

Inflammatory Bowel Disease: Practical Aspects for the Primary Care Provider

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Disclosures

I have no financial disclosures

Objectives

- Recognize the clinical features and complications of inflammatory bowel disease (IBD)
- Differentiate between the two main subtypes of IBD: Crohn's disease and ulcerative colitis
- Identify "red flags" in undiagnosed patients in the primary care setting to determine further workup
- Summarize various diagnostic and treatment options in patients with IBD including medications, surgical management, and dietary therapy
- Describe special considerations for health maintenance in patients with IBD

A visit to the clinic...

- Patient: Vanessa, 19 yo Caucasian female
- Chief complaint: abdominal pain, diarrhea
- HPI: Started noticing periumbilical and RLQ abdominal pain for the past few months. Crampy in quality, lasts several minutes in duration but waxes and wanes throughout the day. Exacerbated postprandially "sometimes," also reports pain prior to defecation. Alleviated following bowel movements on occasion "but not always." Reported having 1-4 formed bowel movements daily until 2 weeks ago. Thought it was due to stress from school.
- For the past 2 weeks: now having mushy to watery stools 4-5 times/day. Has woken from sleep 3-4 nights since onset of looser stools. No sick contacts. States she thinks the diarrhea started after eating Chipotle. No blood in stools but has seen mucus more recently.
- "Something's just not right..."

A visit to the clinic...

- PMHx: seasonal allergies
- Social Hx: drinks “socially on weekends,” smokes 1/2 ppd, sophomore in college
- Family Hx: HTN in father, hypothyroidism in mother, sister with IBS, CVA in maternal grandmother, maternal aunt “avoids gluten”
- Surgical Hx: tympanostomy tubes age 4 for recurrent otitis media
- Medications: cetirizine daily, albuterol inhaler PRN, recently used naproxen BID for shoulder injury after slipping on some ice

Defining Inflammatory Bowel Disease



What is inflammatory bowel disease?

Inflammatory Bowel Disease (IBD) is a chronic disease affecting the gastrointestinal tract

- **No cure**
- 2 main subtypes
 - Ulcerative Colitis (UC)
 - Crohn's disease (CD)

**Indeterminate colitis (IBD-U)
more commonly seen in pediatric
IBD*



Comparing the Two

- **Crohn's disease**

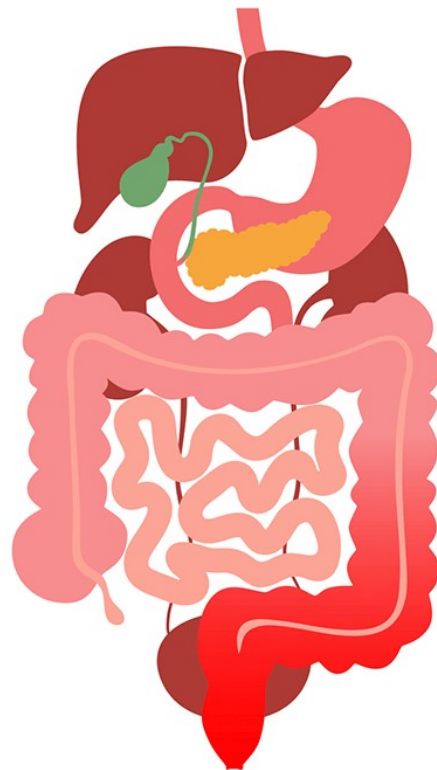
- Can affect any part of the GI tract
- Deep ulcerations (can involve entire bowel wall)
- “Skip lesions”
- Symptoms vary based on disease location

- **Ulcerative colitis**

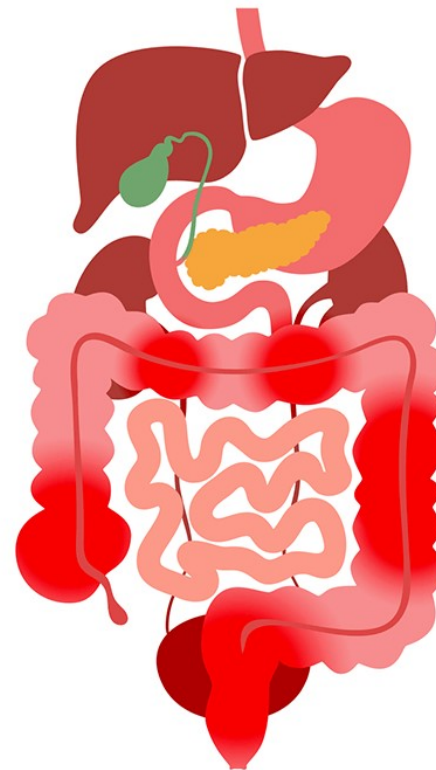
- Location is limited to colon
- Superficial ulcerations (innermost lining of mucosa)
- Continuous pattern
- Symptoms related to large bowel inflammation
 - Diarrhea
 - Hematochezia
 - Urgency
 - Abdominal cramping

Crohn's Disease vs Ulcerative Colitis: *Location, Location, Location!*

INFLAMMATORY BOWEL DISEASE (IBD)



Ulcerative colitis



Crohn's disease

Characteristics of IBD

Crohn's Disease

- Any part of GI Tract
- Discontinuous (skipped lesions)
- Rectal sparing
- Presence of granulomas
- Transmural inflammation
- Fistulas and abscesses
- Strictures = more common
- Perianal Disease

Ulcerative Colitis

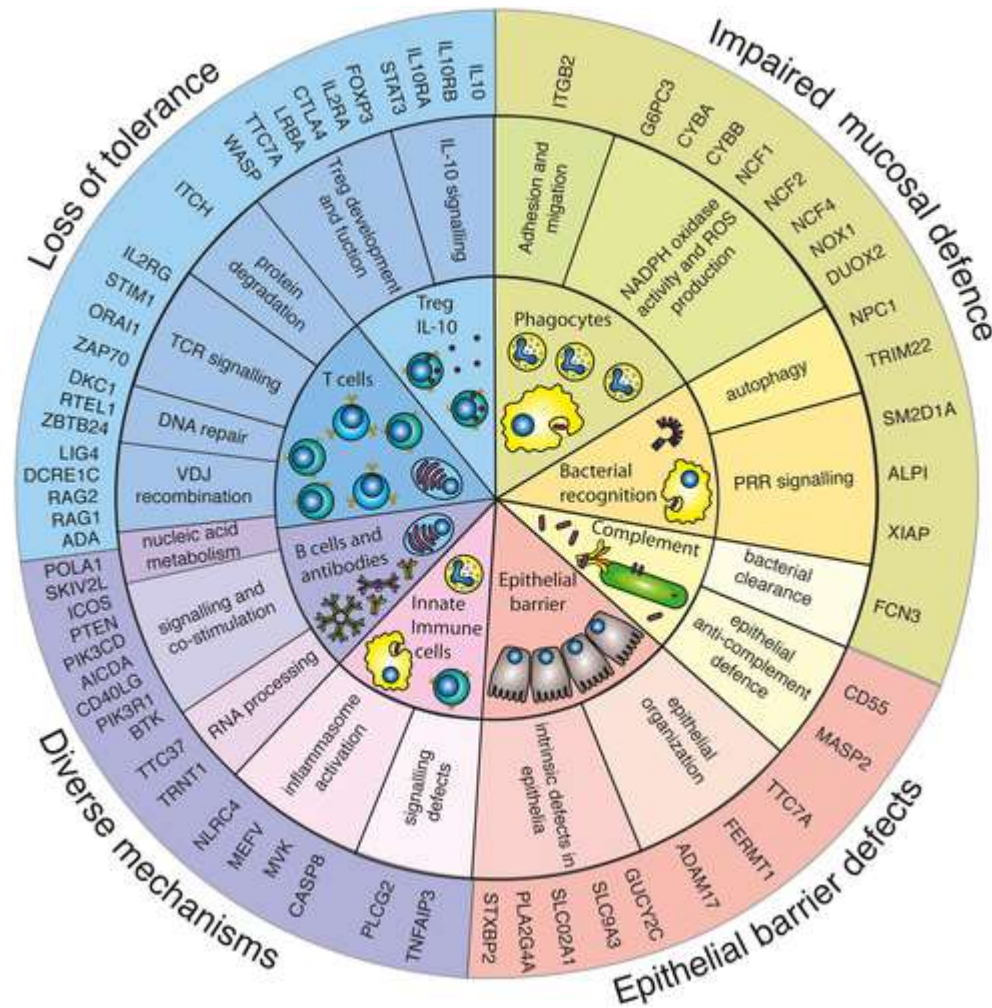
- Colon/rectum only
- Continuous
- No rectal sparing
- No granulomas
- Mucosal inflammation
- Abscesses very rare
- Strictures = rare

**Pediatric patients have more severe/extensive disease than adults, rapid progression is common!*

Very Early Onset (VEO) IBD

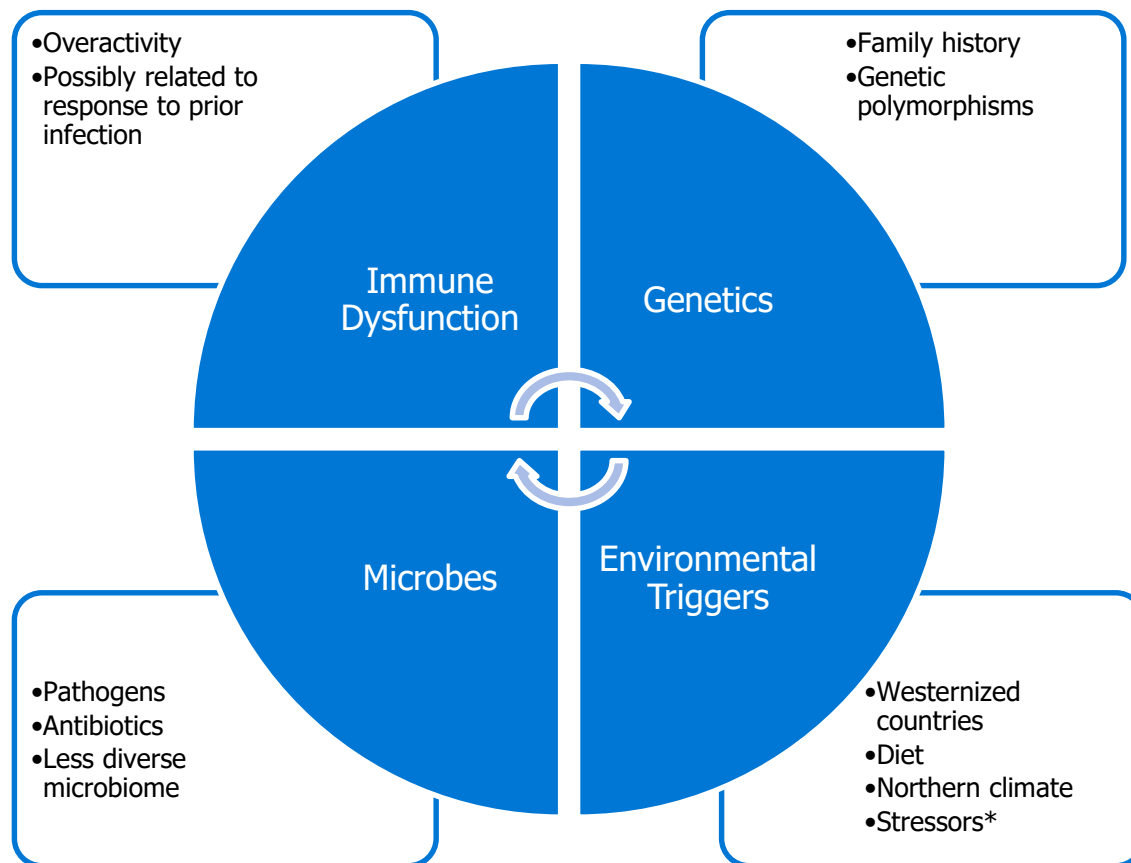
- <6 years of age at time of diagnosis
- Increased severity, aggressive progression, strong family history of IBD, and often poor response to conventional therapies
- Up to 25% patients have underlying immunodeficiency, which may impact response to therapies
 - Monogenic

VEO-IBD Networks



Etiology of IBD

- “It’s complicated”



Genetics: Is IBD inherited?

- Positive family history = greatest single risk factor
- 1.5-28% diagnosed with close relative also with IBD
- Younger age of onset = greater likelihood of family history of IBD
- >130 IBD loci
 - >40 CD specific loci
 - >30 UC specific loci

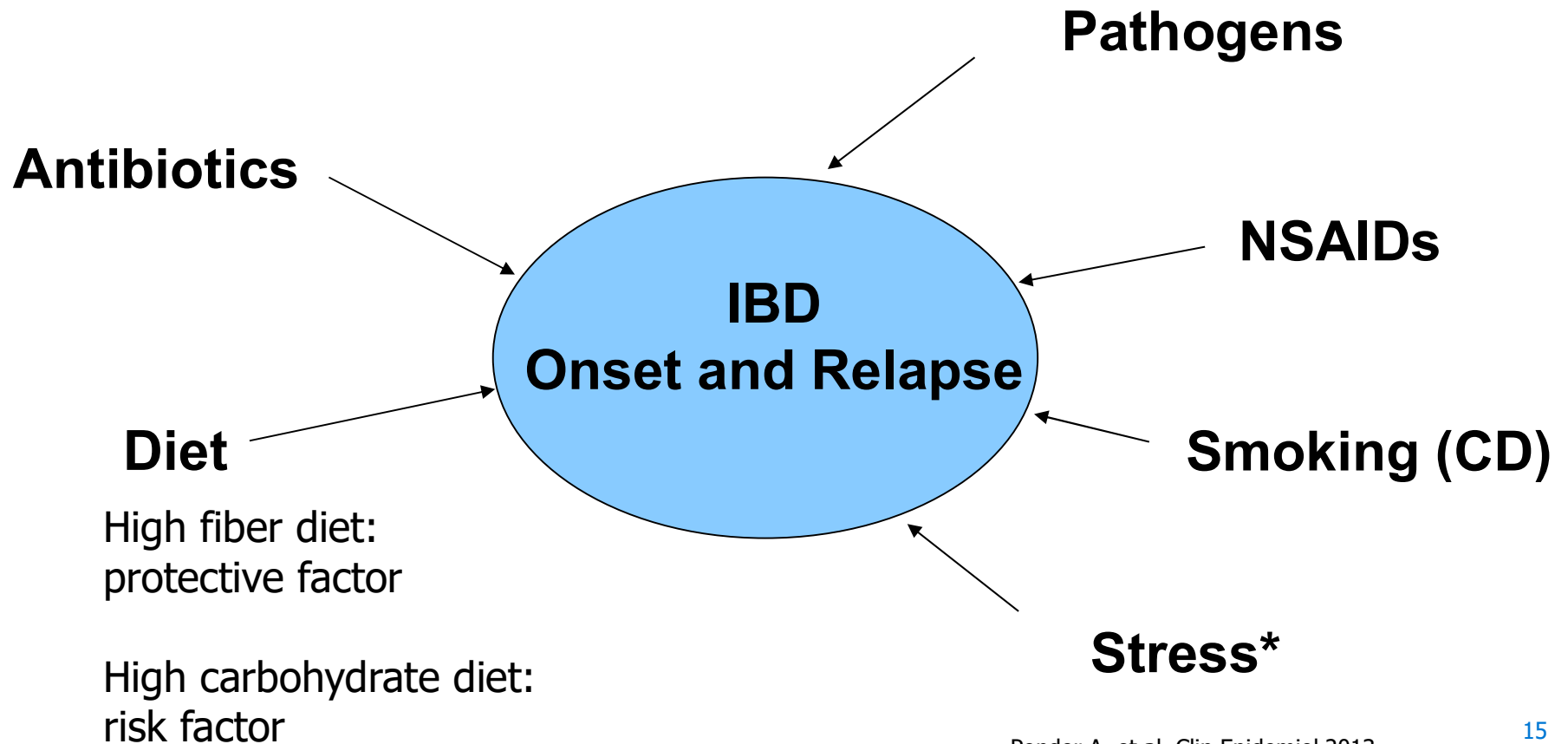


https://www.copaq.ca/wp-content/uploads/2021/08/dna-2789567_1280.png

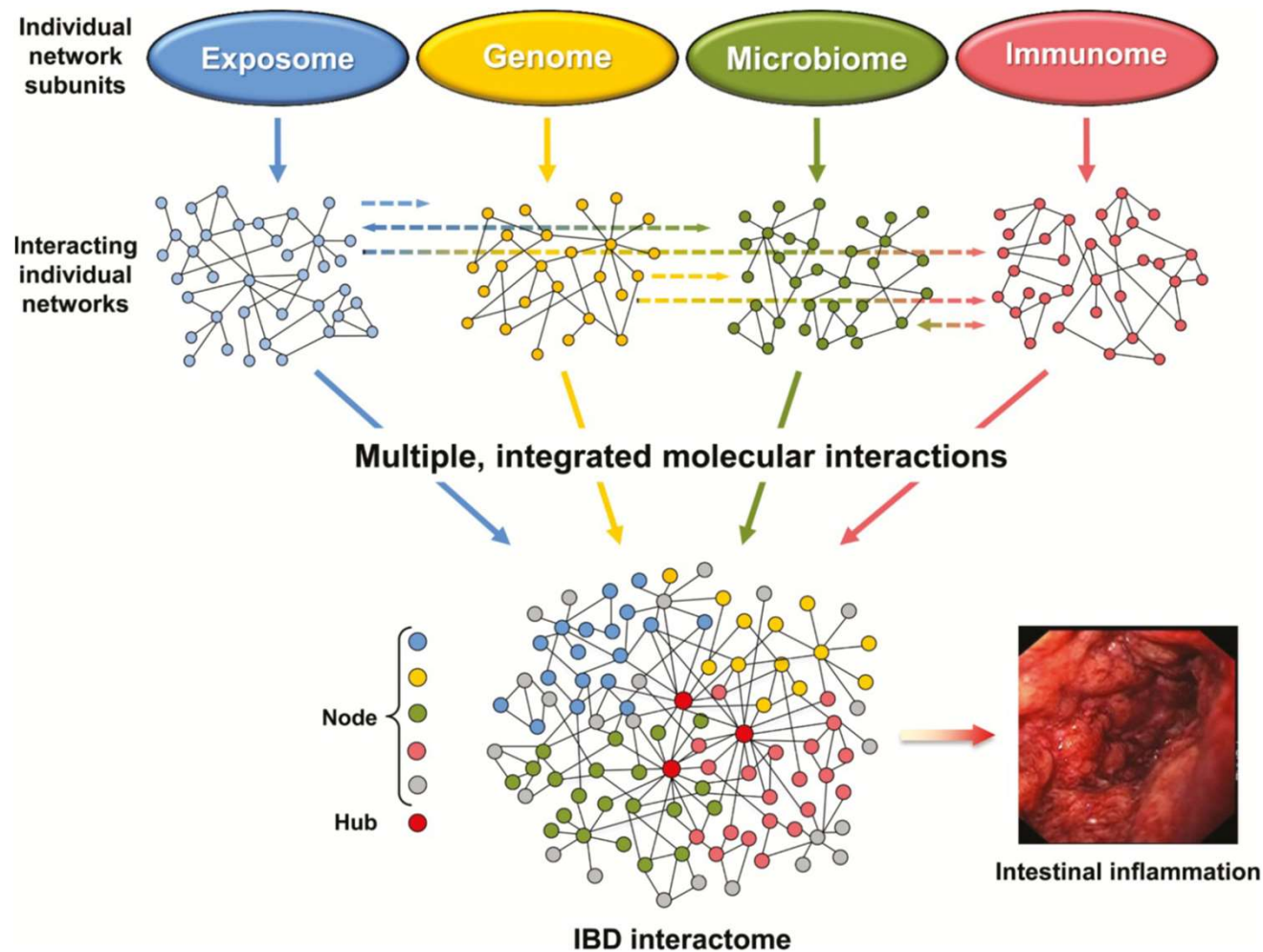
Environmental Triggers

Altered Flora

Altered Barrier Function



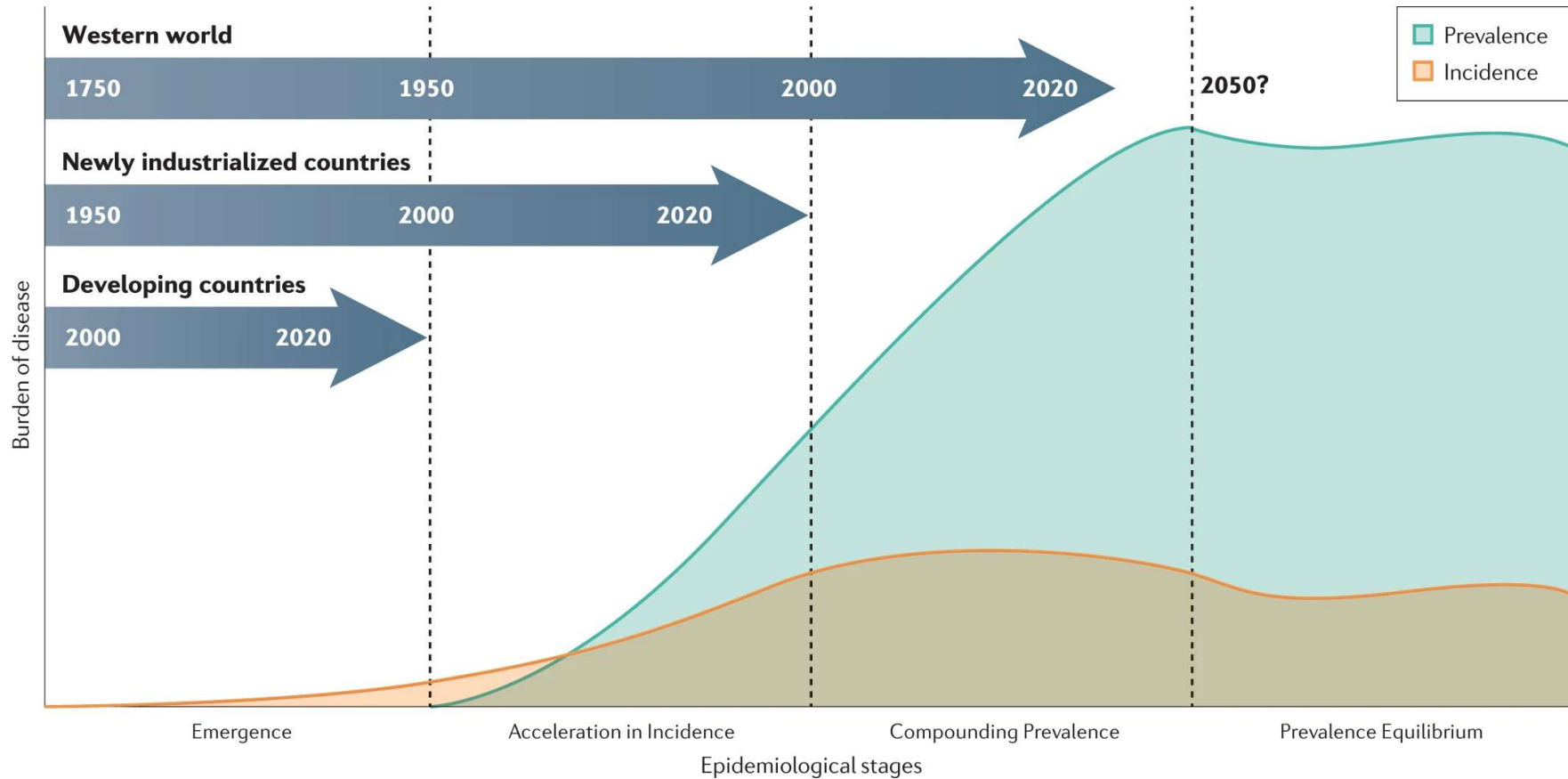
The Perfect Storm



Epidemiology of IBD

- Affects an estimated 3 million Americans
- Can occur at any age, most often diagnosed between the ages of 15-35 **AND** 55-70
 - Increasing incidence of pediatric IBD
- All ethnic backgrounds
 - Caucasian = more common (CD)
 - Increasing in Hispanics & Asians (CD)
 - Older adults → highest increase among non-Hispanic Black individuals
- Affects men and women equally
 - Older men > older women (UC)

Increasing Incidence of IBD



<https://www.nature.com/articles/s41575-020-00360-x/figures/1>
Benchimol EI et al. Inflamm Bowel Dis 2011

Clinical Presentation of IBD



Clinical Presentation of IBD

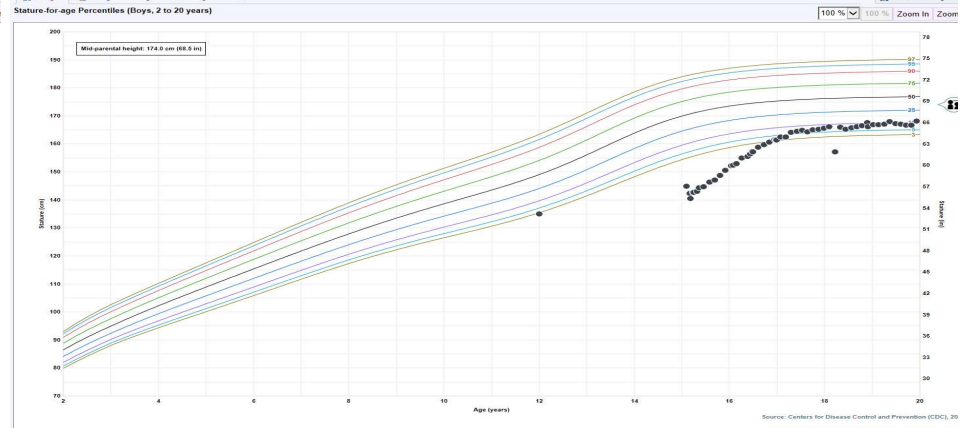
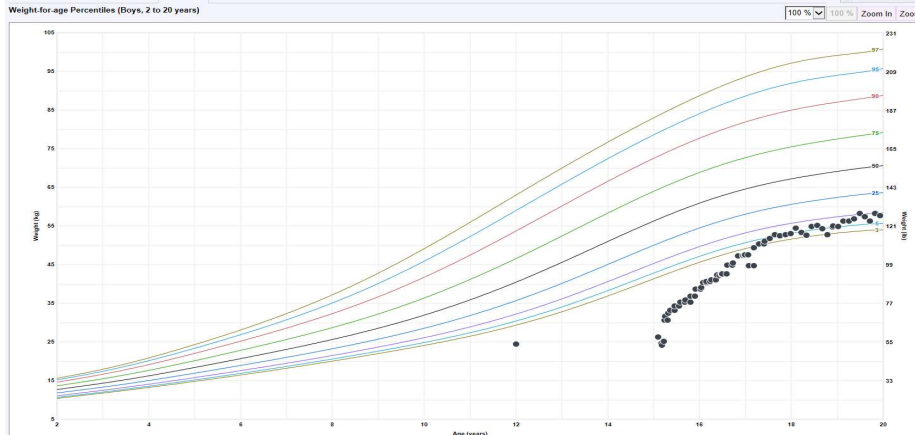
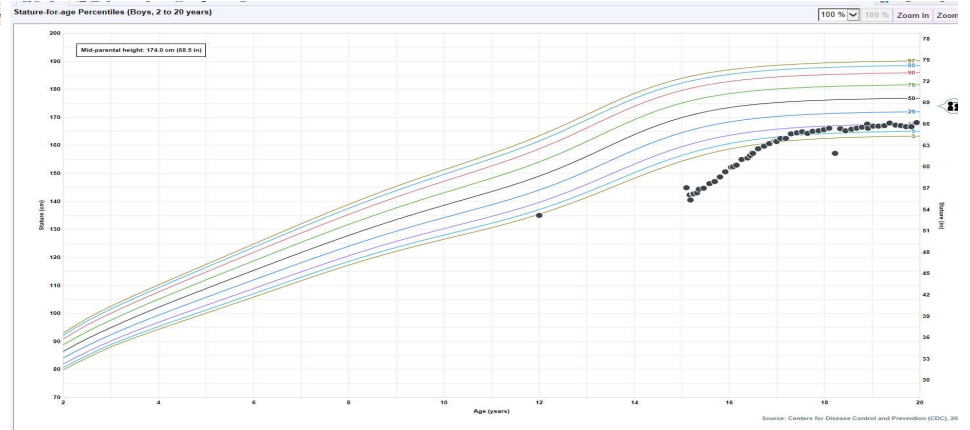
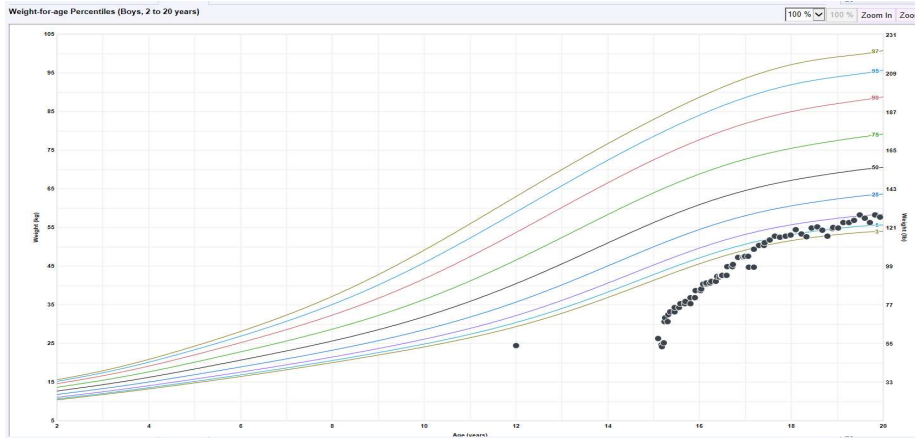
- Classic Presentation

- Gastrointestinal (approx 80%)
 - Abdominal Pain
 - Diarrhea
 - GI bleeding
 - Nausea/vomiting
 - Early satiety
 - Weight loss
 - Oral ulcerations
 - Perianal disease

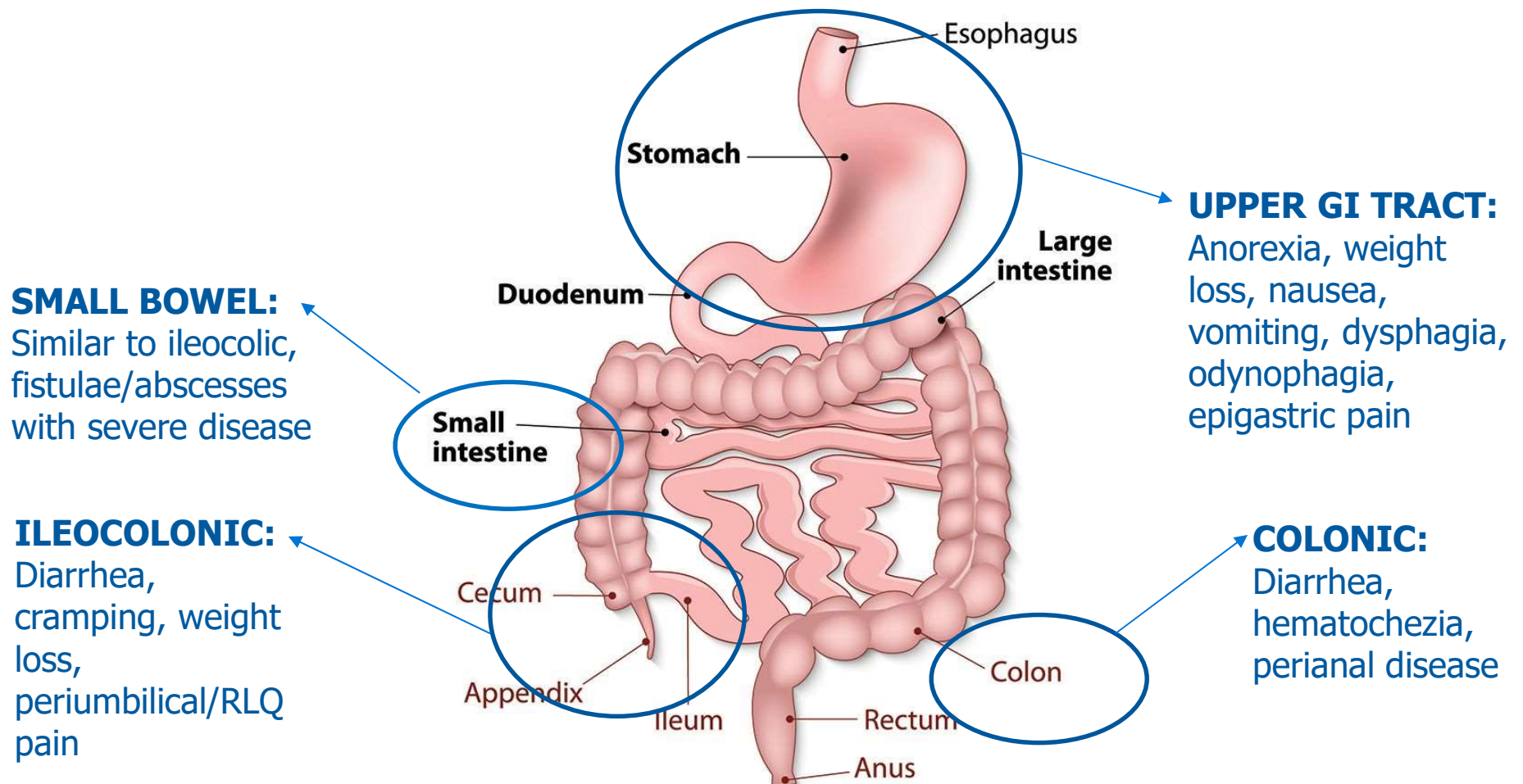
- Atypical Presentation

- Growth Failure (pediatric)
- Anorexia
- Malaise
- Fever of unknown origin
- Endocrine
 - Pubertal Delay (pediatric)
- Hematologic
 - Anemia
 - Micro, macro, or normocytic

Clinical Presentation of IBD: Growth Failure

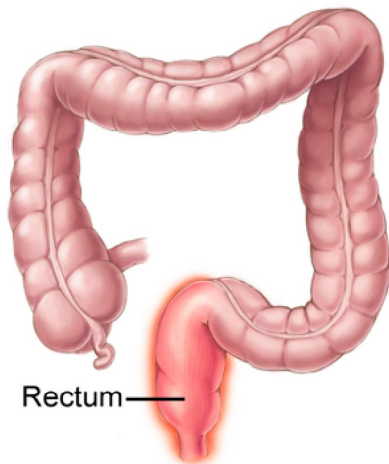


Crohn's Disease Subtypes

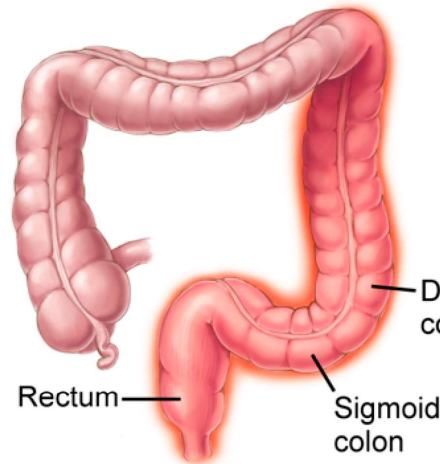


Ulcerative Colitis Subtypes

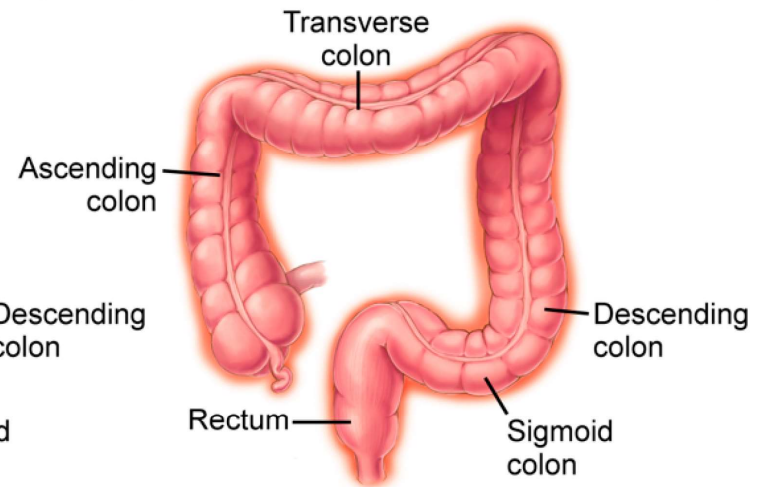
Proctitis Affected Regions



Left-sided Colitis Affected Regions



Extensive (Pan) Colitis Affected Regions



J Gregory ©2019 Mount Sinai Health System

J. Clin. Med. 2020, 9(1), 94; <https://doi.org/10.3390/jcm9010094>

Proctitis

- Rectal bleeding
- Rectal pain
- Urgency
- Formed stools

Left-Sided Colitis

- Anorexia
- Weight loss
- Bloody diarrhea
- LLQ pain

Pancolitis

- Anorexia
- Weight loss
- Bloody diarrhea
- Abdominal pain

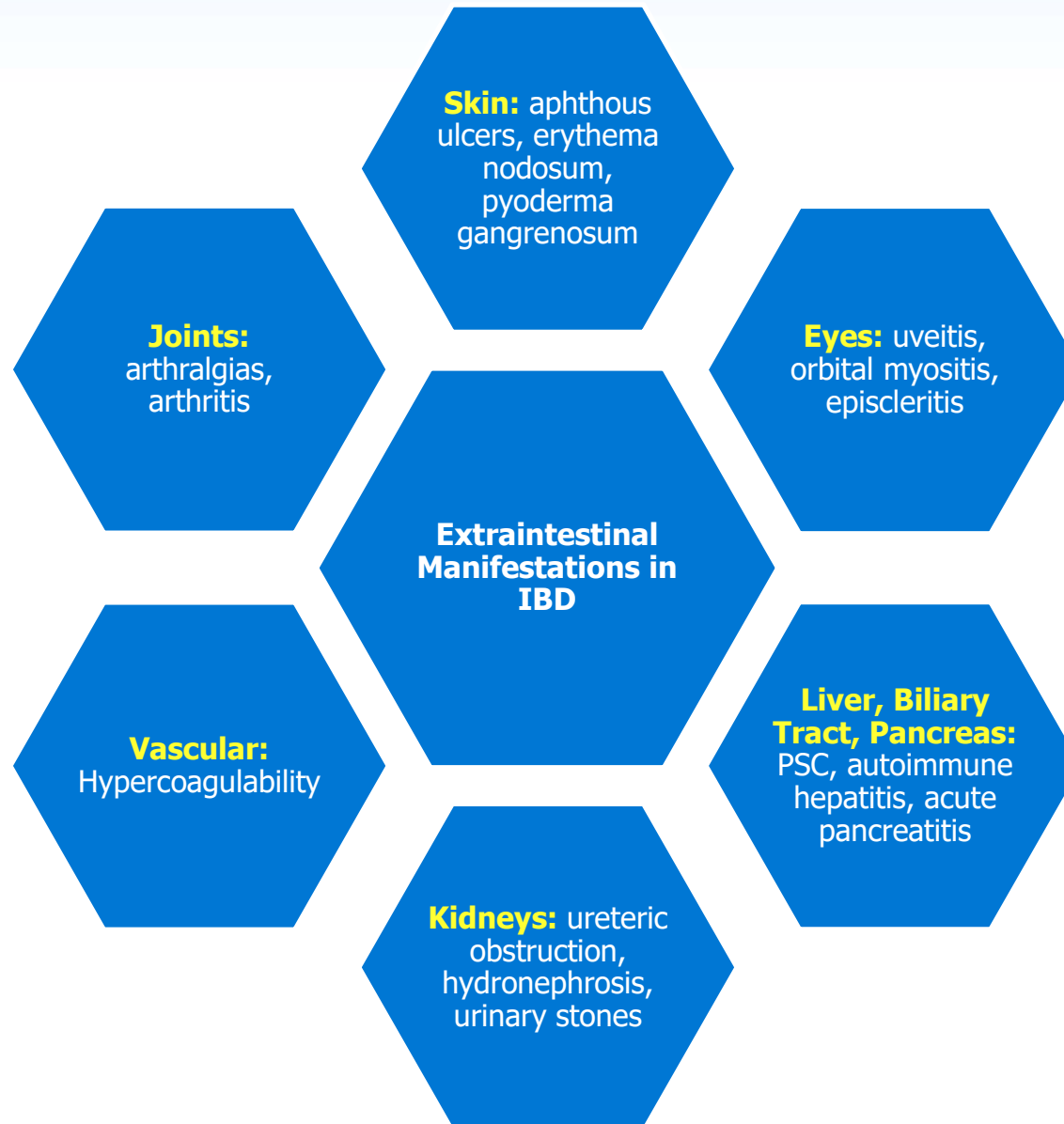
Extraintestinal Manifestations

- May precede GI symptoms
- 25-35% of patients with IBD
- Parallel disease activity, or have course independent of intestinal disease
- Most common in colonic CD



But wait!
There's
MORE!

Extraintestinal Manifestations



Extraintestinal Manifestations



<https://www.aaopt.org/eye-health/diseases/what-is-uveitis>



<https://radiologykey.com/sacroiliitis/>



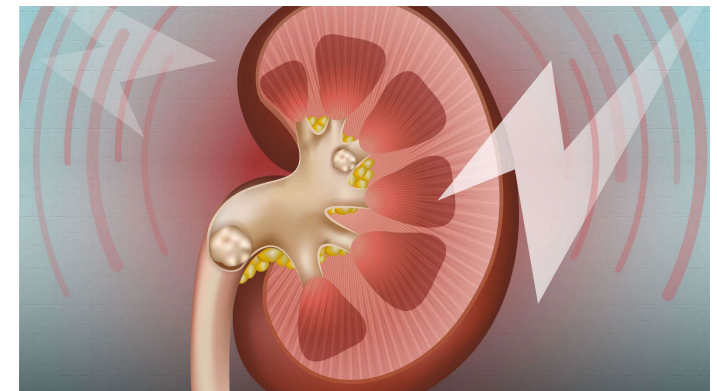
<https://dermnetnz.org/topics/aphthous-ulcer>



<https://carolinefifemd.com/wp-content/uploads/2022/08/Pyoderma-Gangrenosum-4-980x1307.jpg>



<https://www.dermatologyadvisor.com/home/decision-support-in-medicine/dermatology/erythema-nodosum-leprosum-leprosy/>



https://www.uab.edu/news/images/kidney_stones_900.jpg

Diagnosis of IBD

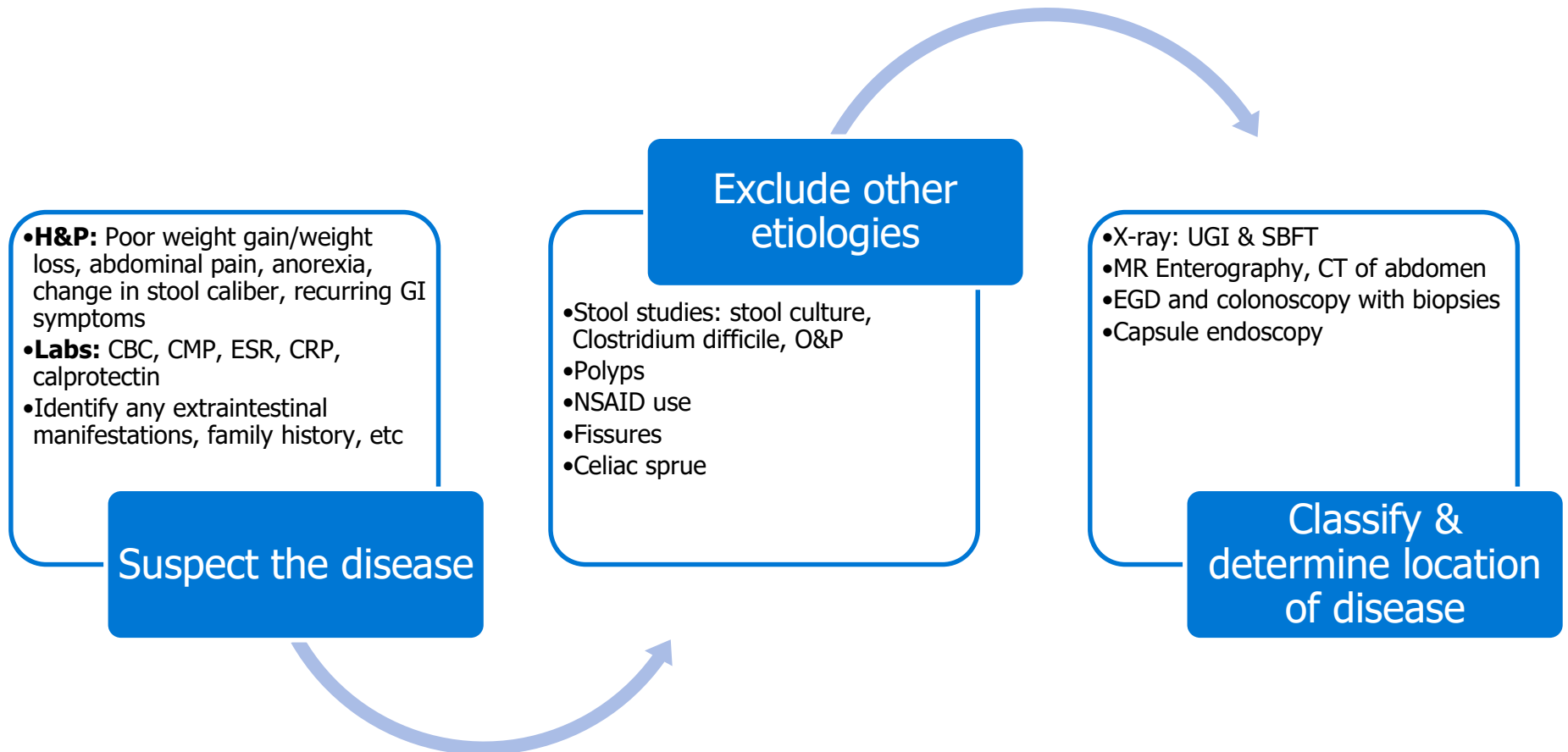


GI Red Flags

- Anorexia
- Poor weight gain/unintentional weight loss
- Dysphagia/odynophagia
- Nocturnal awakening
 - Due to discomfort OR urge to defecate
- Bowel movements
 - Unexplained change in frequency
 - Unexplained change in caliber
- Diarrhea
 - Persistent (>3 days)
 - No apparent correlating factors
- Abdominal pain
 - Persistent
 - No apparent correlating factors
 - Lingers after bowel movements OR relief with vomiting
- Perianal lesions → Look!



Diagnostic Approach to IBD



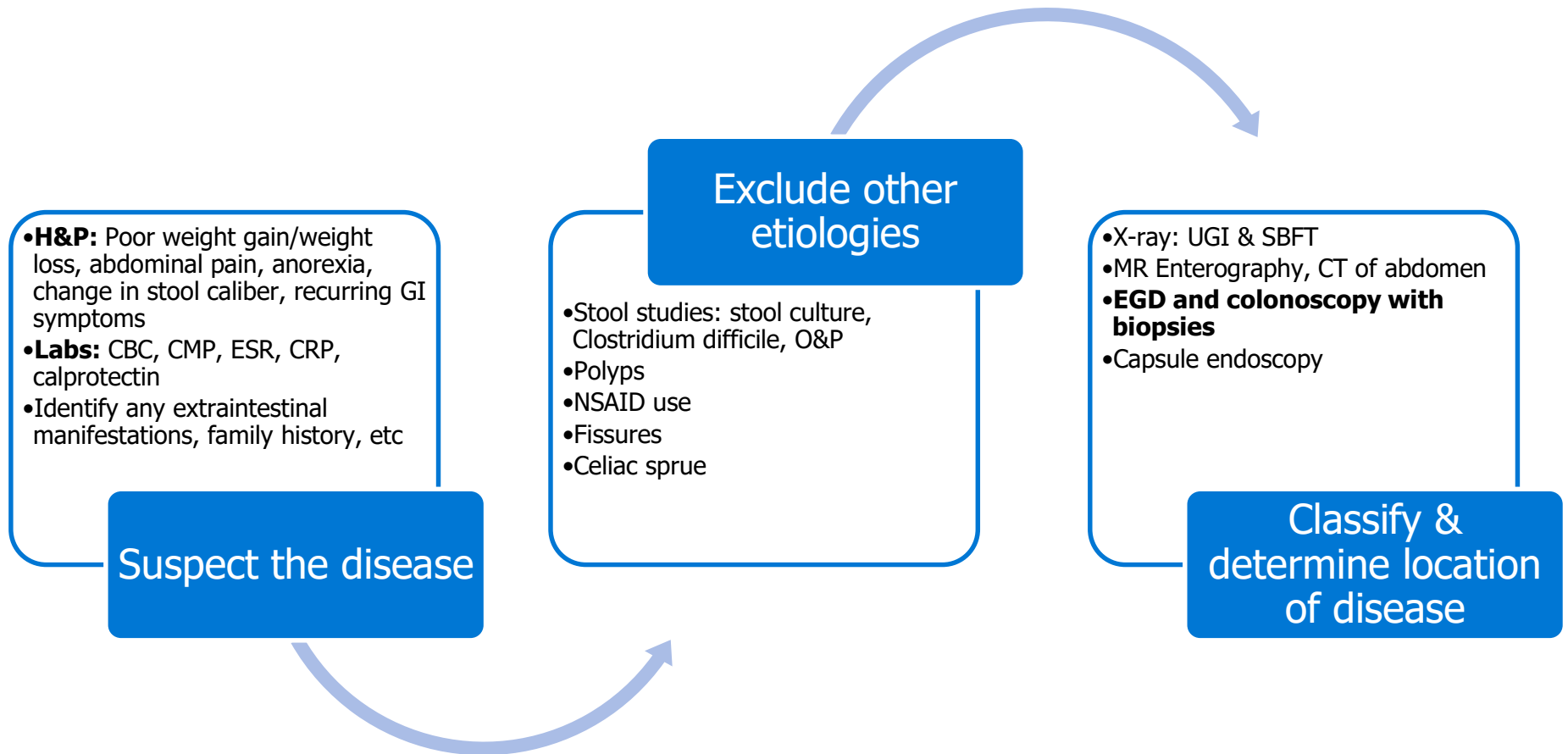
Mimics of IBD

- Irritable bowel syndrome (IBS)
- Celiac sprue
- Infectious diarrhea
 - C. difficile (PCR and EIA toxin)
 - Stool culture
 - Ova & Parasite
- Malignancy
- Fissures
- Hemorrhoids
- Polyps
- NSAID use
- Peptic ulcer disease
 - H. pylori

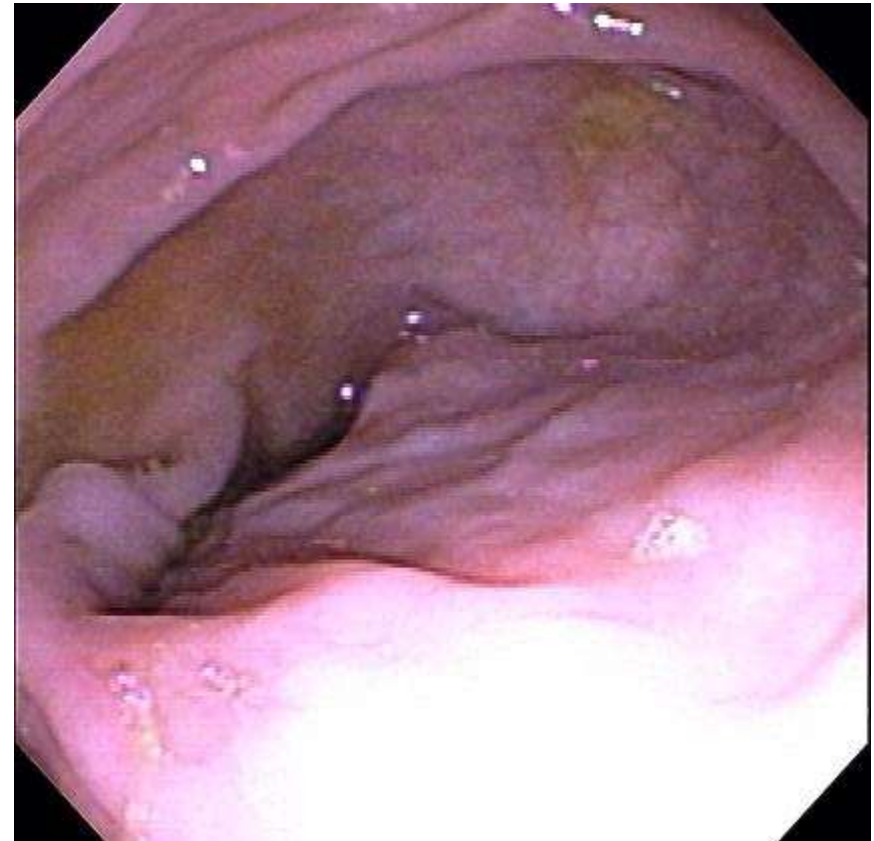


<https://horseyhooves.com/wp-content/uploads/2020/02/Horse-and-zebra-grazing.jpg.webp>

Diagnostic Approach to IBD



What does normal bowel look like?

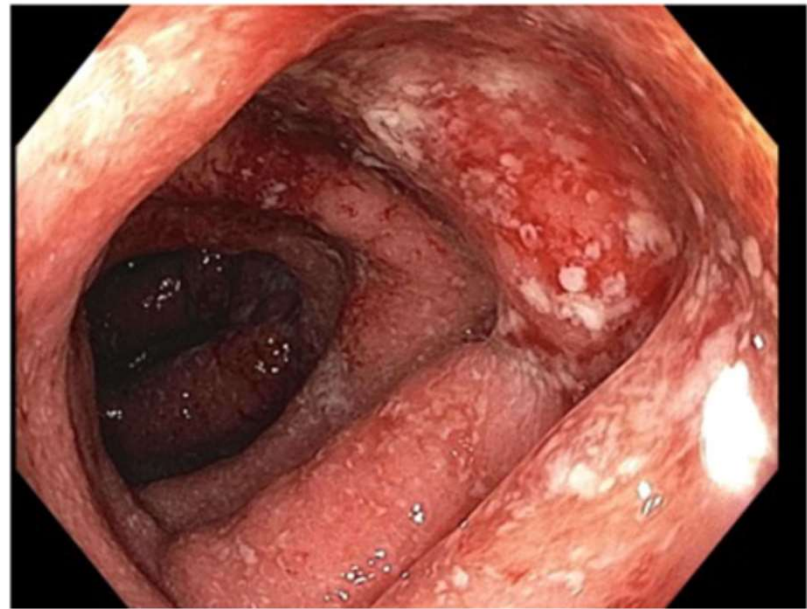


Bowel of IBD Patients

Crohn's Disease

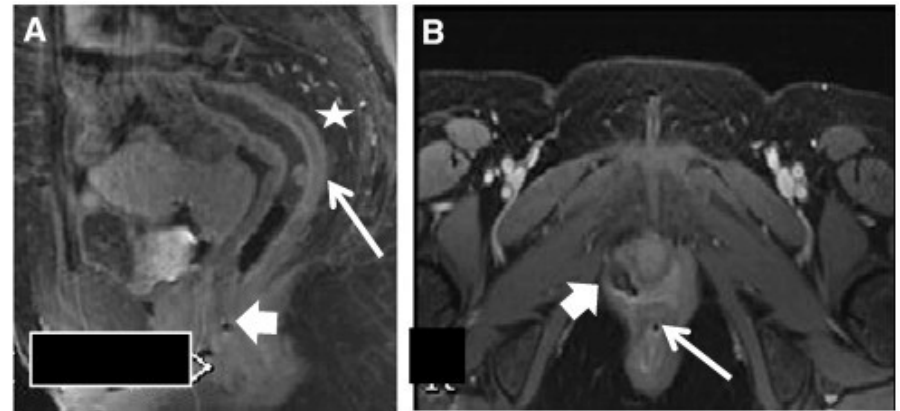


Ulcerative Colitis

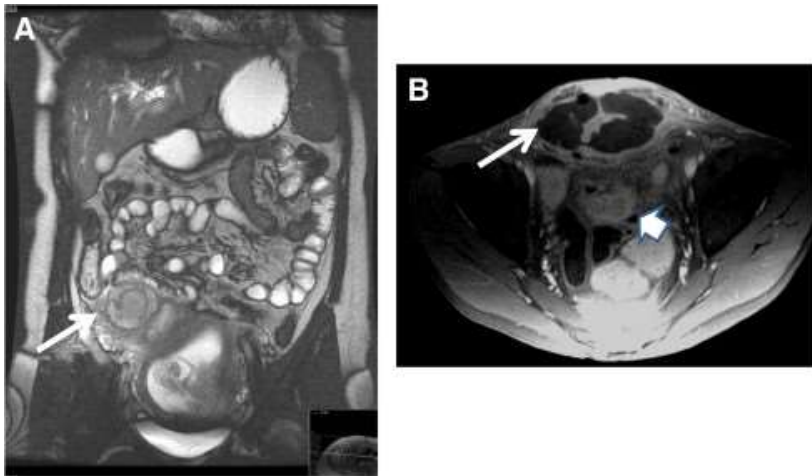


Indications for MR Enterography

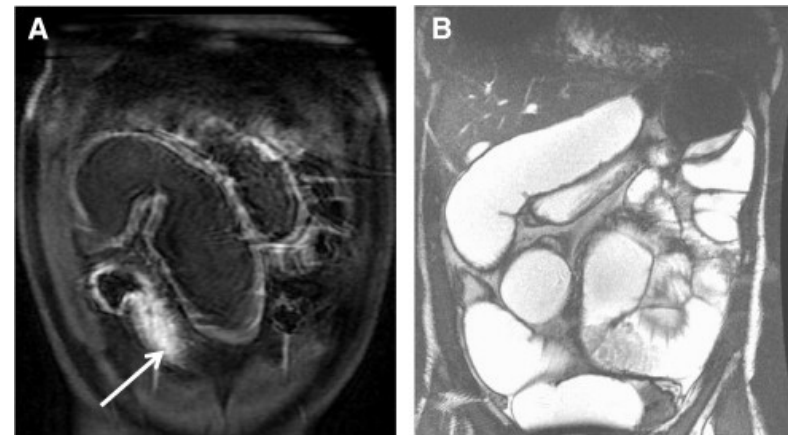
- Assess for small bowel disease
- Evaluate response to medical therapy in small bowel
- Evaluate for possibility of structuring disease, abscesses, fistulizing disease



Rectovaginal fistula



Abdominal wall abscess



Fibrostenotic stricture

Treatment of IBD



Goals of Treatment

- Induce remission of symptoms
- Maintain remission
- Prevent complications of ongoing inflammation
- Optimize growth and development
- Minimize corticosteroid use
- Avoid hospitalizations and surgeries
- Improve quality of life!



Medical Therapies for IBD

Induction of remission

- Corticosteroids
- Anti-TNF therapy
- 5-aminosalicylates (UC)**
- Enteral therapy (CD)

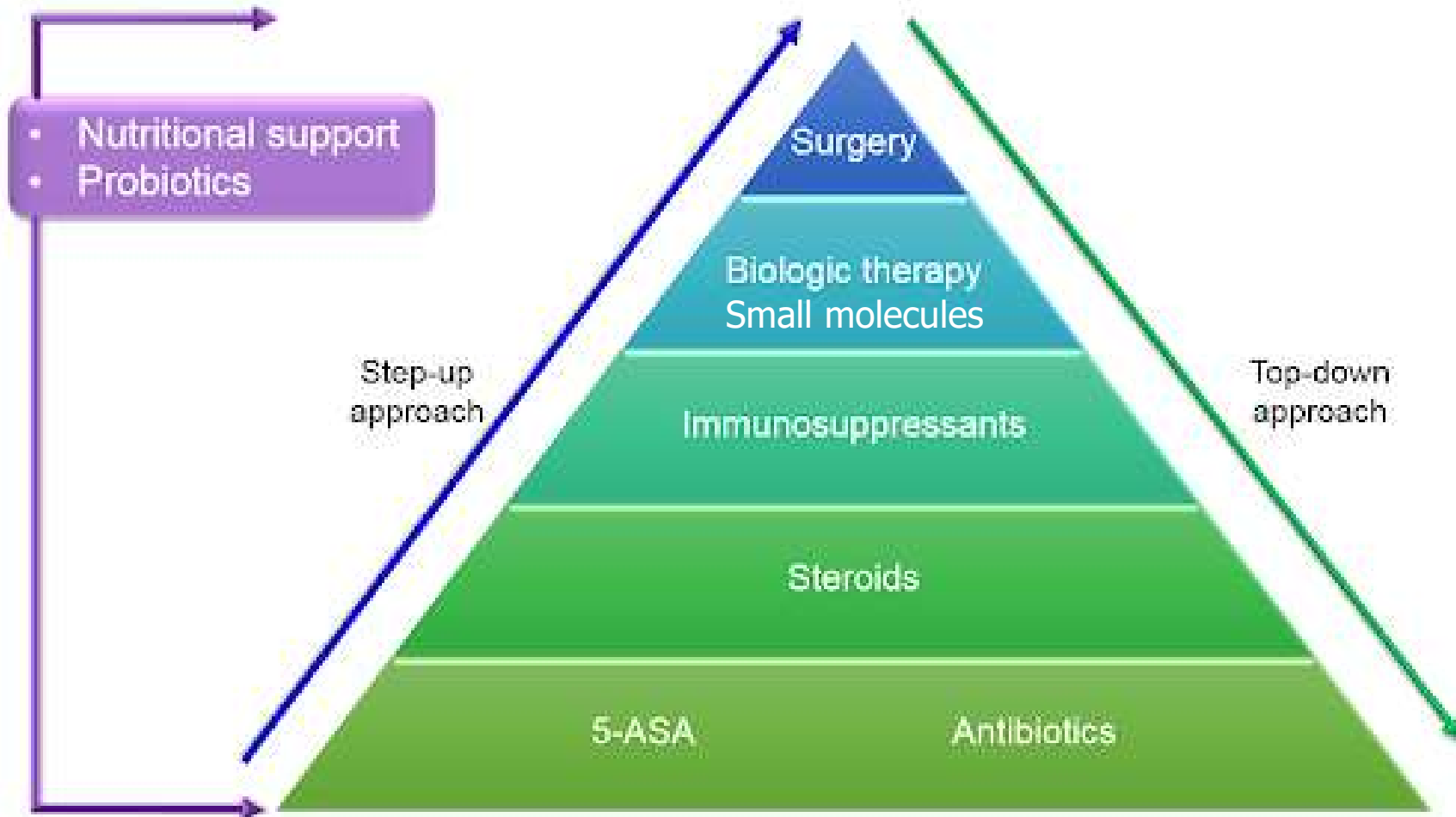
Maintenance of remission

- 5-aminosalicylates (UC)**
- Antibiotics (CD)*
- Enteral therapy (CD)
- Immunomodulators*
- Anti-TNF therapy
- Anti-integrins*
- Anti IL12/23*
- JAK inhibitors*

*Not FDA approved in pediatrics

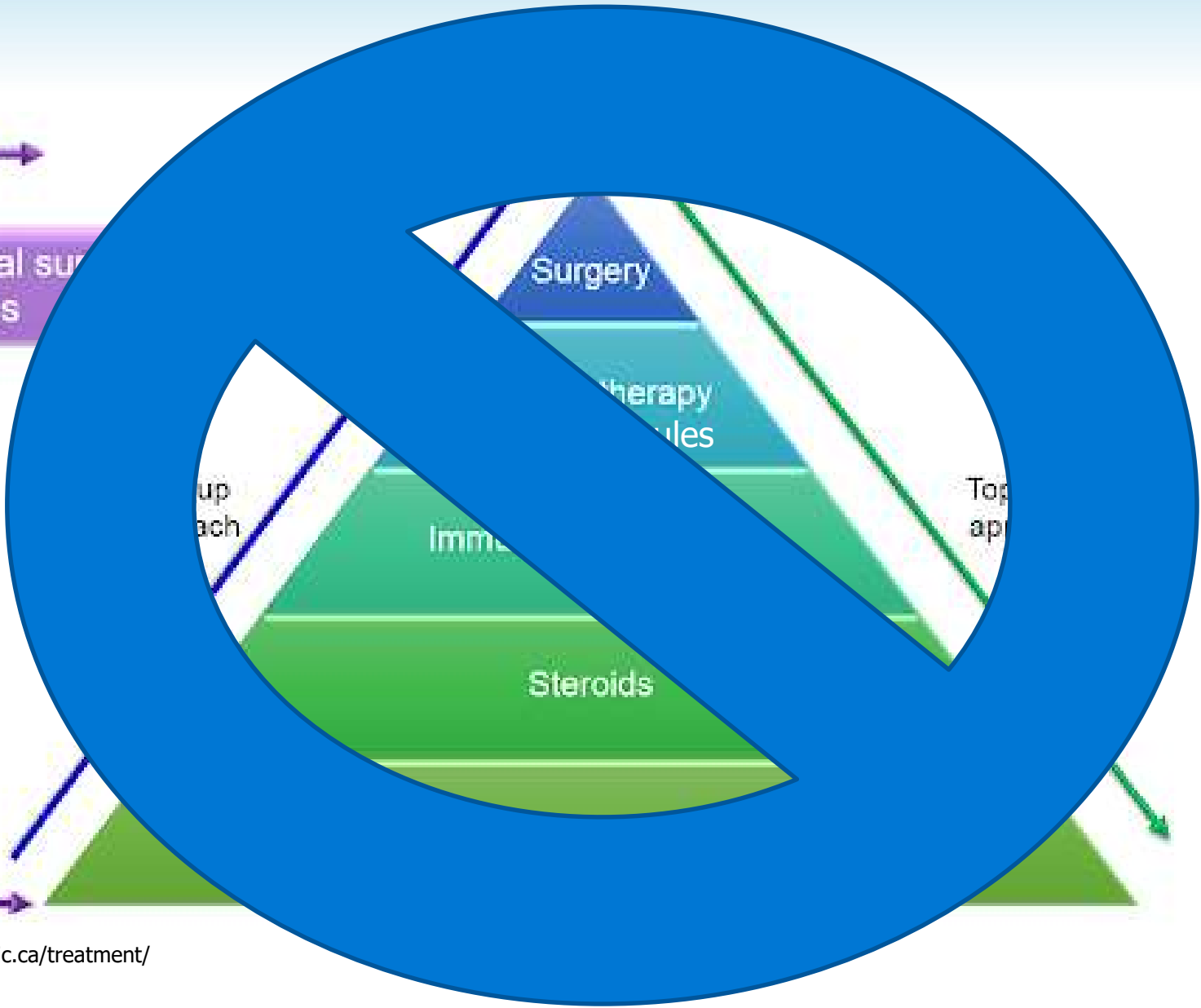
**Only balsalazide is FDA approved in pediatrics

A look back...



<http://www.ibdclinic.ca/treatment/>

- Nutritional support
- Probiotics



<http://www.ibdclinic.ca/treatment/>

Corticosteroids

- Solumedrol IV, prednisone, budesonide (Uceris, Entocort)
 - Suppress immune system
 - Induce remission and treat flare-ups
 - Many side effects!
- Side effects include...
 - Cushingoid appearance
 - Acne
 - Increased appetite → weight gain
 - Mood swings
 - Ankle swelling
 - Easy bruising
 - Stretch marks
 - Osteoporosis
 - Increased risk of infections
 - High blood pressure
 - Diabetes/insulin resistance
 - Cataracts
 - Increased intraocular pressure

Take pred they said,
You'll be fine they said...



Aminosalicylates (5-ASA)

- Oral or rectal preparations
- Medications
 - Sulfasalazine
 - Balsalazide
 - Mesalamine (Asacol, Asacol HD, Delzicol, Pentasa, Apriso, Lialda, Colazal, Rowasa, Canasa)
- Aspirin like compound
- Anti-inflammatory properties locally in the colon and/or small bowel
- Induction and remission of mild-moderate ulcerative colitis for long term therapy (*not Crohn's disease!*)
- Side effects
 - Worsening diarrhea, bloody diarrhea, nausea, headache

This is where the brand matters...

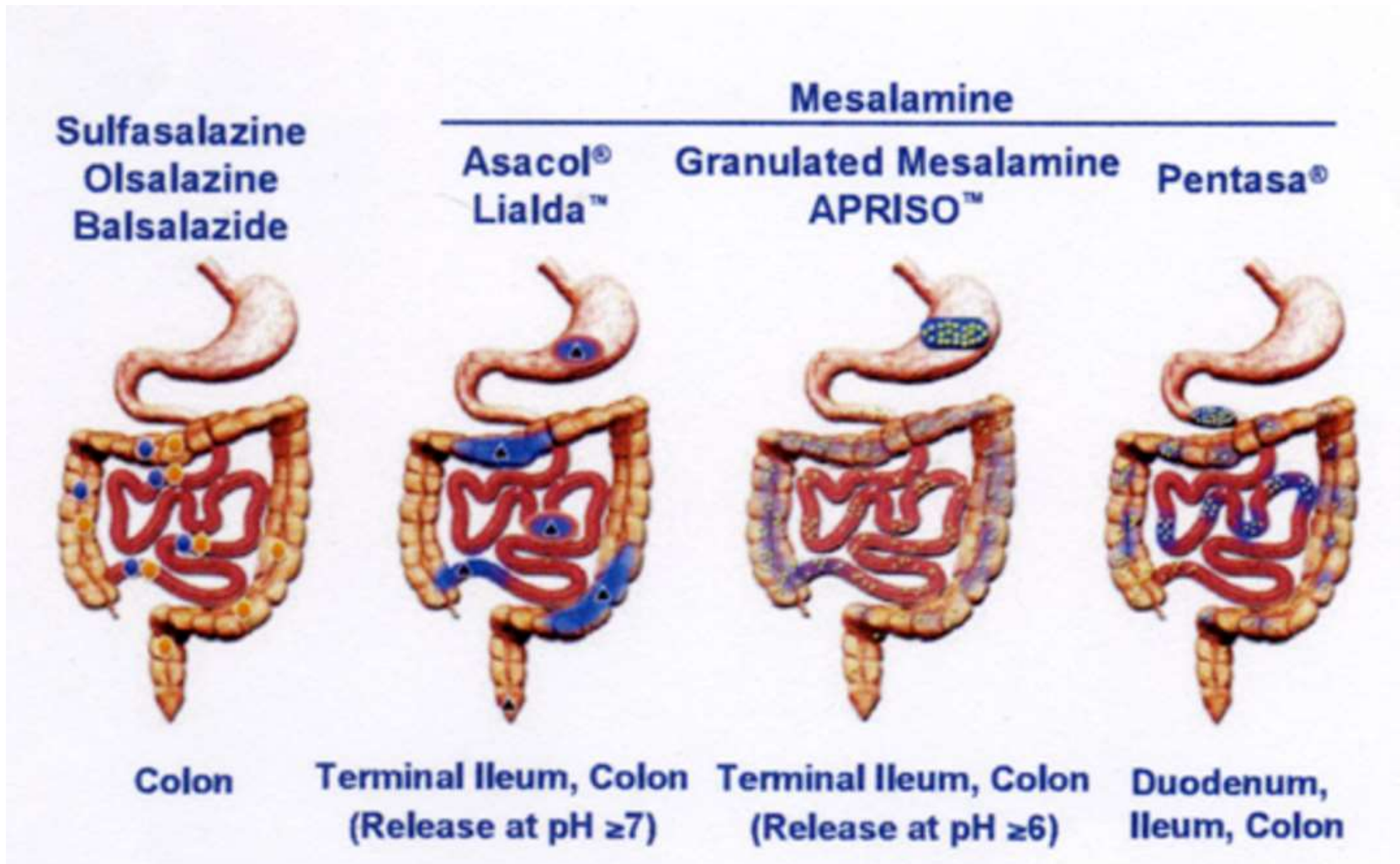


Figure 3.4 : Oral 5-ASA formulations: sites of delivery

Oral Antibiotics in IBD

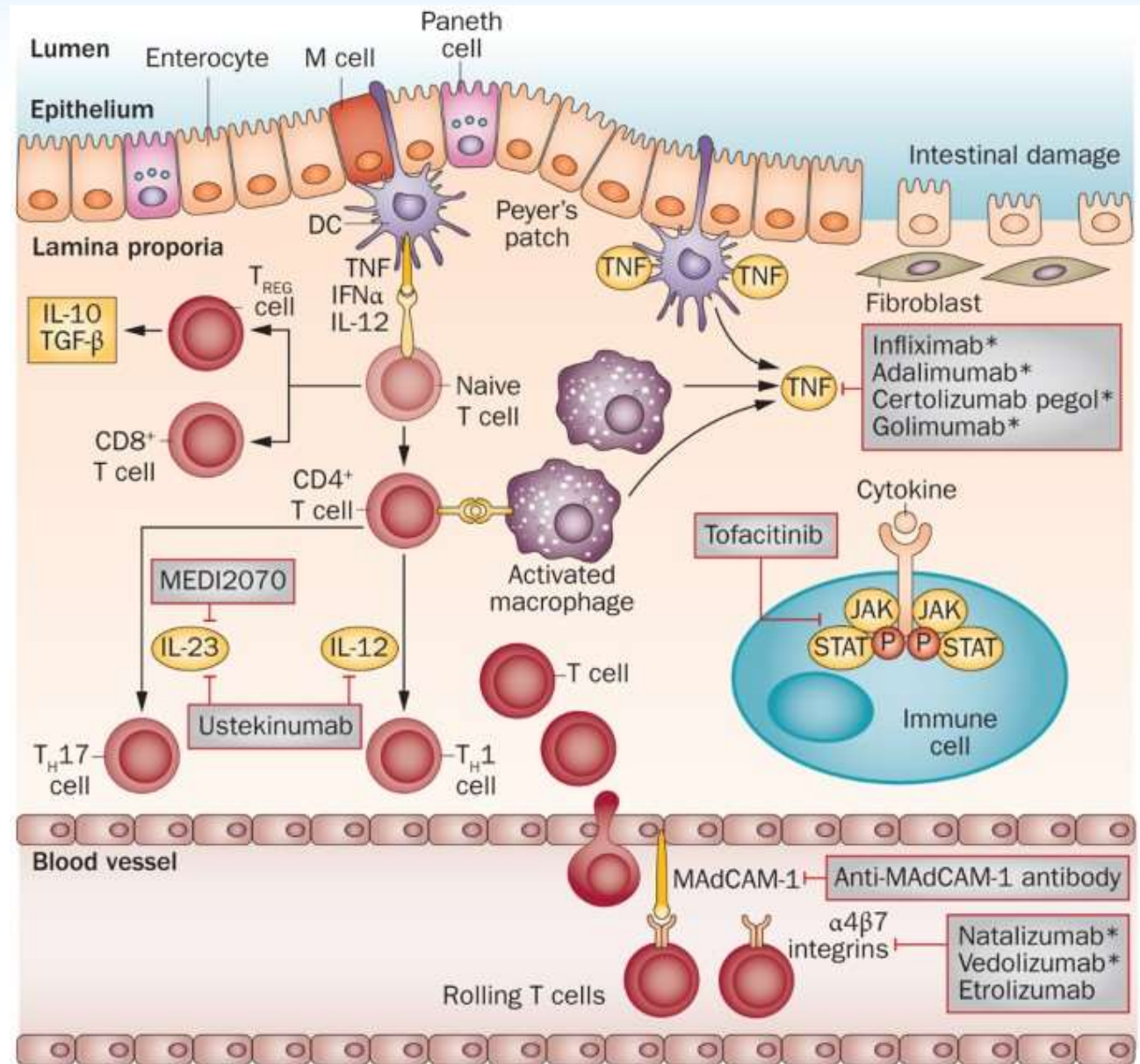
- **Quadruple antibiotic therapy:** amoxicillin, vancomycin, doxycycline, metronidazole
 - Often used in acute severe pediatric UC
 - Alternative or adjunctive therapy to corticosteroids
- **Others:** metronidazole, ciprofloxacin, rifaximin
 - Uses:
 - Treatment of perianal disease (inflamed skin tags, fissures, fistulas, and abscesses)
 - Decrease intestinal inflammation
 - Treat infections

Immunomodulators

- Azathioprine (AZA), 6-mercaptopurine (6-MP), methotrexate (MTX)
- Oral (6-MP, MTX) or SQ injection
- Interfere with DNA and RNA synthesis resulting in immune suppression
- Indicated for moderate-severe disease, fistulae, steroid dependent or refractory disease, maintaining remission
- Slow onset of action (2-3 months)
- Side effects: leukopenia, elevated LFTs, nausea, pancreatitis, increased risk of lymphoma with 6-MP
 - Lymphoma risk associated with initial EBV infection
- Monitor labs closely

Biologics/ Small Molecules

- MOA: Target specific pathways of the immune system in patients with IBD
- 5 classes in IBD currently used (many more underway in clinical trials)
 - Anti-TNF
 - Anti-integrins
 - S1P receptor modulators
 - Anti-IL-12/23
 - JAK inhibitors



Biologics/Small Molecules

Class	Medications	Administration	Onset of action
Anti-TNF (tumor necrosis factor)	<ul style="list-style-type: none"> Infliximab (Remicade, Inflectra, Renflexis)* Adalimumab (Humira)* Golimumab (Simponi) Certolizumab (Cimzia) 	<ul style="list-style-type: none"> IV (infliximab) SQ (adalimumab, golimumab, certolizumab) 	2-4 weeks
Anti-integrins	<ul style="list-style-type: none"> Vedolizumab (Entyvio) <i>Natalizumab (Tysabri)</i> 	<ul style="list-style-type: none"> IV 	Up to 14 weeks
S1P receptor modulators	<ul style="list-style-type: none"> Ozanimod (Zeposia) 	<ul style="list-style-type: none"> Oral 	
IL-12/23 inhibitors	<ul style="list-style-type: none"> Ustekinumab (Stelara) Risankizumab (Skyrizi) 	<ul style="list-style-type: none"> Combination (IV then SQ) 	Up to 12 weeks
JAK inhibitors	<ul style="list-style-type: none"> Tofacitinib (Xeljanz) Upadacitinib (Rinvoq) 	<ul style="list-style-type: none"> Oral 	Up to 8 weeks

*FDA approved in pediatric ulcerative colitis and Crohn's disease

Potential Adverse Events of Biologics/Small Molecules

- Hypersensitivity reactions
 - Immediate
 - Infusion/injection site reactions (3-21%)
 - Delayed
 - Serum sickness
- Increased risk of infection (serious infections 3%)
 - Test for TB and hepatitis B prior to starting
 - Shingles vaccine prior to initiation of JAK inhibitors
- Autoimmune reactions: psoriasis, drug induced lupus
 - Anti-TNF only
- Multiple sclerosis (case reports)
 - Anti-TNF only
- Antibody formation
 - Loss of response to treatment
 - Related to infusion reaction in some patients
- Liver injury
- Increased risk of malignancies
- Hyperlipidemia
 - JAK inhibitors only
- DVT/PE
 - JAK inhibitors only

Potential Adverse Effects of Biologics/Small Molecules

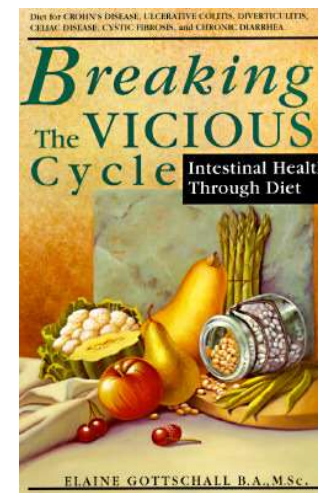
	Anti-TNF	Anti-Integrin	S1P	IL12/23 Inhibitors	JAK Inhibitors
Serious infection	+	-	+	-	+
Herpes zoster	-	-	+	-	+
Non-Hodgkins lymphoma	+	-	-	-	?
Demyelination	+	-	-	-	-
DVT/PE	-	-	-	-	+
Hyperlipidemia	-	-	-	-	+
Arrhythmias	-	-	+	-	-

Dietary Therapy in IBD

- Exclusive Enteral Nutrition (EEN)
 - Formula diet only for 4-12 weeks orally or via a NG tube
 - Can be used as maintenance therapy or bridge to other therapy **in place of steroids**
 - Limitations: COMPLIANCE!
- Specific Carbohydrate Diet (SCD)
 - Grain-free diet low in sugar and lactose → *Breaking the Vicious Cycle*
 - Limitations: very restrictive, little data surrounding efficacy
 - No superiority to Mediterranean diet in clinical trial



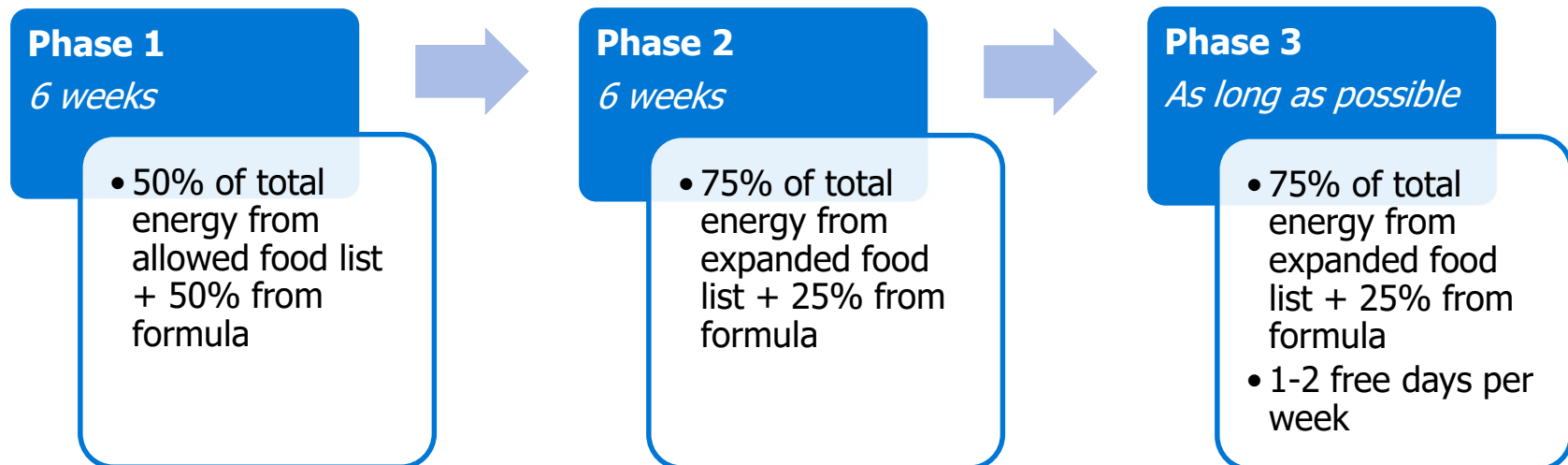
<https://www.ntforibd.org/media/images/toa-heftiba-mZb1YnKJfDU-unsplash.width-600.jpg>



https://www.biblio.com/book/breaking-vicious-cycle-intestinal-health-through/d/1182590957?aid=frg&gclid=Cj0KCOjwMn2iBhCrARIsAG_G2i5_5-68VOVCSWh89cv5vud7ty01TKnbrm9zloDQ6ymZ8wvgrRNXdEaAqJ3EALw_wcB 49

Dietary Therapy in IBD

- Crohn's Disease Exclusion Diet (CDED)
 - 3 phases → start with 50% formula and 50% approved foods, then reduce amount of formula in each phase
 - Limitations: somewhat restrictive, only approved in CD currently



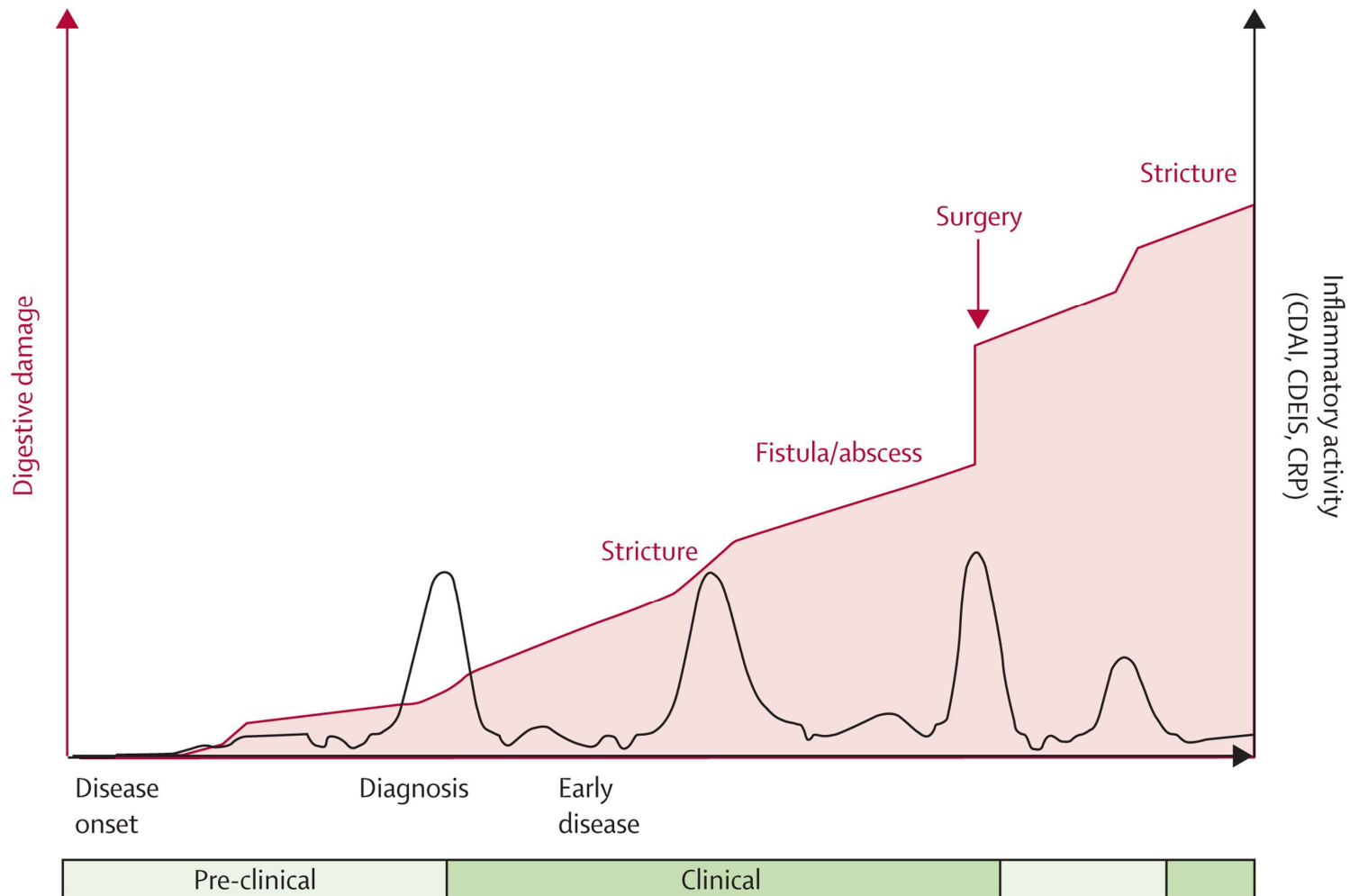
“I think I’ll just put up with the diarrhea then...”

- Ongoing inflammation from IBD has its risks!
 - Colon cancer
 - Blood clots → 3x greater risk than the general population for developing deep vein thrombosis
 - Primary sclerosing cholangitis (PSC)
 - 50% of PSC patients have IBD (more common in UC vs CD)
 - Kidney stones
 - Hospitalizations/surgeries
 - Poor quality of life



<https://www.perthpest.com.au/types-of-pests/bed-bugs/bed-bugs-scared-baby/>

Chronic inflammation = BAD!



Risk Factors for Rapid Progression of Severe Disease

Ulcerative Colitis

- Low risk (40%)
 - Limited extent of disease
 - Mild ulcerations
- High risk (60%) → colectomy
 - Age <40
 - Extensive disease
 - Deep ulcers
 - Steroid dependence
 - Prior hospitalizations
 - Elevated CRP and ESR
 - C.diff or CMV infections

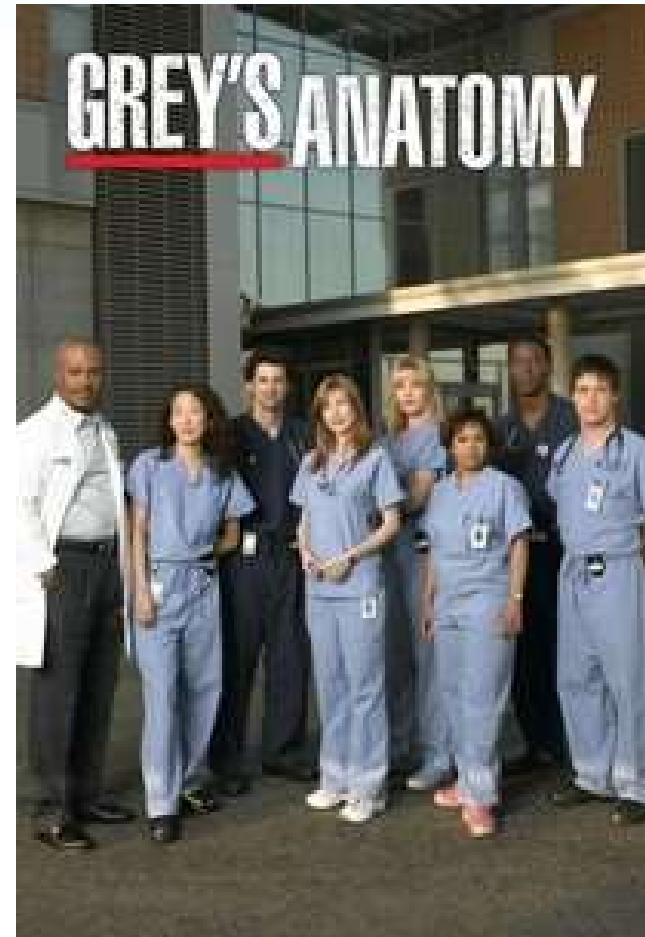
Crohn's Disease

- Low risk (<20%)
 - Age >30
 - Limited extent of disease
 - No perianal involvement
 - Superficial ulcers
 - No prior surgery
 - No stricturing/penetrating phenotype
- High risk (>80%)
 - Age <30
 - Extensive disease
 - Perianal and/or severe rectal disease
 - Deep ulcers
 - Prior surgeries
 - Stricturing and/or penetrating phenotype

Surgery in IBD

Indications:

- Perforation
- Severe disease
- Excessive bleeding
- Intestinal obstruction or stricture
- Fistula/abscess
- Toxic megacolon



https://resizing.flixster.com/1P3B8fjYFSwRnt8PxihRv09n5Nk=/206x305/v2/https://flxt.tmsimg.com/assets/p7894890_b_v10_ad.jpg

Treatment Algorithm for IBD

Mild Disease

UC: 5-ASA +/-
steroid taper

CD: metronidazole,
CDED, sulfasalazine
(colon only),
budesonide x 8
weeks

Moderate Disease

UC: 5-ASA + steroid
taper, vedolizumab,
ozanimod, AZA/6-MP

CD:
immunomodulators,
anti-TNF, IL 12/23
inhibitors

Severe Disease

UC: anti-TNF +
immunomodulator,
JAK inhibitors,
ustekinumab,
ozanimod,
vedolizumab

CD: anti-TNF +
immunomodulator,
IL 12/23 inhibitors

Health Maintenance in IBD



Bone Health

- Osteopenia and osteoporosis are common in patients with IBD
 - Decreased BMD at diagnosis in 43% of CD and 39%, compared to 29% of controls (n=58)
 - Elevated inflammatory cytokines inversely correlated with BMD
- Hypovitaminosis D is prevalent in IBD
 - 25-OH vitamin D levels suboptimal in 58.3%, insufficient in 14.3%, deficient in 5.8% (n=448)
 - Levels inversely associated with ESR



https://monib-health.com/files/blog-post/03afdbd66e7929b125f8597834fa83a4_63_thumb.jpg.webp?_=1640515274

Bone Health Guidelines

- DXA encouraged at baseline and every 1-2 years if low BMD noted
- Regular monitoring of linear growth, growth velocity and pubertal development
- Monitor vitamin D levels at least annually
 - Treat hypovitaminosis D with high doses
 - Once optimal status achieved, continue 800-1000 IU daily
- 1000-1600 mg of elemental calcium daily
- Encourage weight bearing activities and resistance training

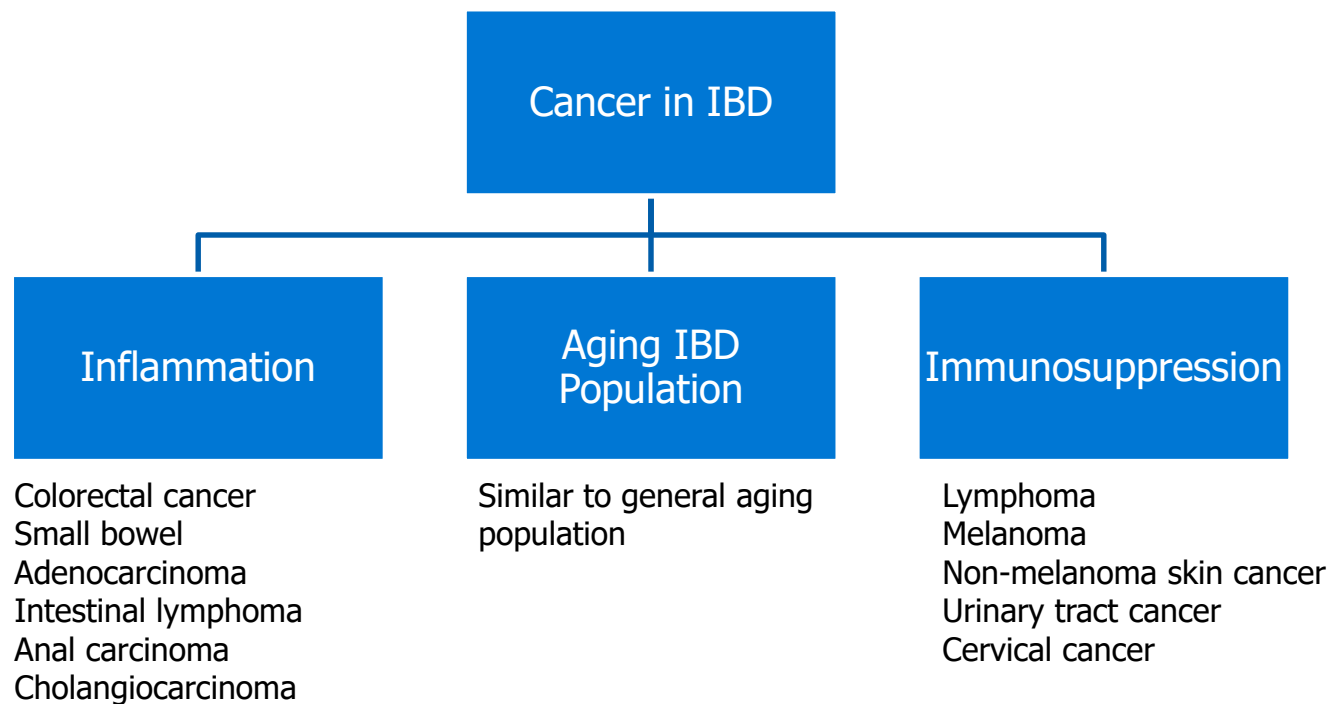
Eye Health

- Annual screening with *ophthalmologist* recommended
 - **IBD-associated manifestations**
 - Uveitis
 - Episcleritis
 - Orbital myositis
 - **Corticosteroid-associated manifestations**
 - Glaucoma
 - Early cataracts




<https://www.aao.org/eye-health/diseases/what-is-uveitis>

Cancer Risk in IBD Patients



Colon Cancer Prevention



So...can I poop
in a box?

- Recommended in patients with history of $>1/3$ colonic inflammation
 - Applies to patients with ulcerative colitis AND Crohn's disease (if meeting above indications)
- **Risk factors:** ongoing inflammation, pseudopolyps, prior dysplasia, mass/stricture, M>F, duration of disease, greater extent of colonic involvement, family history, PSC, younger age of diagnosis
- Screening: colonoscopy 8 years from initial diagnosis, then every 1-3 years thereafter
- Annual screening in patients with PSC
- Cologuard is NOT a substitute!

Cervical Cancer Prevention

- **Annual** Pap smears in young women on immunosuppression
 - Consider starting between age 18-21
- HPV vaccine as scheduled in ALL IBD patients
 - Begin at age 11-12 typically
 - 3 doses at 0, 1-2 months, and 6 months

Cancer Prevention – Skin

- 6-MP/AZA/MTX → increased risk of **non-melanomatous** skin cancers
- Anti-TNF → increased risk of **melanomatous** skin cancers
- Annual dermatology exam recommended in patients on immunosuppression
- Emphasize use of sunscreen (at least SPF 30), sun-protective clothing, etc

Live Vaccines

- Measles/Mumps/Rubella (MMR), VZV (Varicella zoster), intranasal influenza, yellow fever, Rotavirus
- **Indicated in:** patients on dietary therapy, antibiotics, or 5-ASA
- **Contraindicated in:** patients on immunosuppression
 - Ideal world → give live vaccines prior to starting immunosuppression if time allows

Inactivated Vaccines

- Okay to give in **ALL** patients as scheduled
 - Polio: 4th dose at age 4-6
 - DTaP: 5th dose at age 4-6
 - Tdap: age 11, then TD every 10 years
 - HPV: age 11-12 (3-part series)
 - Meningococcal: 1st dose at age 11-12, 2nd dose at age 16
 - Influenza: annually during flu season
 - COVID-19: Primary series + additional dose 4 weeks later (if immunocompromised) + bivalent booster 2 months later
 - Per current CDC guidelines
- Ideally want to time immunosuppression to mount appropriate response
- All should be coordinated with PCP visits

Special Considerations in Immunocompromised patients

- PCV13
 - If PCV7 was given, recommend vaccination with PCV13 for added pneumococcal coverage
- PPSV23
 - Recommended in patients >65 OR in patients with certain medical conditions that can lead to an increased risk for pneumococcal disease
 - If on immunosuppression → give 8 weeks after PCV13 (if recently given), then every 5 years thereafter
- COVID-19:
 - Completion of primary series + additional dose 4 weeks later + bivalent booster at least 8 weeks later
- Herpes Zoster
 - Recommended in patients >50, but given to patients on JAK inhibitors regardless of age
 - If on JAK inhibitors → 2 part series (2-6 months apart)

Mental Health

- Depression and anxiety are higher in the IBD population
 - Burden of living with a chronic illness without a cure
 - Decreased quality of life
 - Poor adherence to therapy/appointments
 - Loss of control
 - Substance abuse
- Frequent screening recommended
- Identify support systems/lack of support

Special Populations in IBD



Pregnancy in IBD

- **Biggest risk to fetus = active disease!**
 - If concerns about medications → discuss with GI before discontinuing treatment!
- PIANO Study
 - NO increased risk of adverse events (congenital malformations, spontaneous abortions, preterm birth, low birth weight) in patients on biologics and/or thiopurines
 - Increased risk of infections if preterm birth
- Medication guidance
 - **Contraindicated:** methotrexate
 - **Avoid:** corticosteroids, ozanimod, JAK inhibitors (tofacitinib, upadacitinib)
 - **Continue:** mesalamine/sulfasalazine, azathioprine/6-MP, anti-TNF, IL 12/23 inhibitors, vedolizumab, low dose aspirin
 - Time last dose of anti-TNF therapy with due date

Pregnancy in IBD

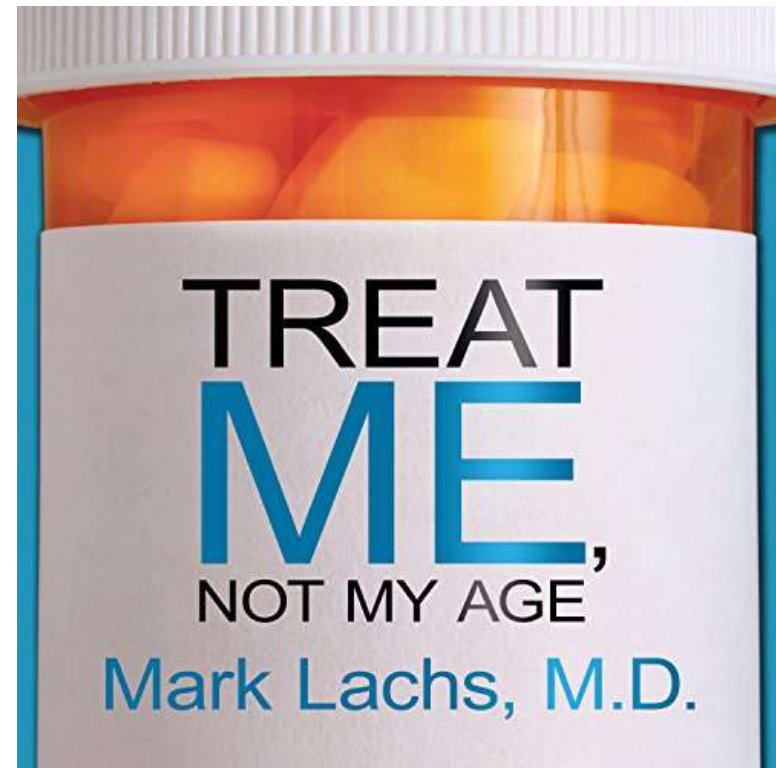
- Breastfeeding is safe for patients on biologics 😊
 - No adverse effects on growth, milestones, or infection rate
 - Not enough data for small molecules
- Infant vaccinations
 - Give all inactivated vaccines as scheduled
 - Avoid live vaccines within the first 6 months if immunosuppressed; 12 months if breastfeeding (Rotavirus)

Aging in IBD

- Older adults are living longer
 - Projected increase of 200% for older adults with IBD
 - 2015: 26% of IBD patients were over age 65
- No change in disease phenotype
- Considerations in aging population
 - Comorbidities
 - Infections
 - Malignancies
 - SCREEN FOR OSTEOPOROSIS!

Aging in IBD

- Medication guidance
 - **Avoid:** thiopurines, corticosteroids
 - **Consider:** vedolizumab, IL 12/23 inhibitors
 - **Discuss based on clinical picture:**
 - Anti-TNF: if minimal melanoma and leukemia/lymphoma risks
 - Methotrexate: if minimal melanoma risks
 - JAK inhibitors: if minimal cancer risks
 - Ozanimod: if minimal leukemia/lymphoma risks



<https://m.media-amazon.com/images/I/513MH6VJ2cL.jpg>

Summary

- Pathogenesis of IBD is multifactorial
 - Genetics, environment, microbiome, immune dysfunction
- IBD is chronic and risks change across the lifespan
- Treatment is multifaceted considering risks of medications, severity of disease and outcomes
- Patients need ongoing monitoring – growth, bone health and immunizations
 - Multidisciplinary approach
- Ultimate Goal = live a normal life!

Back to our patient...

- Patient: Vanessa, 19 yo Caucasian female
- Chief complaint: abdominal pain, diarrhea
- HPI: Started noticing periumbilical and RLQ abdominal pain for the past few months. Crampy in quality, lasts several minutes in duration but waxes and wanes throughout the day. Exacerbated postprandially "sometimes," also reports pain prior to defecation. Alleviated following bowel movements on occasion "but not always." Reported having 1-4 formed bowel movements daily until 2 weeks ago. Thought it was due to stress from school.
- For the past 2 weeks: now having mushy to watery stools 4-5 times/day. Has woken from sleep 3-4 nights since onset of looser stools. No sick contacts. States she thinks the diarrhea started after eating Chipotle. No blood in stools but has seen mucus more recently.

Back to our patient...

- PMHx: **seasonal allergies**
- Social Hx: drinks “socially on weekends,” **smokes** 1/2 ppd, sophomore in college
- Family Hx: HTN in father, hypothyroidism in mother, sister with IBS, CVA in maternal grandmother, maternal aunt “avoids gluten”
- Surgical Hx: tympanostomy tubes age 4 for **recurrent otitis media** → **frequent ABX?**
- Medications: cetirizine daily, albuterol inhaler PRN, recently used **naproxen BID** for shoulder injury after slipping on some ice

Back to our patient...

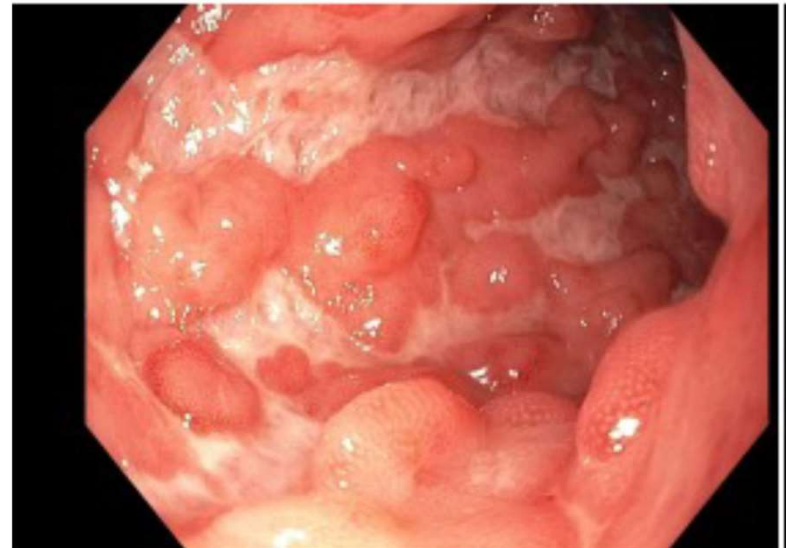
- Vitals: P 96, RR 14, Temp 99.0 F, SpO2 100% RA, Weight 110 lbs (down from 122 lbs 8 months ago), Height 64 inches
- General: Thin-appearing, well-developed female in no acute distress
- Head: Normocephalic, atraumatic
- Eyes: Conjunctival pallor bilaterally, no scleral icterus
- ENT: TM's translucent and mobile, tympanostomy tubes in place bilaterally
- Cardiac: RRR, 2/6 systolic murmur, no rubs or gallops
- Pulmonary: Clear to auscultation bilaterally
- Abdomen: Soft, voluntary guarding, mild TTP in RLQ, bowel sounds normoactive in all 4 quadrants
- Rectal: Normal sphincter tone, deep fissure midline posteriorly,
- Extremities: No cyanosis, edema, or varicosities. Peripheral pulses intact.
- Skin: Good turgor, 2 4-cm circular erythematous lesions on shins bilaterally with TTP
- Musculoskeletal: Normal gait, no asymmetry
- Neurologic: A&Ox3, CN 2-12 intact

Back to our patient...

- Blood work
 - CBC w/ differential: WBC 11.5 H, Hgb 10.6 L, Hct 32.2 L, MCV 64.4 L, Plt 590 H, RDW 16.5 H, ANC 7.9 H
 - CMP: Albumin 3.2 L
 - ESR: 24 H (0-20)
 - CRP: 1.6 H (<0.8)
 - 25-OH Vitamin D: 18 L
 - Ttg-IgA: WNL
 - Serum IgA: WNL
- Stool studies
 - C.diff: negative
 - Stool culture: negative
 - Ova/parasite: negative x 3
 - Fecal calprotectin: 798 H

Back to our patient...

- EGD
 - mild gross ulceration in the esophagus
 - Active chronic inflammation in the stomach
 - 3 pinpoint ulcerations in the duodenum
- Colonoscopy
 - Moderate edema and ulcerated mucosa in the terminal ileum and cecum
 - Areas of healthy mucosa in the ascending colon, sigmoid colon, and rectum
- MRE to assess small bowel involvement
 - Mild wall thickening of the mid to distal ileum



Treatment

- Started on combination therapy with adalimumab and 6-mercaptopurine
- Patient expressed interest in de-escalation of therapy given clinical wellness 6 months after initiation of therapy
- Repeat EGD/colonoscopy at 12 months → normal endoscopically, chronic inflammatory changes in the ileum histologically 😊
- Discuss de-escalation with close monitoring



https://i.dailymail.co.uk/1/2018/03/15/17/2506704-5506129-image-a-46_1521133206723.jpg

Questions?

Thank you!



References

- Askling J, Dickman PW, Karlén P, et al. Family history as a risk factor for colorectal cancer in inflammatory bowel disease. *Gastroenterology*. 2001;120(6):1356-1362. doi:10.1053/gast.2001.24052
- Beaulieu, D. B., Ananthakrishnan, A. N., Martin, C., Cohen, R. D., Kane, S. V., & Mahadevan, U. (2018). Use of biologic therapy by pregnant women with inflammatory bowel disease does not affect infant response to vaccines. *Clinical Gastroenterology and Hepatology*, 16(1), 99-105.
- Benchimol EI, Fortinsky KJ, Gozdyra P, Van den Heuvel M, Van Limbergen J, Griffiths AM. Epidemiology of pediatric inflammatory bowel disease: a systematic review of international trends. *Inflamm Bowel Dis*. 2011;17(1):423-439. doi:10.1002/ibd.21349
- Coward S, Clement F, Benchimol EI, et al. Past and Future Burden of Inflammatory Bowel Diseases Based on Modeling of Population-Based Data. *Gastroenterology*. 2019;156(5):1345-1353.e4. doi:10.1053/j.gastro.2019.01.002.
- Dahlhamer JM, Zammitti EP, Ward BW, Wheaton AG, Croft JB. Prevalence of Inflammatory Bowel Disease Among Adults Aged ≥ 18 Years — United States, 2015. *MMWR Morb Mortal Wkly Rep* 2016;65:1166–1169. DOI: <http://dx.doi.org/10.15585/mmwr.mm6542a3external> icon.
- Dassopoulos T, Cohen RD, Scherl EJ, Schwartz RM, Kosinski L, Regueiro MD. Ulcerative Colitis Care Pathway. *Gastroenterology*. 2015;149(1):238-245. doi:10.1053/j.gastro.2015.05.036
- de Souza HSP, Fiocchi C. Network medicine: a mandatory next step for inflammatory bowel disease. *Inflamm Bowel Dis*. 2018;24:671–679.
- Glassner, K. L., Abraham, B. P., & Quigley, E. M. (2020). The microbiome and inflammatory bowel disease. *Journal of Allergy and Clinical Immunology*, 145(1), 16-27.

References (continued)

- Heyman, M. B., Kirschner, B. S., Gold, B. D., Ferry, G., Baldassano, R., Cohen, S. A., . . . El-Serag, H. B. (2005). Children with early-onset inflammatory bowel disease (IBD): Analysis of a pediatric IBD consortium registry. *Journal of Pediatrics*, 146(1), 35-40.
- Jose, F. A., & Heyman, M. B. (2008). Extraintestinal manifestations of inflammatory bowel disease. *Journal of Pediatric Gastroenterology and Nutrition*, 46(2), 124-133.
- Julsgaard M, Christensen LA, Gibson PR, et al. Concentrations of Adalimumab and Infliximab in Mothers and Newborns, and Effects on Infection. *Gastroenterology*. 2016;151(1):110-119. doi:10.1053/j.gastro.2016.04.002
- Kappelman MD, Moore KR, Allen JK, Cook SF. Recent trends in the prevalence of Crohn's disease and ulcerative colitis in a commercially insured US population. *Dig Dis Sci*. 2013;58(2):519-525. doi:10.1007/s10620-012-2371-5.
- Khan N, Vallarino C, Lissoos T, Darr U, Luo M. Risk of Malignancy in a Nationwide Cohort of Elderly Inflammatory Bowel Disease Patients. *Drugs Aging*. 2017;34(11):859-868. doi:10.1007/s40266-017-0498-y.
- Lindberg BU, Broomé U, Persson B. Proximal colorectal dysplasia or cancer in ulcerative colitis. The impact of primary sclerosing cholangitis and sulfasalazine: results from a 20-year surveillance study. *Diseases of the Colon and Rectum*. 2001 Jan;44(1):77-85. DOI: 10.1007/bf02234825. PMID: 11805567.
- Loftus CG, Loftus EV Jr, Harmsen WS, et al. Update on the incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota, 1940-2000. *Inflamm Bowel Dis*. 2007;13(3):254-261. doi:10.1002/ibd.20029

References (continued)

- Lutgens MW, van Oijen MG, van der Heijden GJ, Vleggaar FP, Siersema PD, Oldenburg B. Declining risk of colorectal cancer in inflammatory bowel disease: an updated meta-analysis of population-based cohort studies. *Inflamm Bowel Dis.* 2013;19(4):789-799. doi:10.1097/MIB.0b013e31828029c0
- Mahadevan U, Long MD, Kane SV, et al. Pregnancy and Neonatal Outcomes After Fetal Exposure to Biologics and Thiopurines Among Women With Inflammatory Bowel Disease. *Gastroenterology.* 2021;160(4):1131-1139. doi:10.1053/j.gastro.2020.11.038
- Matro R, Martin CF, Wolf D, Shah SA, Mahadevan U. Exposure Concentrations of Infants Breastfed by Women Receiving Biologic Therapies for Inflammatory Bowel Diseases and Effects of Breastfeeding on Infections and Development. *Gastroenterology.* 2018;155(3):696-704. doi:10.1053/j.gastro.2018.05.040
- Oliva-Hemker, M., & Fiocchi, C. (2002). Etiopathogenesis of inflammatory bowel disease: The importance of the pediatric perspective. *Inflammatory Bowel Diseases*, 8(2), 112-128.
- Pariente B, Cosnes J, Danese S, et al. Development of the Crohn's disease digestive damage score, the Lémann score. *Inflamm Bowel Dis.* 2011;17(6):1415-1422. doi:10.1002/ibd.21506
- Ponder, A. D., & Long, M. D. (2013). A clinical review of recent findings in the epidemiology of inflammatory bowel disease. *Clinical Epidemiology*, 5, 237-247.
- Rubin, D. T., Abreu, M. T., Rai, V., & Siegel, C. A. (2020). Management of patients with Crohn's disease and ulcerative colitis during the coronavirus disease-2019 pandemic: Results of an international meeting. *American Journal of Gastroenterology*, 159(1), 6-13.

References (continued)

- Rubin DT, Huo D, Kinnucan JA, et al. Inflammation is an independent risk factor for colonic neoplasia in patients with ulcerative colitis: a case-control study. *Clin Gastroenterol Hepatol.* 2013;11(12):1601-8.e84. doi:10.1016/j.cgh.2013.06.023
- Rutter M, Saunders B, Wilkinson K, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. *Gastroenterology.* 2004;126(2):451-459. doi:10.1053/j.gastro.2003.11.010
- Sandborn WJ. Crohn's disease evaluation and treatment: clinical decision tool. *Gastroenterology.* 2014;147(3):702-705. doi:10.1053/j.gastro.2014.07.022
- Sandborn, W. J., Su, C., Sands, B. E., D'Haens, G. R., Vermeire, S., Schreiber, S., . . . Panes, J. (2017). Tofacitinib as induction and maintenance therapy for ulcerative colitis. *New England Journal of Medicine*, 376(18), 1723-1736.
- Sauer, C. G., & Kugathasan, S. (2009). Highlighting pediatric differences in IBD. *Medical Clinics of North America*, 94(1), 35-52.
- Stein, R. B., & Hanauer, S. B. (1999). Medical therapy for inflammatory bowel disease. *Gastroenterology Clinics of North America*, 28(2), 297-321.
- Turner D, Bishai J, Reshef L, et al. Antibiotic Cocktail for Pediatric Acute Severe Colitis and the Microbiome: The PRASCO Randomized Controlled Trial. *Inflamm Bowel Dis.* 2020;26(11):1733-1742. doi:10.1093/ibd/izz298
- Xu F, Carlson SA, Liu Y, Greenlund KJ. Prevalence of Inflammatory Bowel Disease Among Medicare Fee-For-Service Beneficiaries — United States, 2001–2018. *MMWR Morb Mortal Wkly Rep* 2021;70:698–701. DOI: <http://dx.doi.org/10.15585/mmwr.mm7019a2external> icon.