Inflammatory bowel disease and Irritable bowel syndrome

Objectives (regarding the Blueprint):

1. Identify the risk factors and recognize clinical manifestations for inflammatory bowel disease.
2. To be able to act diagnostic plan for patients suspected to have inflammatory bowel disease.
3. To be able to establish a treatment plan for inflammatory bowel disease.
4. To identify the types of irritable bowel syndrome based on the history and examination.
5. List the key points in the management of irritable bowel syndrome.

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Editing File

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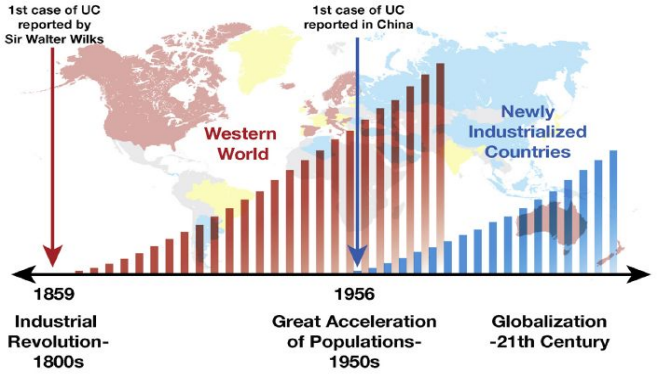
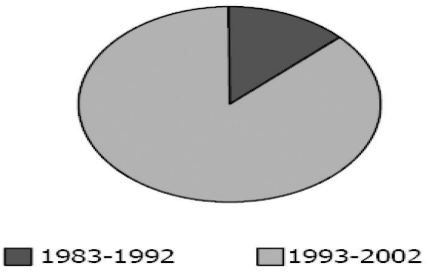
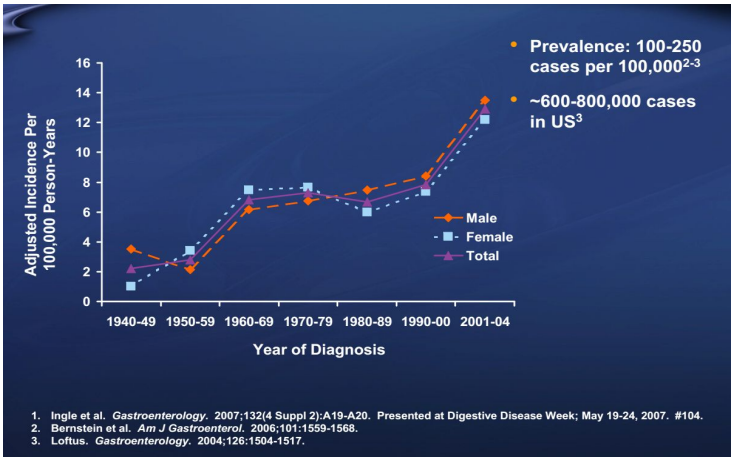
Prevalence of inflammatory bowel disease.



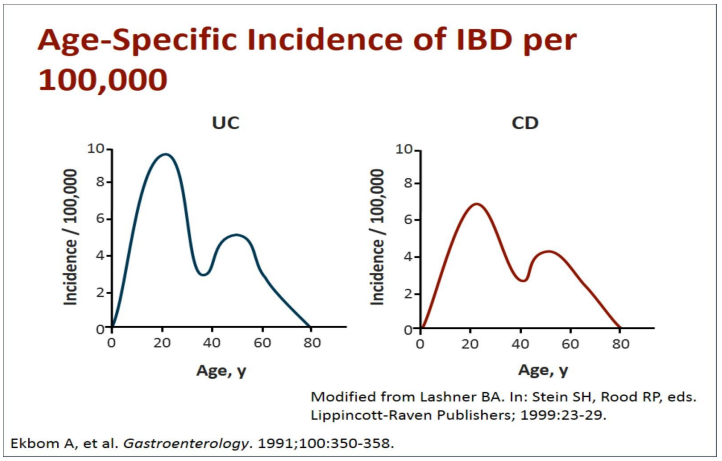
Epidemiology and outcome of Crohn's disease in a teaching hospital in Riyadh



Epidemiology of Crohn's Disease Temporal Trends in Crohn's Disease, Olmsted County, 1940-2004

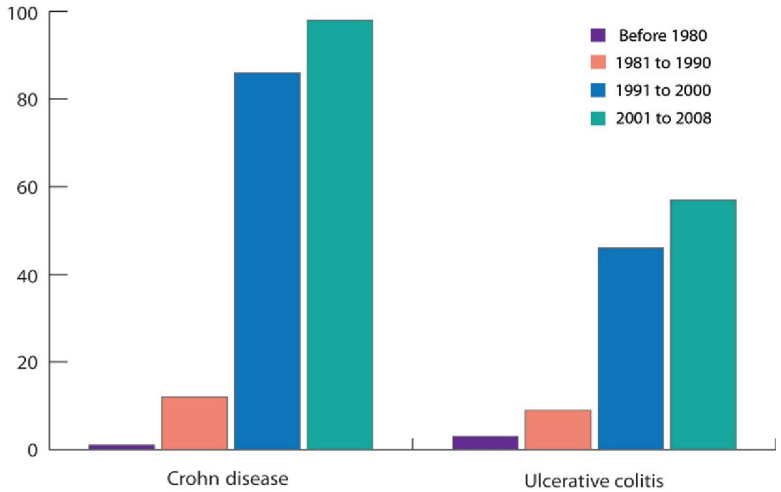


Age, and Impact on life



They have 2 peaks

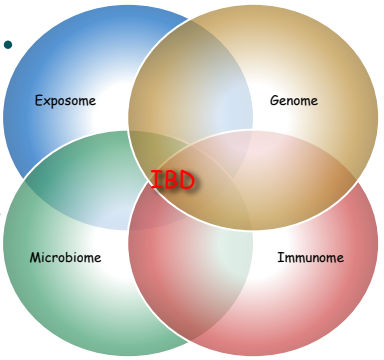
The bar chart shows an increase in number of patients with CD and UC in recent years.



Delay in diagnosis

- In a Swiss IBD cohort, diagnostic delay occurred more commonly in patients with CD compared with ulcerative colitis (median 9 vs 4 months, $p < 0.001$).
- Seventy-five percent of patients with CD were diagnosed within 24 months, compared with 12 months for patients with ulcerative colitis
- Leads to complications and worse outcomes

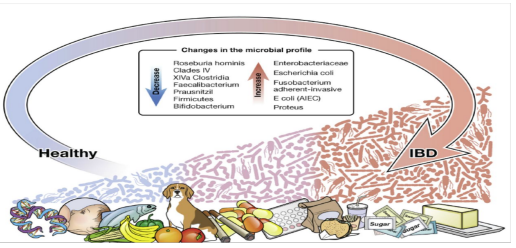
Identify the risk factors and recognize clinical manifestations for inflammatory bowel disease.

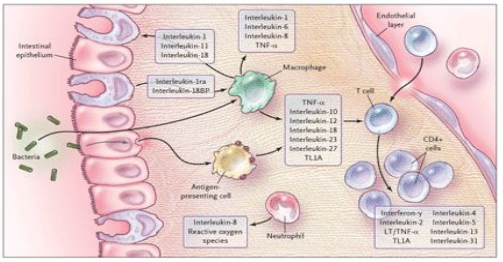


Pathophysiology of IBD

- IBD pathogenesis is complex since an action happens between different factors "omes": genome, exposome, immunome, microbiome.
- Microbiota changes are thought to be a trigger for inflammatory processes in IBD.
- The treatment for IBD now focus on one "ome" which is immunome with immunomodulatiors, anti-TNF, as well as environmental changes (advise the pt to stop smoking, healthy diet).

We mainly control the immunity by medications





Clinical manifestations

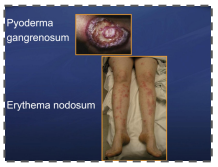
- Ileocecal disease: **abdominal pain**, diarrhea, fever
- Colonic disease: bloody diarrhea, weight loss, fever
- Perianal disease: pain, fistulae, edematous hemorrhoids, fissures
- Rectal-vaginal fistulae: 10% of women with rectal involvement
- Enterovesical fistulae: Recurrent UTIs, pneumaturia

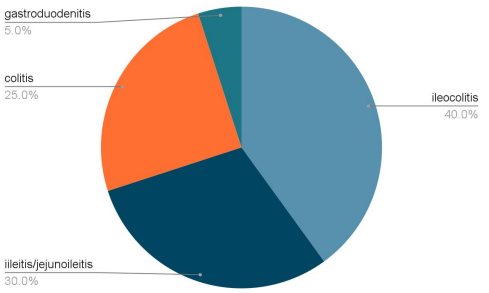
From the history you can differentiate CD from UC
Abdominal pain and diarrhea goes with CD
Bloody diarrhea and urgency goes with UC

Extra-intestinal manifestations

Skin:

- Pyoderma gangrenosum
- Erythema nodosum





Bones and joints: (20-25% of pts)

- Axial skeleton (disease independent)
  - Ankylosing spondylitis
  - Sacroileitis
- Peripheral arthritis (related to disease activity)
  - Type 1: asymmetric, limited
  - Type 2: chronic, symmetric

Eye: episcleritis, uveitis

Kidney: oxalate stones

Hepatobiliary: fatty liver, sclerosing cholangitis

Table 3.11 Extragastrointestinal manifestations of inflammatory bowel disease

Eyes	Uveitis, episcleritis, conjunctivitis
Joints	Arthralgia*, small joint arthritis, monoarticular arthritis (knees and ankles), ankylosing spondylitis, inflammatory back pain
Skin	Erythema nodosum, pyoderma gangrenosum (necrotizing ulceration of the skin, commonly on lower legs)
Hepatobiliary	Fatty liver*, sclerosing cholangitis, chronic hepatitis, cirrhosis, gallstones*
Renal calculi	Oxalate stones in patients with small bowel disease or after resection
Venous thrombosis	

All uncommon, occur in less than 10% of patients other than those marked.*

Identify the risk factors and recognize clinical manifestations for inflammatory bowel disease.

Differential diagnosis:

- Infectious colitis (including C. diff)
- Ischemic colitis
- Drug-induced (NSAID) enterocolitis
- Solitary rectal ulcer syndrome
- Radiation enterocolitis
- Diversion colitis
- Endometriosis
- Malignancy
- Functional (IBS) No weight loss or blood per recrum
- Diverticular disease

Red flags index score[1]

1. Non-healing or complex perianal fistula or abscess or perianal lesions.
2. first-degree relative with confirmed IBD.
3. weight loss (5% of usual body weight) in the last 3 months.
4. chronic abdominal pain (>3 months).
5. nocturnal diarrhea.
6. mild fever in the last 3 months.
7. no abdominal pain 30–45 min after meals, predominantly after vegetables.
8. no rectal urgency.

An RFS ≥8 was significantly associated with having Crohn's disease compared to IBS and healthy controls.

Montreal classification of extent of (UC)

Extent		Anatomy
E1	Ulcerative proctitis	Involvement limited to the rectum (that is, proximal extent of inflammation is distal to the rectosigmoid junction)
E2	Left sided UC (distal UC)	Involvement limited to a proportion of the colorectum distal to the splenic flexure
E3	Extensive UC (pancolitis)	Involvement extends proximal to the splenic flexure

Montreal classification of severity of (UC)

Severity		Definition
S0	Clinical remission	Asymptomatic
S1	Mild UC	Passage of four or fewer stools/day (with or without blood), absence of any systemic illness, and normal inflammatory markers (ESR)
S2	Moderate UC	Passage of more than four stools per day but with minimal signs of systemic toxicity
S3	Severe UC	Passage of at least six bloody stools daily, pulse rate of at least 90 beats per minute, temperature of at least 37.5°C, haemoglobin of less than 10.5 g/100 ml, and ESR of at least 30 mm/h

Vienna and Montreal classification for CD

	Vienna	Montreal
Age at diagnosis	A1 below 40 y	A1 below 16 y
	A2 above 40 y	A2 between 17 and 40 y
		A3 above 40 y
Location	L1 ileal	L1 ileal
	L2 colonic	L2 colonic
	L3 ileocolonic	L3 ileocolonic
	L4 upper	L4 isolated upper disease*
Behaviour	B1 non-stricturing, non-penetrating	B1 non-stricturing, non-penetrating
	B2 stricturing	B2 stricturing
	B3 penetrating	B3 penetrating
		p perianal disease modifier†

*L4 is a modifier that can be added to L1–L3 when concomitant upper gastrointestinal disease is present.

†"p" is added to B1–B3 when concomitant perianal disease is present.

Montreal classification of severity of (UC)

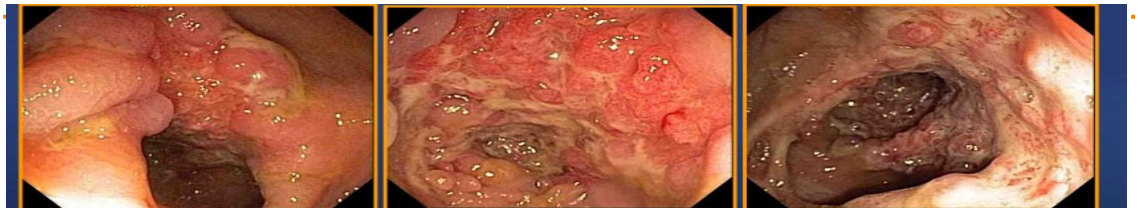
Age at diagnosis (A)			
A1	16 years or younger		
A2	17–40 years		
A3	Over 40 years		
Location (L)		**Upper GI modifier (L4)**	
L1	Terminal ileum	L1 + L4	Terminal ileum + Upper GI
L2	Colon	L2 + L4	Colon + Upper GI
L3	Ileocolon	L3 + L4	Ileocolon + Upper GI
L4	Upper GI	–	–
Behaviour (B)		**Perianal disease modifier (p)**	
B1*	Nonstricturing, nonpenetrating	B1p	Nonstricturing, nonpenetrating + perianal
B2	Stricturing	B2p	Stricturing + perianal
B3	Penetrating	B3p	Penetrating + perianal

1: used for Suspected Crohn's Disease', that reliably discriminates functional gut disorders or normality from CD. its intended to help clinicians in primary or secondary care, and potentially patients, to reliably identify S&S that might lead to the diagnosis of CD before starting any diagnostic workup. The hope is that this Red Flags index will reduce the time to diagnosis and enable intervention at a time when the course of the disease may be changed.

To be able to act diagnostic plan for patients suspected to have inflammatory bowel disease.

Investigations

- Basic workup CBC (anemia, leukocytosis)
- ESR low albumin and electrolytes imbalance
- CRP: Stool culture
  - Advantages:
    - **Short half-life** makes CRP a good marker to detect and follow-up disease activity
    - CRP is a predictor of **relapse** and follow up
  - Limitations:
    - CRP is non-specific, as it is a measure of inflammation, but is not specific to location
    - CD is associated with a strong CRP response in most patients; however, in ulcerative colitis (UC) patients, the CRP response is modest to absent
- Serology
- **Fecal calprotectin:** Protein within the neutrophilic wall
  - Advantages:
    - Calpro makes up for a high proportion of the cytosolic proteins in neutrophils
    - Presence of calpro in feces is proportional to neutrophil infiltration in mucosa and neutrophil shedding in the gut lumen
    - Can be used to **DD IBD from IBS**
    - Calpro is strong marker for disease **activity**
    - Calpro is predictive of **relapse**
  - Limitations:
    - Calpro is not IBD specific
    - Calpro correlates better with colonic CD vs. ileal CD, and an inflammatory phenotype vs. a structuring/penetrating phenotype
- Colonoscopy Cobblestone, erythema, deep ulcer
- Radiological images:
  - US:
    - Accurate technique, non-invasive, and free of ionizing radiation
    - Needs experienced and trained physician, dependent on location and severity of disease
  - CT: Accuracy has not been properly evaluated in prospective studies
  - MRI:
    - Accurate technique, less dependent on experience level or disease location
    - Inferior to endoscopy for detection of mild lesions, but allows for transmural and extraluminal identification of lesions.



To be able to act diagnostic plan for patients suspected to have inflammatory bowel disease.

1st point of diagnosing is identifying **severity**, it helps **guide management**

Clinical Criteria for Crohn's Disease Activity (American College of Gastroenterology Practice Guidelines)

- Mild: Ambulatory, <10% WT loss, minimal impact of quality of life, and no complications
- Moderate: lies in between
- Severe: Persistent symptoms despite therapy, cachexia and presence of complications like abscess, surgery, fistula.

Classification according to disease severity (UC)

Table 4. Proposed American College of Gastroenterology Ulcerative Colitis Activity Index[a]

	Remission	Mild	Moderate-severe	Fulminant
Stools (no./d)	Formed stools	<4	>6	>10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	<75% of normal	Transfusion required
ESR	<30	<30	>30	>30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
FC (μg/g)	<150–200	>150–200	>150–200	>150–200
Endoscopy (Mayo subscore)	0–1	1	2–3	3
UCEIS	0–1	2–4	5–8	7–8

[a]Modified from reference 44.
The above factors are general guides for disease activity. With the exception of remission, a patient does not need to have all the factors to be considered in a specific category.
CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FC, fecal calprotectin; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

Montreal classification for UC

Classified by the extent of the disease

Montreal classification (CD)	**CD (n = 15)**
L1	7% (1/15)
L2	60% (9/15)
L3	33% (5/15)
Montreal classification (UC)-Extent	**UC (n = 13)**
Proctitis E1	8% (1/13)
Left sided UC E2	38% (5/13)
Extensive UC E3	54% (7/13)
Montreal classification (UC)-Severity	**UC (n = 13)**
Clinical remission S0	0
Mild UC S1	54% (7/13)
Moderate UC S2	46% (6/13)
Severe UC S3	0

doi:10.1371/journal.pone.0025417.t001

To be able to establish a treatment plan for inflammatory bowel disease.

Management

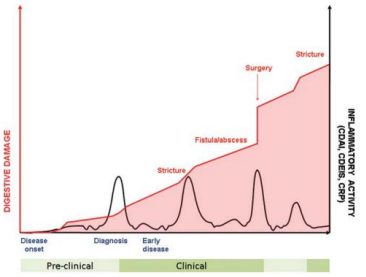
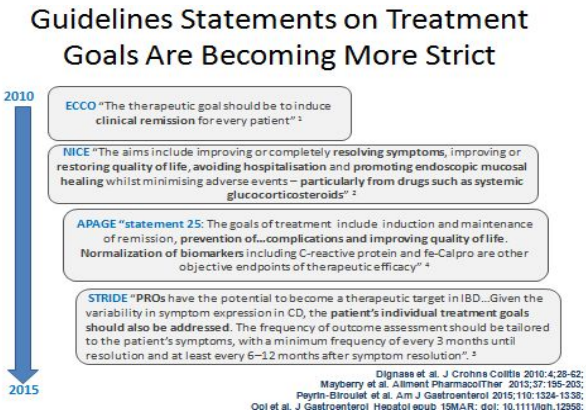


FIGURE 1. Progression of digestive damage and inflammatory activity in a theoretical patient with CD.

Step-up treatment paradigme is **no** longer recommended

Treatment goals in CD:

- ➢ Induce rapid response and maintain steroid-free remission
- ➢ Achieve and maintain complete mucosal healing (MH)
- ➢ Improve quality of life
- ➢ Avoid complications (i.e. hospitalization and surgery)
- ➢ Prevent disease-related mortality
- ➢ Minimize the adverse effects of treatment
- ➢ Avoid treatment-related mortality/morbidity
- ➢ Provide affordable cost for society
- ➢ Provide acceptable benefit-risk



<u>Ultimate goal:</u>

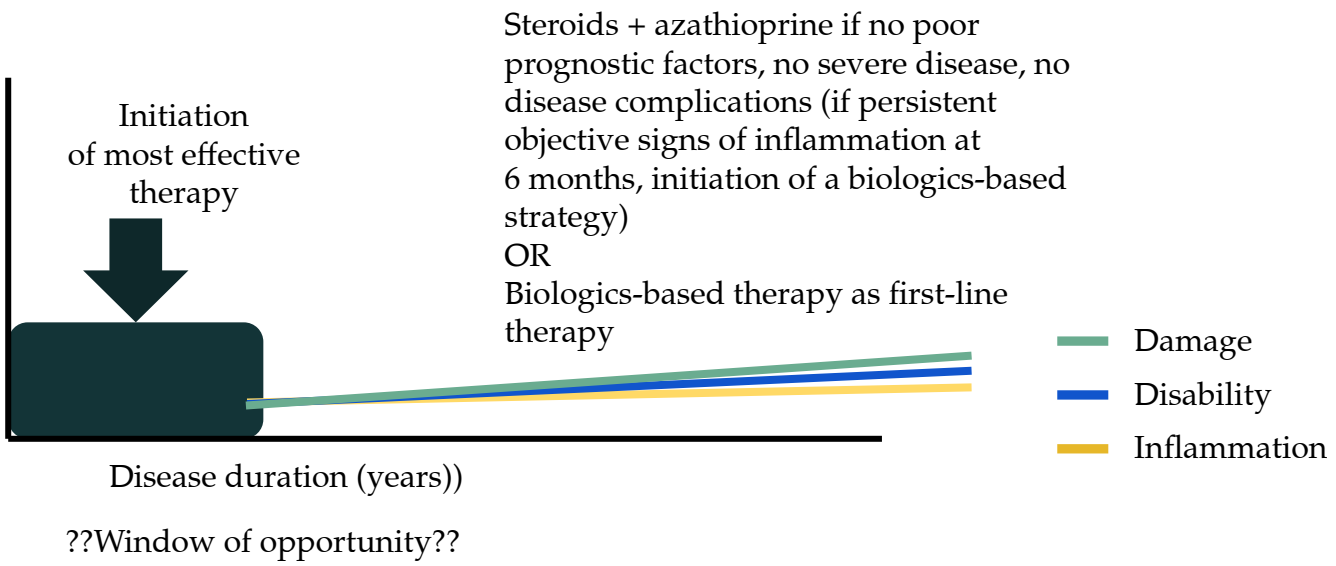
To achieve **disease modification** and to **prevent structural bowel damage**

STRIDE (Selecting Therapeutics Targets in Inflammatory Bowel Disease)

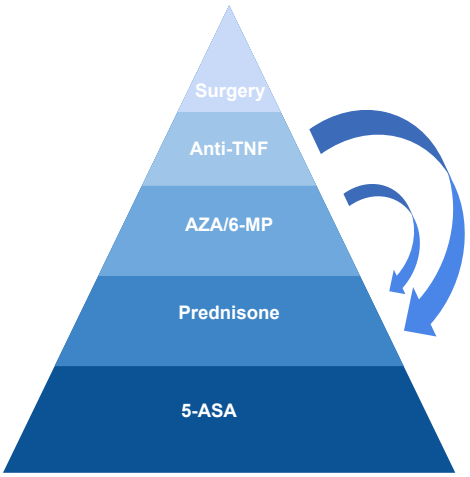
Clinical Recommendation	Endoscopy/imaging	Biomarkers/PROs	Composite endpoint
Resolution of Clinical symptoms and inflammation are the goals of treatment that define the term "remission". Mucosal healing was recommended as the therapeutic goal in clinical practice, because it is associated with better outcomes in both cohort studies and RCTs.	**Absence of ulceration** is the target. Histologic remission is NOT a target. Cross-sectional imaging is not but might have a role in patients with CD who are not assessed by colonoscopy.	**Biomarkers (CRP and fe Calpro) ARE NOT a target**, but adjuvant measures for monitoring of inflammation. The ultimate PRO is the **normalization of quality of life**	**Clinical/PRO remission**: resolution of abdominal pain and diarrhea/altered bowel habit, **assessed at a minimum of <u>3</u> months** during active disease **+** **Endoscopic remission**: resolution of ulceration at ileocolonoscopy (or cross-sectional imaging), **assessed at <u>6- to 9-</u>month intervals** during the active phase

Moving towards disease modification in IBD therapy

A window of opportunity: the concept of disease-modifying drugs (DMAIDs) early in the disease course to change the natural history of Crohn's disease

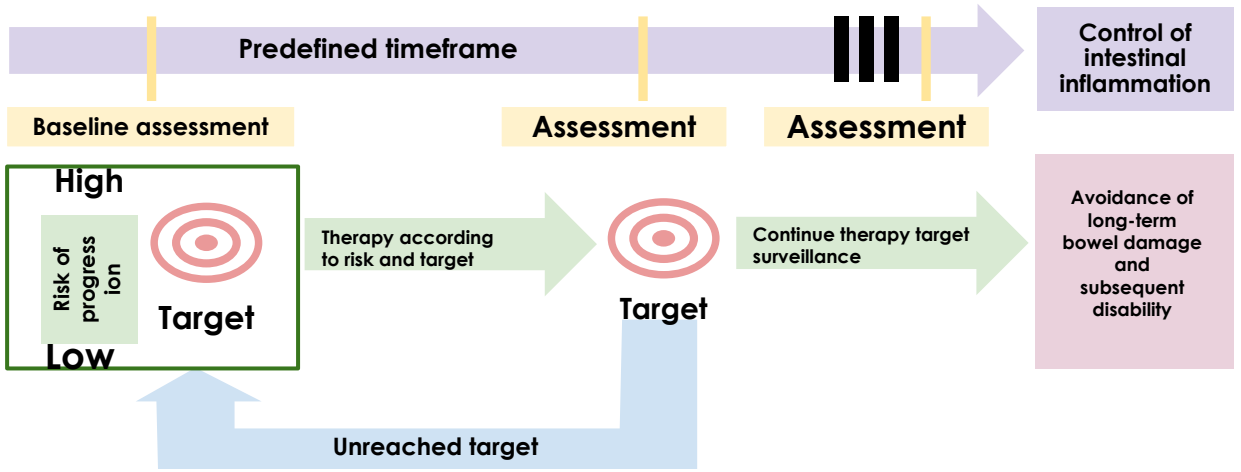


Step-up treatment paradigme in IBD



- Treatment based on disease severity
- Steroids are effective for induction of remission2,3
- Relapse off steroids is high and immunosuppression is often required2–4
- Mucosal healing is not achieved in many patients and surgery is often needed2,3

Treat-to-target concept in Crohn's disease



To be able to establish a treatment plan for inflammatory bowel disease.

Current Therapies for Inflammatory Bowel Disease

Induction agents	Maintenance agents
➢ Corticosteroids ➢ 5-ASA (UC only) ➢ Anti-TNF agents ➢ Vedolizumab ➢ Ustekinumab (Crohn's only) ➢ Exclusive enteral feeding (ileal Crohn's)	➢ 5-ASA (UC only) ➢ Azathioprine / MP ➢ Methotrexate (Crohn's) ➢ Anti-TNF agents ➢ Vedolizumab ➢ Ustekinumab (Crohn's only) ➢ Smoking cessation

Risk Factors for a Disabling Disease Course

Variables	Non-disabling, (%) (n=166)	Disabling, (%) (n=957)	Statistical Univariate Test
Age at Onset			
<40 Year	77.1	87.7	p=0.0004
≥40 Year	22.9	12.3	
Location of the Disease			
Small Bowel Only	44.6	32.8	p=0.002
Small Bowel and Colon	25.9	39.4	
Colon Only	29.5	27.8	
Perianal Lesions at Diagnosis			
Yes	17.5	26.4	p=0.01
No	82.5	73.6	
Requirement for Steroids for Treating the First Flare			
Yes	37.3	65.2	p=0.0001
No	62.7	34.8	

To be able to establish a treatment plan for inflammatory bowel disease.

Importance of Identifying High-Risk Patients

- ➢ Need to determine as early as possible who is at a high risk of developing disease complications
- ➢ Simple demographic and clinical features can help identify high-risk patients at diagnosis and throughout the disease course.

Indolent disease:
Traditional step-up
Avoid intensive therapy, immunosuppression and adverse events

Aggressive disease:
Early intensive therapy
Assure early intensive therapy to avoid complications

Monitoring Tools for Decision Making in the Treatment of CD

1. Symptom-based (CDAI, HBI, IBDQ)
2. Biomarkers(CRP, FeCa)
3. Endoscopic assessment (CDEIS, SES-CD)
4. Cross-sectional imaging (MRI, CT, US)

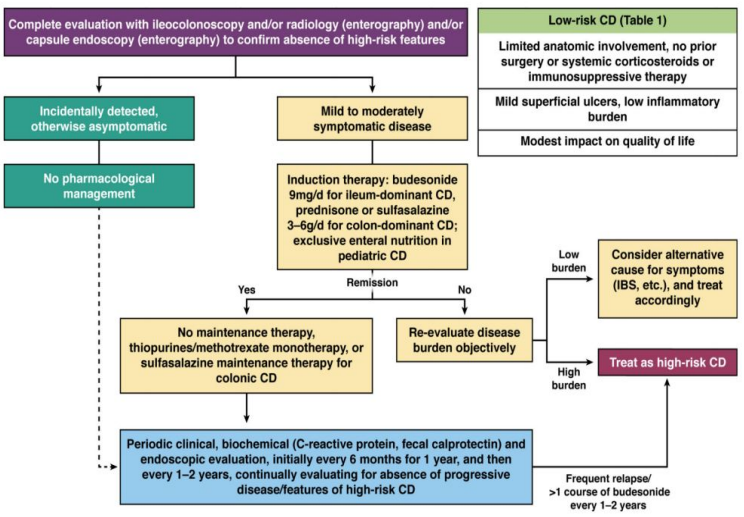


Figure 1.
Proposed algorithm for positioning therapies for patients with low-risk Crohn's disease

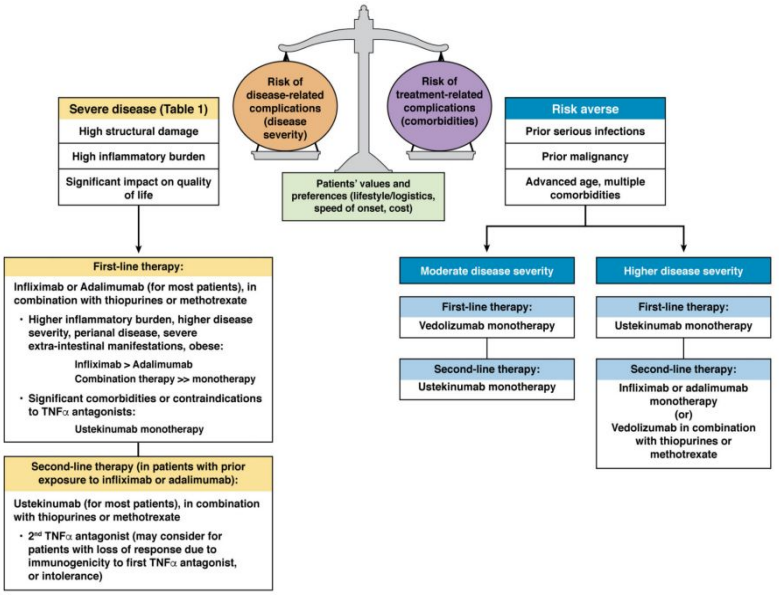
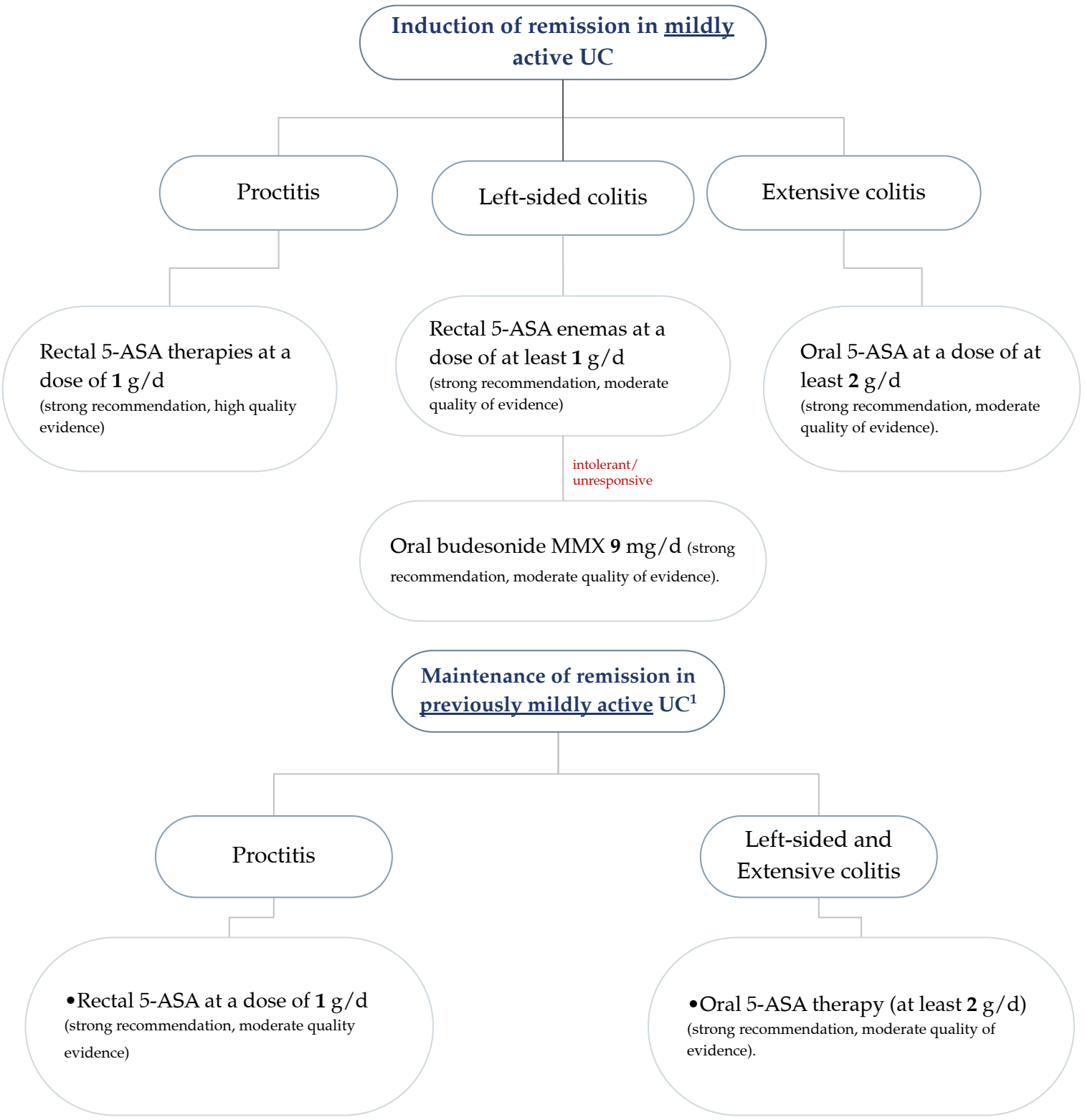


Figure 2.
Proposed algorithm for positioning therapies for patients with high-risk Crohn's disease

To be able to establish a treatment plan for inflammatory bowel disease.

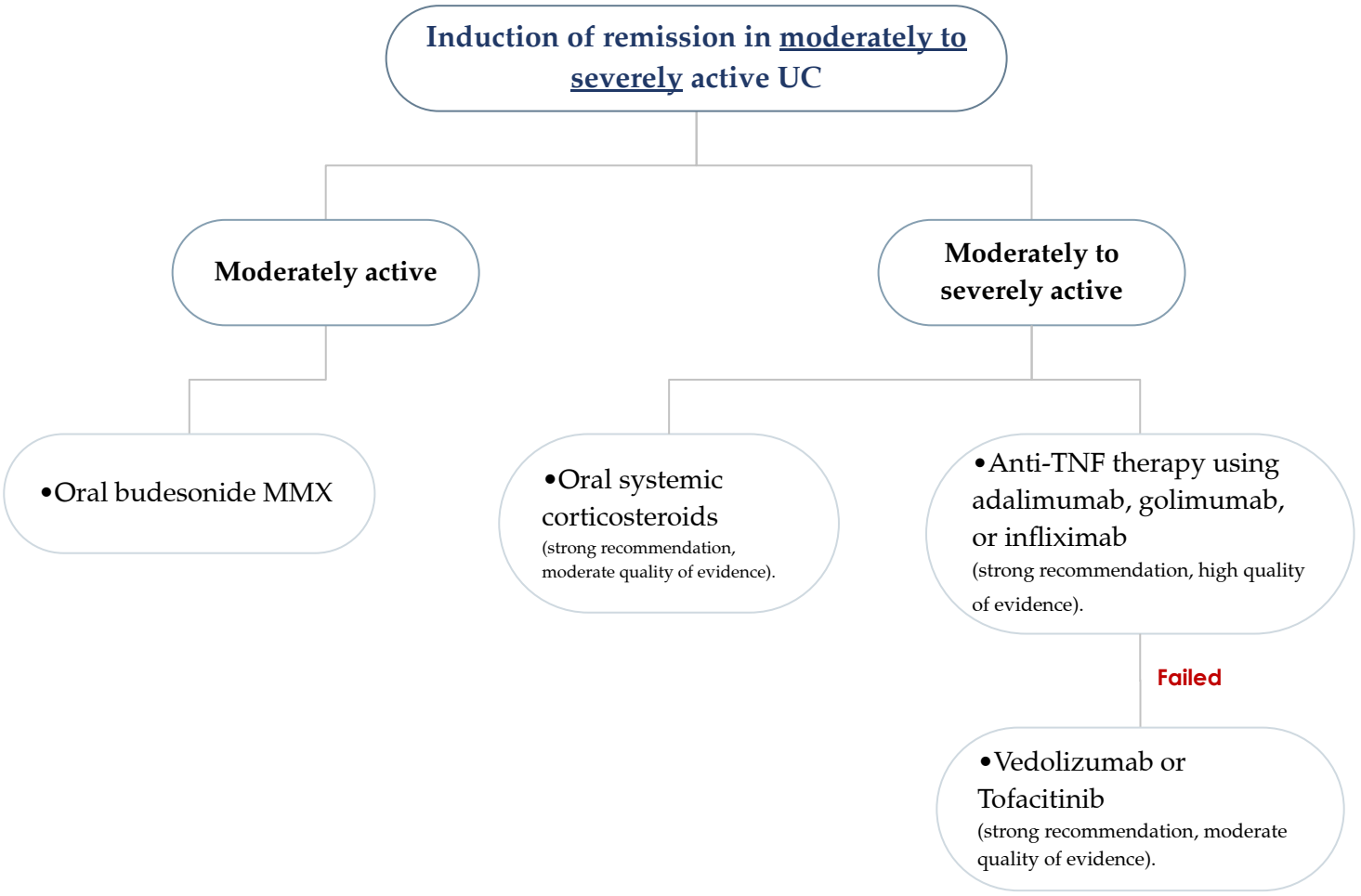


1. We recommend against systemic corticosteroids for maintenance of remission in patients with UC (strong recommendation, moderate quality of evidence).

To be able to establish a treatment plan for inflammatory bowel disease.

Poor prognostic factors in ulcerative colitis

- Age <40 yr at diagnosis
- Extensive colitis Severe endoscopic disease
- Hospitalization for colitis
- Elevated CRP
- Low serum albumin
- The greater the number of poor prognostic factors, the worse the prognosis as measured by the likelihood of colectomy



In patients with moderately to severely active UC, we recommend **vedolizumab** for induction of remission (strong recommendation, moderate quality of evidence).

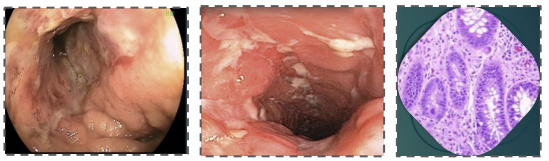
In patients with moderately to severely active UC, we recommend **tofacitinib 10** mg orally b.i.d. for 8 wk to induce remission (strong recommendation, moderate quality of evidence).

In patients with moderately to severely active UC who are responders to **anti-TNF** therapy and now losing response, we suggest measuring serum drug levels and antibodies (if there is not a therapeutic level) to assess the reason for loss of response (conditional recommendation, very low quality of evidence).

Cases (from Dr. Slides)

Case 1:

29 years old female, newly Crohn's disease , A2 L3 B2, c/o post prandial abdominal pain and intermittent **bloody diarrhea** for 4 months, WBC: 7 HGB: 10 CRP: 5 FC: 500 Alb: 2.9. Colonoscopy; inflamed colon with ulceration in TI and stricture (SES-CD score 17). Histopathology, confirmed CD, TB PCR and CMV negative, Fungal culture ; no growth



Server disease

What is the **best next step** in the management ?

A. Budesonide 9 mg daily
B. Start biologic therapy with IMD
C. Refer for Surgical intervention
D. Start Azathioprine 2.5 mg/kg then follow up the response

Answer: B

Case 2:

A 22 year old man with history of UC diagnosed 6 years ago, Mild pancolitis at diagnosis on mesalamine 4 g/day with good adherent, Two months later Admitted with UC flare 12 bowel movements/day, bleeding and mucus discharge, Lost 2-3 kg in the last 2 weeks, has Abdominal pain and distention.

On examination:

Blood pressure 100/60 mmHg. Pulse 95/min, afebrile
Abdomen: mild tenderness all over the abdomen, no signs of peritonitis.
Labs: WBC high 14, Hgb 9.5 g/dL, normal biochemistry, ESR 43 mm/hr, CRP 69 g/dL.

plan:

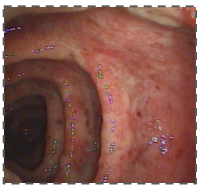
- Admit
- Images
- Stool culture and clostridium difficile
- Nutrition
- VTE prophylaxis

DAY 1

- Patient admitted and start IV methylprednisolone 40 mg IV BID, ciprofloxacin 400 mg IV bid
- C. difficile was negative

DAY 3

- Persistent of diarrhea 10 bowel movement/day with blood
- Hb 8.2, Albumin 27, ESR 57, and CRP=56. Flex sigmoidoscopy:



What is the next therapeutic choice?

A. Infliximab
B. Vedolizumab
C. Antibiotics
D. Colectomy

Answer: A (start anti-TNF if disease still active, if failed consider B

To identify the types of IBS based on the history and examination.

Subtyping syndrome by predominant stool pattern (kumar)

Type	Description
IBS with constipation (IBS-C)	Hard lumpy stools >25% and loose (mushy) or constipation watery stools <25% of bowel movements
IBS with diarrhea (IBS-D)	Loose (mushy) or watery stools >25% and hard (IBS-D) or lumpy stools <25% of bowel movements
Mixed IBS (IBS-mixed)	Hard or lumpy stools >25% and loose (mushy) or watery stools >25% of bowel movements
Unsubtyped IBS (IBS-U)	Insufficient abnormality of stool consistency to meet criteria for IBS- C, D or M

Clinical features	Rome IV criteria for IBS

➢ Abdominal pain
  ○ Frequency, intensity, and localization generally vary widely from patient to patient
  ○ Typically related to defecation
➢ Altered bowel habits: : diarrhea and/or constipation
➢ Other gastrointestinal symptoms
  ○ Nausea, reflux, early satiety
  ○ Passing of mucus, abdominal bloating
➢ Extraintestinal symptoms
  ○ Generalized somatic symptoms (e.g., pain or fatigue, as in fibromyalgia)
  ○ Disturbed sexual function
  ○ Dysmenorrhea
  ○ Increased urinary frequency and urgency
➢ Physical examination: normal
➢ Associated conditions
  ○ Fibromyalgia, chronic fatigue syndrome
  ○ Major depression, anxiety, somatization
  ○ GERD, functional dyspepsia
  ○ Noncardiac chest pain
	Recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with 2 or more of the following:
	➢ Pain related to defecation
	➢ Change in stool frequency
	➢ Change in stool form or appearance
	Alarm features
	➢ Older age of onset (≥50)
	➢ Gl bleeding
	➢ Nocturnal diarrhea
	➢ Worsening pain
	➢ Unintended weight loss
	➢ Abnormal labs (e.g., IDA, electrolyte disorders, increase CRP)
	➢ Positive fecal lactoferrin or calprotectin
	➢ FHx of early colon cancer or IBD

List the key points in the management of irritable bowel syndrome.

IBS Management	
General measures 1. Regular consultations and reassurance that the disease, although chronic, is benign 2. Lifestyle changes: • Dietary adjustments ○ Plenty of fluid ○ High-fiber foods ○ Avoidance of: ■ Gas-producing foods (e.g., beans, onions, prunes) ■ Fermentable, short-chain carbohydrates (e.g., foods with high fructose content: honey, apples, corn syrup) ■ Lactose ■ Gluten • Physical activity • Stress management (identification of stress factors, avoidance techniques, relaxation therapy) 3. Psychological therapy (patients with psychological conditions): e.g., cognitive-behavioral therapy	**Medical therapy** Medical therapy of IBS is symptom-directed: **Diarrhea** ➢ Antidiarrheals (loperamide) ➢ Rifaximin ➢ Alosetron **Constipation** ➢ Soluble fibers/bulk-forming laxatives (psyllium) ➢ Osmotic laxatives (polyethylene glycol) ➢ Lubiprostone (chloride channel activator) **Cramping/pain** ➢ Antispasmodics (dicyclomine, hyoscyamine) ➢ Tricyclic antidepressants (e.g., amitriptyline, nortriptyline)

Conclusion

Emerging strategies are defining improved ways of diagnosing and managing patients with IBD

New therapies provide us with more choice and greater treatment flexibility

- Inhibition of leukocyte trafficking has significant promise
- IL12,23

Our task is to use the right treatment in the right patient at the right time

- Understand best practice
- Optimise your first biologic
- Tailor treatment to patient needs

Ulcerative Colitis

UC is an **inflammatory disease** is a **superficial inflammation** that's **limited to the colon**. Patients present with **bowel urgency**, **frequent bowel movements**, and **bloody diarrhea**. Onset is abrupt and patients often remember when the disease first started. Abdominal pain is unusual; it represents a complication. Diagnosis revolves around **colonoscopy**. UC is a **continuous** lesion, involving the rectum and then extending variably through the colon. UC doesn't extend outside the colon. The end of involved tissue is also **abrupt**. Biopsy of the colon reveals **crypt abscesses** and **superficial inflammation**.

Extraintestinal manifestations include **primary sclerosing cholangitis** (association with **p-ANCA**), erythema nodosum, and aphthous ulcers.

Unlike with Crohn's, **surgical removal of UC is curative**. Because there's a high association with malignant transformation of UC, a **colonoscopy screening** begins at **8 years from diagnosis** and continues **annually** until resection.

Disease severity dictates medical management. For mild disease, **5-ASA compounds** are effective in UC (unlike Crohn's). For moderate disease, immune modulators such as **Azathioprine** and **6-mercaptopurine** are used; **TNF-inhibitors** are used should they fail. Surgery is ultimately curative.

UC Flare

Flares will present with increased number of bowel movements or worsening blood. For flares, **infectious etiologies must be ruled out**, specifically C. Diff. Flares are treated with **steroids** and **antibiotics**.

Mild: **5-ASA Compounds** designed to prevent flare by releasing in the rectum to quiet inflammation. These work for UC
- Sulfasalazine
- Mesalamine

Mod: **Oral steroid** taper quells the acute flare
Then: follow with **immune modulators**
- **Prednisone**
- Azathioprine / 6-Mercaptopurine

Severe: **IV steroids** to quell acute flare, then:
- For UC → **Infliximab** or **Cyclosporine**
- For UC → Resection

SURGERY IS CURATIVE

Screening colonoscopy **q1y** starting at **y8**.

Crohn's Disease

Crohn's disease is an **inflammatory disease** of the bowel **that can extend from the mouth to anus** and can be discontinuous (skip lesions). Patients present with an insidious onset of symptoms and rarely remember the initiation of the disease. They also present with gradually worsening **watery diarrhea** and **weight loss**. Because the inflammation is transmural, it's possible to develop **fistulas** from the bowel to any other organ (entero-entero, entero-vagina, entero-vesicular) or the skin (entero-cutaneous). Because the inflammation can occur anywhere, symptoms are highly variable, which includes nutritional deficiencies. There's a predilection for the **terminal ileum** resulting in **B12 deficiency**. Diagnosis revolves around **endoscopy** and biopsy. Biopsy will reveal **transmural inflammation** and **noncaseating granulomas**.

Extraintestinal manifestations exist, but aren't as specific as in UC. For Step 2, consider Crohn's as having, "no extraintestinal disease," though do know that Rheumatologic complaints can exist.

There's no increased risk of malignancy in Crohn's*. **Resection is NOT curative**, but can be used on limited stretches of bowel that are refractory or particularly burdensome.

5-ASA compounds are still used in Crohn's disease, but there's increasing evidence that **early initiation of disease modifying agents** is superior for the disease course. Azathioprine and 6-mercaptopurine are used in mild and moderate disease. **Anti-TNF** medications are used in severe disease, and, in the absence of infection, are often successful in healing enterocutaneous fistulas. **Dexa-scans** and **Calcium repletion** are usually needed.

Crohn's Flare

Flares will present with increased number of bowel movements, weight loss, and **electrolyte abnormalities**. For flares, **infectious etiologies must be ruled out** - specifically C. diff. Flares are treated with **steroids** and **antibiotics**.

Perirectal disease, such as perianal **abscess**, must be **drained**.

Mild: **5-ASA Compounds** don't really work for Crohn's disease.
- Sulfasalazine

Mod: **Oral steroid** taper quells the acute flare
Then: follow with **immune modulators**
- **Prednisone**
- Azathioprine / 6-Mercaptopurine

Severe: **IV steroids** to quell acute flare, then…
- For CD → **Infliximab**

DO NOT PERFORM SURGERY except for Fistulas (see surgery topics)

Antibiotics are good when there's a perirectal abscess, otherwise no benefit

*severe distal colonic Crohn's = Screen like UC

Lecture Quiz

1:B / 2:B / 3:C

Q1: Which one of these is associated with IBD ?

A. Cataract
B. Ankylosing spondylitis
C. Blindness
D. Diverticulitis

Q2: Patient with extensive ulcerative colitis. Now she has fever, bloody diarrhea for 5-7/ day. She is compliant to 3 mg/dl oral Mesalamine. She took three courses of Steroids in the past 6 months. What would you do for her ?

A. Give glucocorticoids
B. Initiate Azathioprine
C. Increase the dose of mesalamine to 5 mg/dl
D. Add suppository Mesalamine

Q3: A 70-year-old white woman presents with LLQ abdominal pain, low-grade fever, and mild rectal bleeding. Examination shows LLQ tenderness. Unprepped sigmoidoscopy reveals segmental inflammation beginning in the distal sigmoid colon through the mid-descending colon. The rest of the examination is negative.

A. Ulcerative colitis
B. Crohn disease
C. Ischemic colitis
D. Diverticulosis