IBD: Diagnosis & Management with COVID-19 Updates

Lindsay Mohrhardt, DO

Spectrum Health

Disclosures

- None

Case Presentation

- 21 y/o male college student presents with 3 months rectal bleeding
- Admits to urgency with stooling
- States he thought it was all related to stress from school
- Labs drawn revealing anemia, thrombocytosis, elevated CRP
- Denies family history of IBD

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- 27 y/o female chef presents with main complaint of diarrhea
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- Denies rectal bleeding
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Inflammatory Bowel Disease

Ulcerative Colitis	Crohn's Disease
• Affects only the colon mucosa & Submucosa • Extends in a contiguous fashion (usually beginning at the anal verge) • Crypt abscesses on pathology	• Can affect any portion of the GI tract from mouth to anus • Transmural intestinal inflammation • Can have patchy distribution, or skip lesions with areas of uninvolved mucosa • Fistulizing disease & stricturing disease • Can see crypt abscesses and granulomas on pathology

Epidemiology

- Historically thought to be disease of western world
- Incidence of IBD is increasing in US & Globally
- Data from last 10 years shows increase in incidence in newly industrialized countries in Asia (including China & India)
- With aging population, we are also seeing an increase in the prevalence of IBD

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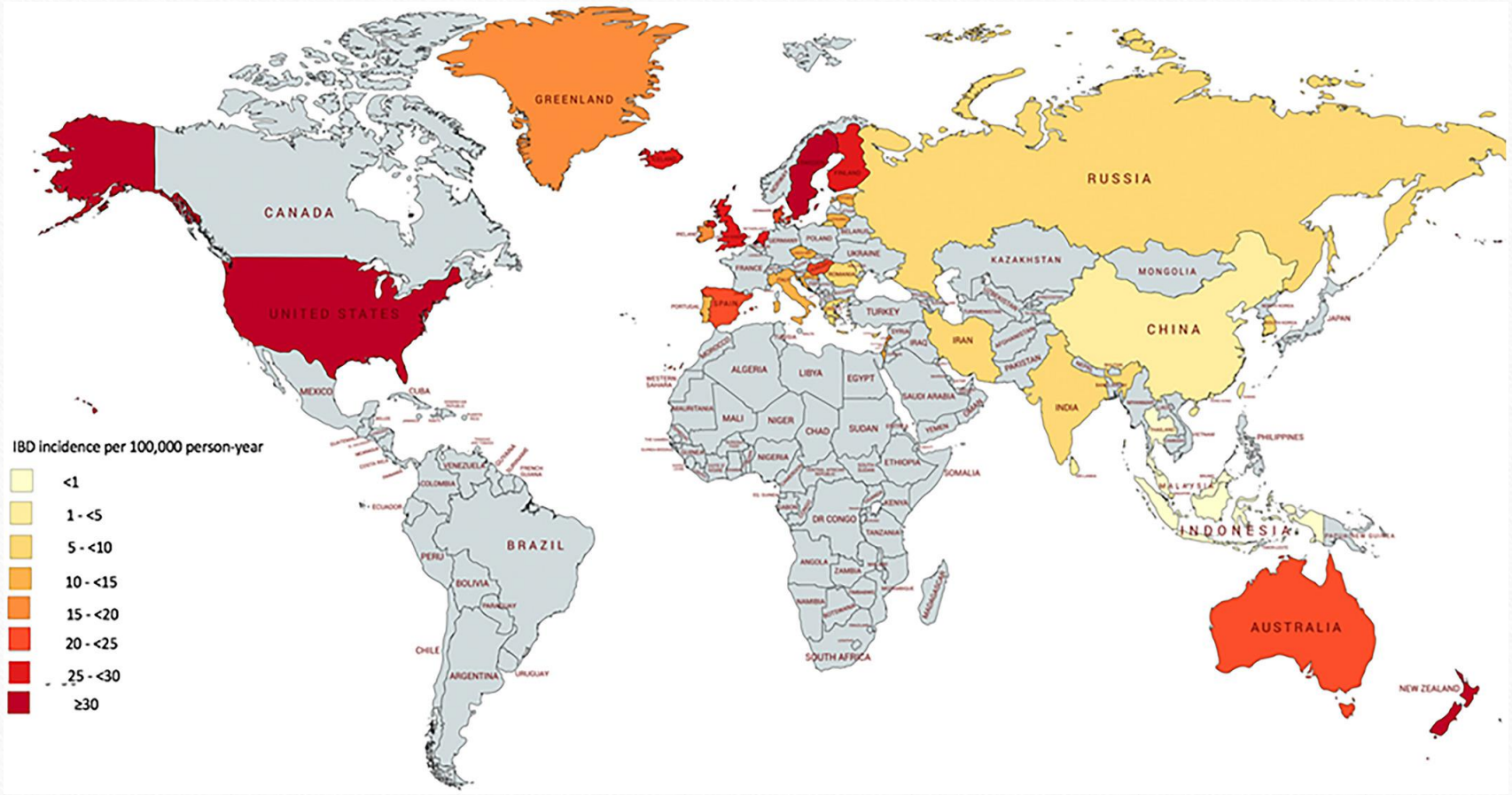
The epidemiology of inflammatory bowel disease: East meets west



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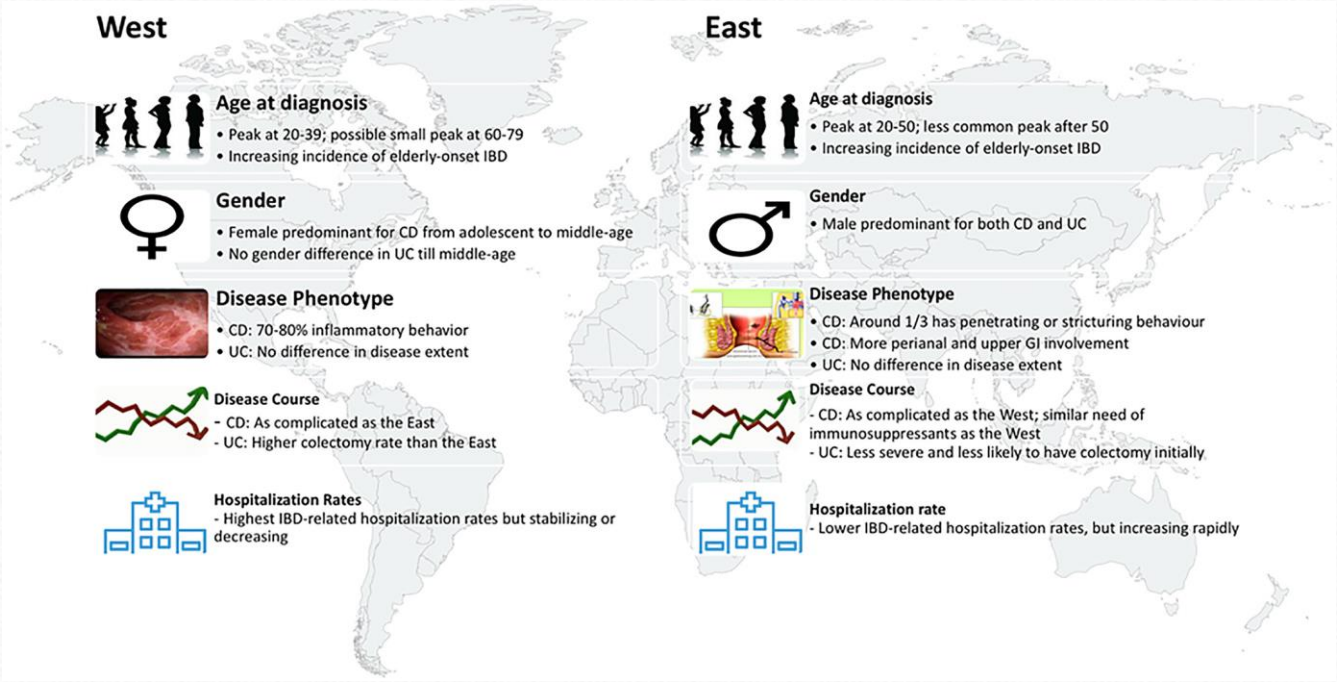
Epidemiology

- Age: average onset 15-30 years with possible 2nd peak age 50-80 years
- Sex: Slight female predominance w/ CD & slight male predominance w/ UC
- Race/ Ethnicity:
  - More common in Jewish
  - Incidence lower in Hispanic and black population as compared to white population

The epidemiology of inflammatory bowel disease: East meets west



Journal of Gastroenterology and Hepatology, Volume: 35, Issue: 3, Pages: 380-389, First published: 09 October 2019, DOI: (10.1111/jgh.14872)

Epidemiology

- Genetics:
  - May play role in IBD
  - Possibly more in CD than UC
  - 1st degree relatives w/ IBD are 3-12 times more likely to develop IBD than general population
  - Over 200 distinct loci for susceptibility

Epidemiology

- Serum Antibody test
  - Anti-Saccaromyces cervisiae (ASCA) found in 96-100% of CD patients, but only 50% sensitive
  - Perinuclear antineutrophilic cytoplasmic antibody (P-ANCA) found in 70% of UC patients, but only 18% of those with CD
  - At this time, there is no recommendation for their use

Tomoko Sairenji MD, MS, Kimberly L. Collins MD and David V. Evans MD
Primary Care: Clinics in Office Practice, 2017-12-01, Volume 44, Issue 4, Pages 673-692, Copyright © 2017 Elsevier Inc.

Epidemiology

- Smoking linked to increase risk of CD, yet seems protective in UC
- In under 20 year old population, appendectomy suggested to protect against development of UC
- Breastfeeding for infants found to be protective
- Association between antibiotic exposure in early childhood and IBD

Presentation

- Clinical symptoms depend on anatomic location and CD vs UC
- Abdominal pain
- Rectal bleeding
- Diarrhea
- Fatigue
- Anemia
- Weight loss
- Palpable abdominal mass
- Extraintestinal manifestations
- Fever

Differential Diagnosis

- Infectious (bacterial, viral, parasitic)
- Microscopic colitis
- Diverticular associated colitis
- Appendicitis
- Ischemic colitis
- Lymphoma
- Solitary rectal ulcer syndrome
- Malignancy
- Typhlitis

Ulcerative Colitis

- 15% of patients may experience an aggressive course
- 20% of patients may require hospitalization for severe disease activity
- 5- & 10- year cumulative risk of colectomy is 10-15% (mainly limited to patients w/ mod-severe disease)

Ulcerative Colitis

- Predictors of an aggressive disease course:
  - Young age at diagnosis (<40 years old)
  - Extensive disease
  - Severe endoscopic activity (large & deep ulcers on endoscopy)
  - Presence of extra-intestinal manifestations
  - Early need for corticosteroids
  - Elevated inflammatory markers

Feurerstein J, Isaacs K Gastroenterology 2020:158:1450-1461

Ulcerative Colitis

- Truelove & Witts criteria
  - Moderate to severe:
    - > 6 bloody bowel movements/ day
    - At least one marker systemic toxicity (HR >90 beats/min, temp > 37.8 C, Hemoglobin <10.5 g/dL, and/ or ESR 30 mm/h)

Crohn's Disease

- Approximately 20% of patients w/ CD were hospitalized every year
- Risk of surgery within 1 year of diagnosis was 24%, 36% at 5 years, and 47% by 10 years
- Outcomes have improved recently
  - Earlier diagnosis
  - Use of biologics
  - Escalation or alteration of therapy

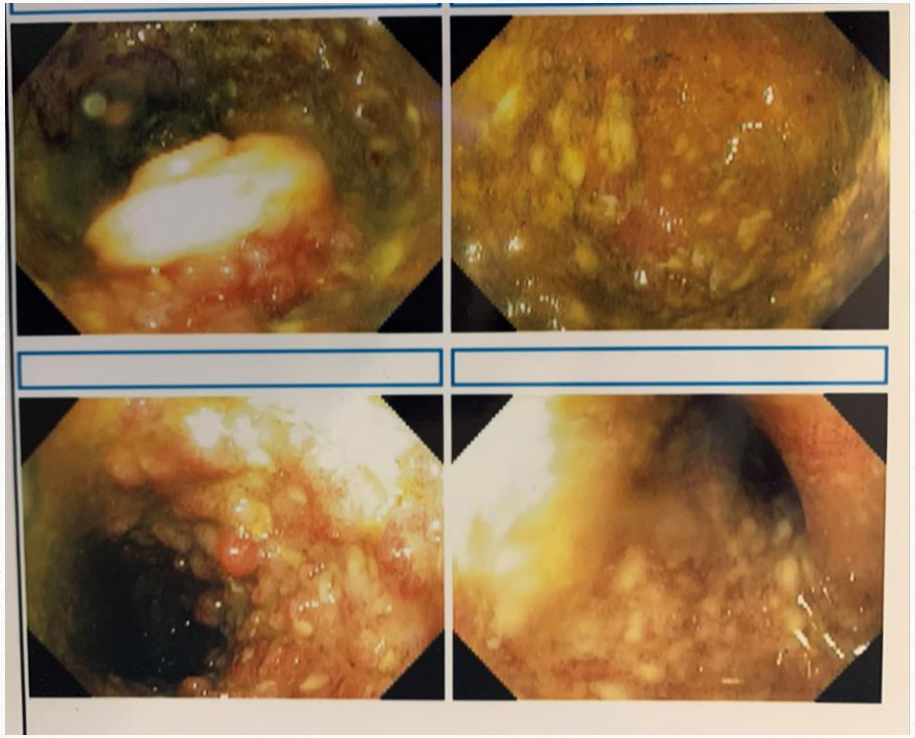
Crohn's Disease

- Contributors to severe disease
  - Large or deep mucosal lesion on endoscopy or imaging
  - Presence of fistula and/or perianal abscess
  - Presence of strictures
  - Prior intestinal resections
  - Extensive disease
  - Anemia
  - Elevated CRP
  - Low albumin

Diagnosis

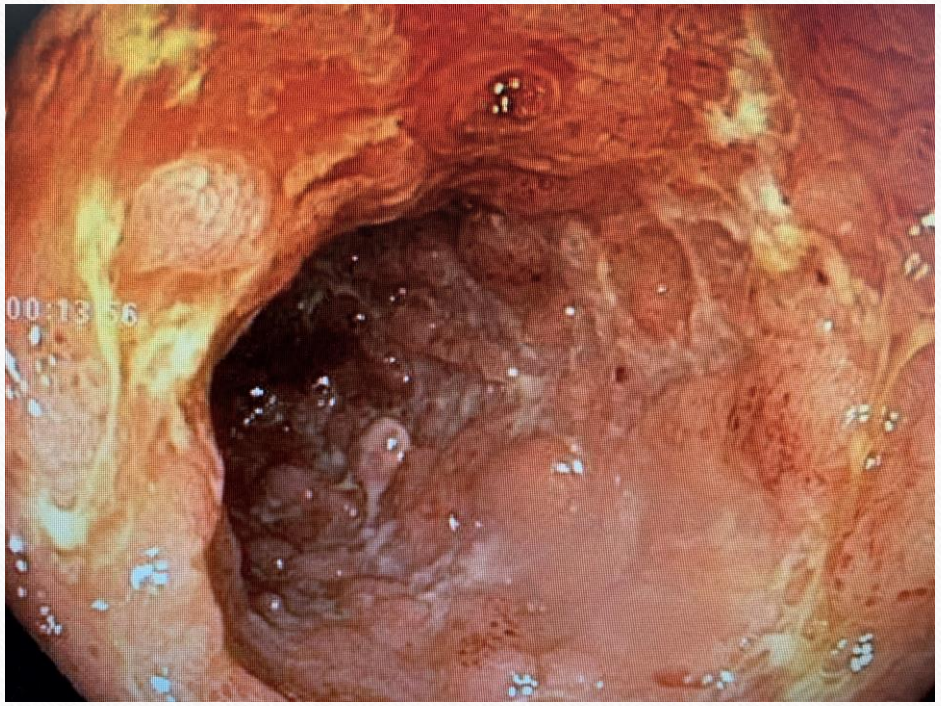
- Labs
  - CBC, CMP, ESR, CRP
  - Stool studies (rule out infectious source), Fecal calprotectin
- Radiology
  - Barium enema (rarely used anymore)
  - CT or MR enterography
  - Regular CT abd/pelvis
- Endoscopy
  - EGD, Colonoscopy, Capsule endoscopy

Diagnosis- Ulcerative Colitis



From personal collection of Lindsay Mohrhardt

Diagnosis



Shared from the personal collection of Dorian T. Jones, MD.

Case Presentation

- 21 y/o male college student presents with 3 months rectal bleeding
- Admits to urgency with stooling
- States he thought it was all related to stress from school
- Labs drawn revealing anemia, thrombocytosis, elevated CRP
- Denies family history of IBD

Answer!

- Ulcerative colitis

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Answer!

- Crohn's Disease

Treatment

- 5-ASA class
  - Sulfasalazine, mesalamine, & diazo-bonded 5-ASA
- Immunomodulator
  - Azathioprine, 6-MP, Methotrexate, corticosteroids
- Biologics
  - TNF-α antagonist, anti-integrin agents, Interleukin 12/23 antagonist

5-ASA

- Sulfasalazine:
  - One of the oldest medications in this class
  - Consists of 5-ASA bonded to sulfapyridine
    - Converted to 5-ASA by colonic bacteria
    - Sulfapyridine is thought to be the contributor to adverse effects of the drug

5-ASA

- Diazo-bonded 5-ASA
  - Prodrug converted to 5-ASA by colonic bacteria
  - Olsalazine
    - Enteric and non-enteric coated
    - Delayed-release enteric coated pH sensitive to release in distal ileum and colon
  - Balsalazide
    - Controlled release delivery beginning in the duodenum and continuing in lower bowel

Topical Mesalamine

- Suppository:
  - Used to treat rectosigmoid disease to 20 cm
- Enema
  - Used to treat left colon to splenic flexure

5-ASA Adverse Effects

- Mesalamine
  - Uncommon idiosyncratic worsening of colitis (presumed hypersensitivity syndrome)
  - Interstitial nephritis
- Diazo-bonded
  - Secretory diarrhea (mainly olsalazine)
  - Rare idiosyncratic worsening of colitis (presumed hypersensitivity syndrome)
  - Rare interstitial nephritis
- Sulfasalazine
  - Interferes w/ folate metabolism
  - Male infertility
  - Rare cutaneous S/E (Stevens-Johnson syndrome)
  - Anemia, leukopenia, pneumonitis
  - Hepatitis

5-ASA Treatment

- Mild to moderate extensive UC
  - Oral mesalamine
- Mild to moderate extensive UC or left sided mild to moderate UC
  - American Gastroenterology Association (AGA) recommends adding rectal mesalamine to oral therapy
- Mild to moderate ulcerative proctosigmoiditis or proctitis
  - AGA recommends using mesalamine enemas (or suppositories) over oral mesalamine

Immunomodulators

- Azathioprine (AZA) is a derivative of 6-mercaptopurine (6-MP)
- Metabolized in liver using two pathways
  - Thiopurine S-methyltransferase (TPMT)
  - Xanthine oxidase
- 10% of population is heterozygous for non-functioning TPMT allele
  - Can result in life threatening myelosuppression
  - Those with intermediate levels can be given lower level of drug

Bass A, Rogatsky, Goldman-Cecil Medicine 32, 156-161. e2

Immunomodulators

- Methotrexate
  - Inhibits dihydrofolic acid reductase
  - Subcutaneous or oral dosing
  - Excreted through the kidneys
    - Dose reduction in renal insufficiency
  - Monitor for liver toxicity and bone marrow suppression
  - Monitor renal function
  - Give folic acid 1mg daily with use
  - Teratogenic (CI in pregnant women, must be using contraception/ birth control)

Bass A, Rogatsky, Goldman-Cecil Medicine 32, 156-161. e2

Anti-TNF Agents

- Infliximab
  - Infusion
- Adalimumab
  - Subcutaneous
- Certolizumab
  - Subcutaneous

Anti-TNF Side Effect

- Increased risk of infection
  - Acute sinusitis
  - Assess for latent TB and Hepatitis B infection before starting and in certain patients, histoplasmosis
- Psoriasis
- Skin cancers
- Worsening or new heart failure
- Rare: Hepatosplenic T cell lymphoma (when used with thiopurine in males <35 yrs)
- Infusion or injection site reaction
- Myalgias, arthralgias
- Autoantibody formation- can cause rare drug-induced lupus-like reaction

Anti-Integrin Agents

- Vedolizumab
  - Humanized Immunoglobulin G1 monoclonal Ab which modulates gut, and not brain
  - Adverse events: nasopharyngitis, headache, nausea, vomiting, arthralgia
- Natalizumab
  - Fell out of favor due to risk of Progressive Multifocal Leukoencephalopathy (PML) caused by reactivation of the Jc Virus

Sandborn W, Feagan B N Eng J 2013; 369:711-721.

Interleukin 12/23 Antagonist

- Ustekinumab
  - One of the newer biologics
  - Common adverse events:
    - Nasopharyngitis
    - Headache
    - Arthralgia
    - URI
  - Rare adverse events:
    - Cancer risk
    - MI

Sands B, Sandborn W N Engl J Med 2019: 381:1201-1214

Biosimilars

- Biologic agent highly similar to an existing FDA –approved biologic agent
  - Chemical activity is similar and no clinically meaningful difference
  - Not considered "generics" which contain the same chemical substance as the original brand drug
- Current biosimilars available for Infliximab and Adalimumab
- Data shows it is ok to switch between drugs and to initiate care with new biosimilars.

Treatment Tips

- NSAIDS are not suggested for use of pain control in IBD patients and can worsen inflammation
- Avoid Narcotics in these patients (risk of decreased motility, megacolon, perforation)
- If you feel a patient needs to stop their medications for whatever reason, make sure the patient contacts their prescriber
- Try to avoid multiple courses of steroids
  - If patient is needing multiple courses of steroids, this means they may need dose escalation or change/ addition of medication

Infectious Complications

- Cytomegalovirus (CMV)
  - Reactivation is common in patient with severe colitis (Ulcerative Colitis or Crohn's Colitis) (prevalence of 4.5-16.6%)
  - Diagnosed by biopsies from colonoscopy
  - High risk of needing colectomy
  - Treatment with Gancyclovir (IV then oral) or Valgancyclovir

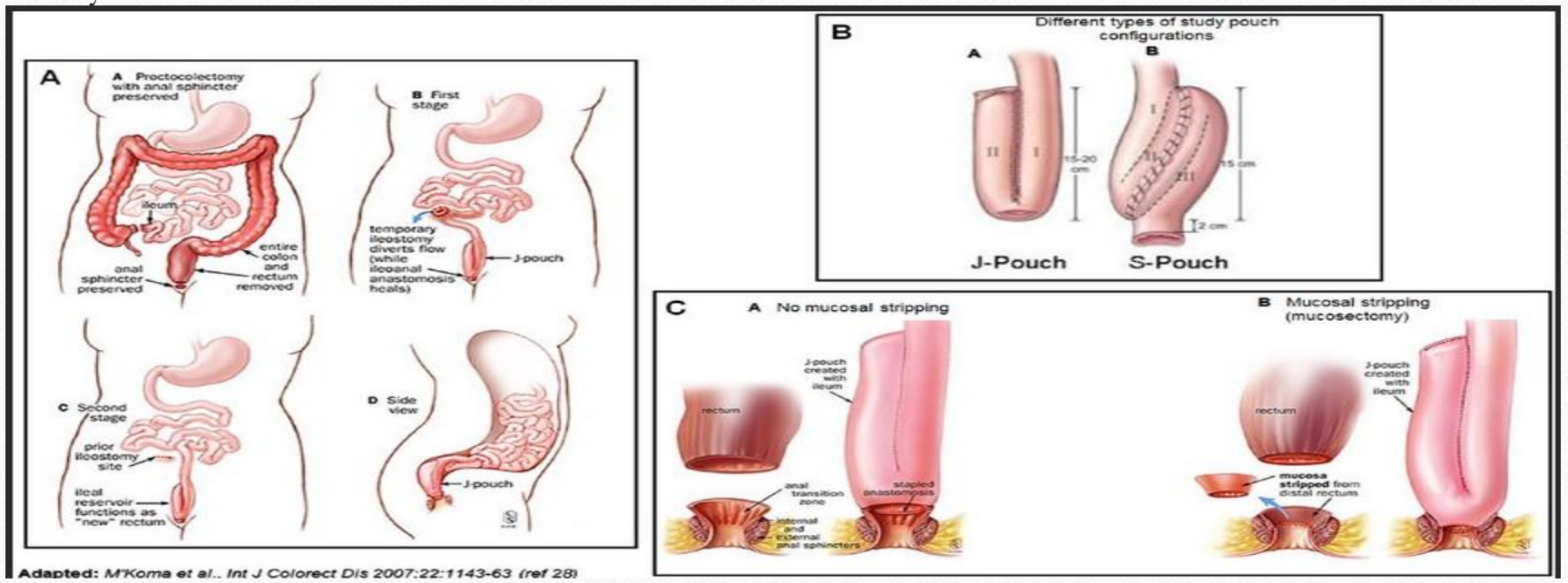
Sager K, Bond A; AP &T; Cytomegalovirus and Inflammatory Bowel Disease; 2015 (41); 725-733.

Infectious Complications

- Clostridium Difficile
  - Pts w/ IBD and C. Diff associated with increased morbidity
    - Escalation in IBD medical therapy, urgent colectomy, and increased hospitalization
  - Steroids are a risk factor for C. Diff, however immunomodulators and biologics are not considered to be increased risk factors
  - Treat 1st line with Vancomycin regimen.
    - Recurrence can be treated with Vanco taper, Fidaxomycin, or fecal transplant
  - Ok to restart patients on biologics 24-48 hours after starting therapy

Pouchitis

- Proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the preferred surgical treatment for refractory UC



Adapted: M'Koma et al., Int J Colorect Dis 2007:22:1143-63 (ref 28)

Pouchitis

- Most common complication occurring after IPAA
  - Acute, chronic/ recurrent, or secondary, occurring due to crohn's disease
- Patients with PSC, NSAID use, & Non-smokers have increased incidence of pouchitis
- Etiology largely unknown
  - Possibly bacterial dysbiosis & alteration in host immunity

Pouchitis

- Symptoms
  - Increased urgency and frequency in stool
  - Blood in stool
  - Abd pain/ cramping
  - Possible fever
- Treatment
  - Antibiotics
  - Small study discussed using Probiotic VSL #3 to prevent pouchitis

Immune-Checkpoint Inhibitors

- New agents for cancer therapy in the last decade
- 10-20% of patients getting Ipilimumab are observed to have colitis
- There can also be a diffuse enteritis
- Ulcerations are diffuse and can affect the entire colon, just like IBD
- Pathology is different than that of IBD
- Patients will need steroids, and possibly infliximab
- Important to get a history and review pathology to distinguish this from IBD

Martins F, Sofiya L, et al; Adverse effects of immune-checkpoint inhibitors: epidemiology, management, and surveillance. Nat Rev Clin Oncol 16, 563-580 (2019)

Health Maintenance Monitoring

Vaccines and Infections

Influenza: All patients >6 months of age should receive annual inactivated influenza vaccine, irrespective of immunosuppression status.

MMR: IBD Patients not immune to MMR should receive a 2-dose series, at least 4 weeks apart. If immune status is uncertain, IgG antibody titer should be checked. MMR should not be given to patients currently on systemic immunosuppressive* therapy.

Pneumococcus: All patients >19 years age receiving systemic immunosuppression* should receive PCV13, followed by PPSV23 at least 8 weeks later, and a booster of PPSV23 5 years later.

Varicella: Seroprotection status should be checked with varicella zoster virus IgG antibodies in all patients without documented vaccination record or exposure. All patients who are not immune should receive a 2-dose series, 4–8 weeks apart, ≥4 weeks before immunosuppression, if therapy can be postponed.

Zoster: All patients receiving JAK inhibitor therapy should receive the recombinant adjuvanted zoster vaccine. Risk of zoster should be considered with combinations of other immunosuppressive* therapies.

TB: Screen for latent TB in all patients with IBD, at baseline. Perform clinical risk assessment for TB exposure annually in all patients with IBD.

Crohn's & Colitis Foundation Professional Education Sub-Committee; Jill Gaidos MD, Alan Moss MD, Mariastella Serrano MD, Gaurav Syal MD • 6/10/2020

Monitoring

Cancer Screening

Colorectal Cancer: All IBD patients with extensive colitis (>1/3 of the colon) for ≥ 8 years should undergo surveillance colonoscopy every 1–3 years, depending on cancer risk;

- IBD patients with a diagnosis of PSC should undergo colonoscopy, starting at the time of PSC diagnosis, and annually thereafter.
- IBD patients with features that are high-risk for developing colon cancer (i.e. prior history of adenomatous polyps, dysplasia, family history of colon cancer and extensive colitis) should have colonoscopies more frequently than every 3 years.

Cervical Cancer: All women with IBD who are being treated with systemic immunosuppression* should undergo cervical cancer by cytology annually (if cytology alone) or every 2 years (if HPV negative).

Skin Cancer: All IBD patients being treated with systemic immunosuppression* should have annual total body skin exams to screen for skin cancer.

Health Maintenance Monitoring

Other Protection

Osteoporosis: Screen for osteoporosis by central (hip and spine) DXA scan in all patients with IBD if ANY risk factors for osteoporosis; low BMI, >3 months cumulative steroid exposure, smoker, post-menopausal, hypogonadism. Repeat in 5 years if initial screen is normal.

Depression/Anxiety: Screen all patients with IBD for depression (PHQ9) and anxiety (GAD7) at baseline, and annually. Refer for counseling/therapy when identified.

Smoking: Screen all patients with IBD for smoking status at baseline, and refer current smokers for smoking cessation therapy.

Crohn's & Colitis Foundation Professional Education Sub-Committee; Jill Gaidos MD, Alan Moss MD, Mariastella Serrano MD, Gaurav Syal MD • 6/10/2020

Extraintestinal Manifestation

- Frequency can range from 6-47%
- Most frequently affect joints, skin, or eyes
  - Less frequently liver, lungs, pancreas
- May present before inflammatory bowel disease diagnosis
- Successful recognition & therapy of EIMS is important for quality of life in IBD patients

Inflamm Bowel Dis. 2015 Aug; 21(8): 1982–1992.

Extraintestinal Manifestations

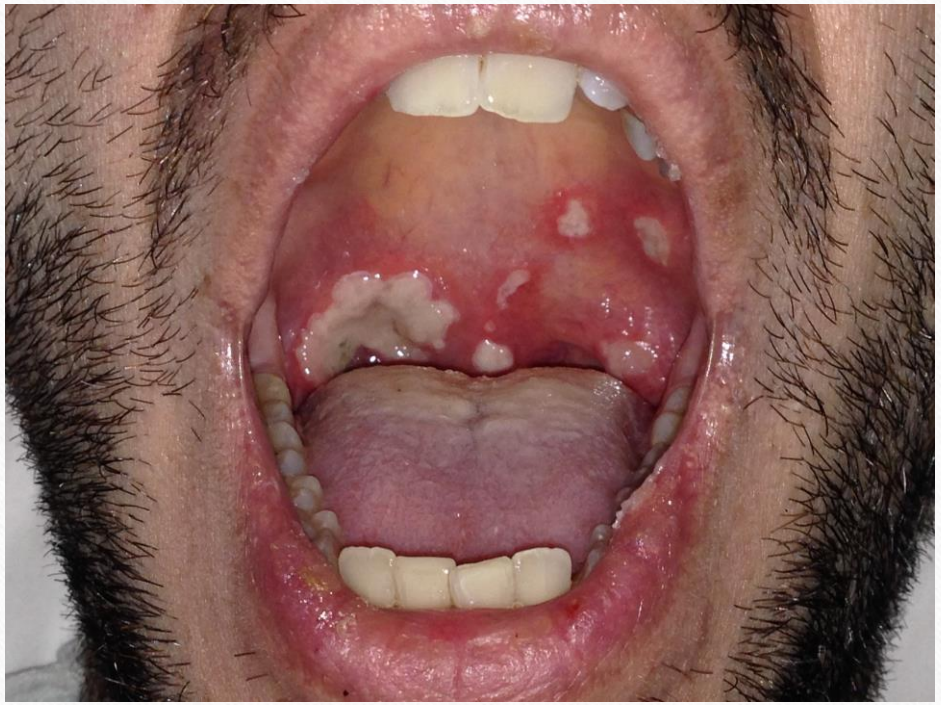
Follows active disease course	Independent of disease activity	Unclear association
• Peripheral arthritis, oral aphthous ulcers, episcleritis, & erythema nodosum	• Uveitis, ankylosing spondylitis (axial arthropathies)	• Pyoderma gangrenosum, primary sclerosing cholangitis

Extraintestinal Manifestations

Musculoskeletal system	• Arthritis: ankylosing spondylitis, isolated joint involvement • Hypertrophic osteoarthropathy: clubbing, periostitis • Other: aseptic necrosis, polymyositis
Dermatologic/Oral system	• Reactive lesions: erythema nodosum, pyoderma gangrenosum, aphthous ulcers, necrotizing vasculitis • Specific lesions: fissures, fistulas, oral Crohn disease, drug rashes • Nutritional deficiencies: acrodermatitis enteropathica, purpura, glossitis, hair loss, brittle nails • Associated diseases: vitiligo, psoriasis, amyloidosis
Hepatopancreatobiliary system	• Primary sclerosing cholangitis, bile-duct carcinoma • Associated inflammation: autoimmune chronic active hepatitis, pericholangitis, portal fibrosis, cirrhosis, granulomatous disease • Metabolic manifestations: fatty liver, gallstones associated with ileal Crohn disease
Hematologic	Anemia, hyperhomocysteinemia
Ocular system	Uveitis/iritis, episcleritis, scleromalacia, corneal ulcers, retinal vascular disease
Metabolic system	Growth retardation in children and adolescents, delayed sexual maturation, osteopenia/osteoporosis
Renal system	Calcium oxalate stones

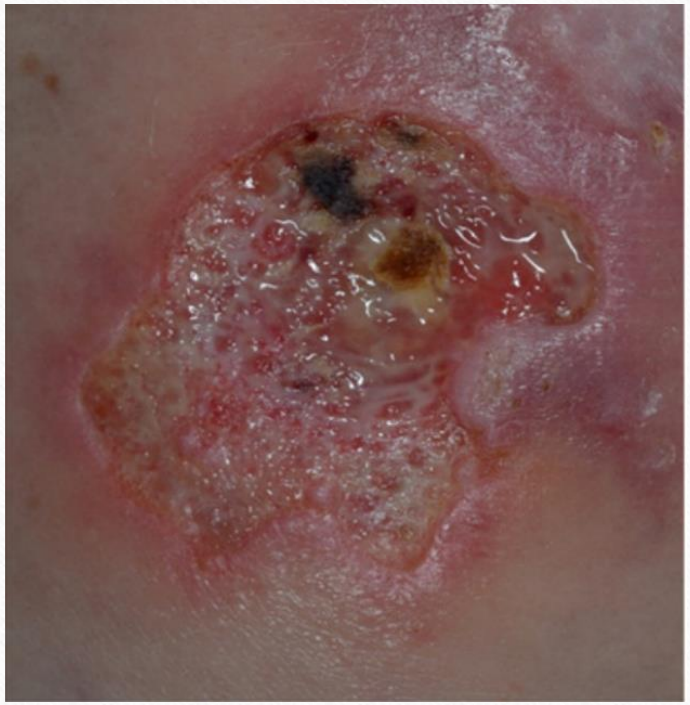
Sairenji T, Collins K. Pri Care, 2017, 44; 673-692

Oral Aphthous Ulcerations



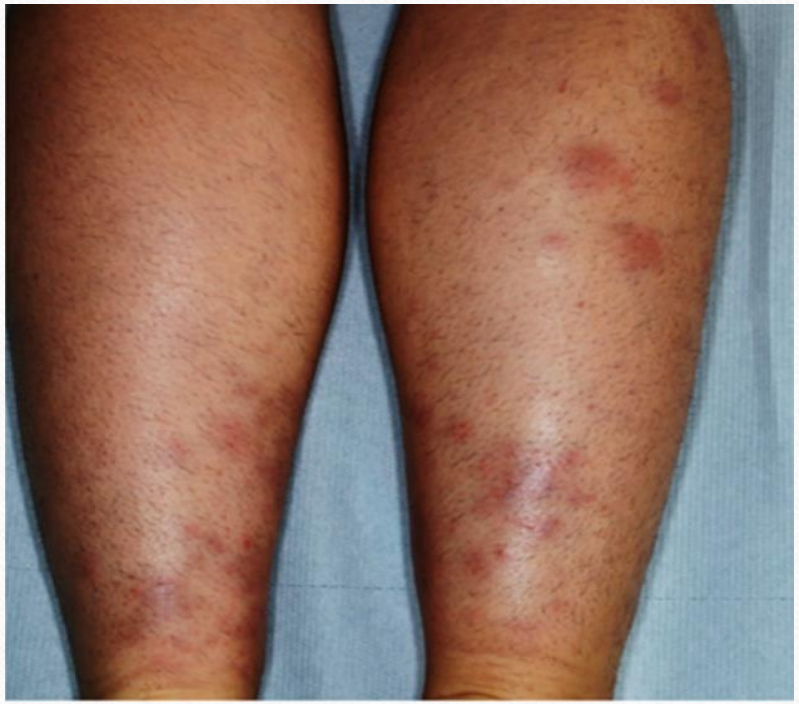
Taken from Lindsay Mohrhardt personal collection

Pyoderma Gangrenosum



Antonelli, E et all. Dermatological Manifestations in Inflammatory Bowel Disease. J Clin Med. 2021; 10(2)364

Erythema Nodosum



Antonelli, E et all. Dermatological Manifestations in Inflammatory Bowel Disease. J Clin Med. 2021; 10(2)364

Treatment EIMs

EIM Organ	Specific EIM	First-line Therapy	Second-line Therapy	References
Joints	Peripheral arthritis	Intraarticular/oral steroids, sulfasalazine, immunomodulators, COX-2 inhibitors; treatment of IBD flare (type 1)	IFX, adalimumab	Generini et al[32]
	Type 1 (large joints)			Herfarth et al[33]
	Type 2 (small joints)			Atzeni et al[34]
	Axial arthropathies	Physiotherapy, COX-2 inhibitors, MTX, sulfasalazine	IFX, adalimumab	Sarzi-Puttini et al[35]
	Ankylosing spondylitis			Kaufmann et al[36]
	Sacroileitis			Generini et al[32]
Skin	Pyoderma gangrenosum	Oral steroids, cyclosporine, immunosupressives	IFX, adalimumab	Brooklyn et al[37]
				Kaufmann et al[36]
				Regueiro et al[38]
	Erythema nodosum	Treatment of IBD flare	IFX, adalimumab	In Bechet's disease
				Tanida et al[39]
	Sweet's syndrome	Topical/systemic steroids	IFX	Vanbiervliet et al[40]
	Aphthous ulcers	Treatment of IBD flare, topical steroids, oral steroids, topical lidocaine	IFX	Kaufman et al[35]
Liver	PSC	Endoscopic retrograde cholangiography for dilatation of dominant strictures, UDCA up to 15 m/kg, controversial for high dose	Transplantation	Singh et al[41]
Eyes	Uveitis	Topical/systemic steroids, cyclosporine	IFX	Fries et al[42]
				Hernandez Garfella[43]
				In Bechet's disease
	Episcleritis	Treatment of IBD flare, topical steroids		Lakatos[44]

Lakatos PL, Lakatos L, Kiss LS, et al. Treatment of extraintestinal manifestations in inflammatory bowel disease. Digestion. 2012;86(suppl 1):28–35

Pregnancy & IBD

- Peak age onset coincides with childbearing years
- 25% of patients will have 1st child after diagnosed with IBD
- Control of disease activity at time of conception is important
- Women are concerned medications will affect their pregnancy adversely and therefore stop them prior to trying to get pregnant
- Uncontrolled disease is associated with high risk of adverse pregnancy outcomes for both mother and fetus

Pregnancy & IBD

- Risk of relapse during pregnancy w/ stable disease is approximately 30%
  - This is similar to non-pregnant patient
- Women with quiescent IBD & no prior pelvic surgery have similar infertility rates (5-14%) as the general population
- Pelvic surgery significantly increases female infertility due to scarring
  - Abdominal surgery which spare the pelvis, or less invasive may preserve fertility
  - Important to counsel women of childbearing years about these risks and alternative approaches

Restellini S, Biedermann L: Update on the Management of Inflammatory Bowel Disease during Pregnancy and Breastfeeding. Digestion 2020;101(suppl 1):27-42. doi: 10.1159/000502886
McConnell R, Mahadevan U:, Gastroenterology Clinics of North America, 2016; 45: 285-301

Pregnancy & IBD

Assess women w/ difficulty conceiving or w/ spontaneous abortions

- Active disease
- Hypovitaminosis D
- Celiac disease

If unable to conceive after 6 months suggest reproductive endocrine referral

Males:

- Zink deficiency in Crohn's disease may impair sperm function
- Sulfasalazine thought to cause reversible infertility (dose dependent oligospermia, reduce sperm motility, & alter sperm morphology)
- Some experts recommend stopping methotrexate 3 months before attempting conception

McConnell R, Mahadevan U:, Gastroenterology Clinics of North America, 2016; 45: 285-301

Pregnancy & IBD Medications

Antibiotics		
Amoxicillin with clavulanic acid	Low risk. Limited data	Preferred antibiotic during pregnancy
Ciprofloxacin	Low risk. Animal data reported anomalies	Short courses for perianal disease
Metronidazole	Low risk. Avoid first trimester. Possible risk of cleft lip	Short courses for perianal disease
Rifaximin	Teratogenicity described in animal models	Avoid
Aminosalicylates		
Balsalazide	Low risk	Maintain prepregnancy dose
Mesalamine	Low risk. Exception: asacol contains dibutylphtalate coating reported to be teratogenic in animal models	Maintain prepregnancy dose. Switch Asacol to another mesalamine agent with equivalent dose
Sulfasalazine	Low risk	Maintain prepregnancy dose. Increase folic acid to 2 mg daily
Corticosteroids		
Budesonide	Low risk	Short courses
Prednisone	Moderate risk. Mother: possible increase risk of gestational diabetes, adrenal insufficiency, premature rupture of membranes. Child: possible increase risk of orofacial cleft (first-trimester exposure), preterm birth, infections	Short courses. Use steroid-sparing agents when possible
Immunomodulators		
Cyclosporine	Possible but limited data with reported increased risk of pregnancy complications, preterm birth, low birth weight	Maintain prepregnancy dose
Methotrexate	Contraindicated: teratogenic and abortifacient	Women must stop the drug 3–6 months before attempting conception
Thiopurines (azathioprine, 6-mercaptopurine)	Low risk in monotherapy Increased risk of infant infections in combination therapy	Maintain prepregnancy dose in monotherapy If patient on combotherapy is in clinical and endoscopic remission with adequate trough levels, consider stopping thiopurine and continuing biologic monotherapy No introduction during pregnancy due to long delay of action and unpredictable risk of developing medullary suppression or pancreatitis

Restellini S, Biedermann L: Update on the Management of Inflammatory Bowel Disease during Pregnancy and Breastfeeding. Digestion 2020;101(suppl 1):27-42. doi: 10.1159/000502886

Pregnancy & IBD Medications

Biologics			
Anti-TNF-α			
IFX	Low risk in monotherapy	Maintain prepregnancy dosing. Consider decreasing the dose or increasing interval of administration depending on second trimester trough levels. Continue dosing until 8–10 week before delivery	Maintain prepregnancy dosing. Stop around week 20–22 in patient in remission
ADA	Low risk in monotherapy	Maintain prepregnancy dosing. Continue dosing until 3–4 week before delivery	Maintain prepregnancy dosing. Stop around week 20–22 in patient in remission
GM	Low risk in monotherapy	Maintain prepregnancy dosing. Continue dosing until 4–6 week before delivery	Maintain prepregnancy dosing. Stop around week 20-22 in patient in remission
CZP	Very low risk. Does not actively cross placenta	Maintain prepregnancy dosing. Continue scheduled dosing through pregnancy	Maintain prepregnancy dosing. Continue scheduled dosing through pregnancy
Anti-integrin			
VDZ	Low risk in monotherapy. Limited data	Maintain prepregnancy dosing. Continue dosing until 8–10 week before delivery	Maintain prepregnancy dosing. Stop around week 20–22 in patient in remission
Anti-interleukins			
UST	Low risk in monotherapy. Limited data	Maintain prepregnancy dosing. Continue dosing until 8–10 week before delivery	Maintain prepregnancy dosing. Stop around week 20–22 in patient in remission

IBD, inflammatory bowel disease; IFX, infliximab; ADA, adalimumab; GM, golimumab; CZP, certolizumab pegol; VDZ, vedolizumab; UST, ustekinumab.

Restellini S, Biedermann L: Update on the Management of Inflammatory Bowel Disease during Pregnancy and Breastfeeding. Digestion 2020;101(suppl 1):27-42. doi: 10.1159/000502886

Breastfeeding & IBD

Aminosalicylates		
Balsalazide	Low risk	Compatible; enters breast milk Potential risk of infantile diarrhea
Mesalamine	Low risk Dibutyl phthalate coating in Asacol HD may be teratogenic in animals	Compatible; enters breast milk Potential risk of infantile diarrhea
Olsalazine	Low risk	Compatible; enters breast milk Potential risk of infantile diarrhea
Sulfasalazine	Low risk; give with folic acid 2 mg daily Reversible oligospermia in men	Compatible; enters breast milk Potential risk of infantile diarrhea
Immunomodulators		
Cyclosporine	Limited data; possible risk of pregnancy complications, preterm birth, low birthweight	Contraindicated; enters breast milk
Methotrexate	Contraindicated: teratogenic, abortifacient Supplement with folic acid Discontinue 3–6 mo before conception	Contraindicated; enters breast milk
Thiopurines (azathioprine, 6-mercaptopurine)	Low risk in monotherapy Delayed infant infections in combination therapy	Compatible; clinically insignificant concentration enters breast milk Wait 4 h after ingestion if able

Biologics		
Adalimumab	Low risk in monotherapy	Compatible; clinically insignificant concentration enters breast milk
Certolizumab pegol	Low risk Does not actively cross placenta	Compatible; clinically insignificant concentration enters breast milk
Golimumab	Low risk in monotherapy	Compatible; undetectable
Infliximab	Low risk in monotherapy	Compatible; clinically insignificant concentration enters breast milk
Natalizumab	Low risk in monotherapy	Compatible; undetectable
Ustekinumab	Limited human data	Likely compatible; limited human data
Vedolizumab	Low risk in monotherapy; limited data	Likely compatible; no human data
Corticosteroids		
Budesonide	Low risk	Compatible; clinically insignificant concentration enters breast milk
Prednisone	Moderate risk; possible orofacial cleft (first trimester exposure), adrenal insufficiency, gestational diabetes, premature rupture of membranes, preterm birth, infant infections	Compatible; clinically insignificant concentration enters breast milk
Antibiotics		
Amoxicillin with clavulanic acid	Low risk; preferred antibiotic during pregnancy	Compatible; enters breast milk
Ciprofloxacin	Low risk; affinity for cartilage	Compatible; enters breast milk
Metronidazole	Low risk; avoid in first trimester due to possible risk of orofacial clefts	Contraindicated; enters breast milk

McConnell R, Mahadevan U:, Gastroenterology Clinics of North America, 2016; 45: 285-301

COVID-19 & IBD

- Ongoing studies regarding IBD and COVID-19
- Initially there were concerns about patients being on immunosuppressive therapies during the COVID-19 pandemic
- More data has since been gathered regarding this patient population and the Coronavirus

COVID-19 & IBD

- Overall, IBD population likely has no increased risk of developing SARS-CoV-2 infection
  - Coronavirus binds to angiotensin-converting enzyme 2 (ACE2), which is present in many organs throughout the body- but highest in the colon and Terminal ileum
    - This may explain why some Covid-19 patients experience GI symptoms
  - *In Vitro* studies have shown there may be a mechanism in IBD related to ACE2 that helps to limit infection with Coronavirus

Kumar A, Arora A; COVID-19 in patients with inflammatory bowel disease. Expert Review Gas Hep; 2020; 14 (12) doi.org/10.1080/17474124.2020.1816822
Monteleone G, Ardizzone S; Are Patients with Inflammatory Bowel Disease at Increased Risk for Covid-19 Infection?. J Crohn's Colitis. 2020; 14(9):1334-1336

Covid-10 & IBD

- Immunosuppressive therapy used in IBD has been known to be a risk factor for infections
- There is some preliminary data to suggest certain biologics may help to block the cytokine storm in severe COVID-19 infections

COVID-19 & IBD

Drug	Recommendation			Level of evidence (I–VII)	Comments
	New treatment	Dose escalation	Dose tapering		
Salicylates	Yes	Yes	NR	V	
Steroids Oral/Systemic Local (Budesonide)	No* Yes	No Yes	Yes* NR	V	*may use lowest possible dose or at least taper to Prednisolone 20 mg/day or equivalent if use is necessary
Azathioprine	No	No	Yes*	V	*pause of Rx till 1–2 weeks after COVID-19 recovery
Methotrexate	No	No	Yes*	V	*pause of Rx till 1–2 weeks after COVID-19 recovery
Anti-TNF agents (Infliximab/Adalimumab)	Yes	Yes	NR/Yes#	V	May consider switching from Infliximab to Adalimumab to permit home based Rx if necessary. # Maintenance dose maybe delayed by 1–2 week(s) if ongoing active COVID-19
Anti-Integrins (Vedolizumab)	Yes	Yes	NR	V	May consider as preferred Rx especially in elderly pt with moderate/severe IBD with comorbidities.

Kumar A, Arora A; COVID-19 in patients with inflammatory bowel disease. Expert Review Gas Hep; 2020; 14 (12) doi.org/10.1080/17474124.2020.1816822

COVID-19 & IBD

- THESE PATIENTS SHOULD BE VACCINATED!!!!

Thank you!