IBD & She
Focusing on Living While Managing IBD

A program for women, their loved ones, and healthcare professionals hosted by two women physician experts and researchers in IBD
Speakers

Sunanda V. Kane, MD, MSPH
Professor of Medicine
Mayo Clinic College of Medicine
Rochester, Minnesota

Uma Mahadevan-Velayos, MD
Associate Professor of Medicine
University of California, San Francisco (UCSF)
Director of Clinical Research
UCSF Center for Colitis and Crohn's Disease
San Francisco, California
Disclosure of Conflicts of Interests

Sunanda V. Kane, MD, MSPH

Dr. Sunanda V. Kane has an affiliation with Kyorin Pharmaceuticals (Speakers Bureau); Shire, Elan (Research).
Today’s Goals

• Identify the gender-specific impact of IBD
  • Understand potential gynecological issues in IBD
  • Highlight intimacy and sexuality
  • Discuss women’s overall general health
  • Recognize the implications of pregnancy, fertility & breastfeeding with IBD
  • Focus on living while managing IBD
Disease Course by Gender

- 10-year study on the rate of relapse of ulcerative colitis in men and women
  - 771 patients from 8 countries
- Relapse rate for women was 20% higher than in men
- Time to first relapse sooner in women than men

The Effect of Smoking on Crohn’s Disease in Women

- There are now two studies that have specifically addressed the gender effect of tobacco.
- Women smokers undergoing surgery are 5 times more likely to have a recurrence than non-smokers, and recur more quickly\(^1\).
- Women smokers hastened onset of disease and increased the need for immunomodulators\(^2\).

\(^1\) Kane SV. *Gastroenterol*. 2002;124(5):A1169.
## Gender-Related Impact of IBD

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reproductive issues</strong></td>
<td>↓ fertility after IPAA or proctocolectomy</td>
<td>↓ fertility with sulfasalazine</td>
</tr>
<tr>
<td></td>
<td>↑ risk of relapse of disease active at time of conception</td>
<td></td>
</tr>
<tr>
<td><strong>Disease-related concerns</strong></td>
<td>↑ concern re: body stigma, loss of bowel control</td>
<td>—</td>
</tr>
<tr>
<td><strong>Sexuality</strong></td>
<td>↓ sexual activity because of dyspareunia, abdominal pain, etc</td>
<td>↓ libido and sexual satisfaction after proctocolectomy</td>
</tr>
</tbody>
</table>
Physical Complications of IBD on Sexuality

- Impact of disease
  - Perianal complications
  - Draining cutaneous fistulae
  - Skin lesions
  - Arthritic deformities
  - Pain
  - Fatigue

- Impact of treatment
  - Surgical scars
  - Stoma
  - Medication side effects
IBD: Systemic Complications

- Eye inflammation*
- Lower bone density*
- Liver and bile duct inflammation
- Gallstones
- Skin lesions
- Kidney stones
- Growth failure in children
- Subfertility*
- Arthritis and joint pains

*Higher incidence in women.
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Menses & Pre-Adolescence

- Possible delayed onset of menses in pre-adolescent girls
- Delayed growth rates
- Delayed maturation & secondary sex characteristics
Menstrual Cycle and Bowel-Pattern Fluctuations

• Bowel-pattern fluctuation is common during the menstrual cycle
• IBD symptoms may increase during the menstrual cycle
• Menses suppression with birth control medication may be needed if debilitating symptoms are present
**Change in Symptoms During Menses**

*P*=0.01 for all disease groups vs control for cyclical symptoms.

**P*=0.03 for all disease groups vs control for abdominal pain.

General Guidelines for Oral Contraceptive (OCP) Use

- OCPs used for contraception should probably have a lower estrogen content
- OCPs should be avoided in women with known history of high coagulation
- OCPs should be avoided in IBD-associated liver disease
What to Expect With Menopause

• Does the course of menopause change when IBD is involved?
• Are the indications more severe/altered from non-IBD related menopause?
• Should female IBD patients be aware of or prevent issues?
  – Vaginal fistulas
Hormone Replacement Therapy (HRT) & Menopause

- 65 patients: 20 UC 45 CD
- Patients on HRT significantly less likely to flare within the first 3 years after menopause

Incidence of Abnormal Pap Smears in IBD

• Abnormal Pap smears associated with both infection and progression to cancer
• Women with IBD were more likely to have an abnormal Pap smear
• Use of azathioprine ↑ risk three-fold

Risk of Abnormal Pap Smears

- Canadian case control study of Pap smears
- 19,692 abnormal results matched to 57,898 controls
- Does not appear to be a difference in ulcerative colitis
- Risk is ↑ 66% in Crohn’s disease when on OCP
- Risk is ↑ 40% when on steroids & immunosuppressants

Conclusion: It is the immune suppression and not IBD that increases the risk for abnormal Pap smears

HPV Vaccines

• Gardasil currently approved for 9-26 years
  – Covers HPV 6,11,16,18
  – Data submitted to FDA for 27-45

• Cervarix
  – Covers serotypes 16,18
  – FDA panel approval for ages 10-25
  – Different formulation
Significance of NOD2

• One copy of mutated gene
  – 1.5- to 4-fold risk
• Two copies: 15- to 40-fold risk
  – 10% of CD patients carry two copies
  – 28% of CD patients carry one copy
  – Actual disease presence with one or two gene copies is less than 10%
Today’s Goals

• Identify the gender-specific impact of IBD
• Understand potential gynecological issues with IBD

• **Highlight intimacy and sexuality**
• Recognize the implications of pregnancy, fertility & breastfeeding with IBD
• Discuss women’s overall general health
• Focus on living while managing IBD
Intimacy and Sexuality

• All relationships are complex
  – IBD adds an additional layer

• Sharing information can relieve stress and anxiety related to holding back and dealing with it alone
  – May be more difficult for new relationships rather than established relationships
  – Who to tell, what to tell, how much to tell
  – IBD affects both partners
Sexuality

• IBD has both direct and indirect effects
• Direct effects
  – Fatigue, diarrhea, abdominal pain
  – Amenorrhea, low libido
  – Surgery related complications
• Indirect effects
  – Depression, altered body image
  – Fear of incontinence
Summary

- Women *are* different from men
- Smoking is BAD
- Menstrual cycle can affect disease course
- Oral contraceptives not likely high risk
- IBD does not affect menopause
- Discuss HPV infection with your physician
Disclosure of Conflicts of Interests

Uma Mahadevan-Velayos, MD

Dr. Uma Mahadevan-Velayos has an affiliation with Centocor, Abbott, UCB, Elan, Biogen, Shire, and Takeda (Consultant); Abbott (Research).
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• **Discuss women’s overall general health**
  • Recognize the implications of pregnancy, fertility & breastfeeding with IBD
• Focus on living while managing IBD
Health Care Maintenance

- **Vaccinations**
  - No live virus vaccines while on biologics or during pregnancy (MMR, varicella)
  - Hepatitis A, B, flu shot

- **Cancer screening**
  - Colonoscopy
  - Pap smear
  - Skin

- **Laboratory tests**
  - Vitamin B12, folate, 25-OH vitamin D, iron, liver, hematocrit
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- **Recognize the implications of pregnancy, fertility & breastfeeding with IBD**
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Before Pregnancy

- Disease under good control
  - 33% chance of flare during pregnancy
- Healthcare maintenance up to date
- Identification of a high-risk obstetrician
- Counseling regarding use of IBD medications during pregnancy and breastfeeding
Common Questions

- Inheritance
- Fertility
- Pregnancy outcomes
- Safety of medications
- Management of flares
Solutions

• Communication with a trustworthy and safe partner
• Getting disease under control
• Sharing your symptoms with your doctor
• Seeking counseling to help with coping with disease
Will My Child Get IBD?

• Increased risk of CD and UC in offspring of patients with IBD
  – 5% if one parent has CD
  – 1.6% if one parent has UC
  – Familial CD has earlier onset than sporadic cases at an average age of 22 years vs. 27 years respectively
• If both parents have IBD, a child’s risk is as high as 35% for developing IBD
• Inheritance is multifactorial with a role for as yet undefined environmental triggers so pregnancy should not be discouraged for this reason

What Are My Chances of Getting Pregnant?

- With both UC and CD, the risk of fertility prior to surgery appears to be similar to the general population
  - For a man or woman with IBD, the chance of conceiving is the same as anyone else their age
- Fertility after surgery for an ileoanal J pouch for ulcerative colitis can drop by 40%–80%

How Will I Do During Pregnancy?

Retrospective cohort study Kaiser Northern California
N=461 IBD, 493 control
5-ASA (51%), corticosteroids (21%), immunosuppressants (4%)

<table>
<thead>
<tr>
<th>Adverse Outcomes</th>
<th>OR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conception (miscarriage)</td>
<td>1.65</td>
<td>1.09–2.48</td>
</tr>
<tr>
<td>LBW, stillbirth, preterm birth</td>
<td>1.54</td>
<td>1.00–2.38</td>
</tr>
<tr>
<td>Complicated labor + delivery</td>
<td>1.78</td>
<td>1.13–2.81</td>
</tr>
<tr>
<td>Newborn outcomes</td>
<td>1.89</td>
<td>0.98–3.69</td>
</tr>
</tbody>
</table>

*Controlled for maternal age, current ETOH, current tobacco, Caucasian ethnicity, number of prenatal visits (except conception)

Most patients are in remission during pregnancy. Even with remission, risk of adverse outcomes are higher.

Risk of flare during pregnancy is 33%

Medical Therapy: FDA Pregnancy Category

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Controlled studies show no risk</td>
</tr>
<tr>
<td>B</td>
<td>No evidence of risk in humans</td>
</tr>
</tbody>
</table>
| C        | • Animal reproduction studies show adverse effects  
          • No adequate studies in humans  
          • Benefits in pregnant women may be acceptable despite potential risk |
| D        | Positive evidence of risk |
| X        | Contraindicated in pregnancy |
Fish Oil

- Essential fatty acids (EFA) and docosahexaenoic acid (DHA)
  - Potential antithrombotic effect
  - Prolong gestation
  - No evidence of prevention of proteinuric pregnancy
- ? benefit in Crohn’s disease

# Safety of Medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA</th>
<th>Birth Defects</th>
<th>Lactation</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesalamine</td>
<td>B</td>
<td>Low risk</td>
<td>Compatible</td>
<td>Rare diarrhea</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>B</td>
<td>Low risk</td>
<td>Compatible</td>
<td>Folic Acid 2 mg daily</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>C</td>
<td>Low risk-T1 cleft palate</td>
<td>Compatible</td>
<td>Gestational DM</td>
</tr>
<tr>
<td>Budesonide</td>
<td>C</td>
<td>Low Risk</td>
<td>Compatible</td>
<td>Little data</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>B</td>
<td>Low risk-T1 cleft palate</td>
<td>Not advised</td>
<td>Short term use</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>C</td>
<td>Not advised – bone</td>
<td>Maybe compatible</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Augmentin</td>
<td>B</td>
<td>Low risk</td>
<td>Compatible</td>
<td>Good alternative</td>
</tr>
</tbody>
</table>
# Safety of Medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA</th>
<th>Birth Defects</th>
<th>Lactation</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathioprine/6MP</td>
<td>D</td>
<td>Low risk</td>
<td>Compatible</td>
<td>Hold BF for 4 hours</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>X</td>
<td>High risk</td>
<td>Not advised</td>
<td>Stop 3-6 mos. prior</td>
</tr>
<tr>
<td>Infliximab</td>
<td>B</td>
<td>Low risk</td>
<td>Compatible</td>
<td>Hold in T3</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>B</td>
<td>Low risk</td>
<td>Compatible</td>
<td>Hold in T3</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>B</td>
<td>Low risk</td>
<td>Compatible</td>
<td>continue</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>C</td>
<td>Low risk</td>
<td>Likely compatible</td>
<td></td>
</tr>
</tbody>
</table>
## Medications to Avoid

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pregnancy Category</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenoxylate</td>
<td>C</td>
<td>Teratogenic in animals</td>
</tr>
<tr>
<td>Loperamide</td>
<td>B</td>
<td>Increase in CV defects in 1 study</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>C</td>
<td>• Animal studies: alendronate crosses placenta</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 24 pregnancies, no increased teratogenic risk(^1)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>X</td>
<td>• Known abortifacent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Teratogenic (skeletal defects; cleft palate)</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>X</td>
<td>• Birth defects</td>
</tr>
</tbody>
</table>

6MP/Azathioprine (D) and Teratogenicity

- 189 pregnant women on AZA contacted 1 of 7 teratogen information services vs. 230 pregnant women who took non-teratogenic treatments\(^1\)
  - Rate major malformations 3.5 % vs. 3.0% \((P=.775)\)
- Swedish Medical Birth Register\(^2\)
  - 476 women used AZA in early pregnancy
  - Most common indication was IBD (>300)
  - Rate of CA 6.2% AZA vs. 4.7% other
    - OR 1.41, 95% CI: 0.98-2.04
  - Increased rate of VSD/ASD
    - OR 3.18, 95% CI: 1.45–6.04

Breastfeeding on AZA/6MP

- 8 lactating women received AZA 75-200 QD
  - Milk and plasma at 30, 60 min and every hour × 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
  - In most cases, will be <10% of maximum concentration

Biologics (B)

Infliximab

Adalimumab

Certolizumab pegol

Monoclonal antibody

Chimeric

Human

PEGylated humanized Fab’ fragment

2 × 20 kDa PEG

PIANO: Pregnancy in Inflammatory Bowel Disease And Neonatal Outcomes

- Patients classified by exposure to four groups of drugs taken b/w conception and delivery: (413 patients)
  - Unexposed: no immunomodulators/biologics
    - Mesalamine, steroids, antibiotics allowed
  - Group A: AZA/6MP
    - +/- Unexposed medications
  - Group B: INF, ADA, CZP
    - +/- Unexposed medications
  - Group AB: Combination therapy
    - +/- Unexposed medications

Mahadevan. Digestive Disease Week, 2010.
PIANO: Pregnancy in Inflammatory Bowel Disease And Neonatal Outcomes

• 413 patients divided into 4 groups:
  – No imm, AZA/6mp, biologic, combination
• Medication use not associated with increased risk of:
  – Any complication
  – Preterm birth, low birth weight
  – Cesarean section
  – Congenital anomalies: 17 anomalies/15 births
• Biologic exp: increased risk of NICU stay
• Combination exp: increased risk of infection at 1 year of age

Join registry: www.ccfa.org/trials
Search: PIANO
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

![Graph showing the relationship between gestational age and IgG levels in the fetal compartment. The graph displays a positive correlation with a coefficient of determination ($r^2=0.87$) and a p-value of $P<0.04$.](Image Courtesy of Sunanda Kane, MD.)


Image Courtesy of Sunanda Kane, MD.
Placental Transfer

- Infliximab crosses placenta at high rate in T3
  - Adalimumab assumed to be same
- Certolizumab with no to minimal transfer
- Current expert recommendation
  - Discontinue infliximab at week 30
  - Discontinue adalimumab at week 30-34
  - Continue certolizumab throughout
  - If mom flares, treat her!
- Breastfeeding compatible
- No live virus vaccine to infant if INF/ADA in utero
  - Babies have normal response to standard vaccines in first 6 months
Delivery

- Delivery is at the discretion of the obstetrician
- Only considerations for Cesarean section specific to IBD
  - Active perianal disease at the time of delivery
  - Ileoanal J pouch
Management of Flares

- Medication choices are similar
  - Avoid new AZA/6mp in pregnancy
  - Avoid mnzd, steroids in T1
- Imaging
  - MRI preferred to CT, though no gadolinium in T1
- Endoscopy
  - Unsedated flexible sigmoidoscopy
- Surgery
  - Indications similar to non-pregnant patient
  - T2 best time to operate
Synopsis

• Chances of getting pregnant similar to the general population
• Small risk of passing on IBD to offspring
• Increased risk of adverse outcomes during pregnancy (though the majority of moms have healthy babies)
• Most medications compatible with use in pregnancy and breastfeeding
• Recommendations:
  – Control disease prior to conception
  – Continue most medications
  – Multidisciplinary approach: high-risk obstetrician, pediatrician, surgeon if needed
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• Focus on living while managing IBD
Focus on Living While Managing IBD

• Make a life plan: education, family, friends, hobbies
• Educate yourself on your disease
• Maintain communication with your GI & your GYN
  – Stay up to date on doctor visits
• Create a support system
  – Family members, friends, IBD community
  – IBD support groups
    • Online
    • In person
  – Accept support from others
  – Offer support when you can
Focus on Living While Managing IBD

• Stress is inevitable and can exacerbate symptoms
  – Minimize stressful situations
  – Find outlets to help yourself deal with & work through stress

• Combating pain
  – Chart your pain and symptoms
  – Communicate with your doctor
  – Work with pain management team

• Combating exhaustion
  – Maintain a balanced diet
  – Manipulate your schedule to get enough sleep for your body
  – Build your support system, ask for help when you need it
Questions & Answers
Program Evaluation
www.RMEI.com/CCFAevaluation

CNE Credit (for nurses only)
Please complete the evaluation form online at www.cmeuniversity.com.
Click on “Find Post-Test/Evaluation by Course” on the navigation menu, and search by project ID 7342. Upon successfully completing the evaluation, your certificate will be made available immediately.

Please print your certificate for your records.