
2023 SCSG
GI SYMPOSIUM

Care of the IBD Patient

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Disclosures

- None

Objectives

- Differentiate key differences between ulcerative colitis (UC) and Crohn’s disease (CD).
- Identify new therapies to treat UC and CD.
- Utilize a treat to target approach for IBD patients.

Ulcerative Colitis and Crohn’s Disease

Comparing Crohn's Disease vs Ulcerative Colitis

Ulcerative colitis

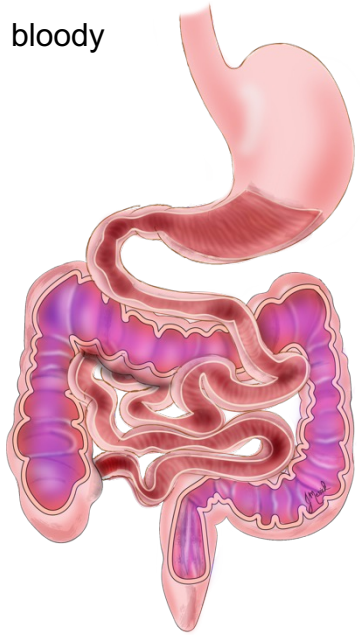
Presenting symptoms
Abdominal pain, rectal bleeding, bloody diarrhea

Location
Limited to the colon

Pattern
Continuous; starts in the rectum and progresses proximally

Rectal involvement
Very common

Perianal involvement
Uncommon



Crohn's disease

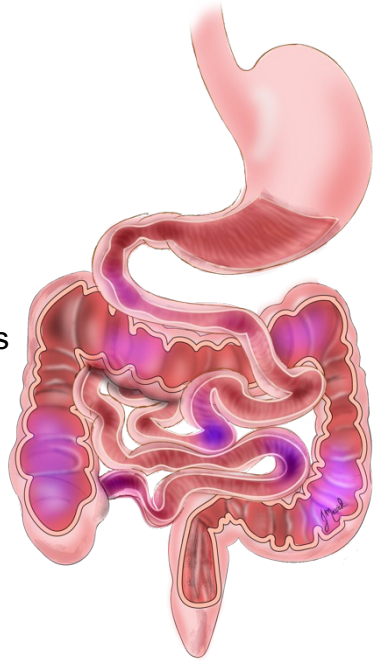
Presenting symptoms
Abdominal pain, diarrhea, nausea, vomiting, weight loss

Location
May affect entire GI tract

Pattern
Discontinuous with skip lesions primarily in SI and colon; most commonly in terminal ileum and cecum

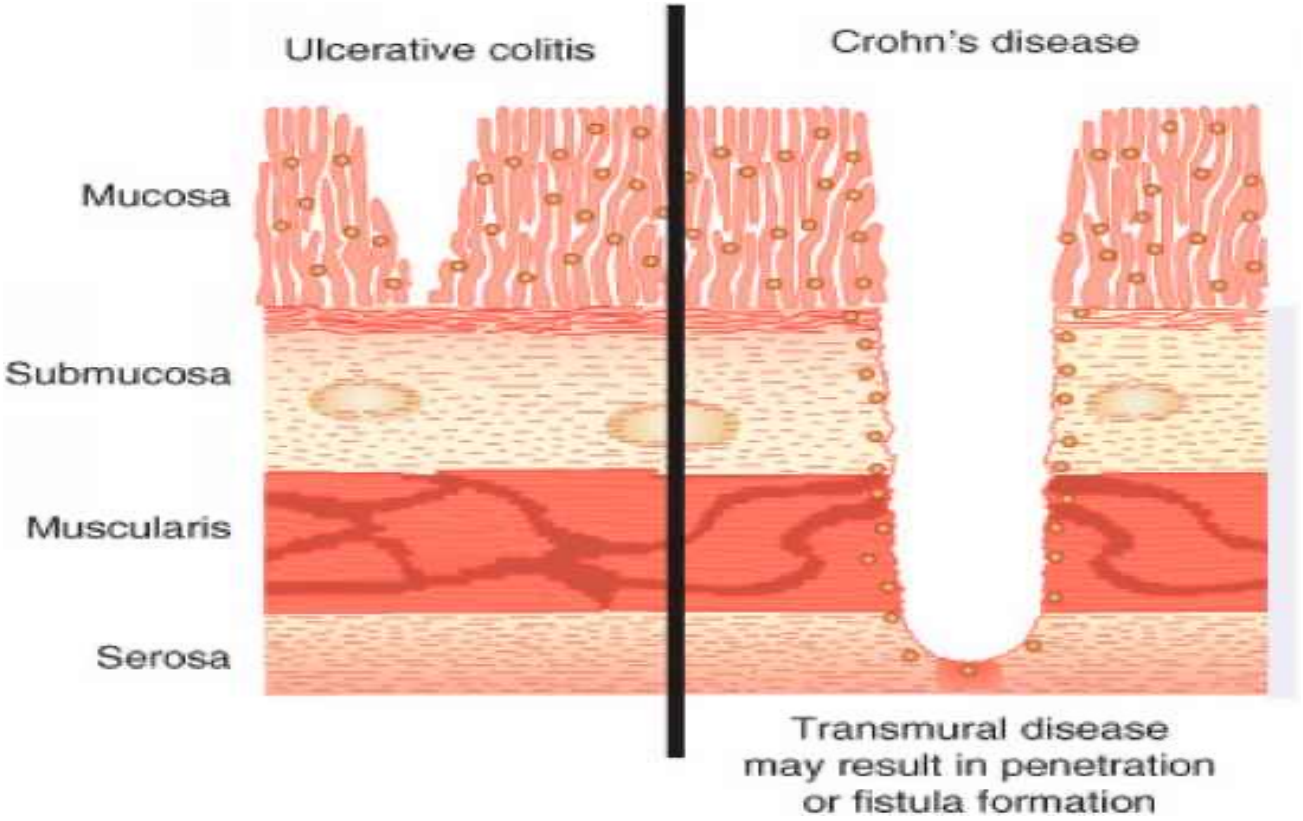
Rectal involvement
Uncommon

Perianal involvement
Common



Baumgart DC, Sandborn WJ. *Lancet.* 2007;369(10):1641-1657.

Comparing Crohn's Disease vs Ulcerative Colitis



Not Just Real Estate – Ulcerative Colitis Location, Location, Location!

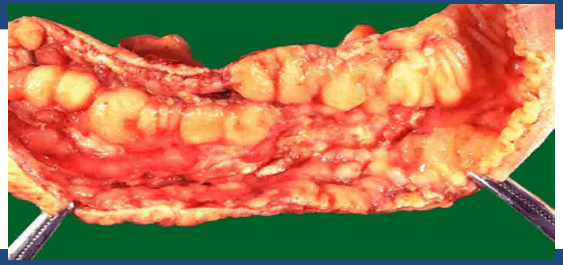
- Usually effects large intestine/colon only
  - 40-50% rectal or rectosigmoiditis
  - 30-40% left sided
  - 20% pan colitis-involves entire colon
- Always begins in the rectum; can proceed proximally in continuous fashion

- Symptoms vary by location:
  - Proctitis Constipation, rectal bleeding, tenesmus
  - Left Sided (up to splenic flexure) Urgency, frequency, blood and mucus
  - Pancolitis Anemia, fatigue, anoxeria, weight loss, urgency, frequency, passing blood alone, tenderness on palpation

Crohn's Disease: Characterized by Inflammation of the ENTIRE GI Tract

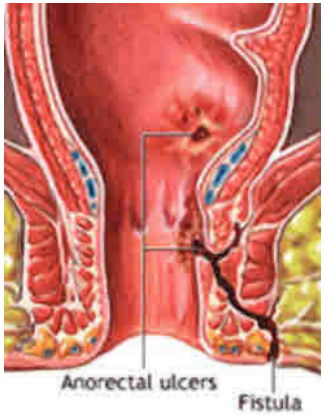
Inflammation

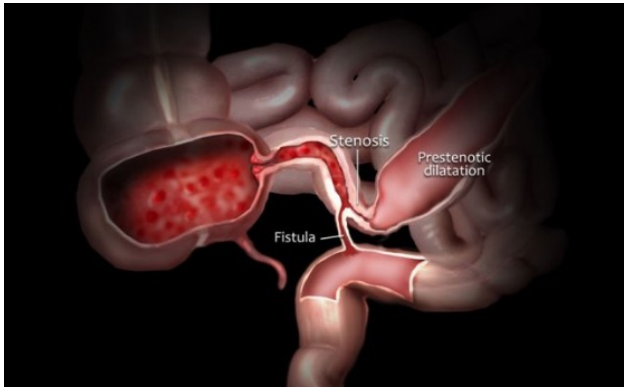
- Patchy / non-continuous
- Throughout GI tract
- Cobblestone pattern of ulceration
- Affects all the bowel wall (mucosa to serosa)

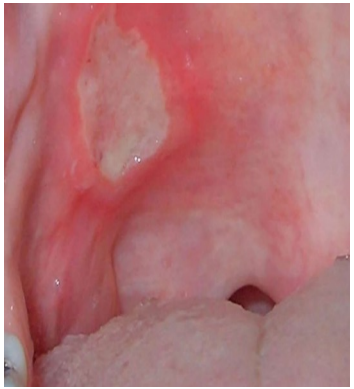


Complications

- Ulcers
- Fistulae
- Perforation
- Abscess formation
- Stricture
- Bowel obstruction
- Increased cancer risk



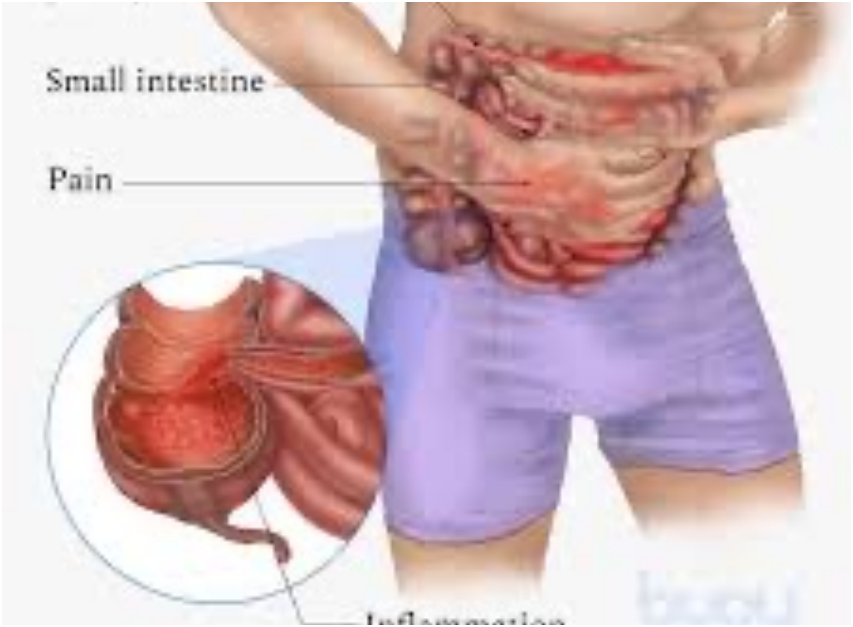




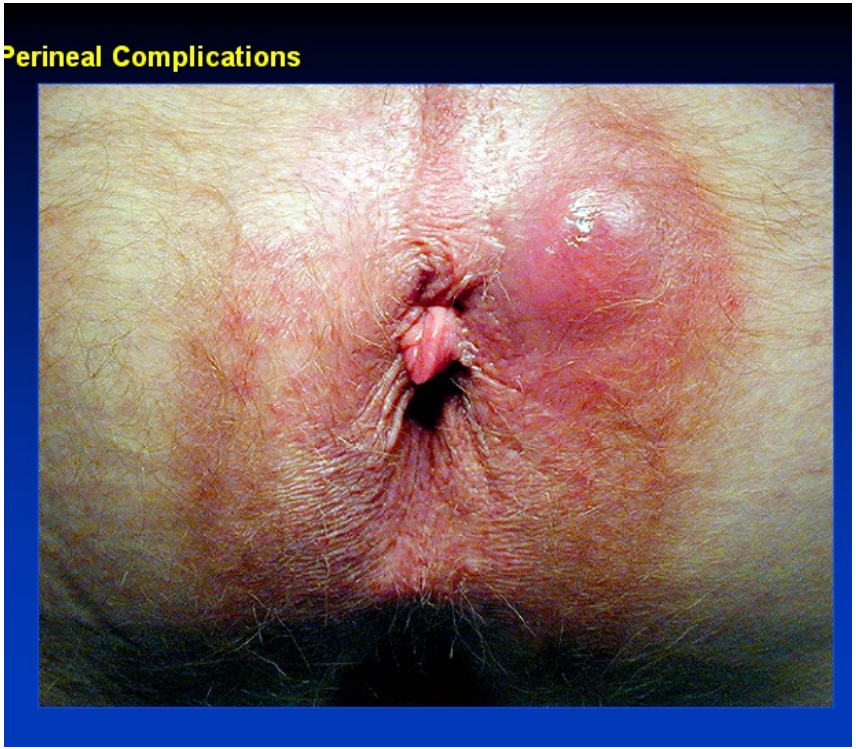
De Lange. BMC Gastroenterology 2004;4:9

Symptoms: Crohn's Disease

- Dependent on the location of the disease- Location, Location, Location!
- Abdominal pain
- Diarrhea
- Blood in stool
- Fatigue
- Weight loss
- Fistulas



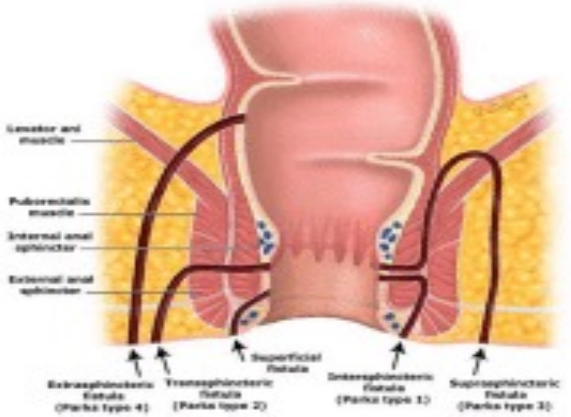
Perianal Abscess

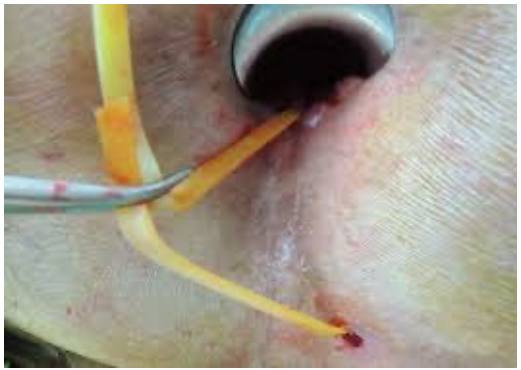


- MRI pelvis view
- Antibiotics
- Referral for colorectal surgery

Fistula

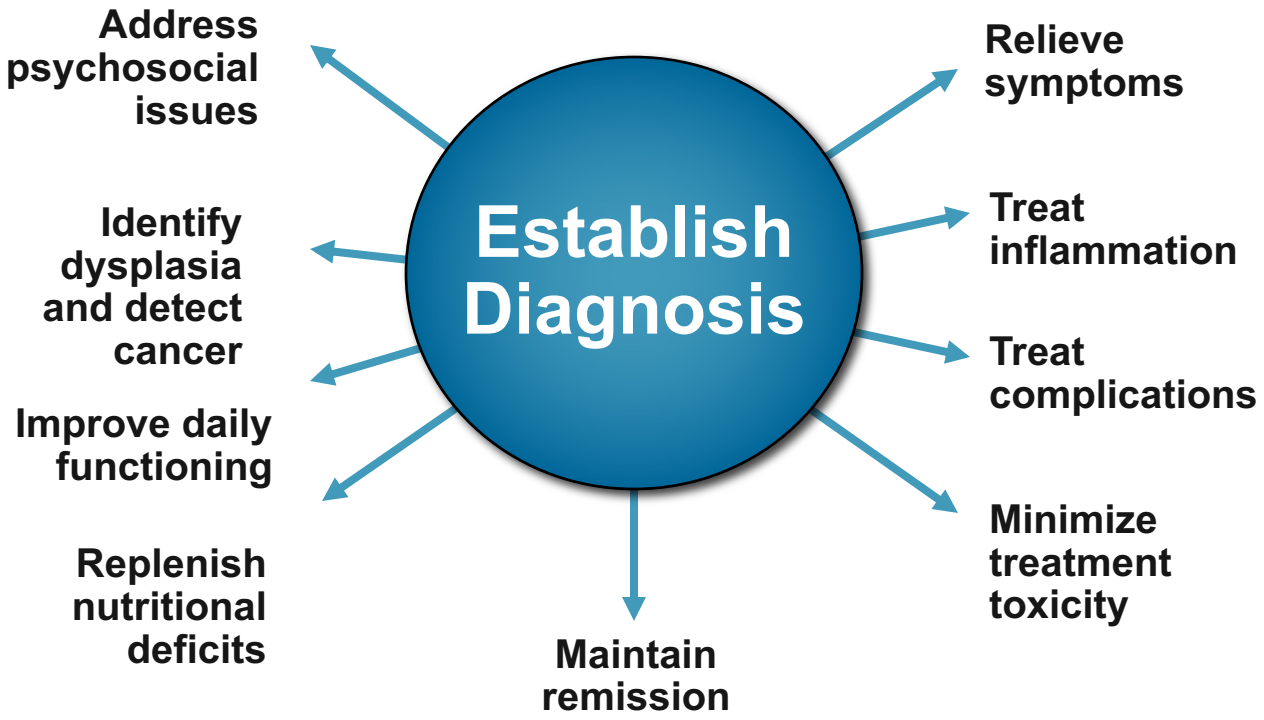
- Almost always only in CD, not UC
- Rarely at presentation or diagnosis, but 25-30% of all CD patients will develop ne or more fistulas in their lifetime
- Fistulas develop due to inflammation, “roadblock” for stool
  - Rectovaginal
  - Perianal
  - Enteroenteric
  - Colovesical
- Manage by treating inflammation
  - Increase dosages needed
  - Anti-TNFs most effective with most evidence
  - No steroids
  - Concomitant antibiotics- Cipro (ciprofloxacin) / Flagyl (metronidazole)
- Setons placed for perianal disease, by a colorectal surgeon





Management of IBD

IBD: Management Goals



Evolution in IBD Management

- Old way of thinking
- How sick is the patient today?
  - Mild, moderate or severe?
- Loss of response
  - Switch therapy
- Variation in follow up
- Reactive Care

- New way of thinking
- What is the patient's risk of developing a complication, flare or surgery in the future?
- Loss of response
  - Check levels/antibodies assess disease.
  - Treat to Target
- Tight control follow up visits
- Proactive Care

Barriers to Early Intervention

- A fundamental problem in IBD management is that we wait for patients to become “sick enough” to use our best drugs and miss window of opportunity
- We focus too much on disease activity (symptoms) as opposed to overall disease severity (history and damage)
- We focus too much on risk of the therapies and not risk of the disease

Disease Activity

Reflects cross-sectional assessment of biologic inflammatory impact on symptoms, signs, endoscopy, histology and biomarkers

How is your patient TODAY?

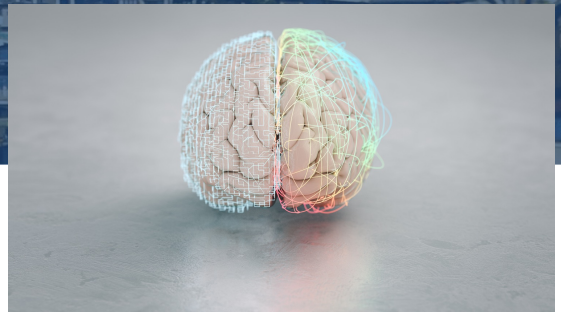
Disease Severity

Includes longitudinal (disease course) and historical factors that provide a more complete picture of the prognosis and overall “burden” of disease

What has your patient’s disease course been like over their history since diagnosis?

Pariente B et al. *Inflamm Bowel Dis*. 2011;17:1415-1422; Colombel JF et al. *Gastroenterology*. 2017;152:351-361.e5.

New Way of Thinking about IBD



We want to identify patients
before they have severe disease

We want to identify patients
at risk for severe disease

Drug Therapies for IBD – old and NEW!

Immunomodulators:
Azathioprine
6-MP
Methotrexate
cyclosporine

Supportive Agents:
Pain management
Anti-diarrheal
Bile sequestrants
Anti-depressant
Anti-spasmodic

Corticosteroids:
Hydrocortisone
Prednisone
Methyl-prednislone
Budesonide

Aminosalicylates:
Sulfasalazine
Mesalamine
Balsalazide
Olsalazine

Biologics:
Anti-TNF
Ustakinumab
Vedolizumab

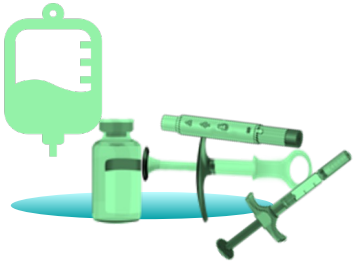
Antibiotics:
Cipro
Flagyl
Vanco

Small Molecules:
JAK
S1P

Biologics and Small Molecules

Class	Agent	Administration	CD	UC
Anti-TNF	Infliximab	IV	X	X
	Adalimumab	SQ	X	X
	Certolizumab	SQ	X	
	Golimumab	SQ		X
Anti-integrin	Vedolizumab	IV	X	X
IL 12/23 inhibitor	Ustekinumab	IV induction, then SQ	X	X
IL 23 inhibitor	Risankizumab	IV induction, then SQ	X	
JAK inhibitor	Tofacitinib	PO		X
Selective JAK inhibitor	Upadacitinib	PO		X
S1P1 inhibitor	Ozanimod	PO		X

Positioning FDA approved therapies in moderate to severe Ulcerative Colitis



TNF antagonists

- IV vs SC options
- Rapid onset of action (IV hospitalized patients)
- Best with immunomodulator
- Infection risk
- Lymphoma risk (with IM)
- EIMs, EN, Psoriasis

JAK inhibitors (tofacitinib, upadacitinib)

- Oral
- Rapid onset of action
- **Monotherapy**
- UPA after TNF failure
- TOFA best for severe disease
- Infection risk (zoster)
- MACE
- Not for biologic naive

Anti-adhesion molecules (vedolizumab)

- IV
- VDZ>ADA (VARSITY)
- Monotherapy or combination therapy?
- Live vaccinations OK
- Pregnancy data?
- Older patients or those with comorbidies

IL 12/23 inhibitor (ustekinumab)

- IV then SQ
- Low immunogenicity
- Monotherapy or combination therapy?
- Excellent safety profile
- Older patients or those with comorbidities
- Psoriasis

S1p receptor modulator (ozanimod)

- Only Oral 1st line therapy
- Best for use after failure of 5ASA
- No pregnancy data
- C/I bradycardia

IM, intramuscular; JAK, janus kinase; SC, subcutaneous; IV, intravenous.

Hindryckx P et al. *J Crohn's Colitis.* 2018;12(1):105–119.

Positioning FDA approved therapies in moderate to severe Crohn's Disease

TNF antagonists

- More rapid induction than anti-adhesion molecules
- Stronger evidence for clinical remission
- Some evidence of endoscopic healing

Anti-adhesion molecules
Vedolizumab

- Significant benefit in maintenance of remission, but slower onset of action
- Better results in anti-TNF-naïve patients
- Gut-selective with good safety profile

IL 12/23 inhibitor (Ustekinumab, Risankizumab)

- Similar induction success as anti-TNF agents
- Efficacy in anti-TNF-naïve and -failure patients
- Safety superior to anti-TNF therapies
- Low rate of immunogenicity
- Good use if concomitant psoriasis

Hindryckx P et al. *J Crohn's Colitis.* 2018;12(1):105–119.

4-step approach to picking the right drug for the right patient

1. Patient's risk of disease-related complications
2. Comparative efficacy of therapies
3. Patient's risk of treatment-related complications
4. Comparative safety of therapies

What Should We Tell Our Patients?

- All medications associated with adverse events
- Most serious adverse events are extremely rare (e.g. infection,lymphoma, MS, renal failure)
- For most patients….
  - When applied for appropriate indications
  - Benefits of IBD medications outweigh the risks
  - Particularly if the patient is responding

C. Everett Koop (Former US Surgeon General)

“Drugs don’t work in patients who don’t take them”

Treat to Target

Why do we need TDM in clinical practice?

Response rates

- 10-30% of IBD patients are primary non-responders
- Annual risk for loss of response to IFX or ADA estimated to be 13% and 24% respectively (secondary non-responders)
    - Immunogenicity
    - **Suboptimal dosing**

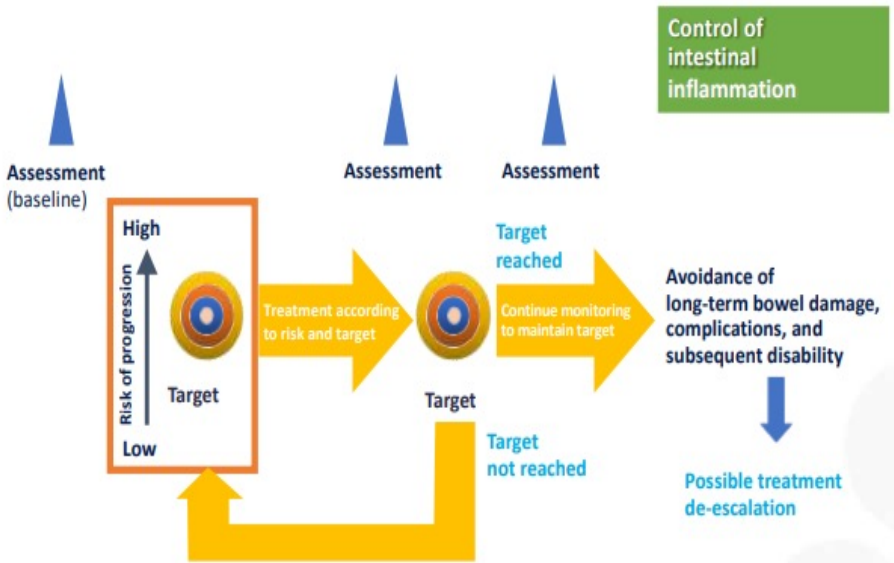
Loss of response

1. Is it the right dose? Get trough drug levels and increase the dose or decrease the interval. Most relevant (most data) on anti-TNF

2. Does the patient have antibodies? Switch within class (anti-TNF 1 to anti-TNF 2 to ??? or Switch out of class (other MOA)

3. Has the drug had enough time? The patient should be in clinical remission with the loading dose – if not, something isn't right. Treat the whole patient, not just the test.

How Does This Translate to Clinical Practice?



- Baseline assessment with endoscopy, imaging and lab values
- Start therapy
- Assess for early response with lab values and Patient Reported Outcomes
- Perform REPEAT assessment in 4-6 months for mucosal healing with endoscopy, imaging and lab values
- IF mucosal health is achieved, continue therapy and perform assessments as necessary
- IF active disease is found, utilize therapeutic drug monitoring to optimize medication and make changes to therapy
- Repeat endoscopy, imaging and labs every 4-6 months until mucosal healing is achieved

Bouguen G et al. *Clin Gastroenterol Hepatol*. 2015;13(6):1042-1050; Colombel JF et al. *Gastroenterology*. 2017;152(2):351-361.

Suggested biologic levels in clinical practice

Biologic	Target after loading dose (µg/mL)	Maintenance trough (µg/mL)
Infliximab	Week 2 >23 / Week 6 >10	3-7, 10 for perianal CD
Adalimumab	Week 6 10-15	5-7
Certolizumab pegol	Week 6 >32	15 - 20
Vedolizumab	Week 6 >37.1 / week 14 >18.4	>12.7
Ustekinumab	Week 8 4 - 7	>1, >4.5, >7?

Cheifetz, AS et al. (2021).Am J Gastroenterol; 116(10):2014-25.

Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE)

Recommendations from International Organization for the Study of Inflammatory Bowel Disease (IOIBD) based on literature and expert opinion

Target for Ulcerative Colitis

Resolution of rectal bleeding and diarrhea/altered bowel habits (PRO remission)

AND

Endoscopic remission defined as Mayo endoscopic score of 0 or 1

Target for Crohn's Disease

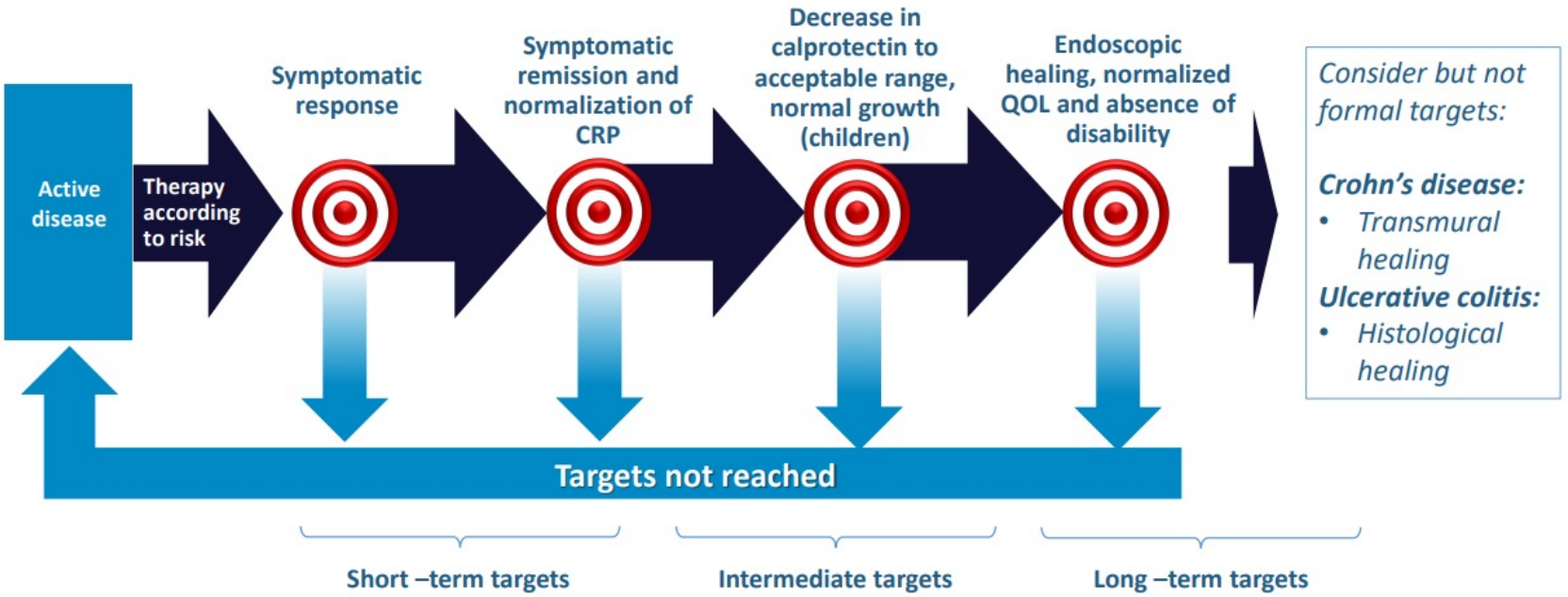
Resolution of abdominal pain and diarrhea/altered bowel habits (PRO remission)

AND

Endoscopic remission defined as resolution of ulcerations OR resolution of inflammation on cross-sectional imaging

Peyrin-Biroulet L et al. *AJG*. 2015.

(STRIDE 2) Treatment Targets in Both Crohn's Disease and Ulcerative Colitis



Turner D et al. *Gastroenterology*. 2021;160:1570-1583

What's the Target? Can It Always Be Reached?

- When is improvement / healing "good enough"?
- Perfect is the evil of good
- TDM most relevant for anti-TNFs
- Surgery is part of the algorithm!
  Not a personal failure
- Alleviate complications
- Alleviate symptoms
- Prevent organ damage
- Achieve best possible quality of life

Treat to Target: Standardized; Yet Personalized

- Risk stratify patients according to prognosis
- Identify a target/goal of therapy with a patient
- Identify a time-frame for reassessment an a plan for “what if…”
- PROACTIVE REASSESSMENT
- Reassess regularly, whether patients are doing well, doing poorly, on therapy, or not

- **Monday Challenge: What proportion of your IBD patients have a follow up visit scheduled?**

Standardize, so You Can Personalize!

Standardize the When

- After starting/changing therapy
- First follow up visit?
- Proactive TDM
- First colonoscopy /imaging
- Crohn's surgery
- Starting post op therapy?
- First colonoscopy?
- Drug specific monitoring
- Routine Labs?
- TDM?
- Health Care Maintenance

Personalize the What/HOW

- Which drug to choose
- What they've been on before
- Special circumstances: EIM, Elderly, Pregnant
- How to optimize the drug
- Mono/combo therapy
- Dose de-escalate

Conclusions

- Ulcerative colitis and Crohn’s Disease (IBD) are complex, chronic inflammatory disorders that affect the entire GI tract.
- Symptoms vary based on location of disease – range from diarrhea, abdominal pain, weight loss, tenesmus, bloody stools and fever.
- Complications of Crohn's disease include perianal disease, fistulas and small bowel obstructions.
- Management goals for IBD include reduction of inflammation, mucosal healing and improved quality of life by reducing symptoms
- New medications are available for patients – “drugs don’t work in patients who don’t take them”
- Treat to target approach goes beyond symptom management and aims to prevent organ damage and to change the progressive course of IBD.
- A personalized approach and proactive re-assessment are key for optimal care of the IBD patient.