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Inflammatory Bowel Diseases for the General Internist

When to Consider and How to Optimize Care?

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OU PHYSICIANS CROHN'S AND COLITIS CLINIC

10/05/2019

Disclosures

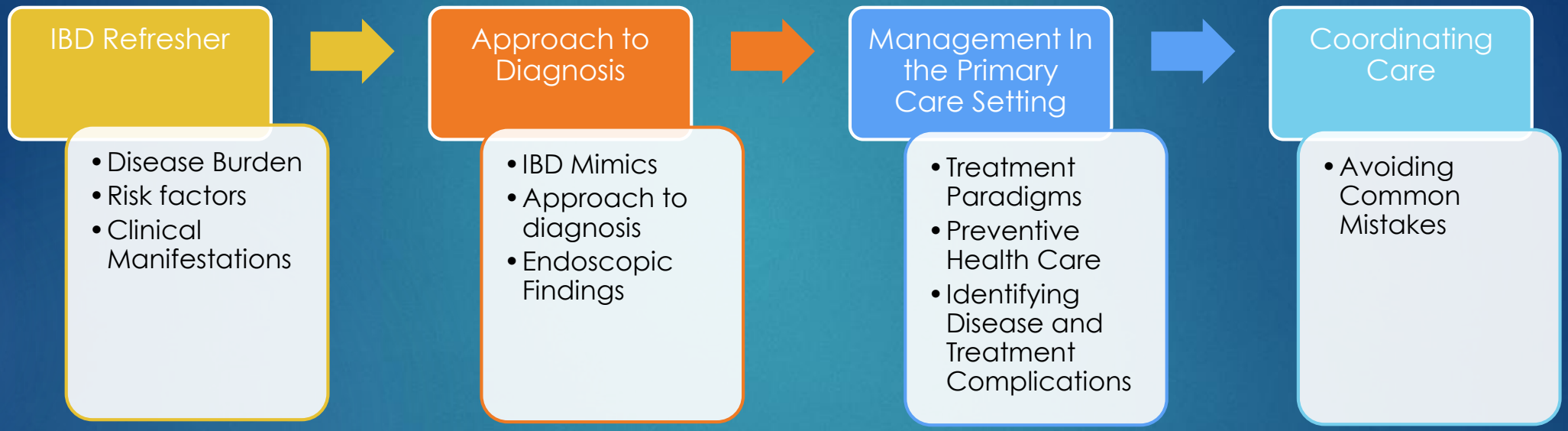
- **I have no conflicts of interest to disclose in relation to this presentation**

Objectives

At the conclusion of this presentation, participants will be able to

1. Recognize the signs and symptoms of inflammatory bowel diseases and identify candidates for endoscopic evaluation and gastroenterology referral
2. Recognize disease and treatment complications and coordinate care with managing gastroenterologist
3. Promote appropriate preventive health services for IBD population
4. Answer common IBD patient questions in the primary care setting

Outline


IBD Refresher
• Disease Burden
• Risk factors
• Clinical Manifestations
Approach to Diagnosis
• IBD Mimics
• Approach to diagnosis
• Endoscopic Findings
Management In the Primary Care Setting
• Treatment Paradigms
• Preventive Health Care
• Identifying Disease and Treatment Complications
Coordinating Care
• Avoiding Common Mistakes

A Common Concern

A 26-year-old female has small and large bowel Crohn's disease diagnosed 5 years ago. She has required multiple courses of steroids and a distal ileum stricture resection in the past but has done better since starting therapy with azathioprine and infliximab 2 years ago.

She reports occasional bloating and mild abdominal cramping relieved by passing stool. Otherwise she feels well.

Colonoscopy one month ago showed scattered aphthae in the terminal ileum and a small ulcer in the ascending colon. Overall this represents a marked improvement compared to prior exams. Her blood work is unremarkable.

She is concerned about the long-term health impact of current immunosuppressants and would like to discuss her options.

Back

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Which of the following management decisions is correct?

A “drug holiday” with close monitoring is safe given sustained clinical remission for over one year

Should patient plan to get pregnant, stop both medications and switch to oral mesalamine to reduce risk of congenital malformations

Continue both azathioprine and infliximab and optimize therapy

Influenza and pneumococcal vaccines are contraindicated in the setting of anti-TNF use but can be used with azathioprine

Poll Everywhere

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Disease Burden

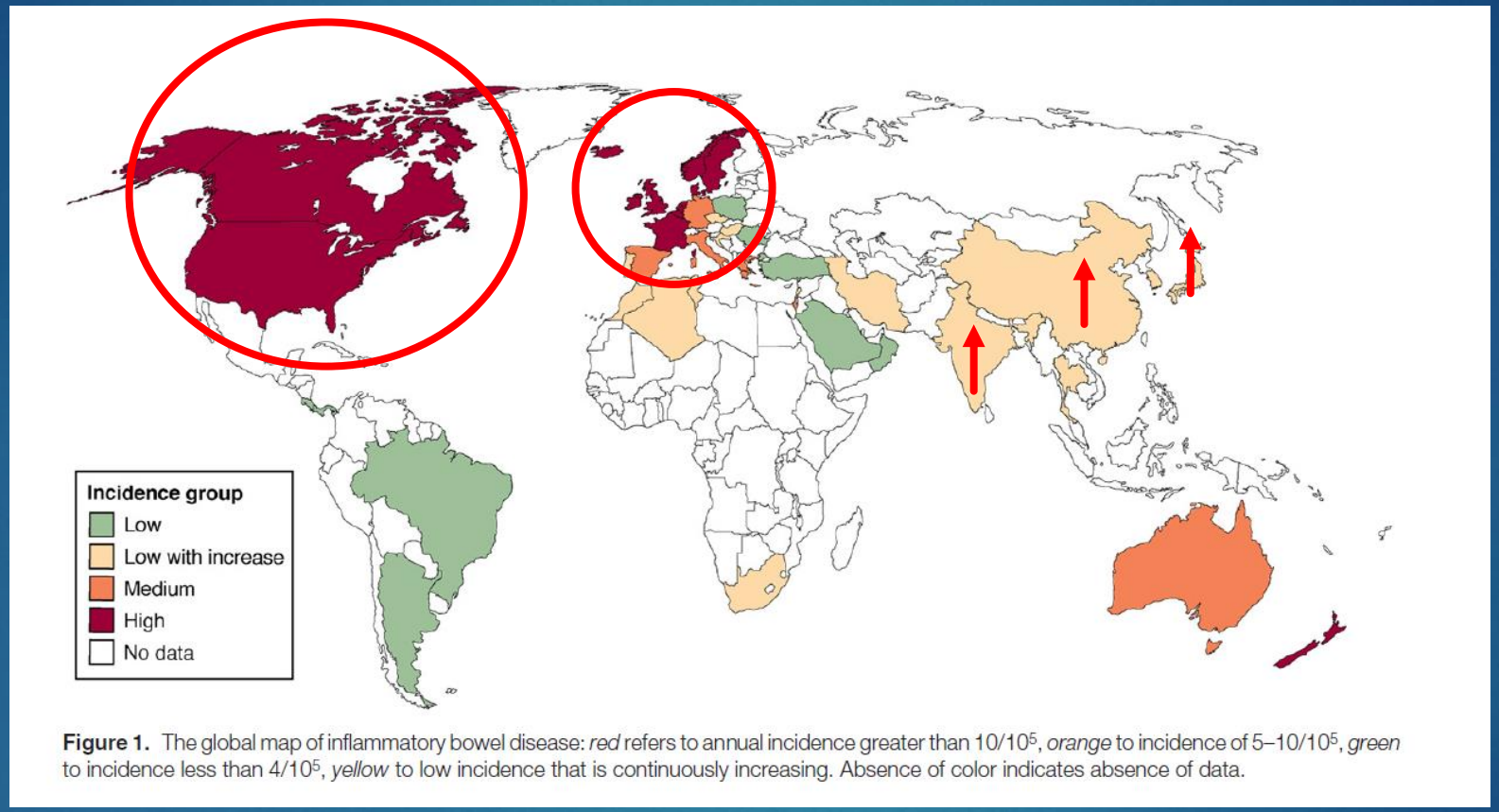
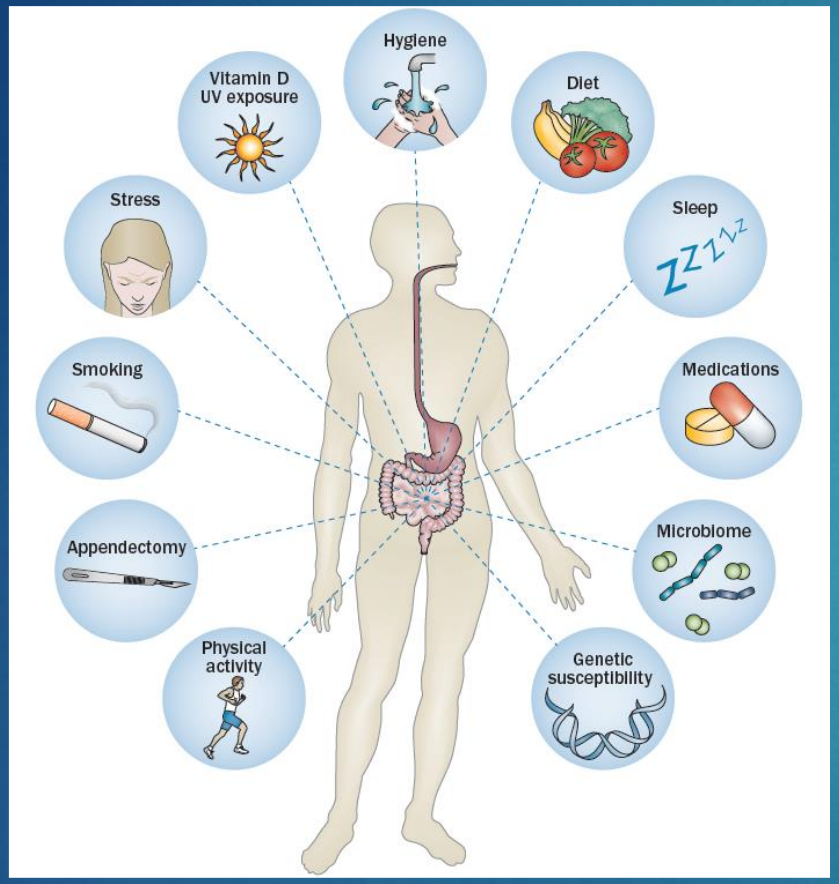


Figure 1. The global map of inflammatory bowel disease: *red* refers to annual incidence greater than $10/10^5$, *orange* to incidence of $5–10/10^5$, *green* to incidence less than $4/10^5$, *yellow* to low incidence that is continuously increasing. Absence of color indicates absence of data.

0.5-1% of population suffer from IBD in the US

Loftus et al. Gastroenterology 2004
Cosnes et al. Gastro 2011

Why Me?



Intestinal Dysbiosis

+

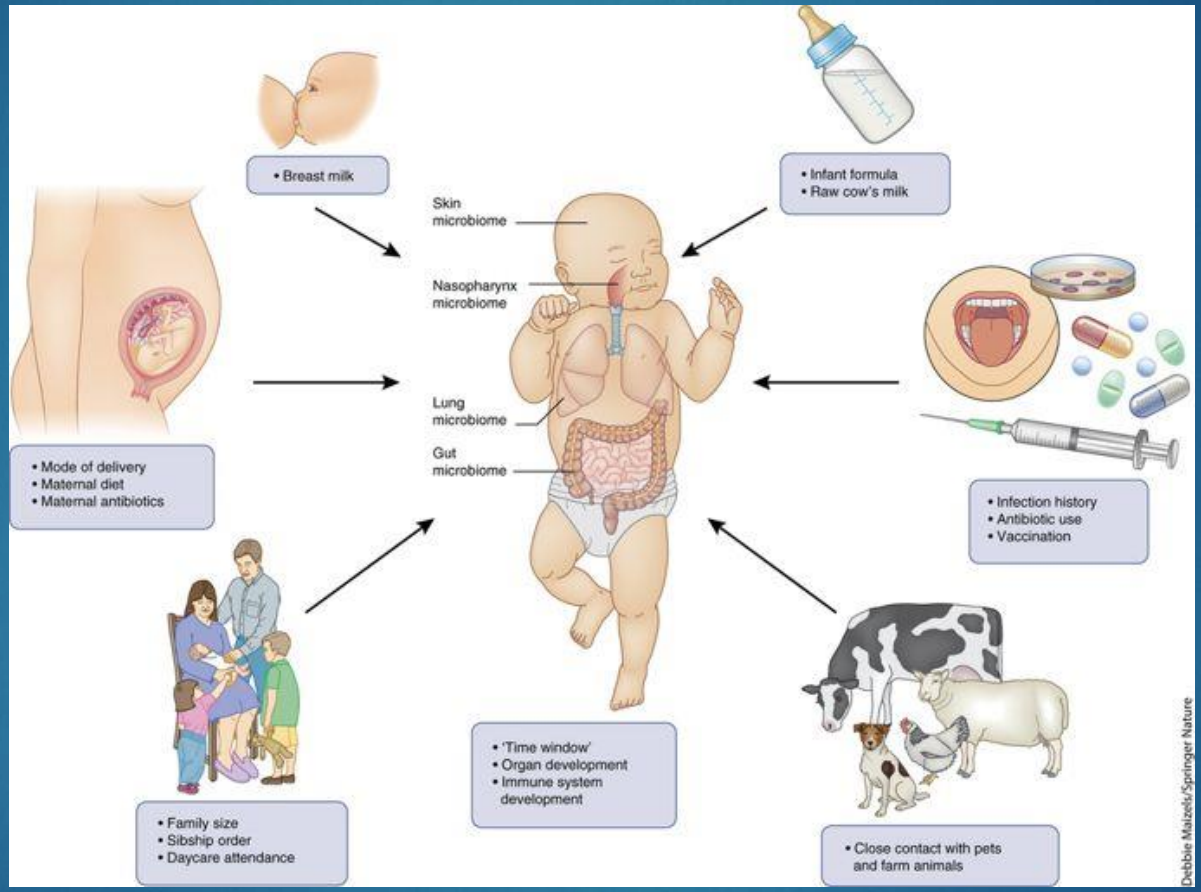
Genetically Susceptible Host

↓

Inappropriate chronic inflammatory response

Ananthakrishnan, A. N. *Nat. Rev. Gastroenterol. Hepatol.* 2015

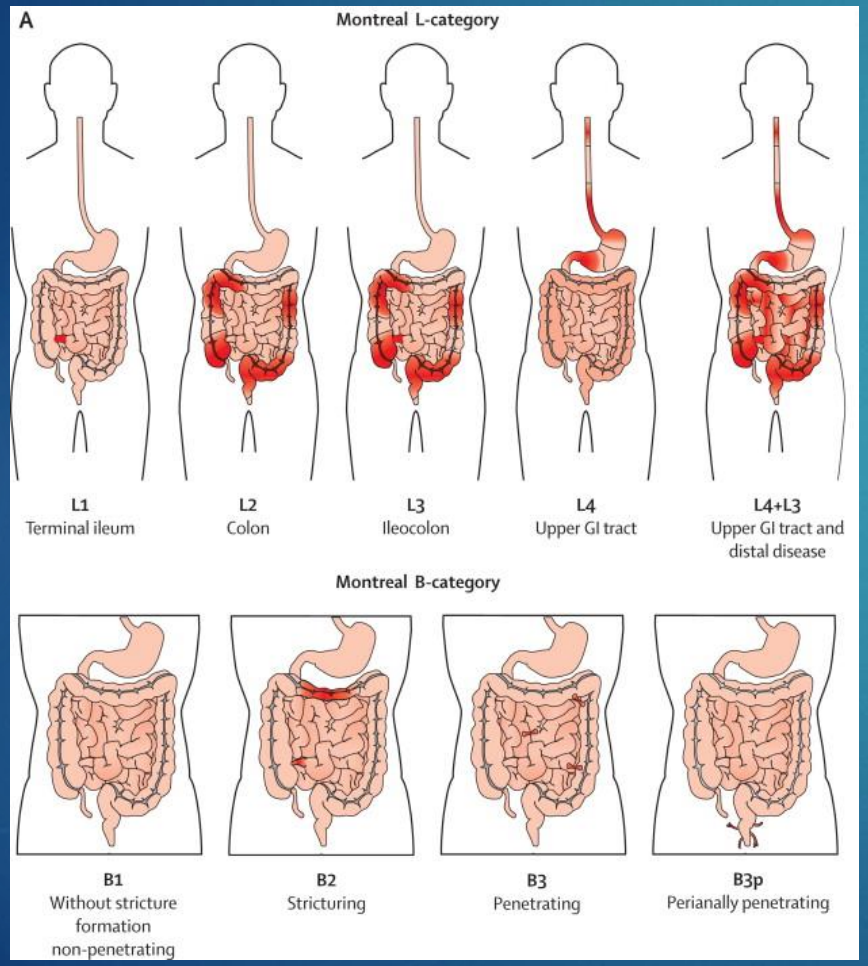
Hygiene Hypothesis



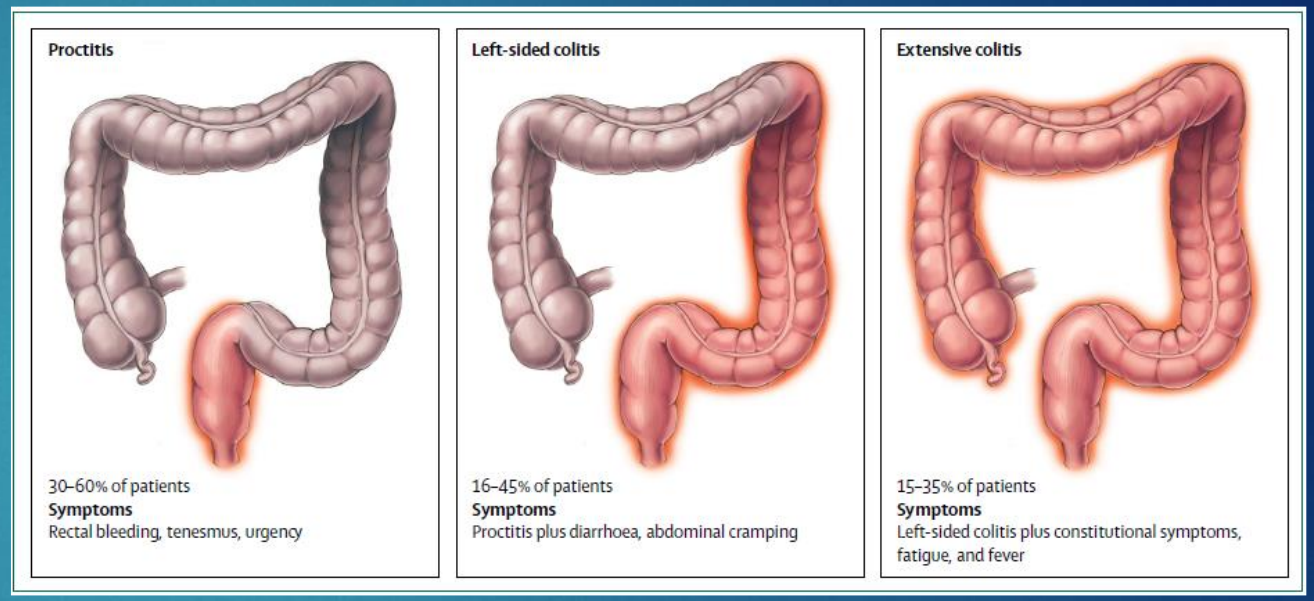
Summers et. al Gut 2005
Lashner et. AJG 2008
Schölmerich et al. JCC 2017

Disease Distribution

Crohn's Disease



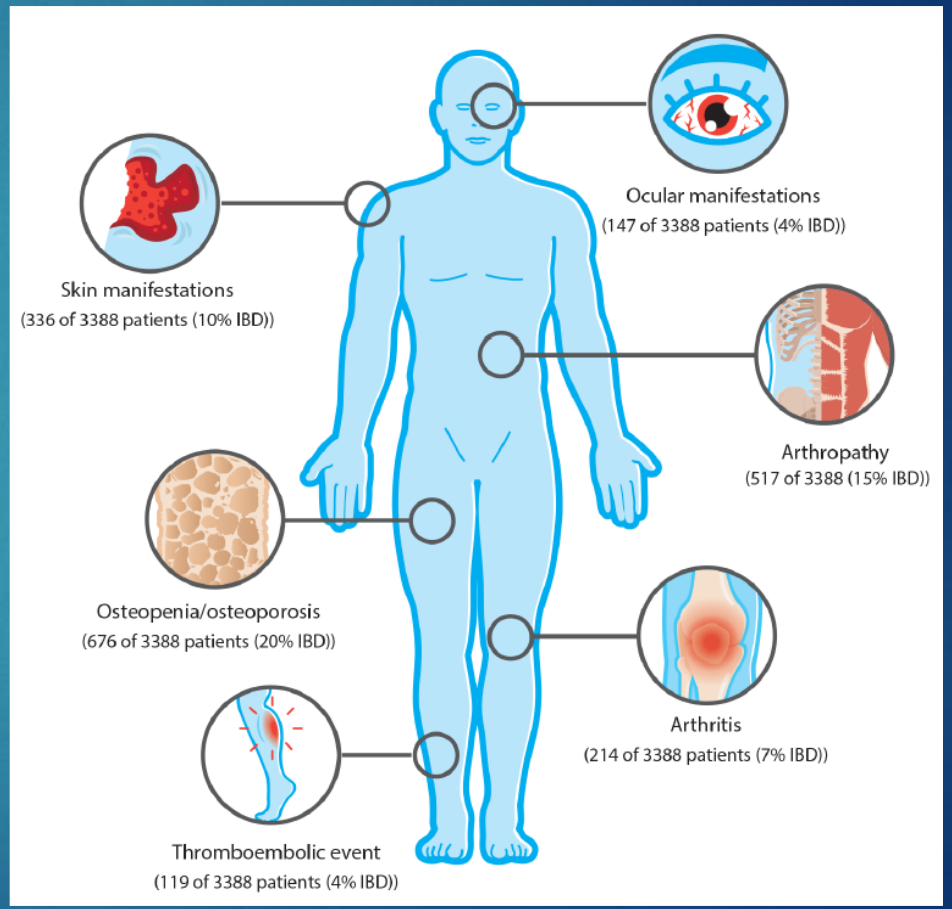
Ulcerative Colitis



Ungaro et al. Lancet 2017
Sandborn et al. Lancet 2012

Think Systemic Disorders

- Extraintestinal manifestations may precede diagnosis
- Most mirror intestinal disease activity
- Some ophthalmologic manifestations are medical emergencies



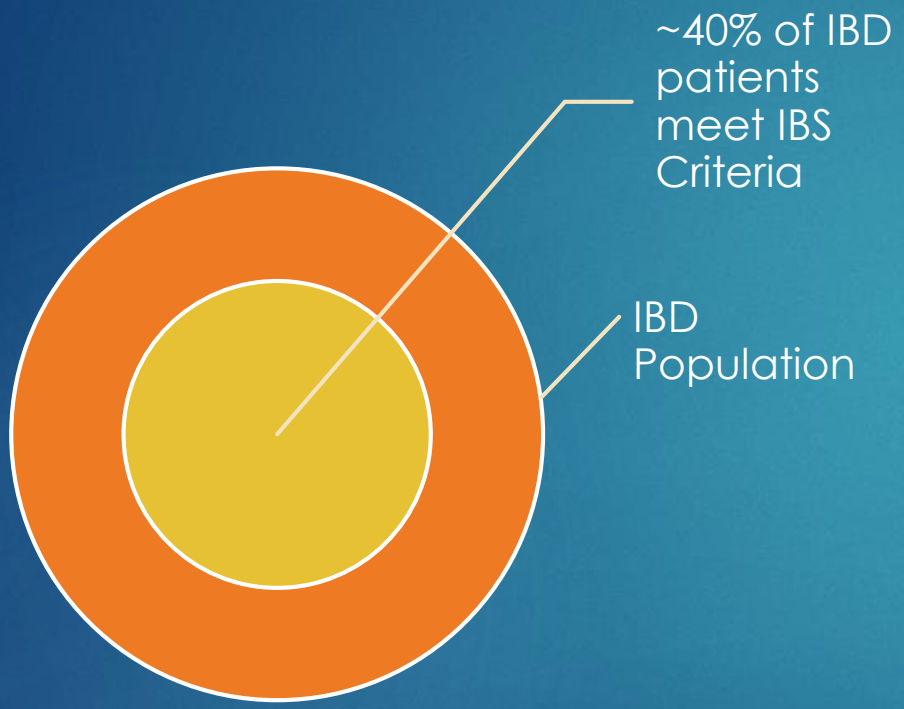
Vavricka et al. Inflamm Bowel Dis 2015
Spekhorst et al. BMJ 2017

Approach to Diagnosis

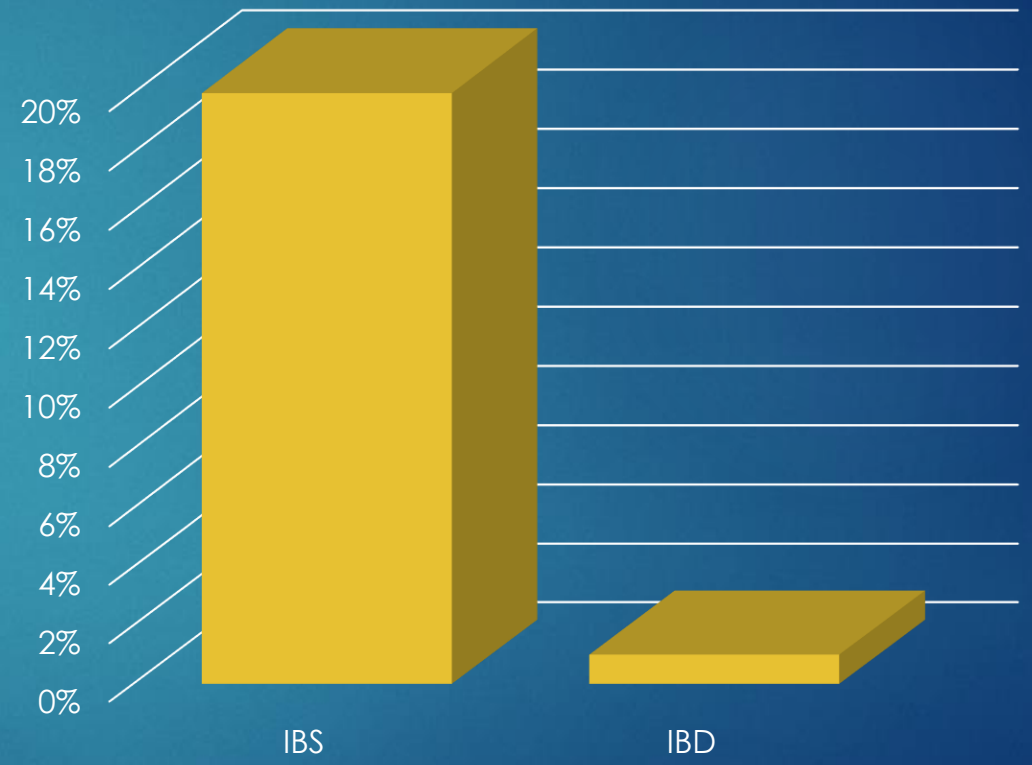
- CD and UC have overlapping features with other GI disorders
- **No single test is accurate enough to diagnose IBD**
  - Diagnosis relies on a combination of clinical features, laboratory, endoscopy and imaging tests
- Right demographic
  - Peak age for CD is 20–30 years and for UC 30–40 years

Inflammatory vs Functional?

IBS-IBD Overlap

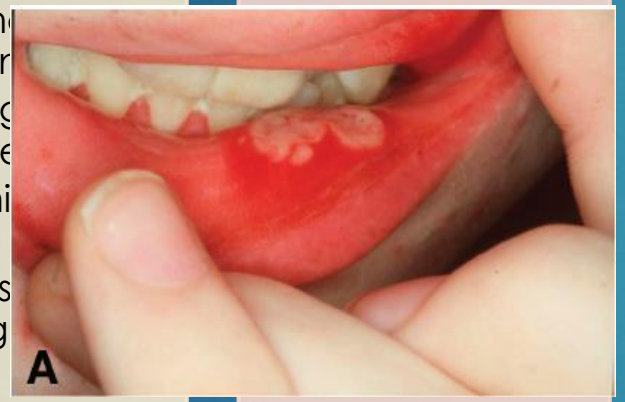
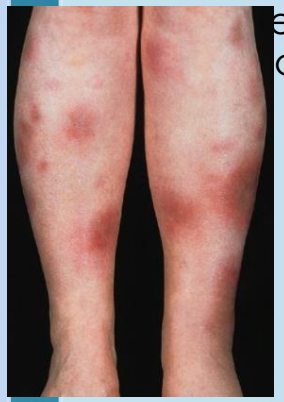


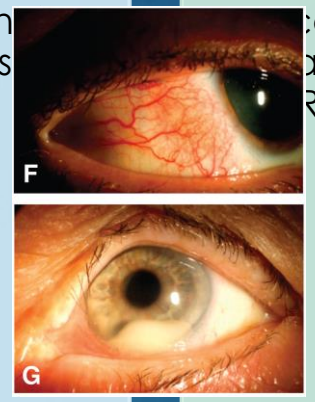
Population Prevalence



Lovell et al. Clin Gastroenterol Hepatol. 2012
Halpin et al. *Am J Gastroenterol* 2012

Clinical Pearls

Chronic Diarrhea with Inflammatory Features	Chronic Abdominal Pain	Systemic Symptoms	Family History of IBD	Concomitant Autoimmune Disorders
• Nighttim occurrer • Fecal urg and tene • Blood mi stool • Lack of s food trig			en as 	eliac ase, Psoriasis, RA, MS



Laboratory (Alarm) Features

- Iron deficiency anemia
- Vitamin B12 and folic acid deficiencies (CD)
- Hypoalbuminemia
- Elevated inflammatory markers
  - Can be used to screen patients with suspected functional diarrhea for IBD

Test	Sensitivity	Specificity
CRP	49%	92%
Fecal Calprotectin	88%	73%
Stool Lactoferrin	82%	79%

Table. Diagnostic accuracy for assessment of endoscopic disease activity in IBD

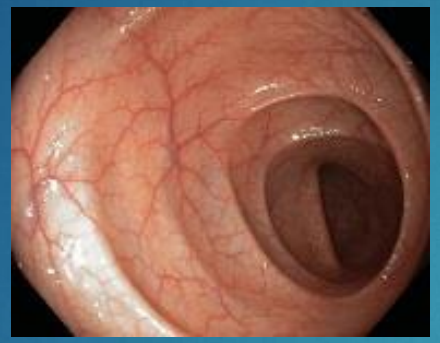
Mosli et al. Am J Gastroenterol 2015
Smalley et al. Gastro 2019

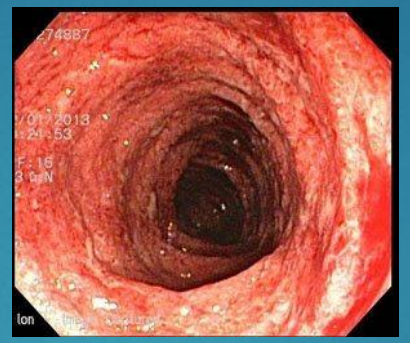
IBD Serology Panels

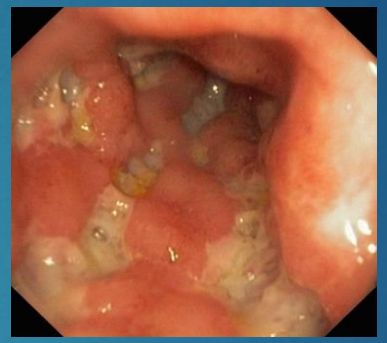
- Contain autoantibodies and antimicrobial antibodies
  - *IBDsgi diagnostic* assay adds several genetic risk markers (Prometheus Laboratories)
- **One stop test to diagnose IBD? <u>NO</u>**
  - Variable component sensitivities
  - Low disease prevalence limits positive predictive value
  - 2018 and 2019 ACG CD and UC clinical guidelines recommend against use

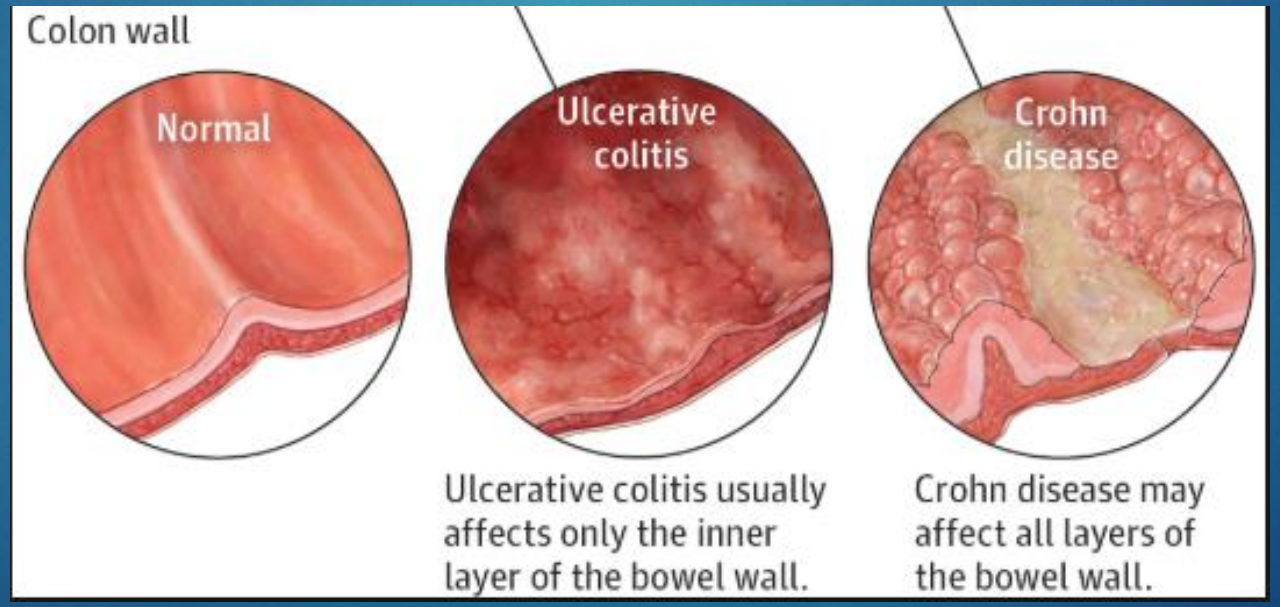
Sands et al. CGH 2018

Ileo-Colonoscopy: Gold Standard



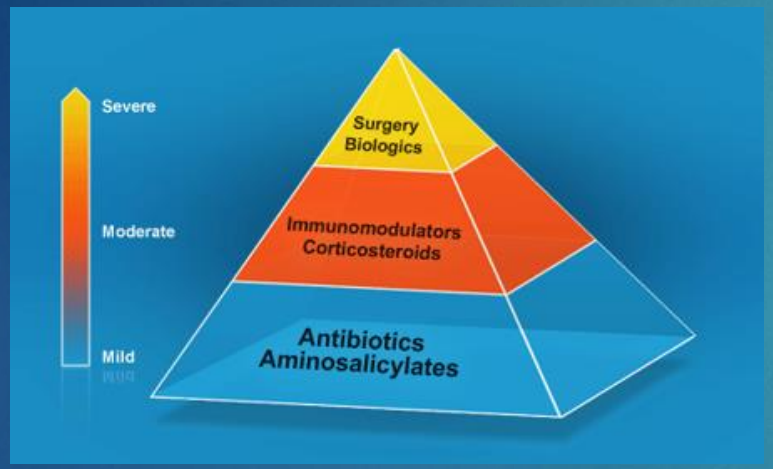






Shifting Treatment Paradigms

Traditional Approach



Therapeutic Targets

4. Change Disease Course

3. Deep Remission

Attainable in some patients

2. Mucosal Healing

1. Steroid Free Clinical Remission

Attempt in all patients

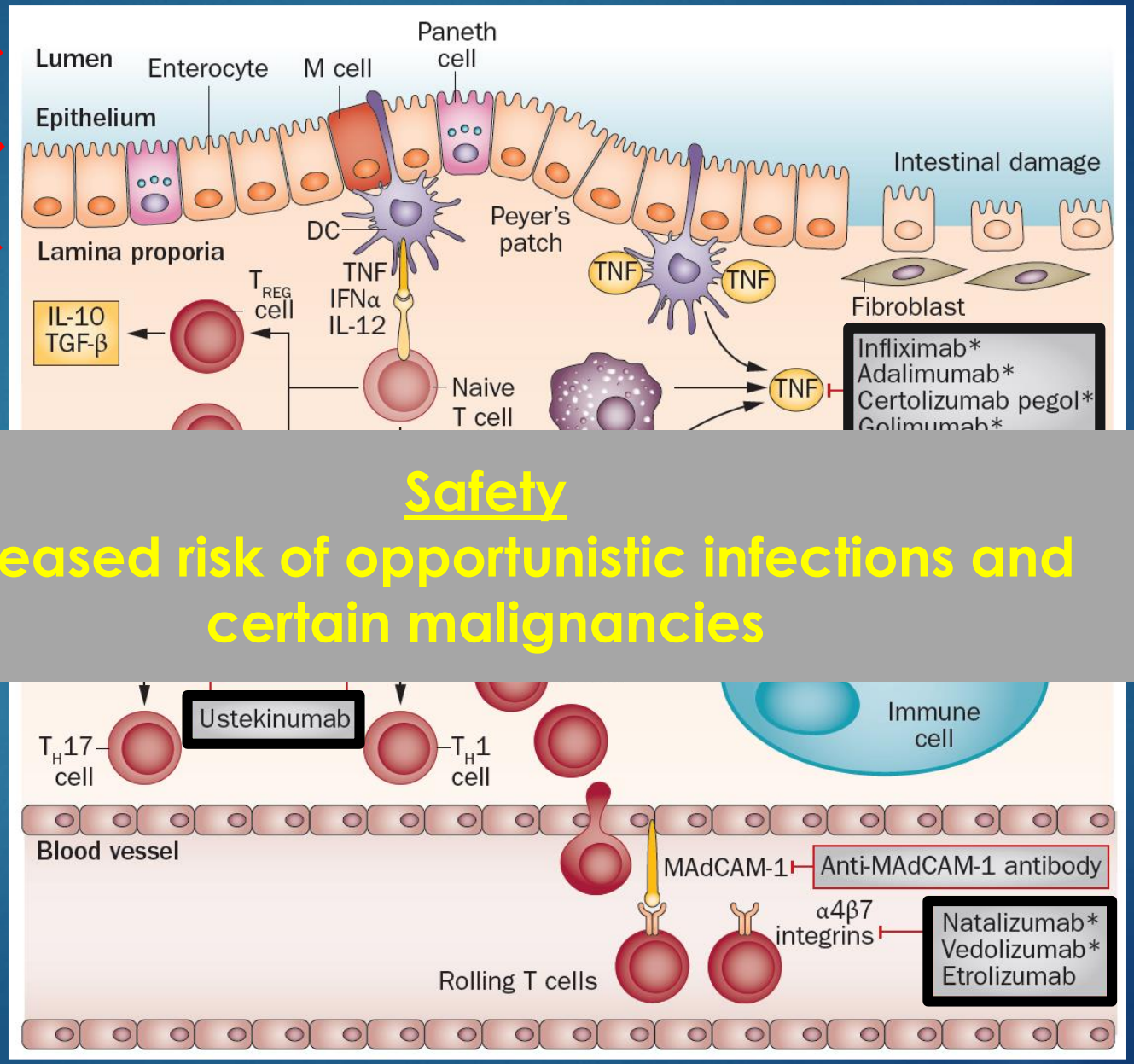
Treat Early (therapeutic window) → Use Effective Therapy → Optimize Therapy → Prevent Complications and Avoid Surgery

Treatment Options

- 5-ASA (mesalamine): mild to moderate UC only
- Steroids (Conventional and Budesonide): induction of remission
- Immuno-modulators: Azathioprine/6-MP and Methotrexate
- Biologics
- JAK inhibitor (small molecule)
  - Tofacitinib (approved in 2018 for UC only)

Biologic Drug	Commercial Name	FDA Approval	Indication
Infliximab	Remicade®	1998	CD and UC
Adalimumab	Humira®	2002	CD and UC
Certolizumab	Cimzia®	2008	CD
Golimumab	Simponi®	2009	CD and UC
Vedolizumab	Entyvio®	2014	CD and UC
Ustekinumab	Stelara®	2016	CD

Biologics



Safety

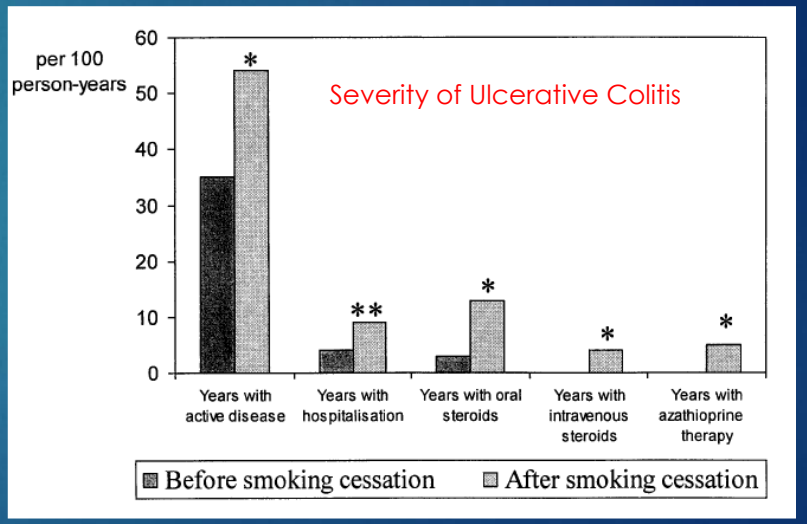
Increased risk of opportunistic infections and certain malignancies

Danese et al. nrgastro 2016


Preventive
Care

Smoking Cessation

- Crohn's disease patients should be counselled to quit smoking
  - Inferior response to biologics
  - Higher risk of disease recurrence after surgery
  - Higher risk of stricturing disease and perianal disease complications
- Ulcerative Colitis
  - Smoking cessation is associated with worsening disease activity



Beaugerie et.al Am J of Gastroenterol 2001
Farraye et al. *Am J Gastroenterol* 2017

Vaccines

- 1.5-3 fold increase in incidence of influenza, pneumococcal disease and Zoster in IBD population
- Risk increased by but not always related to immuno-suppressive medications

- 64% of GIs believed PCP should determine which vaccinations to give
- 83% believed PCP should administer the vaccines

- Only 37% of family practitioners felt comfortable providing primary care (including vaccines) across a range of IBD severity

Kants et al. *Am J Gastroenterol* 2015
Tinsley et al. Inflamm Bowel Dis 2018
Long et al. Aliment Pharmacol Ther 2013
Wasan et al. Inflamm Bowel Dis 2011
Selby et al. Dig Dis 2011

Vaccination Best Practices

INFLUENZA VACCINATION

Recommendations

1a. All adult patients with IBD should undergo annual vaccination against i… *very low lev…*

1b. Those on im… contacts sho… influenza va… vaccine. *Co… evidence.*

PNEUMOCOCCAL VACCINATION

Recommendation

2. Adult patients with IBD receiving immunosuppressive ther… …ccination with both the …ith national guidelines. *…y low level of evidence.*

Live vaccines are contraindicated in patients on biologics, high dose steroids or high dose immunomodulators

…AND HUMAN

…, and HPV should be administered as per ACIP guidelines. *Conditional recommendation, with very low level of evidence.*

HERPES ZOSTER VACCINATION

Recommendation

3. Adults with IBD over the age of 50 should consider vaccination against herpes zoster, including certain subgroups of immunosuppressed patients. *Strong recommendation, with low level of evidence.*

Farraye et al. *Am J Gastroenterol* 2017

Osteoporosis

- Related to malabsorption, negative effects of pro-inflammatory cytokines and adverse reactions from medications (steroids)
- DXA screening for patients with one or more risk factors
  - **Chronic corticosteroid therapy (>3 months)**
  - Postmenopausal women
- Correct Vitamin D deficiency to >30 ng/ml (immunoregulatory effects)

Ali et al. Am J of Medicine 2009
Bernstein et al. Gastroenterology 2003
Kabbani et al. AJG 2016

Preventive Care-Other

- Skin cancer risk
  - Melanoma ~30% ↑ (with anti-TNF use)
  - Non-melanoma skin cancers 2 fold ↑ (with thiopurine use)
  - Screening dermatology visit: case-by-case surveillance strategy
- Cervical cancer
  - Women with IBD on immunosuppressive therapy should undergo annual cervical cancer screening

Farraye et al. *Am J Gastroenterol* 2017


WHY?
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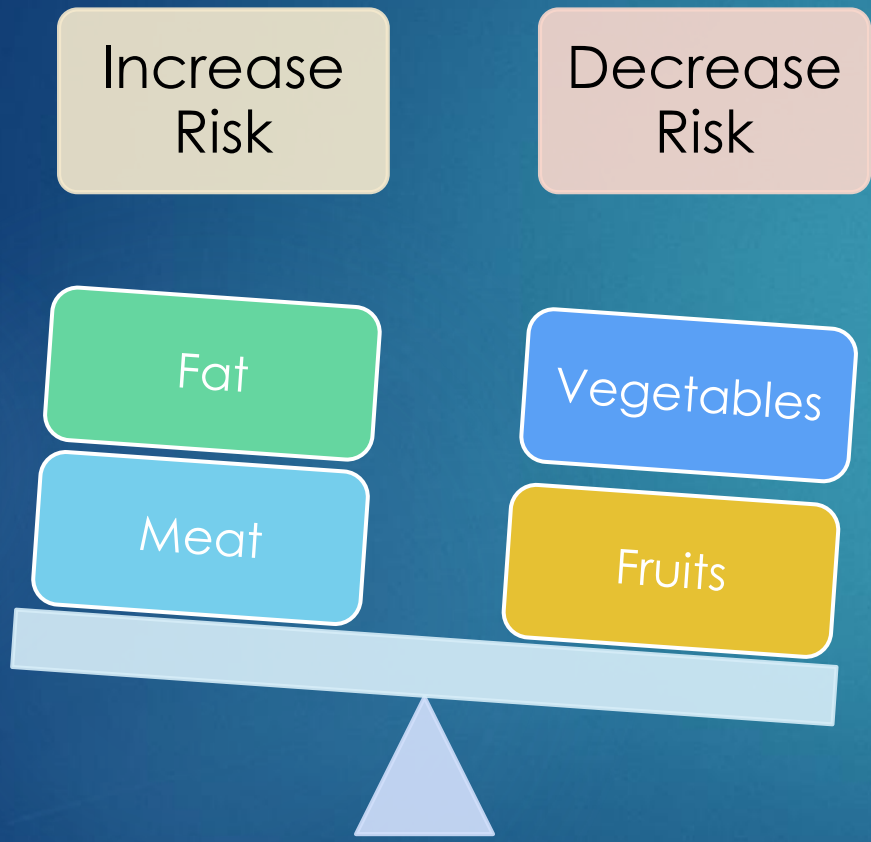
What Should Patients with IBD be Eating?



- **No special "anti-inflammatory diet"** (Exclusive and partial enteral nutrition are used infrequently in adult patients with CD)
- Low fiber diet if stricture
- Low FODMAP and gluten free helpful for patients with concomitant IBS and celiac disease

Hou et al. *Am J Gastroenterol* 2011
Hwang et al. Inflamm Bowel Dis 2014

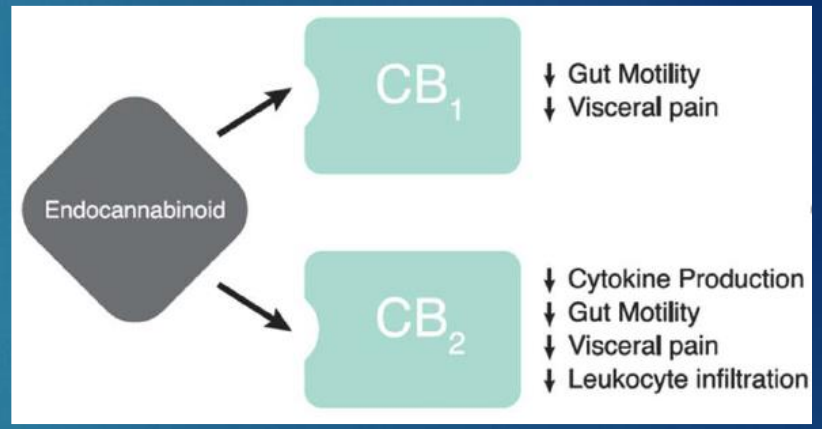
Fecal Microbiota Transplantation *Magic Bullet?*

- 2/3 RCTs on the use of FMT in UC achieved their primary end point of clinical remission
  - Remission rates 20-30%
- No RCTs in Crohn's disease
- Currently, only accepted application is recurrent C.difficile colitis (investigational with IND enforcement discretion)

Narula et al. Inflamm Bowel Dis 2017

What about Supplements?

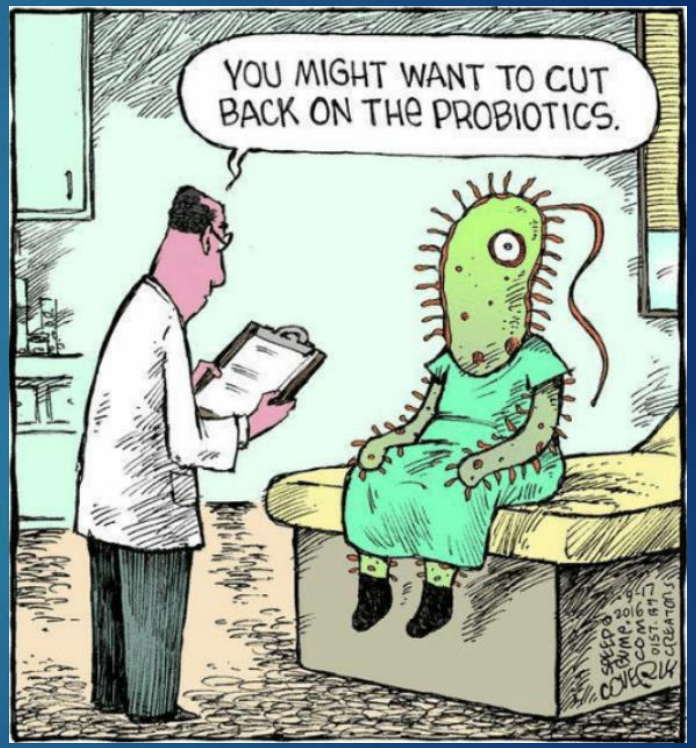
- Omega-3 fatty acids --- No
- Curcumin --- Maybe
  - Mild to moderate UC
  - Daily dose 2-3 g in addition to mesalamine
- Cannabis --- ??
  - Symptom improvement in Crohn's disease but no evidence of objective improvement in bowel inflammation
  - Negative Study in UC
  - CBD vs THC? Oral vs smoked?



Quezada et al. Inflamm Bowel Dis 2016

And Probiotics?

- Crohn's Disease
  - No benefit in inducing or maintaining remission or in preventing relapse of CD after surgery
- Ulcerative Colitis (mild to moderate)
  - **VSL#3** may be effective in inducing remission
  - **E. coli Nissle 1917** may be as effective as 5-ASAs in preventing relapse



Derwa et al. Aliment Pharmacol Ther. 2017

NSAID Use

- Use common in IBD population
- Conflicting evidence but overall in favor of increased risk of disease activity with frequent NSAID use
- Avoid all NSAIDs if possible
  - Cox-2 blockers may be safer

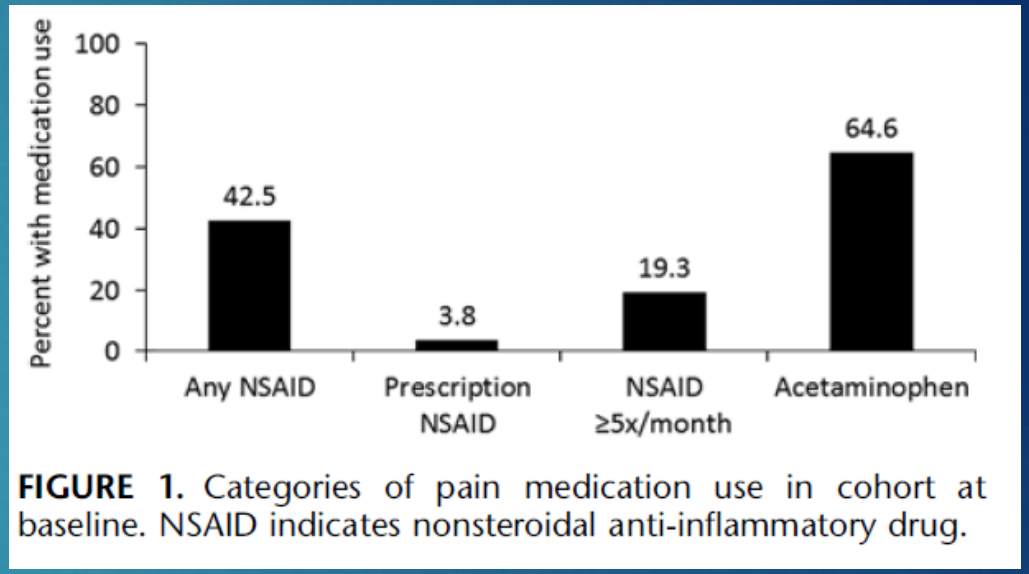


FIGURE 1. Categories of pain medication use in cohort at baseline. NSAID indicates nonsteroidal anti-inflammatory drug.

Kefalakes et al. Eur J Clin Pharmacol 2009
Long et al. Clin Gastroenterol 2016
Wallace et al. Gastro & Hepatology 2011

Narcotics

- Use tripled over past 2 decades
  - Presence of psychiatric illness and use of narcotics among top factors associated with high costs of IBD care
- Use of strong opiates is associated with increased all-cause premature mortality
- Reserve for acute pain only
  - Tramadol and codeine may be safe

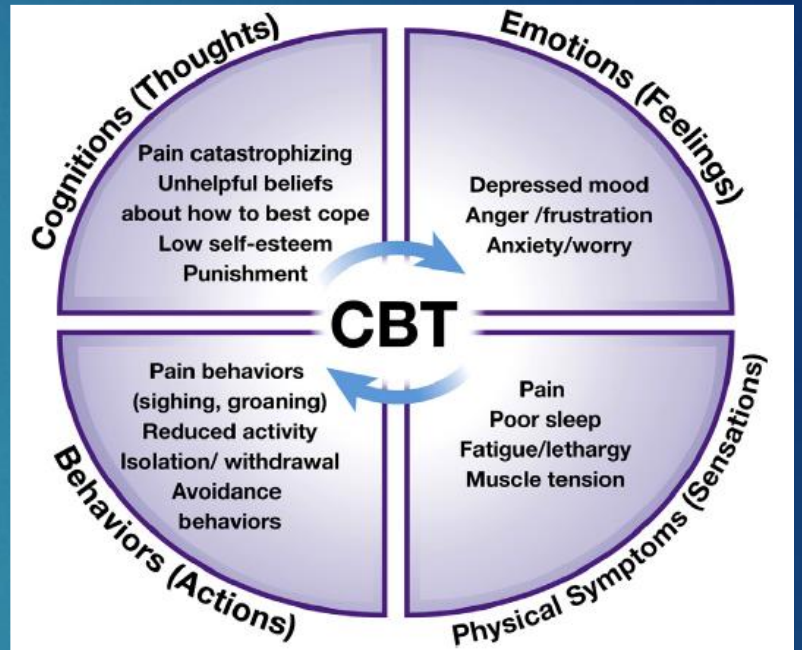
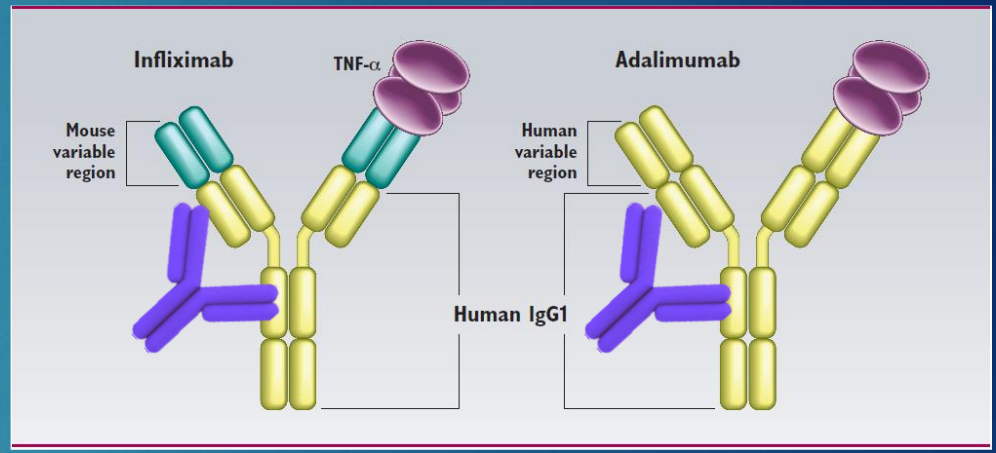


Figure 2. Emotional, cognitive, behavioral, and physical targets of CBT in treating chronic pain in IBD.

Burr et al. Clin Gastroenterol Hepatol 2018
Regueiro et al. Gastro 2017

Interrupting Biologic Therapy and "Drug Holidays"

- Interruption risks the formation of antibodies thus decreasing clinical efficacy
  - Elective surgeries can be scheduled at drug trough level
- Drug holidays only for patients in clinical (and preferably endoscopic) remission
  - 1 year relapse ~50%



Vermeire et al. *Ther Adv Gastroenterol* 2018
Vaughn et al. Inflamm Bowel Dis 2015
Louis et al. Gastro 2012

Healthy Mother---Healthy Baby

1. Preconception counseling critical to positive pregnancy outcomes
2. Anti-TNF and azathioprine are **safe** during pregnancy and breastfeeding
3. Avoid live vaccinations within the first 6 months for newborns exposed to maternal anti-TNFs

Take Home Messages

1. Inflammatory Bowel Diseases are chronic morbid GI conditions commonly affecting younger adults
2. Distinction from more common functional bowel disorders is essential for early diagnosis and treatment
3. Optimizing care goes beyond anti-inflammatory therapy and includes essential preventive services
4. Care of IBD patients is multidisciplinary which makes coordination between health services critical to good outcomes

A Common Concern

A 26-year-old female has small and large bowel Crohn's disease diagnosed 5 years ago. She has required multiple courses of steroids and a distal ileum stricture resection in the past but has done better since starting therapy with azathioprine and infliximab 2 years ago.

She reports occasional bloating and mild abdominal cramping relieved by passing stool. Otherwise she feels well.

Colonoscopy one month ago showed scattered aphthae in the terminal ileum and a small ulcer in the ascending colon. Overall this represents a marked improvement compared to prior exams. Her blood work is unremarkable.

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Influenza and pneumococcal vaccines are contraindicated in the setting of anti-TNF use but can be used with azathioprine

Poll Everywhere

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Questions?

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