GI Alliance

Advancing GI Patient Care 2021

SATURDAY, JULY 24, 2021

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IBD in Pregnancy
Clinical Care Pathway
IBD Parenthood Project

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TDDC – Dallas, TX

Disclosures

- Governance
  - Chief of Gastroenterology – Texas Health Dallas
  - Chair Elect – American Board Internal Medicine Board of Directors
  - Member – TDDC Clinical Governance Board
- Research
  - AbbVie
  - Eli Lilly
  - Gilead Sciences
  - UNC TOUR

Outline

- Background
  - Inflammatory Bowel Disease (IBD)
  - IBD Parenthood Project
- Clinical Care Pathways
  - Pre-conception
  - Pregnancy
  - Delivery
  - Post-partum
- Summary

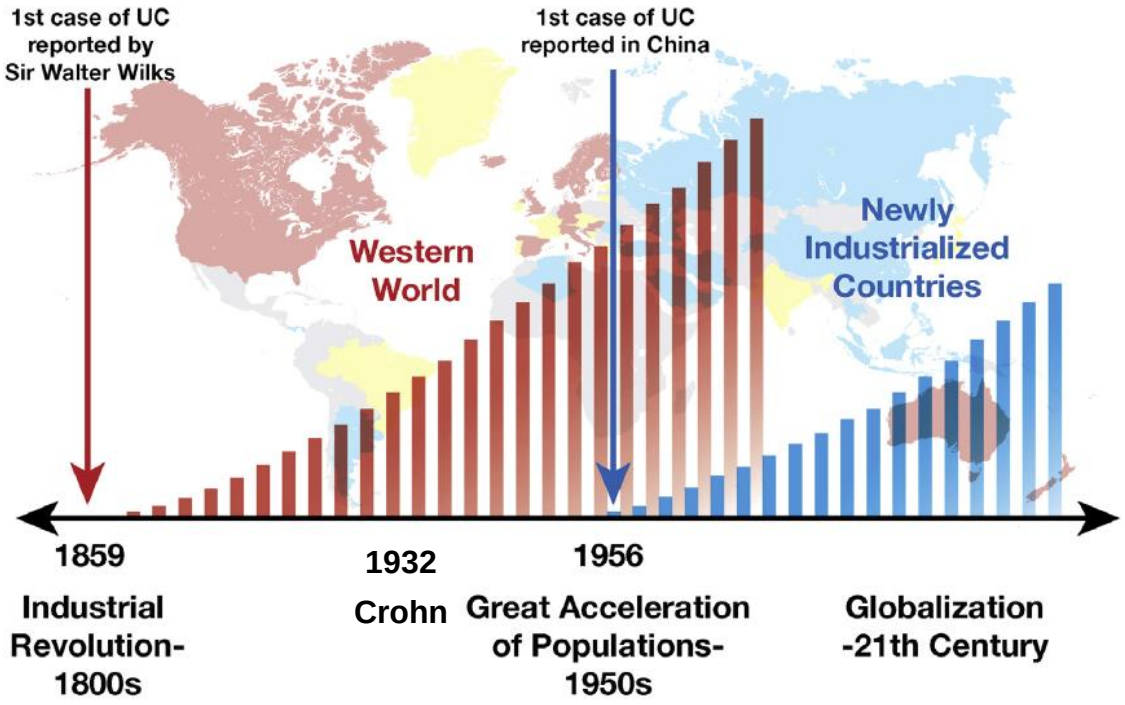
Inflammatory Bowel Disease

- Immune-mediated condition of unknown etiology
- Chronic
- Relapses and remissions
- Substantial impact

Inflammatory Bowel Disease (IBD)

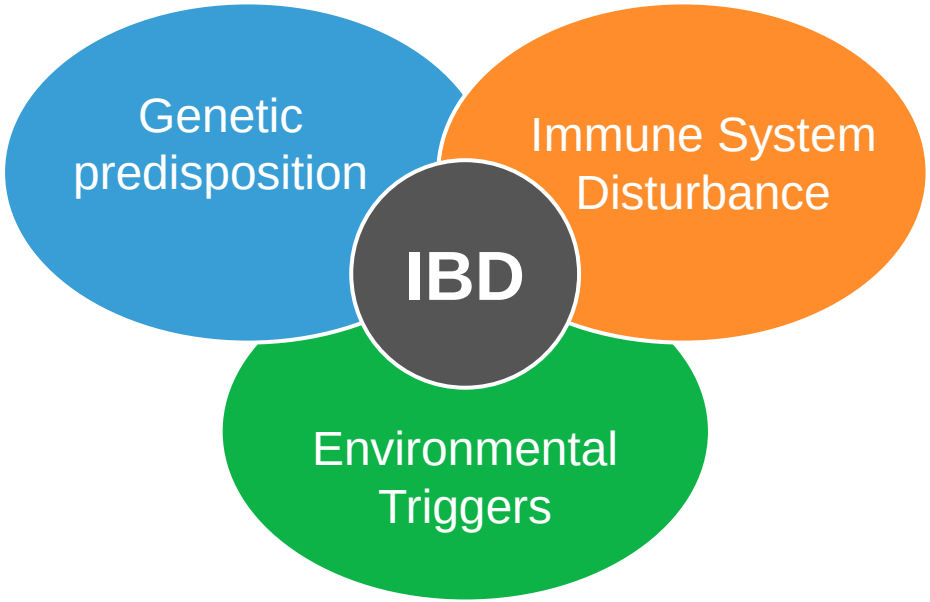
- Crohn's disease (CD)
  - Inflammation at any location in along the GI tract
    - 35% ileocecal, 35% ileal, 20% colonic
    - Transmural and patchy with creeping fat
  - Complications: strictures, fistulas and abscesses
    - By 10 yrs, ~50% of patients have required surgery
- Ulcerative colitis (UC)
  - Starts in rectum and continuous extension limited to colon
  - Only affects mucosal layer
- Indeterminate colitis

IBD History & Global Burden



Kaplan & Ng. *Gastroenterology*. 2017; 152: 313-21.

IBD Pathogenesis



Crohn’s & Colitis Foundation.

IBD in the US

1.6 Million

People have IBD in the U.S.

50%

Are women and most will have the condition during childbearing years – from before getting pregnant to after birth

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Fear

- Impact of IBD and its therapies on:
  - Pregnancy
  - Infant outcomes
- Impact of pregnancy on:
  - IBD
  - Maternal health

Voluntarily Childless

18%
OF WOMEN WITH IBD ARE **VOLUNTARILY CHILDLESS (VC)**

VS.

6%
OF THE GENERAL POPULATION

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Background

Consensus Conference
July 26-27, 2018

Partners

Partner organizations in the development of the Clinical Care Pathway

Society for Maternal-Fetal Medicine	Crohn's & Colitis Foundation	Girls With Guts .org
AUTHORITY	**EMPOWERMENT**	**PERSPECTIVE**
Society specializing in the care of high-risk pregnancy, offering unique access to practice professionals, as well as like-minded, agenda-setting organizations.	Leading IBD patient organization, providing invaluable partnership and expertise in patient education and advocacy.	Not-for-profit organization dedicated to empowering women living with IBD, supported by their built-in network of like-minded patients.

Multidisciplinary Working Group

Spectrum of providers that a woman with IBD may seek treatment from before, during, and after pregnancy

Gastroenterology

Maternal-fetal medicine

Teratology

Lactation

Patient stakeholders

Goals

- Provide guidance on the continuum of care
- Best practices
- Practical resource
  - Providers
  - Patients

Publications

Gastroenterology 2019;156:1508–1524

AGA SECTION

Inflammatory Bowel Disease in Pregnancy Clinical Care Pathway: A Report From the American Gastroenterological Association IBD Parenthood Project Working Group

Uma Mahadevan,[1] Christopher Robinson,[2] Nana Bernasko,[3] Brigid Boland,[4] Christina Chambers,[4] Marla Dubinsky,[5] Sonia Friedman,[6] Sunanda Kane,[7] Jacob Manthey,[8] Jason Sauberan,[9] Joanne Stone,[5] and Rajeev Jain[10]

[1]University of California, San Francisco, San Francisco, California; [2]Bon Secours St Francis and Summerville Medical Center, Charleston, South Carolina; [3]Penn State Health, Milton S. Hershey Medical Center, Hershey, Pennsylvania; [4]University of California, San Diego, California; [5]Icahn School of Medicine at Mount Sinai, New York, New York; [6]Brigham and Women's Hospital, Boston, Massachusetts; [7]Mayo Clinic, Rochester, Minnesota; [8]American Gastroenterological Association, Bethesda, Maryland; [9]Sharp Neonatal Research Institute, San Diego, California; and [10]Texas Digestive Disease Consultants, Texas

CLINICAL GUIDELINES

Inflammatory Bowel Disease in Pregnancy Clinical Care Pathway: A Report From the American Gastroenterological Association IBD Parenthood Project Working Group

Uma Mahadevan[1], Christopher Robinson[2], Nana Bernasko[3], Brigid Boland[4], Christina Chambers[4], Marla Dubinsky[5], Sonia Friedman[6], Sunanda Kane[7], Jacob Manthey[8], Jason Sauberan[9], Joanne Stone[5], Rajeev Jain[10]

Inflamm Bowel Dis • Volume 25, Number 4, April 2019

Special Report ajog.org

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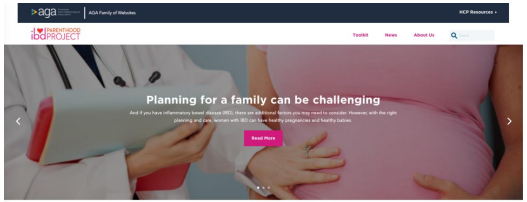
American Journal of Obstetrics & Gynecology APRIL 2019



Care Coordination Team

- Gastroenterologist specializing in IBD
- Obstetrician
- Maternal-fetal medicine (MFM) specialist
- Nutritionist
- Lactation specialist
- Colorectal surgeon, if needed

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Care Coordination Team

Due to variation in access, availability, and preference:

IBD Care	Obstetric Care
Gastroenterologist, general	MFM
Advanced Practice Provider (APP)	Obstetrician
Surgeon	Family practitioner
Primary care provider	Midwife
Emergency department	Emergency department

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

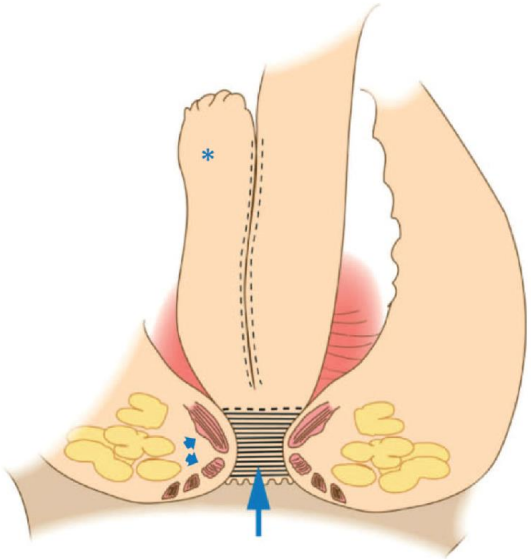
Risks of IBD to a Pregnancy

- Miscarriage
- Delivery of small-for-gestational-age infant
- Premature delivery
- Poor maternal weight gain
- Complications of labor and delivery
  - Preeclampsia
  - Placental abruption
  - Increased probability of cesarean section

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Role of Team Members

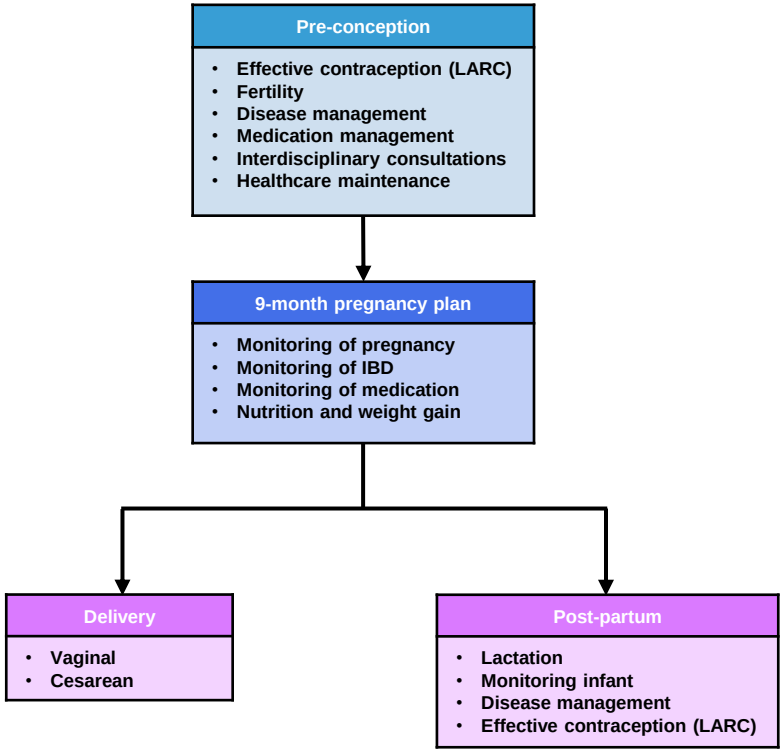
- MFM Specialist and Obstetrician
  - Mode of delivery
  - Type of monitoring
  - Frequency of visits
  - Prior surgery
    - laparotomy, ostomy,
    - ileal pouch-anal anastomosis (IPAA)
- Gastroenterologist
  - Coordinate IBD care
- Nutritionist



Adapted from McGuire BB. Ileal pouchanal anastomosis.

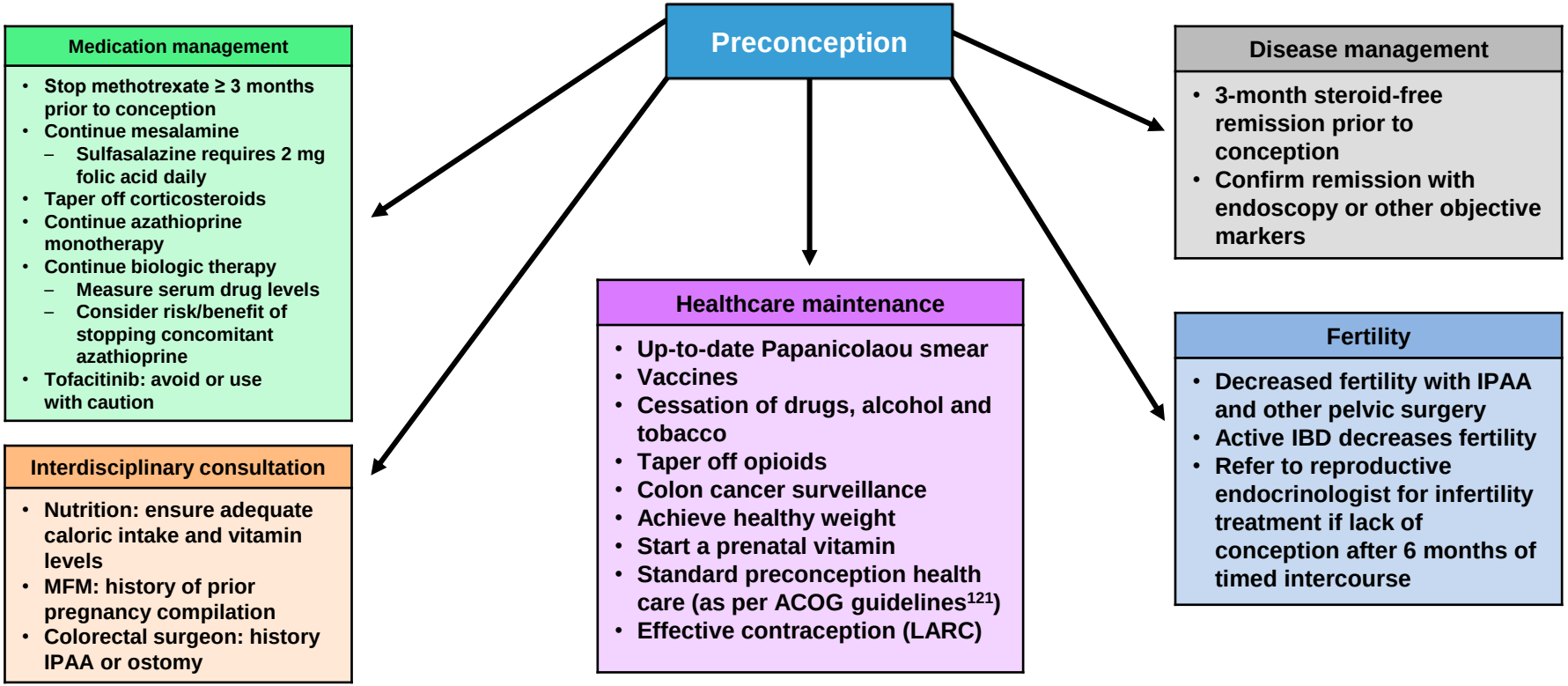
Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24; *Br J Surg*. 2007; 94: 812–823.

Overview of Clinical Pathway



Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Family Planning and Preconception



Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Contraception

- Safest and most effective birth control option
- Long-acting, reversible contraception (LARC)
  - Hormonal or nonhormonal intrauterine device
  - Contraceptive implant
- Preference for non-estrogen containing contraception
  - Increased risk of venous thromboembolism in IBD
- Pill efficacy may be decreased
  - Active small bowel inflammation
  - Extensive resection
  - Rapid bowel transit

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Genetic Risk

- IBD Type: CD > UC
- Parent: Paternal > Maternal
  - Incidence Rate Ratio (IRR)
    - Maternal CD: 6.3
    - Maternal UC: 3.7
  - Both parents: ~30% (based on 2 small studies)
  - Multiple family members
- Age of Onset: Younger > Older

Danish Study 1977-2011
N = 8,295,773
IBD 45,780

200 million person yrs

CD 0.25%
UC 0.35%

4-6 fold increased risk

Absolute Risk: 1-2.1%

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24; Moller FT et al. *Am J Gastroenterol*. 2015; 110: 564-71.

Fertility Concerns

- Rates are similar to general population IF:
  - Remission
  - No prior IBD-related surgery
    - Ileal pouch-anal anastomosis (IPAA), proctectomy & ostomies
      - Inflammation and scarring of the fallopian tubes
- Voluntarily childless 18%
- Medical therapy does **not** decrease fertility
  - Biologics, steroids, thiopurines, methotrexate and mesalamine

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

9-Month Plan

IBD remission

IBD monitoring

- GI visit trimester 1 or 2 and then as needed
- Labs at least every trimester: complete blood count, liver enzymes, albumin (combine with OB labs)

Maternal/fetal monitoring

- Routine antepartum care
- Trimester 3 fetal growth ultrasound
- Examine perineum for evidence of active disease
- Counseling on mode of delivery

IBD flare

IBD monitoring

- GI follow-up every 2 weeks (patient portal, live, video)
- Adjust medication
- Monitor labs, calprotectin
- Management of flares (Table 1)

Maternal/fetal monitoring

- Consider fetal growth surveillance every 4 weeks after 24 weeks
- Recommend antepartum surveillance for patients with active disease in trimester 3
- Recommend ultrasound cervical length screening at 18-22 weeks gestation with follow-up if indicated by short cervix (< 25 mm) per usual obstetric indications
- Nutrition counseling
- NST/BPP for usual indications
- Patients on steroids should have early glucose screen
- Counseling on mode of delivery

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

9-Month Plan

Medication (Table 2)

- Stool softeners as needed
- Appropriate antimicrobials as needed
- Aminosalicylates and thiopurine monotherapy can continue throughout
- Corticosteroids are not maintenance therapy
  - Use as indicated for flares
- Biologics should continue throughout pregnancy without interruption
  - Can time last dose in trimester 3 to deliver infant at presumed drug trough

Nutrition and weight gain

- Prenatal vitamin
  - Iron may worsen abdominal pain
- Trimester 1: check iron/B12 levels
- Adequate folate supplementation
- Monitor gestational weight gain, which can be low in IBD
- Nutrition consult if needed
  - Post-surgical changes
    - Short bowel
    - Ostomy
  - Inadequate weight gain
  - Active disease

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

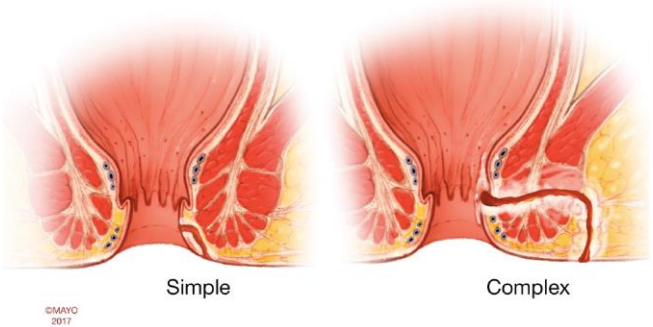
Gestational Weight

- Risk of not achieving target gestational weight gain for BMI
  - CD 2x
  - UC 1.5x
- Inadequate gestational weight gain associated with 2x risk for small-for-gestational – age infants
- Correlation with disease activity and reduced gestational weight gain
- Inadequate gestational weight gain – 2.5x risk of preterm birth

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Pregnancy & IBD Concerns

- IBD flares complicate 30-35% of pregnancies
- Active perineal disease associated with 10-fold increase for 4th degree laceration
  - Anorectal fistula/abscess
  - Rectovaginal fistula
  - Anal fissure or stenosis



Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Options for Flare Management

Table 1

Laboratory values	Endoscopy	Radiologic imaging	Surgery	Medication
• Standard IBD laboratory values checked • Trends for CRP and ESR may be helpful • Fecal calprotectin • Serum drug concentrations • Possibly elevated in pregnancy: – ESR – CRP • Alkaline phosphatase (also elevated in lactation) • Reduced in pregnancy: – Hemoglobin – Albumin	• Perform for strong indications: – Determining IBD disease activity – When result will change management • Flexible sigmoidoscopy is preferred over pan-colonoscopy when possible; can be performed unsedated, unprepped, and in any trimester	• MRI and CT have similar diagnostic accuracy for assessing IBD • Gadolinium should be avoided in pregnancy • The cumulative radiation exposure of a single CT scan (about 50 mGy) is below the level of concern • Ultrasound, where available is appropriate for terminal ileal disease	• Surgical intervention may be needed for: – Acute refractory colitis – Perforation – Abscess – Severe hemorrhage – Bowel obstruction	• Manage similar to nonpregnant IBD patients • Exceptions: • Thiopurine-naïve patients: avoid first start in pregnancy due to concerns for distinctive rare adverse reactions • Methotrexate contraindicated • Tofacitinib: avoid due to limited human data

CRP, C-reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate; MRI, Magnetic resonance imaging.

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Imaging During Pregnancy

- Sonography is limited after 28-30 wks gestation as fetus obscures bowel.
- MRI – safety has not been definitively proven
  - Static magnetic field, tissue heating from radiofrequency pulses, high acoustic noise level & gadolinium contrast (avoid during 1st trimester).
- CT acceptable if needed (<50 mGy) with single study
- Sonography & MRI > CT because of the lack ionizing radiation. (GRADE: Strong recommendation, very low-quality evidence)

Nguyen GC et al. Toronto Consensus Statement. *Gastroenterology*. 150: 734–57; 2016.

Endoscopy During Pregnancy

- Endoscopic procedures should only be performed for strong indication & if possible deferred to 2nd trimester. (ASGE & ECCO)
  - Maternal & fetal hypoxia, teratogenicity of medications and premature birth.
  - Avoid benzodiazepines in 1st trimester
- Position: left lateral or left pelvic tilt
  - Supine position: gravid uterus compressing aorta and IVC leading to maternal hypotension and decreased placental perfusion.
- Periprocedural fetal monitoring coordinated w/OB
- In pregnant women with suspected IBD or IBD flare, we recommend use of flexible sigmoidoscopy or colonoscopy if the results will affect the antenatal management of IBD.
  (GRADE: Strong recommendation, very low-quality evidence.)

Nguyen GC et al. Toronto Consensus Statement. *Gastroenterology*. 150: 734–57; 2016.

Pregnancy & IBD Therapy

What medications should be stopped?

- Dibutyl Phthalate containing mesalamines
  - Asacol HD®.[1]
- Methotrexate
  - Known teratogen, abortifacient.[2]
  - When to stop? Out of body in 1 week. Recommend 1-3 months.
- Corticosteroids
  - More of an issue with disease control than drug toxicity.
  - Low birth weight, preterm birth, gestational diabetes.
- Tofacitinib
  - Very limited human data. Animal data shows malformations [PI].
  - 158 cases (96 healthy), 11 maternal in IBD.

1. *Reprod Toxicol*. 2013 Jun; 37: 1-5. doi: 10.1016/j.reprotox.201; 2. *Arthritis Rheumatol*. 2014 May; 66 (5): 1101-10.

Pregnancy & IBD Therapy

What medications should be continued/used?

- 5-aminosalicylates
  - No increased risk of birth defects.[1]
  - No increased risk of renal insufficiency.[2]
- Antibiotics
  - Metronidazole – low risk, but all data from bacterial vaginosis.[3]
  - Ciprofloxacin – low risk, but limited data. Avoid.
  - Amoxicillin-Clavulanic Acid – low risk. ? NEC not consistent when given for PROM.
- Azathioprine/6mercaptopurine
  - No increased risk of birth defects.[4]
  - Risk with combination therapy?[5]

1. *Gastroenterology*. 2014 Jan; 146 (1): 76-84; 2. *Lancet*. 344 (8922): 620-621; 3. *Curr Drug Saf*. 2015; 10 (2): 170-9;
4. *Am J Gastroent*. 2013 Mar; 108 (3): 433-40; 5. *Gastroenterology*. 2016 Jul; 151 (1): 110-9.

Pregnancy & IBD Therapy

What medications should be continued/used?

- Anti-tumor necrosis factor alpha
  - No increased risk of birth defects, infections in infant.[1]
  - Continue drug through pregnancy. Stopping associated with flares.[1]
  - Placental transfer, except certolizumab.
- Ustekinumab
  - Low risk [206 pregnancies in clinical trials].
  - Placental transfer.
- Vedolizumab
  - Low risk [27 preg.].[2]
  - Placental transfer, ? Madcam and adherence.

1. Luu. *AJG*. 1457; 2. *Aliment Pharmacol Ther*. 2017 Apr; 45 (7): 941-950.

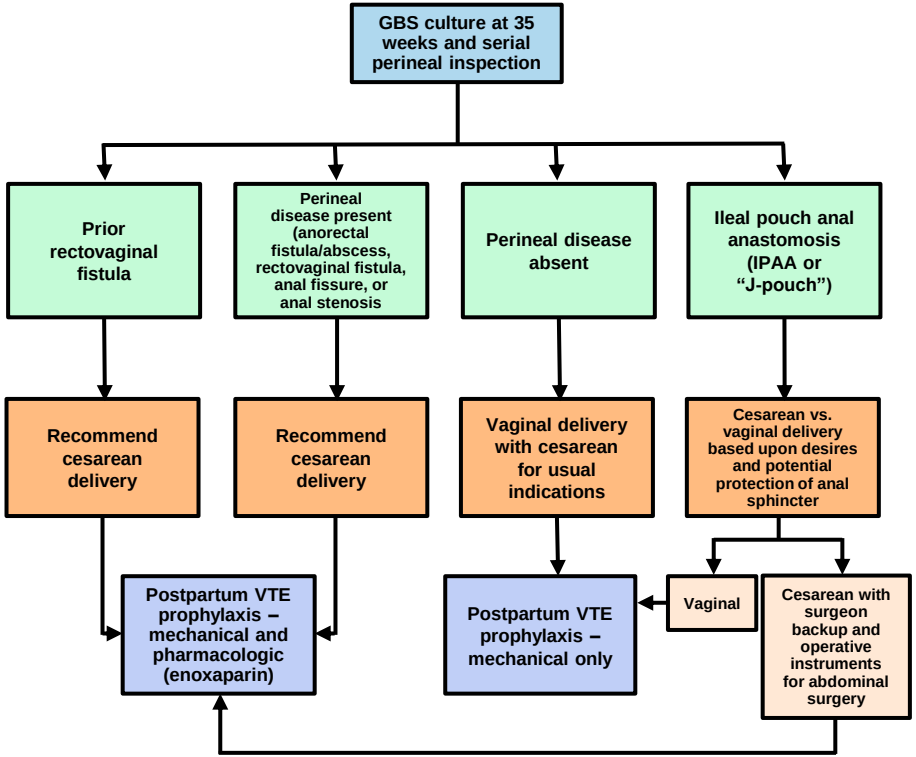
Timing of Last Dose of Biologics

Minimize transplacental transfer by achieving trough level at estimated date of confinement (EDC)

Adalimumab	Plan Final pregnancy injection 2-3 wk before EDC and resume postpartum[a] (1-2 wk if weekly dosing)
Certolizumab pegol	May continue scheduled dosing throughout pregnancy.
Golimumab	Plan final pregnancy injection 4-6 wk before EDC and resume postpartum[a]
Infliximab	Plan final pregnancy infusion 6-10 wk before EDC and resume postpartum[a] (If every-4-wk dosing, then 4-5 wk before EDC) Base dosing on prepregnancy weight during pregnancy and immediate postpartum
Natalizumab	Plan final pregnancy infusion 4-6 wk before EDC resume postpartum[a]
Ustekinumab[b]/ Vedolizumab[b]	Plan final pregnancy dose 6-10 wk before EDC and resume postpartum[a] (If every-4-week dosing, then 4-5 wk before EDC

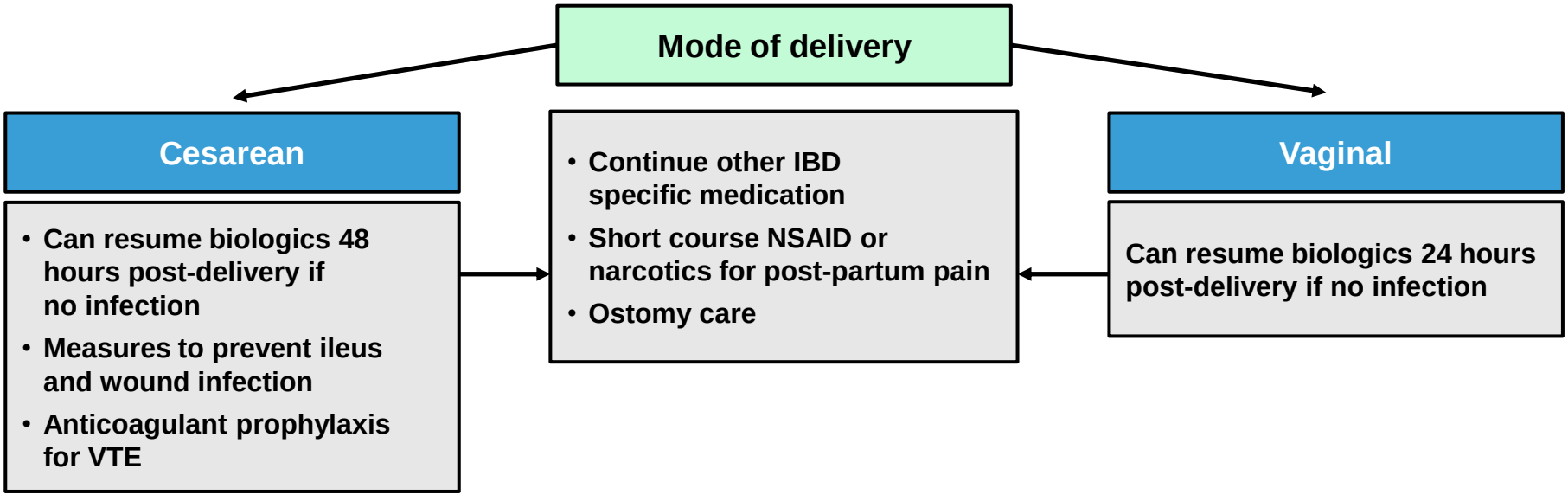
Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Mode of Delivery Algorithm



Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

IBD Therapy After Delivery



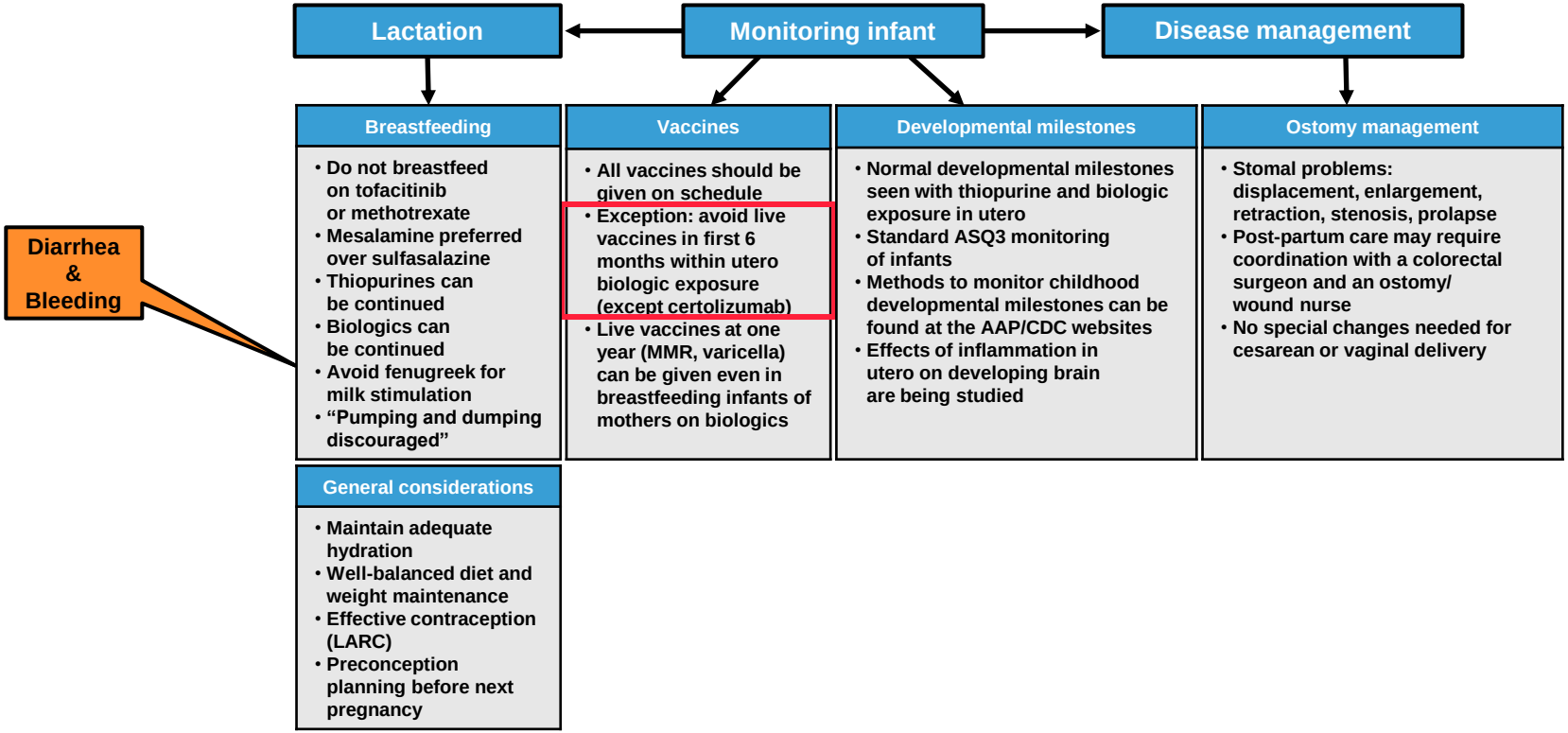
Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Anticoagulation Prophylaxis

- Any patient admitted with IBD flare
- Anticoagulant thromboprophylaxis may be extended up to 3–6 weeks postpartum in patients:
  - history of venous thromboembolic disease event or
  - other high-risk factors
- Medical therapy:
  - Unfractionated heparin, low-molecular weight heparin, and warfarin are appropriate to prescribe to breastfeeding women
  - AVOID:
    - Oral direct thrombin (Pradaxa, dabigatran) and,
    - Factor Xa inhibitors (Eliquis, apixaban; Xarelto, rivaroxaban)

Mahadevan U et al. *Gastroenterology*. 2019; 156: 1508-24.

Post-Delivery Care



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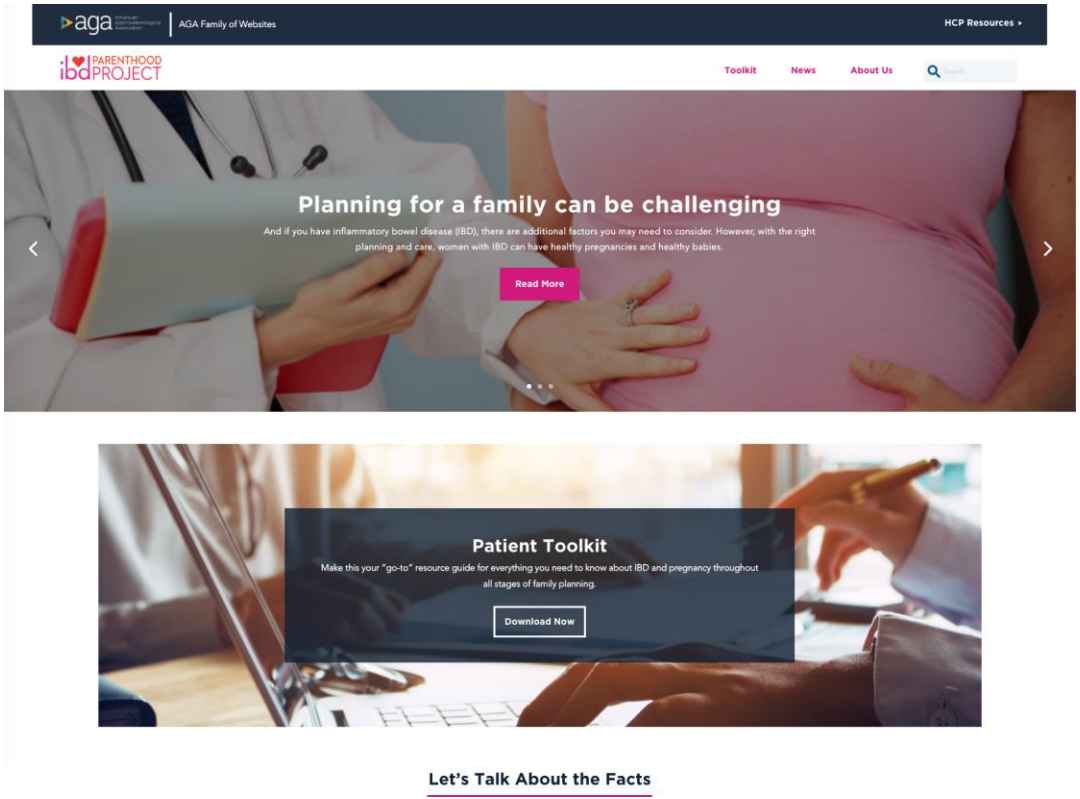
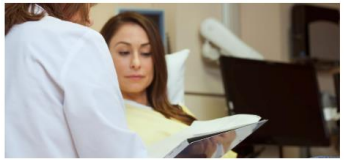
IBD Parenthood Project



http://www.ibdparenthoodproject.gastro.org/.

Patient Toolkit



Flowchart: Diagnosed with IBD?

Follow this flowchart to learn who should be involved in your care and how they should work together.

Read More >

Infographic: Prepare for better care

Discover key topics to think about through all stages of family planning (conception, pregnancy and after delivery).

Read More >

Infographic: Have a healthy pregnancy

Learn what you can do to make sure things go well.

Read More >

Discussion Guide: Speak up for what you need

Start a conversation with this guide to get the care you're looking for.

Read More >

Checklist: Plan ahead

Think of questions to ask your doctors to guide open and ongoing conversations.

Read More >

Fact Sheet: Know the truth

Separate myths from facts to feel empowered on the road ahead.

Read More >

FAQ: Get answers

Read these FAQs about proper planning and care to move forward with confidence.

Read More >

Fact Sheet: Post-delivery considerations

Key considerations for managing your health and the health of your newborn.

Read More >

Summary

- IBD Parenthood Project
  - http://www.ibdparenthoodproject.gastro.org/
- Clinical pathways
  - Pre-conception
  - Pregnancy
  - Delivery
  - Post-partum
- Patient Toolkit

aga American Gastroenterological Association

Society for Maternal-Fetal Medicine

CROHN'S & COLITIS FOUNDATION

Girls With Guts .org