Inflammatory bowel disease: clinical overview and update

AAMS 8th Annual Fall Symposium
October 12, 2019

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Presentation objectives

- Provide a high-yield clinical overview of inflammatory bowel disease (IBD).
- Identify typical (and avoidable) clinical pitfalls in IBD.
- Review practical vignettes illustrating a spectrum of common IBD scenarios.
- Time for Q&A.

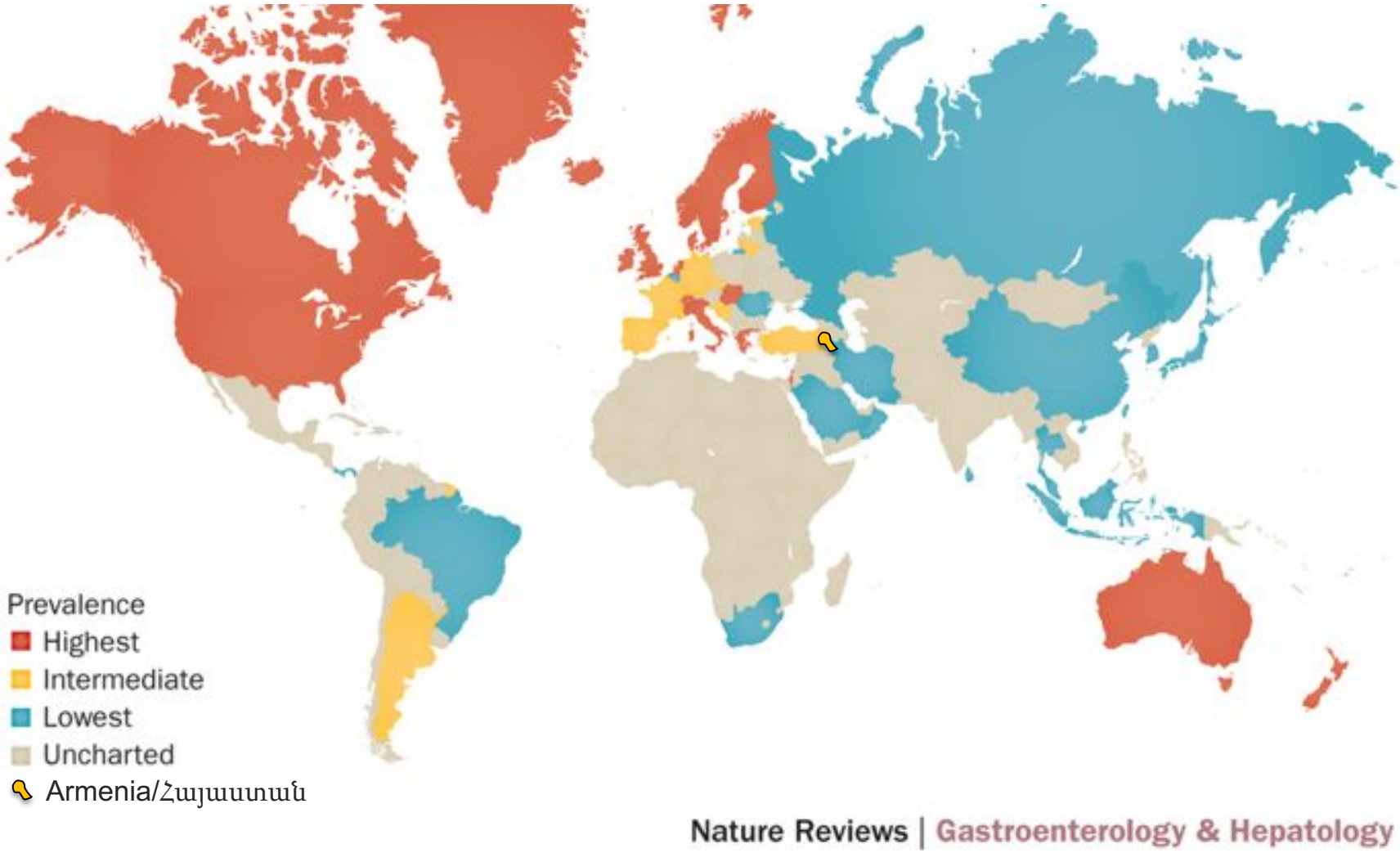
Presentation outline

- Provide a high-yield clinical overview of inflammatory bowel disease (IBD).
  - **Background**
  - Symptoms and associated conditions
  - Diagnosis
  - Pre-treatment evaluation
  - Treatment goals and options
- Identify common (and avoidable) clinical pitfalls in IBD.
- Practical interactive IBD vignettes.
- Time for Q&A.

Clinical Epidemiology of IBD

- IBD is an umbrella term which includes Crohn's disease (CD) and ulcerative colitis (UC)
  - Both are characterized by idiopathic chronic inflammation
    - Can be relapsing and remitting in nature
  - Neither has a specific "cause", but both are immune-mediated
- ≈1 in 400 in USA have IBD (prevalence ≈1,000,000 adults)
  - Similar prevalence in males and females
  - Individuals of all ages can have IBD (pediatric, adult, geriatric)
  - Incidence of IBD is rising, especially in developing countries
- In the USA, IBD is associated with $6.3 billion in direct costs per year

Worldwide prevalence of IBD



Presentation outline

- High-yield clinical overview of IBD.
  - Background
  - **Symptoms and associated disorders**
  - Diagnosis
  - Pre-treatment evaluation
  - Treatment goals and options
- Common (and avoidable) clinical pitfalls in IBD.
- Practical interactive IBD vignettes.
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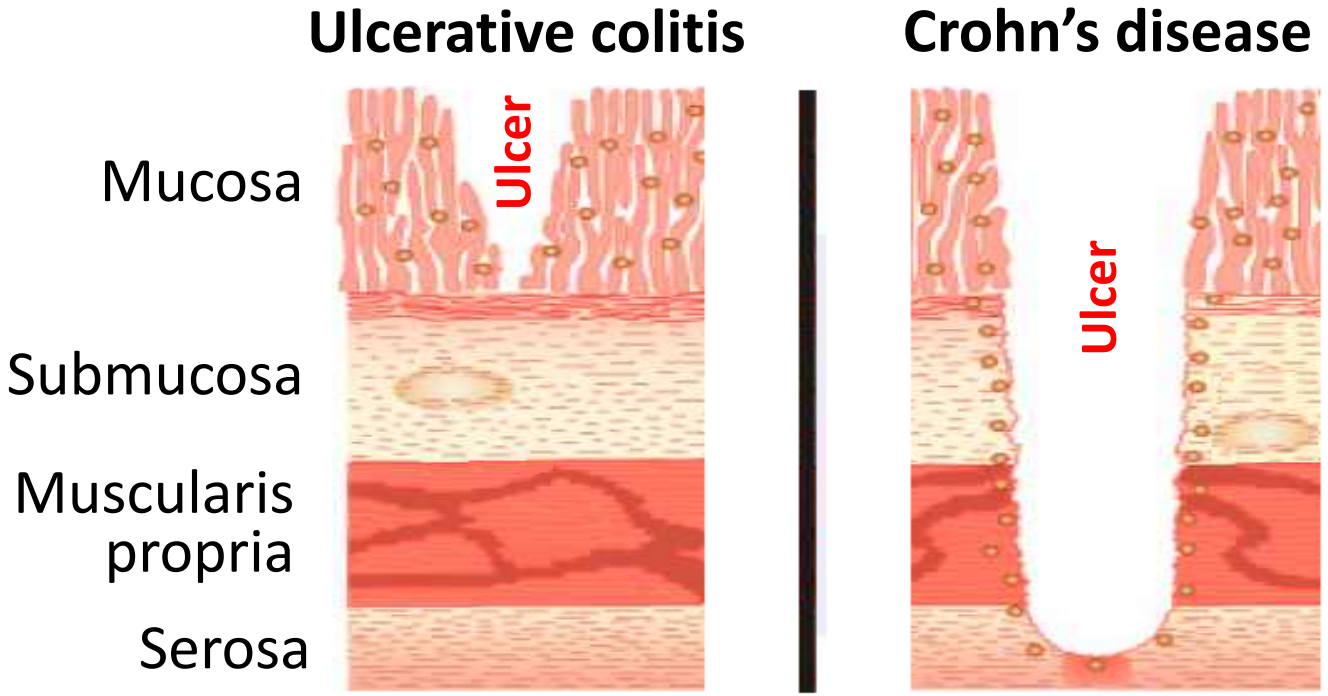
Symptoms of IBD – very variable!

- Depend largely on the:
  - location, extent, and severity of inflammation/tissue injury
  - how healthy the remainder of the GI tract is
  - the degree of chronic vs. superimposed acute (active) inflammation
- Can range from subclinical or extremely subtle to life-threatening such that may be…
  - an incidental finding (e.g. picked up on CT for other reason)
  - diagnosed during workup of chronic microcytic (or normocytic) anemia
  - the etiology of septic shock and need for emergent surgery

Symptoms in UC vs. CD

- UC and CD generally differ in the distribution and depth of disease involvement
  - UC typically only affects the colon (large intestine) and is mucosally-based
  - CD can affect the colon, small intestine, stomach, and more and can be/is often a transmural disease



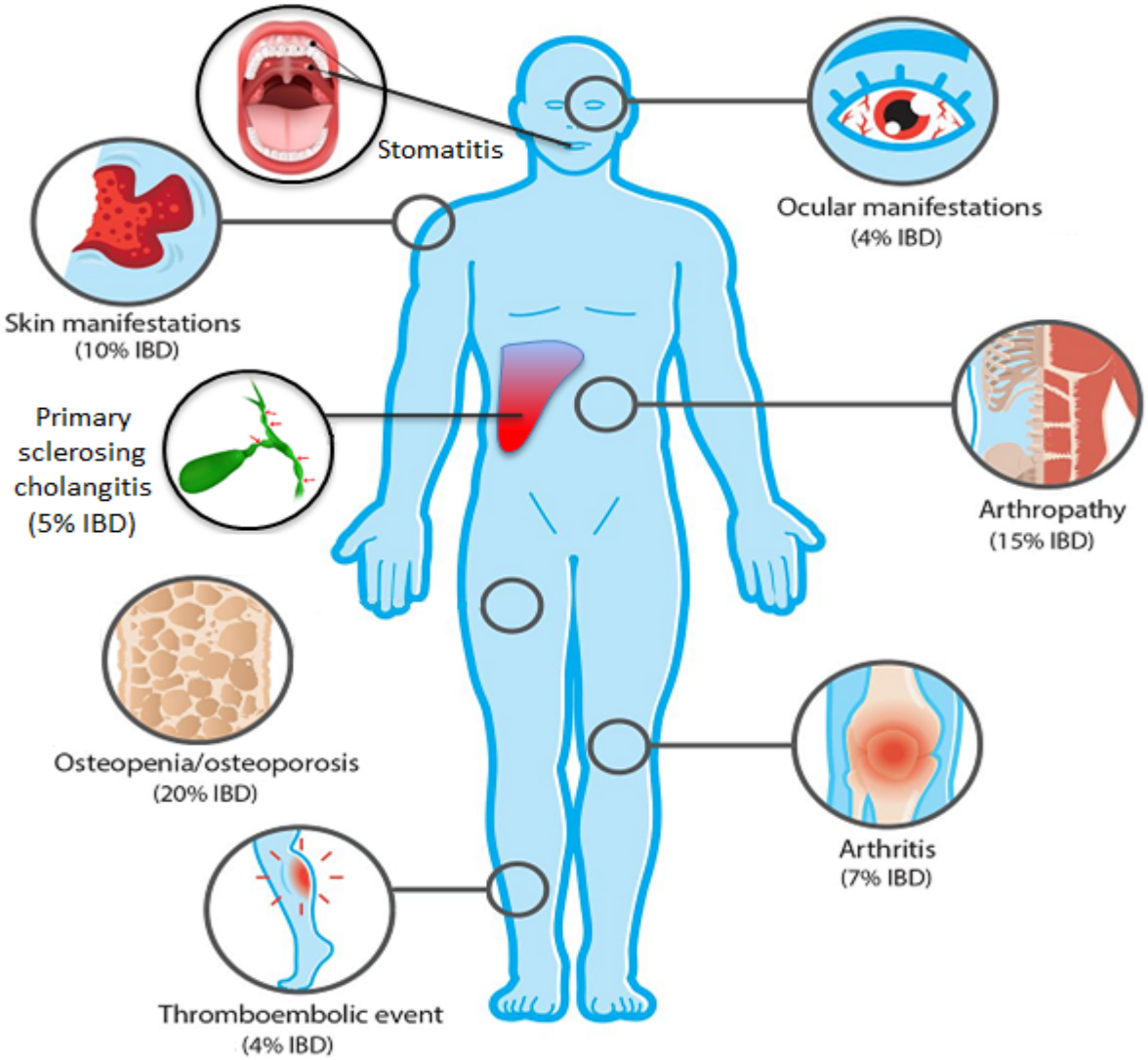
Commonly reported symptoms of IBD

- Symptoms may (but need not) include:
  - Bloody bowel movements/bloody diarrhea
  - Abdominal cramping/pain, pelvic pain
  - Fecal urgency, nocturnal bowel movements
  - Unexplained weight loss (failure to thrive in peds)
  - Fatigue
- Intermittent flares (i.e. acute worsening) may occur periodically over the course of the disease

Extra-intestinal manifestations of IBD

- Some symptoms of IBD are not “intestinal”; these are referred to as extra-intestinal manifestations (EIMs)
- EIMs have multi-system involvement, including:
  - Hepatobiliary (mainly primary sclerosing cholangitis [PSC])
    - Present in 5% of patients with IBD; IBD present in 70% of those with PSC
  - Vascular
    - Increased risk of arterial and venous thromboembolism
      - Risk highest during inpatient flare (17x); need DVT prophylaxis
  - Ocular (e.g. uveitis, episcleritis)
  - Dermatologic (e.g. rashes, hair loss)
  - Rheumatologic/musculoskeletal (e.g. spondyloarthropathy)
  - Renal (e.g. calcium oxalate stones)
- 10% of patients will have one or more of the above EIMs.
  - Small subset of patients have *only* EIMs (i.e. no “intestinal” symptoms)

EIMs of IBD at a glance



Dutch IBD Biobank. BMJ Open. 2017 Nov 8;7(11):e016695.

Complications of IBD

- Differ somewhat between CD and UC
- Potential complications seen (primarily) in CD:
  - Mesenteric abscess
  - Fistulization
    - perianal, entero-enteric, entero-colonic, colo-vaginal
  - GI-tract stricture formation (most often small bowel)
- Complications potentially seen in CD or in UC:
  - Toxic megacolon, colonic perforation
  - Nutritional deficiencies
  - Impaired health-related quality of life (HRQoL)

Additional IBD-associated disorders

- Infections related to IBD (or its therapy)
  - *C. difficile* colitis
  - Immunosuppressive therapy-related infection
    - Cytomegalovirus (CMV), *Mycobacterium tuberculosis*
- Malignancy related to IBD (or its therapy)
  - Colorectal cancer, lymphoma, skin cancer

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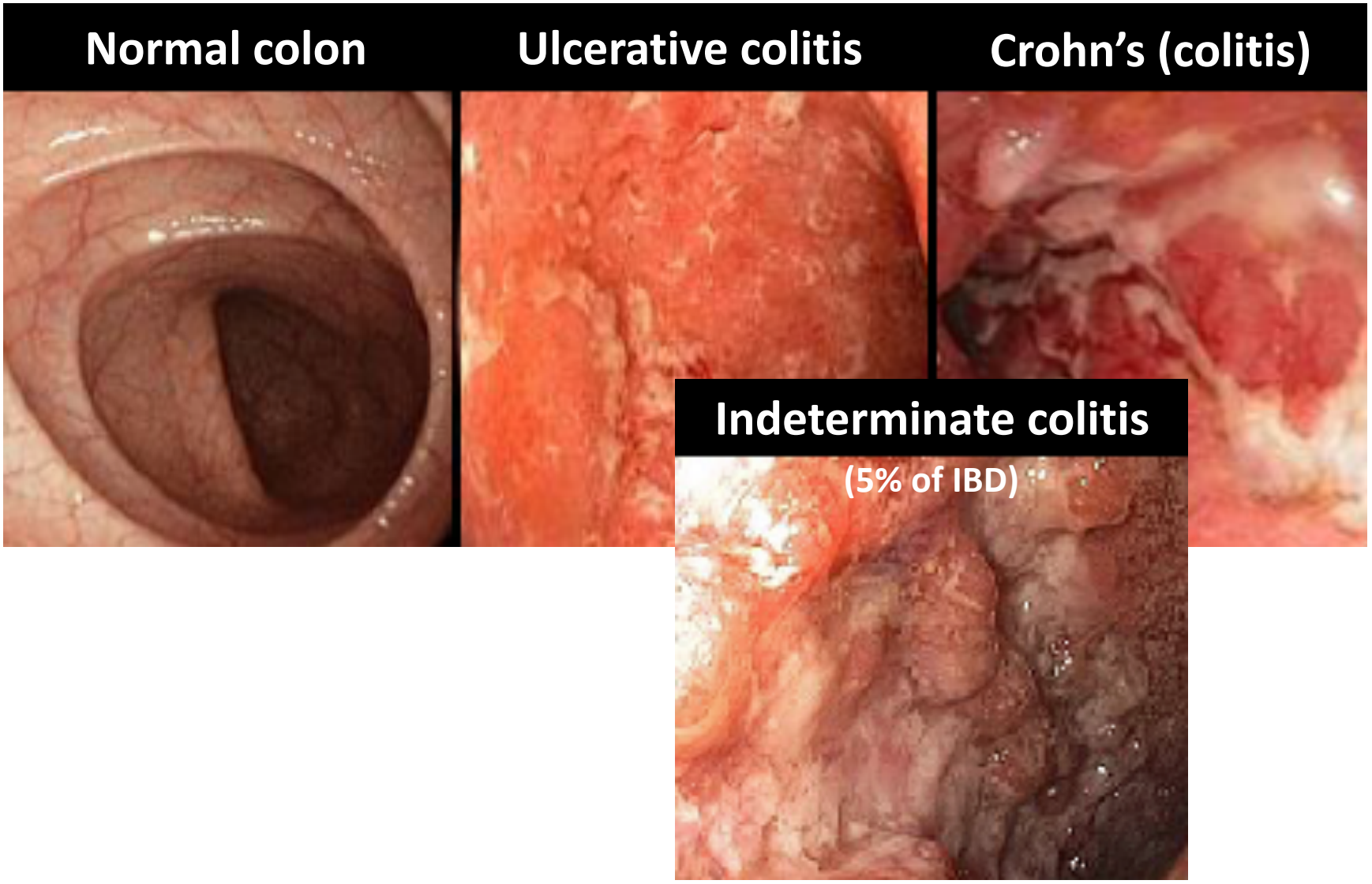
IBD is a multi-modal diagnosis

- Depends on:
  - 1) Symptoms
  - 2) Laboratory tests
  - 3) Abdominal imaging
  - 4) Endoscopy
    - Colonoscopy +/- upper endoscopy (and occasionally enteroscopy)
  - 5) Histopathology (of mucosal biopsies or surgical specimens)
- Some patients will have normal values/findings for one or more of the above 5 components
  - Of the 5 components, #4 and #5 are the most accurate/critical
- IBD can co-exist with other GI disorders
  - e.g. irritable bowel syndrome (IBS)

Lichtenstein GR, et al. Am J Gastroenterol. 2018 Apr;113(4):481-517.

Colonoscopic appearance of IBD



Differential diagnosis of IBD

- Depends on the type, extent, and severity of IBD.
- Entities commonly on the differential include:
  - Peptic ulcer disease
  - GI-tract infection
    - *E. coli*, *Campylobacter*, *Yersinia*, *Shigella*, TB, others
  - Acute diverticulitis
  - Acute appendicitis
    - May have actually been Crohn's disease
      - Interestingly, cohort studies (and murine models) have demonstrated the preventive effect of appendectomy on the development of UC
  - Pancreatitis

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Pre-treatment evaluation of IBD

- Successful treatment depends on several variables, including:
  - correct diagnosis
    - IBD vs. non-IBD
      - if IBD, CD vs. UC
  - accurate assessment of disease extent and severity
    - e.g. is the inflammation limited to just the rectum? Is it pan-colonic? Is it patchy throughout the colon?
    - e.g. is the inflammation mild or is it severe?
  - various patient-level factors
    - E.g. comorbidities, allergies, medication-related preferences, etc.

Tenets of clinical evaluation of IBD

- When evaluating a patient presenting with
  - a suspected flare of known (i.e. already diagnosed) IBD or
  - symptoms which may be due to IBD (i.e. new diagnosis),

  the following elements are needed:
  - a thorough history
    - e.g. new medications, exposures/sick contacts, travels, occupation, medico-surgical history, family history
  - physical examination
  - laboratory testing
  - imaging
  - endoscopy
    - *not always needed for an IBD flare (e.g. if responding appropriately)

Laboratory testing in the evaluation of IBD

- Helps to determine the etiology and/or severity of the condition/symptoms
  - (be they IBD or otherwise [e.g. infectious colitis])
- Generally would include:
  - CBC (with differential)
  - Complete metabolic panel (or basic metabolic panel plus serum liver tests)
  - C-reactive protein (CRP) +/- ESR
  - INR (surrogate for various things, e.g. fat-soluble vitamin deficiency, concomitant liver disease)
  - Stool culture (make sure includes assessment for *C. difficile*) and stool ova and parasites (e.g. to rule out *Giardia* infection)

Imaging in the evaluation of IBD

- The imaging test of choice usually depends on:
  - the setting (ED vs. urgent care vs. elective outpatient)
  - the specific nature of the disease/symptoms
  - patient-level considerations (e.g. age, claustrophobia, etc.)
- Ultrasound is minimally informative in IBD
- Routine X-ray (e.g. KUB) can help rule-in or rule-out obstruction, but otherwise low sensitivity/specificity
- CT is preferred over either of the above, though if without IV and oral contrast, diagnostic performance is hampered
- If wanting to evaluate the small bowel in particular:
  - Should order enterography
    - Consider MR rather than CT in young patients (or if iodinated contrast allergy)

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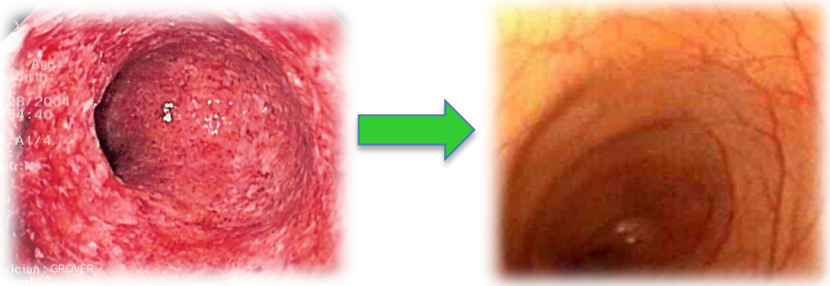
Goals of treatment in IBD



- Mucosal healing.
  - This is assessed endoscopically
- Histologic healing
  - Based on biopsies obtained during endoscopy
- Feeling better physically (back to normal)
  - Note: low correlation between patient symptoms and endoscopic findings
    - Patients with severe, active IBD may not feel poorly
    - Patients with well-treated IBD may still have symptoms (e.g. IBS)
- Restoring HRQoL
  - A comprehensive approach which also evaluates for and addresses stress, anxiety, and depression
- Reducing complications, social/occupational burden, costs

Lichtenstein GR, et al. Am J Gastroenterol. 2018
Moradkhani A,..., Tabibian JH. J Crohns Colitis. 2013 Jul;7(6):467-73.

IBD treatment considerations

- The best treatment is that which most effectively and safely achieves the goals of treatment.
  - This notion is referred to as a "treat to target" algorithm in IBD
    - Need to match the disease, its severity, and the patient who has the disease (his/her comorbidities, preferences, etc.) with one (or more) of the many existing IBD therapies.
- IBD treatment is categorized (conceptually and practically) as either:
  - **Induction** of remission
  - **Maintenance** of remission
- Some medications can be used for both induction and maintenance of remission (and some can not)

Talley et al. Am J Gastroenterol. 2011
Scott F et al. Curr Gastroenterol Rep 2016.
Lichtenstein GR, et al. Am J Gastroenterol. 2018 Apr;113(4):481-517.

IBD treatment options

- In general, for induction of remission:
  - For mild colitis, oral (and/or rectal) 5-ASA agents
    - e.g. mesalamine, sulfasalazine
  - For moderate-severe colitis/IBD, corticosteroid therapy
    - e.g. IV methylprednisolone, oral prednisone, or oral budesonide
  - For severe colitis/IBD, biological therapy (plus corticosteroid)
    - e.g. infliximab, adalimumab, vedolizumab, ustekinumab

- In general, for maintenance of remission:
  - For mild colitis, similar to above, 5-ASA agents (may use lower dose vs. induction)
  - For moderately severe IBD, an immunomodulator
    - e.g. oral azathioprione, +/- 5-ASA agent
  - For severe IBD, biological therapy, +/- immunomodulator

Talley et al. Am J Gastroenterol. 2011
Scott F et al. Curr Gastroenterol Rep, 2016
Lichtenstein GR et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018

Treatment doesn't always go as planned

- Response to (and safety of) IBD treatment needs to be periodically examined.
  - These examinations (by labs, imaging, endoscopy, symptoms, etc.) should occur more frequently earlier on (i.e. while trying to induce remission)
  - Examinations can be spaced out once IBD in remission
- Sometimes the best IBD treatment (in theory) ends up not working well – no crystal ball
  - Be prepared to change/modify therapy
  - Work together with your patient on this
    - Take into account his/her concerns, preferences

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Treatment pitfalls in IBD

- Mismatch between disease severity and medication used
  - e.g. not starting immunomodulatory or biological therapy early enough
- Underdosing:
  - 5-ASA:
    - induction dose ≠ maintenance dose; the former is often higher
  - Thiopurines (azathioprine and 6-MP) and biological therapy
    - dosing should be weight-based in most cases (e.g. x mg/Kg of body weight/day)
- Using a medication as a monotherapy when combination therapy would be more effective in achieving remission.
- "Crisis management" rather than proactive treatment/monitoring.
  - Stopping therapy prematurely for what is a chronic disease
- Using corticosteroids long-term (i.e. for maintenance of remission)
  - Remember, corticosteroids are induction medicines in IBD
  - Once patient improves with corticosteroids, need an "exit strategy"

Lichtenstein GR et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018
Ko CW et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology. 2019

Miscellaneous/general clinical IBD pitfalls

- Delay in diagnosis
  - Consider IBD in the differential diagnosis of patients with:
    - fecal urgency, tenesmus, chronic bloody stools/bloody diarrhea, or fistulae
    - avoid precociously attributing signs/symptoms to IBS, hemorrhoids, etc
- Not vaccinating patients about to start and while on immunosuppressants
  - e.g. pneumococcal polysaccharide vaccine.
- Inadequate bone mineral density and Vitamin D testing.
- Insufficient attention to patient concerns/preferences
  - e.g. in dietary interventions/modifications
  - not referring for mental health needs, clinical trials

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Ko CW et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology. 2019
Moradkhani A, …, Tabibian JH. Dig Dis Sci. 2011
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Vignette 1

- A 35 year old male patient presents to primary care clinic with 4 months of bloody bowel movements on nearly a daily basis. He also reports mild lower abdominal discomfort. He states his stools are generally soft, and he will have a bowel movement 2-3 times per day. All of the following would be indicated at this juncture EXCEPT:
  - A) Abdominal ultrasound
  - B) Stool culture
  - C) CBC
  - D) CRP
  - E) Obtaining family history

Vignette 2

- A 22 year old female is admitted to the hospital for progressive bloating-type abdominal pain over the last 3 months and objective findings (labs and CT) compatible with IBD. She undergoes EGD and colonoscopy the following day; EGD is normal, while colonoscopy shows mild-moderate inflammation in the cecum and terminal ileum. Biopsies of the ileum and cecum are obtained and reveal active ileitis and colitis with architectural distortion and crypt abscesses. Stool studies are negative for infection. Which medication would you start her on now for this new diagnosis of Crohn's disease?
  - A) Oral 5-ASA (mesalamine)
  - B) Cipro and flagyl
  - C) Corticosteroids
  - D) Fiber (Metamucil®)
  - E) Nightly 5-ASA enemas

Vignette 2 – part 2

- The 22 year old female in the previous vignette responds well to intravenous corticosteroids (methylprednisolone 20 mg q8h). On hospital day 3 she is transitioned to oral steroids (prednisone 40 mg/day). Which of the following is the most appropriate discharge plan with regard to IBD treatment?
  - A) Continue on 40 mg/day for 4 weeks, and then monitor
  - B) Switch prednisone to mesalamine upon discharge, and then add a biological therapy if needed
  - C) Decide on and begin an immunomodulator, and begin tapering steroids in 2 weeks
  - D) Start gluten-free diet and continue on low-dose prednisone

Thank you AAMS leadership, members, and guests