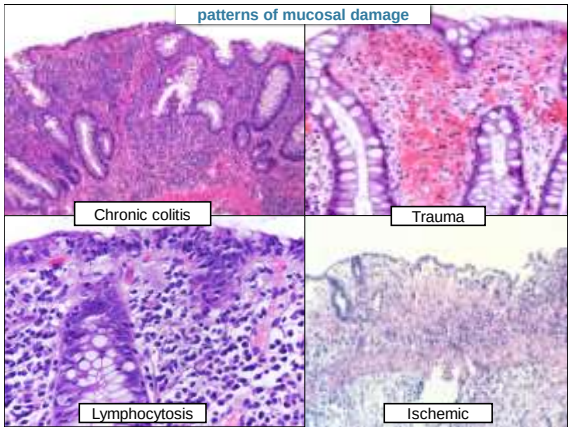
Non IBD-Colitis: How to communicate with the clinicians

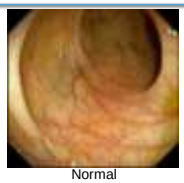
Gregory Y. Lauwers, M.D.
Vice Chairman
Department of Pathology
Director, Gastrointesinal Pathology Service
Massachusetts General Hospital
Professor of Pathology
Harvard Medical School, Boston, MA
glauwers@partners.org



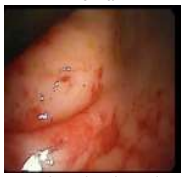
Patterns of mucosal damage=Dx

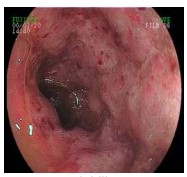
• Chronic colitis	IBD; healed isch.;RT; infection
• Diffuse active colitis	IBD;infection;diverticular dis.
• Focal active colitis	Early IBD;infection;drugs;
• Lymphocytosis	Lymphocytic /collagenous C.
• Ischemic type injury	Vascular/low flow;infection
• Apoptotic “colopathy”	Drugs;Infection;Trauma
• Traumatic changes	Drugs;bowel preparation

Patterns of mucosal damage-endoscopy


Normal

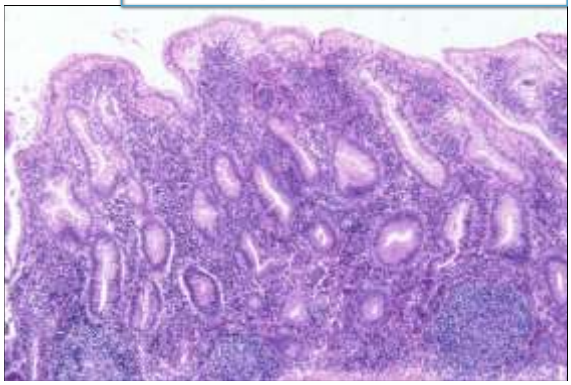

Pseudomembranes


Edema / Ecchymosis

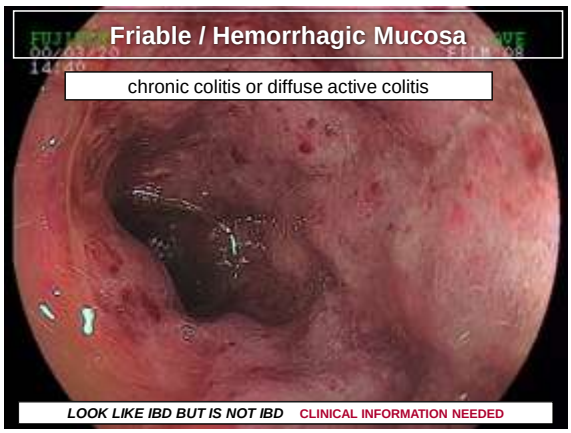

Friability

CASE 1

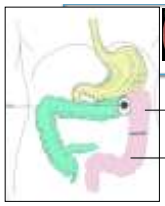
68 M. Requisition sheet: "colitis"



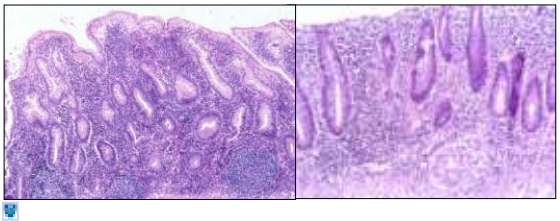
Friable / Hemorrhagic Mucosa



Diversion Colitis in defunctionalized bowel

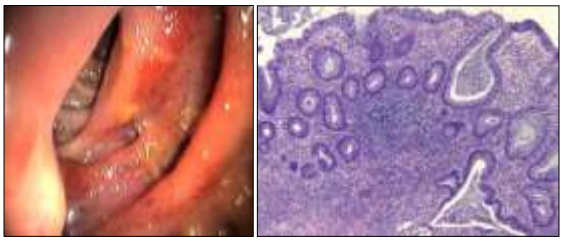


RX:short-chain fatty acids (restauration of fecal stream)



Diverticular associated Colitis

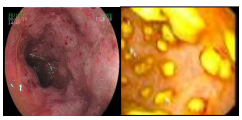
- Can cause segmental strictures-no punched-out ulcers or fissuring.



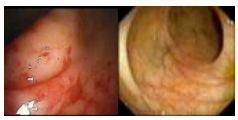
- Diff. Dx: left sided UC w/ rectal sparing or left sided CD.
- Distinction rests on clinical features

Infectious colitis

- Acute onset bloody diarrhea (usually 2-4 wk course – ASLC)



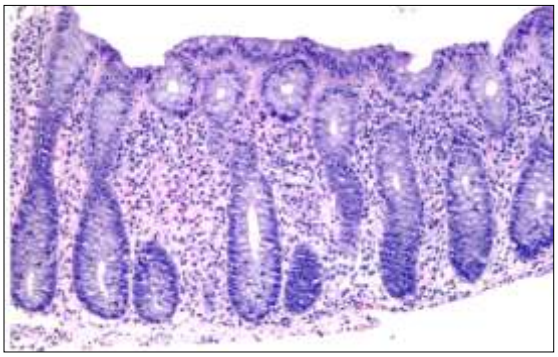
Acute/full blown (specific etiologies)



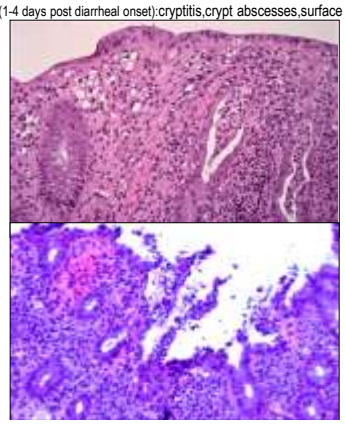
Early stage/resolving (partially treated)

- Bx may be necessary to distinguish between infectious colitis & new onset IBD

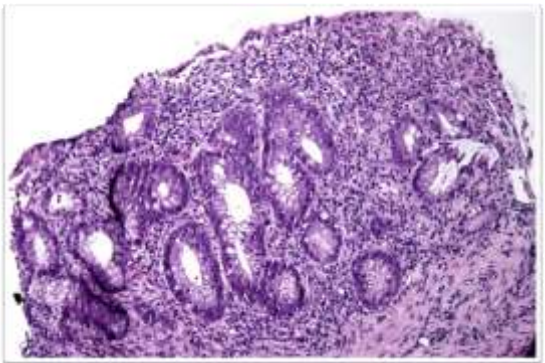
Early Changes: Edema, Neutrophil infiltrate and epithelial damage



Peak activity (1-4 days post diarrheal onset):cryptitis,crypt abscesses,surface damage w/ erosions



Aeromonas species Colitis

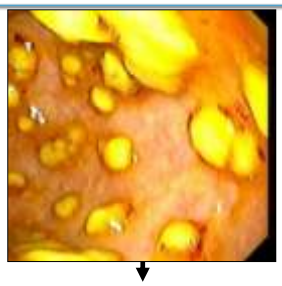


Mucosal atrophy & basal plasmacytosis <5% of cases at 1 year

Acute Infectious-type Colitis

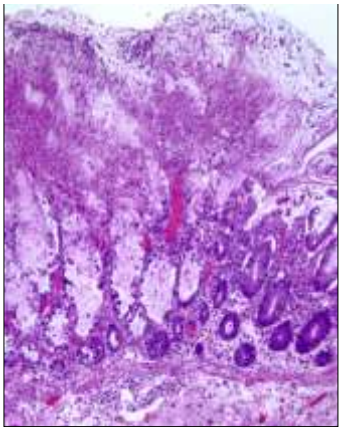
- In most cases cannot distinguish between the different entero-invasive bacteria.
- Pathogens identified in 30-40% of pts (when cultured)
- ***Campylobacter jejuni sp,***
- *Clostridium difficile*
- *Salmonella,*
- *Shigella*
- *Chlamydia*
- *Yersinia enterocolitica*
- *E. coli 0157:H7.*
- *Aeromonas species*

Pseudomembranes



- Pseudomembranous colitis
- Specific features

(Acute ischemic colitis)

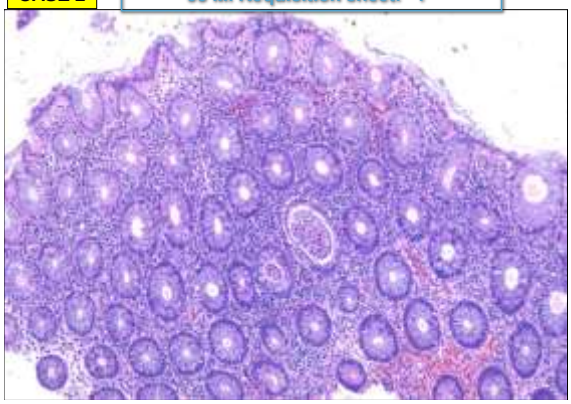


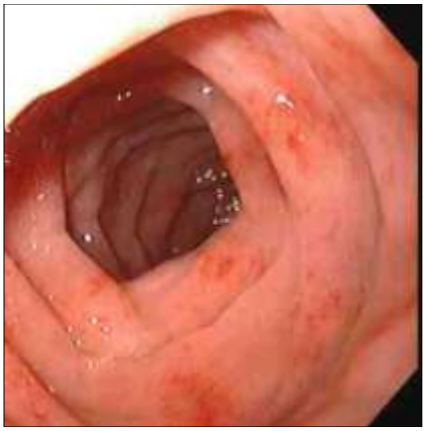
Acute colitis with pseudomembranes

- Clostridium Difficile:
  - Antibiotic and other drugs associated
- Other Infections:
  - Shigella, E. Coli 0157:H7
- Drug/Toxin:
  - Chlorpropamide, Mercuric Compound, NSAIDS, Golds
- Superimposed on lesions/mass:
  - SRUS, cap polyposis
- Ischemia:
  - segmental distribution (microscopic dx)

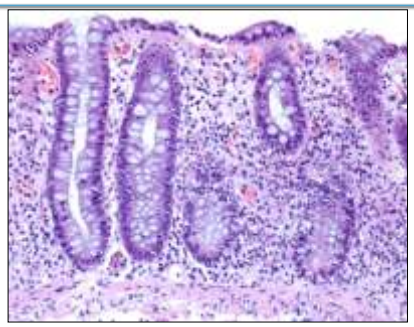
CASE 2

55 M. Requisition sheet: "?"





Focal active colitis (focal isolated neutrophilic crypt injury)



Other changes: crypt abscess, apoptosis, aphthous erosions

Focal active colitis*

	ADULTS		PEDS
Acute infectious colitis*	55%	48%	
Ischemic colitis	5%	10%	
Crohn's disease	0	13%	
Ulcerative colitis	0	0	
Allergic colitis	0	0	
Hirschprung's	0	0	
Irritable Bowel Syndrome	14%	-	
Incidental (no diarrhea)	26%	29%	

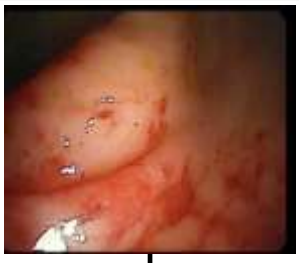
(*Drug effect and particularly NSAIDs should also be considered)

- *110 biopsies with FAC
  - 19% positive for *Campylobacter jejuni* DNA by PCR.

Schneider EN. Am J Surg Path 2006;30:782-785

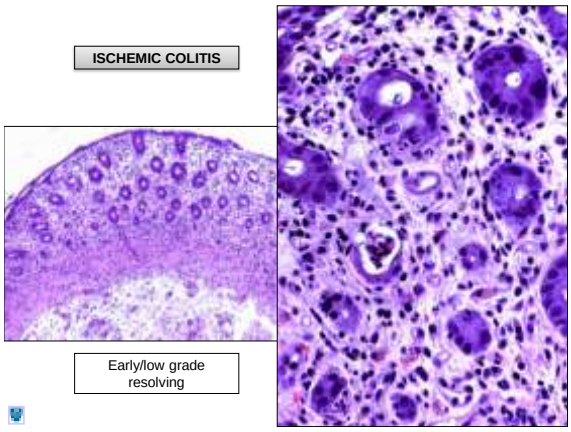
Am J Surg Pathol. '03;27:1134-8. - Hum Pathol. '97;28:729-33. - Mod Pathol. '98;789-94.

Edema / Ecchymosis



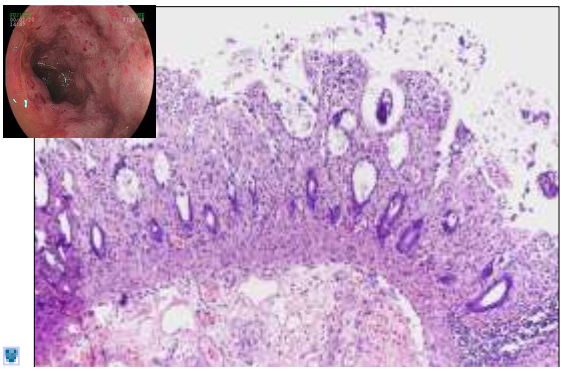
Acute colitis w/ or w-o ischemic features (e.g., infectious)

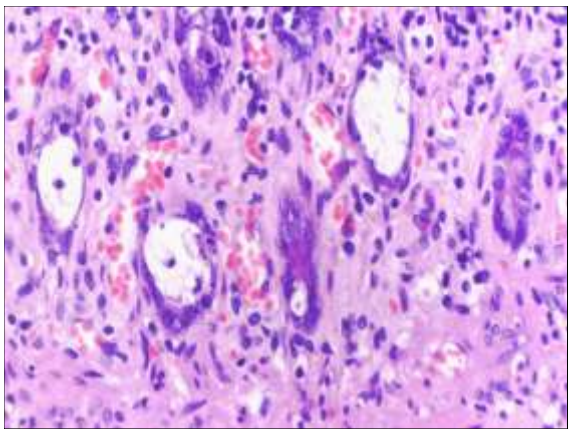
ISCHEMIC COLITIS



Early/low grade resolving

Ischemic colitis-severe

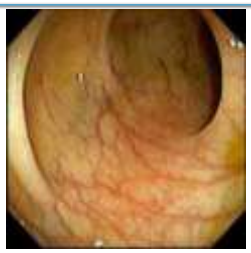




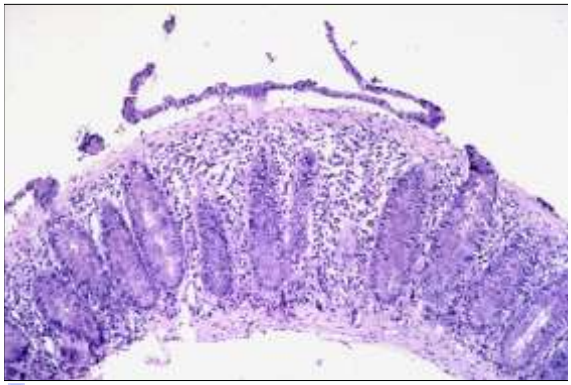
Causes of Ischemic Colitis

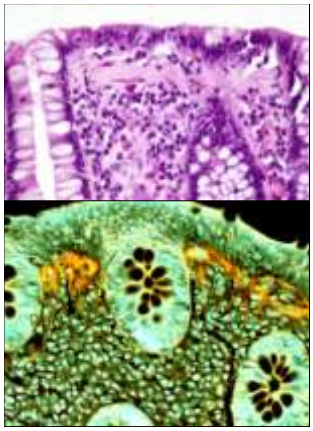
- Low Blood Flow (shock / cardiac failure)
- Thromboses & Emboli
- Mechanical (volvulus,hernia,adhesions, tumors)
- Vasculitis, Diabetes mellitus,
- Trauma, Surgery, Radiation injury
- ***Hematologic disorders***
  - sickle cell disease , distance runner , Protein C/S antithrombin III deficiencies
-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

Normal endoscopy

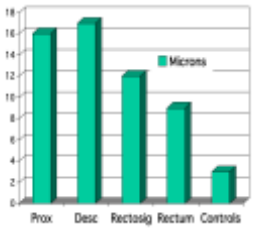


Collagenous colitis
Lymphocytic colitis
Focal active colitis
Others (IBS)





Thickness of Collagen by Site



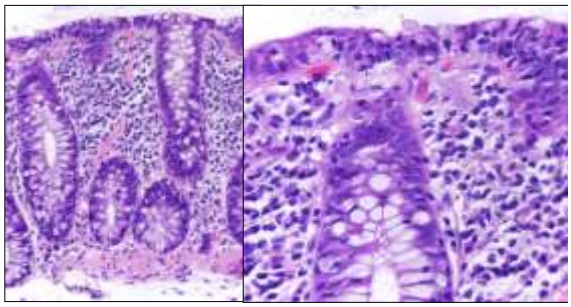
(Human Pathol 18:839-848, 1987)

Collagenous colitis

Etiology

- Idiopathic (most cases) - Luminal agent important since disappearance of collagen on diversion of fecal stream
- Drugs – NSAID's, others
- Autoimmune disease – strong association with many autoimmune diseases especially – autoimmune thyroid disease and rheumatoid arthritis
- Celiac disease (reported in up to 25%)

Lymphocytic colitis



IELs (intraepith. lymphocytes in surface /glds) **>15/100 epith. cells**

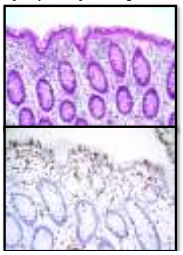
Lymphocytic colitis

- Etiology
  - Idiopathic (~ 75%) – association with autoimmune disease or presence of autoantibodies in many cases
  - 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, PPI's and SSRI's; also herbal remedies, ticlopidine, carbamazepine
  - Autoimmune disease – Hashimoto thyroiditis
  - *Infection – Brainerd diarrhea, resolving infective colitis*
  - *Others – Crohn disease/ulcerative colitis, food allergy, IBS, autism, CVID*

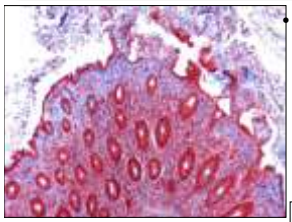
Colonic lymphocytosis-Diff. Dx

- Increased intraepithelial lymphocytes but no appreciable lamina propria inflammation.
- Sometimes reported as *'pauci-cellular lymphocytic colitis'* is ch[(7-20/100 EC) or patchy intraepithelial lymphocytosis]
- Be careful in the cecum

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

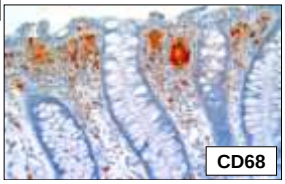


Atypical patterns of microscopic colitis



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

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



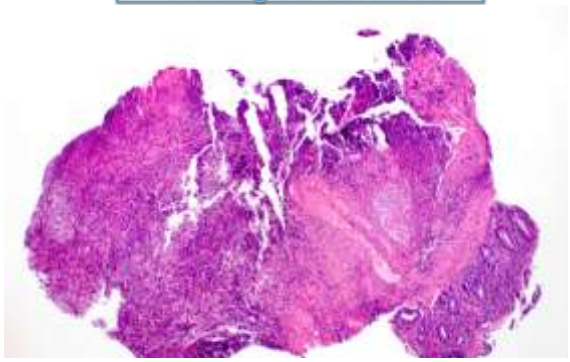
IBD-Like Morphology is rare Collagenous & Lymphocytic Colitis

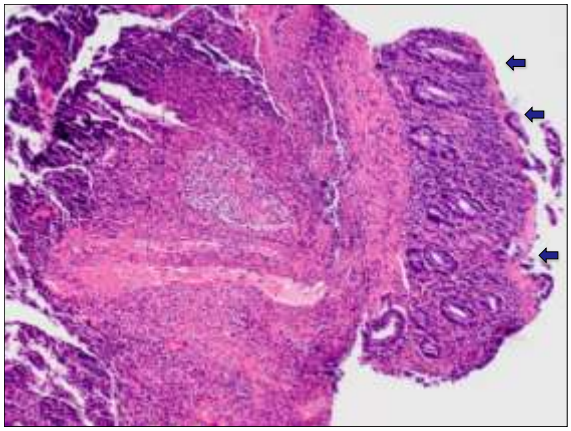
Crypt disarray <10% / active inflammation ~35%

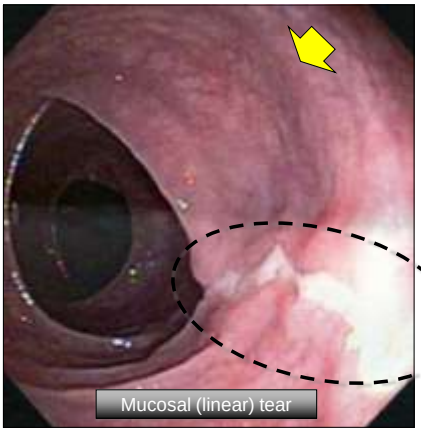
Ayata et al. AJSP 2002;26:

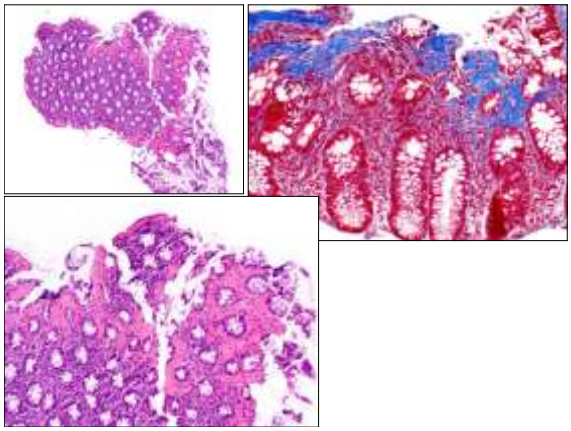
CASE 3

72 F. watery diarrhea
Working Dx: Infectious









Granulomas in colonic biopsies

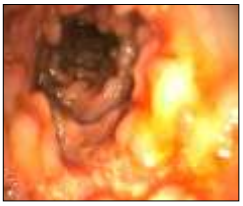
- IBD: Crohn disease and U.C. (mucin granuloma)
- Sarcoidosis
- Systemic Infection (TB, histoplasmosis)
- GI infections (salmonella,yersinia,campylobacter)
- Venereal infections (syphilis, LGV)
- Drugs (e.g.,diclofenac)
- Foreign Body (talc, starch, barium)
- Inherited (CGD, Hermansky-Pudlak syndrome)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

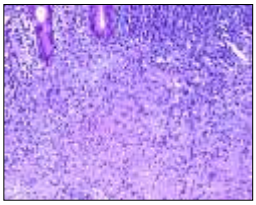
Approach to colonic granulomata

- 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

Tuberculosis





Pathologic features favoring TB over Crohn disease

J Clin Pathol 2006;59:840-44

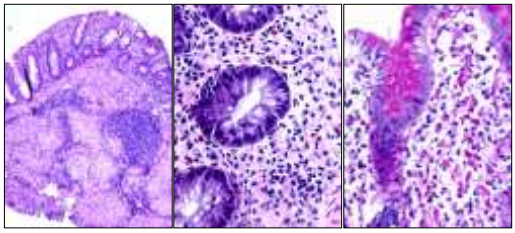
confluent granulomata (50% vs 0%)
≥10 granulomata/biopsy site (33% vs 0%)
Caseous necrosis (22% vs 0%

Am J Gastroenterol 2010;105:642-51

Absence of focally enhanced colitis (64% vs 32%)
No involvement of Sigmoid colon (89% vs 33%

Chronic Granulomatous Disease

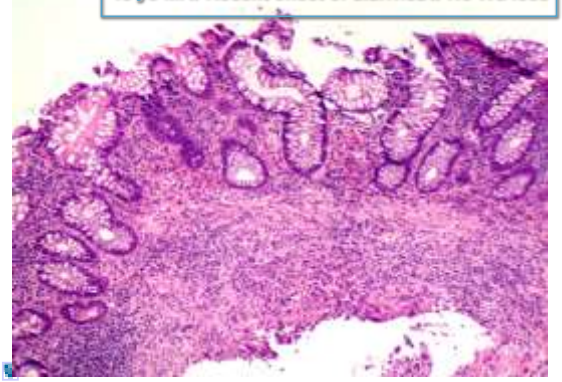
•2/3 X linked;1/3 AR: NADPH oxidase abnormality w/ inability to kill bacteria.

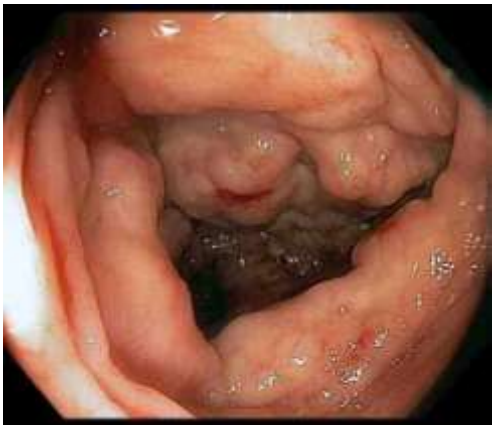


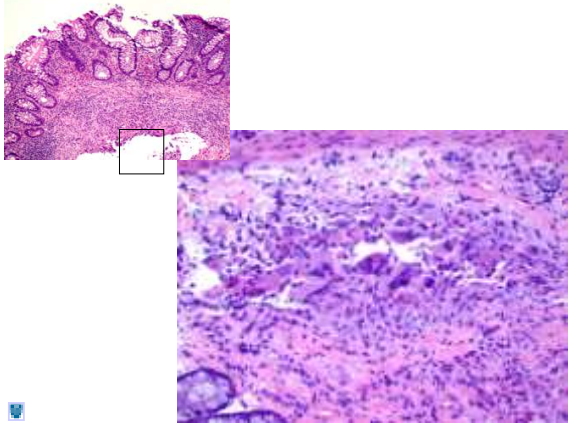
•Granulomas: consequence of persistent/recurrent infection
•Resembles Crohn disease both histologically and clinically
•Pigment laden macrophages in non inflammed areas are a clue to diagnosis

CASE 4

45 yo M. // Recent onset of diarrhea // No Wt. loss





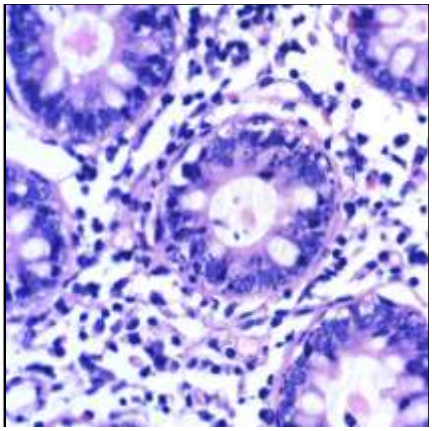


Pneumatosis intestinalis

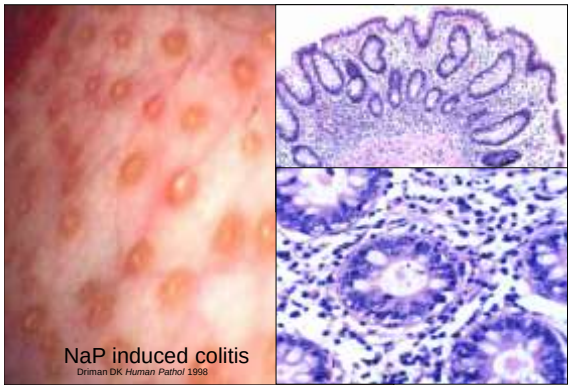
- Collection of gas in the bowel wall.
- Pathogenesis?
  - intraluminal gas, pulmonary gas, luminal bacteria.
- Various “etiologies”: traumatic, mechanical, inflammatory, autoimmune, collagen-vascular, infectious, and drug-induced etiologies.

CASE 5

- 63 yr M

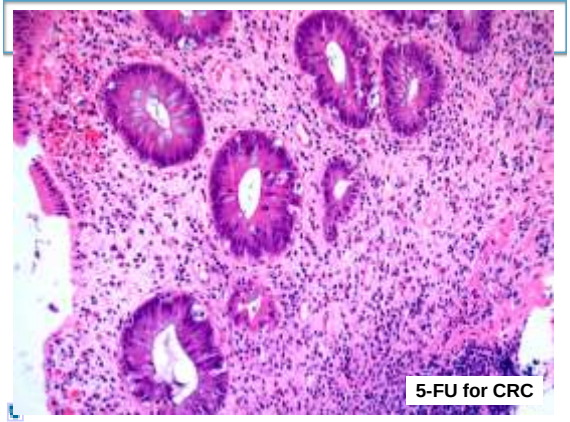


- Tubular adenoma 3 yrs prior // F. up colonoscopy

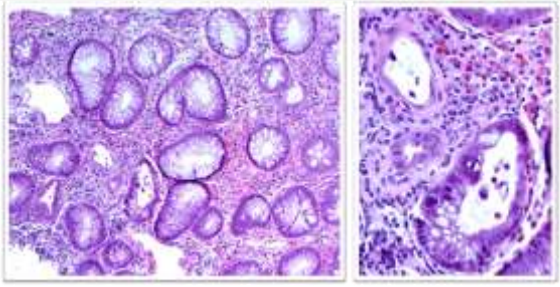


Drug-induced colonopathy/colitis

• **Erosions and ulcers**	NSAIDs, KCl
• **Strictures**	KCl, pancreatic enzyme replacement
• **Microscopic colitis**	PPIs, ticlopidine, ranitidine, simvastatin, flutamide, carbamazepine, paroxetine, sertraline, penicillin V,cyclo 3Fort, NSAIDs
• **Pseudomembranous colitis**	Antibiotics, PPIs
• **Neutropenic enterocolitis**	Cytosine arabinoside, cisplatin, vincristine, adriamycin, 5-FU, mercaptopurine
• **Malakoplakia**	Corticosteroids
• **Sigmoid diverticular perforation**	Corticosteroids
• **Ischemic colitis**	Digitalis, diuretics, BCP, ergotamine, cocaine, Kayexalate, glutaraldehyde, sumatriptan, *α*-interferon, dopamine, methysergide, NSAIDs
• **Focal active colitis**	NaPO4, NSAIDs
• **Epithelial atypia mimicking dysplasia**	IV cyclosporin
• **Apoptosis**	NSAIDs, NaPO4, melanosis, 5-FU, Mycophenolate Mofetil

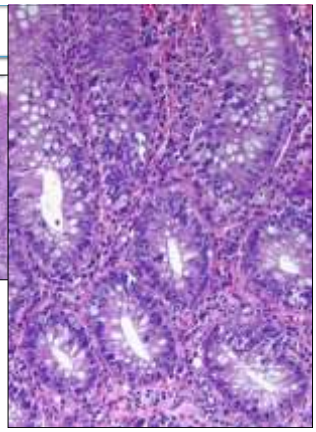


Mycophenolate Mofetil



- Differential diagnosis: i) GVHD; ii) Ischemia iii) Crohn disease

NSAIDs



- Collagenous colitis
- Focal active colitis.
- Reactive epithelial changes
- Apoptosis.
- Ulcerations.
- Eosinophilic colitis

Eosinophilic colitis - diagnosis

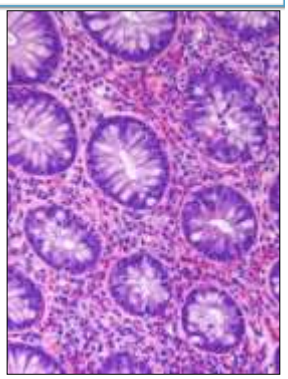
- Normal colonic eosinophil count not well defined
- Varies - Right colon > left colon
  - Season (higher numbers in spring)
  - Geography (high numbers closer to tropics)

- Rare
- Isolated to colon or part of a more generalised GIT eosinophilic disorder
- All ages, slight bimodal age distribution - young children and adults (20-50)

Pascal R et al Mod Pathol 1997;10(4):363-365

Eosinophilic Colitis - dx

- Uniformly >20/HPF
- Degranulation
- Eos in crypt and/or surface epithelium.
- Eos crypt abscess
- Epithelial injury
- Eos through the musc. mucosae into superficial submucosa
- Relative absence of other inflammatory cells

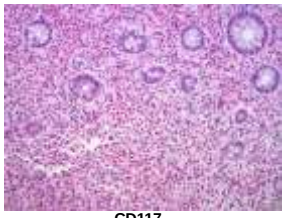


Causes of eosinophilic colitis/colonic eosinophilia

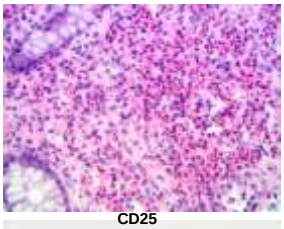
- **Hypereosinophilic syndrome**
- **Parasitic infection** eg. Enterobius, Strongyloides, others
- **Allergy –** Food - Cows milk, Soy protein, allergic proctocolitis
- **Drugs –** NSAID's, Gold, L-Tryptophan, Carbamazepine, Methotrexate, Tacrolimus, Azothioprine, Rifampicin, Clozapine
- **Connective tissue disorders**
- **Vasculitis –** Churg – Strauss syndrome
- **Neoplasia** - Lymphoma, Langerhans cell histiocytosis, Systemic Mastocytosis, myeloid neoplasms
- **Inflammatory fibroid polyp**
- **Inflammatory bowel disease**
- **Solid organ and bone marrow transplantation**
- **Idiopathic**

48 year old female

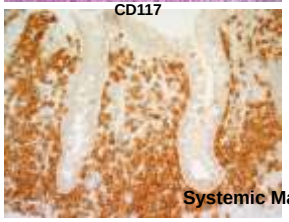
- Diagnosed 3 years earlier with eosinophilic colitis
- Diarrhea and intermittent nausea and vomiting

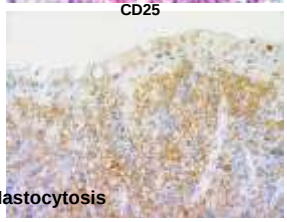


CD117



CD25





Systemic Mastocytosis

Diagnosis of Colitis Other Than Inflammatory Bowel Disease