

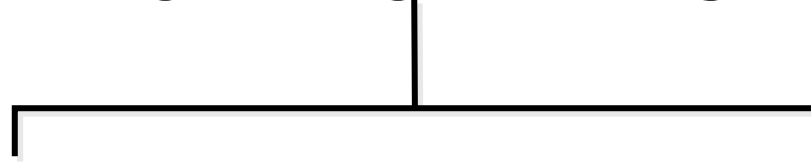
Contemporary Management of Inflammatory Bowel Disease (IBD): What Do I Treat and What Do I Send?

James Lord, MD, PhD

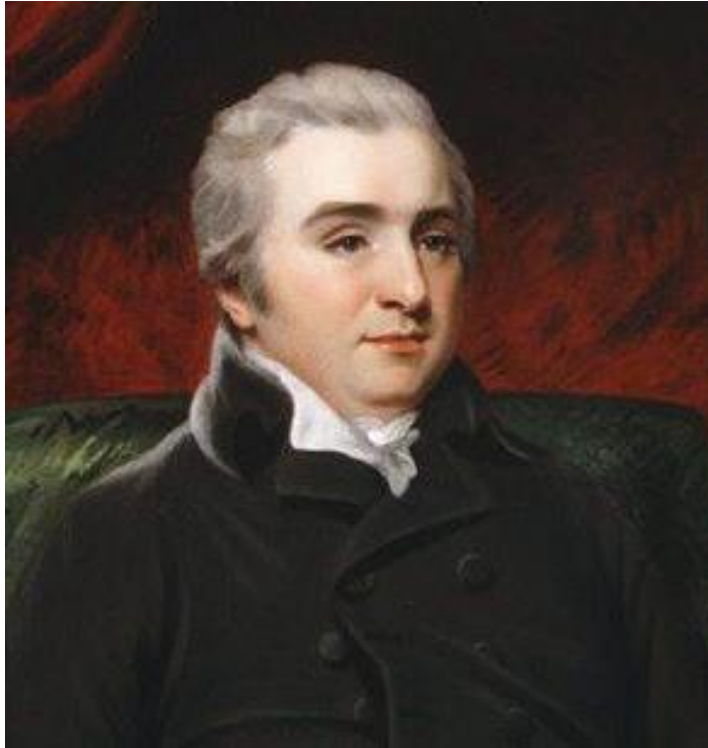
Benaroya Research Institute

Virginia Mason Franciscan Health

INFLAMMATORY BOWEL DISEASE (IBD)



Ulcerative Colitis (UC)



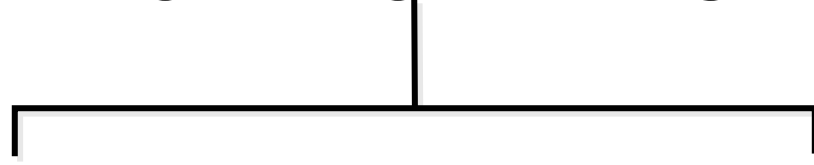
Maybe described by by Matthew Baillie in *Morbid Anatomy*, 1793?

Crohn's Disease (CD)

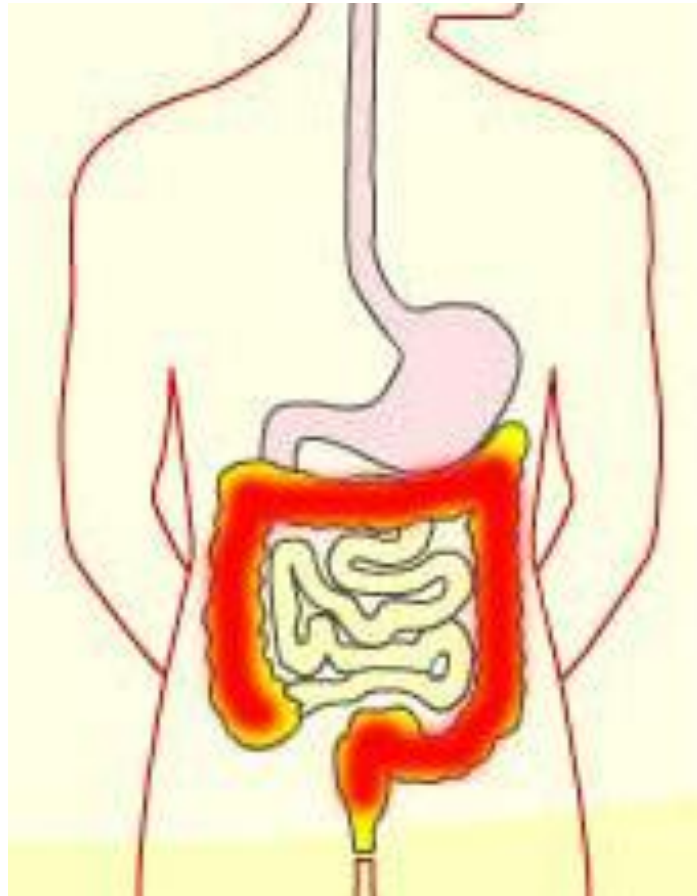


Described by Burrill Crohn et al, 1932, Mt Sinai Hospital, NYC

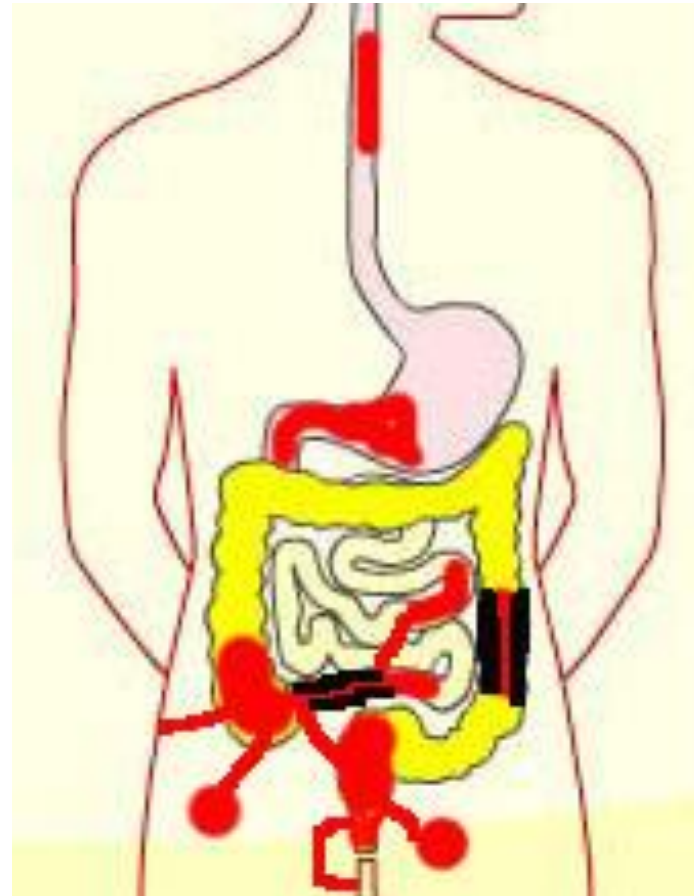
INFLAMMATORY BOWEL DISEASE (IBD)



Ulcerative Colitis (UC)

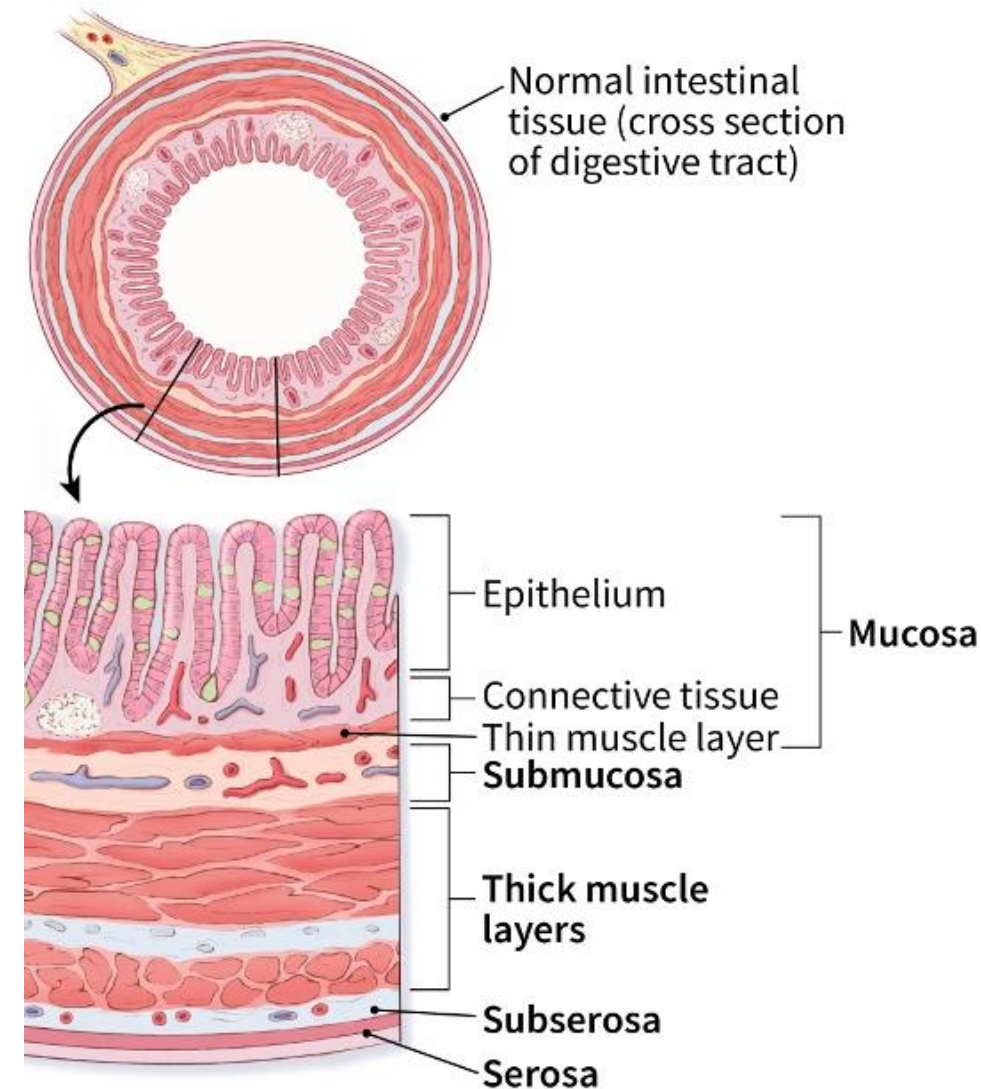


Crohn's Disease (CD)



IBD Can Vary By

- Anatomic distribution of inflammation
 - Gross:
 - UC: how much of colon is involved?
 - Crohn's: is colon and/or small intestine involved, and where?
 - Microscopic:
 - Mucosal inflammation (UC, Crohn's)
 - Submucosal/transmural inflammation (Crohn's)
- Severity of inflammation
- Structural complication (Crohn's)
 - Stricture
 - Fistulas
- Extra-intestinal complications



Peripheral pauciarticular arthritis

Axial spondyloarthropathy



Arthritis



Skin conditions

Erythema nodosum

Pyoderma gangrenosum

Primary sclerosing cholangitis (PSC)



Liver disorders



Kidney disorders

Nephrolithiasis

episcleritis

Iritis

uveitis



Eye Inflammation



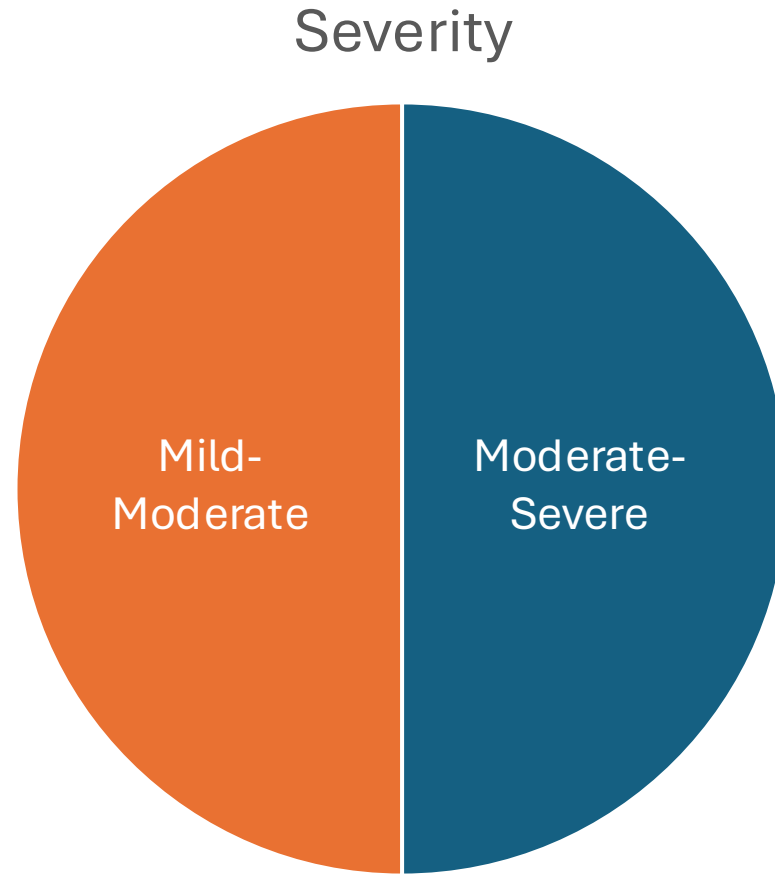
Osteoporosis



Anemia

Ulcerative Colitis

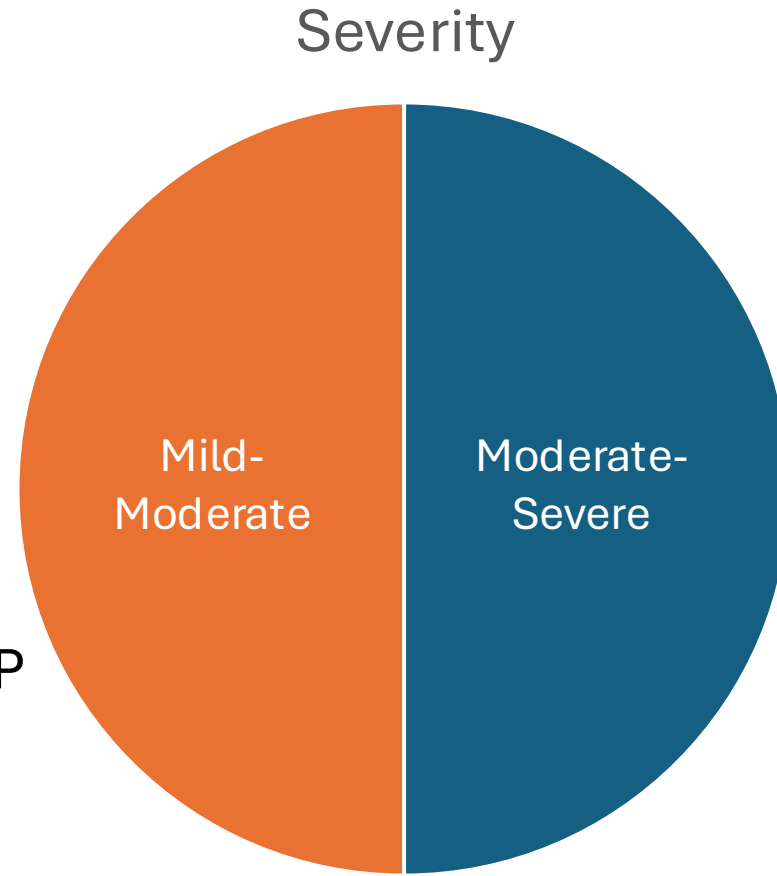
- Can induce remission with steroids (\leq annual)
 - Ideally budesonide 9 mg tabs (6 mos OK)
 - Rectal steroids
 - Prednisone (<1 mo)
- Can induce/maintain remission with 5'ASA
 - Mesalamine
 - Oral
 - Rectal
 - Balsalazide
 - Sulfasalazine



- Requiring systemic steroids > annually or >1 mo for induction
- Need advanced therapy for maintenance
 - Biologics
 - Vedolizumab
 - Anti-IL-23
 - Anti-TNF
 - Oral agents
 - Thiopurines
 - JAKinibs
 - S1PR agonists

Ulcerative Colitis

- Steroids are easy to Rx as a short-term fix
 - Though neither safe nor effective long-term
- 5'ASA's are comparatively inexpensive and harmless
 - Can be managed by PCP alone



- Advanced therapies require specialists
 - \$\$\$ → Complex / laborious insurance preauthorizations
 - Complex therapeutic drug monitoring algorithms
 - Pre-treatment screening requirements
 - On-treatment monitoring requirements
 - Rapidly changing treatment options / recommendations

Who Can Do What for UC?: Diagnostics

Primary Care/ER can:

- Quantify inflammation:
 - Blood: CRP
 - Stool: Calprotectin
- Exclude infectious mimics:
 - Acute: Enteric pathogen panel, C. difficile
 - Chronic: O&P, giardia
- Evaluate deficiencies:
 - Iron, ferritin (bleeding)
 - Albumin

Gastroenterologist should:

- Do colonoscopy to:
 - Stage inflammation
 - Exclude CMV
 - Exclude neoplasia
- Evaluate eligibility for advanced therapies:
 - TB screen (Qgold)
 - HBV screening
 - TPMT/NUDT15 genotyping
- Therapeutic drug monitoring

Who Can Do What for UC?: Treatment

Primary Care/ER can Rx:

- 5' aminosalicylates
 - Mesalamine (PO/PR)
 - Sulfasalazine (PO)
 - Balsalazide (PO)
- Steroids
 - Prednisone (PO)
 - Budesonide (PO, PR)
 - Hydrocortisone (PR)

Gastroenterologist should Rx:

- Immunomodulators
 - Thiopurines
 - Azathioprine
 - 6-mercaptopurine
 - Methotrexate (only w/ anti-TNF)
- Biologics
 - Anti-TNFs
 - Vedolizumab
 - Anti-IL-(12/23)s
- New advanced oral therapies
 - JAKinibs
 - Tofacitinib
 - Upadacitinib
 - S1P agonists

5' aminosalicylates: mesalamine

- Many trade names, but now mostly generic
- Minimally absorbed (basically topical)—very safe
- Initial oral dose (for symptomatic patient): 4.8 gm/day x mos
- Maintenance oral dose (for asymptomatic patient): 2.4 gm/day
- Can also be used rectally for distal UC:
 - For left-sided UC: mesalamine enema QHS
 - For distal proctitis only: mesalamine suppository QHS
 - Don't need to hold it in all night—think of it as paint

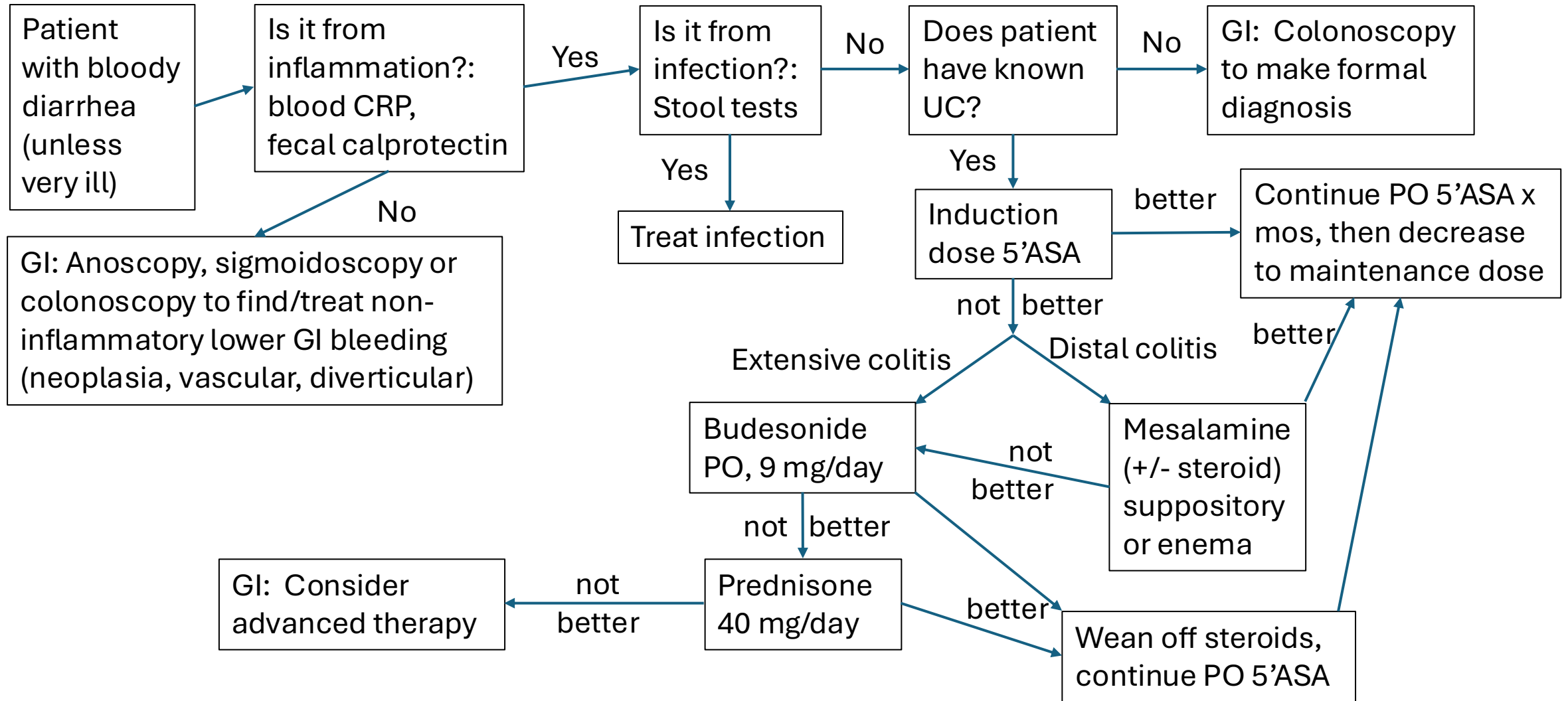
Other 5' aminosalicylates

- Sulfasalazine:
 - Cheapest IBD drug
 - Beware sulfa allergies, pancreatitis, nausea
 - Monitor for agranulocytosis, renal injury
 - Not delayed release—requires BID-QID dosing
 - Induction dose 4 gm/d divided, maintenance dose 2 gm/day
- Balsalazide:
 - Cost between sulfasalazine and mesalamine
 - Huge pills and a lot of them (3 pills, 750 mg ea, TID = 6.75 gm/day)

Steroids

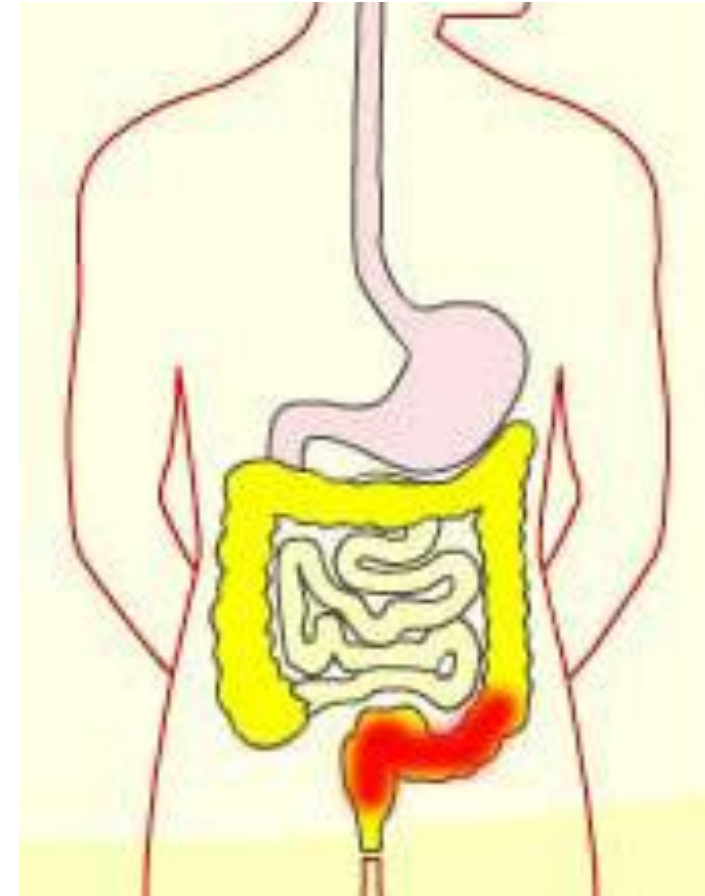
- Useful to INDUCE, not MAINTAIN remission
 - Potently immunosuppressive, but also block mucosal healing
- Prednisone
 - Fast, cheap and powerful, but more dangerous/toxic than most IBD meds
 - Use for as short a time as possible
 - Use no more than 40 mg/day
 - Taper daily dose by 5-10 mg every 3-7 days as tolerated until off
 - If unable to taper off or used > annually, consider advanced therapy (GI)
- Budesonide
 - Weaker than prednisone but much safer (minimal systemic exposure): 6-12 mos OK
 - 9 mg tabs release in colon (for UC), but often denied by insurance
 - 3 mg tabs (use 3 per day) release in small bowel (for Crohn's), inferior but adequate for UC
- Rectal steroids
 - Hydrocortisone or budesonide
 - Can be a suppository, enema or foam
 - Less effective than mesalamine PR, so rarely useful

An Initial Algorithm for UC



UC Case 1

- 25 yr old male with no PMH
- 1 month of bloody diarrhea 3x/day
- Urgency but no incontinence
- Nocturnal stooling 1-2x/wk
- Colonoscopy shows red, edematous distal colon without ulceration
- Biopsies consistent with UC
- CRP is 18
- CBC & CMP normal



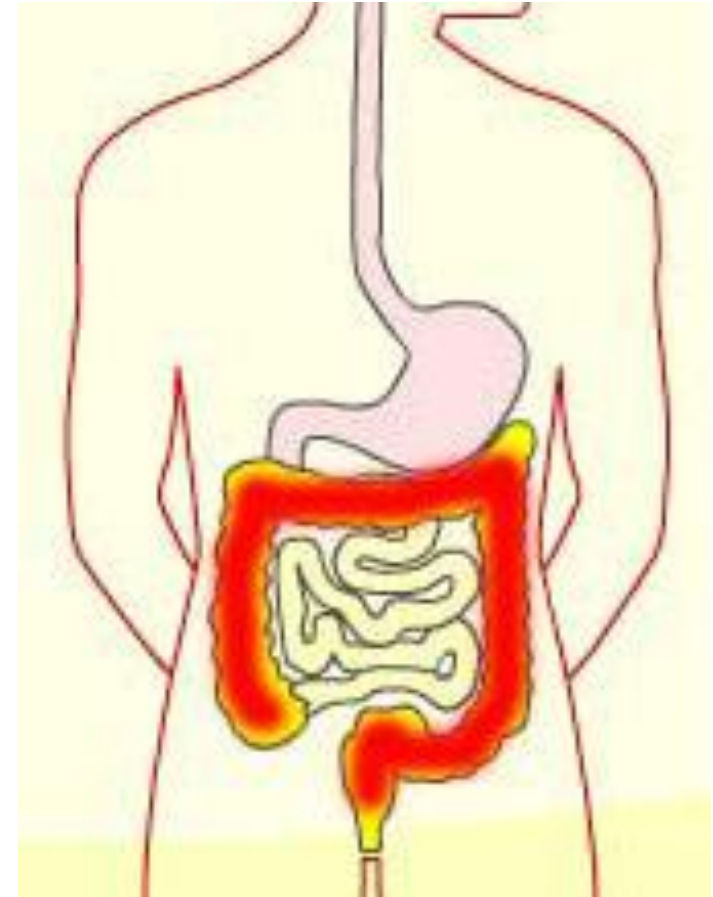
Treat or refer?

Treatment options for mild UC

- For any mild UC
 - Oral 5'aminosalicylates (5'ASA) (indefinite)
 - Mesalamine (cheap)
 - Balsalazide (cheaper)
 - Sulfasalazine (cheapest)
 - Oral budesonide (temporary, <6 mos)
 - 9mg tabs are built to release in colon for UC (but often not covered)
 - 3 mg tabs (x3) are built to release in the small bowel for Crohn's
- For left-sided UC only (rectum, sigmoid, +/- descending colon)
 - Mesalamine enemas (more effective than steroid enemas)
- For proctitis (rectum) only
 - Mesalamine suppositories

UC Case 2

- 30 year old female with left-sided UC diagnosed 2 yrs ago, on mesalamine
- 2 months of progressive bloody diarrhea, now 8x a day, 1x/night
- Colonoscopy now shows erythema, edema, adherent mucous, shallow ulcers throughout colon (pancolitis)
- Hct 31, MCV 77, CRP 32, Alb 3.1
- Otherwise normal CBC, CMP



Treat or refer?

Treatment options for moderate UC (old)

- Systemic steroids (prednisone): only a “bridge” therapy
 - Taper pt off over 1-2 mos, if not faster
 - Too toxic for long term use
 - Might recover 5'ASA-responsive UC, but usually not
- Thiopurines (azathioprine, 6-mercaptopurine)
 - Now rarely used as primary monotherapy (newer agents more effective & safer)
 - Require close lab monitoring due to liver/hematologic risk
 - Very slow (mos) to reach steady-state/benefit
 - Check TPMT (and if Asian, NUDT15) to optimize 1st dose, exclude rare homozygotes
 - Can optimize dose with metabolite (6-TGN, 6-MMPN) monitoring
 - Avoid if history of pancreatitis, non-melanoma skin cancer, EBV lymphoma, HPV

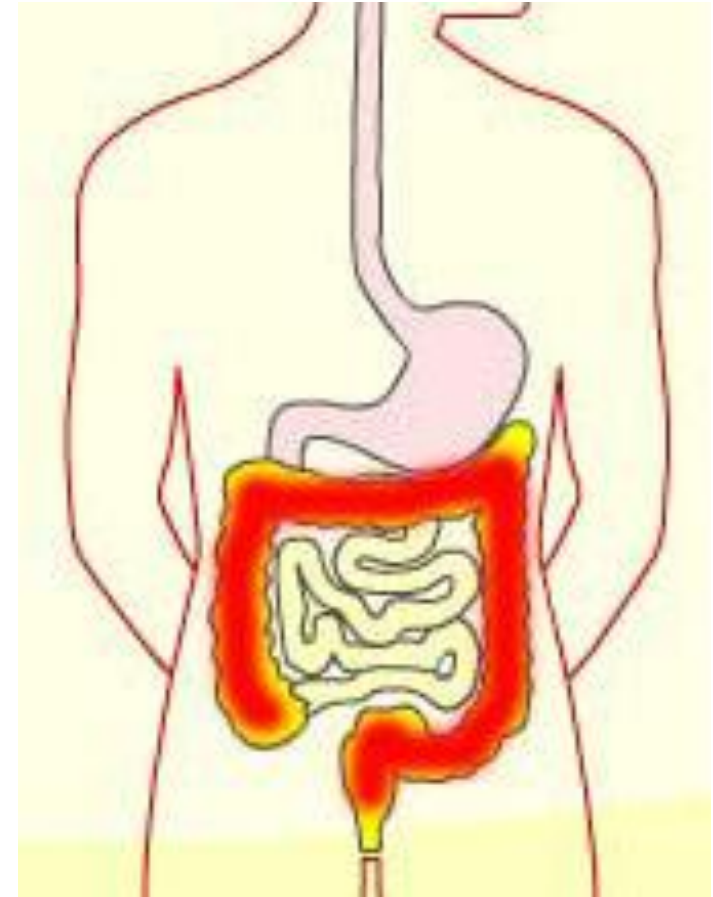
Treatment options for moderate UC (new)

- **Biologics**
 - Anti-Integrin (vedolizumab): Slow and safe, IV or SQ
 - Anti-IL-(12/23) (ustekinumab, risankizumab, guselkumab, mirikizumab): Slow and safe, IV, then SQ
 - Anti-TNF (infliximab, adalimumab, golimumab): Slightly faster & slightly less safe, immunogenic (beware anti-drug antibodies), IV or SQ
 - Can reduce immunogenicity with immunomodulators (thiopurine, methotrexate)
 - Use methotrexate with caution in fertile women
 - Fear of hepatosplenic T cell lymphoma with thiopurines in males <35yo
- **Novel small molecule (oral) therapies**
 - S1PR agonists (ozanimod, etrasimod): safe, but limited efficacy
 - JAK inhibitors (tofacitinib, upadacitinib): potent, VERY fast, less safe
 - Black box warning reserves use for biologic failures

UC Case 3

- 22 year old male with a preadolescent history of lymphoma
- 2 weeks of severe bloody diarrhea >20x/day, abd pain, fever, wt loss
- CT and colonoscopy 1 wk ago show severe UC (pancolitis), no lymphoma, CMV, C. diff
- Prednisone 40 mg PO QD for past wk having no effect on symptoms
- Hct 18, MCV 82, CRP 110, Alb 2.2, AP 320, WBC 14, granulocytosis

Treat or refer?

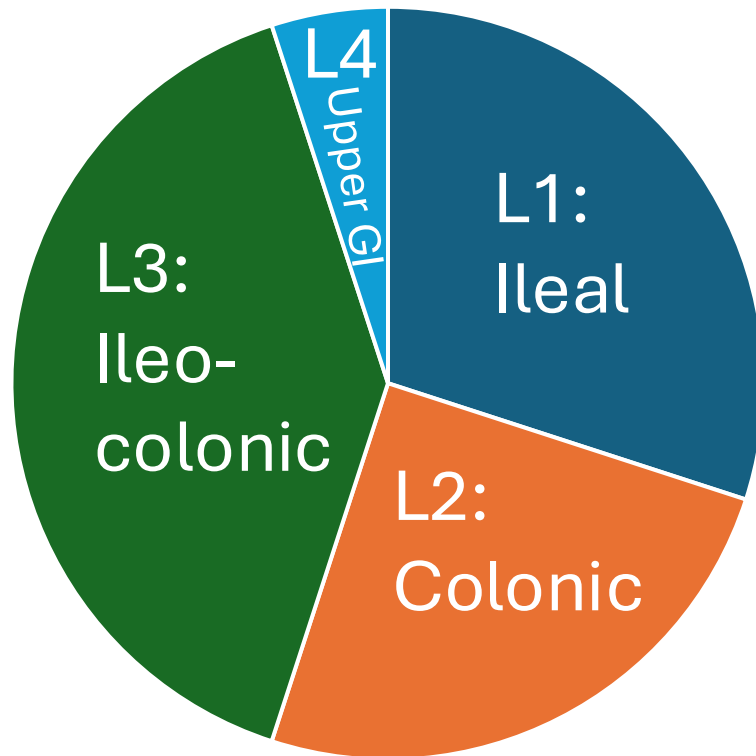


Treatment Options for severe UC

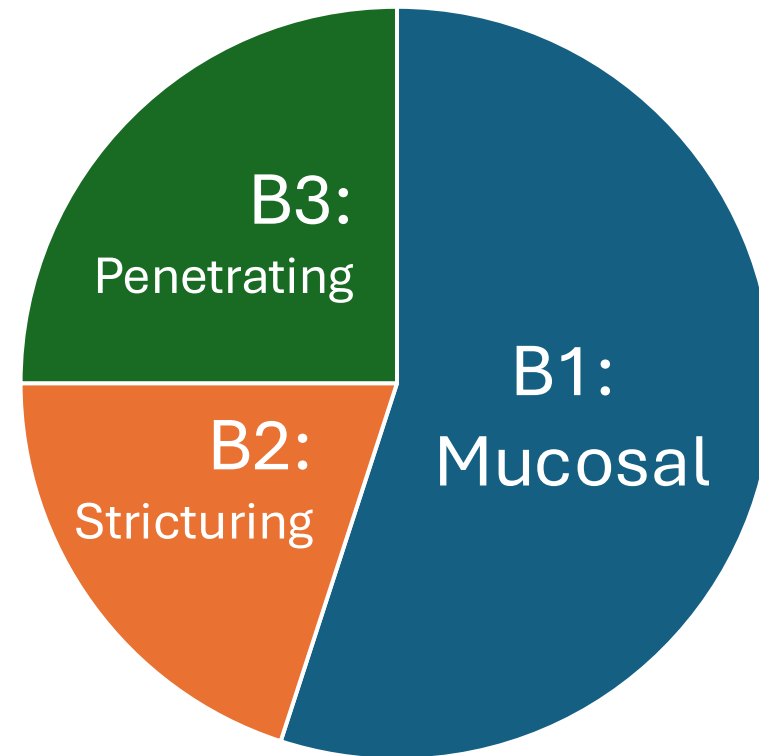
- Inpatient IV steroids (methylprednisolone)
 - If no improvement within 3-5 days, MUST do more:
- Urgent ileostomy (+/- subtotal colectomy with eventual J-pouch)
- IV Infliximab (at increased dose [10-20mg/kg])
 - Repeat in 1 wk if not improving
- JAK inhibitor (upadacitinib more potent than tofacitinib)
 - Faster than infliximab
 - Hard to get for inpatients
 - Often denied for anti-TNF-naïve
 - Can appeal urgently for mitigating circumstances (disease acuity, h/o lymphoma?...)
- Calcineurin inhibitors (cyclosporine, tacrolimus)
 - Rarely ever used now due to toxicity, infection risk

Crohn's Disease: more heterogeneous than UC

Anatomic Location

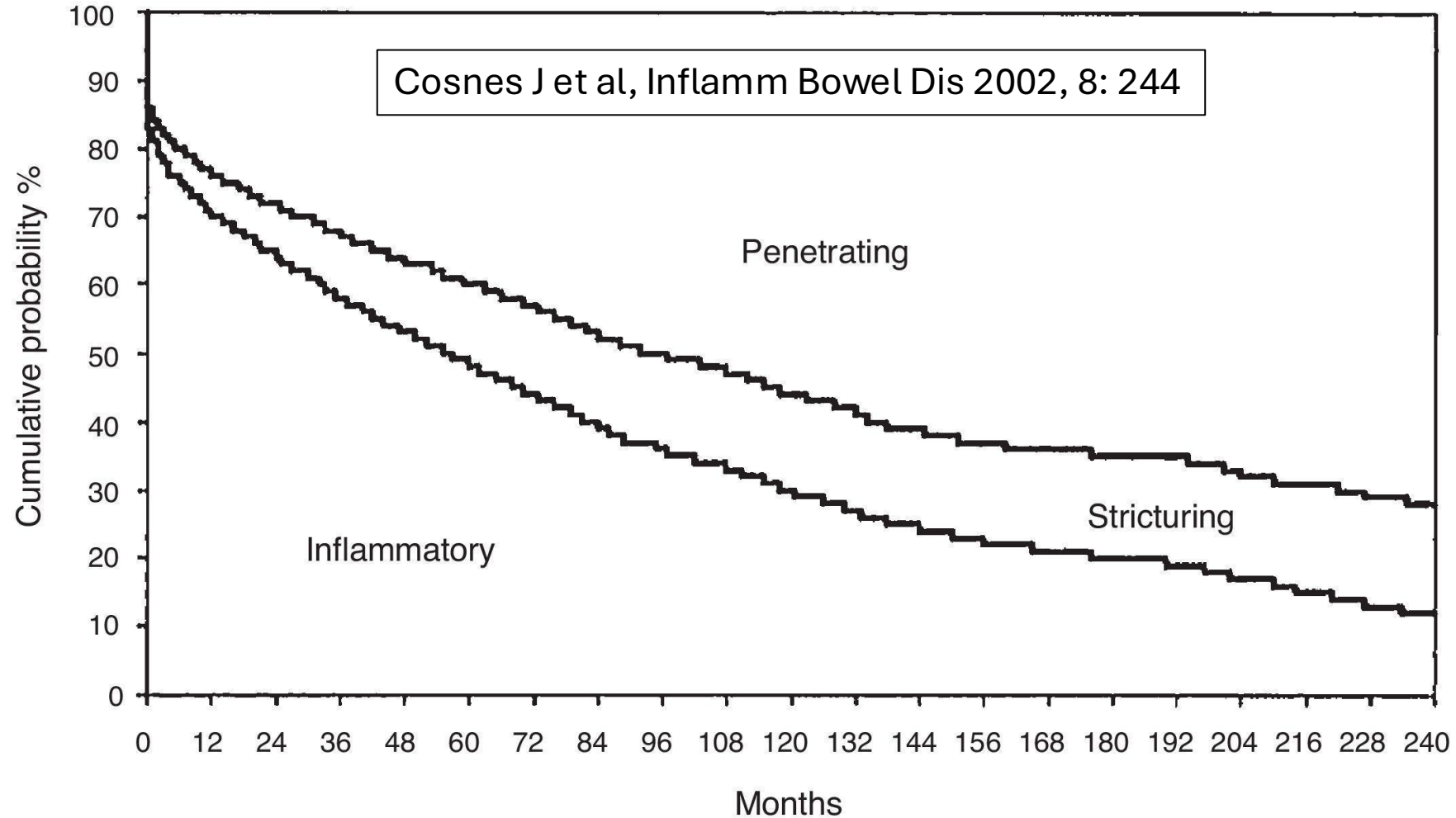


Behavior at Diagnosis*



*over time, B1 progresses to B2 and B3

Crohn's disease behavior progresses over time



No evidence that existing therapies halt (or even slow) this progression

L2, B1 Crohn's can be managed like UC

Anatomic Location

Behavior at Diagnosis



Mild:

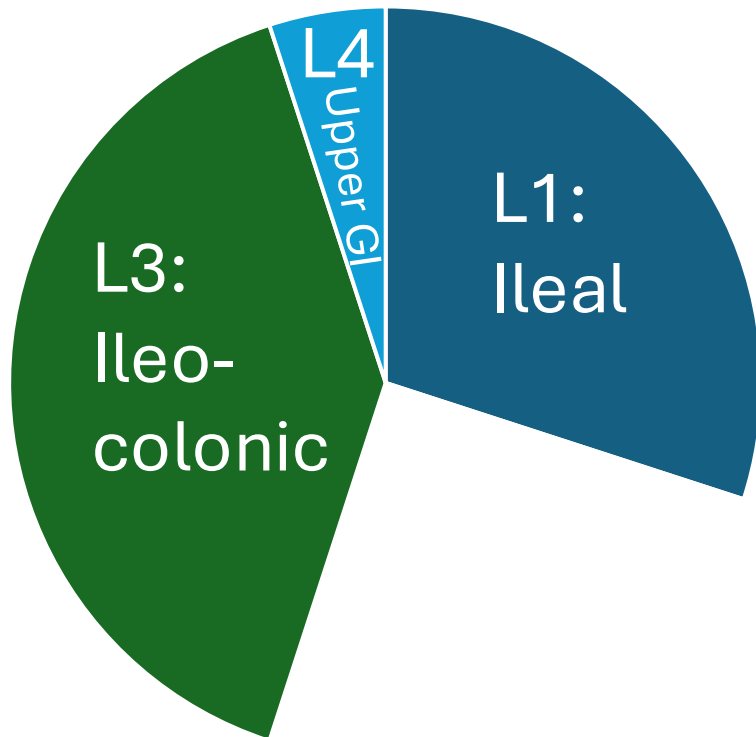
- 5'aminosalicylates
- Episodic budesonide

Moderate to Severe:

- Anti-integrin (vedolizumab)
- Anti-IL-(12/23)
- Anti-TNF + immunomodulator
- Janus kinase inhibitor

More proximal Crohn's has fewer options

Anatomic Location



Mild:

• ~~5-aminosalicylates~~

- Episodic budesonide

Moderate to Severe:

- **Anti-integrin (vedolizumab) ??**
- Anti-IL-(12/23)
- Anti-TNF + immunomodulator
- Janus kinase inhibitor

B3: Penetrating Crohn's has even fewer effective treatment options

Behavior



Mild:

- ~~5'aminosalicylates~~
- ~~Episodic budesonide~~

Moderate to Severe:

- ~~Anti-integrin (vedolizumab)~~
- Anti-IL-(12/23) ??
- Anti-TNF + immunomodulator
- Janus kinase inhibitor

B2: Stricturing Crohn's has no effective pharmaceutical treatment options

Behavior



Mild:

- ~~5'aminosalicylates~~
- ~~Episodic budesonide~~

Moderate to Severe:

- ~~Anti-integrin (vedolizumab)~~
- ~~Anti-IL-(12/)₂₃~~
- ~~Anti-TNF + immunomodulator~~
- ~~Janus kinase inhibitor~~

B2: Stricturing Crohn's is currently managed structurally, not pharmacologically

Behavior



Strictures < 5cm, without fistulas:

- Endoscopic balloon dilation

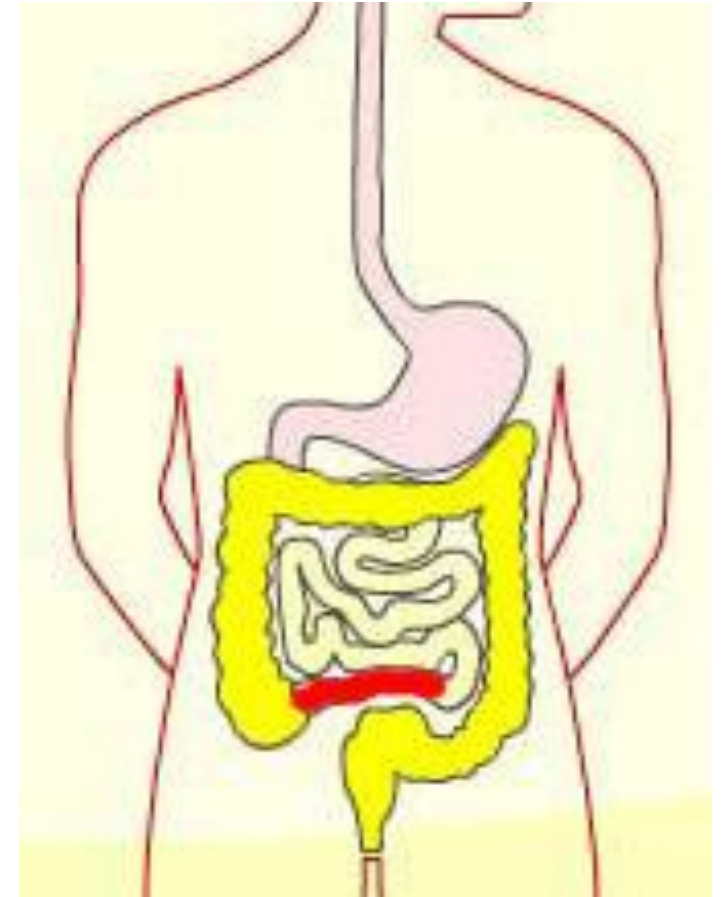
Strictures >5cm or with fistulas:

- Surgical resection
- Surgical bypass
- Stricturoplasty

Crohn's case 1:

- 50 yr old man with ileal aphthae and granulomas found on screening colonoscopy
- Insists he never uses NSAIDs
- No symptoms
- Normal CBC, CMP, CRP

What should be done?

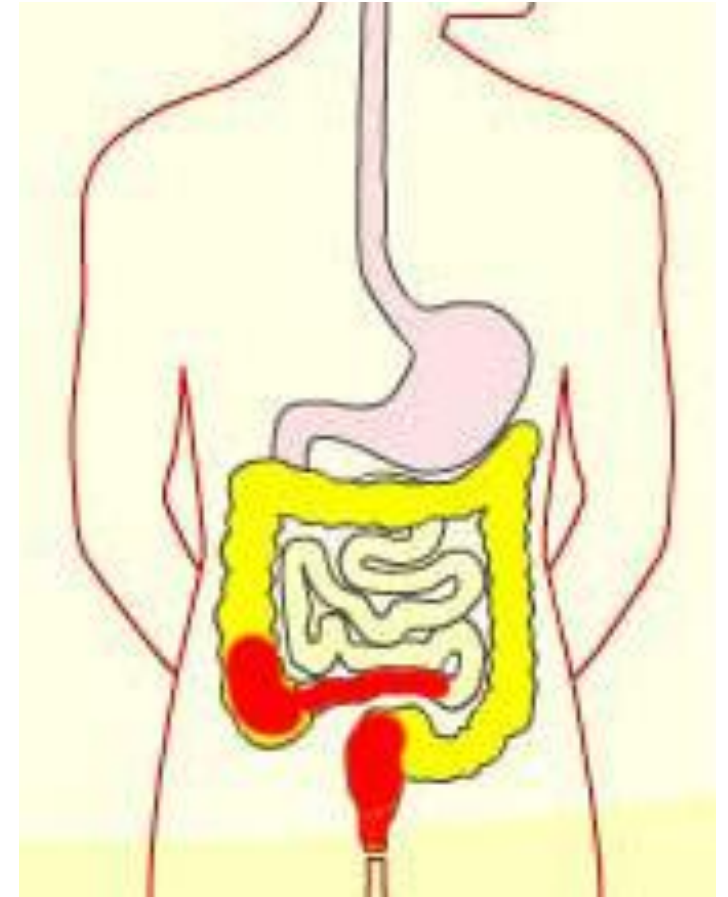


NOTHING

- There are no good long-term treatments for asymptomatic mild ileal Crohn's disease
- If patient endorsed any symptoms, a limited course of ileal-release (3 mg tabs) budesonide could be used to see if there is any improvement, to warrant long-term treatment
- Otherwise, it is reasonable to watch and wait for any progression

Crohn's case 2:

- 32 yo woman with abdominal pain, urgency (tenesmus) and non-bloody diarrhea 3x/day x 3 wks
- Colonoscopy/biopsy shows patchy aphthous, granulomatous inflammation in rectum, cecum and ileum
- No fistulas or strictures on CT enterography
- Hct 35, MCV 80, CRP 11
- Otherwise normal CBC, CMP



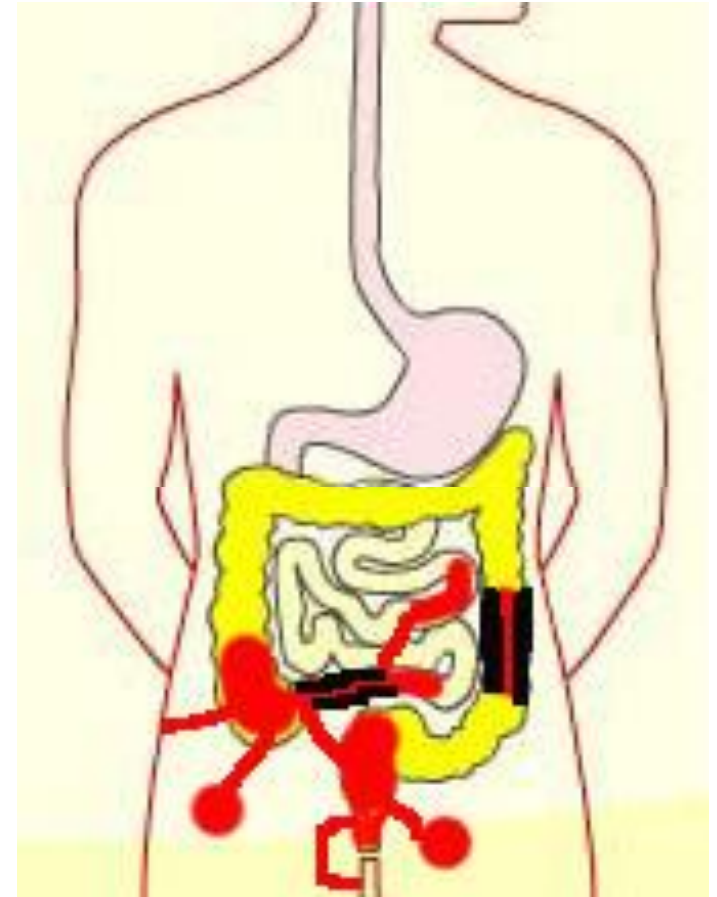
What should be done?

Treatment for mild but symptomatic Crohn's

- 5' aminosalicylates (PO +/- PR) might help colonic mucosal Crohn's
 - Can monitor efficacy on colon (L>R) via fecal calprotectin
 - No demonstrable 5'ASA benefit for ileal disease
 - But colon (esp rectum) may be primary source of symptoms
- If symptoms persist, trial of ileal release budesonide tabs to see if symptoms are responsive and hence inflammatory
- If so, biologic therapy may be justified
 - Anti-IL-(12/23) (ustekinumab, risankizumab, guselkumab, mirikizumab)
 - Anti-TNF (infliximab, adalimumab, certolizumab pegol)
 - Anti-integrin (vedolizumab)

Crohn's Case 3:

- 48 yr old man with 12 yr h/o Crohn's presents with N/V, abdominal pain and fever of 38
- Was previously on anti-TNF + azathioprine, vedolizumab, now on risankizumab + methotrexate
- Was in ER 2 wks ago, Rx'd 40 mg/d prednisone, has been on this since w/ no improvement
- CT shows ileocolitis, multiple strictures, partial obstruction, fistulas, intra-abdominal and perianal abscesses



Treat or refer?

How NOT to manage complex Crohn's

- 5'ASAs
 - Useless outside colon (ileitis)
 - Useless for transmural complications (strictures, fistulas)
- Chronic steroids (prednisone)
 - Prevents mucosal healing, fistula closure
 - May ultimately increase structural defects
- Serial bowel resections instead of advanced pharmacology
 - Were once the leading cause of short gut and intestinal transplantation

Treatment of complex Crohn's

Fistulas, strictures, and treatment-refractory Crohn's are best managed by a well-coordinated multidisciplinary team:

- Colorectal surgeons
 - Fistulotomies/setons
 - Diverting stoma
 - Resections/stricturoplasty
- Interventional radiologists
 - Percutaneous drainage
- Therapeutic endoscopists
 - Deep enteroscopy (double-balloon)
 - Balloon dilations
- Gastroenterologists with IBD experience and resources
 - Advanced/combination therapies (insurance appeals)
 - Clinical trials

IBD-focused multidisciplinary centers

- In Seattle
 - Children's Hospital (Drs. Wabeh, Suskind, Zheng, Young)
 - University of Washington Medical Center (Drs. Lee, Saxena, Barahimi, Jacobs)
 - Virginia Mason Franciscan Health (Drs. Zisman, Lord, Rosenfeld)
 - Swedish Providence (Drs. Harper, Wong, Iles-Shih)
- Nationally
 - Cedars Sinai, Los Angeles CA
 - Mayo Clinic, Rochester, MN
 - University of Chicago, Chicago, IL
 - Mount Sinai, New York, NY
 - Many other major academic medical centers

IBD-Specific Preventative Care

Some age-specific health maintenance recommendations should be offered much earlier in IBD patients

- Vaccinations
- Cancer screening
- Bone densitometry

Vaccination at any age

Many IBD patients either are or could be on an immunosuppressant

- Anti-TNFs (infliximab, adalimumab, golimumab, certolizumab)
 - Increased risk of influenza, pneumococcal pneumonia
 - Annual Flu shot
 - Pneumococcus-21 or Pevnar 20 >5 years after last Pneumovax or Pevnar-13
- JAKinibs (Upadacitinib, tofacitinib)
 - Increase reactivation of Zoster (shingles)
 - Shingrix, 2 doses, 2-6 mos apart
 - Generally weaker anti-viral immunity (interferons are JAK-dependent)
 - Annual Flu shot
 - Covid boosters

When to vaccinate relative to IBD medication?

- Anti-TNFs and JAKinibs blunt protective response to vaccines
- Ideally vaccinate before starting therapy, but seldom practical
- Holding JAKinib for 3 days prior to vaccination and resuming 1-2 wks after might improve vaccine response without risk
- Holding anti-TNF for vaccine is less safe/effective
 - Risks anti-drug antibodies → ruin anti-TNF safety/efficacy for future
 - Would require months without anti-TNF to clear drug → risks IBD flare
- Timing of vaccine relative to biologic dose makes no difference
 - Biologics are dosed to remain saturating even at “trough” (right before next dose), so biologic effect never diminishes

Colon cancer screening

- Do NOT use FOBT/FIT or Cologuard in IBD patients (high false +s)
- If IBD involves <30% of the colon (eg: just proctitis in UC), timing/methodology otherwise no different from anyone else
- If >30% of colon, start dysplasia surveillance colonoscopies Q1-2 yrs 8-15 (usually 10) years after initial diagnosis
 - Q1yr if white-light with 4-quadrant random biopsies
 - Q2yrs if chromoscopy (blue dye) with targeted biopsies/resections
- Exceptions:
 - If also primary sclerosing cholangitis, colonoscopy Q1yr immediately upon IBD diagnosis
 - If any dysplasia identified, colonoscopies much more frequently (eg: Q 6 mos until gone)

Other cancer screening (Thiopurines)

- HPV:
 - Azathioprine and 6-MP clearly increase cervical cancer risk
 - Unclear if newer agents do (JAKinibs impair immunity vs other herpes viruses, like varicella)
 - No clear recommendations on how to alter pap reccs for thiopurine recipients
 - AGA 2025: “Shared decision-making and individual risk stratification are encouraged”
- Non-melanoma skin cancer:
 - Only associated with thiopurines, no other IBD drugs
 - Maybe a dedicated skin exam every 1-2 yrs? No clear recommendations.
- Waning use of thiopurines and rising use of HPV vaccines and sunscreen makes these recommendation less important for IBD

Bone health

- IBD can cause osteoporosis through several mechanisms
- Screen with DEXA scan regardless of age and sex if:
 - History of prolonged prednisone use (mos-yrs)
 - History of extended ileal resection (>45 cm): Ca⁺⁺/vit D malabsorption
 - Long periods of uncontrolled inflammation: IL-6 → osteoclasts
- Subsequent frequency of DEXA depends on patient characteristics (no algorithm specific to IBD)
 - Age, sex
 - BMI
 - Ongoing steroid use, inflammation
 - Vitamin D levels

Summary (2026)

- Up to half of UC patients can maintain remission with 5'ASA drugs alone, can be Rx'd by PCP
- Crohn's usually needs a gastroenterologist
 - Too heterogenous to be algorithmic
- Preventative care for IBD patients differs from general population
 - Vaccinate early and often
 - Colon cancer screening recs unique to IBD are complicated
 - Low threshold for DEXA

The Future?

- Always more new classes of drugs coming
 - Anti-TL1A, obefazimod, oral anti-IL-23R/integrins, PDE inhibitors...
- Combinations of drugs will work better than monotherapies
 - VEGA/DUET trials: anti-IL-23 + anti-TNF
- Blood tests might predict IBD
 - Autoantibodies (vs integrin $\alpha\beta6$) in UC: Japan
 - Multiple factors in Crohn's: Europe (INTERCEPT)
- Appendectomy might treat or prevent UC (ACCURE, COSTA)
- CAR T cells might treat refractory UC