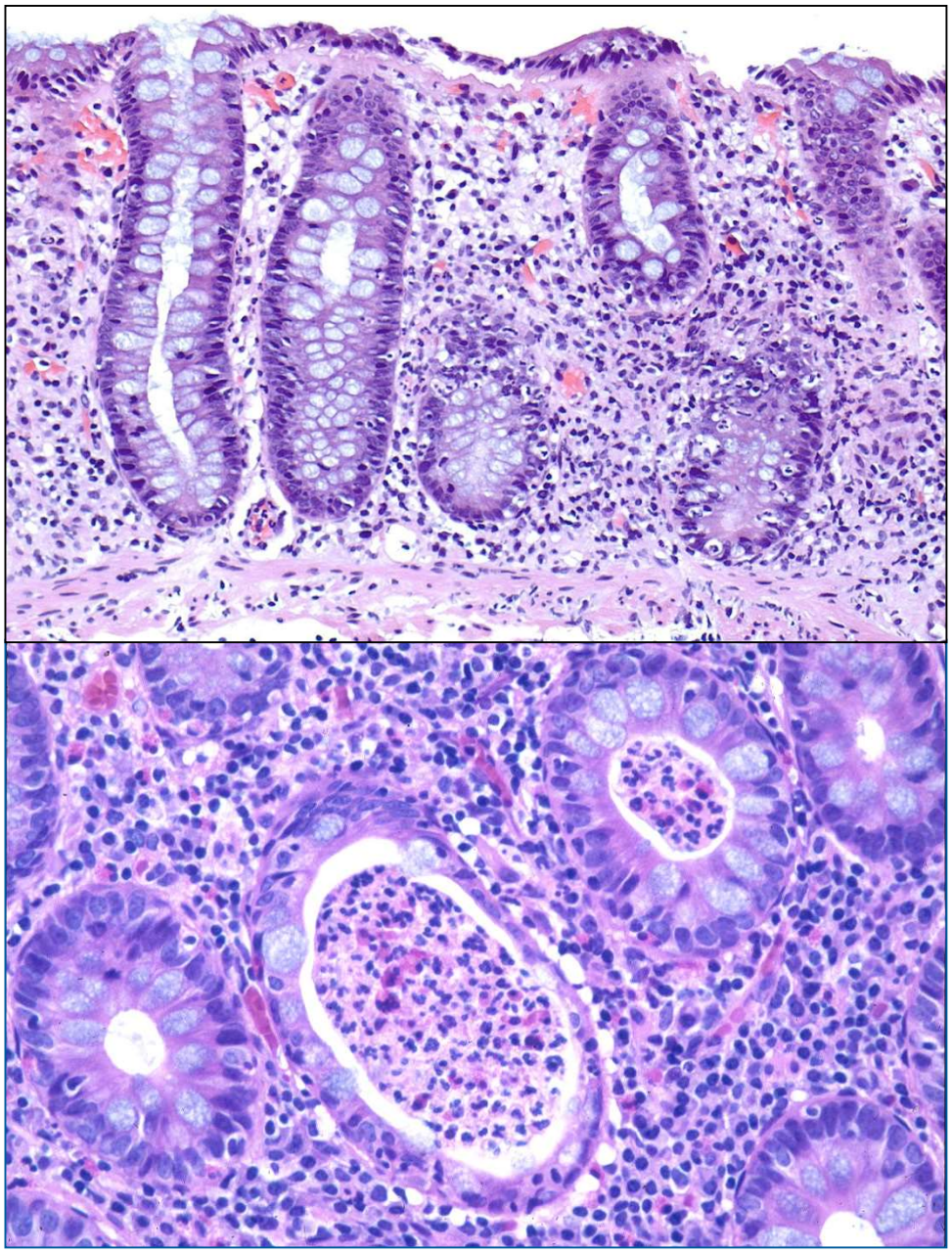
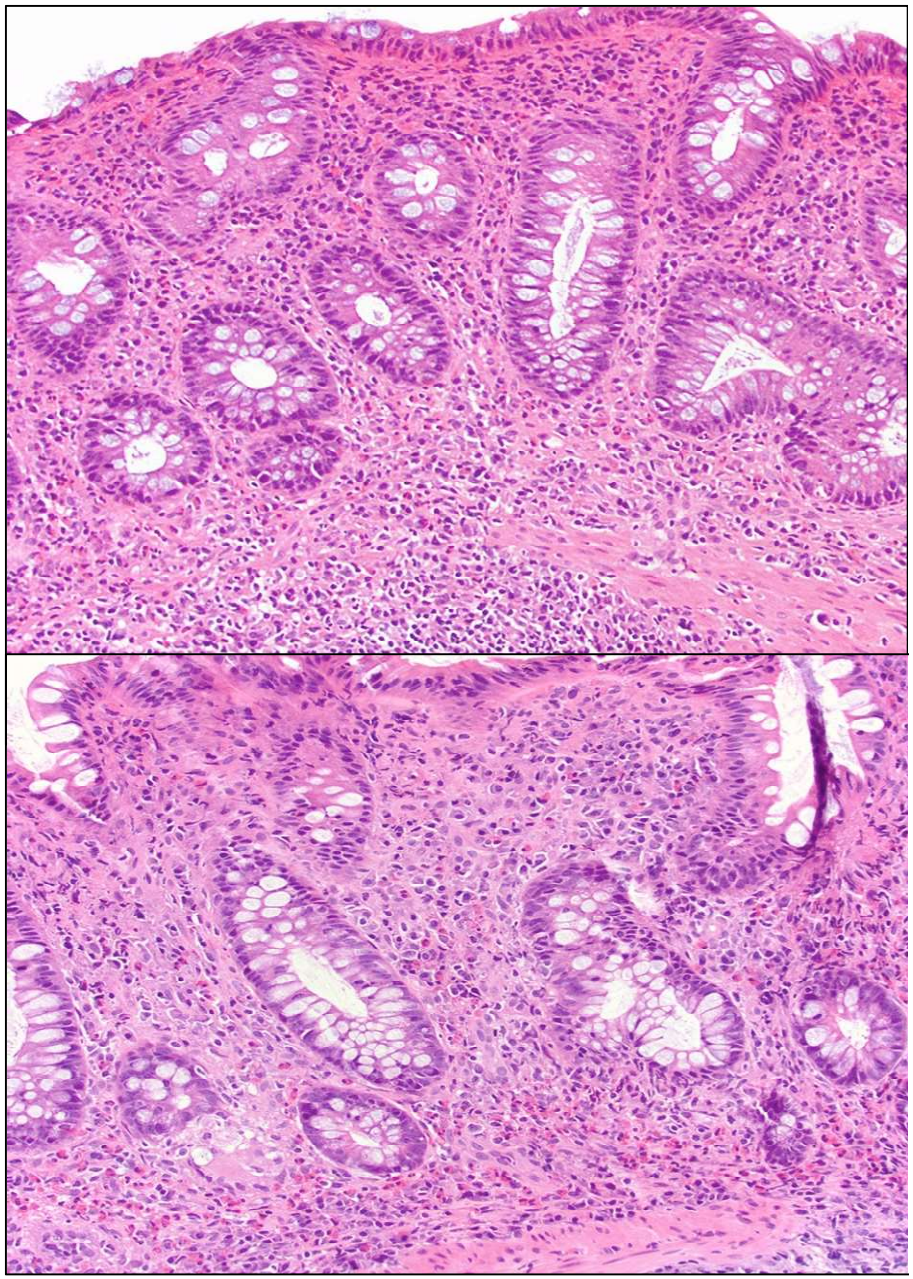
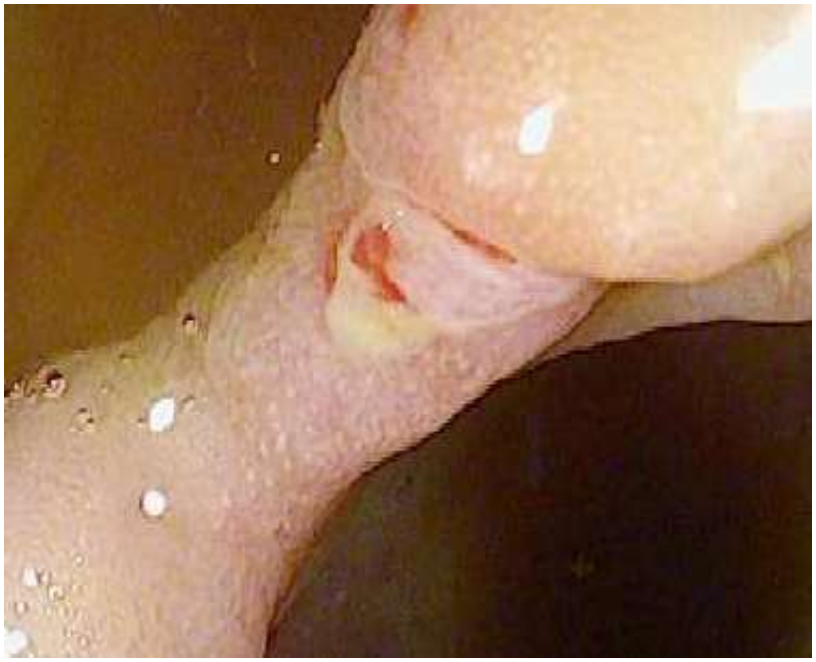
Focal active colitis

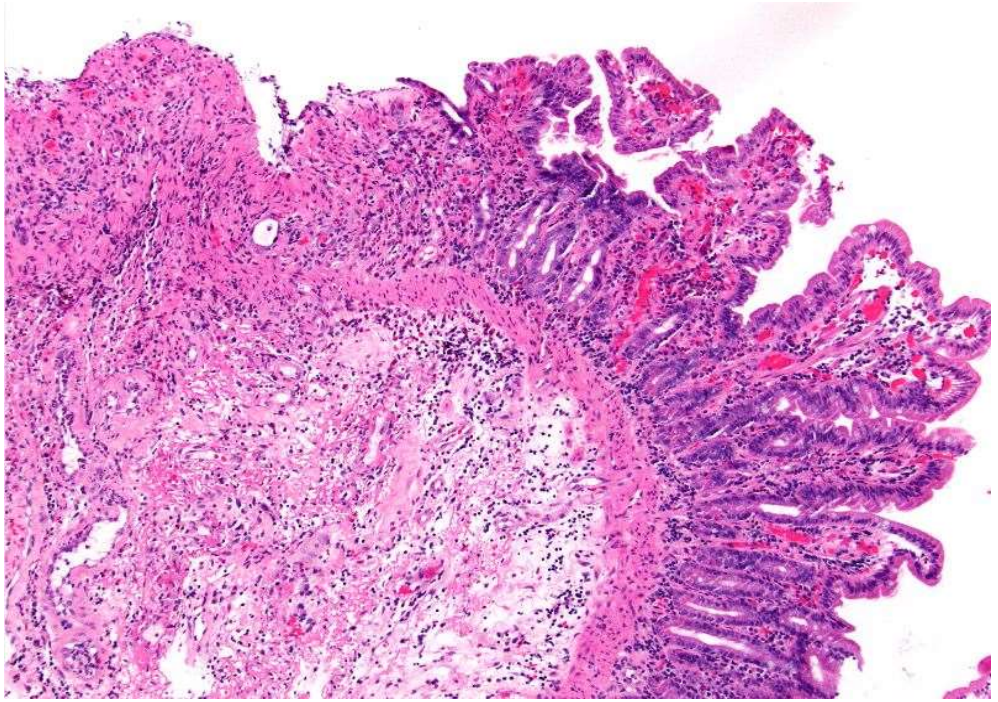


Right sided ‘NSAIDs chronic colitis’





- NSAIDS – Ulcer can occur anywhere in colon, but more common on right side.

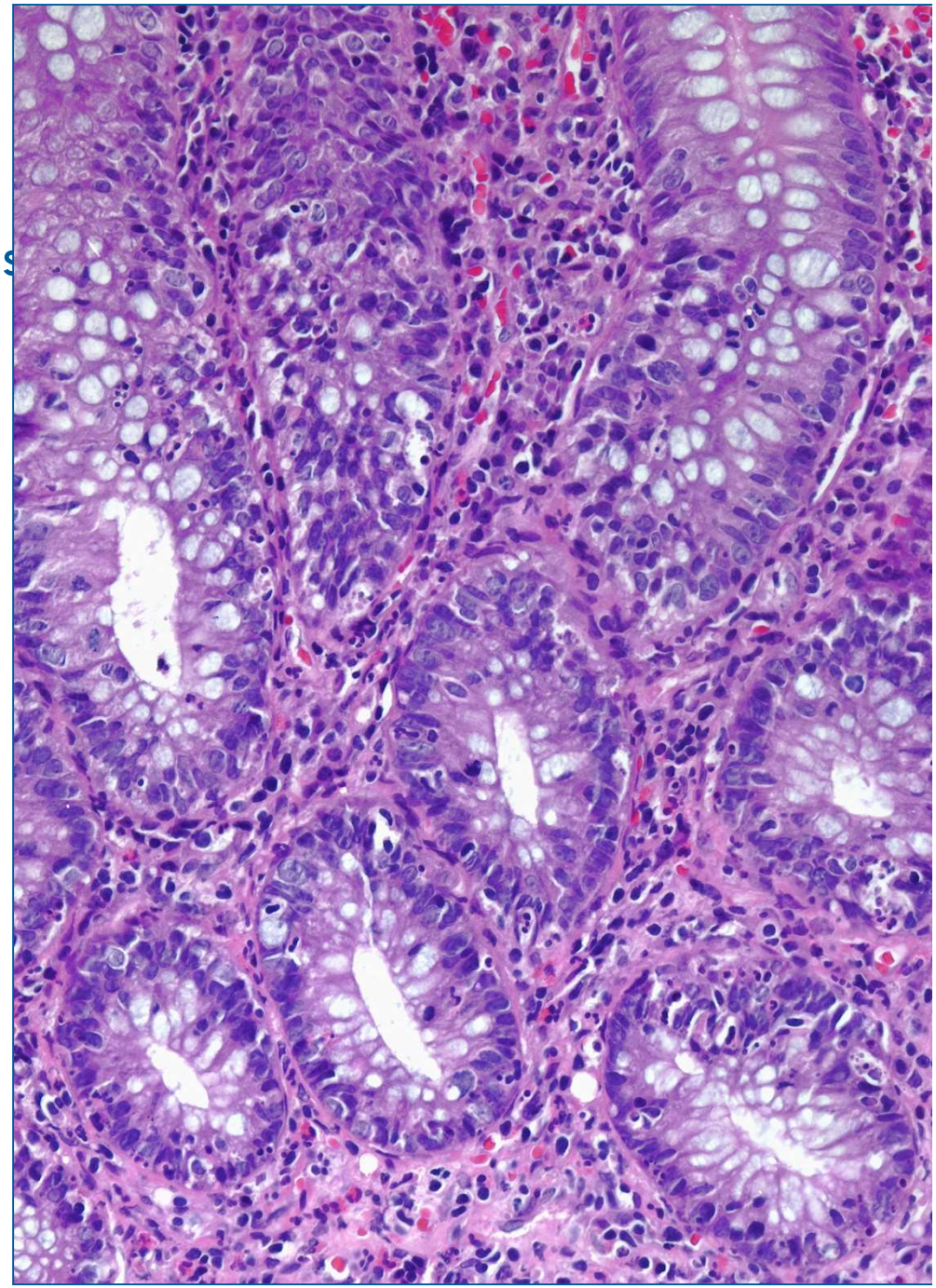


- sharply circumscribed with ischemic-type histology

Solitary cecal ulceration, ulceration secondary to a diverticulum, local ischemia, stercoral ulceration and solitary rectal ulcer syndrome need to be ruled

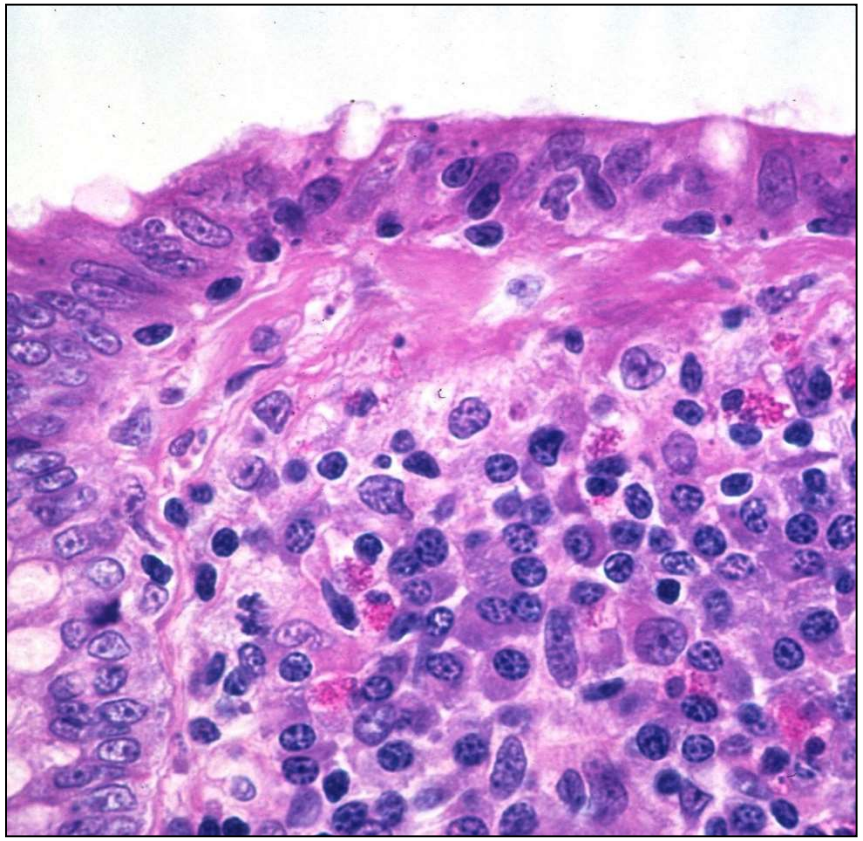
NSAIDs colitis

- Crypt disarray, erosion, cryptitis & crypt abscesses but:
  - *(no marked cryptic architectural distortion)*
  - *No basal lymphocytic infiltrate*
- Reactive epithelial changes
- Apoptosis.
- Mild/marked (inflammation:
  - lymphocytes, plasma cells, neutrophils



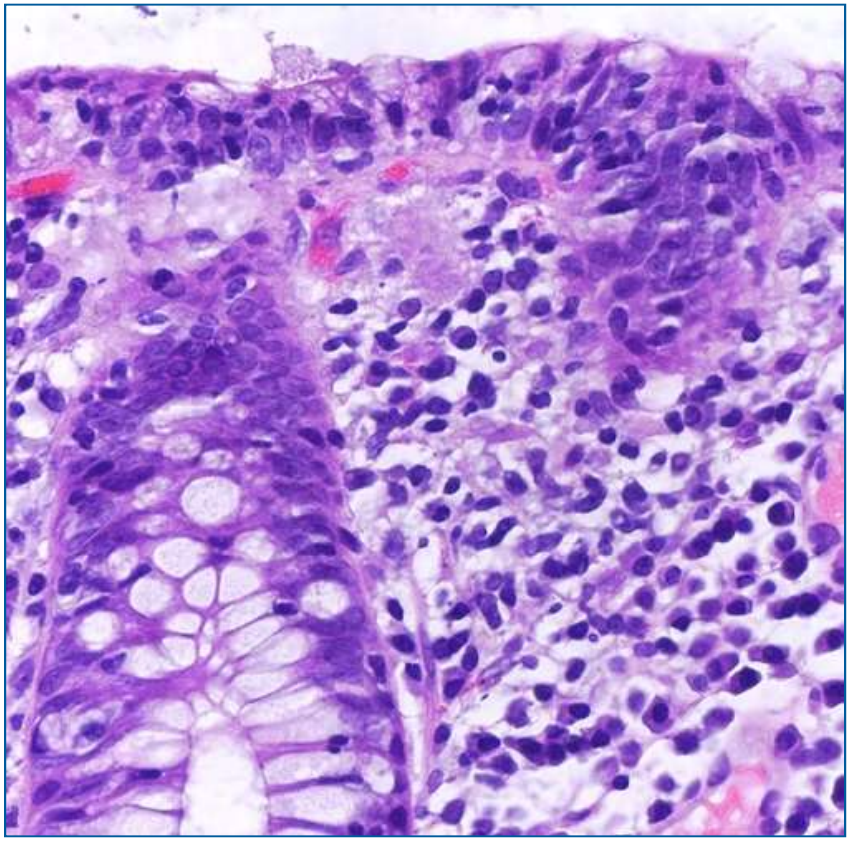
Goldstein *Am J Clin Pathol* 1998

Collagenous Colitis



NSAIDs, Olmesartan, others

Lymphocytic colitis (10%)



NSAIDs, PPI, SSRI; herbal remedies, ticlopidine, carbamazepine

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NSAIDS and 'microscopic colitis'

Collagenous colitis

- *Case control study of 31 pts w/ collagenous colitis*
  - 19 patients using NSAIDs (vs. 4 controls)
  - All developed diarrhea after beginning NSAID therapy
  - 3 improved with discontinuation of NSAIDs
  - 1 re-challenged: recurrence of diarrhea

Riddell et al. Gut 1992

Lymphocytic colitis

- *40 pts w/ lymphocytic colitis*
  - Half taking NSAIDs
  - Patients on NSAIDs had higher intraepithelial lymphocyte counts
  - However, no correlation between NSAID use and clinical course

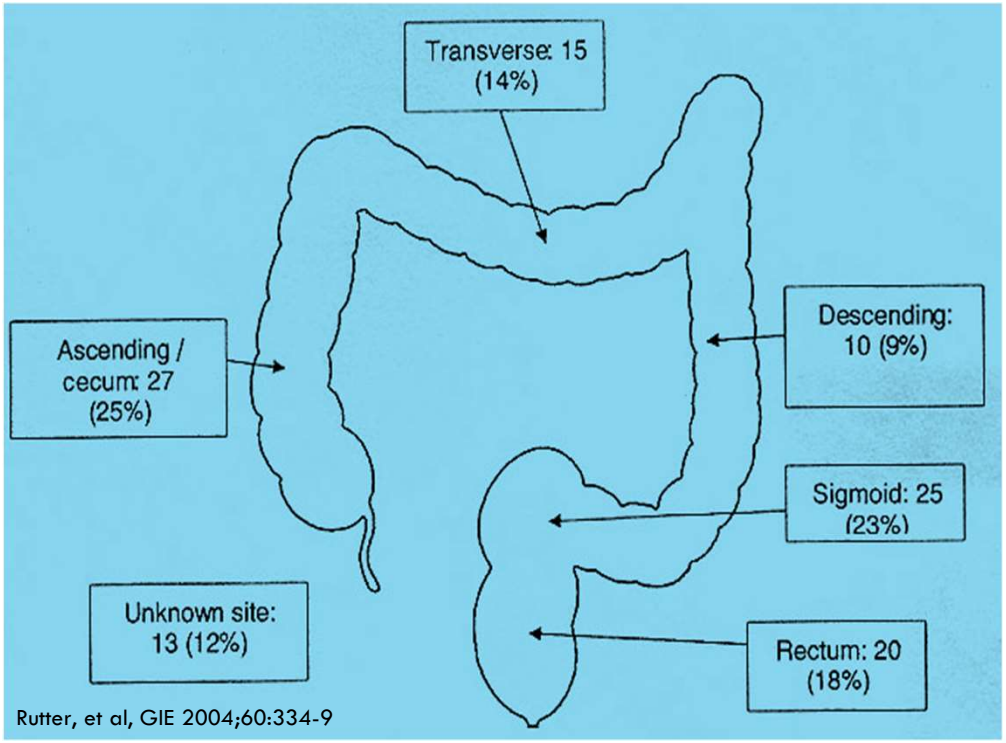
Wang N, et al. Am J Surg Pathol 1999

Dysplasia in Inflammatory Bowel Disease

Dysplasia is frequently synchronous to CRC:

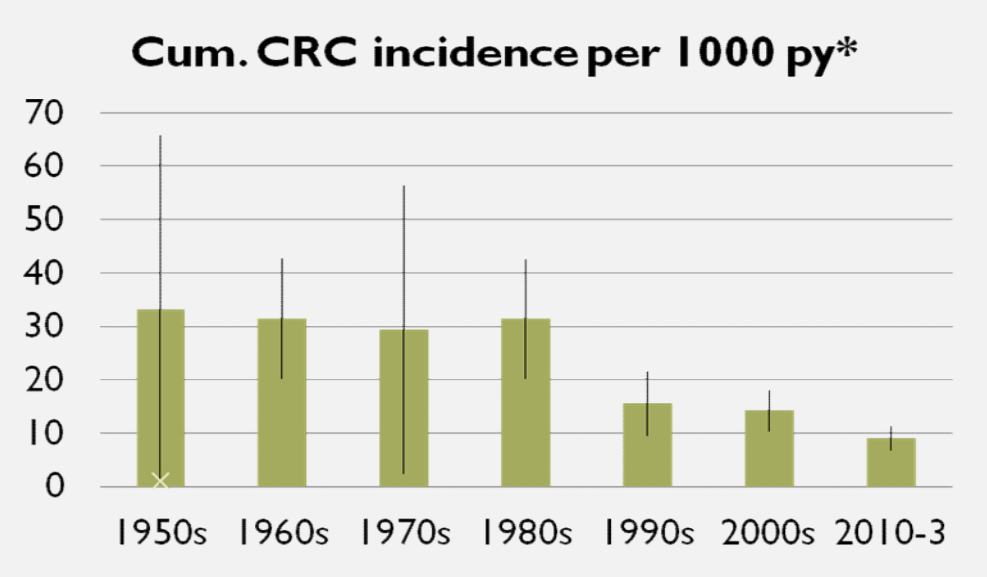
- 74% of 50 colectomy (average of 27 bloks)
- 92% of UC cases (76% LGD;85% HGD)
- 27% to 100% of patients w/ Crohn's colitis

Distribution of 104 dysplasias & 6 CAs in 56 UC patients



- **3% of CRC and 11% of dysplasia found during initial colonoscopy**

Medical therapy & surveillance have been effective in decreasing the incidence of CRC in IBD……



* Castaño-Millo et al. Aliment Pharmacol Ther 2014;39:645-9

…..while endoscopic surveillance can be credited with earlier diagnosis of CRC and better prognosis

Author	Locale and study dates	Cancers within surveillance	5-year survival	Cancers outside of surveillance	5-year survival	*P* value
Giardiello[28]	Johns Hopkins, 1956–1991	18*	88%	22	15%	<0.001
Choi[27]	Lahey Clinic, 1974–1991	19	77%	22	36%	0.026
Connell[29]	St. Mark's, 1947–1992	16	87%	114	55%	0.024

*Includes cancers detected at surveillance colonoscopy or prophylactic colectomy.

Loftus, J Clin Gastroenterol 2003; 36:S79-S83

Unequivocally neoplastic lesions

NEGATIVE

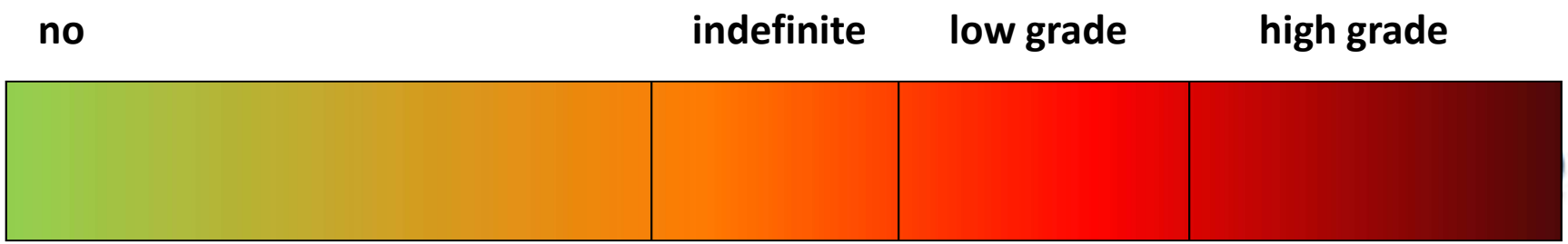
- Range of epithelia from truly normal, normalized, reactive and regenerative
- Diagnosis of dysplasia is based on recognition of what is perceived as *not* dysplasia

LOW-GRADE DYSPLASIA

- Resemble sporadic adenomas
- Lack of maturation & top-down pattern
- Limited glandular distortion
- Pencil-shape hyperchromatic nuclei
- Limited nuclear stratification
- Reduced differentiation
- Increased proliferation
- Clonal character

HIGH-GRADE DYSPLASIA

- Marked architectural distortion
- Lack of maturation
- Marked nuclear stratification
- Marked nuclear enlargement
- Marked nuclear hyperchromasia
- Mitoses onsurface
- Reduced differentiation
- Increased proliferation
- p53 overexpression or loss

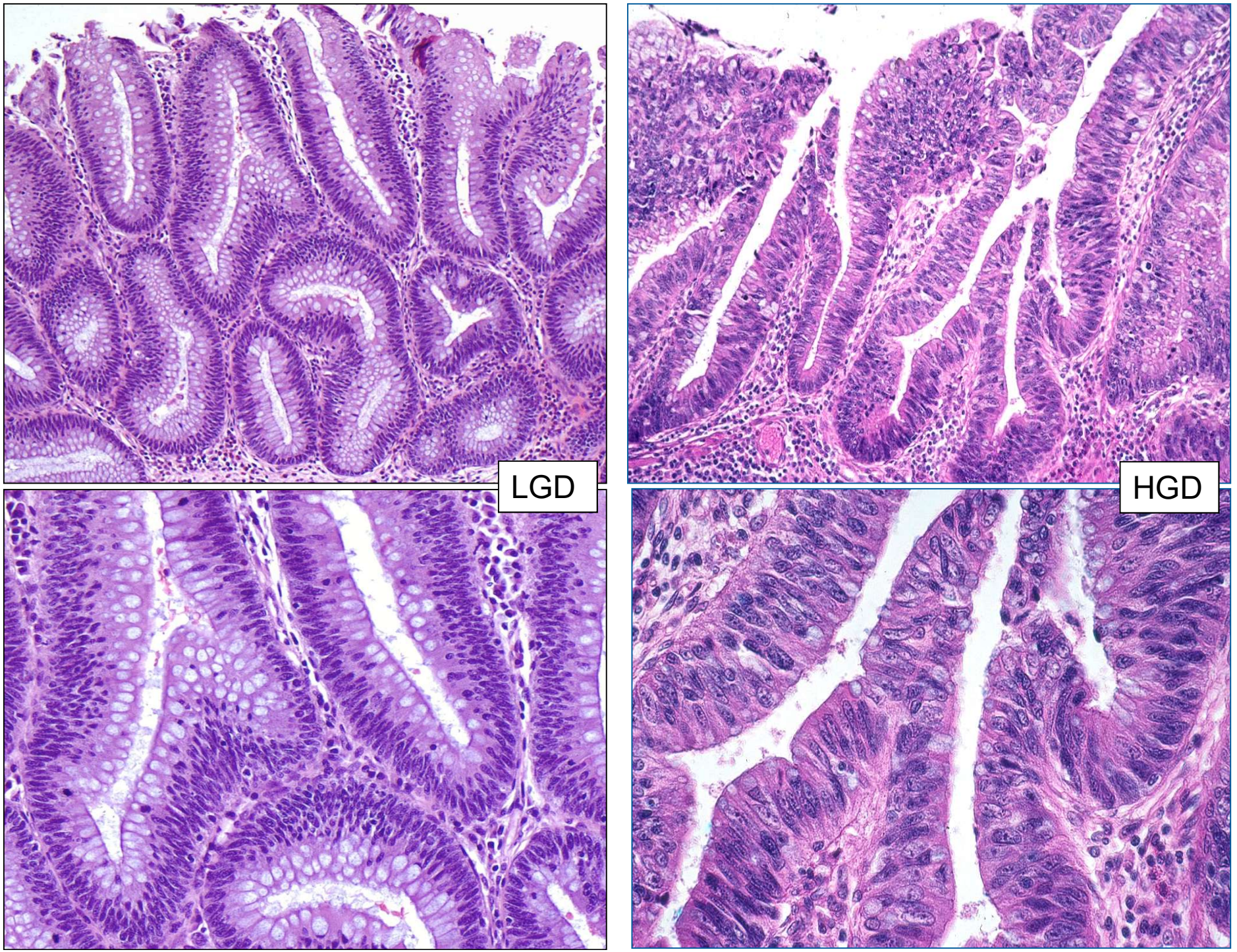


Inter-observer agreement in assessing dysplasia

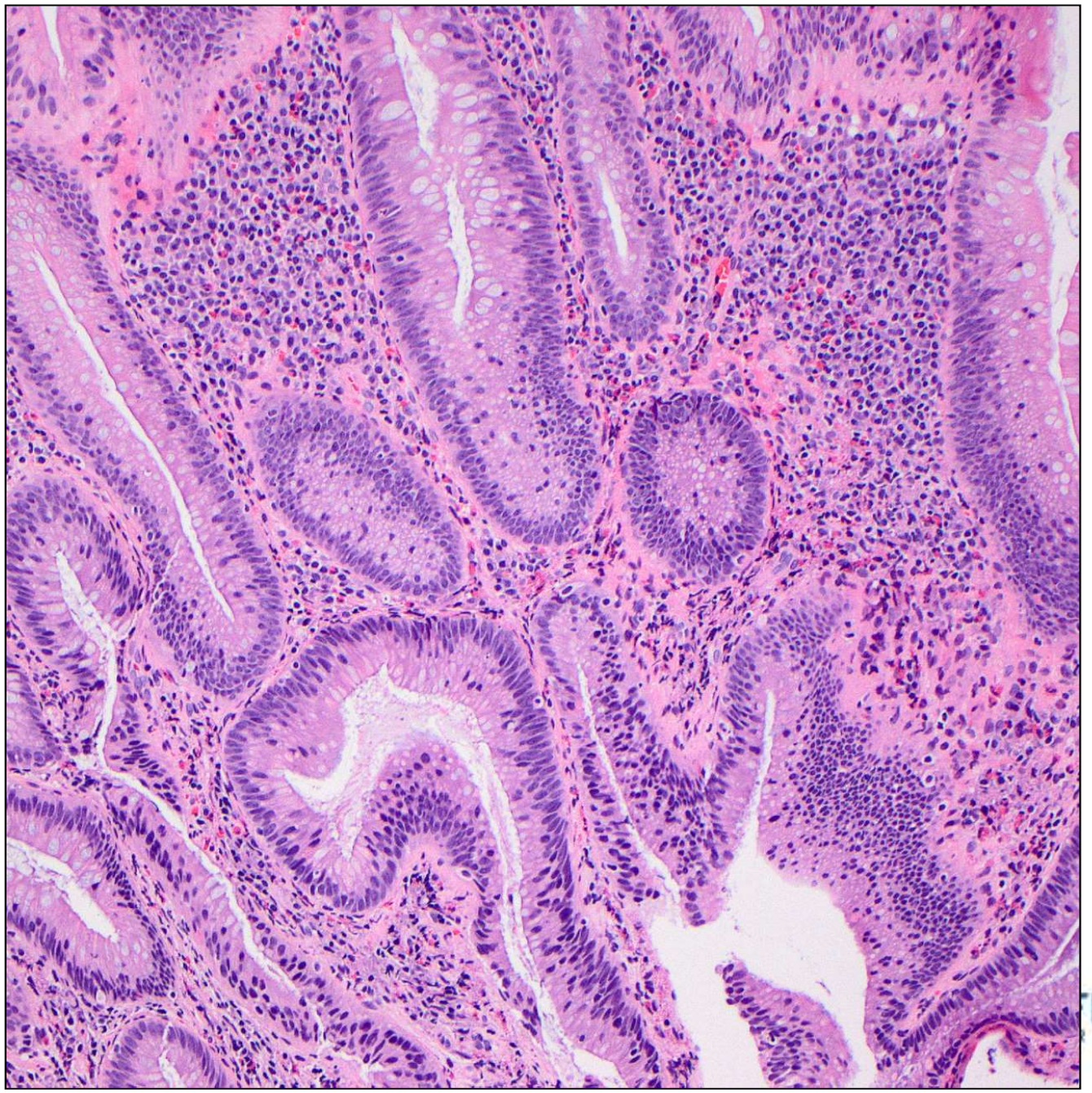
- Overall: fair ($\kappa \sim 0.3$)
- Indefinite & LGD: poor to fair ($\kappa \sim 0.0$-0.3)
- Negative & HGD: good ($\kappa \sim 0.3$-0.5)
- Similar agreement for GI specialists & general pathologists
- Weaknesses in study design
  - Lack of "real life" histological context
  - Assessment of precision, not accuracy (outcomes)

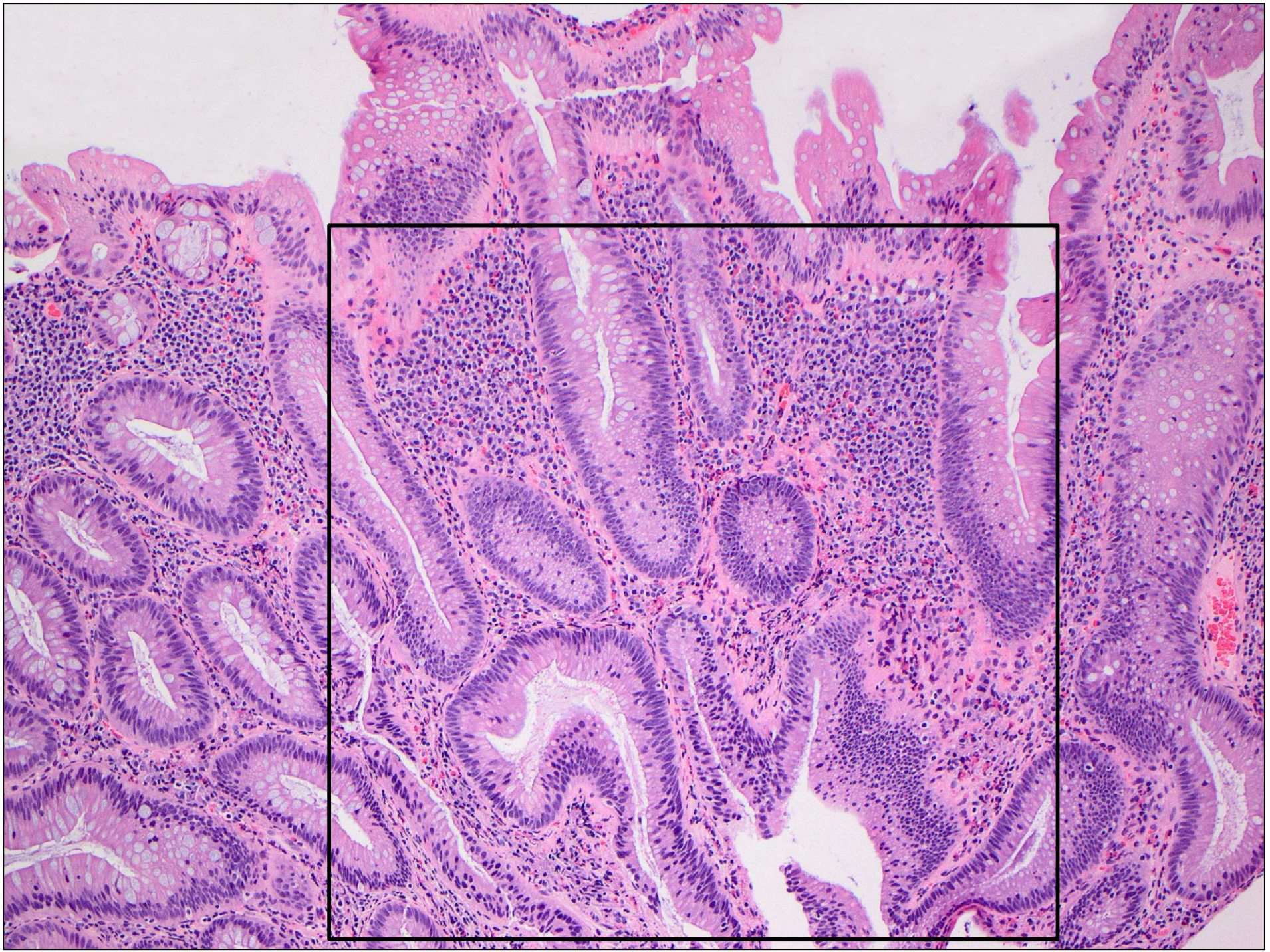
Impediments to accurate grading of dysplasia

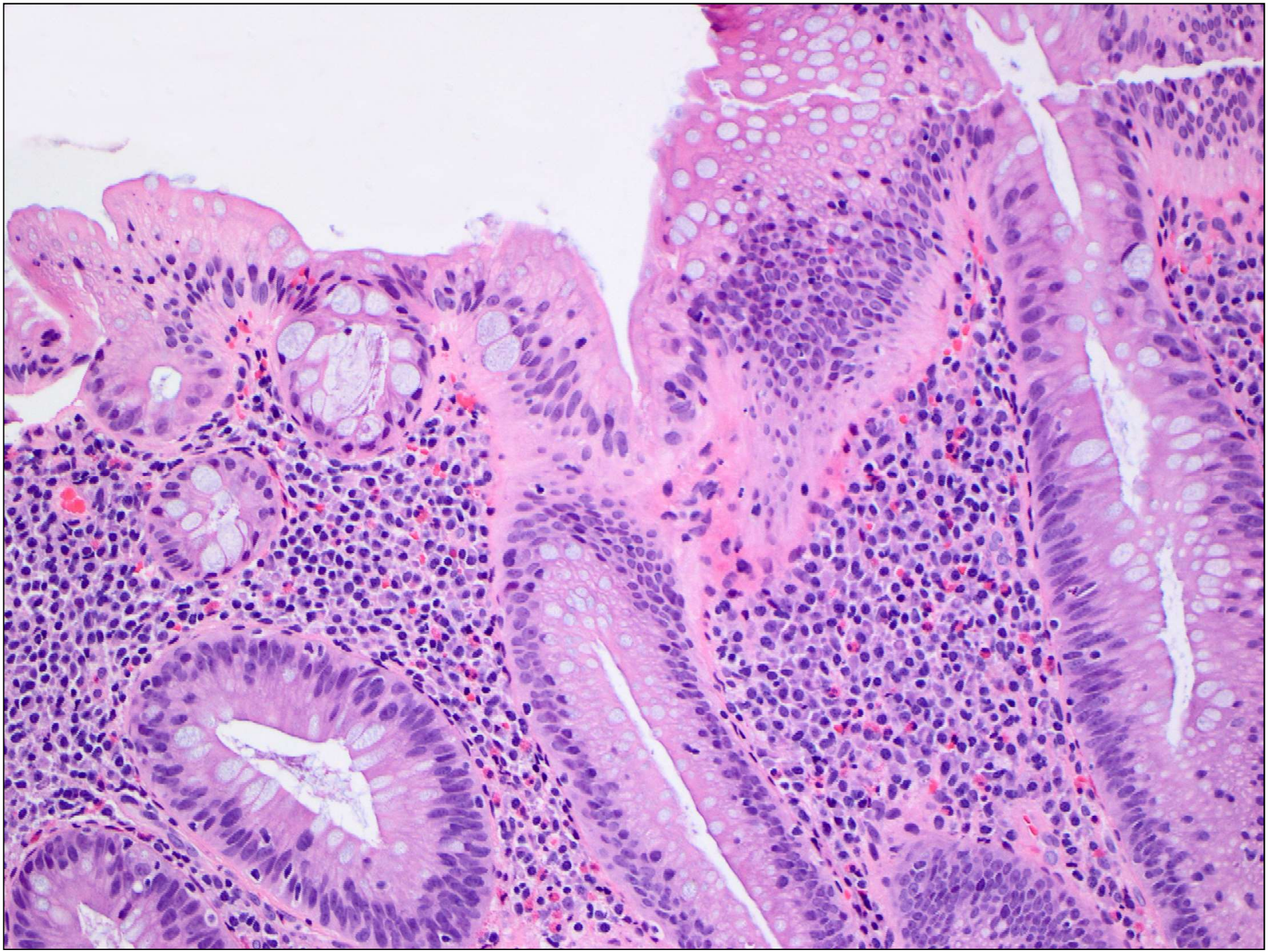
- Technical (fixation, processing, sampling)
- Overlapping features of dysplastic and reactive changes (active inflammation, post-inflammatory regeneration)
- Synthesis of several histologic parameters which may have conflicting significance
- Histological diversity of dysplastic changes


LGD
HGD

Surveillance dilemma: dysplasia or not?



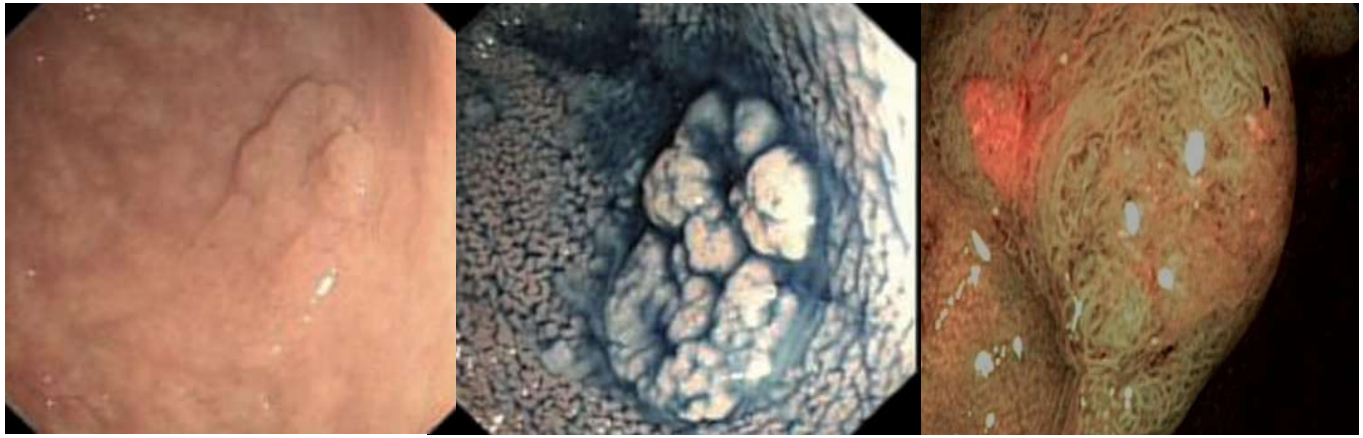


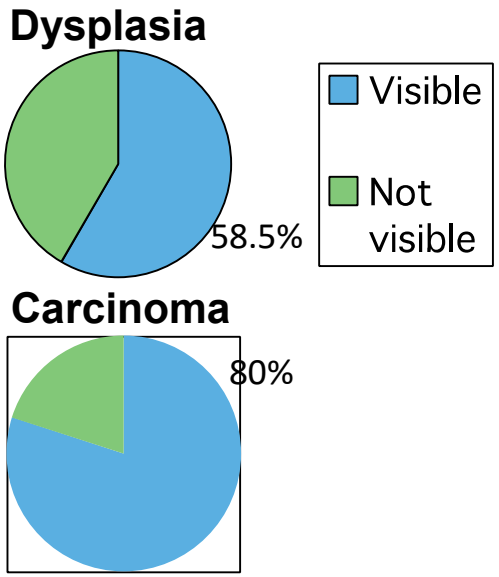


Dysplastic lesions in IBD were once reported to not always be endoscopically visible but with newer technologies, investigators now recognize that most of these lesions are visible

Review of 1339 surveillance endoscopies in 622 pts
128 lesions identified:65 dysplastic lesions and 10 CAs

Gastrointest Endosc 2007:65:998-1004





- Proportion of pts w/ dysplasia is 0-10% greater with chromoendoscopy
- # of dysplastic lesions detected is greater in patients who had both chromoendoscopy & white-light examination with the number of lesions discovered increased by almost 2-fold (RR 1⁄4 1.9, 1.4-2.7)
- Chromoendoscopy increases the duration of colonoscopy by a mean of 11 minutes (range 9-12 minutes).

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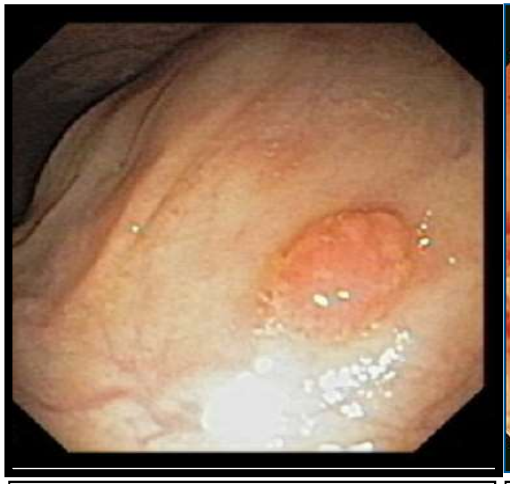
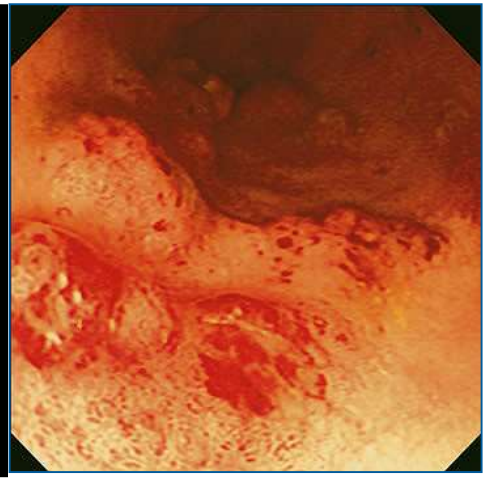
Gastroenterology 2015;148:639–651

Clinically relevant classification of Dysplasia in IBD

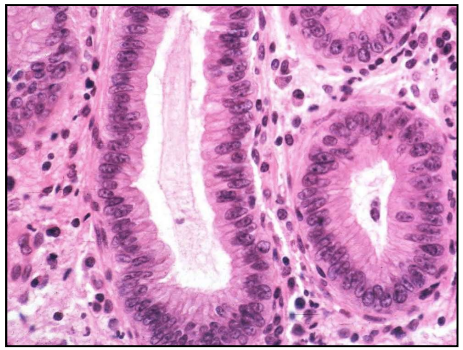
1. **Endoscopic (gross)**
   a. **Flat (endoscopically undetectable)**
   b. **Elevated (endoscopically detectable)**
      - **Adenoma like**
      - **Non Adenoma like**

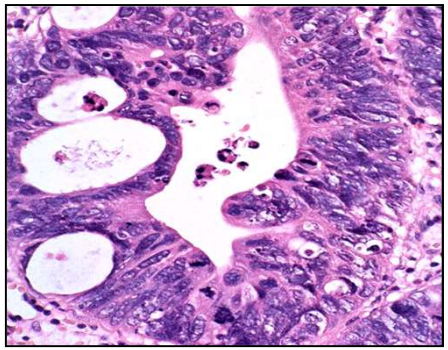




•Sessile/pedunculated •Well circumscribed •Smooth surface •Visible borders •Non ulcerated •No stricture •No mucosal tethering	•Sessile •Poorly circumscribed •Irregular surface •Indistinct border •Ulceration/necrosis •Stricture •Tethering
LGD	HGD

2. **Microscopic:**
   - **Negative**
   - **Indefinite**
   - **Positive (LGD – HGD)**





Progression of *flat* & outcome study of *polypoid* dysplasia

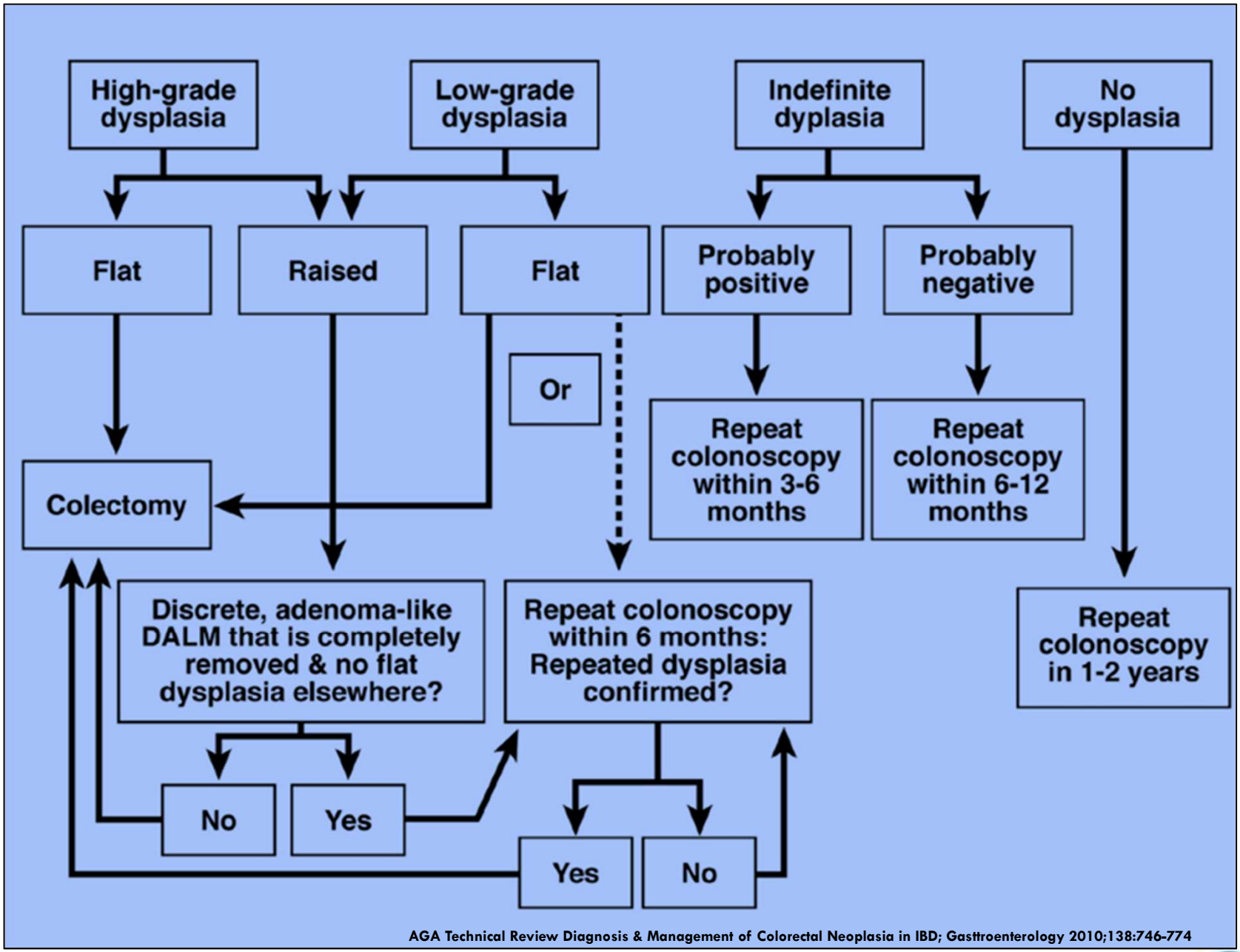
Gastroenterology 1999 ;117:1295-300.

Mean follow up: 15 months (4.5-50.5)

DIAGNOSIS	46 Patients w/ FLAT Low Grade Dysplasia	
	Colectomy <6 mo. after Dx (n=11)	Colectomy after F.U* (n=14)
Carcinoma	**2**	**5**
HGD	**1**	**3**
	27%	**57%**
LGD	**7**	**5**
Negative	**1**	**1**

Clin Gastro Hepatol 2004;2:534-541.

Feature	UC patient groups		Non-UC patients
	Adenoma-like DALM	Sporadic adenoma	Sporadic adenoma
No. of patients	24	10	49
Mean follow-up (mo)	82.1	71.8	60.4
Pts who developed additional polyps	15 (62.5%)	5 (50%)	24 (49%)
Pts who developed flat dysplasia	1 (4%)	0 (0%)	0 (0%)
Pts who developed adenocarcinoma	1 (4%)	0 (0%)	0 (0%)



AGA Technical Review Diagnosis & Management of Colorectal Neoplasia in IBD; Gasttroenterology 2010;138:746-774

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With more surveillance colonoscopies come more unconventional lesions that need to be fully evaluated….

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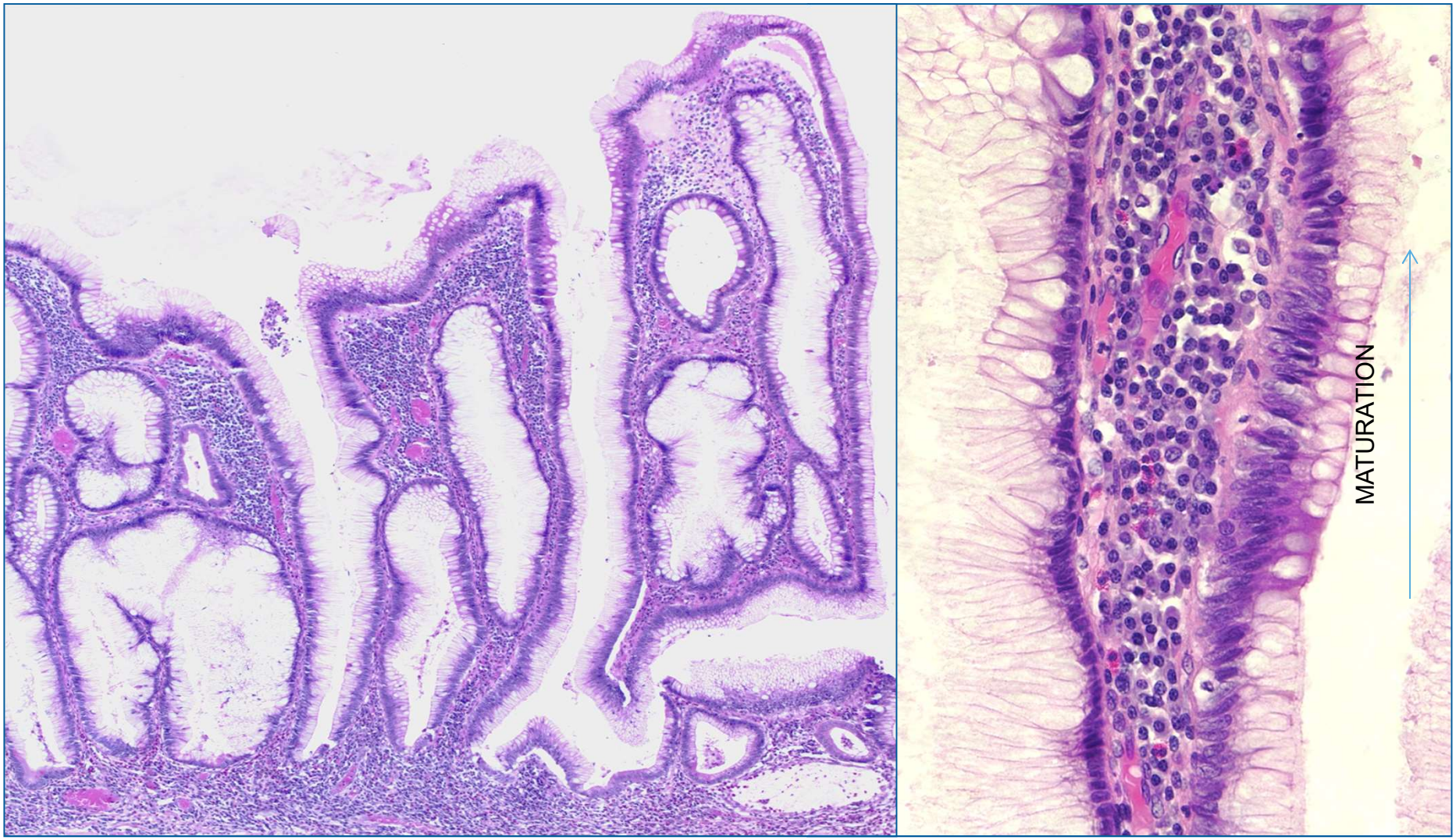
Villiform hypermucinous dysplasia



Extensive; Flat, villiform or nodular; Frequently ill-defined borders

Direct progression to cancer; 61% KRAS mutations

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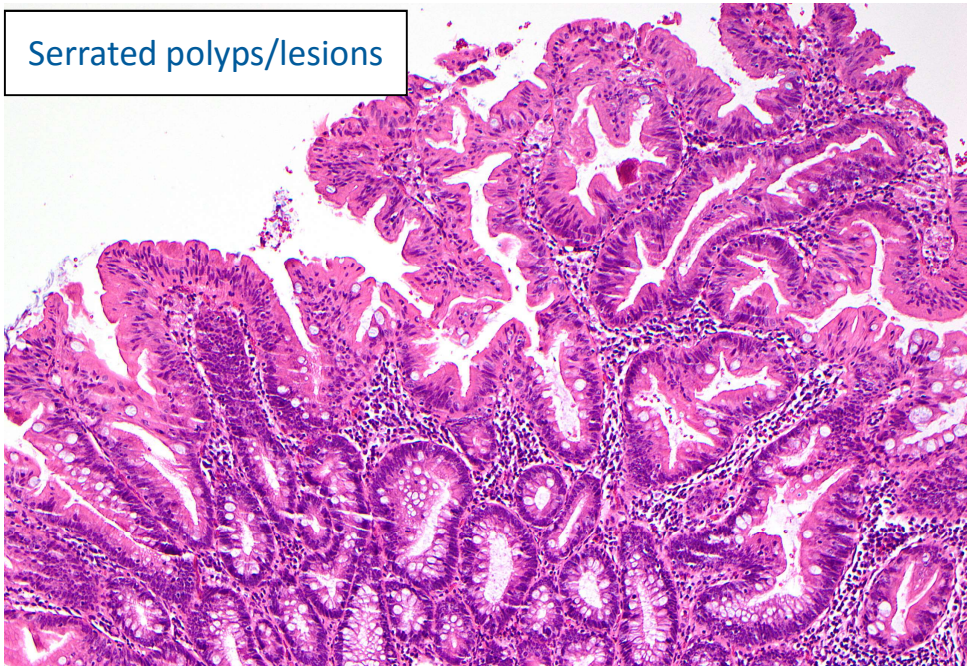
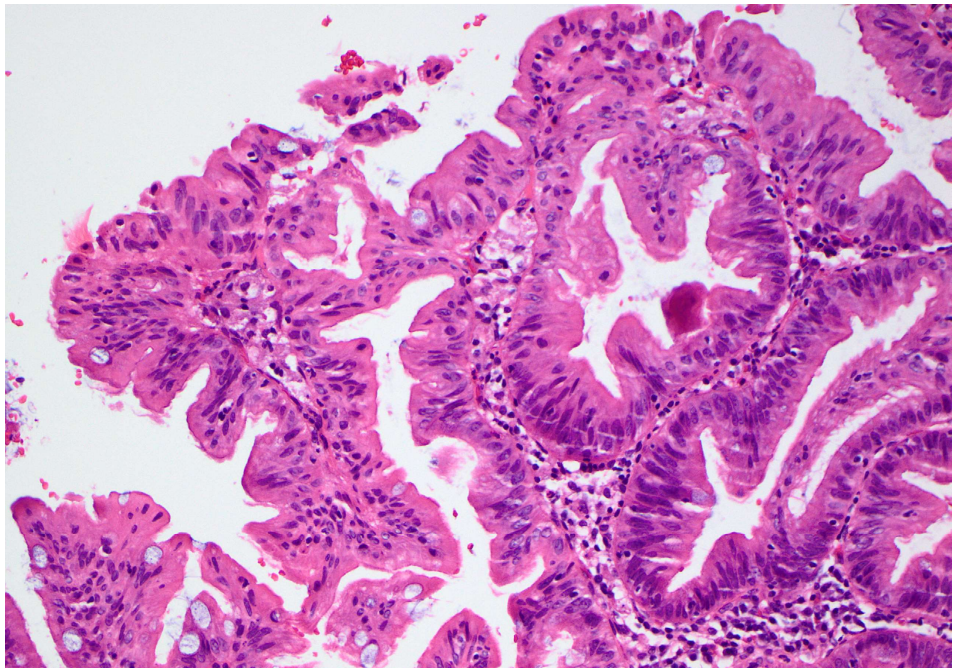
Anderson et al. Gut 1999;45:686-92

Serrated polyps/lesions



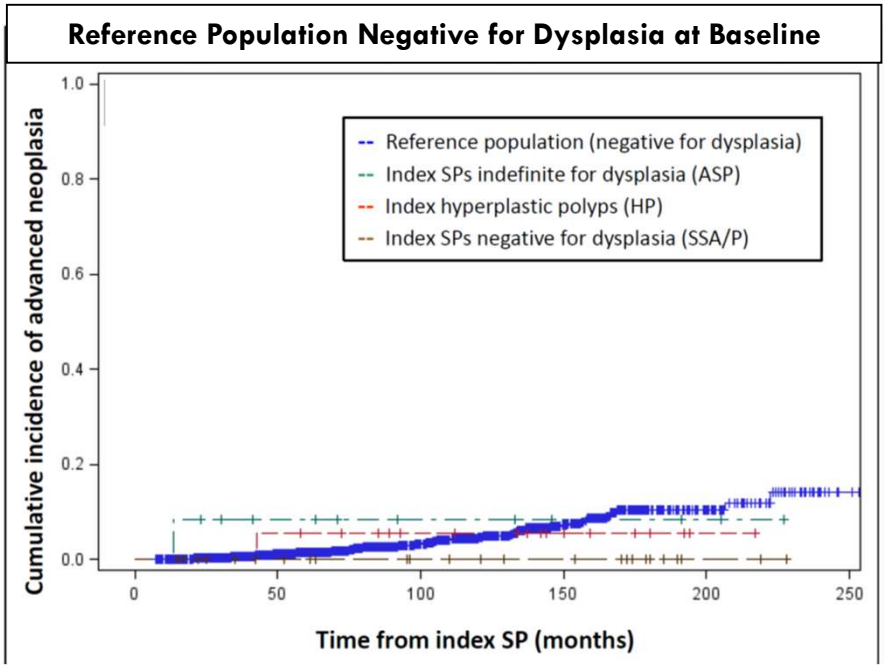


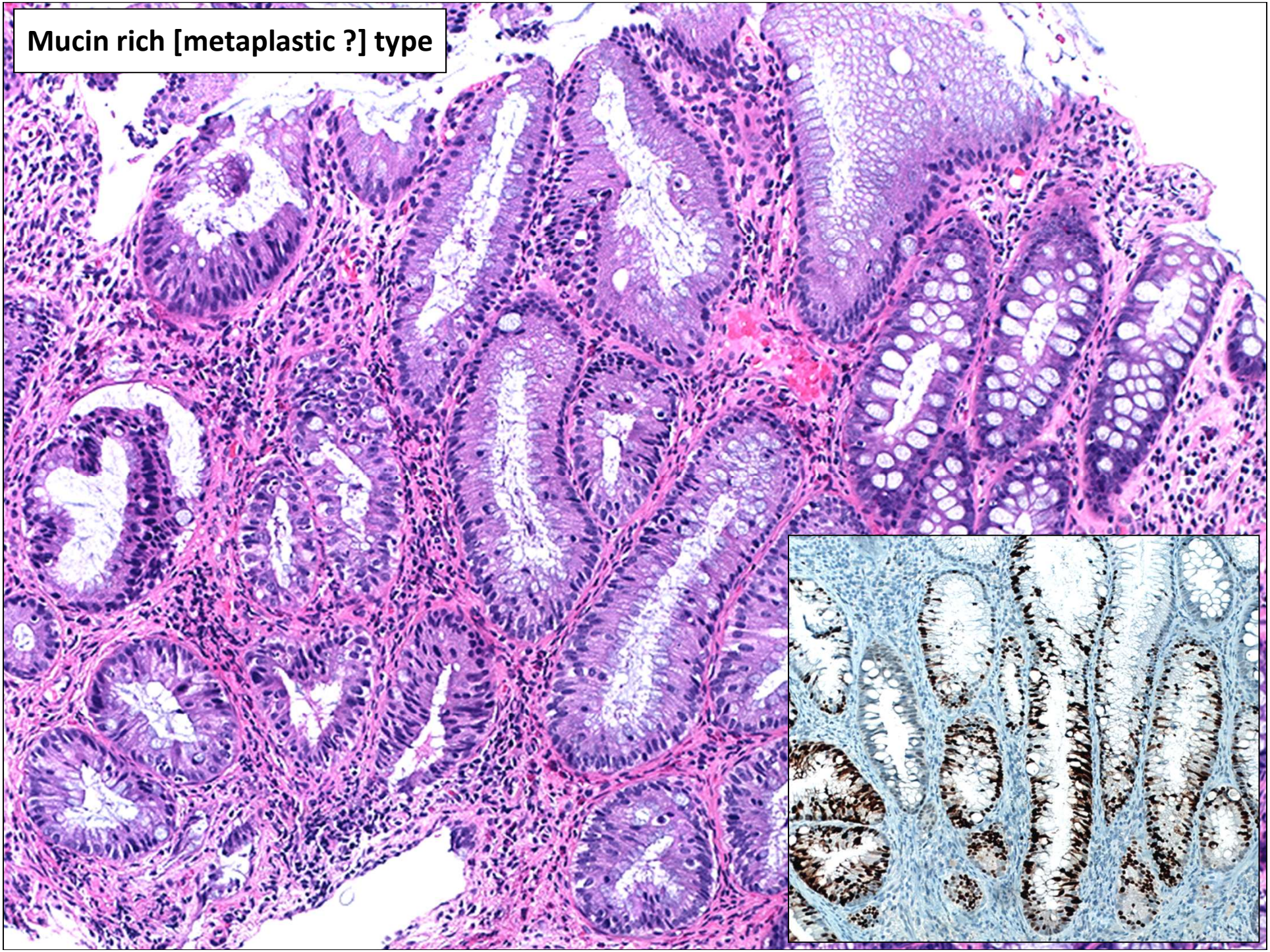
1.9 % of UC & CD pts. w/ serrated epithelial change; No CRC; 10 SSPs (0.2%) Aliment Pharmacol Ther 2014;39:1408-17

Highest grade prevalent neoplasia /pt and type

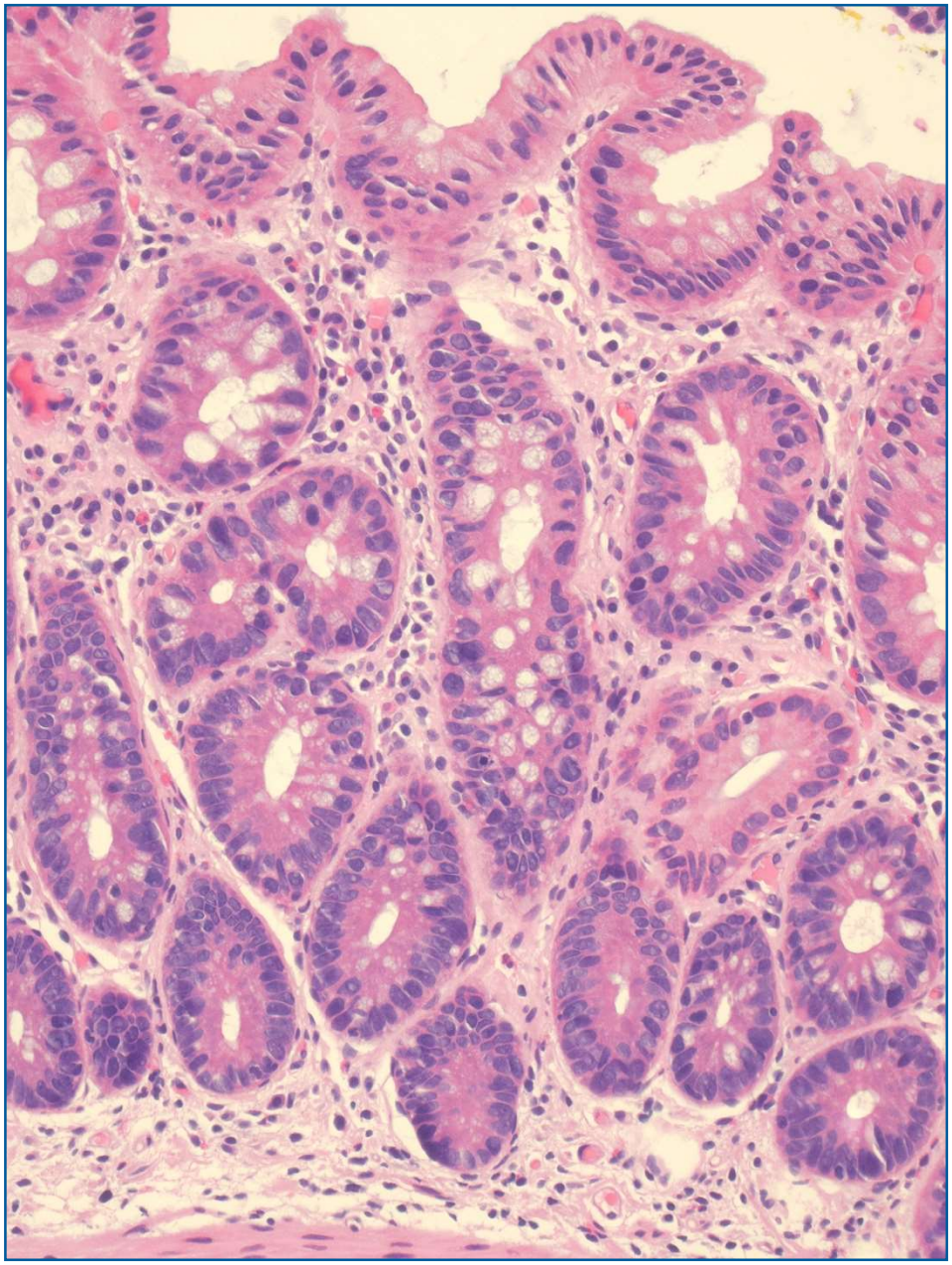
	TSA-LIKE (N = 25)	SP-IND (N = 18)	SSA-LIKE (N = 35)	HP (N = 28)
No neoplastic events	6 (24%)	11 (61%)	31 (89%)	**22 (79%)**
LGD	13 (52%)	4 (22%)	3 (9%)	**2 (7%)**
HGD	4 (16%)	2 (11%)	0 (0%)	**2 (7%)**
ACA	**2 (8%)**	**1 (6%)**	**1 (3%)**	**2 (7%)**

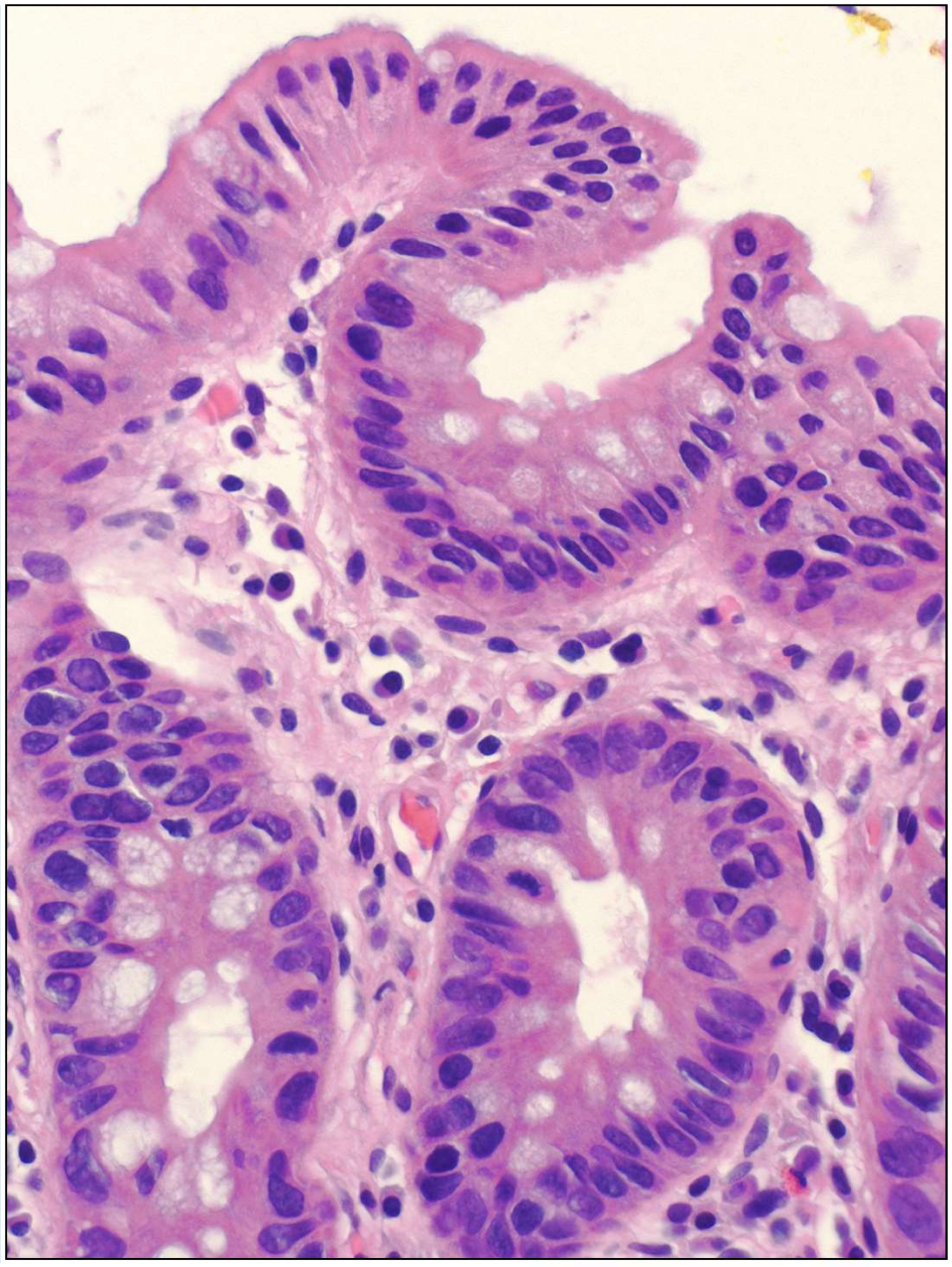
Ko. HM. Abstract #668-USCAP-Baltimore 2013




Mucin rich [metaplastic ?] type

Low Grade – yet unnamed dysplasia





Classification, clinical implications and management of dysplasia in IBD based on grade

Grade	*Probability of CRC at immediate colectomy*	*5-y progression to HGD or CRC*	*Recommended management*
Negative		1.1% (4% in 10y)	Surveillance 1-2y
Indefinite		9-13%	Repeat <3-6 mo., accelerated surveillance
Flat LGD	16-34%	10-54%	Accelerated surveillance or colectomy
Flat HGD	42-67%		Colectomy
Raised dysplasia (non-adenoma)	31-65%		Local resection or colectomy

Dysplasia in IBD

TAKE HOME MESSAGE

- Growing list of lesions w/ neoplastic potential lacking conventional morphologic evidence of dysplasia
- Importance to be aware of these lesions for both for diagnosis & risk stratification
- Morphologic and molecular characterization are needed to better understand these lesions and might facilitate:
  - *histological diagnosis*
  - *risk stratification*
  - *investigation into pathogenesis*
  - *molecular diagnosis*

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Thank You!

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