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'm mostly just plagued by the prednisone side effects.

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. And is there something I can do to improve my vitamin deficiencies? I already take a multi-vitamin.

Thanks,
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).

Causes of Sexual Dysfunction in IBD

- Increased disease activity
- Surgery
- Depression
- Hypogonadism

Infertility: When to Refer for Intrauterine Insemination (IUI) or In Vitro Fertilization (IVF)

Fertility

- When to refer for work up:
  - >1 year in any IBD patient
  - Any post surgical IBD pt with irregular cycles
  - >3 menstrual cycles in a post surgical patient


Sexual Function and Fertility in Women After Total Proctocolectomy and Ileostomy

- UC (n=41); CD (n=30)

<table>
<thead>
<tr>
<th></th>
<th>Pre-op</th>
<th>Post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal discharge</td>
<td>9%</td>
<td>49%</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>12%</td>
<td>27%</td>
</tr>
<tr>
<td>Pregnancy within 5 years of follow up</td>
<td>72%</td>
<td>37% (p&lt;0.001)</td>
</tr>
<tr>
<td>C-section post-op</td>
<td></td>
<td>6/27 patients</td>
</tr>
</tbody>
</table>

Ulcereative Colitis - Ileal Pouch-Anal Anastomosis

Risk of Infertility in UC Increases Threefold After Ileal Pouch-anal Anastomosis (IPAA)*

<table>
<thead>
<tr>
<th>Study</th>
<th>Relative Risk (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wikland</td>
<td>1.93 (0.92, 4.03)</td>
<td>9.9</td>
</tr>
<tr>
<td>Oresland</td>
<td>14.40 (0.98, 211.94)</td>
<td>1.2</td>
</tr>
<tr>
<td>Counihan</td>
<td>3.60 (1.39, 9.35)</td>
<td>9.1</td>
</tr>
<tr>
<td>Sjogren</td>
<td>1.00 (0.32, 3.10)</td>
<td>9.1</td>
</tr>
<tr>
<td>Hudson</td>
<td>3.38 (1.66, 6.89)</td>
<td>5.8</td>
</tr>
<tr>
<td>Olsen</td>
<td>3.62 (2.42, 5.41)</td>
<td>44.1</td>
</tr>
<tr>
<td>Johnson</td>
<td>2.89 (1.47, 5.68)</td>
<td>20.9</td>
</tr>
<tr>
<td>Overall</td>
<td>3.17 (2.41, 4.18)</td>
<td></td>
</tr>
</tbody>
</table>

* Compared to medical management

**Hysterosalpingography after IPAA**

- 21 patients with UC after IPAA
- Hysterosalpingography normal in only 7
- Bilateral occlusion of the fallopian tubes in 2
- Unilateral occlusion in 9
- Fallopian tubes adherent to the bottom of the lesser pelvis in 10 patients


**Does Laparoscopic vs Open IPAA Surgery Make a Difference?**

- Less adhesion formation after lap vs open colectomy
- Cross-sectional study, Netherlands and Belgium
- Laparoscopic (n=27); 19 pregnant, 1 IVF
- Open (n=23); 9 pregnant; 4 IVF
- Shorter time to pregnancy with laparoscopic IPAA: p=.023

Fertility in Non-Surgically Treated IBD

- Systemic review of 11 studies
- Women with CD: 11-44% reduction in fertility (all voluntary)
- Men with CD: 18-50% reduction in fertility (probably voluntary)
- Women and men with UC: No reduction in fertility


Voluntary Childlessness is Increased in Women With IBD

- Survey study in women; 110 CD, 59 UC; ages 15-44
  - 92% white
  - 44% bachelor’s degree (national level 17%)
  - 29% graduate degree (national level 9.8%)
- Voluntary childlessness:
  - CD: 18% versus 6.2% national average; p<0.001
  - UC: 14%; p < 0.08
- Number of children
  - CD: 0.8, UC 0.6 (p<0.001 versus census data of 1.18)

### Reasons Women With IBD Have for Not Wanting Children

<table>
<thead>
<tr>
<th>Concerns</th>
<th>(N=37 patients)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerns of having a worsening of my disease as a result of the pregnancy</td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>Concern for the possibility of genetically passing the disease to my child</td>
<td></td>
<td>73</td>
</tr>
<tr>
<td>Concern for not being able to care for a child</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>Concerned about the added stress of raising a child</td>
<td></td>
<td>65</td>
</tr>
<tr>
<td>Concern for having a recurrence of my disease as a result of pregnancy</td>
<td></td>
<td>57</td>
</tr>
</tbody>
</table>

Increase in Preterm Birth With Moderate to High Disease Activity

<table>
<thead>
<tr>
<th></th>
<th>Crude Relative Risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW</td>
<td>1.1</td>
<td>0.3-4.0</td>
</tr>
<tr>
<td>LBW at term</td>
<td>0.9</td>
<td>0.1-8.5</td>
</tr>
<tr>
<td><strong>Preterm birth</strong></td>
<td><strong>3.4</strong></td>
<td><strong>1.1-10.6</strong></td>
</tr>
<tr>
<td>Congenital Anomalies</td>
<td>0.4</td>
<td>0.0-3.9</td>
</tr>
</tbody>
</table>

Danish population based study: Pregnancies with disease activity at any time (n=71) were compared to pregnancies without any disease activity (n=86).


Pregnancy Outcomes in a Large HMO Population

- Retrospective cohort study of all women in Northern California Kaiser Permanente: 1995-2002
- 461 pregnant women with IBD matched to 493 pregnant women without IBD
  - Biologics/immodulators 4%
  - Corticosteroids 21%
  - 5-ASAs 51%
  - 80% mild disease throughout pregnancy

Effect of IBD on Pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Conception Outcome</th>
<th>Pregnancy Outcome</th>
<th>Pregnancy Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD</td>
<td>1.65 (1.09-2.48)</td>
<td>1.54 (1.00-2.38)</td>
<td>1.78 (1.13-2.81)</td>
</tr>
<tr>
<td>UC</td>
<td>2.78 (0.68-11.3)</td>
<td>1.48 (0.91-2.39)</td>
<td>1.51 (0.9-2.53)</td>
</tr>
<tr>
<td>CD</td>
<td>2.53 (0.24-27.2)</td>
<td>1.40 (0.75-2.63)</td>
<td>2.33 (1.24-4.37)</td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td>2.42 (1.28-4.55)</td>
<td>2.90 (1.45-5.78)</td>
<td>1.95 (0.9-4.2)</td>
</tr>
<tr>
<td>Surgery</td>
<td>2.26 (1.12-4.55)</td>
<td>1.28 (0.57-2.86)</td>
<td>2.99 (1.39-6.43)</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

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]


First Trimester Considerations

- Nausea, decreased appetite, fatigue
- Iron, B12, folate deficiency
- Ionizing radiation
  - Fetal risks of anomalies, growth restriction, or abortions are not increased with radiation exposure of < 5 rad (50mGv)
  - Fetus CNS at greatest risk at 8 to 15 weeks
  - No proven risk < 8 weeks or > 25 weeks
### American College of Radiology Relative Radiation Levels

<table>
<thead>
<tr>
<th>Relative Radiation Level</th>
<th>Adult Effective Dose Estimate Range (mGy)</th>
<th>Pediatric Effective Dose Estimate Range (mGy)</th>
<th>Example Examinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Ultrasound, MRI</td>
</tr>
<tr>
<td>🎁</td>
<td>&lt;0.1</td>
<td>&lt;0.03</td>
<td>Chest radiography, hand radiography</td>
</tr>
<tr>
<td>🎁</td>
<td>0.1-1</td>
<td>0.03-0.3</td>
<td>Pelvis radiography, mammography</td>
</tr>
<tr>
<td>🎁 🎁</td>
<td>&gt;1-10</td>
<td>0.3-3</td>
<td>Abdomen CT, nuclear medicine bone scan</td>
</tr>
<tr>
<td>🎁 🎁 🎁</td>
<td>&gt;10-30</td>
<td>&gt;3-10</td>
<td>Abdomen CT with and without contrast administration, whole body PET</td>
</tr>
<tr>
<td>🎁 🎁 🎁 🎁</td>
<td>&gt;30-100</td>
<td>&gt;10-30</td>
<td>CT angiography chest, abdomen and pelvis with contrast administration, transjugular intrahepatic portosystemic shunt placement</td>
</tr>
</tbody>
</table>

### Second Trimester Considerations

- Risk of recurrence low
- 10-20 pound weight gain
- Safest time to operate
- CT OK after 25 weeks
Third Trimester Considerations

- Anemia can be severe\(^1\)
- Increased risk of preterm births\(^2\)
- Corticosteroids - monitor size of baby by serial ultrasound
- Stress dose steroids during labor if needed

\(^1\)Porter et al., Br J Obstet Gynecol 1986;93:1124.
\(^2\)Baird et al., Gastroenterology 1990;99:987.

Delivery

- UC: normal labor and delivery
- IPAA 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)\(^2\)
- ? Long term function (10-20 years out)
- Ostomy - stomal prolapse

\(^1\)Remzi et al., Dis Colon Rectum 2005;9:1691.
**Mode of Delivery: Recommendations**

- C-section in patients with active perirectal, rectovaginal, or perianal fistulas

---

**Continence in Pregnant Women Following Ileal Pouch-Anal Anastomosis**

<table>
<thead>
<tr>
<th></th>
<th>Before Pregnancy</th>
<th>During Pregnancy</th>
<th>1-24 Mos After Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaginal Delivery</strong>&lt;br&gt;(n=12)</td>
<td>2.66 ± 3.17</td>
<td>6.25 ± 5.15</td>
<td>3.25 ± 4.97</td>
</tr>
<tr>
<td><strong>C-Section</strong>&lt;br&gt;(n=14)</td>
<td>1.5 ± 1.99</td>
<td>2.42 ± 3.03</td>
<td>1.57 ± 2.17</td>
</tr>
<tr>
<td><strong>Vaginal and C-Section</strong>&lt;br&gt;(n=3)</td>
<td>2.33 ± 3.21</td>
<td>9.66 ± 4.72</td>
<td>6.66 ± 1.15</td>
</tr>
<tr>
<td><strong>Total (n=29)</strong></td>
<td>2.06 ± 2.61</td>
<td>4.75 ± 4.74</td>
<td>2.79 ± 3.80</td>
</tr>
</tbody>
</table>

“The greatest risk to pregnancy is active disease, not active medicine”.

David Sachar, M.D.

Fetal Risk Categories

A Controlled studies in pregnant women show no risk
B Safe in animals, no studies in women or not safe in animals but safe in women
C Adverse effects in animals, no studies in women
D Evidence of human fetal risk but benefits may be acceptable
X Contraindicated
### 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></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></td>
<td></td>
</tr>
</tbody>
</table>


### Summary: 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></td>
<td>Cyclosporine</td>
</tr>
</tbody>
</table>

Corticosteroids

- Generally safe\textsuperscript{1,2}
  - Glucose intolerance (mom)
  - Hypertension (mom)
- Use for moderate to severe disease
- Safe in nursing

\textsuperscript{1}Present, Advanced Therapy of IBD 2001;129:613.

No Increased Major Congenital Anomalies With Medication Use For IBD During Pregnancy

- UK 1990-2010 mother-child linked dataset
- 1703 children of mothers with IBD;
  384,811 children of mothers without IBD
- Major CAs associated with:
  - 5-ASAs: OR 0.82 (95% CI, 0.42-1.61)
  - Corticosteroids: OR 0.48 (95% CI, 0.15-1.50)
  - 6-MP/AZA: OR 1.27 (95% CI, 0.48-3.39)

Ban et al., Gastroenterology 2014;146:76-84.
Azathioprine Safety: Spanish Cohort

- 571 IBD pregnancies in Spain (53% CD; 21% active disease during pregnancy)
- 253 pregnancies in patients exposed to IM (187) or anti-TNF (66) during/within 6 months of pregnancy
  - 74% IM monotherapy; 11% anti-TNF agent; 15% combination therapy

<table>
<thead>
<tr>
<th></th>
<th>Exposed (253)</th>
<th>Unexposed (318)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s Disease</td>
<td>73%</td>
<td>37%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IBD Surgery</td>
<td>37%</td>
<td>6%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>History: Tobacco Use</td>
<td>21%</td>
<td>13%</td>
<td>0.01</td>
</tr>
<tr>
<td>Active IBD</td>
<td>27%</td>
<td>19%</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Conclusion:
- There was no increased risk of poor pregnancy outcomes in Spanish IBD patients on immunosuppressant therapy.
- Thiopurines only predictor of favorable Global Pregnancy Outcome OR 1.67, 1.03-2.7


Thiopurines and Fetal Anemia; Should We Test Newborns?

- 30 patients on azathioprine (28 patients, median dose 1.93 mg/kg) or 6-MP (two patients, doses 1.32 and 0.94 mg/kg)
- During pregnancy, median 6-TGN decreased over time (p=0.001). while 6-MMP increased, without causing maternal myelotoxicity or hepatotoxicity.
- After delivery, both 6-TGN and 6-MMP levels returned to preconception baseline levels.
- No data on TPMT phenotype or genotype

Thiopurines and Fetal Anemia; Should We Test Newborns?

- Fetal 6-TGN concentrations correlated positively with maternal 6-TGN levels (p<0.0001). (n=25 of 31 infants)
- Median 6-TGN infant: mother = 42:92 pmol/8x10^8
- No 6-MMP was detected in the newborns except 1
  - Pancytopenia and high alk phos (severe pre-eclampsia)
- 63% had anemia at birth: (n=16 of 31 infants)
  - Median Hb 9.25 mmol/l [8.25-9.60]
- 6-TGN 230 vs 90 in infants with anemia
- Congenital Anomalies: 2/31 (6.5%); clubfoot, ptosis


Long-term Follow-up of Children Exposed to 6-MP/AZA in Utero

- Prospective study of 30 children exposed in utero to 6-MP/AZA (median age 3.8 years [2.9-4.7]).
- Validated questionnaire to assess physical, cognitive, and social aspects of health status in preschool children
- Assessment of child’s growth parameters, MD visits, labs, illnesses
- No affect on long-term development or immune function

Meij et al., APT 2013;38:38-43.
Breastfeeding and AZA/6-MP

- 8 lactating women received AZA 75-200mg QD
- Milk and plasma at 30, 60 min and every hour X 5
- Variation in bioavailability reflected in wide range in milk and plasma first 3 hours
- Major excretion in breast milk within 4 hours of drug intake
- Worst case scenario: max concentration 0.0075 mg/kg/24hr. In most cases, will be <10% of maximum concentration

Christensen APT 2008;28:1209-1213.
Transfer Across Placenta

- Fetal immunity is acquired by transfer of Ab as IgG from maternal to fetal circulation
- IgG is actively transported across the placenta
  - Smooth linear rise in fetal IgG as early as 13 weeks (earliest examined), after 32 weeks, significant increase in ratio
- Preferential transport:
  - IgG1 > IgG4 > IgG3 > IgG2
- Certolizumab is a Fab’ fragment
  - Likely passive diffusion

Kane AJG Jan 2009;104:228-233

Placental Transfer of IgG Ab

- INF and ADA are IgG1 antibodies
- Fc portion of IgG actively transported across placenta by specific neonatal FcR
- Highly efficient transfer in 3rd T leads to elevated levels of drug in newborn

\[ r^2=0.87, p<0.04 \]

Image Courtesy of Sundana Kane MD
- 462 women exposed to anti-TNF agents during pregnancy (IFX, ADA, CRT)
- Low risk – no increased CAs, stillbirths, spontaneous abortions or preterm deliveries

Narula et al: Meta-analysis of 5 studies; anti-TNF versus controls
- No significant adverse pregnancy outcomes, spontaneous abortions, preterm births, low birth weights or CAs
Biologics: Placental Transfer

- **Infliximab**:
  - Study of 11 mothers on IFX
  - In all cases, infant and cord IFX level were greater than mother. 6 months to clear

- **Adalimumab**
  - Study of 10 mothers on ADA
  - In all cases, infant and cord ADA level was greater than mother. Up to 4 months to clear
  - ¾ pts who stopped ADA 35 days prior to delivery had a flare

- **Certolizumab**
  - Study of 10 mothers
  - In all cases, infant and cord levels were less than 2 mcg/ml even if mom dosed the week of delivery


The PIANO Registry

Uma Mahadevan, Christopher Martin, Christina Chambers, Sunanda Kane, Marla Dubinsky, William J. Sandborn, Bruce E. Sands & the CCFA Clinical Research Alliance
The PIANO Registry

- Use a prospective national sample of children born to women with IBD to:
- Determine whether *in utero* medication exposure affects the rates of
  - Pregnancy and newborn adverse outcomes
  - Newborn growth
  - Congenital anomalies

Mahadevan et al., Digestive Disease Week, Chicago, May 2014

Methods

- Prospective cohort of pregnant women with IBD identified and followed at 30 member sites of the CCFA clinical alliance
- Data collected by telephone or by in person; questionnaire at intake, each trimester, at delivery, months 4, 9, 12, annually years 1-4
- Mother’s medication exposure, IBD history, disease activity (HBI, SCCAI) and complications during pregnancy and post-partum were recorded
Methods

- Classified into four groups based on exposure to drugs taken between conception and delivery
- Unexposed: (can include steroids, ASA, antibiotics)
- Group A: Azathioprine/6-mercaptopurine
- Group B: Biologics (IFX, ADA, CZP,NAT)
- Group AB: Combination AZA/Biologic
- Exposure was defined as any use of AZA/6MP or a biologic agent at any time from 3 months prior to LMP to the end of the pregnancy

RESULTS

<table>
<thead>
<tr>
<th>Women Enrolled (11/12/2013)</th>
<th>1289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancies Ended (live birth)</td>
<td>1085 (1039)</td>
</tr>
<tr>
<td>• Still pregnant</td>
<td>109</td>
</tr>
<tr>
<td>• Missing outcomes</td>
<td>67</td>
</tr>
<tr>
<td>• Excluded/Withdrawn</td>
<td>28</td>
</tr>
<tr>
<td>• Reached 1 year of age</td>
<td>958</td>
</tr>
<tr>
<td>• Completed 1 yr questionnaire</td>
<td>417</td>
</tr>
</tbody>
</table>

| Unexposed | 356 |
| • No medications | 39 |

| Group A (AZA/6MP) | 230 |
| Group B (Biologics) | 392 |
| Group AB (Combination) | 107 |

| Infliximab (+multiple exp) | 246(26) |
| Adalimumab | 149(25) |
| Cetolizumab | 63(14) |
| Natalizumab | 9 (1) |

Multiple Exposure: 32
- IFX/ADA (18) IFX/CZP (7) ADA/CZP (5) ADA/CZP/NAT (1) IFX/ADA/CZP (1)
### Maternal Demographics

<table>
<thead>
<tr>
<th></th>
<th>Total Population</th>
<th>Ref</th>
<th>A</th>
<th>B</th>
<th>AB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>1085</td>
<td>356</td>
<td>230</td>
<td>392</td>
<td>107</td>
</tr>
<tr>
<td><strong>Mean Maternal Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Range (18-47)</td>
<td>32</td>
<td>31</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td><strong>Median Dx Duration (yrs)</strong></td>
<td>Range (0-32)</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td><strong>Crohn’s Disease</strong></td>
<td>(59.4%)</td>
<td>138</td>
<td>131</td>
<td>297</td>
<td>78</td>
</tr>
<tr>
<td><strong>Ulcerative Colitis</strong></td>
<td>(38.3%)</td>
<td>206</td>
<td>93</td>
<td>91</td>
<td>26</td>
</tr>
<tr>
<td><strong>Indeterminant</strong></td>
<td>(2.3%)</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td><strong>Smokers: current</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2%)</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>(29%)</td>
<td>28%</td>
<td>29%</td>
<td>29%</td>
<td>6%</td>
</tr>
<tr>
<td><strong>Mean # Pregnancies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Range (1-11)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

*7 women received their diagnosis of IBD during pregnancy

### Adverse Pregnancy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Group A (aza) RR (CI)</th>
<th>Group B (bio)</th>
<th>Group AB (combo)</th>
<th>Group AB (UC only)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Complication</strong></td>
<td>1.1 (0.8-1.5)</td>
<td>1.2 (0.9-1.5)</td>
<td>1.2 (0.8-1.8)</td>
<td>2.0 (0.8-4.9)</td>
</tr>
<tr>
<td><strong>SAB</strong></td>
<td>1.2 (0.4-3.3)</td>
<td>1.7 (0.7-3.8)</td>
<td>1.5 (0.5-5.0)</td>
<td>2.9 (0.5-15.9)</td>
</tr>
<tr>
<td><strong>Preterm Birth</strong></td>
<td>1.0 (0.5-1.8)</td>
<td>0.9 (0.5-1.5)</td>
<td><strong>2.6 (1.4-4.8)</strong></td>
<td><strong>4.9 (1.6-14.6)</strong></td>
</tr>
<tr>
<td><strong>LBW</strong></td>
<td>0.9 (0.4-1.8)</td>
<td>1.2 (0.6-2.1)</td>
<td>1.6 (0.7-3.6)</td>
<td><strong>6.1 (2.0-19.1)</strong></td>
</tr>
<tr>
<td><strong>IUGR</strong></td>
<td>1.3 (0.4-4.4)</td>
<td>1.0 (0.4-2.6)</td>
<td>1.3 (0.3-6.0)</td>
<td>0.6 (0.1-5.3)</td>
</tr>
<tr>
<td><strong>Cesarean</strong></td>
<td>1.1 (0.8-1.6)</td>
<td><strong>1.3 (1.0-1.8)</strong></td>
<td>1.4 (0.9-2.2)</td>
<td>1.5 (0.6-3.6)</td>
</tr>
<tr>
<td><strong>NICU</strong></td>
<td>1.2 (0.7-2.2)</td>
<td>1.3 (0.8-2.1)</td>
<td><strong>1.9 (1.0-3.7)</strong></td>
<td><strong>3.9 (1.4-11.5)</strong></td>
</tr>
<tr>
<td><strong>Congenital Anom</strong></td>
<td>1.3 (0.7-2.3)</td>
<td>1.1 (0.7-1.9)</td>
<td>1.5 (0.7-3.3)</td>
<td>1.1 (0.2-5.3)</td>
</tr>
</tbody>
</table>

* Adjusted for none/mild vs. mod/severe disease activity
**P <0.05
**Removed steroids from ref
Summary

- Infants exposed to AZA/6-MP and anti-TNF agents
  - Do not have higher rates of congenital anomalies
  - Have higher rates of preterm birth when exposed to combination therapy
  - Infants born to mothers with UC who were exposed to combination therapy also had increased rates of preterm birth, low birth weight, NICU stay

Breastfeeding

- **Infliximab**
  - Breastmilk 1/200th mother’s level (n=1)\(^1\)
  - Peak concentrations in BM 100 ng/ml
  - Induction therapy: (n=1) infant levels 1700 ng/ml (maternal level 78,300 ng/ml)\(^3\)

- **Adalimumab**
  - Breastmilk 1/200th mother’s level(n=1)\(^2\)
  - Adalimumab undetectable in infant serum (n=1)\(^3\)

- **Certolizumab**
  - Not detected in breast milk (n=1)\(^4\)

---

Timing of biologics

- Current expert recommendation
  - Last dose infliximab at week 30 gestation *
  - Last dose adalimumab at week 30-34 *
    *If flaring, continue throughout pregnancy
  - Continue certolizumab throughout pregnancy
  - If mom flares, treat her!
- Breast feeding compatible


Vaccinating the Infant

- Live vaccines for first 6 months of life:
  - Rotavirus, intranasal influenza, BCG
- Avoid live vaccines in infants exposed in utero to IFX or ADA if serum levels are detectable
- CZP concentrations thought to be undetectable by time of rotavirus vaccination (2 months)

Take Home Points

- IBD patients (except those with IPAAAs and ostomies) have mostly normal fertility
- Patients with IBD have a higher C-section rate, a higher rate of adverse conception and pregnancy outcomes, and a higher rate of pregnancy complications
- Patients with IBD have a higher incidence of obstetric complications.
- Patients should be in remission when trying to conceive
- Increased disease activity can negatively affect a pregnancy more than most IBD medications
- Vaginal delivery after IPAA may be associated with future fecal incontinence

Definition of Outcomes

- Adverse conception outcomes:
  - Spontaneous abortion, abortion for unknown reason
- Adverse pregnancy outcomes:
  - Preterm birth (< 37wk), small for gestational age (birth weight <10th percentile for gestational age), stillbirth (death of fetus after 20th week of pregnancy)
Definition of Outcomes

- Pregnancy complications:
  - Abruptio placenta, placenta previa, pre-eclampsia/eclampsia, infection, premature rupture of membranes, prolonged rupture of membranes, chorioamnionitis, fetal distress, urine group B streptococcus, maternal blood transfusion, death of mother

- Adverse newborn outcomes:
  - NICU admission, newborn seizure, infant mortality

Continence Grading Scale

<table>
<thead>
<tr>
<th>Type of Incontinence</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never</td>
</tr>
<tr>
<td>Solid</td>
<td>0</td>
</tr>
<tr>
<td>Liquid</td>
<td>0</td>
</tr>
<tr>
<td>Gas</td>
<td>0</td>
</tr>
<tr>
<td>Wears pad</td>
<td>0</td>
</tr>
<tr>
<td>Lifestyle alteration</td>
<td>0</td>
</tr>
</tbody>
</table>

0=perfect
20=complete incontinence

Jorge et al., Dis Colon Rectum 1993; 36:77-97
Pelvic Floor Disorders

- Spontaneous vaginal birth vs. C-section (n=1011)
  - Stress incontinence (OR 2.9, 95% CI 1.5-5.5)
  - Prolapse to or beyond the hymen (OR 5.6, 95% CI 2.2-14.7)
- Operative vaginal birth significantly increased the odds for all pelvic floor disorders, especially prolapse
  - (OR 7.5, 95% CI 2.7-20.9)
- Forceps deliveries and perineal lacerations, but not episiotomies, were associated with pelvic floor disorders 5-10 years after a first delivery