Women and Inflammatory Bowel Disease

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Background:
Ulcerative colitis (UC) and Crohn’s disease (CD)

• Increasing incidence over the last 50 years
• Peak incidence: 15-35 years
• The diseases have an unpredictable cyclic pattern of relapses and remissions
• A relapse is characterised by inflammation of the small or large intestines
• Relapses can be characterized as mild, moderate or severe

UC: Presenting Symptoms

- Bloody diarrhea
- Abdominal cramping
- Urgency
- Weight loss
- Fevers
- Symptoms depend upon extent and severity of inflammation
Endoscopic Spectrum of Severity
UC – Spectrum of Disease

Normal

Mild

Moderate

Severe

Reprinted with permission from AGA Clinical Teaching Project. IBD. 3rd ed. 2002.
CD: Presentation

- Diarrhea
- Chronic abdominal pain and tenderness
- Weight loss
- Fever
- Perianal disease
- Symptoms vary with location of disease
CD: Clinical Features

Inflammation
- Abdominal pain
- Tenderness
- Diarrhea
- Weight loss

Obstruction
- Cramps
- Distention
- Vomiting

Fistulization
- Diarrhea
- Pain
- Air/feces in urine
- Types
  - Enteroenteric
  - Enterovesical
  - Retroperitoneal
  - Enterocutaneous

Adapted with permission from AGA Gastroenterology Teaching Project. 3rd ed. 2002.
Outline

• Birth control
• Sexual function
• Fertility in IBD
• Planning a pregnancy
• Managing IBD during pregnancy
• Delivery recommendations
• Post-partum management of IBD and breast feeding
• Menopause
Contraception: Questions

• Will certain types of contraception make IBD worse?
  – Contraception use should not worsen bowel symptoms (and may improve them if they are cyclical)

• Is contraception needed and/or effective in IBD?
  – Contraception is effective
  – Planning pregnancy is crucial in IBD

• Are any contraceptive methods that should not be used in women with IBD?
A few considerations

• If patients have significant inflammation affecting absorption, this may decrease the efficacy of an oral contraceptive (the pill)

• Women with IBD have a 2-3 fold increased risk of blood clots, and combination contraception (with estrogen) may also increase risk of blood clots to 2x baseline

• IUDs are thought to be safe, but the data are limited
Risk of hormonal contraceptives

• Low-dose (containing ≤35 \( \mu g \) ethinyl estradiol) combined oral contraceptives, the combined hormonal patch, and the combined vaginal ring.

• For women with mild IBD and no other risk factors for a blood clot (venous thromboembolism), the benefits generally outweigh the risks.

• For women with IBD who are at increased risk for blood clot (e.g., those with active or extensive disease, surgery, immobilization, corticosteroid use, vitamin deficiencies, or fluid depletion), the risks generally outweigh the benefits.

MMWR Recomm Rep 2010;59(RR-4):1-86.
Selected reproductive matters in IBD:
Sexual function, fertility, and conception

Father with IBD

Effects of:
- Disease activity
- Medications
- Surgery
- Depression
- Hypogonadism

Mother with IBD

Effects of:
- Disease activity
- Medications
- Surgery
- Depression
- Hypogonadism

Fertility

Conception

Pregnancy

Viable intrauterine pregnancy

Pregnancy loss/ectopic pregnancy

Sexual function
Sexual function in Crohn’s disease and ulcerative colitis

What we know:
1. There is an increased prevalence of sexual dysfunction women (and men) with IBD
2. Causes of sexual dysfunction in IBD
3. Treatment of sexual dysfunction in the general population

Knowledge gaps:
1. How to accurately measure the presence of and degree of sexual dysfunction in patients with IBD
2. Treatment of sexual dysfunction in patients with IBD
Factors that can affect sexual function in IBD

- Scars
- Ostomies
- Feeding tubes
- Pain/nausea
- Reduced self-esteem
- Loss of former identity
- Anxiety over disclosure
- Antidepressants
- Corticosteroids: body image
- Immunosuppressant
- Opiates
- Diarrhea
- Fatigue / low libido
- Body image/appearance
- Perianal complications
- Draining fistulae
- Skin/Arthritic lesions
- Pain
- Disease Activity
- Medication
- Depression
- Surgery
- Scars
- Ostomies
- Feeding tubes
- Pain/nausea
- Disease Activity
- Depression
- Surgery
- Medication

Disease Activity, Depression, Surgery, Medication are interconnected.
Female Sexual Dysfunction in IBD

Percentage of respondents who felt that CD or UC contributed to the following perceptions/symptoms in sexual relationship (> 50% of the time)

- Embarrassment
- Less attractive to partner
- Negative affect
- Fatigue
- Reduced desire
- Fear of ostomy leak
- Fear of pain
- Fear of passing urine
- Fear of passing stool
- Fear of passing gas
- Fear of intimacy
- Rectal pain
- Abdominal pain
- Increased consciousness during intercourse
- Caused problems during sex
- Prevented sexual activity
- Delayed start of sexual relationship
- Prevent start of sexual relationship
- Distress

N=244

De Silva, DDW 2016
Solutions for non-IBD patients which may be helpful for our IBD patients

- Pelvic floor physical therapy with an experienced therapist
- Myofascial release at specific vaginal/pelvic trigger points
- Biofeedback therapy; vaginal dilators
- Before therapy for sexual dysfunction, address mood, self-image, stressors, and relationship issues and provide referrals

Female Sexual Dysfunction Algorithm

Gyn Exam
- Manage active gyn issues

Depression?
- Stress?
- Abuse?
- Medications?
- Manage active IBD issues

Sexual interest/arousal disorder
- Psych, counseling, mindfulness therapy

Orgasmic disorder

Genitopelvic pain disorder
- Pelvic floor PT
Selected reproductive matters in IBD: Sexual function, fertility, and conception

Father with IBD

- Effects of:
  - Disease activity
  - Medications
  - Surgery
  - Depression
  - Hypogonadism

Mother with IBD

- Sexual function
- Fertility
- Conception
- Pregnancy

Effects of:
- Disease activity
- Medications
- Surgery
- Voluntary childlessness
- Ovarian reserve

Pregnancy loss/ectopic pregnancy

Viable intrauterine pregnancy

Pregnancy
Fertility in Crohn’s disease and ulcerative colitis

• What we know:
1. There is increased voluntary childlessness – women “volunteering” NOT to have children
2. IBD surgery decreases fertility – ileostomy, ileoanal pouch anastomosis

• What we are beginning to understand:
1. The effect of laparoscopic surgery and assisted reproduction (IVF) on fertility in patients with IBD
2. Patients with Crohn’s disease have decreased ovarian reserve\(^1,2\)
3. Patients with active disease probably have decreased fertility\(^3\)
4. The rate of ectopic pregnancies is increased in patients with Crohn’s disease\(^4\)

\(^1\)Freour, Inflamm Bowel Dis 2012; \(^2\)Senates, J Crohns Colitis 2013; \(^3\)Ban et. al. APT 2015; 42(7): 855-66; \(^4\)De Silva et al., Advances in IBD 2016.
Fertility in Crohn’s disease and ulcerative colitis: What we don’t know

**Knowledge gaps:**

1. The rate of pregnancy loss
2. The effect of subclinical disease on fertility
3. The effect of IBD medications on fertility
Ovarian reserve in Crohn’s disease

**Definition:** The capacity of the ovary to provide egg cells that are capable of fertilization resulting in a healthy and successful pregnancy.

**Measurement:** anti-Mullerian hormone (AMH) is a good indicator of ovarian reserve

Low ovarian reserve in CD associated with:
- Age >30y
- Colonic disease
- Higher disease activity
- Disease duration >5y
- Surgery did not affect ovarian reserve

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1 Freour, Inflamm Bowel Dis 2012; 2 Senates, J Crohns Colitis 2013
Ileal Pouch-Anal Anastomosis (IPAA)
Fertility after ileal pouch anal anastomosis (IPAA)

- 2-3 fold increased risk of infertility after IPAA\(^1,2,3\)
- Reduction in fertility from 72 to 37% after surgery\(^4\)

1. Waljee et. al., Gut, 2006; 55: 1575
Does laparoscopic vs. open IPAA surgery make a difference?

• Cross-sectional study, Netherlands and Belgium; 27 laparoscopic, 23 open
  – Shorter time to pregnancy with laparoscopic IPAA: \( p=0.023 \)^1

• French study of 63 patients who underwent laparoscopic IPAA, 73% of them for ulcerative colitis, 17% for familial adenomatous polyposis^2
  – 73% of women who attempted pregnancy were successful in conceiving

Infertility in IBD: When to refer for assisted reproductive technology treatment (IVF)

Fertility

- When to refer for work up:
  - >1 year of infertility in any IBD patient
  - Any post surgical IBD patient with irregular cycles
  - >3 cycles without success in a patient s/p IPAA (colectomy with J pouch) or proctectomy

Assisted reproduction (IVF) in women with IBD in Denmark

- Danish Birth Registry and IVF Registry
- Outcome live birth per IVF treatment cycle
- UC + IVF: live birth rate 27% lower than infertile women in the general population
- CD + IVF: live birth rate also lower by 23%
- CD + CD surgery + IVF: live birth rate lower by 49%
Fertility: Conclusion

• Aside from increased voluntary childlessness, decreased fertility in IBD is due to surgery for IBD and probably increased disease activity
• Patients with Crohn’s disease probably have decreased ovarian reserve
• Laparoscopic surgery probably improves fertility in patients with IBD + ileoanal pouch anastomosis
• Women with IBD do not have the same success with IVF as women in the general infertile population
Selected reproductive matters in IBD: Pregnancy

Effects of:
- Medications
  - Adverse Effects
  - Adherence
- Surgery
- Disease activity

Recommended mode of delivery
- Adverse Birth Outcomes
- Medications and Lactation

Long term effects during childhood and adulthood

Pregnancy

Birth

Postpartum
Pregnancy and Moderate to Severe UC

- 32 year old woman, previously normal pregnancy and vaginal delivery 2 years ago
- Reported bloody diarrhea and abdominal pain the “moment I got pregnant”
- Flex sig during 8\textsuperscript{th} week of pregnancy showed moderate to severe UC
- Placed on oral prednisone
- Decreased BMs and blood on 40mg and symptoms returned when down to 30mg
Milestones of Gestation / Prenatal Care

Establish PNC

0  2  4  12  18  23  24  35  37  39  40

LMP  Conception  Expected period  Established placental perfusion  Completion morphologic development  Down’s screening/PNC Testing  Morphology screening u/s  Viability  Gestational diabetes screening  NICU admissions NOT mandated  Term  Elective delivery acceptable
Data

- Up and down on prednisone, unable to go below 30mg and worsened during second trimester
- Failing 60mg oral prednisone at 23 weeks gestation
- PE: tender mid epigastric area and LLQ pain
- HGB 9.6
- CRP 44.6
- Admitted for IV solumedrol
- Sigmoidoscopy - moderate chronic active colitis
Sigmoidoscopy
Clinical Course

- Better on IV solumedrol X 7 days
- Home on oral prednisone and worsening after one week
- Readmitted 2 weeks later
- She is now 25 weeks pregnant - What would you do next? Are anti-TNFs safe during pregnancy?
- Do we know why women with UC tend to flare more during pregnancy than women with Crohn’s disease?
Are anti-TNFs Safe?

Recent meta-analysis showed no statistically significant differences in unfavorable pregnancy outcomes, rates of abortion, preterm birth, low birth weight or congenital anomalies in women taking anti-TNFs.

Impact of IBD on Pregnancy
Crohn’s vs. UC

**Crohns**

<table>
<thead>
<tr>
<th>Time (trimester)</th>
<th>CD non-pregnant</th>
<th>CD pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>1</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
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<td>4</td>
<td>56</td>
<td>51</td>
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$P = 0.2049$

**UC**

<table>
<thead>
<tr>
<th>Time (trimester)</th>
<th>UC non-pregnant</th>
<th>UC pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>111</td>
<td>111</td>
</tr>
<tr>
<td>1</td>
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<td>111</td>
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<td>2</td>
<td>108</td>
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<td>3</td>
<td>99</td>
<td>76</td>
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<td>4</td>
<td>86</td>
<td>71</td>
</tr>
<tr>
<td>5</td>
<td>82</td>
<td>64</td>
</tr>
</tbody>
</table>

$P < 0.0001$

_N. Pedersen et al_. *Aliment Pharmacol Ther* 2013; 38: 501-512
Clinical Course

- She received induction infliximab and IV solumedrol
- Better after one week and discharged home
- Bloody diarrhea after several days and readmitted 2 weeks later – salmonella infection
- Better on antibiotics and sent home after one week
- More bloody diarrhea and switched to oral medrol still at high doses, given 2nd dose infliximab induction no response
Medication Safety

- Does she need a C-section?
- Does she need early delivery?
- Will delivering her baby make the UC better?
Delivery

- Infliximab is not working and medrol is not working – she is now 32 weeks and 5 days pregnant – she has premature rupture of membranes and abruption and has a spontaneous vaginal delivery
- Baby has APGARs of 9 and 9 and does well
Post-delivery

- She failed infliximab + azathioprine, vedolizumab and tofacitinib and eventually has a colectomy
- Pathology of her colon:
Gross Pathology
Gross Pathology
Impact of pregnancy on maternal IBD

<table>
<thead>
<tr>
<th></th>
<th>IBD (ulcerative colitis and Crohn’s disease)</th>
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</thead>
<tbody>
<tr>
<td>% patients in remission during pregnancy</td>
<td>% patients with aggravated or persistent disease activity during pregnancy</td>
</tr>
<tr>
<td>Remission at the time of conception 70</td>
<td>30</td>
</tr>
<tr>
<td>Active disease at the time of conception 30</td>
<td>70</td>
</tr>
</tbody>
</table>

Preconception care leads to less disease relapse during pregnancy

- Prospective study; 2008-2013
- Females of reproductive age with IBD attending IBD Pregnancy Outpatient Clinic (POC)
- Study group (n=149): preconception IBD POC counseling (30 minute consult)
- Control group (n=105): patients attending IBD POC when already pregnant
- Results:

<table>
<thead>
<tr>
<th></th>
<th>Control group (105)</th>
<th>Study group (149)</th>
<th>P value</th>
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<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>
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<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>

Preventing possible adverse outcomes

- Low birth weight and preterm birth are the main predictors for perinatal mortality and morbidity.
- Impaired intrauterine growth predicts chronic diseases in adulthood.
Risk of adverse events

- Meta-analysis of 23 studies including over 15,000 women with IBD comparing odds of adverse events between pregnant women with and without IBD
- Effects of flare on these outcomes are unknown
- Medications were not controlled for

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
</tr>
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<tbody>
<tr>
<td>Preterm Birth</td>
<td>1.85</td>
<td>1.67-2.05</td>
</tr>
<tr>
<td>Small for Gestational Age Birth Weight</td>
<td>1.36</td>
<td>1.16-1.60</td>
</tr>
<tr>
<td>Congenital Anomalies</td>
<td>1.29</td>
<td>1.05-1.58</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>1.57</td>
<td>1.03-2.38</td>
</tr>
</tbody>
</table>
Outcomes of obstetric hospitalizations in women with IBD

- 2005 National Inpatient Sample (US)
- 4.21 million deliveries; 2372 CD, 1368 UC
- Increased risk of:
  - C section – OR 1.72 [1.44-2.04] CD; 1.29 [1.01-1.66] UC
  - Blood transfusions – OR 2.2 [1.51-5.26] CD
  - Protein-calorie malnutrition – OR 20 [8.8-45.4] CD; 60.8 [28.2-131] UC

Nguyen et al., Clin Gastroenterol and Hepatol 2009;7:329.
Complications from IBD during pregnancy and delivery

- Medical, birth, Patient and Prescribed Drug Registers of all residents in Sweden (inpatient and outpatient records)
- 1209 UC; 787 CD; 10,773 controls
- October 2006-December 2009
- DVT UC: OR 3.78 [1.52-9.38]
- Antepartum hemorrhage CD: OR 1.66 [1.12-2.45]
- Emergency C-section UC: OR 1.39 [1.13-1.70]; CD: OR 1.50 [1.17-1.92]

Treatment of inflammatory bowel disease (IBD) 20 - 5 years ago

- Biological therapy was considered only for those who have a moderate-severe disease or failed other medications
- It was introduced for treatment of IBD in the late 90s
Treatment of moderate to severe IBD in 2018

- Surgery
- Total Parenteral Nutrition (Crohn’s disease only)
- Small molecules (UC only)
- Prednisone/Budesonide
- Biologics + Immunomodulators
Biologics and small molecules: Many new treatments, not enough data in pregnancy

- Infliximab (Remicade)
- Adalimumab (Humira)
- Certolizumab (Cimzia)
- Vedolizumab (Entyvio)
- Natalizumab (Tysabri)
- Ustekinumab (Stelara)
- Tofacitinib (Zeljanz)
Pregnancy planning

• Important to discuss pregnancy with patients who are planning to conceive in the near future
• Factors that may affect IBD during pregnancy
  – Disease status at conception
  – Medication use and/or continuation
• Often recommended for a patient to meet with or be followed by high-risk OB
Summary: Safety of IBD medications during pregnancy

<table>
<thead>
<tr>
<th>Evidence Favors Benefit Over Any Risk</th>
<th>Less Data/ Benefit Thought to Outweigh Risks</th>
<th>Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral, topical 5-ASA</td>
<td>Aza/6MP</td>
<td>Asacol HD? (Diphenylthalate)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Cyclosporine</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Anti-TNFs</td>
<td>Thalidomide</td>
</tr>
<tr>
<td>Anti-diarrheals</td>
<td>Vedolizumab/Ustekinembab</td>
<td></td>
</tr>
</tbody>
</table>

Human placental transfer

- Fetal immunity is acquired by transfer of Ab as IgG from maternal to fetal circulation
- IgG is actively transported across the placenta
- All 4 subclasses of IgG can pass to the fetus
  - Preferential transfer of IgG1
- IgG transferred via the placenta will persist longer in the newborn than the mother

Distribution of IgG concentration during gestation in the umbilical vein

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When Do You Stop Anti-TNFs?

• London Position Statement of the World Congress of Gastroenterology: infliximab, adalimumab and certolizumab are considered low risk and can be continued during conception and at least the first 2 trimesters of pregnancy

• ECCO: Discontinue anti-TNF medication around gestational week 24-26 but decision to discontinue should be determined individually based on maternal disease activity

• US: Medication often stopped at end of 2nd trimester though decision is case by case, and we continue medications if women are flaring
How long are levels detectable in offspring?

Figure 4. Mean (±SEM) and fitted neonatal clearance of adalimumab and infliximab.

Julsgaard et. al. Gastroenterology April 2016; 151:110-119
Hi Sonia and Beth-Ann,

I started Stelara and stopped the Azasan and am weaning off the prednisone. My Crohn's symptoms are much better than they were!

I went to see my gynecologist today, and I am pregnant. I have an ultrasound tomorrow morning, but she thought that I was fairly early on.

That said, I'm really concerned. As this was not a planned pregnancy, I was/am taking some medications (Percocet, Azasan, Prednisone) that I worry could hurt the baby. Not to mention my low levels of B12 and vitamin D...the silver lining is I'm on day 2 of no smoking, and think this time quitting will stick!

Specifically I'm worried about the Percocet. I typically take 2.5mg once or twice a day, but last month I was using up to 10mg a day, as I was in a lot of pain.
Patient History

- 55 cm of ileal CD resected 5 years ago
- Failed all anti-TNFs and MTX
- CD recurrence better on Stelara and Azasan (brand name azathioprine)
- Unplanned pregnancy
IBD Medications and Pregnancy

• Are you concerned about any of these medications taken during pregnancy?
• Specifically: Stelara (ustekinumab), azathioprine, prednisone?
• Is any trimester more dangerous than any other in terms of taking these medications?
• What about the safety of other IBD therapies? Vedolizumab? Tofacitinib?
Vedolizumab

- 24 pregnancies in exposed females and 15 pregnancies in partners of exposed men
- 1 congenital anomaly (agenesis of corpus callosum) among 24 pregnancies in VDZ-exposed females
  - Occurred in the baby of a healthy volunteer; unclear if related to VDZ given the virtual elimination of VDZ at the estimated time of organogenesis of the corpus callosum

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Number and outcome of pregnancies in female participants and partners of male participants in the clinical development programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy outcome</td>
<td>Placebo ($n^* = 3/4$)</td>
</tr>
<tr>
<td></td>
<td>Healthy volunteers</td>
</tr>
<tr>
<td>Live birth</td>
<td>0/0</td>
</tr>
<tr>
<td>Congenital anomaly</td>
<td>0/0</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>1/0</td>
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<tr>
<td>Elective termination</td>
<td>0/0</td>
</tr>
<tr>
<td>Undocumented‡</td>
<td>0/0</td>
</tr>
</tbody>
</table>

CD, Crohn’s disease; UC, ulcerative colitis.

*Number of pregnancies in female study participants/number of pregnancies in partners of male study participants.
†Includes the congenital anomaly outcome.
‡Includes pregnancies that were on-going at last participant contact.

Mahadevan et. al. APT 2017; 45: 941-950
Ustekinumab

- Data and safety are based on case reports
- One case report of an uncomplicated pregnancy in a woman with Crohn’s disease on combo therapy with ustekinumab and azathioprine\(^1\)
- Measurement of cord blood levels were nearly two-fold that of maternal drug levels at delivery (37 weeks) after maintenance of therapy every 4 weeks until gestational week 33\(^2\)

\(1\) Cortez et. al. J Clin Pharm Ther 2017, 42: 234-236. \(2\) Rowan et. al. JCC 2017 epub
Tofacitinib

- 18 RA & 16 psoriasis pregnancies
- First trimester exposures only
- 21 pregnancies resulted in a live birth
  - Healthy newborn: 18
  - 1 low birth weight
  - 1 preterm
- Congenital malformation: 1
- More data are needed

Tofacitinib

- 11 UC pregnancies in the clinical trials
- First trimester exposure only
- 2 spontaneous abortions
- 2 medical terminations
- 4 healthy babies
- 3 lost to follow-up

Outcome

• Vaginal delivery at 38 weeks, 4 days - healthy baby
• She wants to breastfeed on Stelara - is this OK? What do you tell patients about breastfeeding on biologics and azathioprine/6-MP?
Breastfeeding Benefits

• Reduced infant infectious disease
  – Diarrhea
  – ENT infections
  – Pneumonias
• Reduced long term risk of asthma
• Reduced long term risk of obesity
• Reduced risk of SIDS
• Reduced maternal breast/ovarian CA
• Health care costs lower (3x) among breastfed mother-baby diads.

Consult – stricturing ileal CD in Mid-pregnancy

- GI consult- 23 week pregnant female with 10 year history of CD of ileal, had only been on 6-75mg MP + prednisone (on and off)
- Now on 20mg of prednisone
- Nausea/vomiting, no flatus, abdominal distention
The image reveals a 7 to 10 cm long stricture at the terminal ileum (white arrows) causing obstruction and significant dilatation of the proximal small bowel (white asterisk). A fetus is seen in the uterus (dashed white arrows).
What would you do now?

• She can drink fluids but cannot eat despite steroids being increased to IV solumedrol 20mg q 8 hours
• Still obstructed
• Which is safer, surgery or TPN?
• What is the hesitancy in using TPN and are there different considerations for a pregnant person?
• Any use for infliximab?
How do we evaluate disease activity during pregnancy?

www.beliefnet.com

www.syrvet.com

www.active8health.net
Management of the flaring IBD Pregnant Patient

• Medication choices are similar
  – Avoid new aza/6mp in pregnancy.
  – Okay to start biologics.
  – Avoid metronidazole in first trimester (T1)

• Laboratory/Stool Tests
  – C. difficile
  – Fecal calprotectin
  – Albumin may be low; mild anemia normal, ESR/CRP may be elevated due to pregnancy

• Imaging
  – MRI preferred to CT, though no gadolinium in T1
  – Ultrasound!

• Endoscopy: Unsedated flexible sigmoidoscopy

• Surgery: Indications similar to non-pregnant patient; T2 best
Delivery Considerations

• Most patients: normal labor and delivery
• Ileoanal pouch anastomosis and vaginal delivery: A word of caution
• Higher incidence of anterior sphincter defects by endoanal sonography and lower anal squeeze pressures in vaginal delivery versus C-section\(^1\)
• Good short to medium term pouch function (0-5 years)\(^2\) and no significant change in pouch function after vaginal delivery
• ? Long term function (10-20 years out)

\(^1\)Remzi et al., Dis Colon Rectum 2005;9:1691
\(^2\)Nelson et al., Dis Colon Rectum 1989;32:384
Mode of Delivery: Recommendations

• Absolute Indications for C-section:
  – Active perianal disease
  – Perirectal, rectovaginal, or perianal fistulas
Post-Delivery Considerations

• When to restart therapy
  – Immediately, while in the hospital
• Vaccination recommendations for the baby
• Medications that are safe during breastfeeding
# Neonatal Vaccination Schedule

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type</th>
<th>Birth</th>
<th>2mo</th>
<th>4mo</th>
<th>6mo</th>
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</thead>
<tbody>
<tr>
<td>Hepatitis B (HBV)</td>
<td>Inactivated Viral</td>
<td>X</td>
<td></td>
<td></td>
<td>X---</td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis (Dtaph)</td>
<td>Inactivated Bacterial</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus Influenzae</em> (HiB)</td>
<td>Inactivated Bacterial</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (PCV)</td>
<td>Inactivated Bacterial</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Polio (IPV)</td>
<td>Inactivated Viral</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Rotavirus (RV)</td>
<td>Live Viral</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
Are vaccinations effective in babies exposed to biologics?

- PIANO registry
- 26 babies not exposed to biologics during pregnancy and 153 exposed to biologics in utero
- No significant difference in proportion of 7 month old infants with protective antibody titers to Hepatitis B or tetanus toxin after vaccination

Beaulieu et. al., CGH 2017, epub
## Safety of IBD medications during breastfeeding

<table>
<thead>
<tr>
<th>Safe to Use when Indicated</th>
<th>Limited Data Available but Appear Low Risk</th>
<th>Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral, topical 5-ASA</td>
<td>Azathioprine</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>6-MP</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Anti-TNFs</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td></td>
<td>Vedolizumab/Ustekinimab</td>
<td>Cyclosporine</td>
</tr>
</tbody>
</table>

Pregnancy summary

• Best outcomes for women with IBD are in those with planned pregnancies
• Ensure preconception counseling and collaboration with an OBGYN or Maternal Fetal Medicine before and during pregnancy
• Do not alter best practices for IBD management due to pregnancy in women with active disease
• Infliximab has a slower clearance from the neonatal circulation than adalimumab and levels can be present as late as 12 months
• Combination therapy with anti-TNF + azathioprine/6-MP is associated with a greater risk of neonatal bacterial infections
Hormone replacement therapy and IBD

• Prospective cohort study of 108,844 postmenopausal US women (median age 54 years) enrolled in 1976 in the Nurses’ Health Study without a prior history of CD or UC

• Compared to women who never used hormones, the risk for ulcerative colitis was 1.71 (95% CI, 1.07-2.74) among women who currently used hormones and 1.65 (95% CI, 1.03-2.66) among past users.

• No difference in risk according to hormone type.

• No increased risk of Crohn’s disease.

THANK YOU