INFLAMMATORY BOWEL DISEASE & CASES

Anil Seetharam MD

11.10.15

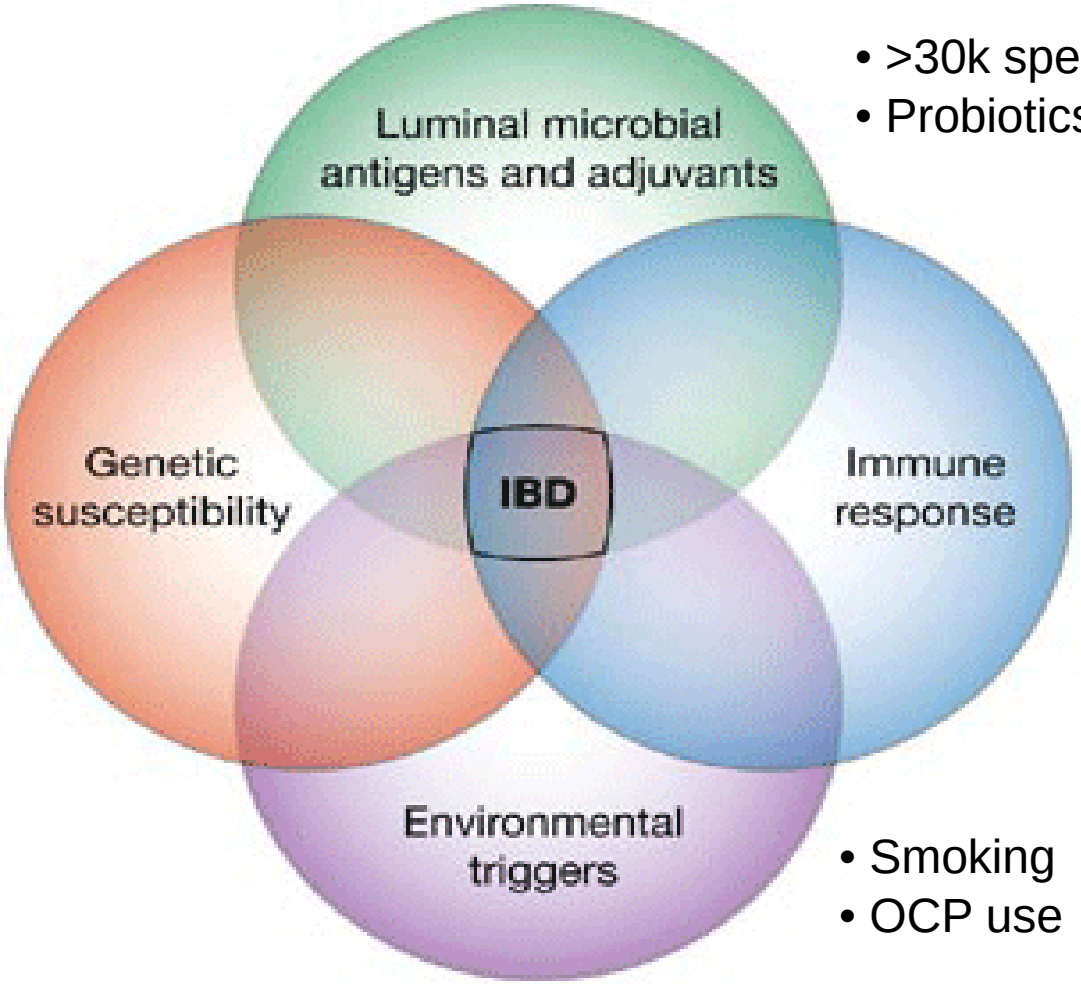
Outline

- Inflammatory Bowel Disease Pathogenesis
- Diagnosis
- Extra intestinal Manifestations
- Complications
- Management
- Cases

Inflammatory Bowel Disease: The Big Picture

- Uncontrolled and dysregulated inflammation of the GI tract in a genetically susceptible individual

- IBD Runs in families 10-15x in 1st degree relatives
- NOD2 mutation Ch 16-- "overeactive immune cells"



- >30k species of bacteria
- Probiotics, antibiotics

- GI tract is an immune organ: Tolerance, Innate, Adaptive immunity

- Smoking
- OCP use

Ulcerative Colitis

- Chronic idiopathic inflammatory disorder of the GI mucosa
- Superficial inflammation extending contiguous fashion beginning at anal verge to involve portion or all colon
- 25 cases/100,000; slightly higher incidence in males, 30-40yrs
- Classic symptoms: bloody diarrhea, tenesmus, fecal urgency
- Location (from rectum)
  - -Just rectum: *proctitis*
  - -To sp flex: *left sided*
  - -Proximal to sp flex: *Extensive*
  - -Entire colon: *Pancolitis*

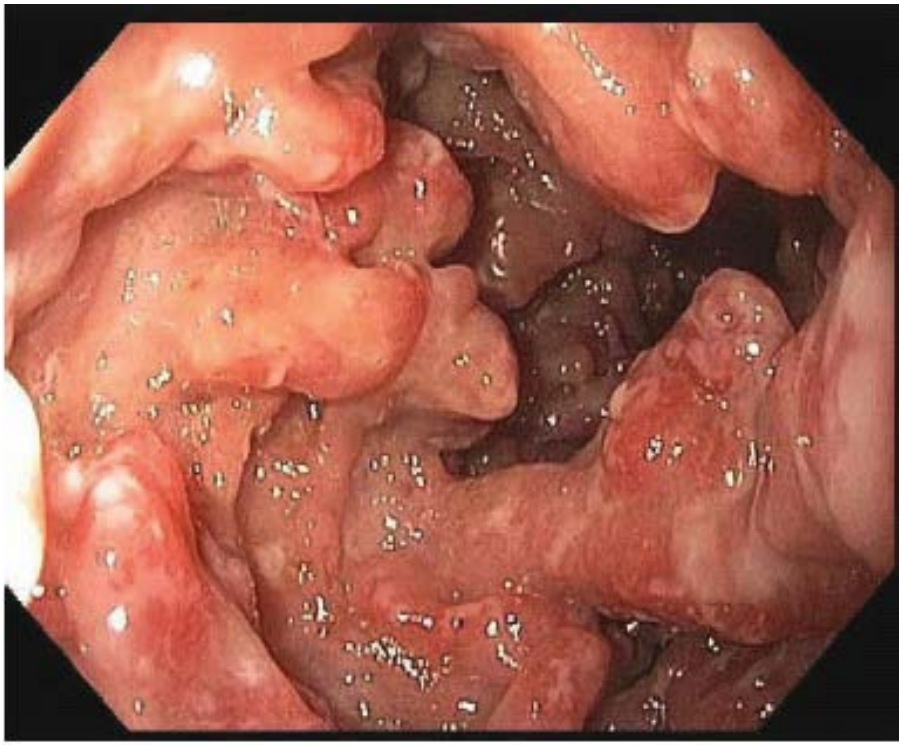
Crohn's Disease

- Chronic idiopathic transmural intestinal inflammation
- Can involve any portion of the GI tract, classically involves the ileocecal region and does not involve the rectum; patchy distribution: "skip lesions"
- 20 cases/100,000, slightly higher incidence females, age 20-30 peak incidence
- Classic symptoms: fever, weight loss, diarrhea, pain, mass

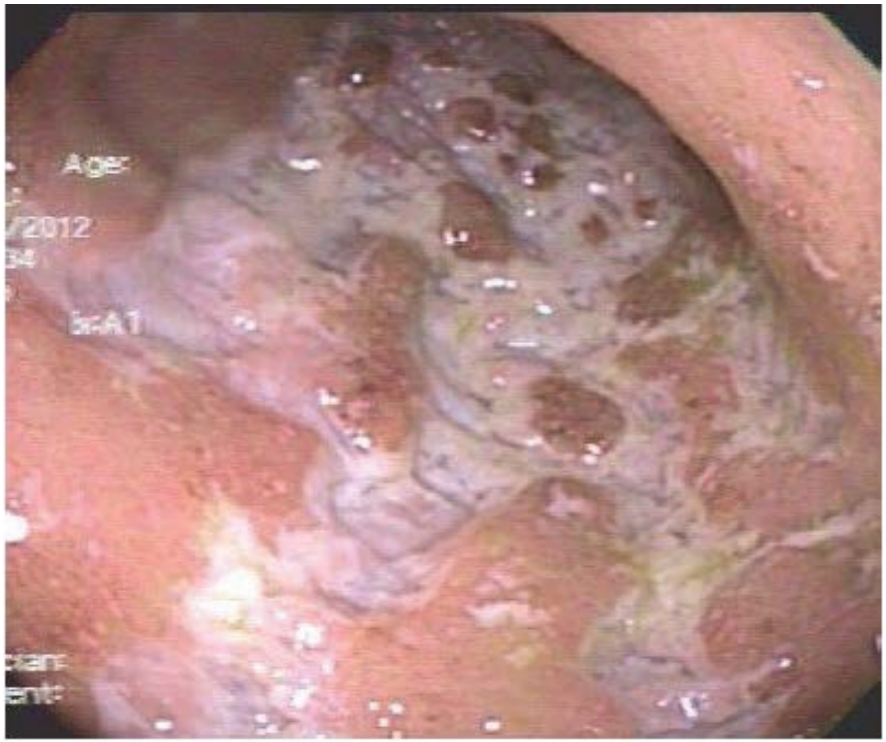
Making The Diagnosis

- No ONE TEST makes the diagnosis of inflammatory bowel disease
- History: GI symptoms Labs: Albumin, CRP, ESR, CBC
- Radiography (beyond just CT)
  - SBFT: evaluation of strictures
  - VCE: evaluate small bowel mucosa
  - MRE: fistulas, perianal disease

Endoscopic and Histologic Assessment is Key



UC: contiguous ulceration, rectum involved, pseudopolyps severe



CD: deep, “rake ulcerations”, rectum spared, skip lesions—”cobblestoning”

- Histologic assessment IS CRITICAL
  - Looking for features of **CHRONICITY ON BIOPSY**
  - Neutrophils are recruited early in any colitis (Acute) and aren’t helpful
  - Lymphocytes, crypt architectural distortion, basal lymphoid aggregates
    - UC: crypt distortion
    - CD: Non caseating granulomas on biopsy (rare)

Differential Diagnosis

Infectious Conditions
- Bacteria
  - Bacterial toxins
    - Toxigenic *E. coli*
    - *Clostridium difficile*
  - Bacterial invasion
    - *Salmonella*
    - *Shigella*
    - *Campylobacter*
    - *Yersinia*
    - *Mycobacterium*
    - Gonorrhea
    - *Aeromonas*
    - Lymphogranuloma venereum
- Parasites
  - Amebiasis
  - Chlamydia
  - Schistosomiasis
- Viruses
  - Cytomegalovirus
  - Herpes simplex
  - Adenovirus

Noninfectious Conditions
- Collagenous colitis
- Lymphocytic colitis
- Diverticular-associated colitis
- Diversion colitis
- Ischemic colitis
- Medication-induced colitis
- NSAID-induced enterocolitis
- Gold-induced enterocolitis
- Chemical colitis
- Glutaraldehyde-induced colitis
- Radiation enterocolitis
- Appendicitis
- Neutropenic enterocolitis
- Solitary rectal ulcer syndrome
- Malignancy
- Carcinoma
- Lymphoma
- Leukopenia
- Mesenteric venous thrombosis
- Typhlitis

Ulcerative Colitis

- Gradual or sudden onset of increased bowel movements, bloody, cramping and abd pain
- Diarrhea usually worse in the morning, postprandial
- Mild activity—exam is often benign
- Course variable: long periods of remission
- Nicotine is thought to confer protection
- Disease refractory to medical therapy: colectomy is curative
  - Ileal pouch, anal anastamosis→pouchitis

Crohn's Disease

- Symptoms depend on the location of disease activity
- Colonic disease behaves a lot like UC
- Transmural inflammation creates problems: fistulizing disease, fibrostenotic disease
- Course highly variable
- Nicotine makes worse
- Treatment: largely medical
  - Surgery Ileocolonic resection, SB resection for strictures

Distinguishing UC from CD

Characteristic	UC	CD
Rectal Bleeding	Usual	Sometimes
Abdominal Pain	Rare	Often
Perianal Disease	Extremely Rare	5-10%
Upper GI Symptoms	Never	Occasional
Cigarette Smoking	Rare	Common
Malnutrition	Sometimes	Common
Rectal Disease	Usual	Rare
Continuous Disease	Usual	Rare
Crypt Abscesses	Common	Rare
Granulomas	Never	10-20%
Skip Lesions	No*	Common
Ileal Involvement	No*	Common
Fistulas	Never	Common
Transmural inflammation	No	Common

Extraintestinal Manifestations

- Disorders of skin, eyes, joints, and mouth. Most parallel underlying intestinal disease activity and respond to GI treatment

- Skin
  - Pyoderma Gangrenosum: idiopathic skin ulceration at sites of trauma, lower extremities, UC>CD

  - Erythema Nodosum: tender, reddish purple nodules on extensor surface of lower extremities

- Ocular Manifestations
  - Uveitis: photophobia, headache, blurred vision; independent of bowel activity

  - Scleritis/Episcleritis: mild itching

EIMs continued

- Peripheral arthropathy
  - Pauciarticular (Type 1): < 5 joints, big (knees, elbows, ankles) responds well to bowel treatments
  - Polyarticular (Type 2): > 5 joints, small, doesn't respond well to bowel treatments
- Axial arthropathy
  - Spondylitis, HLA-B27
  - Sacroilitis
  - Very difficult management, does not respond to bowel treatments

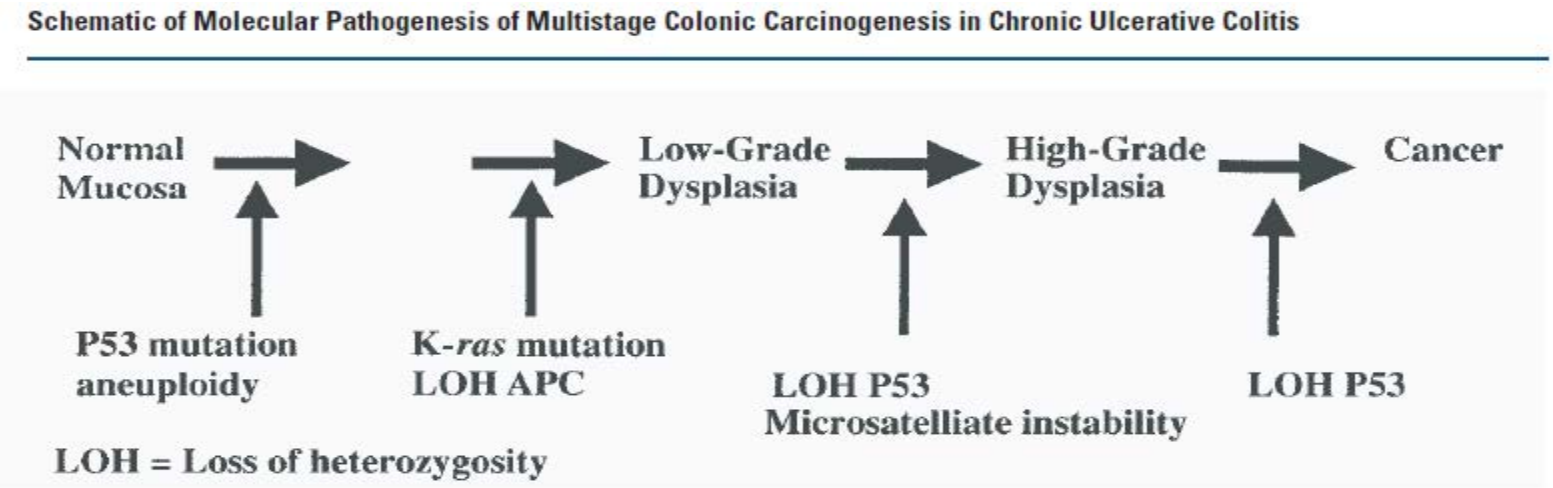
Complications

- Decreased Bone Mineral Density
  - Malabsorption of calcium and vitamin D or chronic steroids
- Thrombotic Events
  - 3-4 increased risk of DVT
- Nephrolithiasis
  - Calcium oxalate or uric acid stones
- Anemia
- Primary Sclerosing Cholangitis
  - Narrowing, stricturing of the extrahepatic ducts
  - More common in UC (5-10%) than CD

Biggest Complication: Colorectal Cancer

UC: 10-25 fold Increased risk of CRC
CD: 2-3 fold increased risk of CRC; 5-6 fold increased risk in Crohn's Colitis

Risk is directly related to duration of colitis



• Anyone with IBD and documented duration longer than 8-10 years needs surveillance colonoscopy with biopsies (every 10cms) every 1-2 years

•Surveillance for dysplasia
•Low grade dysplasia can be followed; High grade=Colectomy

Therapy Goals

- Induce Remission
- Maintain Remission
- Alleviate or minimize intestinal symptoms
- Alleviate of minimize extra intestinal symptoms
- Minimize toxicity
- Improve quality of life
- Maintain adequate nutrition

Aminosalicylates

Delivery	Proprietary name	Unit dose	Generic name	Site	Dose (g/day)
Oral Tablet					
	Azulfidine	500 mg	Sulfasalazine	Colon	3–6 g/day
	Asacol	400 mg	Mesalamine	Distal ileum	1.6–4.8 g/day through colon
	Asacol HD	800 mg	Mesalamine		
	Dipentum	250 mg	Olsalazine	Colon	1.5–3 g/day
	Colazal	750 mg	Balsalazide	Colon	6.75 g/day
	Apriso	375 mg	Mesalamine	Distal Ileum through colon	1.5–3.0 g/day
	Lialda	1200 mg	Mesalamine MMX	Colon	2.4–4.8 g/day
Oral Capsule					
	Pentasa	250 or 500 mg	Mesalamine	Duodenum through colon	2–4 g/day
Suppository					
	Canasa	1000 mg	Mesalamine	Rectosigmoid to 20 cm	0.5–1.0 g/day
Enema					
	Rowasa	1 or 4 grams	Mesalamine	Left colon to splenic flexure	1–4 g/day

Immune Modifiers

- Azathioprine
  - Prodrug non-enzymatically converted to 6-MP
  - 6MP is metabolized to 6TGN which has favorable activity
  - TPMT is involved in process, if not present, unfavorable metabolites
  - UC and fistulizing CD
- Methotrexate
  - 15mg IM weekly for CD, not approved for UC
- Cyclosporine
  - Rarely used, a lot of toxicity

Biologics

- Infliximab, anti TNF
  - 5mg/kg at 0,2,6 weeks
  - Infusion every 8 weeks for maintenance
- Adalimumab, anti TNF
  - Subcutaneous, loaded, every 2 weeks
- Certolizumab, anti TNF-Fab fragment
  - Subcutaneous, loaded, every 4 weeks
- Natalizumab, anti integrin
  - Infusion every four weeks
  - Progressive multifocal leukoencephalopathy (PML)

Steroids

- Mainstay for quick induction
- Oral is equivalent to parenteral
- Dosing is critical: 1mg/kg daily
- Can be given topically

- Budesonide (entocort) controlled ileal release, extensive 1st pass metabolism, less adrenal suppression

Inpatient Management of Flares

- Revisit the diagnosis: biopsy proven? Chronicity
- Restage the disease
- What was the last flare like? Symptom diary
- Rule out infection or secondary process
- If you are going to use steroids, dose appropriately
- If distal symptoms, treat distally
- Have an exit strategy in mind if steroids are started
  - Clear taper in mind
  - Preparation for immune modifier or biologic
    - TB testing, TPMT testing, Hep B studies
  - If not DRAMATICALLY BETTER, is it necessary to get surgery involved?

29 y/o with PMHx of ulcerative colitis presents to establish. UC diagnosed at age of 18 when he developed bloody BMs and tenesmus; colonoscopy w biopsy showed chronic colitis. He received a short course of steroids at diagnosis and has been on oral mesalamine 3 grams daily for the last 10 years. He feels well and has 1 BM daily without blood and no abdominal pain. Current lab evaluation includes: Hgb: 15.0 g/dL, Alb: 4.1, Cr: 0.5. He has not seen a GI since diagnosis and doesn't see the need. Which of the following is correct regarding management of UC in this patient:

A) Initiation of steroid therapy is needed for active disease

B) Biologic therapy should be considered given aminosalicylate use for over 10 years

C) Request for colonoscopy is indicated for surveillance of CRC given disease duration of 11 years

D) CRC screening is indicated and can be accomplished with FOBT given age

You refer the 29 year old with UC for colonoscopy. Results show no macroscopic disease and biopsies are consistent with mild, chronic colitis with no dysplasia. He remains well on mesalamine for the next year with no bowel issues. He returns to you 1 year later for annual physical. He has no major complaints but feels a bit fatigued.

Annual lab evaluation includes: Hgb: 15.0 g/dL, Alb: 4.1, Cr: 0.5, ALT: 8, AST: 10, Tbil: 1.8 and ALP: 400. You notice Tbil and ALP were normal one year ago. Which of the following tests is indicated for further workup:

A) X-Ray of the spine

B) Magnetic Resonance Cholangiopancreatography (MRCP)

C) 24 hour urine protein collection

D) Evaluation of peripheral blood smear for hemolysis

32 y/o with hx of ileocolonic Crohn's Disease presents for evaluation of fatigue. Diagnosis made by colonoscopy at age 18 when she presented with RLQ pain. Managed with entocort from age 18-22 but developed intermittent small bowel obstruction from ileal stricturing requiring hospitalization. She underwent induction with infliximab and remained in remission from age 22-28. She redeveloped small bowel obstruction and underwent an ileocolonic resection at age 28. She has felt well without pain since and has been maintained on flagyl for disease recurrence. Lab evaluation reveals: Hgb: 7.5, Plts: 250k, MCV: 110, ESR: 1, Ferritin and Iron Battery within normal limits, Haptoglobin normal. Which of following is the most likely etiology of her anemia:

A) Chronic inflammation

B) Iron deficiency from occult GI bleeding

C) Resection of the terminal ileum

D) Side effect of chronic flagyl use

You are taking care of a 26 y/o WM in the hospital with a diagnosis of Ulcerative Pancolitis. Disease was in remission on Infliximab q8 weeks (last dose 1 week ago) for the last 2 years with 1-2 BMs daily, no blood or abdominal pain. This changed 2 days ago with the onset of severe rectal urgency and 10 bloody BMs daily. Admission is noteable for stable vital signs. Admit labs include: WBC: 4.0, Hgb: 10.0 g/dL, Cr: 0.5g/dL, ESR: 100, stool cultures/c. diff negative.

-You commence 1 mg/kg of prednisone orally. After 6 days, vitals and lab parameters have not changed and the patient is having 8 bloody bowel movements daily with continued urgency. Which of the following is an appropriate next course in management:

A) Add rectal mesalamine preparation for distal symptoms

B) Consider change in biologic therapy from infliximab

C) Consider colorectal surgery consult for discussion of colectomy

D) All of the Above