Irritable Bowel Syndrome, Diverticular disease, and Inflammatory Bowel Disease

Hiram Ortega-Cruz
Gastroenterologist
Primer Simposio del Oeste
Academia de Medicina General De Puerto Rico

Inflammatory Bowel Disease et al Objectives

- Discuss IBS, diverticular disease, and IBD
- Compare and contrast Crohn’s disease and ulcerative colitis
- Discuss medical therapy and patient compliance techniques
- Discuss systemic manifestations of IBD

Case

- 23 yo female with intermittent abdominal pain, bloating, and loose, nonbloody stools.
- FamHx - negative for GI illnesses
- Above sx present for at least five years
- Dx?

Irritable Bowel Syndrome

Irritable Bowel Syndrome Diagnosis

- Abdominal pain associated with disturbed defecation and relieved with defecation
- Stools looser or more frequent at pain onset
- Feeling of incomplete evacuation
- Mucus per rectum
- Visible abdominal distention (bloating)
- Labs and sigmoidoscopy negative

Irritable Bowel Syndrome

- Diagnostic tests?
- **There are none** - this is purely a clinical diagnosis and a diagnosis of exclusion
- Consider the following:
  - CBC, CMP (Chem-20), ESR, hCG, KUB, UA

Celiac Disease

- With any new diagnosis of IBS, entertain the Dx of celiac disease in your Ddx.
- Tissue transglutaminase and other labs tests to confirm
- Gluten free diet

Irritable Bowel Syndrome Treatment

- Reassurance!
- Identify and correct precipitating factors (lactose intolerance, anxiety disorder, etc)
- Reduce stress
- Diet therapy - eat fiber!

Irritable Bowel Syndrome

- *Diagnostic criterion**
- Recurrent abdominal pain or discomfort** at least 3 days/month in the last 3 months associated with *two or more of the following:*
  - Improvement with defecation
  - Onset associated with a change in frequency of stool
  - Onset associated with a change in form (appearance) of stool
- * Criterion fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis
- ** “Discomfort” means an uncomfortable sensation not described as pain.
- http://www.theromefoundation.org/assets/pdf/19_RomeIII_apA_885-898.pdf

Irritable Bowel Syndrome Treatment

- Drug therapy
- Constipation - bulking agent (psyllium), lactulose/milk of magnesia
- Diarrhea - bulking agent, loperamide, cholestyramine
- Bloating - simethicone (OTC)
- Pain/cramping - dicyclomine/Bentyl, Donnatal, hyoscyamine/Levsin

The Rome Criteria III

http://www.romecriteria.org/questionnaires/

Case

- 64 year old male with three day h/o left lower quadrant abdominal pain. Has had fever of 102 today. Still passing some gas.
- FamHx - no colon cancer
- ROS - no melena, no BRBPR, no screening flex sig done to date.
- Labs - WBC = 15, bands = 18%
- Dx?

Diverticular Disease

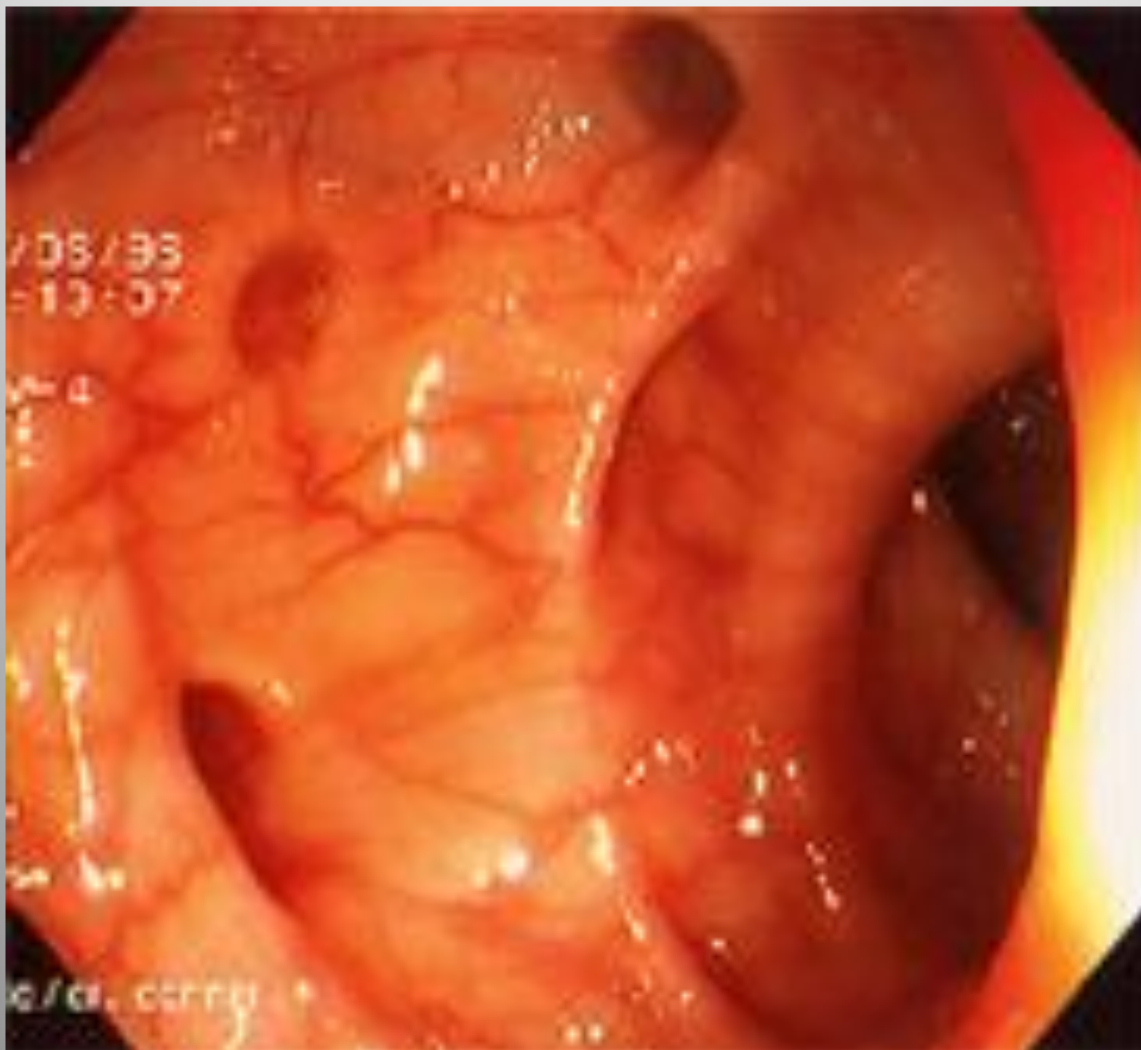
Diverticular Disease

- Diverticulosis
  - Herniation of the mucosal lining of the intestine through a defect in the muscular layer of the intestine
  - One-third + of people aged 50
  - Two-thirds + of people aged 80
  - A rough rule of thumb: incidence = age

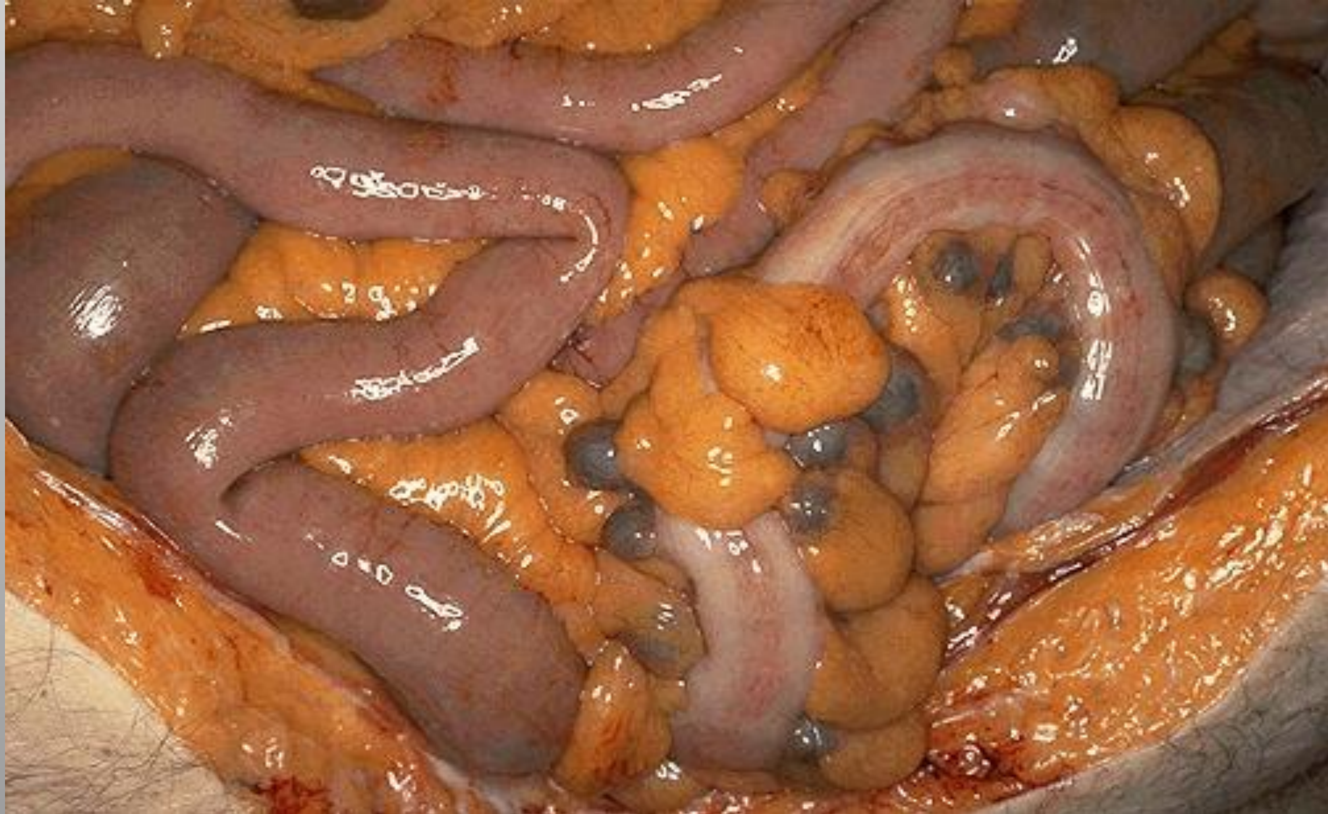
Diverticular Disease

- Diverticulosis
  - Characteristic findings on radiologic or endoscopic exam
  - No fever or leukocytosis
  - Possibly some intermittent left lower quadrant pain
  - Usually asymptomatic
  - **Eat more fiber!!!**

Diverticular Disease



Diverticulosis



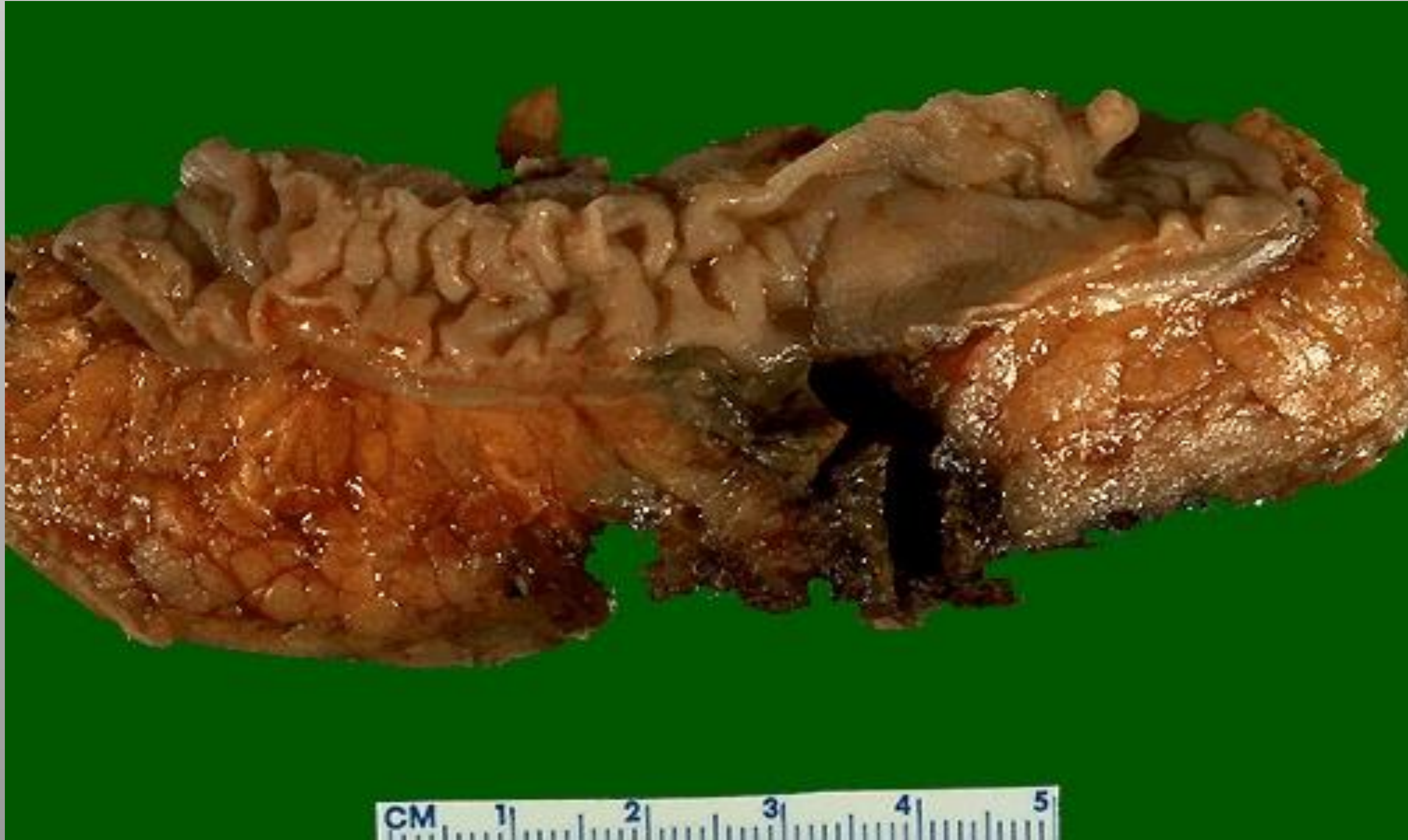
Diverticular Disease

- Diverticul***itis***
  - Acute abdominal pain
  - Constipation or bowel irregularity
  - LLQ tenderness and possible mass
  - Fever and leukocytosis
  - Characteristic radiographic signs

Diverticular Disease

- Diverticul***itis*** - Treatment
  - Antibiotics
  - Liquid diet or NPO
  - Can be managed as an outpatient in mild cases
  - NG tube if obstructed
  - 10-20% of patients have a recurrence
  - Surgery is an option in appropriate cases

Diverticulitis



Case

- 29 year old woman with episodes of bloody diarrhea for 1 week. Has had similar episodes in past, but they resolved after 2 weeks on their own. No melena.
- FamHx - no colon cancer
- No ill contacts
- Dx?

Inflammatory Bowel Disease
IBD (not IBS)

Inflammatory Bowel Disease

- Two major types of IBD
- Crohn's disease
  - Incidence – 3.1-14 per 100,000 persons
  - Prevalence - 174 per 100,000 persons
- Ulcerative colitis
  - Incidence – 2.2-14.3 per 100,000 persons
  - Prevalence - 214 per 100,000 persons

Inflammatory Bowel Disease

- Etiology - not clearly discernable. Possible combination of genetic predisposition and environmental exposures.
- Crohn's Disease - affects mouth to anus and has ***transmural*** involvement
- Ulcerative colitis - strictly affects the colon and has ***mucosal*** involvement

Crohn's Disease

- Epidemiology
  - Risk of relapse 53% at 1 yr, 85% 5yrs
  - 40-60% patients hospitalized
  - Risk of surgery 58% overall

Crohn’s Disease

- Symptoms
  - Right lower quadrant pain and diarrhea, usually intermittent in nature
  - Hematochezia occurs in a minority of patients
  - Low fever and weight loss also possible
  - High fever and pain may be indicative of a complication, e.g., perirectal abscess.

Crohn's Disease

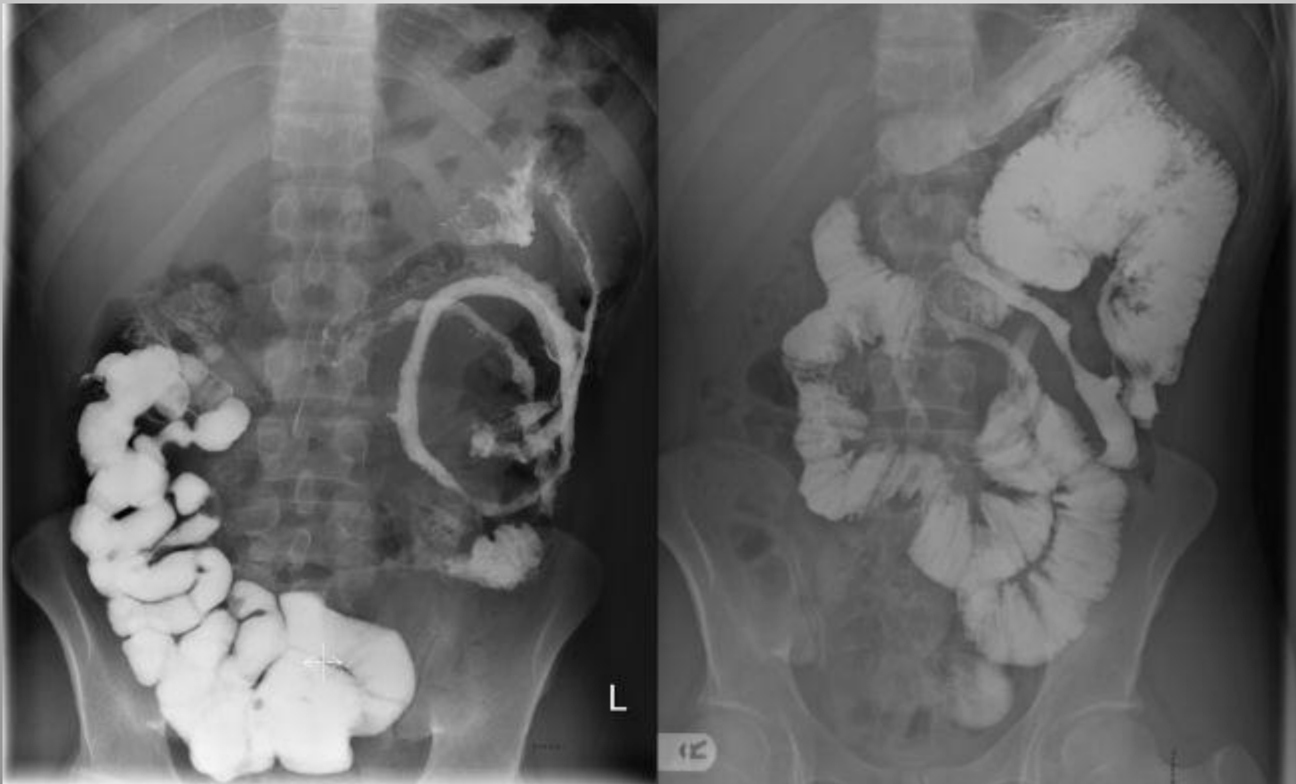
- Signs
  - Abdominal TTP, especially RLQ
  - Palpable mass in RLQ is possible
  - Rectal exam may reveal a perirectal mass
  - Abdominal distention/SBO picture
  - Peritoneal signs in patients who have fistulized or ruptured.

Crohn's Disease

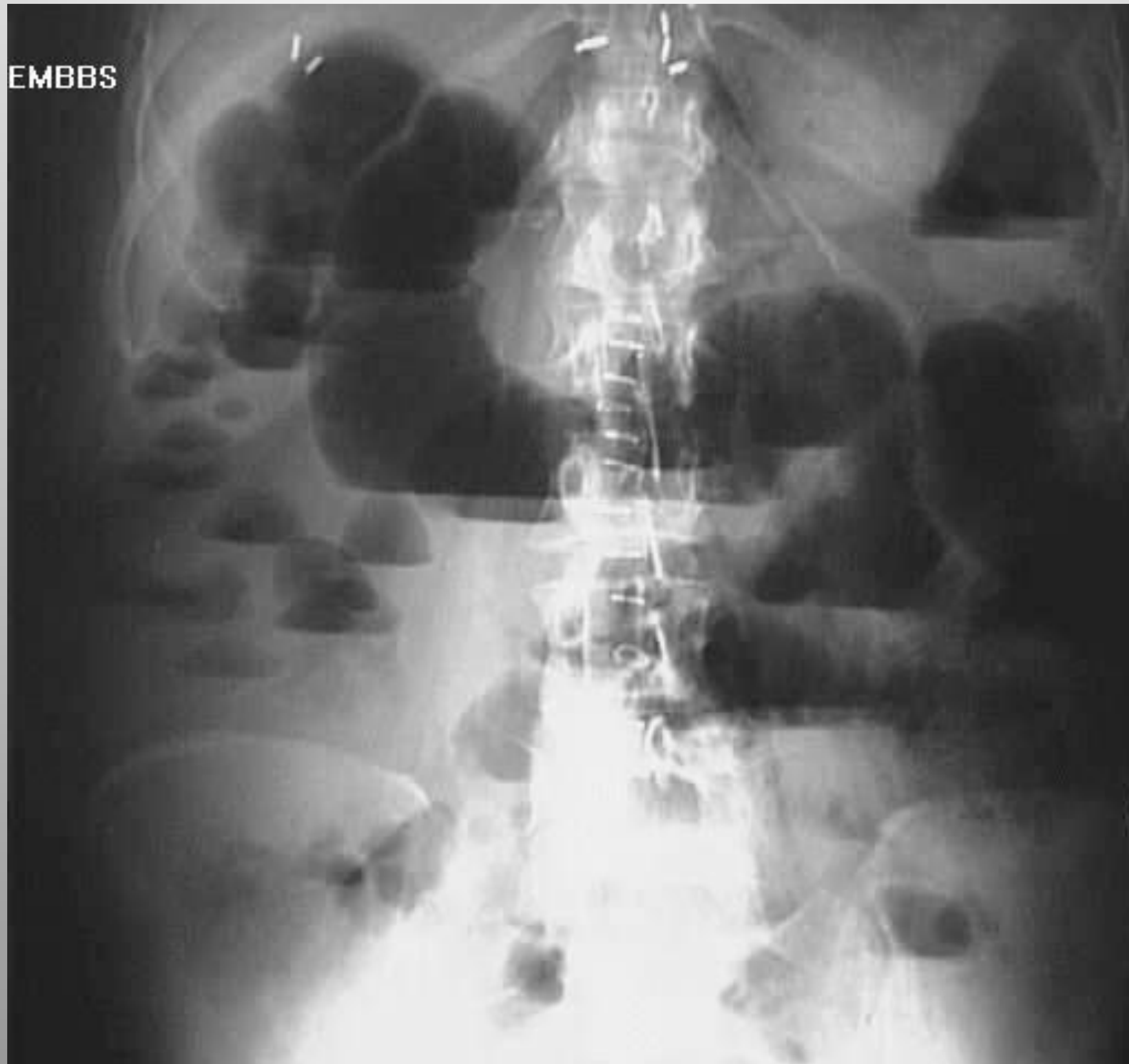
- Lab findings - generally nonspecific
  - ESR usually elevated - may be normal when disease in remission
  - Anemia - both low iron from anemia of chronic disease and low B12 secondary to ileal involvement or resection
  - Leukocytosis and thrombocytosis
  - Hypoalbuminemia

Crohn's Disease

- Imaging Studies
  - Small bowel follow through - drink barium and take pictures as it transits the small bowel



Small Bowel Obstruction



Crohn’s Disease

- Imaging Studies
  - Colonoscopy preferable over BE in evaluating the colon
  - BE can evaluate for fistulas and strictures
  - Colonoscopy may take biopsies in addition to direct visualization.
  - Both can provide evaluation of the terminal ileum to help distinguish Crohn’s from UC

Crohn’s Disease

- Capsule Endoscopy
  - Swallow a small pill that is a video recorder.
  - Records a video image of the small bowel.
  - Transmits an image to a video receiver that then visualizes the small bowel.

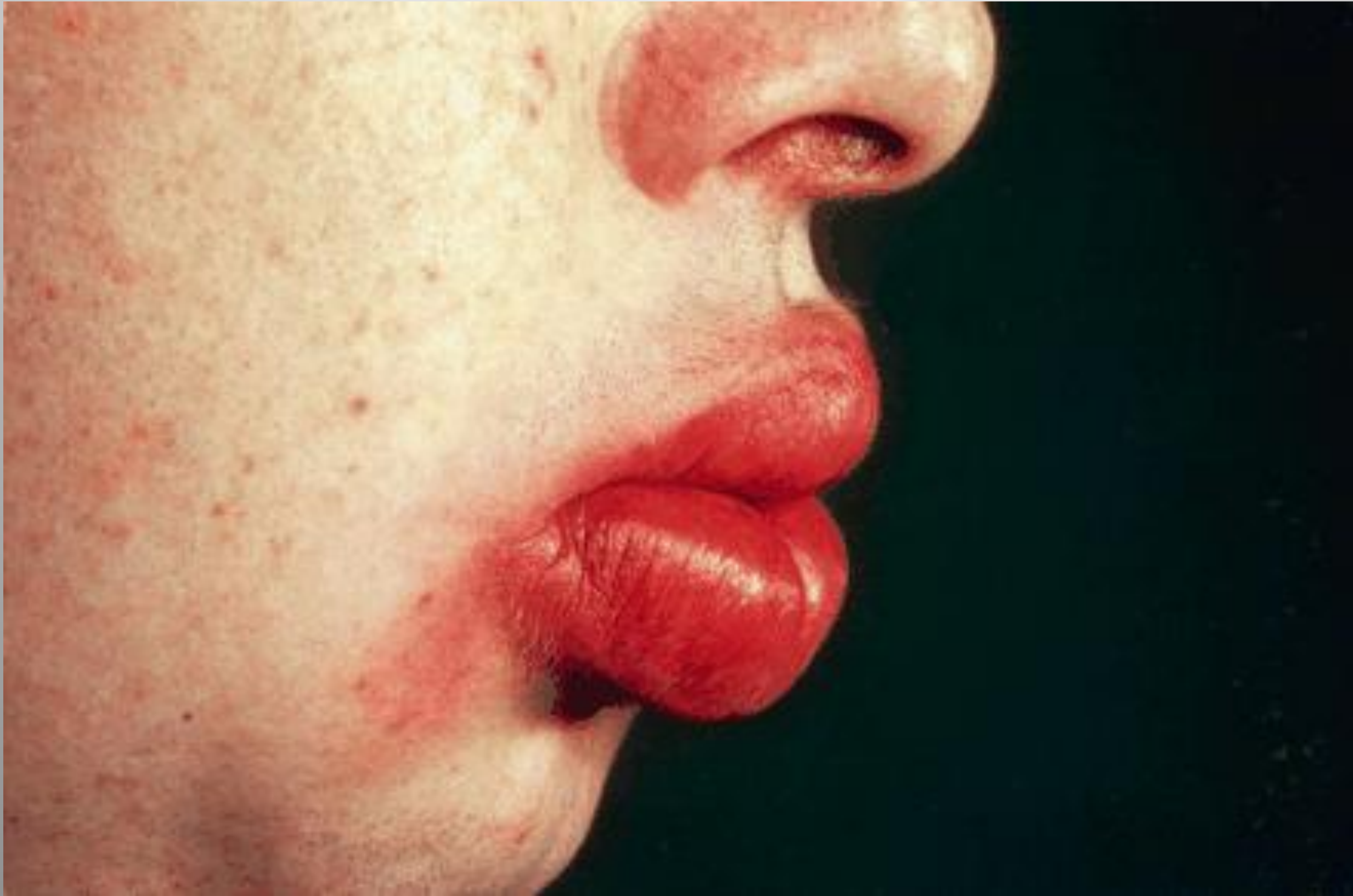
Crohn's Disease

- Imaging Studies
  - Abdominal CT - not useful as an initial diagnostic study but is extremely helpful in managing complications of Crohn's disease. E.g., evaluating for an intra-abdominal abscess or fistula

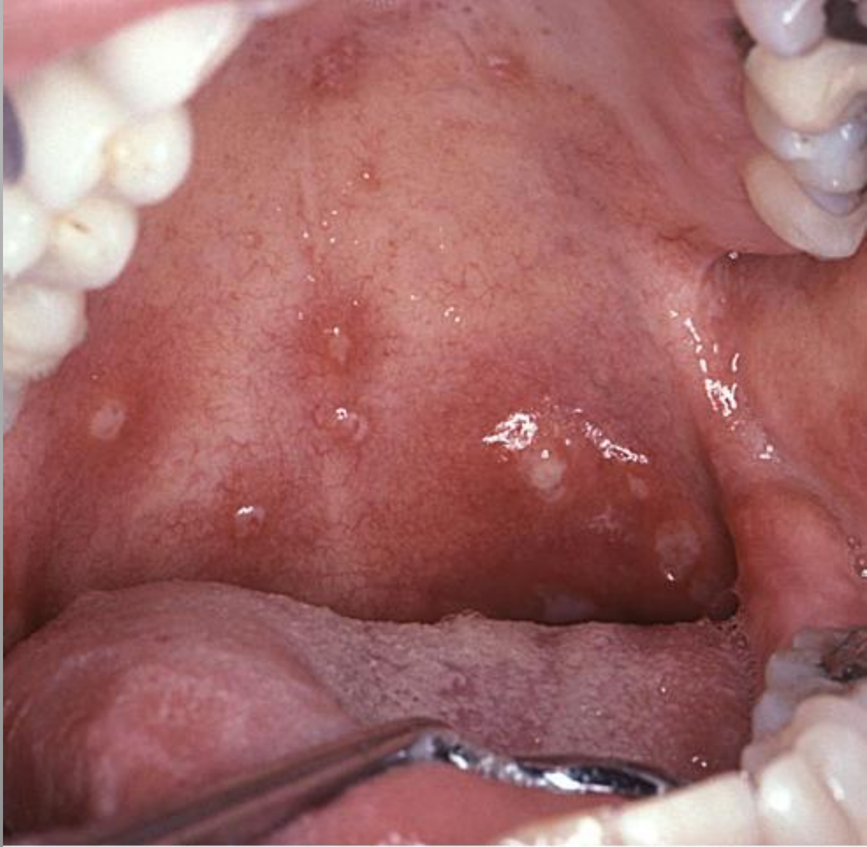
Crohn’s Disease

- Classic findings
  - Skip lesions - Crohn’s does not affect the intestinal mucosa in a continuous fashion
  - Cobblestoning owing to mucosal fissures
  - Luminal narrowing/strictures - string sign
  - Fistulas
  - Aphthous ulcers

Angular Cheilitis



Aphthous Ulcers



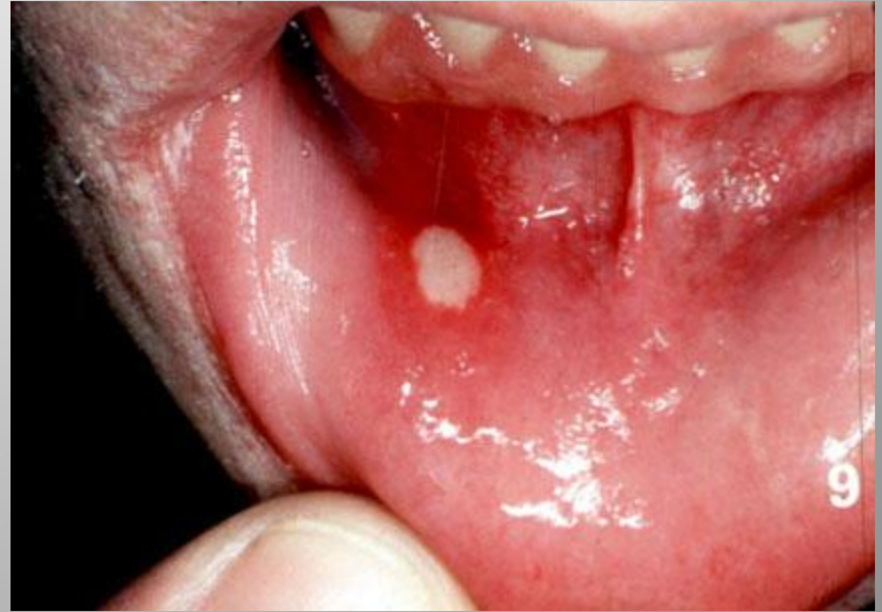
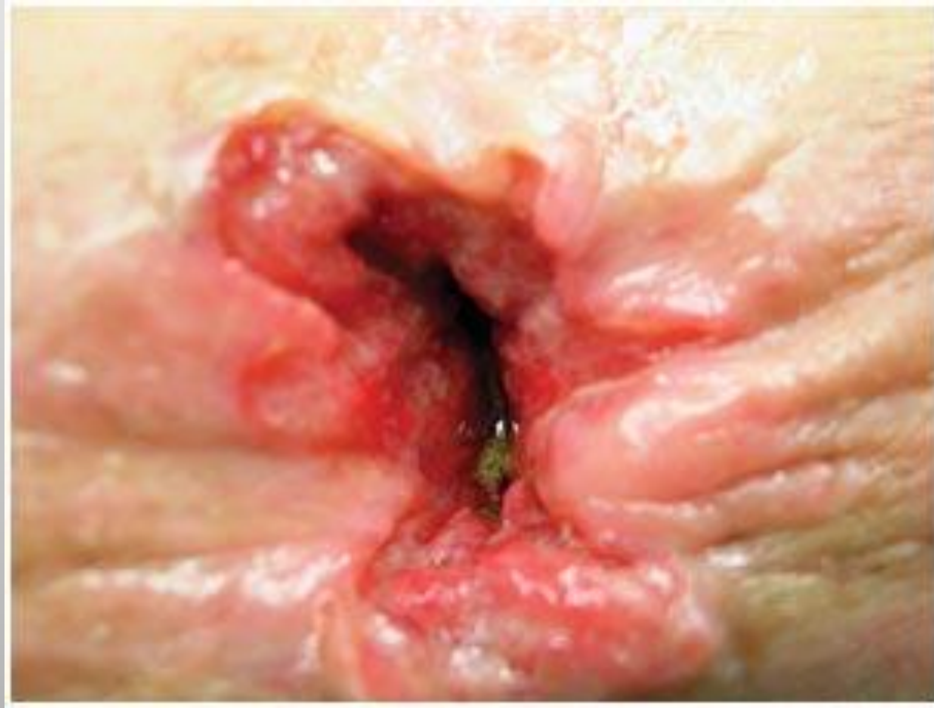


Figure 1 Image of a fissure in ano suspicious for squamous cell carcinoma in a 56-year-old female patient with ileocolic Crohn's disease



Galandiuk S and Davis BR (2008) Infliximab-induced disseminated histoplasmosis in a patient with Crohn's disease
Nat Clin Pract Gastroenterol Hepatol doi:10.1038/ncpgasthep1119

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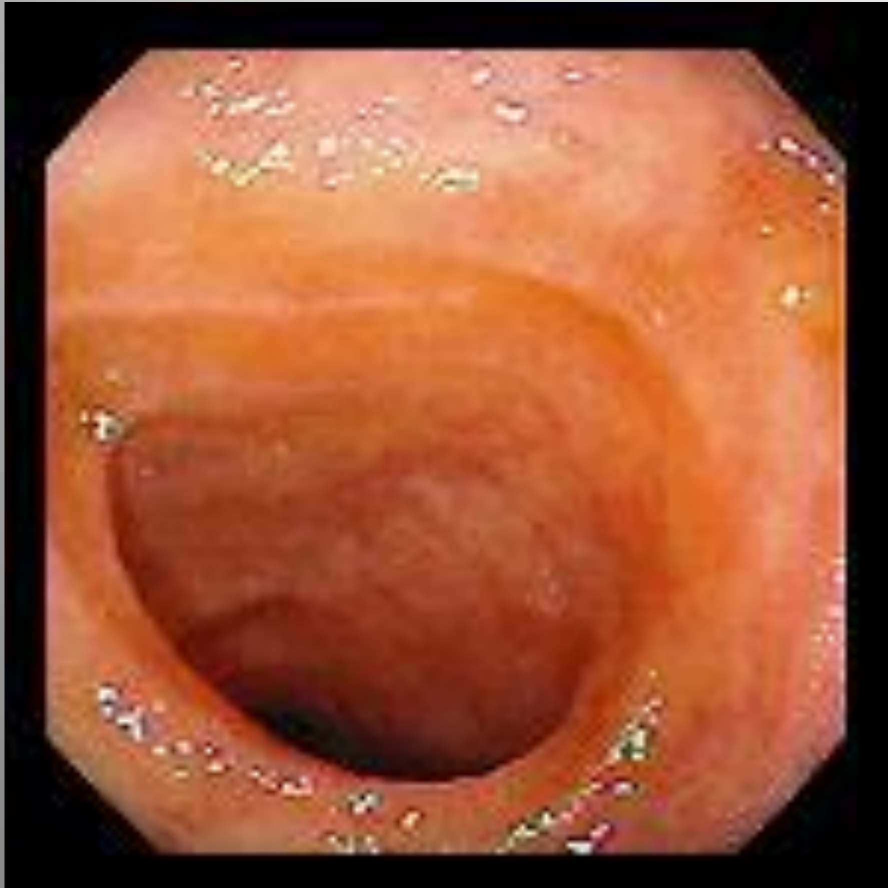
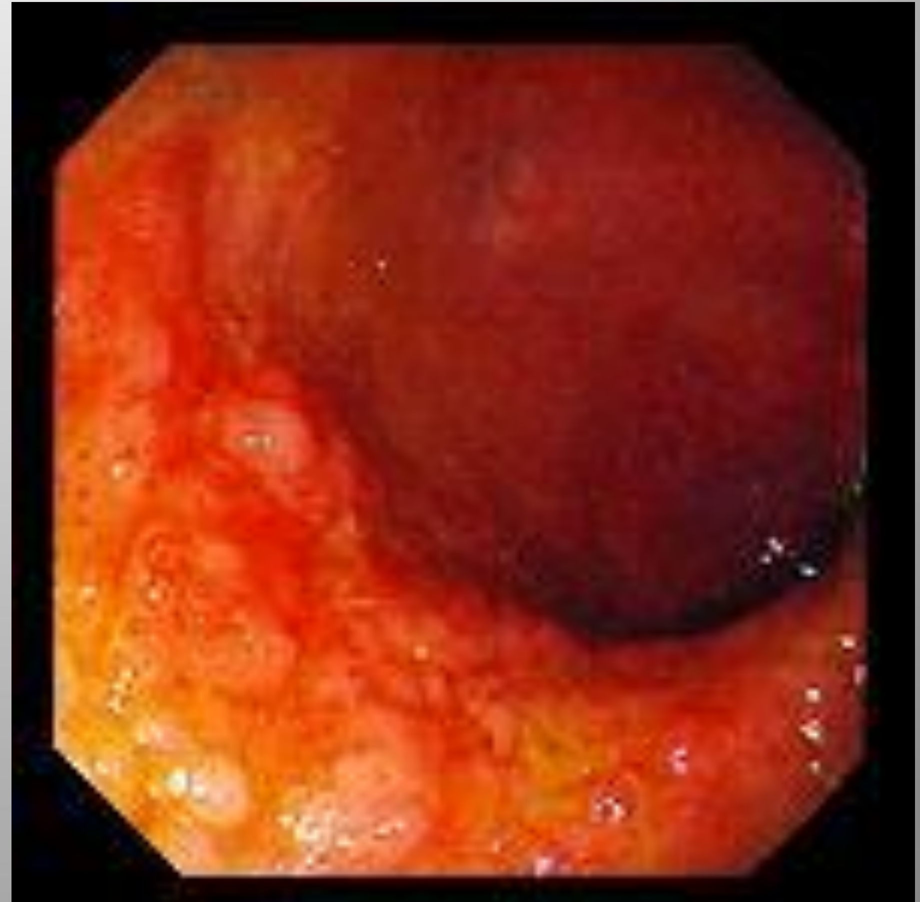
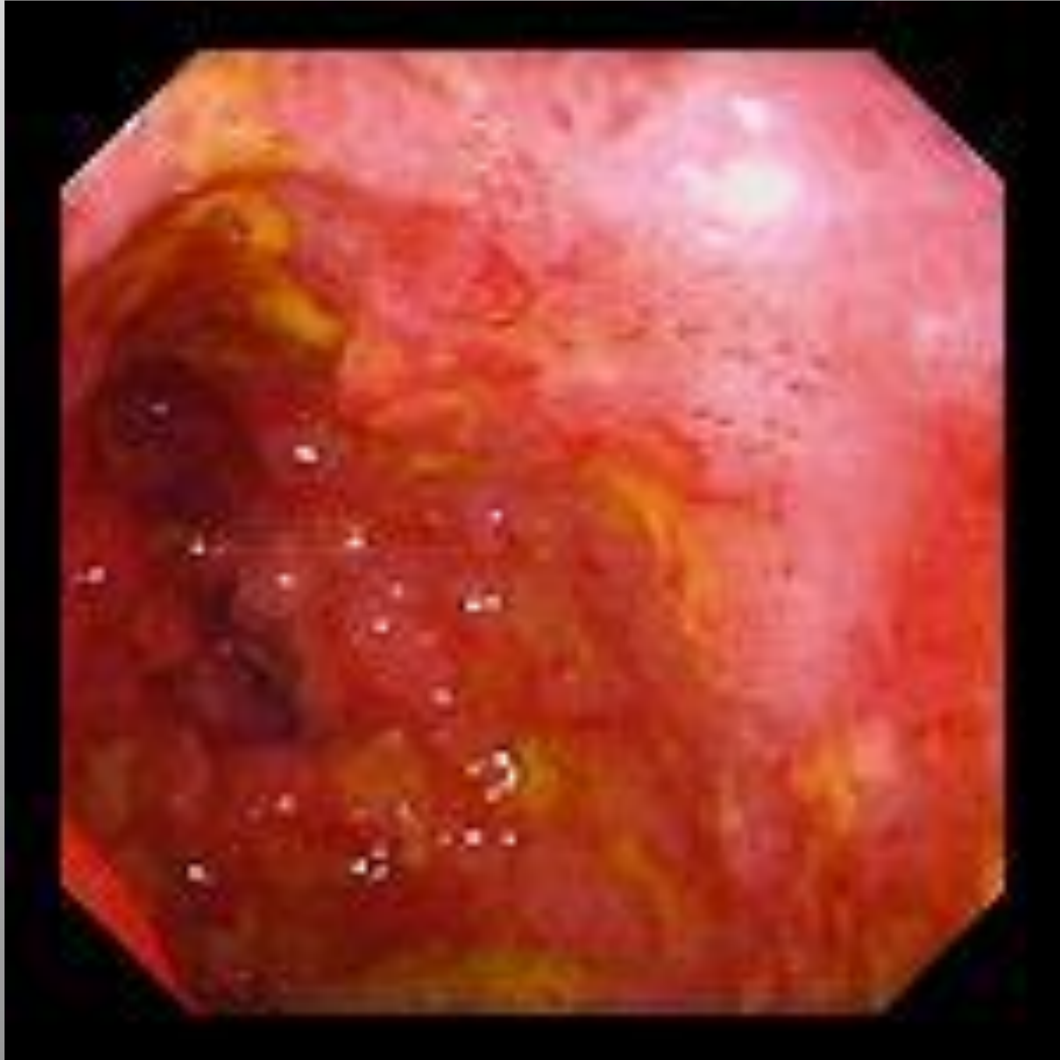
Crohn's Disease

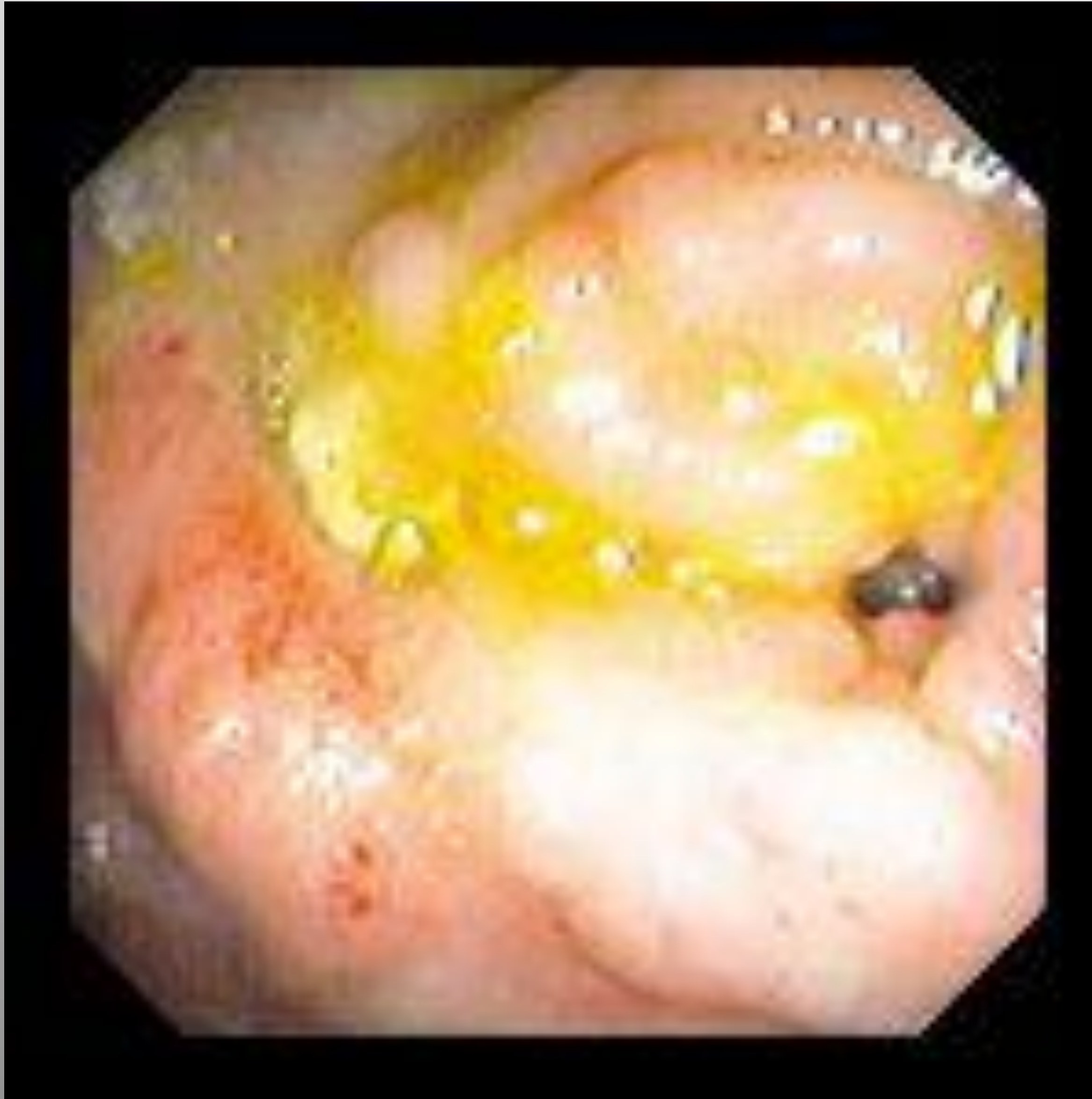




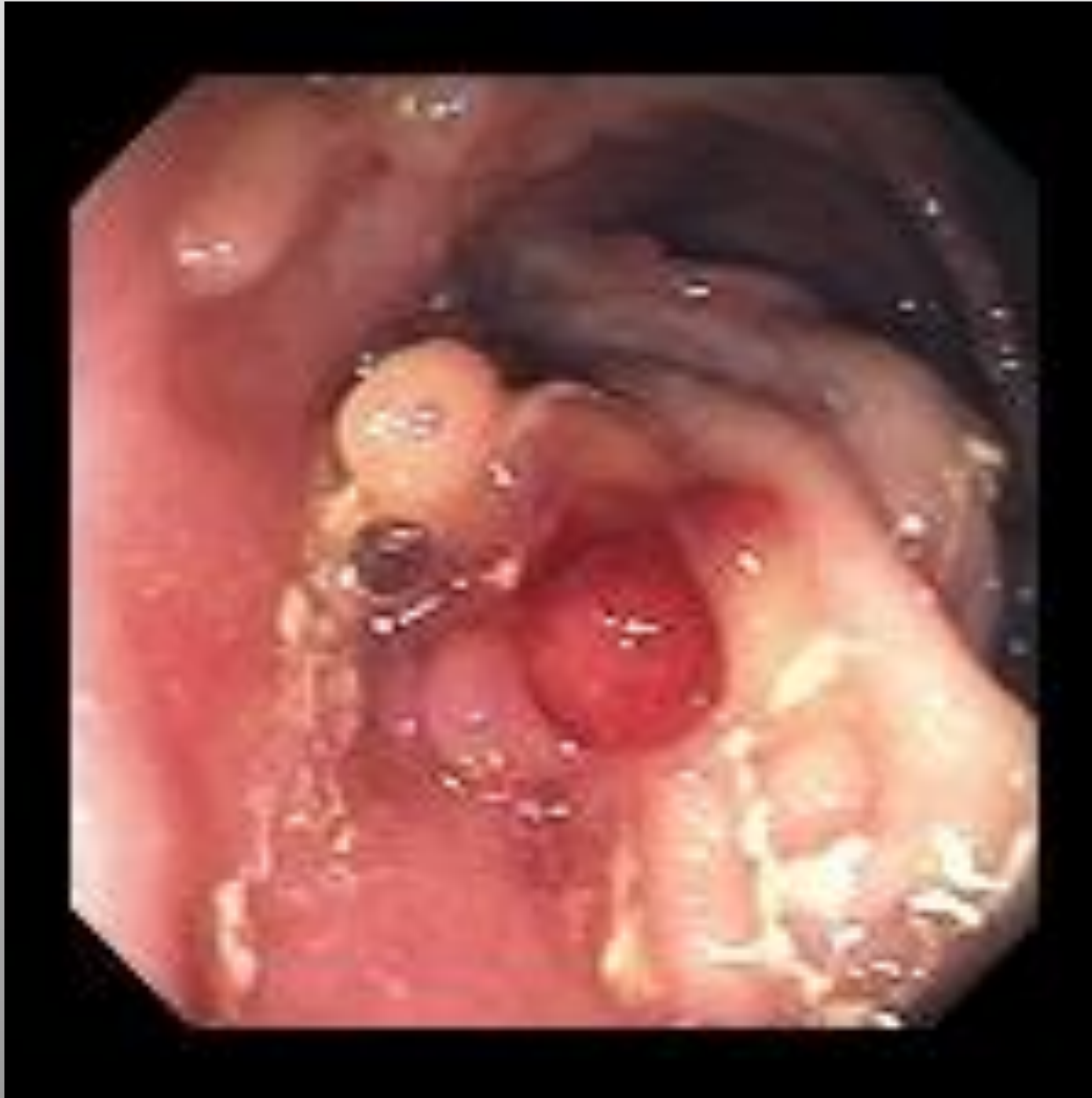
Crohn's Disease

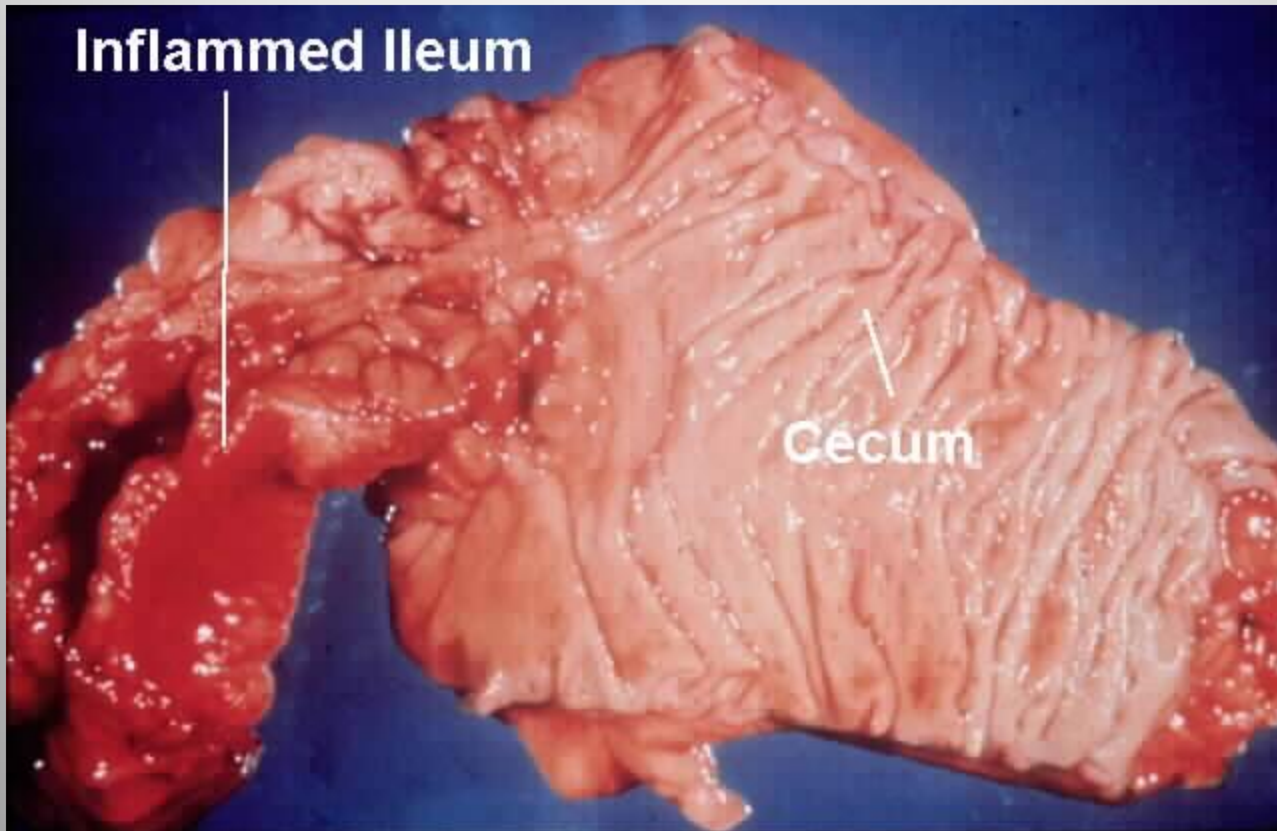


Crohn's Disease



Crohn's Disease




Inflammed Ileum
Cecum

Crohn's Disease

Crohn's Disease

Pattern	% at presentation
Ileocecal disease	40-50
Small bowel only	30-40
Colon only	20

Crohn’s Disease

- Differential diagnosis of ileocecal small bowel disease:
- Acute appendicitis with RLQ pain
- Ectopic pregnancy, tubo-ovarian abscess/PID
- Cecal diverticulitis
- Yersinia enterocolitica
- CMV in immunocompromised host
- Lymphoma, cecal carcinoma

Crohn's Disease

- Differential diagnosis:
- Colonic disease - infectious
  - Bacterial colitis - Salmonella, Shigella, Campylobacter
  - Ameba
  - CMV
- Colonic disease - noninfectious
  - Ulcerative Colitis, radiation, ischemia

Crohn's Disease

- Complications
  - Fistula formation - up to 40% of patients
  - Enteroenteric
  - Enterovesicular - recurrent UTIs and pneumaturia
  - Enterocutaneous - rectovaginal, fistula-in-ano

Crohn's Disease

- Complications
  - Perforation/abscess formation
  - Stricture/ small bowel obstruction
  - Nutritional deficiencies - Disease involvement at the terminal ileum as B12 and fat-soluble vitamin defiency (ADEK).

Ulcerative Colitis

Ulcerative Colitis

- Symptoms
  - Bloody diarrhea
  - Crampy abdominal pain
  - Tenesmus - urgent feeling of needing to evacuate to the rectum.
  - Fever, weight loss also possible
  - 15-25% have extra-intestinal manifestations

Ulcerative Colitis

- Signs
  - LLQ pain - mild to severe
  - Can be very ill in patients with toxic megacolon: fever, tachycardia, orthostasis

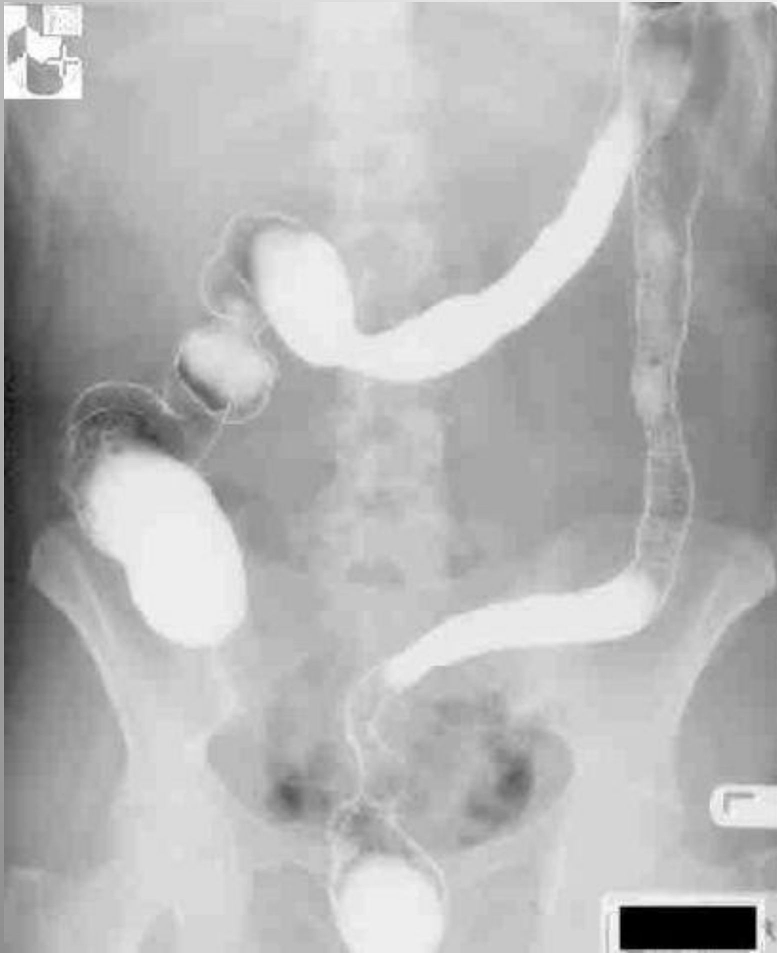
Ulcerative Colitis

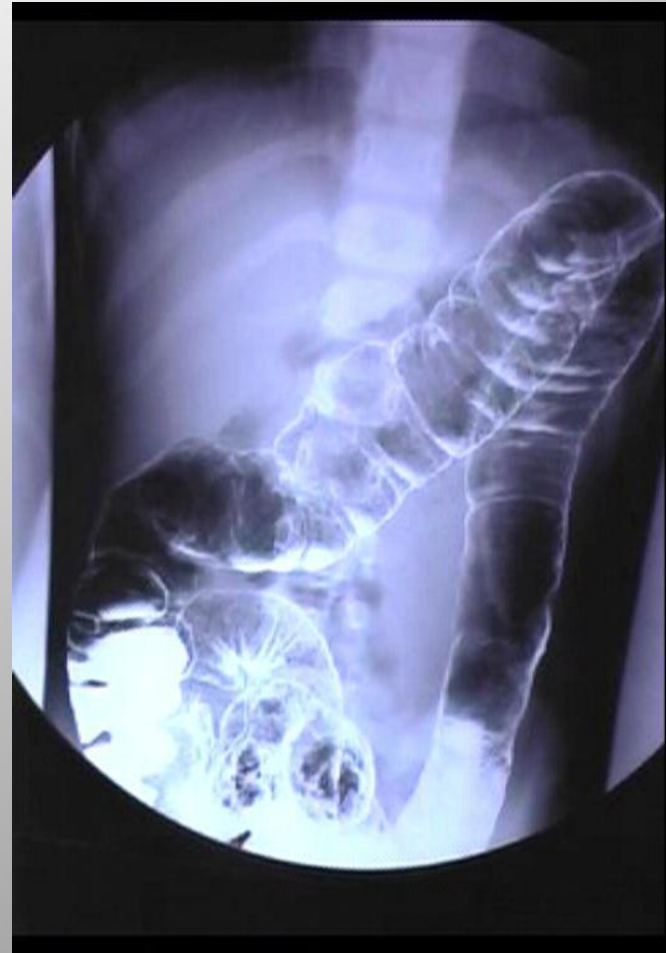
- Lab Findings - as in Crohn's, nonspecific
  - ESR usually elevated in active disease
  - Mild anemia
  - Leukocytosis
  - Thrombocytosis (acute phase reactant)
  - Stool studies negative (culture, C.diff toxin, O&P)

Ulcerative Colitis

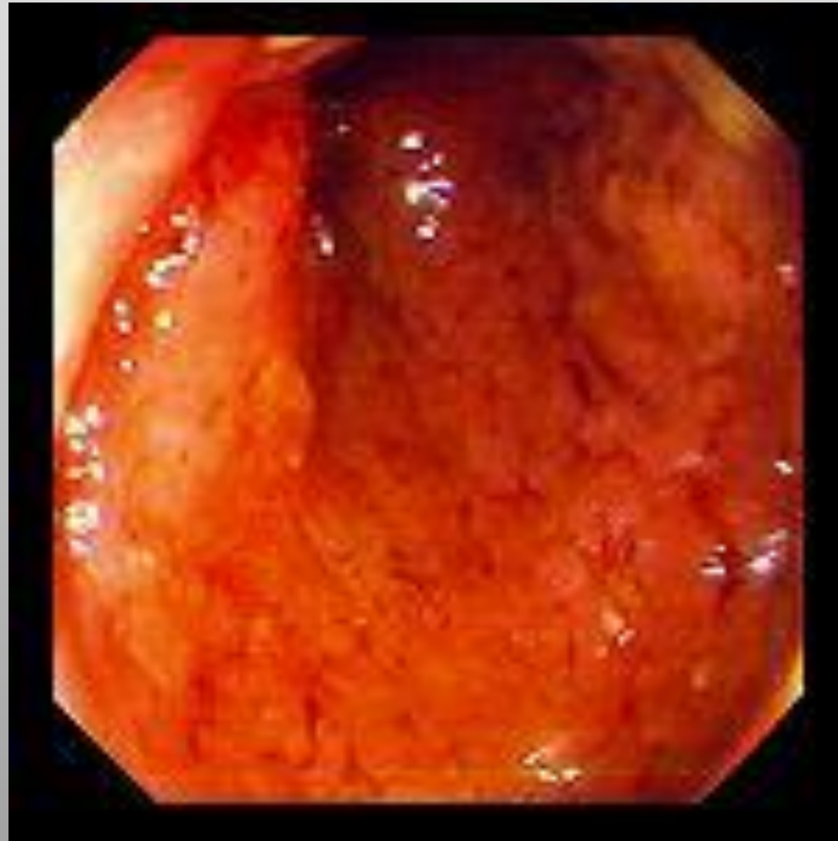
- Imaging Studies
  - As disease affects the rectum and extends proximally, endoscopic evaluation allows for direct visualization for staging and biopsy sampling.
  - Contrast radiography/ACBE may show mucosal changes and distal ulcers.
  - Classic long-standing finding is the lead pipe colon.

Lead pipe colon

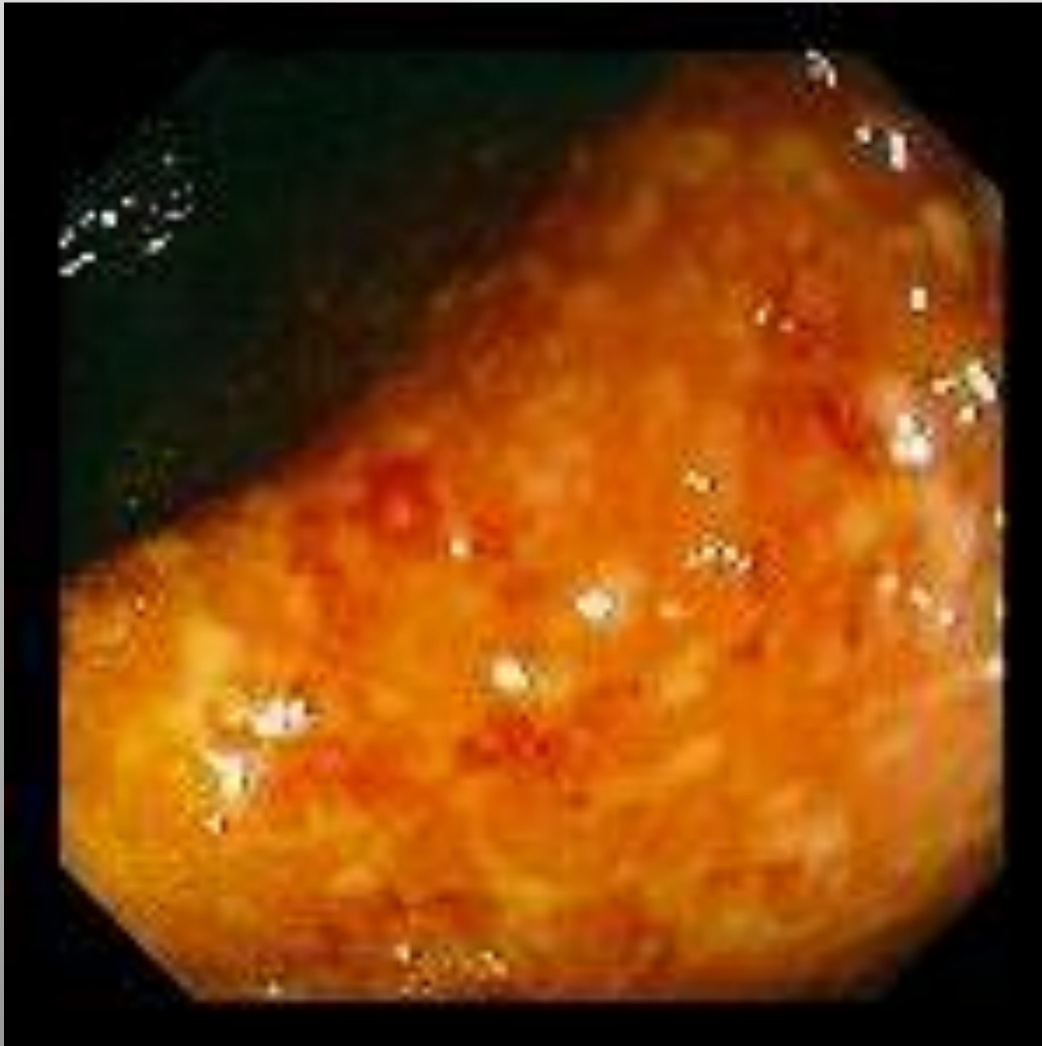




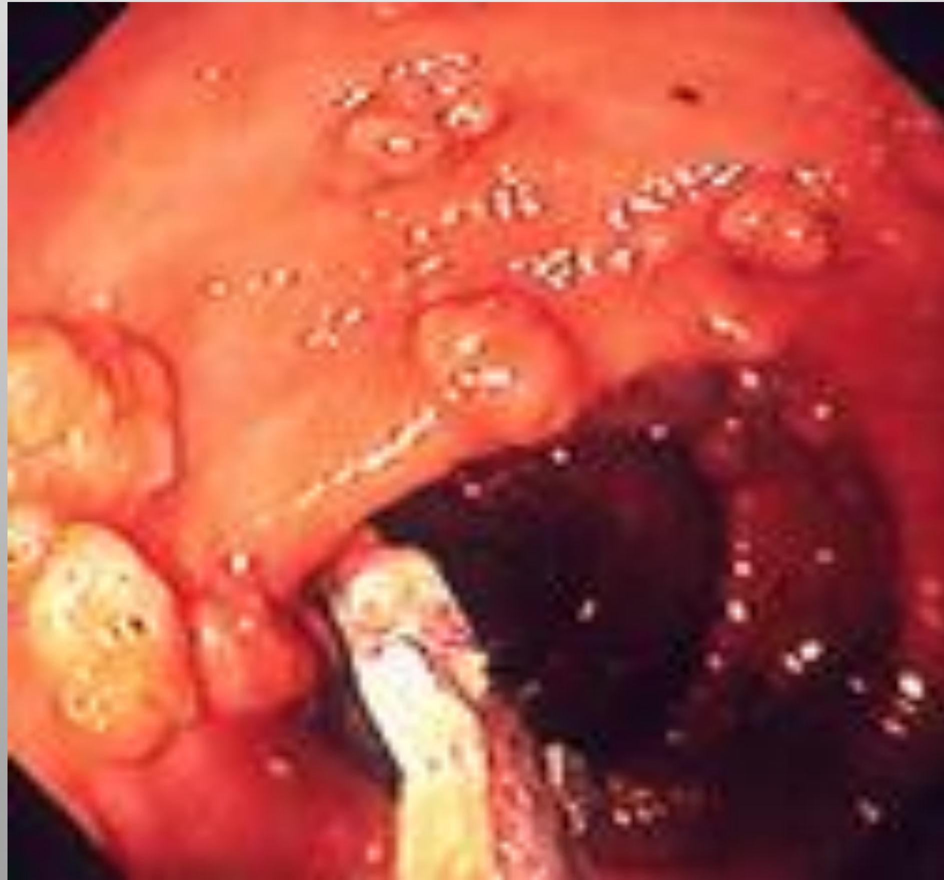
Ulcerative Colitis



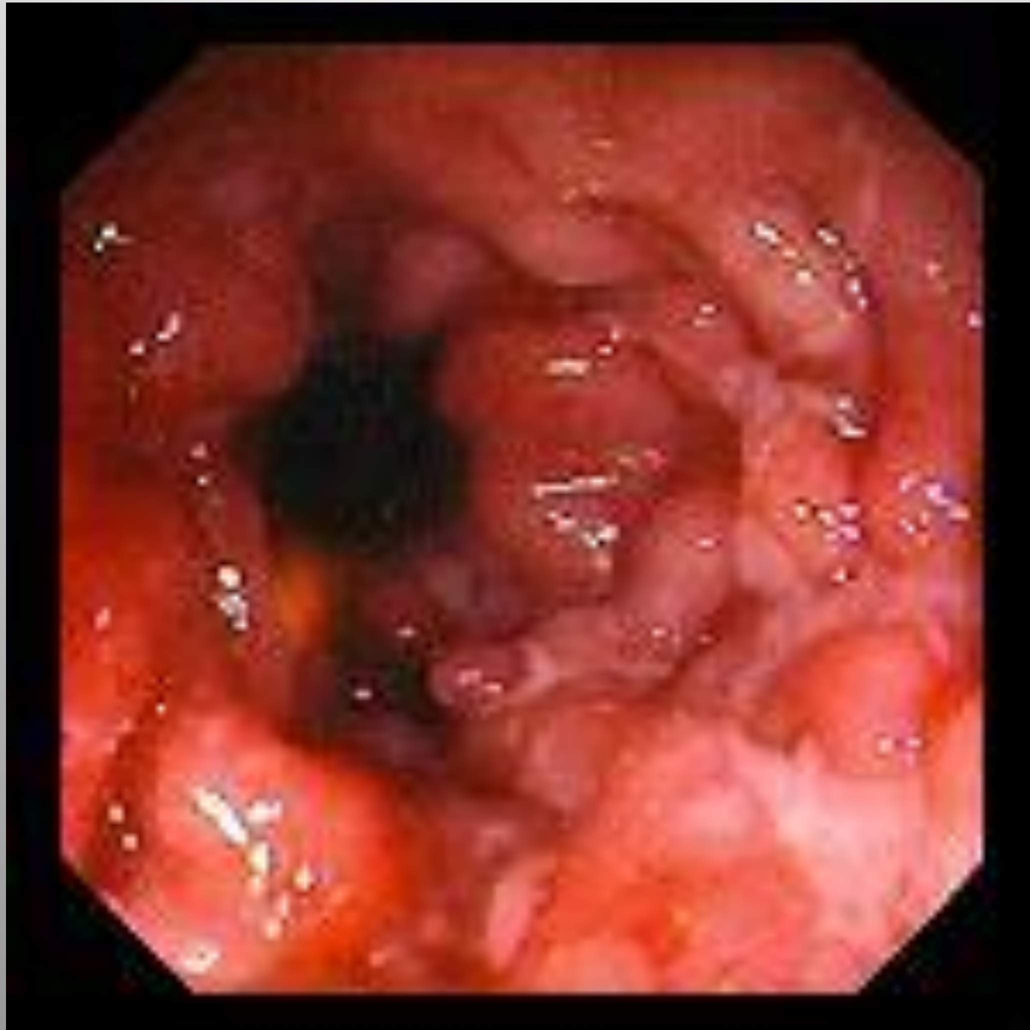
Ulcerative Colitis



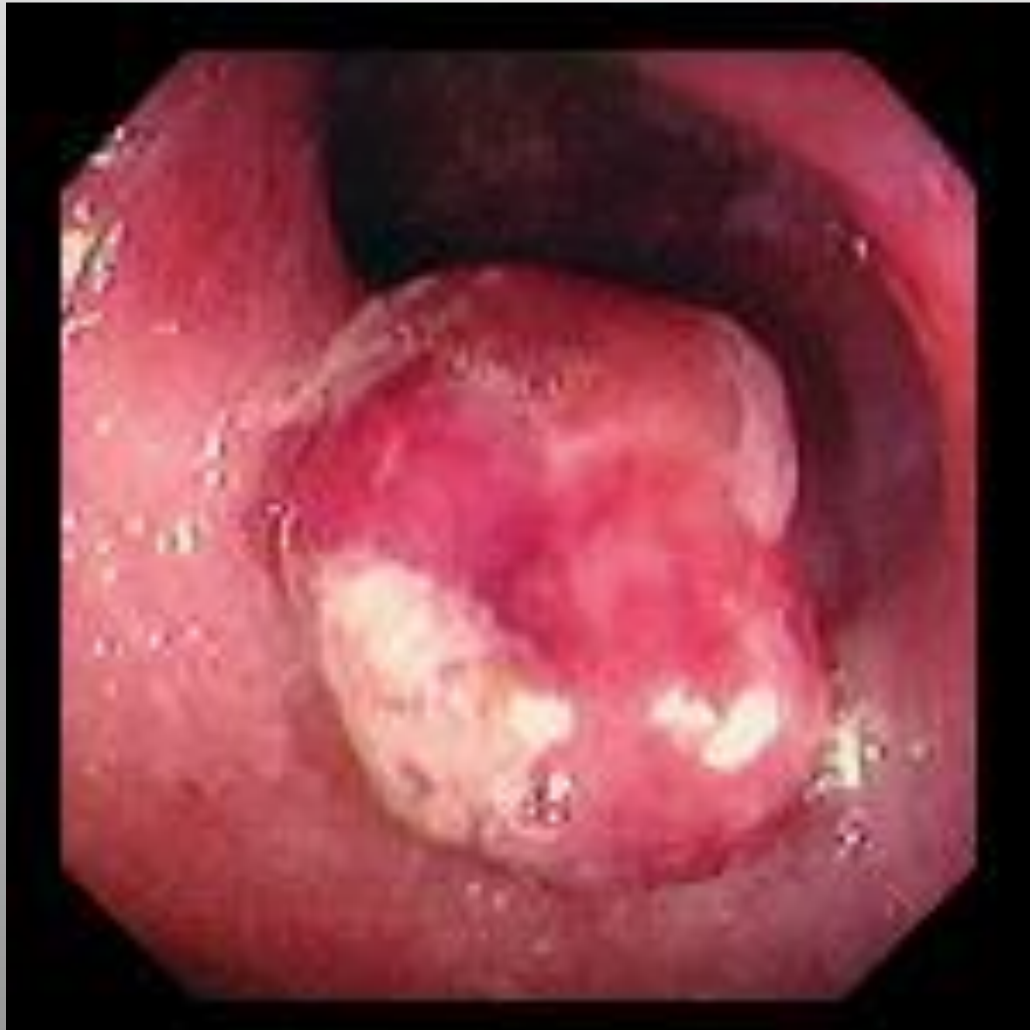
Ulcerative Colitis



Ulcerative Colitis



Ulcerative Colitis



Ulcerative Colitis

- Differential Diagnosis
  - Infection: Campylobacter, Shigella, Salmonella, Yersinia, E. coli 0157:H7, amebiasis, Clostridium difficile
  - Noninfectious: Crohn's disease, ischemic colitis, radiation colitis
  - Immunocompromised host: CMV, HSV, GC, Blastocystis hominis, Chlamydia

Ulcerative Colitis

- Complications
  - Toxic Megacolon: 15-50% mortality
  - Perforation
  - Cancer: increasing risk of dysplasia with increased time from onset of disease.

Time from onset:	20	30
Risk of cancer	8%	18%

Ulcerative Colitis

- Cancer
  - In “usual” colon adenocarcinoma, the cancer starts as a polyp sitting on or above the mucosal surface.
  - In UC, the dysplastic changes occur in flat epithelium. Thus, cancer is not seen until it is a late finding.
  - This is the reason that multiple biopsies are taken during screening colonoscopy in patients with UC.

Ulcerative Colitis

- Prognosis
  - Severity of disease is somewhat predictive of the future course and the need for colectomy.
  - In one study, the colectomy rate was 24% at 10 years and 30% at 25 years.
  - Rate of colectomy is much higher in patients with pancolitis. Those with isolated ulcerative proctitis have essentially the same cancer risk as the baseline population.
  - **<u>Of note, total colectomy is 100% curative!</u>**

IBD markers

- p-ANCA: 25% positive in CD & 75% in UC
- ASCA: 50-75% positive in CD (very specific), not so well for UC
- OmpC: 50% positive in CD

✓ At this time there is no recommendation for routine diagnosis or management in IBD

Summary

	Ulcerative Colitis	Crohn's
Clinical findings		
– Perianal Disease	Rare	Common (1/3 pts)
– Fistulas	Rare	Common (up to 40%)
– Abscess	Rare	20%
– Stricture	Rare	Common
Colonoscopy findings		
– Rectal involvement	Always	Usually spared
– Pattern	Continuous from rectum	Skip lesions
Radiologic findings		
– Ileal involvement	Rare, backwash ileitis	75%
Histologic findings		
– Depth of inflammation	Mucosa to submucosa	Transmural
– Granulomas	Uncommon	20% of biopsies

IBD - Treatment

- Medications used in treatment
  - 5-aminosalicylic acid (5-ASA)/mesalamine
  - Different preparations of 5-ASA include:
  - Asacol, Rowasa, Pentasa (tradenames)
  - 5-ASA is a topically active anti-inflammatory agent for inflamed intestinal mucosa.
  - Chronic 5-ASA requires folate therapy.

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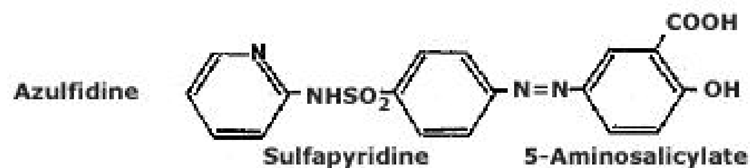
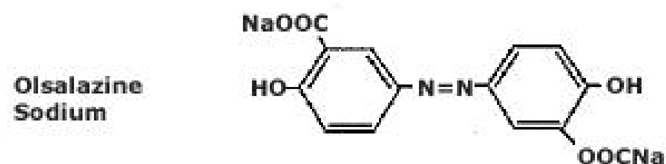
Structures of sulfasalazine, mesalamine, and olsalazine

Azulfidine



Mesalamine

Olsalazine Sodium



Sulfasalazine is a composite molecule composed of 5-aminosalicylic acid (5-ASA) linked by an azo bond to sulfapyridine. Mesalamine is the 5-ASA moiety alone, while olsalazine consists of two 5-ASA molecules joined by an azo bond.

IBD - Rx

- Sulfasalazine/Azulfidine - composed of sulfapyridine and 5-ASA molecules. Bacteria in the terminal ileum cleave the drug into these respective components. Because of where in the intestinal tract the drug becomes active, sulfasalazine is usually used to Rx UC and active ileitis in Crohn's. Sulfapyridine is responsible for the sulfa-related adverse drug reactions of this drug.

IBD - Rx

- Olsalazine/Dipentum - two 5-ASA molecules bound by a diazo bond. Delivered intact to the terminal ileum and there it is cleaved by bacteria.
- Useful in treating UC.
- Side effect of note - ileal secretory diarrhea secondary to the diazo bond. Occurs in 5-10% of treated patients.

IBD - Rx

- Mesalamine
  - Pentasa: 5-ASA packaged in ethylcellulose granules that are slowly released from the jejunum to the colon.
  - Used to Rx Crohn's disease.
  - 4 gm per day most helpful in Crohn's, but requires taking 16 tablets.
  - 2-3 gm/d for active UC, 1-2 gm/d for maintenance of UC

IBD - Rx

- Mesalamine
  - Asacol - enveloped in a pH-sensitive coating which delivers drug to the distal ileum and colon.
  - 2.4 - 4.6 gm/d for UC.
  - Can be used to maintain remission in Crohn’s disease in Crohn’s of the terminal ileum.

IBD - Rx

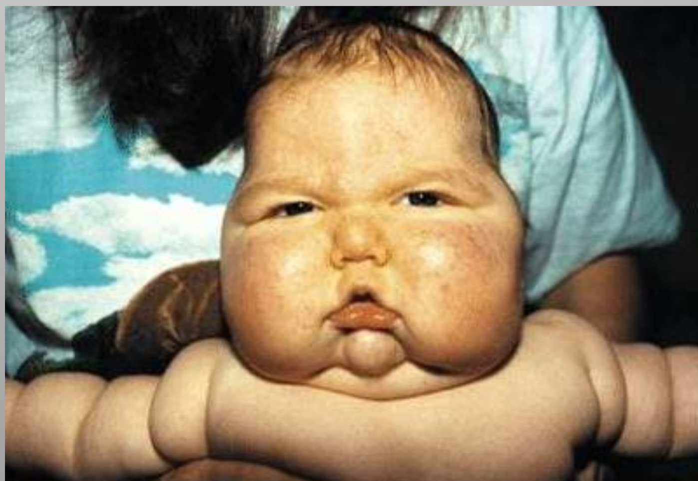
- Mesalamine
  - Rowasa - enema or suppository form of mesalamine.
  - Useful for distal proctosigmoiditis/UC. Not helpful in treating perirectal Crohn’s disease.
  - Little systemic absorption, few side effects.
  - Rowasa works best if given HS and retained overnight.

IBD - Rx

- Corticosteroids - extremely useful for treating acute flares and in maintaining remission in moderate to severe disease.
- Start Solu-medrol at 125mg IV q6hr, then switch to po Prednisone at 40-60mg qD.
- Taper over 8-12 weeks if possible.

Corticosteroids Side Effects

- Cushingoid appearance
- Osteoporosis
- Hypertension
- Diabetes
- Peptic ulcer
- Psychosis
- Aseptic necrosis of bone/hip
- Neuropathy
- Myopathy



IBD - Rx

- Immunosuppressive drugs
  - Azathioprine and 6-Mercaptopurine
    - Purine analogs that may inhibit T cell function
  - Infliximab (Remicade ®), Adalimumab(Humira ®) used for more severe disease
    - Tumor Necrosis Factor (TNF)
- Antibiotics - acute treatment
  - metronidazole/Flagyl - covers anaerobic bacteria. Especially useful in perirectal disease.

IBD - Rx

- Education
- Support groups
- Psychologic therapy as indicated
- Don’t lose sight of the fact that we are treating patients, not diseases.

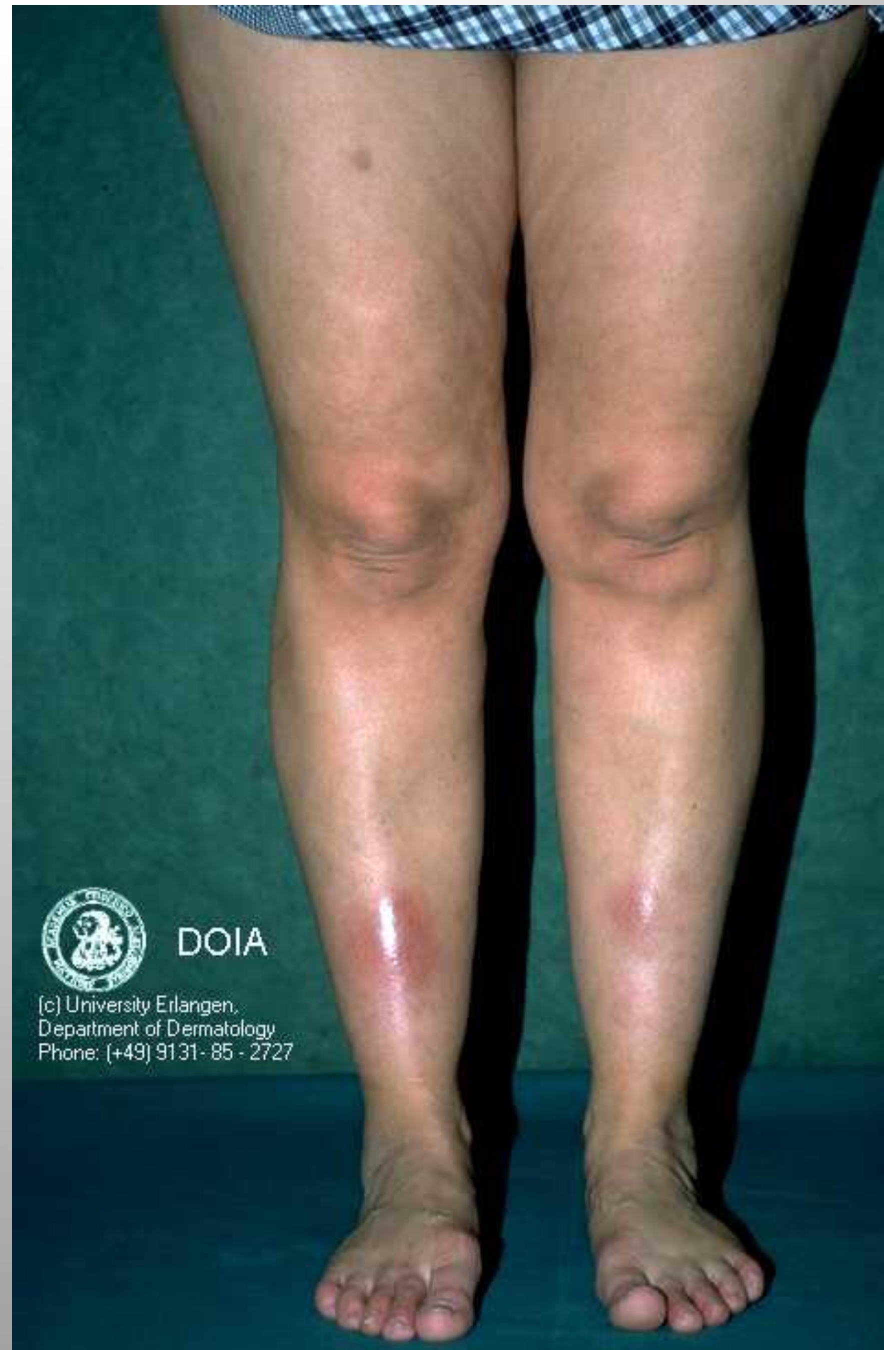
Extra-intestinal Manifestations of IBD

- Reactive arthropathy - present with active disease
- Episcleritis - seen more commonly in Crohn’s disease
- Erythema Nodosum - Crohn’s > UC
- Pyoderma Gangrenosum - UC > Crohn’s

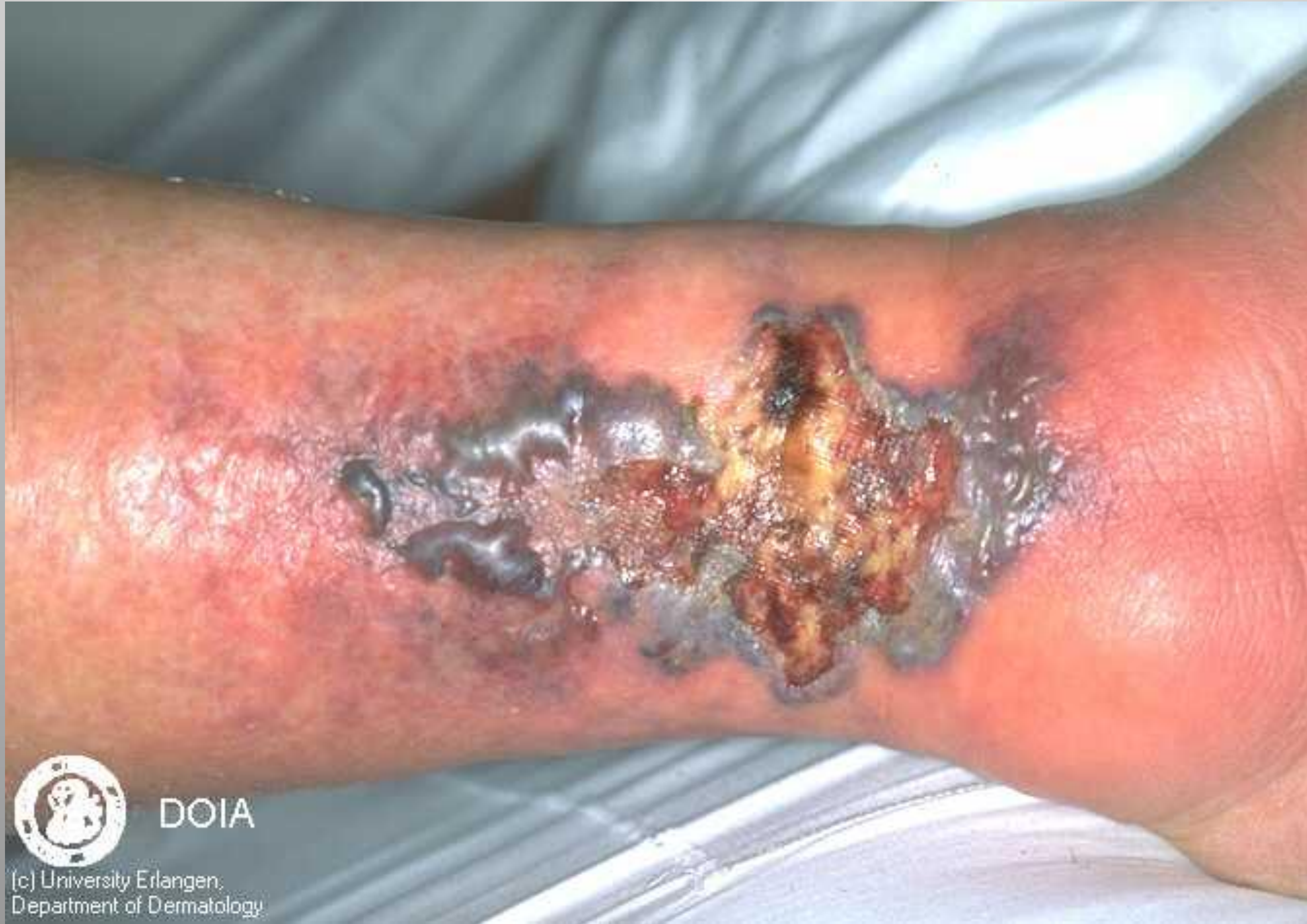
Extra-intestinal Manifestations of IBD

- Sacroiliitis - 10% patients with IBD. Association with HLA-B27
- Uveitis and episcleritis
- Primary sclerosing cholangitis - usually with UC
- PSC also at increased risk

Erythema Nodosum



Pyoderma Gangrenosum



Thanks

Questions?