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Interactive Case: Uncomplicated Pregnancy in IBD

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Background

- There is a lack of reproductive counseling for women with IBD
- Knowledge gaps can contribute to higher rates of poor medication adherence and/or “voluntary childlessness”
- Nurses and advanced practice providers are well positioned to provide patient education, pregnancy counseling, and steps that can be taken to ensure safe outcomes for the pregnant IBD patient

Lori M. Gawron, Jessica Sanders, Katelyn P. Steele, Ann D. Flynn, Reproductive Planning and Contraception for Women with Inflammatory Bowel Diseases, Inflammatory Bowel Diseases, Volume 22, Issue 2, 1 February 2016, Pages 459–464.

Rachel Winter, Bente M. Nørgård, Sonia Friedman, Treatment of the Pregnant Patient with Inflammatory Bowel Disease, *Inflammatory Bowel Diseases*, Volume 22, Issue 3, 1 March 2016, Pages 733–744.

Williams A-J, Karimi N, Chari R, et al. Shared decision making in pregnancy in inflammatory bowel disease: design of a patient orientated decision aid. *BMC Gastroenterol*, 2021;21(1):1–18.

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Objectives

- The learner will be able to discuss preconception planning with an IBD patient
- The learner will be able to assess the impact of various IBD treatments during pregnancy
- The learner will be able to describe monitoring strategies during a normal pregnancy to ensure a safe pregnancy and delivery

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Case Introduction

- Sarah is a 23-year-old female who was diagnosed with moderate/severe left sided ulcerative colitis four years ago
- She is treated with infliximab 5 mg/kg IV every eight weeks and 50 mg azathioprine po daily
- Her last colonoscopy one year ago revealed mild inflammation in the rectum and was otherwise normal

Initial Visit

- Continues IFX 5mg/kg IV q8w + AZA 50mg po daily
- 2-3 soft BM/day without abdominal pain or bleeding for the past year
- Weight has been stable; BMI 20
- Labs are unremarkable aside from HGB 11 and MCV 75
- Physical Exam: Unremarkable
- Works as a teacher full time; she is getting married in six months

Sarah's Concerns

- "I'm not sure if I want to have children. I don't want my IBD to flare."
- Preconception Planning *(See slide 16)*
- "Is it safe for me to continue my medication while I am pregnant and while I am breast feeding?"
- Medication Safety *(See slide 17)*

Assessment

- Ulcerative colitis: Clinical remission on IFX/AZA
- Microcytic anemia: unknown source
- Preconception planning *(See slide 16)*

Plan

- Continue present therapy *(See slide 21)*
- Schedule endoscopy *(See slide 19)*
- Obtain IFX trough/antibody *(See slide 18)*
- Check nutritional markers -- iron, vitamin B12, vitamin D, folate *(See slide 22)*
- Review health maintenance - vaccination & cancer screening *(See slides 23 & 24)*

Follow-Up After Lab Review

- Infliximab level was 2, no antibodies
- IFX increased to 10 mg/kg every eight weeks, AZA 50 mg daily continued
- Patient started on multivitamin with iron due to iron deficiency
- Patient vaccinated with annual influenza vaccine and COVID booster
- Patient referred to dermatologist for full skin surveillance

Sarah Returns to Clinic Four Months Later

- Continues IFX 10 mg/kg IV q8w + AZA 50 mg po daily
- One formed BM/day without abdominal pain or bleeding
- Reports being six weeks pregnant
- Colonoscopy was not completed as previously recommended

Disease Surveillance During Pregnancy

- Endoscopy *(See slide 19)*
- Imaging *(See slide 26)*
- Labs *(See slide 27)*
- Referral *(See slide 28)*

Follow-Up

- Sarah returns and is doing well, no complaints
- Labs Hgb 14, MCV 96, Calprotectin 25
- Remains on infliximab 10 mg/kg q 8 weeks – levels rechecked IFX 8, no antibodies
- “I’m feeling really well, I think I’d prefer to stop my medication.”

Monitoring

- Sarah is seen every two to three months until delivery
- Weight and labs are stable
- Infliximab is scheduled through week 32 and two days after delivery
- Patient is provided information regarding vaccinations for newborn *(See slide 23)*
- Patient will be scheduled for colonoscopy in the future, either after breastfeeding or if she has any symptoms

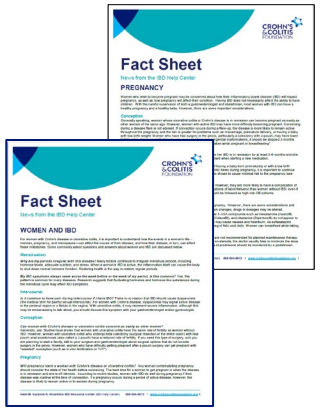
Normal Pregnancy

- Sarah is seen for infusion two days after delivery
- Reports normal vaginal delivery, no complications
- Infant and mother are doing well, breastfeeding is going well
- No bowel changes at this time
- Weight and labs are stable

Crohn's & Colitis Foundation Resources

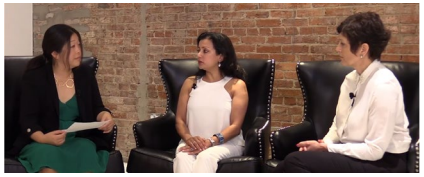
Patients

- Fact sheets: (https://www.crohnscolitisfoundation.org/)
  - Pregnancy
  - Women and IBD
- Support groups:
  - Online: www.crohnscolitiscommunity.org
  - In-person: Locate at www.crohnscolitisfoundation.org
- IBD Help Center: available by email (info@crohnscolitisfoundation.org), phone (888-694-8872), or online chat



Providers

- *Inflammatory Bowel Disease in Pregnancy Clinical Care Pathway: A Report From the American Gastroenterological Association IBD Parenthood Project Working Group* (https://doi.org/10.1093/ibd/izz037)
- Other educational videos on pregnancy: (https://www.crohnscolitisfoundation.org/prescribers)



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Preconception Planning

- Up to 50% of patients have poor knowledge of IBD and IBD-related treatments during pregnancy. This often leads to nonadherence in therapy.

- Preconception counseling can help patients build confidence when deciding about childbirth by addressing the impact of pregnancy on IBD and the safety of IBD medical therapy.

Wierstra, K., Sutton, R., Bal, J., Ismond, K., Dieleman, L., Halloran, B., ... & Huang, V. (2018). Innovative Online Educational Portal Improves Disease-Specific Reproductive Knowledge Among Patients With Inflammatory Bowel Disease. *Inflamm Bowel Dis.*

Williams A-J, Karimi N, Chari R, et al. Shared decision making in pregnancy in inflammatory bowel disease: design of a patient orientated decision aid. *BMC Gastroenterol*. 2021;21(1):1–18.

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Medication Safety During Pregnancy/Lactation

Drug	Recommendation in Pregnancy	Recommendation in Lactation
Aminosalicylates	- Low risk - Safe to be continued throughout pregnancy - Increase folate supplementation to 2 mg daily with sulfasalazine use	- Mesalamine is preferred - Sulfasalazine should be avoided (increased hemolysis risk)
Immunomodulators		
Methotrexate	- High risk - Contraindicated—Stop at least 3 months prior to conception. Take folic acid	- Avoid during lactation given limited data
Thiopurines	- Low risk - Safe to continue, avoid new starts	- Safe to continue, undetectable levels in breastmilk
Biologics		
Infliximab (Remicade)	- Low risk	- Safe to continue
Adalimumab (Humira)	- Low risk	- Safe to continue
Certolizumab (Cimzia)	- Low risk	- Safe to continue
Golimumab (Simponi)	- Low risk	- Safe to continue
Ustekinumab (Stelara)	- Low risk	- Safe to continue
Vedolizumab (Entyvio)	- Low risk	- Safe to continue
Natalizumab (Tysabri)	- Low risk	- Safe to continue
Small Molecules		
Tofacitinib	- Presumed to cross placenta, limited data - Discontinue 1 month prior to conception	- Avoid given limited data
Upadacitinib	- Presumed to cross placenta, limited data - Discontinue 1 month prior to conception	- Avoid given limited data
Ozanimod	- Presumed to cross placenta, limited data - Discontinue 3 months prior to conception	- Avoid given limited data

Laura C. Sahyoun, Jill K. J. Gaidos, A Practical Approach to IBD Care in the Pregnant Patient, *Current Gastroenterology Reports*, Volume 24, 23 November 2022, Pages 201–209, https://doi.org/10.1007/s11894-022-00856-3.

Therapeutic Drug Monitoring

Agent		Induction		Post-induction		Maintenance	
		Reactive	Proactive	Reactive	Proactive	Reactive	Proactive[a]
Infliximab[b]	Recommendation	Consider	Consider	Recommend	Consider	Recommend	Recommend
	Target	Week 2: 20–25 μg/mL Week 6: 15–20 μg/mL		Week 14: 7–10 μg/mL		5–10 μg/mL	
Adalimumab	Recommendation	Consider	Consider	Recommend	Consider	Recommend	Recommend
	Target	Week 4: 8–12 μg/mL		Week 12: 8–12 μg/mL		8–12 μg/mL	
Golimumab	Recommendation	N/A	N/A	Consider	Consider	Consider	Consider
	Target			3–7 μg/mL		1–3 μg/mL	
Certolizumab	Recommendation	N/A	N/A	Consider	Consider	Consider	Consider
	Target			32–36 μg/mL		13–15 μg/mL	
Vedolizumab[b]	Recommendation	Consider	Consider	Consider	Consider	Consider	Consider
	Target	Week 6: 33–37 μg/mL		Week 14: 15–20 μg/mL		15–20 μg/mL	
Ustekinumab	Recommendation	N/A	N/A	Consider	Consider	Consider	Consider
	Target			Week 8: 3–7 μg/mL		1–3 μg/mL	
Thiopurines	Recommendation	Not recommended[c]	Consider[d]	Recommended	Recommended	Recommended	Recommended
	Target	Week 4: 235 pmol/8 × 10^8 RBC		Week 12: 235 pmol/8 × 10^8 RBC		235 pmol/8 × 10^8 RBC	

NOTE: Level recommendations are drawn from Cheifetz et al. These are broad targets, often based on limited evidence and, as per the main text, may need to be adjusted depending on disease phenotype and therapeutic goal.
N/A, not applicable; RBC, red blood cells.

a. At least once per year.
b. Intravenous preparation.
c. Week 4 is too early to identify primary nonresponse.
d. Poor adherence, underdosing, and abnormal metabolism can be identified by week 4.

Irving P, Gecse K. Optimizing therapies using therapeutic drug monitoring: current strategies and future perspectives. Gastroenterology. 2022; 162 (5): 1512- 24

Endoscopy

- Women with IBD who are considering pregnancy are recommended to have endoscopic assessment of inflammation prior to conception
- There is an increased risk of premature birth, low fetal birth weight, and congenital anomalies if babies are conceived in the setting of active IBD

Cornish J, Tan E, Teare J, et al. A meta-analysis on the influence of inflammatory bowel disease on pregnancy. *Gut.* 2007;56(6):830–837.

Nguyen GC, Seow CH, Maxwell C, et al. The Toronto consensus statements for the management of inflammatory bowel disease in pregnancy. *Gastroenterology*. 2016;150(3):734–757. e731.

IBD Medications During Pregnancy

- Biologics are safe to use during pregnancy and do not increase rates of preterm birth, stillbirth, congenital malformation, or low fetal birth weight
- There are no differences in pregnancy outcomes between mothers with IBD exposed to biologics while pregnant versus unexposed to biologics with the exception of higher rates of C-section
- If anti-TNF therapy is discontinued prior to 24 weeks gestation, compared to continued through pregnancy, there is an increased risk of IBD flare during pregnancy and postpartum

Nielsen OH, Gubatan JM, Juhl CB, Streett SE, Maxwell C. Biologics for inflammatory bowel disease and their safety in pregnancy: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2022;20(1):74–87.

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.

Gisbert JP, Chaparro M. Safety of new biologics (vedolizumab and ustekinumab) and small molecules (tofacitinib) during pregnancy: a review. Drugs. 2020;80(11):1085–1100.

Continuing Medications

- Pregnancy outcomes are improved when the patient is in steroid-free clinical remission on a safe medication regimen for at least 3 months prior to conception

- Infliximab drug clearance decreases during pregnancy, resulting in higher serum drug concentrations. This is unique to infliximab compared to other biologic therapies. Nonetheless, IFX dosing during pregnancy should be based on pre-pregnancy weight

Mahadevan U, Robinson C, Bernasko N, et al. Inflammatory bowel disease in pregnancy clinical care pathway: a report from the American Gastroenterological Association IBD Parenthood Project Working Group. Inflamm Bowel Dis. 2019;25(4):627–641.

Flanagan E, Gibson P, et al. Infliximab, adalimumab and vedolizumab concentrations across pregnancy and vedolizumab concentrations in infants following intrauterine exposure. Alimentary Pharmacology and Therapeutics, 52(10), 1551–1562.

Nutritional Screening

- Low vitamin D levels can be linked to lower conception rates and live births

- Folic acid should be administered in every pregnancy (400 mcg/day). Higher doses of folic acid (2 mg/day) are recommended for women with ileal disease, with prior exposure to methotrexate, or on current medications that affect folate metabolism

Mullin GE. Micronutrients and inflammatory bowel disease. *Nutr Clin Pract*. 2012;27(1):136–7.

Fung JL, Hartman TJ, Schleicher RL, Goldman MB. Association of vitamin D intake and serum levels with fertility: results from the Lifestyle and Fertility Study. Fertil Steril. 2017;108(2):302–311

Van Assche G, Dignass A, Reinisch W, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Special situations. *J Crohns Colitis*. 2010;4(1):63–101.

Vaccination

Vaccines	Which Patients	How Often
☐ COVID-19 vaccine (Moderna, Pfizer, Novavax)	All patients with IBD.	Follow recommendations for the general population.
☐ Influenza, Fluzone High Dose, Flublok recombinant, Fluad adjuvanted	All adult patients with IBD should receive a standard dose. Those on Anti-TNF monotherapy should receive a high dose influenza vaccine.[1] Older Adults aged ≥65 should receive the high dose, recombinant or adjuvanted inactive influenza vaccine.[2]	Annually.
☐ Pneumococcus (PCV 15, PCV 20 or PPSV23)	All patients ≥19 years age receiving systemic immunosuppression.*	Vaccine naïve should receive PCV20 or PCV 15 then 8 weeks apart PPSV23 in one year. Those previously vaccinated with PCV13 and PPSV23 should receive one PCV 20 at least one year since last dose of pneumococcal vaccine. Older adults > 65 should receive a dose of PCV 20.
☐ Recombinant Herpes Zoster (RZV) (adjuvanted- non-live) SHINGRIX	All patients with IBD ≥19 years of age.[3]	Should receive two dose recombinant herpes zoster vaccine 2–6 months apart.
☐ Human Papilloma Virus (HPV) 9valent GARDASIL	All Adults 18–26. Adults 26-45* shared decision who are likely to have a new sexual partner.	Should receive 3 doses series 0, 1–2 months and 6 months.
☐ Hepatitis B Heplisav® Engerix® or Recombivax®:	All adult patients with IBD. Universal vaccination is recommended for all adults 19–59.[4]	Heplisav®: Two dose series (HepB-CpG) at 0 and 1 month. Engerix® or Recombivax®: Three doses series on 0, 1, 6-month schedule 3 doses series Hep A-Hep B (Twinrix® at 0, 1, 6-months).
☐ Measles, Mumps, and Rubella (MMR) two-dose live vaccine	Patients with IBD not immune to MMR. If immune status is uncertain, obtain immunization history. IgG antibody titer can be checked but not recommend by ACIP. MMR live vaccine should not be given to patients currently on systemic immunosuppressive therapy.[5]	Should receive a 2-dose series, at least 4 weeks apart.
☐ Varicella two-dose live vaccine	Documentation of two doses or varicella vaccine. Serology not recommended by ACIP for evaluation of vaccine induced immunity in those with appropriate documentation.[6]	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.

Cancer/Other Screenings

Cancer Screening	Which Patients	How Often
☐ Colorectal	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.	Patients with IBD with a diagnosis of PSC should undergo colonoscopy, starting at the time of PSC diagnosis, and annually thereafter. Patients with IBD 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	All women with IBD who are being treated with systemic immunosuppression.*	Should undergo cervical cancer by cytology annually (if cytology alone) or every 3 years (if HPV negative).[7]
☐ Skin	All IBD patients being treated with systemic immunosuppression.*	Should have annual total body skin exams to screen for skin cancer.
Other Screenings	**Which Patients**	**How Often**
☐ Mental Health	All	Annual; Depression (PHQ2) and anxiety (GAD7) at baseline, and then annually. Refer for counseling/ therapy when identified.
☐ Osteoporosis	All	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, hypo-gonadism. Repeat in 5 years and no sooner than 2 years[3] if initial screen is normal. Vitamin D (800-1000 IU per day) and calcium (1200 mg/day) for Women >65 yo, male > 70 yo (regardless of clinical risk factors).
☐ Smoking	All	Refer current smokers for smoking cessation therapy.
☐ Latent infections Hepatitis B and tuberculosis	Patients with IBD starting on anti-TNF therapy.	Evaluate prior to starting anti-TNF therapy.
☐ Nutritional deficiencies	Patients with IBD annually.	Ferritin, Transferrin %, Vitamin D, Vitamin B12, and Vitamin B6.

Crohn's & Colitis Foundation Professional Education Sub-Committee; Freddy Caldera, MD, Shubha Bhat, PharmD, Shail Govani, MD | 8/29/2022

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Endoscopy During Pregnancy

- Endoscopy can be safely performed during all trimesters of pregnancy, but should be avoided unless clinically necessary

- Endoscopy should be done with the lowest level of sedation possible (i.e., un-sedated flexible sigmoidoscopy over colonoscopy) with fetal monitoring by an OB

Amandeep K. Shergill, Tamir Ben-Menachem, et al. Guidelines for endoscopy in pregnant and lactating women. *Gastrointestinal Endoscopy*. Volume 76, Issue 1, 14 May, 2012, Pages 18-24.

Alison De Lima, Boris Galjart, et al. Does Lower Gastrointestinal Endoscopy During Pregnancy Pose a Risk for Mother and Child? - A Systemic Review. *BMC Gastroenterology*, Volume 15, Issue 1, 12 February 2015, Pages 1-11.

Imaging During Pregnancy

- Should only be completed when deemed necessary for treatment
- Intestinal ultrasound is the safest imaging modality in pregnancy. Evaluation of the terminal ileum is limited after 20 weeks gestation
- If IUS is not available, MRI is preferred over CT in pregnancy. Gadolinium should be avoided in the first trimester

Emma Flanagan , Emily K. Wright, et al. Monitoring Inflammatory Bowel Disease in Pregnancy Using Gastrointestinal Ultrasonography. *Journal of Crohn's and Colitis*, Volume 14, Issue 10, 5 October 2020, Pages 1405-1412.

Myriam D. Stern, Uri Kopylov, et al. Magnetic Resonance Enterography in Pregnant Women with Crohn's Disease: Case Series and Literature Review. BMC Gastroenterology. Volume 14, Issue 1, 16 August 2014, Pages 1–9.

Monitoring Disease Activity in Pregnancy

- Hemoglobin - altered by pregnancy as well as disease
- Albumin – altered by pregnancy as well as disease
- ESR - not accurate in pregnancy
- CRP – slight elevation in pregnancy, typically still within normal range
- Fecal Calprotectin – not affected by pregnancy, most accurate noninvasive marker of inflammation during pregnancy

Rachel Winter, Bente M Norgard, et al. Treatment of the Pregnant Patient with Inflammatory Bowel Disease. Inflammatory Bowel Diseases, Volume 22, Issue 3, March 2016, Pages 733-744.

Mette Julsgaard, Christian L. et al. Fecal Calprotectin Is Not Affected by Pregnancy: Clinical Implications for the Management of Pregnant Patients with Inflammatory Bowel Disease. *Inflammatory Bowel Diseases,* Volume 23, Issue 7, 1 July 2017, Pages 1240-1246.

Referral to High-Risk Maternal Fetal OB

- Women with IBD are at risk for poor maternal weight gain, preterm delivery, and delivery of small-for-gestational-age newborns. These risks should be monitored by a maternal fetal medicine (MFM) specialist

- MFM specialists have training and expertise in high-risk pregnancies and deliveries, including in women with IBD who have had prior abdominal surgery like an ostomy, ileal pouch anal anastomosis, or perianal fistula

Uma Mahadevan, Christopher Robinson, et al. Inflammatory Bowel Disease in Pregnancy Clinical Care Pathway: A Report from the American Gastroenterological Association IBD Parenthood Project Working Group, *Inflammatory Bowel Diseases*, Volume 25, Issue 4, April 2019, Pages 627-641, https://doi.org/10.1093/ibd/izz037.

Vaccinations

- Infant should receive all non-live vaccines on time
- Live vaccines including rotavirus and oral polio should be held until 9 months of age

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.