Gastrointestinal disorders in women: what an obstetrician/ gynecologist needs to know

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Objectives

Identify gastrointestinal disorders that impact patients seen in an OB/GYN practice

a. constipation
b. fecal incontinence
c. inflammatory bowel disease
d. colorectal cancer including Lynch syndrome

Recognize the specific disease, signs, symptoms, differential diagnosis related to these disorders and diagnostic testing necessary to determine treatment plans

Incorporate evidence-based medicine into the treatment and management of disease process, and utilize appropriate follow up or use of consultants

Chronic constipation

- How do you define it?
- What are the types ?
- What work up do you recommend ?
- How do you treat?

Case 1

- 42 year old lady with 3-4 BM's/week and chronic straining x 1 year
- Sits on the toilet for at least half an hour with a feeling of incomplete evacuation
- Failed laxatives OTC –miralax and senna tea
- No alarm features
- Saw a GI physician
  - Normal colonsocopy
  - Started on amitiza 24 mcg twice daily
  - Stools became watery –still has incomplete evacuation

Definition: Rome III criteria

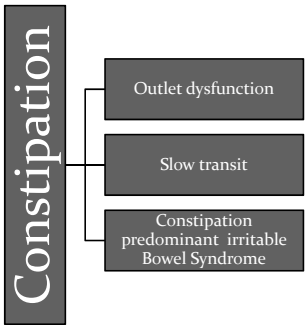
1. Must include 2 or more of the following:
   a. Straining during at least 25% of defecations
   b. Lumpy or hard stools in at least 25% of defecations
   c. Sensation of incomplete evacuation for at least 25% of defecations
   d. Sensation of anorectal obstruction/blockage for at least 25% of defecations
   e. Manual maneuvers to facilitate at least 25% of defecations (eg. digital evacuation, support of the pelvic floor)
   f. Fewer than 3 defecations per week
2. Loose stools are rarely present without the use of laxatives
3. There are insufficient criteria for IBS

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

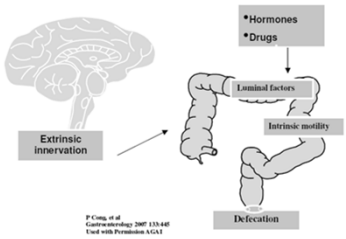
Take home message

- Infrequent defecation alone is not sufficient to define constipation
- The majority of constipated persons do not have <3 bowel movements/week

Types of constipation



PATHOPHYSIOLOGY OF CHRONIC CONSTIPATION



SOME DRUGS ASSOCIATED WITH CONSTIPATION

- Anticholinergics
  - Antispasmodics
  - Antidepressants
  - Antipsychotics
- Cation-containing agents
  - Iron supplements
  - Aluminum (antacids, sucralfate)
- Neurally active agents
  - Opiates
  - Antihypertensives
    - Calcium channel blockers
  - Ganglionic blockers
  - Vinca alkaloids
  - 5HT3 antagonists

Work up- what do we have in our toolbox

A task force convened by the ACG concluded that there are inadequate data to support the routine use of flexible sigmoidoscopy, colonoscopy, barium enema, thyroid tests, serum calcium, and other tests in patients with chronic constipation without alarm symptoms or signs; these include hematochezia, weight loss > 10 lbs., family history of colon cancer or IBD, anemia, positive fecal occult blood tests, and acute onset of constipation in elderly persons.

Thus, the routine approach to a patient with chronic constipation without alarm signs or symptoms should be empiric therapy.

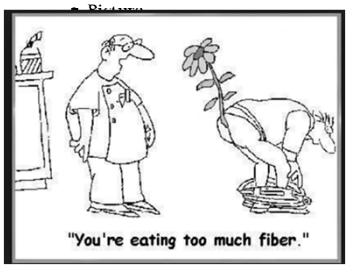
Work up- what do we have in our toolbox

- History and a physical examination
  - Bristol Stool Scale
- Anorectal manometry
- Sitz marker study
- Smart pill
- Colonoscopy ? (if there are alarm symptoms or patient at risk for colon cancer, IBD etc)

Treatment

Role of fiber

- No evidence that it improves symptoms
- May exacerbate symptoms of bloating, distension and pain even when used judiciously
- Use soluble fiber if need be



Types of available laxatives

Bulk Agents
Psyllium
Methycellulose
Bisacodyl
Calcium Polycarbophil
Wheat dextrin

Nonabsorbed Substances
PEG
Lactulose*
Sorbitol*
Magnesium salts

Diphenylmethanes
Bisacodyl

Anthraquinones
Senna

Newer Agents
Tegaserod *(**restricted**)
Lubiprostone*
Linaclotide

*Prescription only

Myth

Chronic use of stimulant laxatives is harmful to the colon and will lead to cathartic colon

LAXATIVE USE: Tegaserod

Withdrawn from the market due to increased risk of cardiovascular events

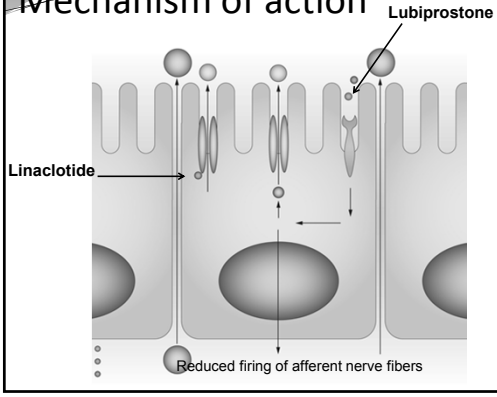
Osmotic laxative: Polyethylene glycol

- Grade A recommendation
  - Safe and effective even in elderly patients
  - Less expensive
- a recent meta-analyses
  - Number needed to treat was 3 (95% CI,2 to 4)
- Improvement in 52% of PEG and 11% of placebo subjects ($p < 0.001$)
- Increasing bowel frequency
  - Between group difference was 1.56 spontaneous bowel movements [SBMs]/week, $P < 0.0001$
- Not helpful in pain

Newer agents ….

- Lubiprostone
- Linaclotide

Mechanism of action



Lubiprostone

- Superior to placebo in several large, multicenter RCTs involving chronic constipation and IBS-C
  - Increase in the number of SBMs
  - Improved stool consistency
  - Reduced straining, bloating

Johanson et al, Am J Gastroenterol 2008;103:170–177

Lubiprostone …

- Study of 240 patients
  - Greater number of SBM' s at week 1-4 (5.69 *vs* 3.46, *P* = 0.0001)
- Within 24 hrs of drug administration
  - 56.7% vs 37 % reported a SBM placebo (*P* = 0.0024)
- Within 48 h
  - 80% and 60.7% of these patients reported a SBM (P = 0.0013)

Johanson et al, Am J Gastroenterol 2008;103:170–177

Lubiprostone

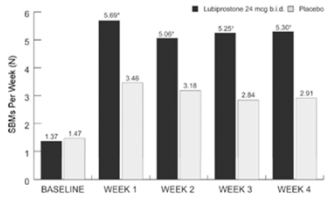


Figure 2. Frequency of SBMs at baseline and for weeks 1–4 with lubiprostone 24 mcg twice daily or placebo (ITT population with L
0001 *versus* placebo; †$P \leq 0.002$ *versus* placebo (van Elteren's test stratified by pooled center).

Johanson et al, Am J Gastroenterol 2008;103:170–177

Lubiprostone

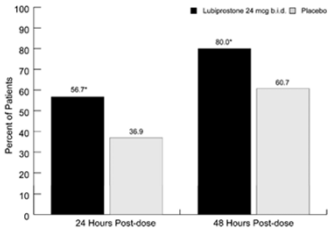


Figure 3. Proportion of patients who had experienced a SBM at 24 or 48 h after the initial dose of study medication (ITT population). *$P \leq$ 0.0024 *versus* placebo (Cochran-Mantel-Haenszel test stratified by pooled center).

Johanson et al, Am J Gastroenterol 2008;103:170–177

Lubiprostone

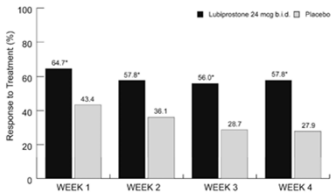


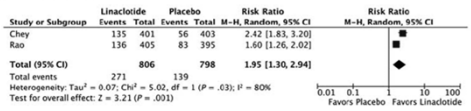
Figure 4. Percentage of patients that were full responders (SBM frequency of ≥3 per week) with lubiprostone 24 mcg twice daily or placebo (ITT population with LOCF). *$P < 0.004$ *versus* placebo (van Elteren's test stratified by pooled center).

Johanson et al, Am J Gastroenterol 2008;103:170–177

Linaclotide

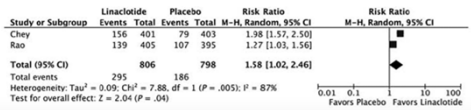
A FDA Responder

Improvement of ≥30% from baseline in average daily worst abdominal pain + increase of ≥1 CSBM from baseline for 50% of weeks



B Abdominal Pain Responder

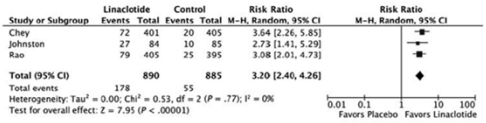
≥30% decrease in worst abdominal pain for 75% of weeks



Linaclotide….

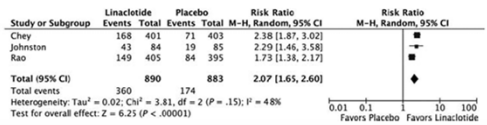
C CSBM Responder

≥3 CSBMs and an increase of ≥1 CSBM from baseline for 75% of weeks



D Adequate Relief Responder

Reported adequate relief for 75% of weeks



Approximate cost of available laxatives

Laxative	Dose	Cost in $
Senna	17.2 mg (2 tabs daily)	2.7
Psyllium	11 g (1 rounded tsp 1-3 times daiy)	11-35
Bisacodyl	10 mg (2 tabs daily)	7.5
Milk of Magnesia	2.4 gms (2 tbsp daily)	11.4
Sorbitol	21 gms (30 cc daily)	21.0
Lactulose	20 gms (30 cc daily)	40.0
PEG	17 gms in 8 ounces of water	21.0
Lubiprostone	24 mcg (1 tab twice daily)	207 $$$
Linaclotide	290 mcg (1 tab daily)	

Approximate 30 day cost

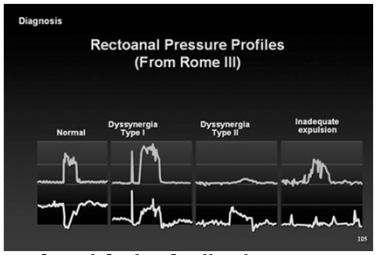
Case 1…

Bristol Stool Chart

Type 1	Separate hard lumps, like nuts (hard to pass)
Type 2	Sausage-shaped but lumpy
Type 3	Like a sausage but with cracks on the surface
Type 4	Like a sausage or snake, smooth and soft
Type 5	Soft blobs with clear-cut edges
Type 6	Fluffy pieces with ragged edges, a mushy stool
Type 7	Watery, no solid pieces. Entirely Liquid

Case 1

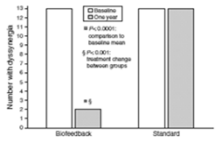
- Anorectal manometry revealed anismus

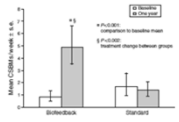


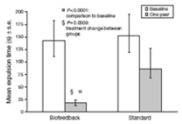
- Referred for biofeedback x 6 sessions
- Improved dramatically

Biofeedback in outlet dysfunction

- Superior to standard treatment at 1 year
- ↑↑ in no. of complete, spontaneous BM's
- Improvement in balloon expulsion
- Normalization of dyssenergia
- Normalization of colonic transit







Rao et al. Am J Gastroenterol 2010;105:890–896

Refractory constipation: subtotal colectomy

At least five criteria should be met prior to consideration of surgery

- Chronic, severe, and disabling symptoms from constipation that are unresponsive to medical therapy.
- Slow colonic transit of the inertia pattern
- The patient does **not** have the following
  - intestinal pseudoobstruction
  - pelvic floor dysfunction/dyssenergia
  - abdominal pain as a prominent symptom.

Outcomes

- 13 studies of 362 patients
  - Mean follow up of 106 months
  - Patient satisfaction was 88%
- Long-term morbidity following subtotal colectomy for constipation

• Reoperation	40%	36%
• Abdominal Pain	90%	54%
• Bloating	80%	76%
• Urge to Defecate	45%	--

Careful selection of patients is important

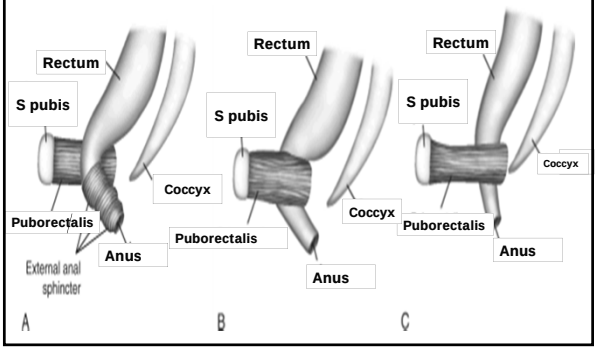
Nyam DC et al.Dis Colon Rectum. 1997;40(3):273.

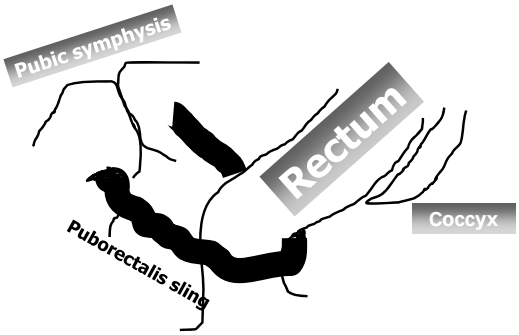
Fecal incontinence

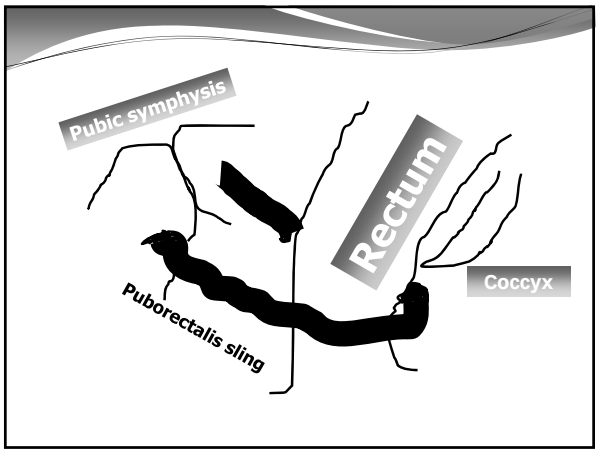
Fecal incontinence

- Prevalence ranges from 2.2-15.3%
- Increases with age
  - 4% between 40-49 years
  - 11.6% > 80 years
- 47% in nursing home residents in Wisconsin

Mechanisms of continence



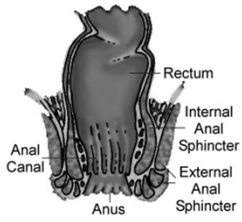




Pathophysiology :

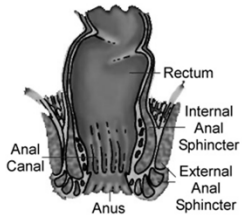
- Internal anal sphincter -70% of resting tone
- External anal sphincter
- Puborectalis-maintains an acute angle
- Rectal compliance and rectal sensation

Fecal incontinence : Mechanisms



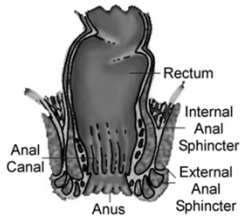
- Rectal sensation
  Perception of "call to stool
- Rectal accomodation
- Diabetes mellitus, neuropathy
- CNS disorders
  Dementia
  Mental retardation
  Stroke Brain tumor
  Proctitis (IBD,radiation

Fecal incontinence : Internal anal sphincter



- 70% of resting tone.
- Diabetes mellitus
- Sphinceterotomy
- Smooth muscle diseases, *progressive systemic sclerosis*,

Fecal incontinence : External sphincter & puborecatlis



- Maintains anal closure and anorectal angle
- Childbirth injury, pudendal neuropathy, "idiopathic" incontinence, surgical damage to external anal sphincter
- Skeletal muscle diseases *myasthenia gravis*, *myopathies*, and *myotonic dystrophy*

Other causes:

- Diarrhea
- Constipation (overflow incontinence)
- Ingestion of mineral oil, olestra, or orlistat

Evaluation of incontinence

- History
- Physical exam
- Lab tests

Flex sigmoidoscopy

Anorectal manometry

EMG – to assess for pudendal neuropathy

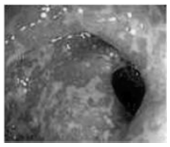
Anorectal ultrasound

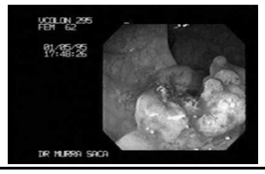
MRI

Physical exam

- Examination of the perianal area
  - chemical dermatitis suggesting chronic incontinence
  - fistula
  - prolapsing hemorrhoids
  - rectal prolapse
- Anal wink- if absent suggest neuronal damage
- Rectal Exam

Flexible sigmoidoscopy





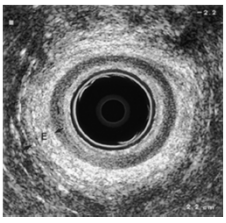
Anorectal manometry

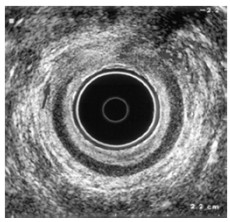
- maximal resting anal pressure
- amplitude and duration of squeeze pressure
- threshold of conscious rectal sensation, rectal compliance, and rectal and anal pressures during straining
- the rectoanal inhibitory reflex (not necessary for continence)

Pudendal nerve EMG

- Operator dependent
- Poor correlation with clinical symptoms and histologic findings
- Not predictive of surgical outcomes

Anorectal ultrasound





Therapy

- Medical therapy
- Biofeedback
  - more helpful with urge incontinence
- Sacral nerve stimulation
- Injection of bulking agents
- Surgery

Medical management

- Bulking agents
- Loperamide superior to diphenoxylate
- Hyoscamine
- Bowel regimen program
- Amitryptiline
- Phenlyephrine gel

Biofeedback

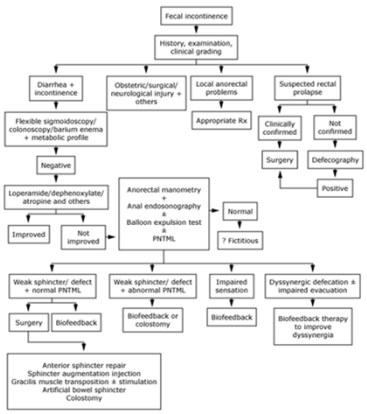
- Safe – may be useful in patients with weak sphincters and/or impaired rectal sensation
- No significant benefit compared with standard care (largest randomized controlled trial)

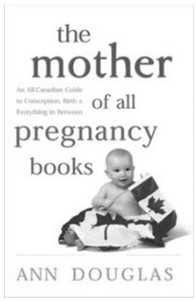
Surgery

- Anterior overlap repair of the external anal sphincter
  - resolves symptoms in approximately 80 % of patients with obstetric damage
  - long term outcome less optimistic

Sacral nerve stimulation

- Improvement observed in 83%
- Symptomatic response maintained after implantation of a permanent pacemaker in 48/75 patients over 1 year





Impact of gender on IBD

- 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

Hoie O. *Am J Gastro*. 2007;102(8):1692-1701.

The Effect of Smoking on Crohn's Disease in Women

- 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 nonsmokers
- and recur more quickly
- Women smokers hastened onset of disease and
- increased the need for immunomodulators

Kane SV. *Gastroenterol*. 2002;124(5):A1169.
Cosnes J. *J Clin Gastro and Hepatol*. 2004;2:41-48.

Incidence of Abnormal Pap Smears in IBD

- Women with IBD were more likely to have an abnormal Pap smear
- Use of azathioprine increases the risk three-fold
- Canadian case control study of Pap smears
  - 19,692 abnormal results matched to 57,898 controls
  - Risk is 40% when on steroids & immunosuppressants

Kane SV. *Am J Gastroenterol.* 2008;103(3):631-636.
Singh H. *Gastroenterol*. 2009;136:451-458

Fertility

What Are My Chances of Getting Pregnant?

- Fertility rates in IBD (both men and women) similar to the general population 8-10%
- Fewer children than in the general population
  - Body image issues
  - Relationship difficulties (dyspareunia, decreased libido)
  - Inappropriate medical advise

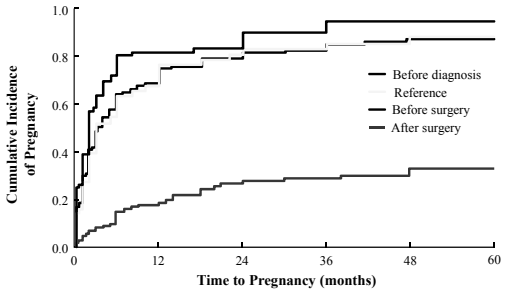
In men…..

- Sulfasalazine –reversible dose related decrease in sperm count (60%)
- Reversed after 2 months of discontinuation

Special situations IPAA- in UC

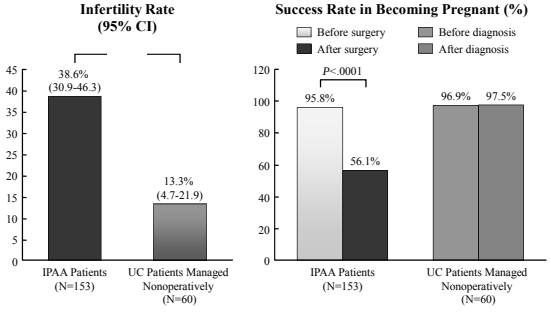
- Increase in fecundity (waiting time to pregnancy)after IPAA
  - Likely due to tubal occlusion from adhesions
  - Increase in dyspareunia (22-38%)
  - Increase in sexual satisfaction (improved general health)

IPAA: Cumulative Incidence of Pregnancy Within 5 Years



Reprinted from Olsen KØ, et al. *Gastroenterology.* 2002;122:15-19 with permission from American Gastroenterological Association.

Female Infertility After IPAA for UC



Johnson P, et al. *Dis Colon Rectum.* 2004;47:1119-1126.

Crohn's disease

- Fertility not decreased in inactive disease
- Active disease –decrease in fertility due to adhesions of fallopian tube

Effects of IBD on pregnancy

How Will I Do During Pregnancy?

Retrospective cohort study
Kaiser Northern California

- n=461 IBD, 493 controls
- 5ASA(51%)
- corticosteroids (21%)
- immunosuppressants (4%)

Adverse Outcomes	OR* (95% CI)
Conception (miscarriage)	1.65 (1.09–2.48)
LBW, stillbirth, preterm birth	1.54 (1.00–2.38)
Complicated labor + delivery	1.78 (1.13–2.81)
Newborn outcomes	1.89 (0.98–3.69)

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

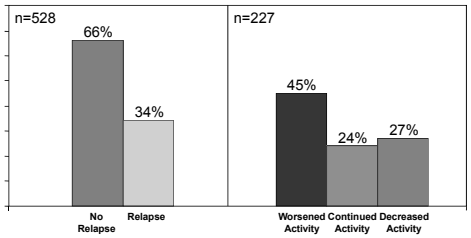
Mahadevan U, et al. *Gastroenterol.* 2007;133:1106.

Effects of pregnancy on IBD

- Course of disease not affected in patients with inactive UC
  - -1/3 relapse during pregnancy and puerperium
- Active disease at time of conception
  - -2/3 worsen or have persistent activity

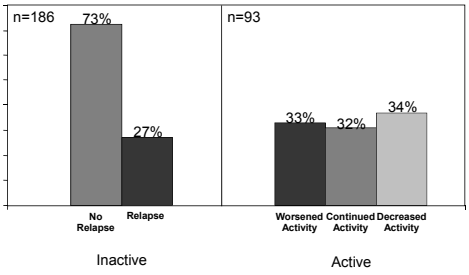
First attack of UC during pregnancy-aggressive course

Effect of Pregnancy on UC: Disease Activity at Conception



Miller JP. *J R Soc Med.* 1986;79:221-5.

Effect of Pregnancy on CD: Disease Activity at Conception



Miller JP. *J R Soc Med.* 1986;79:221-5.

Effects of active UC

- Active nonfulminant UC-abortion stillbirth rate of 18-40%
- Fulminant UC requiring surgery –abortion and stillbirth rate of 60%

Pregnancy outcomes: population based studies

	IBD	UC	CD
Preterm Birth	X	X	X X
LBW	X		X X
SGA			X
Congenital Malformation		X	
Caesarean Section	X		

Kornfeld: Am J Obstet Gynecol 1997 (n=756 IBD)
Fonager: Am J Gastroenterol 1998 (n=510 CD)
Norgard: Am J Gastroenterol 2000 (n=1531 UC)
Dominitz: Am J Gastroenterol 2002 (n=107 UC, 155 CD)

Medications in IBD –FDA category

A	B	C	D	X
	Azulfadine Mesalamine Balsalazide Flagyl Infliximab	Quinolones CSA Tacrolimus Budesonide Prednisone No rating	Azathioprine 6 MP	Methotrexate Thalidomide

Will My Child Get IBD?

- Increased risk of CD and UC in offspring of patients with IBD1
  - 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 respectively3
- If both parents have IBD, a child's risk is as high as 35%
- for developing IBD2
- Inheritance is multifactorial
  - undefined environmental triggers
- Pregnancy should not be discouraged for this reason

Orholm M. *Am J Gastroenterol*. 1999;94(11):3236-3238.
Bennett RA. *Gastroenterology*. 1991;100(6):1638-1643.
Polito JM. *Gastroenterology.* 1996;111(3):580-586.

Health Care Maintenance

- Vaccinations
  - No live virus vaccines while on biologics or during pregnancy (MMR, varicella)
  - Hepatitis A, B, flu shot
- Cancer screening
  - Colonoscopy
  - Annual Pap smear
- Laboratory tests
  - Vitamin B12, folate, 25-OH vitamin D, iron, liver, hematocrit

Safety of Medications

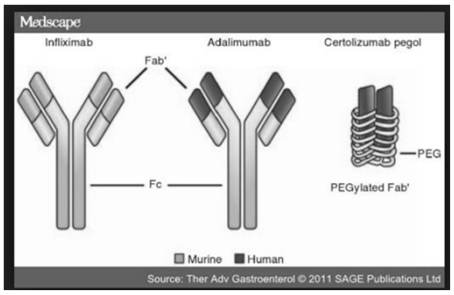
Drug Lactation	FDA	Birth Defects	Lactation	Notes
Mesalamine	B	Low risk	Compatible	
Sulfasalazine	B	Low risk	Compatible	
Corticosteroids	C	Low risk- T1 cleft palate	Compatible	
Budesonide	C	Low Risk	Compatible	
Metronidazole	B	Low risk- T1 cleft palate	Not advised	
Ciprofloxacin	C	Not advised – bone	Avoid use- maybe compatible	
Augmentin	B	Low risk	Compatible	

Medications to avoid

Drug	Pregnancy Category	Comments
Diphenoxylate	C	Teratogenic in animals
Loperamide	B	Increase in CV defects in 1 study
Bisphosphonates	C	Crosses the placenta in animal studies . No increased risk in one study of 24 patients
Methotrexate	X	Known abortifacient Teratogenic (skeletal defects; cleft palate)
Thalidomide	X	Birth defects

Ornoy. Reproductive Toxicology. 2006;22:578.

Biologic agents in IBD



Use of biologic agents in pregnancy

- Infliximab crosses placenta at high rate in the 3rd trimester
- 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
- Breastfeeding compatible

Thank you