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INDIANAPOLIS, INDIANA

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ACG 2022
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THE AMERICAN COLLEGE OF GASTROENTEROLOGY
Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR
ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2023 for this activity.
MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 29 – Thursday, July 21, 2022
Vascular Diseases of the GI Tract
Paul Feuerstadt, MD, FACG
Thursday, July 21, 2022 at Noon Eastern and NEW! 8pm Eastern!

Week 30 – Thursday, July 28, 2022
Diagnosis and Management of Barrett’s Esophagus: An Updated ACG Guideline
Nicholas J. Shaheen, MD, MPH, MACG
Thursday, July 28, 2022 at Noon Eastern and NEW! 8pm Eastern!

Visit gi.org/ACGVGR to Register
Disclosures

Eugenia Shmidt, MD
No relevant financial relationships

Raina Shivashankar, MD
AbbVie: Clinical trial funding, speakers’ bureau
Janssen: IBD fellowship funding, advisory board

*All of the relevant financial relationships listed for these individuals have been mitigated
ACG Virtual Grand Rounds
Fertility, Preconception and Pregnancy in IBD

Eugenia Shmidt, MD
Assistant Professor
Co-Director, Inflammatory Bowel Disease Program
University of Minnesota

Objectives

• Characterize the impact of IBD and IBD-related surgery on fertility
• Emphasize the importance of multidisciplinary preconception care
• Discuss what to expect in pregnancy and how to prevent flares and manage disease
• Review mode of delivery, breastfeeding and infant care
Age at IBD diagnosis overlaps with sexual maturation, family planning


Fears drive voluntary childlessness

<table>
<thead>
<tr>
<th>Patients' Concerns about Pregnancy</th>
<th>Yes [%]</th>
<th>No [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Considered becoming pregnant</td>
<td>68.7</td>
<td>31.3</td>
</tr>
<tr>
<td>Fear of IBD causing harm to the baby</td>
<td>62.6</td>
<td>37.4</td>
</tr>
<tr>
<td>Fear of IBD medications causing harm to the baby</td>
<td>73.1</td>
<td>26.9</td>
</tr>
<tr>
<td>Fear of passing on IBD to the baby</td>
<td>67.8</td>
<td>32.2</td>
</tr>
<tr>
<td>Fear of having a complicated pregnancy because of IBD</td>
<td>63.3</td>
<td>36.7</td>
</tr>
<tr>
<td>Fear of not being able to take care of the baby because of IBD</td>
<td>13.1</td>
<td>86.9</td>
</tr>
<tr>
<td>Fear of not becoming pregnant</td>
<td>22</td>
<td>78</td>
</tr>
</tbody>
</table>

Case #1 Question

A 23-year-old woman with severe ulcerative colitis who has failed multiple immunosuppressive agents. You are discussing elective restorative proctocolectomy with ileal pouch-anal anastomosis (RPC/IPAA) as the next step.

What can reduce risk of infertility the most?
   A. Laparoscopic (vs. open rectal dissection)
   B. Abdominal colectomy now. Delay rectal dissection until after family is complete
   C. Ask the colorectal surgeon to use adhesion barrier during open rectal dissection
   D. Cryopreservation of eggs now before surgery

Case #1 Answer

A 23-year-old woman with severe ulcerative colitis who has failed multiple immunosuppressive agents. You are discussing elective restorative proctocolectomy with ileal pouch-anal anastomosis (RPC/IPAA) as the next step.

What can reduce risk of infertility the most?
   A. Laparoscopic (vs. open rectal dissection)
   B. Abdominal colectomy now. Delay rectal dissection until after family is complete.
   C. Ask the colorectal surgeon to use adhesion barrier during open rectal dissection
   D. Cryopreservation of eggs now before surgery
Infertility in the general population

- Infertility: failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse.\(^1\)
- Affects 6-15\(^\%\)^2,3
- Risk factors\(^2\)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>aOR for Infertility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>~11*</td>
</tr>
<tr>
<td>Race</td>
<td>1.44**</td>
</tr>
<tr>
<td>Education level</td>
<td>0.5***</td>
</tr>
</tbody>
</table>

* Nulliparous, ages 40-44
** non-Hispanic, black
*** 16 years of education

Fertility after Pouch Surgery

- **Open** technique increases infertility by > 3 fold\(^1\)
- **Laparoscopic** technique associated with lower infertility risk\(^2\) and shorter time to pregnancy\(^3\)

\(^1\) Rajaratnam SG et al. J Int J Colorectal Dis. 2011
\(^3\) Gorgun et al. Surgery. 2019
Crohn’s disease vs. non-IBD

- Time to pregnancy is higher after surgery

<table>
<thead>
<tr>
<th></th>
<th>Crohn’s after surgery (n=67)</th>
<th>Crohn’s without surgery (n=206)</th>
<th>UC (n=340)</th>
</tr>
</thead>
<tbody>
<tr>
<td>aRRR for time to pregnancy &gt;12 mo</td>
<td>2.54 (1.39-4.65)</td>
<td>1.16 (95% CI, 0.7-1.93)</td>
<td>1.10 (95% CI, 0.80-1.51)</td>
</tr>
</tbody>
</table>

aRRR=adjusted relative risk ratios

- Ovarian reserve is lower

- Age >25
  - OR 10.03 (95% CI, 1.90-52.93, \(P=0.007\))

- Active disease
  - (OR, 27.99 (95% CI, 6.13-127.95, \(P<0.001\))


Fertility in Non-surgical IBD

- Systematic review including 11 studies

- CD: 17-44% reduction in fertility but linked to voluntary childlessness

- UC: no reduction in fertility

- Flare associated with reduced fertility

1. Tavernier N. Aliment Pharmacol Ther 2013
Summary: Fertility in IBD

<table>
<thead>
<tr>
<th>Surgery (RPC/IPAA in UC)</th>
<th>No Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s disease</td>
<td>Affected by active disease</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>Affected by active disease</td>
</tr>
</tbody>
</table>

- "Grain of salt": prospective data lacking from patients pre-pregnancy
- Fertility Clinic Referral
  - All IBD: 6 months
  - IBD + ≥ 40 yo: 4 months

Ban et al. Aliment Pharmacol Thera 2015

ART is successful in UC after IPAA

BUT live birth rates are reduced after IPAA failure (HR 0.36, 95% CI, 0.14-0.92)

3. Laube et al. AJG 2021
Assisted Reproductive Technology in IBD

• Danish nationwide cohort study, 1994-2013\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>NS for live births or pregnancies, per SR/MA(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC</td>
<td>0.73 (0.58-0.92)</td>
<td></td>
</tr>
<tr>
<td>CD</td>
<td>NS in full model</td>
<td></td>
</tr>
<tr>
<td>CD after surgery</td>
<td>0.51 (0.29-0.91)</td>
<td></td>
</tr>
</tbody>
</table>

• Decreased chances of live birth related to fertilization and implantation, not carrying pregnancy to term\(^2\)

2. Friedman et al. Gut. 2017
3. Laube et al. AJG. 2021

Summary: ART success

<table>
<thead>
<tr>
<th>Surgery</th>
<th>No Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn's disease</td>
<td></td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>Mixed Data</td>
</tr>
<tr>
<td>* If no pouch failure</td>
<td></td>
</tr>
</tbody>
</table>

Early referral to fertility specialist

American College of Gastroenterology
Case #2: Question 1

During an office visit, a 29-year-old woman with Crohn’s ileocolitis tells you she wants to get pregnant. She wonders if she will have active disease during pregnancy. How do you respond?

A. It depends on her disease activity at the time of conception
B. She has a 33% chance of disease staying the same, 33% chance of disease worsening and 33% chance of disease improving
C. Most likely, she will have active disease during pregnancy
D. Most likely, she will have inactive disease during pregnancy

Case #2: Answer 1

During an office visit, a 29 year-old woman with Crohn’s ileocolitis tells you she wants to get pregnant. She wonders if she will have active disease during pregnancy. How do you respond?

A. It depends on her disease activity at the time of conception
B. She has a 33% chance of disease staying the same, 33% chance of disease worsening and 33% chance of disease improving
C. Most likely, she will have active disease during pregnancy
D. Most likely, she will have inactive disease during pregnancy
Pregnancy may decrease IBD-related inflammation

Rate of disease relapse 4 years after delivery was lower than during the 3 years prior to the first pregnancy2

1. van der Giessen et al. Gut. 2020
2. Kim et al. Gastroenterology. 2021

Disease course during pregnancy might be different for UC and CD

- ECCO EpiCom: First prospective study of disease activity during pregnancy
- Most flares occurred in T1, T2 and immediate post partum
- Flares more common in UC (vs CD)
- In UC, flare was driven by pregnancy
- In CD, flare was driven by disease activity
- PIANO: Higher rates of flares, lower rates of remission in UC (vs. CD)

Pedersen N. et al. AP&T. 2013
Mahadevan et al. Gastroenterology. 2021
Active disease at conception increases risk of flare during pregnancy, poor pregnancy outcomes

- Large, prospective cohort from a single center in Rotterdam
- 298 pregnancies in 229 IBD patients
- 226 live births recorded, 9 birth defects
- Active disease at conception associated with disease relapse during pregnancy with an OR 7.66 (3.77-15.54)
- UC patients experienced relapse more often than CD, aOR 3.71 (1.86-7.4)
- Active disease in nulliparous women led to more spontaneous abortion and low birth weight

De Ima-Karagiannis A. Am J Gastroenterol 2016

Preconception care decreases disease relapse during pregnancy, voluntary childlessness

<table>
<thead>
<tr>
<th>N= 254</th>
<th>Control group (105)</th>
<th>Study group (149)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folate intake</td>
<td>46</td>
<td>87</td>
<td>0.0001</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>1</td>
<td>19</td>
<td>0.0001</td>
</tr>
<tr>
<td>Discontinuation of IBD meds due to concerns of side effects</td>
<td>8</td>
<td>0</td>
<td>0.0033</td>
</tr>
<tr>
<td>Periconceptual disease activity</td>
<td>16</td>
<td>12</td>
<td>0.68</td>
</tr>
<tr>
<td>Disease activity during pregnancy</td>
<td>34</td>
<td>20</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Cross-sectional prospective questionnaire across 8 Mediterranean centers

Impact of education:

# Pregnancies
Voluntary childlessness

North American Guideline

Statement 1:
• “We recommend that women of reproductive age with IBD receive preconception counseling to improve pregnancy outcomes”
  • Strong recommendation, very low quality evidence


Case #2: Question 2

Your 29 yo patient with Crohn’s ileocolitis develops active disease and she wants to get pregnant now. You counsel her that if she were to get pregnant now, she would be at increased risk for which of the following outcomes?

A. Cesarean section
B. Preterm prelabor rupture of membranes
C. Early pregnancy loss
D. Active disease during pregnancy
E. All of the above
Case #2: Answer 2

Your 29 yo patient with Crohn’s ileocolitis develops active disease and she wants to get pregnant now. You counsel her that if she were to get pregnant now, she would be at increased risk for which of the following outcomes?

A. Cesarean section  
B. Preterm prelabor rupture of membranes  
C. Early pregnancy loss  
D. Active disease during pregnancy  
E. All of the above

Pregnancy related outcomes in IBD

Fecal calprotectin correlates to disease activity in pregnancy in mod-severe IBD

- Danish cohort of 219 pregnancies with IBD on anti-TNF therapy
- 346 FC measurements
- Disease activity assessment: HBI, SCCAI or clinical symptoms
- FC cut-off of 200 mg/kg:
  - sens 70%–80%, spec 67%–73%, PPV 67%–74%
- Inactive: 80-120
- Mild: 259-349
- Mod-severe: 778-1277

Kammerlander H. Inflamm Bowel Dis. 2018.
University of Minnesota MFM expert recommendations

Mild Disease
No medications or Amniosalicylates only

- Fetal Monitoring
  - Comprehensive US 18-20 weeks
  - Growth US at 26 and 34 weeks

- Timing of Delivery
  - Consider at 39 weeks

Moderate/Severe Disease
Treated with medications OTHER THAN aminosalicylates

- Fetal Monitoring
  - Comprehensive US 18-20 weeks
  - Growth US q 4 weeks at 24 weeks
  - Weekly BPP at 32 weeks

- Timing of Delivery
  - Recommend at 39 weeks

BPP, biophysical profile

Case # 2: Question 3

- Your patient with Crohn’s ileocolitis is in her late first trimester of pregnancy. She reports abdominal cramping and loose stools. You rule out infection. Fecal calprotectin is 675 mg/kg. Which modality below is unsafe to work up the disease?
  A. MRI scan with gadolinium contrast
  B. Fecal calprotectin
  C. Colonoscopy with sedation, with appropriate fecal monitoring
  D. None of the above
Case # 2: Answer 3

• Your patient with Crohn’s ileocolitis is in her second trimester of pregnancy. She reports abdominal cramping and loose stools. You rule out infection. Fecal calprotectin is 675 mg/kg. Which modality below is unsafe to work up the disease?
  A. MRI scan with gadolinium contrast
  B. Fecal calprotectin
  C. Colonoscopy with sedation, with appropriate fecal monitoring
  D. None of the above

Disease activity assessment during pregnancy

• Serology
  • hemoglobin, platelets, iron, albumin; ↑ESR, WBC
• Imaging
  • MRI, US > CT
  • Avoid gadolinium, especially in T1
  • Iodinated contrast crosses placenta, but likely clinically safe, if necessary
• Endoscopy
  • Fetal monitoring (previable vs. viable)
• Sedation

Safety of lower GI endoscopy in IBD

- Case control study of pregnant IBD patients matched to age, medications and disease activity
  - Cases: did not respond to medication for flare within 1 week
  - Controls: responded to medication for flare within 1 week
- 2008-2014
- 42 IBD women (12 colonoscopies, 35 flex sig) vs. IBD controls without endoscopy
  - Sedation: none (23), midazolam (3), fentanyl (9), midazolam + fentanyl (7), unknown (5)
- Median birth weight lower in cases but no difference in spontaneous abortions, gestational age, birth defects or APGAR scores

Methylene blue, indigo carmine for chromoendoscopy
- Risks > benefits

Pregnancy-onset IBD (POIBD)

- UC > CD in POIBD vs non pregnancy–diagnosed IBD
- Symptom onset perhaps more common in T1
- Birth outcomes similar to non-POIBD
- 4-fold increase in risk of disease-related hospitalizations

2. Yu et al. Inflammatory bowel diseases. 2021
Case #2: Question 4

Your patient with active Crohn’s ileocolitis underwent an ileocolonoscopy safely and was found to have active disease, with an SES-CD score of 15. You told her that you would like to escalate her therapy. She states that her obstetrician (ob) told her to avoid IBD medications in pregnancy. You call the ob and share that most IBD medications are safe in pregnancy, except for methotrexate and:

A. small molecules
B. vedolizumab and ustekinumab
C. golimumab
D. mesalamine

Case #2: Answer 4

Your patient with Crohn’s ileocolitis underwent an ileocolonoscopy safely and was found to have active disease, with an SES-CD score of 15. You told her that you would like to escalate her therapy. She states that her obstetrician (ob) told her to avoid IBD medications in pregnancy. You call the ob and share that most IBD medications are safe in pregnancy, except for methotrexate and:

A. small molecules
B. vedolizumab and ustekinumab
C. golimumab
D. mesalamine
Corticosteroid use

- Association with oral facial clefts unlikely, although stat power may be low
- Role of disease activity

<table>
<thead>
<tr>
<th>Adverse Outcome</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm birth (&lt;37 weeks)</td>
<td>1.79 (1.18-2.73)</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>1.76 (1.07-2.88)</td>
</tr>
<tr>
<td>NICU admission</td>
<td>1.54 (1.03-2.30)</td>
</tr>
<tr>
<td>Serious infections* @ 9mo, 12 mo</td>
<td>2.9 (1.2-6.8)</td>
</tr>
</tbody>
</table>

* Use in T2/T3, controlled for disease activity


Mesalamine is safe in pregnancy

- Meta-analysis of 7 studies
- 642 received 5-ASAs, 1,158 did not
- Previous concern regarding DBP in formulation, now changed
- If on sulfasalazine, supplement with 2 mg folate daily

<table>
<thead>
<tr>
<th>Outcome</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA</td>
<td>1.16</td>
<td>0.76-1.77</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>2.38</td>
<td>0.65-8.72</td>
</tr>
<tr>
<td>SA</td>
<td>1.14</td>
<td>0.65-2.01</td>
</tr>
<tr>
<td>Preterm</td>
<td>1.35</td>
<td>0.85-2.13</td>
</tr>
</tbody>
</table>

Rahimi R. Reprod Toxicol. 2008
Safety of thiopurines in pregnancy

**Piano Registry**
- 242 exposures
- No increased risk:
  - pregnancy-related complications
  - congenital malformations
  - infant infection rates at 12 mo
  - developmental milestones at 12 mo (48 mo)

**French national health data system**

<table>
<thead>
<tr>
<th></th>
<th>Thiopurine only (n=3,554) vs none aOR (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Still birth*</td>
<td>2.04 (1.18-3.55)</td>
</tr>
<tr>
<td>C section</td>
<td>1.19 (1.09-1.31)</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>0.79 (0.67-0.92)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>1.76 (1.55-2.00)</td>
</tr>
<tr>
<td>Very preterm birth</td>
<td>1.85 (1.37-2.50)</td>
</tr>
<tr>
<td>Large for gestational age</td>
<td>1.39 (1.13-1.53)</td>
</tr>
</tbody>
</table>

*rate of 0.5% vs. 1% (unexposed), anti-TNF monotherapy (0.4%) and combination groups (0.7%)  

1. Mahadevan et al. Gastroenterology. 2021  

---

**Case #2: Question 5**

Your pregnant patient with Crohn’s ileocolitis is started on infliximab and achieves clinical remission. She is now 20 weeks pregnant. How should her disease be managed through the end of pregnancy?

A. stop infliximab now  
B. stop infliximab in the third trimester  
C. continue infliximab through pregnancy  
D. continue infliximab but at a lower dose
Case #2: Answer 5

Your pregnant patient with Crohn’s ileocolitis is started on infliximab and achieves clinical remission. She is now 20 weeks pregnant. How should her disease be managed through the end of pregnancy?

A. stop infliximab now
B. stop infliximab in the third trimester
C. continue infliximab through pregnancy
D. continue infliximab but at a lower dose

Biologics are safe

PIANO

• 869 pregnant women exposed to biologics
  • 421 IFX, 279 ADA, 135 CTZ, 11 GOL, 15 NAT, 41 VDZ, 18 UST
  • No difference (vs. no exposure) in pregnancy complications, except CS rates

Meta-analysis: 48 studies

• ~7,000 pregnancies with biologic exposure
  • IFX, ADA, CTZ, GOL, VDZ, UST
  • Rates of the following comparable to the gen pop:
    • Early pregnancy loss
    • Preterm birth
    • Stillbirth
    • Low birth weight
    • Congenital malformations

Babies exposed to most biologic therapies *in utero* have high drug levels

Fc portion of IgG antibodies are actively transported across placenta by neonatal Fc receptor

<table>
<thead>
<tr>
<th>Drug</th>
<th>N</th>
<th>Ratio infant/maternal level</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFX</td>
<td>51</td>
<td>2.2</td>
</tr>
<tr>
<td>ADA</td>
<td>35</td>
<td>1.5</td>
</tr>
<tr>
<td>UST</td>
<td>3</td>
<td>1.4</td>
</tr>
<tr>
<td>VDZ</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td>CZP</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>

Kanis S et al. J Crohns Colitis 2018

Outcomes in children exposed to anti-TNF, thiopurines

- In utero exposure to anti-TNF, thiopurine or combination vs. no exposure
- Initiative of Crohn’s and Colitis (ICC)
  - 20 centers across Netherlands, retrospective study
  - 1000 children born to IBD mothers 1999-2018, 5 year follow up
  - No difference in antibiotic treated infections, hospitalization for severe infection, adverse reactions to vaccination, growth failure, autoimmune diseases, malignancies
- PIANO (n=320)
  - No difference in developmental milestones or infection rates at 12 months

What Do The Beacons Say?

**Toronto Consensus Statement (2016)**
- Continue anti-TNF and thiopurine therapy
  - Caveat: low quality evidence

**AGA Care Pathway (2019)**
- Stop biologics at 22 weeks' gestation

**ECCO (2015)**

---

Biologics SHOULD be continued through pregnancy

- Meta-analyses of patients who continued (vs. discontinued) biologics in T3
  - 3 studies, 455 patients: Ø preterm birth
  - 4 studies, 621 patients: Ø low birth weight
  - 3 studies, 455 patients: Ø congenital malformations

- Interrupting anti-TNF therapy increases relapse risk
- Maternal disease activity is an independent risk factor for spontaneous abortion

2. Luu et al. Am J Gastroenterol. 2018
Fine tuning in clinical practice

- Consider checking trough level before conception and in T2
  - Pregnancy affects clearance of biologics differently
- If possible, adjust schedule so that the biologic is given soon after delivery
- Consider checking thiopurine metabolites in T2


Vedolizumab is safe in pregnancy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Vedolizumab (vs. unexposed or anti-TNF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage</td>
<td>Ø1,2</td>
</tr>
<tr>
<td>Birth weight</td>
<td>Ø1,2, 3</td>
</tr>
<tr>
<td>Apgar score</td>
<td>Ø1,2, 3</td>
</tr>
<tr>
<td>Prematurity</td>
<td>Ø1,2, 3</td>
</tr>
<tr>
<td>Congenital abnormalities</td>
<td>Ø1,2, 3</td>
</tr>
<tr>
<td>Malignancies (up to 1 year)</td>
<td>Ø1</td>
</tr>
<tr>
<td>Infant infections</td>
<td>Ø1,2, 3</td>
</tr>
<tr>
<td>Developmental milestones</td>
<td>Ø2</td>
</tr>
</tbody>
</table>

1. Moens et al. Aliment Pharmacol Ther. 2020
2. Chambers et al. Poster at ACG 2020. (OTIS)
Ustekinumab is safe in pregnancy

206 reports available (164 PsO, 6PsA, 36 CD)

Mahadevan et al. DDW 2018.

Limited data on risankizumab

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of Maternal Pregnancies (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth without congenital anomaly*</td>
<td>7</td>
</tr>
<tr>
<td>Live birth with congenital anomaly</td>
<td>0</td>
</tr>
<tr>
<td>Elective termination†</td>
<td>5</td>
</tr>
<tr>
<td>Elective termination with fetal defects</td>
<td>2</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>4</td>
</tr>
<tr>
<td>Pregnancy ongoing</td>
<td>3</td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>1</td>
</tr>
</tbody>
</table>

*Data through March 29, 2019.
†6 live births without complications; 1 live birth was a 36 week infant born premature due to maternal eclampsia. The infant had no complications.
‡No reported fetal defects or an examination for fetal defects was not performed.
Source: Data on file, AbbVie.
Safety of small molecules

<table>
<thead>
<tr>
<th></th>
<th>JAK inhibitors</th>
<th>S1P Receptor Modulators</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Animal studies</strong></td>
<td>Harmful (at very high concentrations)</td>
<td>Harmful S1P receptor involved in vascular formation during embryogenesis</td>
</tr>
<tr>
<td><strong>Clinical trial data</strong></td>
<td>n=11 maternal UC n=158 RA, P5, P5a</td>
<td>n=36 RMS</td>
</tr>
<tr>
<td></td>
<td>No increased rates of miscarriages or congenital malformations</td>
<td>No increased rates of miscarriages</td>
</tr>
<tr>
<td><strong>Breastfeeding</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Half life</strong></td>
<td>Short</td>
<td>Long (avoid x 90 d prior to conception)</td>
</tr>
</tbody>
</table>

2. Mahadevan U. et al. Inflamm Bowel Dis 2018

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Mode of delivery

- **GBS culture at 36 weeks and serial perineal inspection**
  - **Prior rectovaginal fistula**
    - Recommend cesarean delivery
  - **Perineal disease present (unrepaired fistula, anorectal or anal stenosis or anal stenosis)**
   - Perineal disease absent
   - Heal pouch anal anastomosis (PAA or "2-pouch")
   - Vaginal delivery with cesarean for usual indications
   - Cesarean vs. vaginal delivery based upon desires and potential protection of anal sphincter

- **Postpartum VTE prophylaxis—mechanical and pharmacologic (enoxaparin)**
  - Cesarean with surgeon backup and operative instruments for abdominal surgery

Mahadevan et al. Gastroenterology. 2019
Fears drive breastfeeding avoidance

- Personal preference
- Too ill from IBD
- Concern about exposing baby to IBD medications
- Doctor’s recommendation
- Other

Breastfeeding

Safe
- 5-ASAs
  - Mesalamine, balsalazide and olsalazine > sulfasalazine
- Biologics
  - Transferred to breastmilk in miniscule amounts
  - No adverse effects (up to 1 year) on growth, developmental milestones or infection rates
- Thiopurines

Unsafe
- Methotrexate
  - Paucity of data
  - Small molecules

Increased risk of new-onset psychiatric diagnosis in postpartum period in IBD

- 3,721 women with IBD vs. 798,908 women without IBD
- Outcome: incidence of **new-onset mental illness** from conception to 1 year post partum
- Elevated risk occurs in:
  - Post partum period (aHR 1.20, 95% CI 1.09 to 1.31)
  - Crohn’s disease (aHR 1.12, 95% CI 1.02 to 1.23)
- Women with IBD are at increased risk for mood or anxiety disorders, substance use disorders

_Vigod et al. Gut. 2019._

Vaccinations

- Infants with _in utero_ exposure to biologics (except certolizumab pegol) in T3 should avoid all live vaccines x 6 months
  - Unless serum levels are undetectable
  - Oral rotavirus (US), BCG, oral polio

_Mahadevan et al. Gastroenterology. 2019_
Summary

• Infertility increases after RPC/IPAA, Crohn’s surgery and in active disease
• Prior to conception, clinical and endoscopic remission should be achieved.
• Active disease (not meds) = biggest threat to Mom and Baby
  • Continue biologics through pregnancy
• Check fecal calprotectin at preconception, T1, T2, T3 and postpartum
• In most cases, vaginal delivery is safe
• Avoid methotrexate and ozanimod x 3 mo before conception.
• For now, avoid JAK inhibitors in pregnancy and lactation
• Breastfeeding is safe with biologics

Thank you, ACG!
Questions and Answers

Eugenia Shmidt, MD

Raina Shivashankar, MD

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