

Digestive Health Disease In Women

Nicole Kershner
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Topics to be discussed...

- Sex difference in GI physiology
- GERD and dyspepsia
- Irritable Bowel syndrome
- Constipation
- Pelvic Floor Dysfunction
- Fecal Incontinence
- Chronic Pelvic Pain
 - Endometriosis
- IBD and women
- Liver Disease and Women
 - EtOH, Autoimmune, PBC, Gallstones, Liver Lesions
- Abuse and GI disorders
- Colorectal Cancer in women

Sex Differences in Gastrointestinal Physiology

- 1) Genetics - enhanced expression of X-linked genes in women
- 2) Hormones – progesterone, estrogen, and testosterone
- 3) Environmental/Social factors - Women are higher users of health care than men in the United States
- 4) Differences in hormones and body composition



Sex Differences in Gastrointestinal Physiology

- Body Composition (women vs. men):
 - Higher percentage of body fat
 - Less bone mass
 - Less muscle mass
- Structural Differences
 - Gastrointestinal system:
 - Shorter esophagus in women (regardless of height)
 - Brain:
 - Differences in pain threshold and cognitive style
 - Heart:
 - Less ventricular mass, smaller chamber in women
 - Reproductive system
 - Pelvic Floor
- Possible Differences in Drug Metabolism?

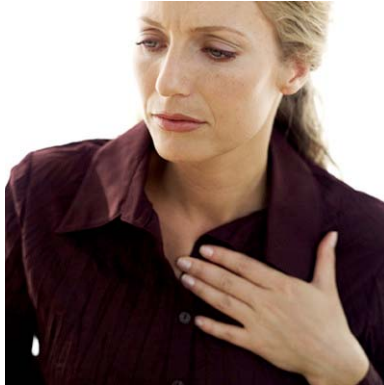
Sex Differences in Gastrointestinal Physiology

Hormones

- Estrogen - may have protective role in the development of colorectal cancer
- Progesterone - may reduce spasm and relax smooth muscle, reduces gallbladder activity, and may lower esophageal sphincter pressure
- Testosterone – in women, this hormone helps maintain muscle mass and plays a role in libido. Hormone replacement therapy (HRT) can lead to testosterone decline

Gastroesophageal Reflux Disease and Dyspepsia

- Women have higher frequency and severity of GERD symptoms for the same endoscopic grades of esophagitis



- Women are less likely to have erosive esophagitis and Barrett's Esophagus
- Physiologic fluctuations of sex hormones during menstrual cycle do not predispose to GERD
 - This is despite a significant rise in progesterone level when going from the follicular phase into the luteal phase – no significant differences in LES pressure or esophageal acid exposure

Gastroesophageal Reflux Disease and Dyspepsia

- Rome III Criteria of Functional Dyspepsia
 - One or more of: postprandial fullness, early satiety, epigastric pain, epigastric burning AND no structural disease to explain symptoms
- Women are more likely to:
 - present with a combination of symptoms (20% of females vs. 10% males)
 - more likely to have early satiety (36% of females vs. 28% of males)
 - less likely to have frequent upper abdominal pain (32% of females vs. 52% of males)

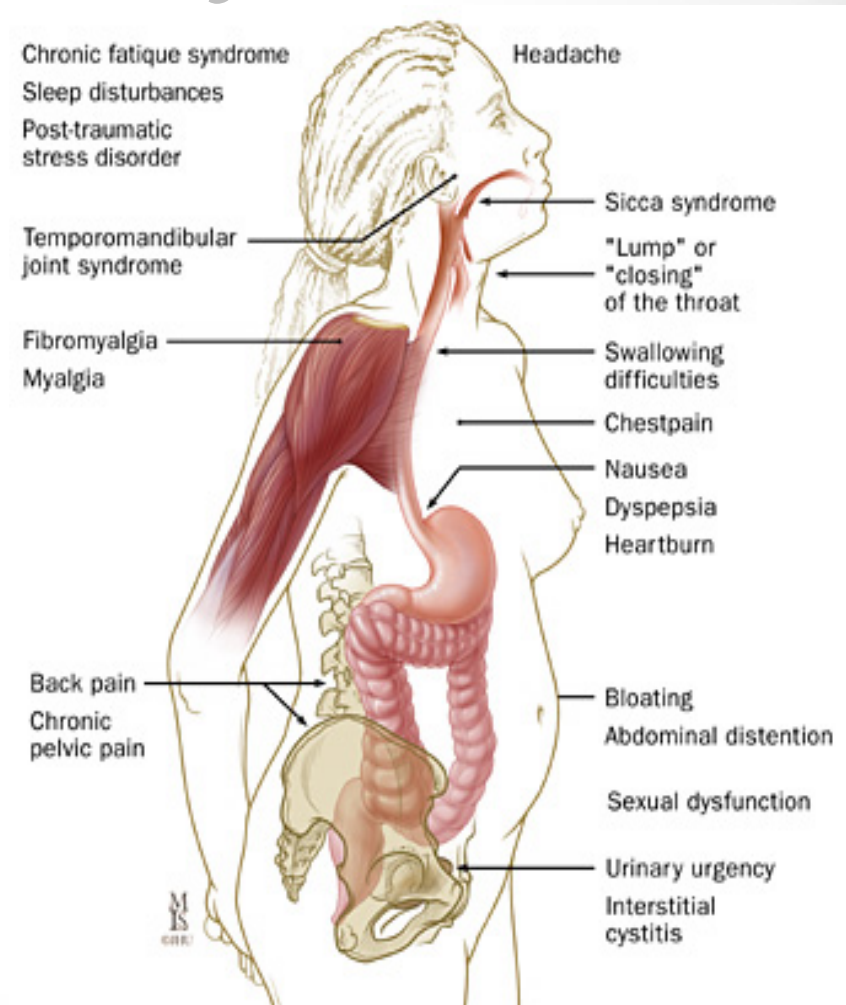
It's not a real job unless it's caused
you to have IBS.



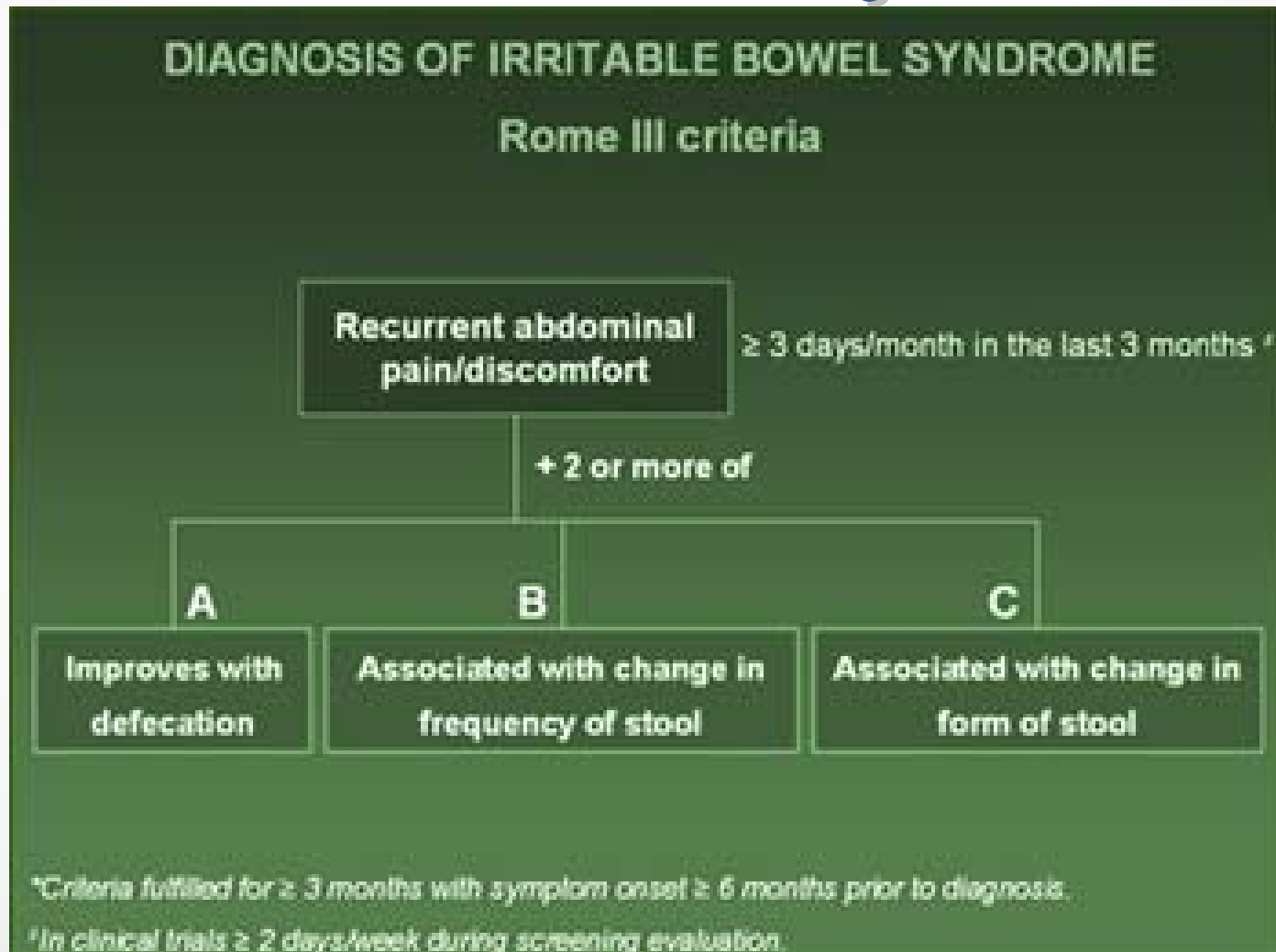
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Irritable Bowel Syndrome

- The most common functional bowel disorder
- In the health care-seeking population, women outnumber men 3 to 1
- Observed gender differences diminish with age



Irritable Bowel Syndrome



Irritable Bowel Syndrome

- Although IBS patients are predominately female – there appears to be an even greater sex difference in the subgroup of IBS with constipation than in other subgroups
- Women also report more non-pain-related symptoms, including nausea, alterations of taste and smell, morning muscle stiffness, greater food sensitivity and greater medication side effects

Irritable Bowel Syndrome

- Traits related to social factors:
 - Bowel functioning may be perceived as a source of embarrassment or shame
 - Because of our society's focus on thinness in women; bloating and constipation may not represent a physical discomfort so much as a source of psychological stress
- Psychological Factors:
 - In one study, IBS patients had a greater level of psychological disturbance than either IBS non-patients (non-seekers of health care) or controls. In fact, IBS non-patients were not psychologically different from normal.
 - Another study demonstrated that female IBS patients had higher scores for depression and long standing anxiety and lower scores for energy. Women also demonstrated higher scores on the hysteria scale suggesting greater somatization or fear of pain.

Irritable Bowel Syndrome and Menses

- No significant differences have been seen in most symptoms of IBS, but one study found that women with IBS using OCPs have lower cognitive, anxiety, and depression symptoms.
- Symptoms of IBS are generally more pronounced in the pre-menses period
- In another study, it was demonstrated that during menses, rectal distension was associated with increased abdominal pain, bloating, and rectal sensitivity compared to other phases of the menstrual cycle

Irritable Bowel Syndrome and Rectosigmoid Sensitivity

- Sex significantly influences perceived sensitivity to rectosigmoid distension.
- Women with IBS demonstrate the greatest sensitivity to rectosigmoid distension when compared to healthy women and male IBS patients and controls.



If 2 out of 3 people suffer from constipation, does that mean one person enjoys it?



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Constipation

- Bloating, hard stools, difficult stool passage, sensation of incomplete evacuation, and frequent straining are more commonly reported symptoms
- Prevalence in N. America is ~ 15% with a female-male ratio of 2.2:1 (symptoms advance w/age, >65)
- Causes:
 - Functional constipation (includes idiopathic and IBS-C)
 - Defecation disorders (pelvic floor dyssynergia, excessive perineal descent, mechanical obstruction)
 - Slow-transit constipation (least common)

Constipation

- History and Physical
 - Inquire about previous pelvic surgeries and vaginal deliveries
 - Examine for previous episiotomies and obstetric scars



Constipation

- In the absence of alarm signs/symptoms, there is no evidence to support the use of laboratory testing, X-rays, or endoscopy in the routine management of constipation
- There is good evidence in support of physiologic testing (manometry, colon transit studies) in order to direct treatment



Functional Constipation

Rome III criteria for functional constipation

Two or more of the following symptoms for the last 3 months, with symptom onset at least 6 months before diagnosis: (1) straining in $\geq 25\%$ of defecations, (2) lumpy or hard stools in $\geq 25\%$ of defecations, (3) sensation of incomplete evacuation in $\geq 25\%$ of defecations, (4) sensation of anorectal obstruction/blockade in $\geq 25\%$ of defecations, (5) manual maneuvers to facilitate $\geq 25\%$ of defecations, (6) < 3 bowel movements per week.

Loose stools not present (without laxative use).

Insufficient criteria for irritable bowel syndrome.

ACG definition of constipation

Unsatisfactory defecation characterized by infrequent stools, difficult stool passage, or both. Difficult stool passage includes straining, sense of difficulty passing stool, incomplete evacuation, hard/lumpy stools, prolonged time to stool, or need for manual maneuvers to pass stool. Chronic constipation defined by presence of these symptoms for ≥ 3 months.



Abbreviation used: ACG, American College of Gastroenterology.

Defecation Disorders

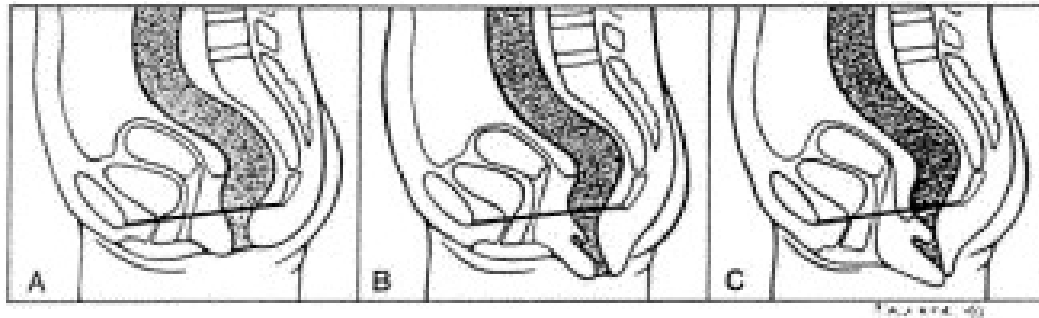
- **Functional Defecation Disorders: Rome III Criteria**
 - The patient must satisfy diagnostic criteria for functional constipation**
 - During repeated attempts to defecate must have *at least two* of the following:
 - Evidence of impaired evacuation, based on balloon expulsion test or imaging
 - Inappropriate contraction of the pelvic floor muscles (i.e., anal sphincter or puborectalis) or less than 20% relaxation of basal resting sphincter pressure by manometry, imaging, or EMG
 - Inadequate propulsive forces assessed by manometry or imaging
- Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

**** Diagnostic criteria for functional constipation:**

- (1.) **Must include *two 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 (e.g., digital evacuation, support of the pelvic floor), (f) Fewer than three defecations per week.
- (2.) **Loose stools are rarely present without the use of laxatives.**
- (3.) **Insufficient criteria for irritable bowel syndrome.**

Defecation Disorders

- Pelvic floor dyssynergia is the paradoxical contraction or failure of relaxation of the pelvic floor muscles with bearing down
- In older women, there may be failure of the anorectal angle to open or excessive perineal descent that leads to problems with rectal evacuation

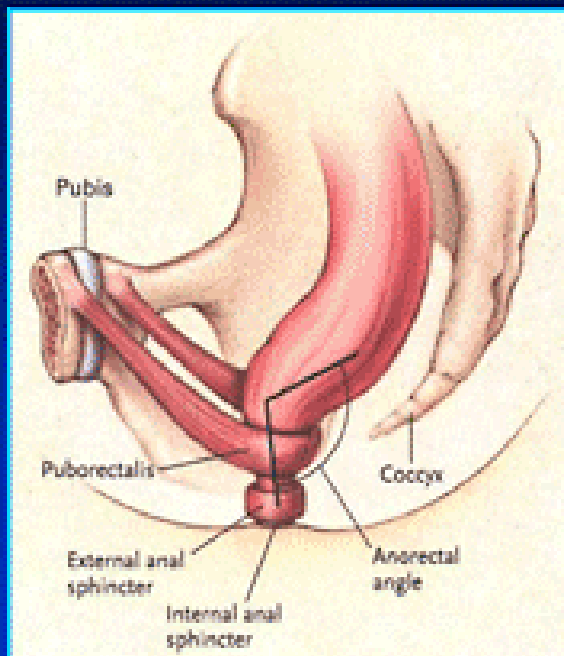


- Pelvic Floor Dysfunction accounts for 1/3 of constipation cases in the community setting, but up to 70% in a tertiary care center setting

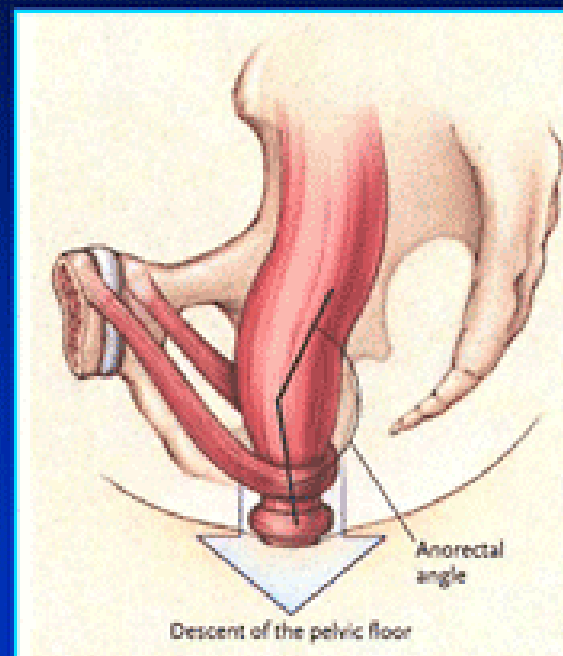
Pelvic Floor

Normal Anorectal Physiology

At Rest



With Straining



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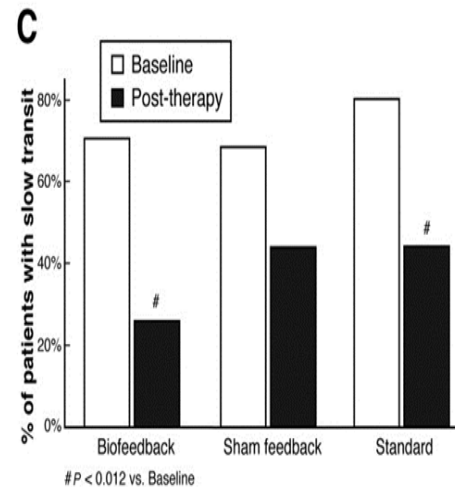
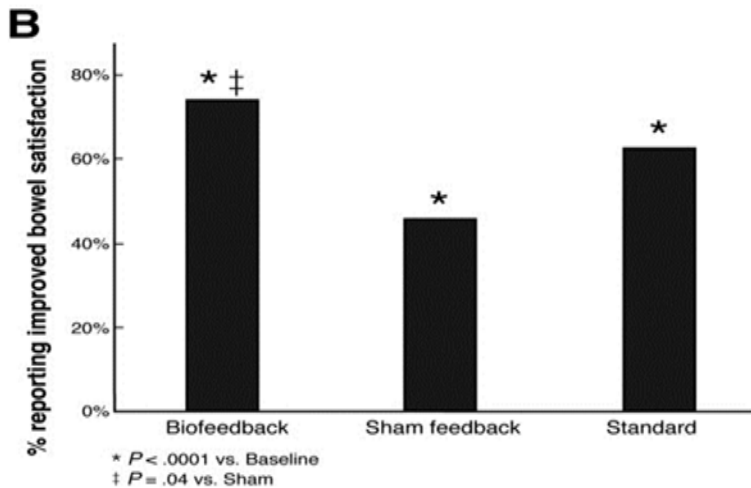
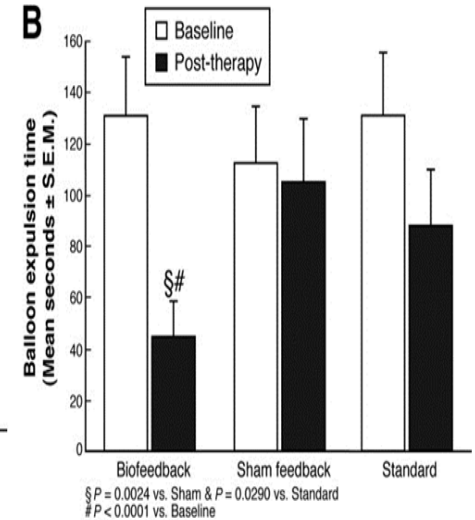
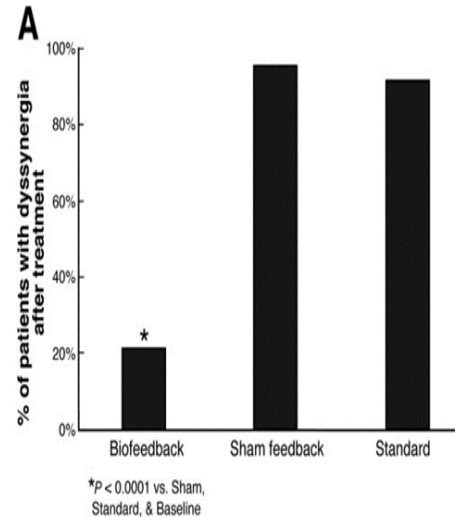
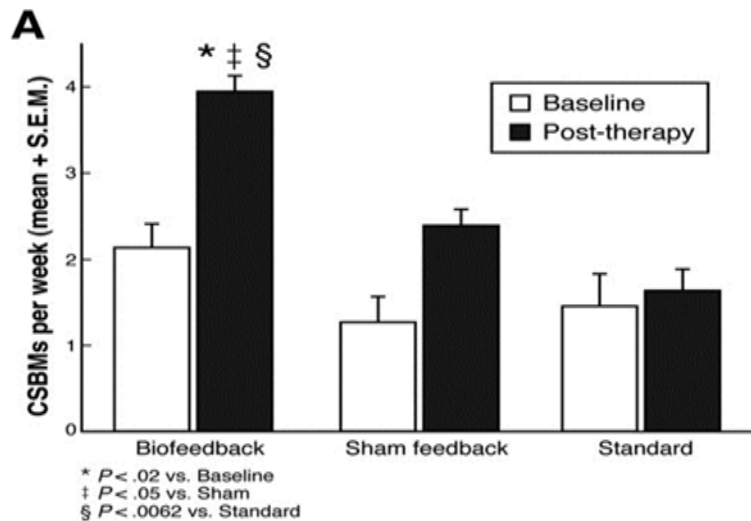
Defecation Disorders

- Increased muscle tension may result from symptoms of anxiety and/or psychological stress
 - Sexual abuse has been reported in 22% of women with functional defecation disorders and 40% of women with lower gut disorders (this includes functional defecation disorders)
- Generally believed that functional defecation disorders are likely to be acquired behavioral disorders
 - 2/3 of patients learn to relax the external anal sphincter and puborectalis muscles appropriately when provided with biofeedback training

Defecation Disorders

- Biofeedback is an effective treatment
 - Patients receive visual or auditory feedback on striated muscle activity recorded by anal or perianal electromyography or pressure sensors (modify behavior through trial and error)
 - Controlled and uncontrolled studies suggest a success rate of 67-80% after pelvic floor retraining
- RTC of Biofeedback, Sham Feedback, and Standard Therapy for Dyssynergic Defecation (Rao, et al, Clinical Gastroenterology and Hepatology 2007)
 - Investigated the efficacy of biofeedback (manometric-assisted anal relaxation, muscle coordination, and simulated defecation training; biofeedback) with either sham feedback therapy (sham) or standard therapy (diet, exercise, laxatives; standard) in 77 subjects (69 women) with chronic constipation and dyssynergic defecation. At baseline and after treatment (3 months), physiologic changes were assessed by anorectal manometry, balloon expulsion, and colonic transit study and symptomatic changes and stool characteristics by visual analog scale and prospective stool diary.

Defecation Disorders



Defecation Disorders

- Botulinum type A toxin injected into the puborectalis muscle may be effective in the treatment of defecatory disorders involving spastic pelvic floor muscles
- Surgery can be considered in patients with refractory constipation due to pelvic floor dysfunction and functionally significant rectoceles



Slow-Transit Constipation

- Least common form of constipation
- Main complaint of infrequent bowel movement
 - Symptoms include: frequent urge to defecate, bloating, abdominal pain, and abdominal discomfort
- Commonly occurs with puberty
- Histology – changes in the number of myenteric plexus neurons expressing the excitatory neurotransmitter substance P, abnormalities in the inhibitory neurotransmitters vasoactive intestinal peptide and nitric oxide, and a reduction in the number of interstitial cells of Cajal
- Treatment: Misoprostol and colchicine along with Miralax. Consider subtotal colectomy and ileorectal anastomosis in severe, refractory cases

Fecal Incontinence

- Fecal incontinence is an involuntary loss of liquid or stool that is a social or hygiene problem

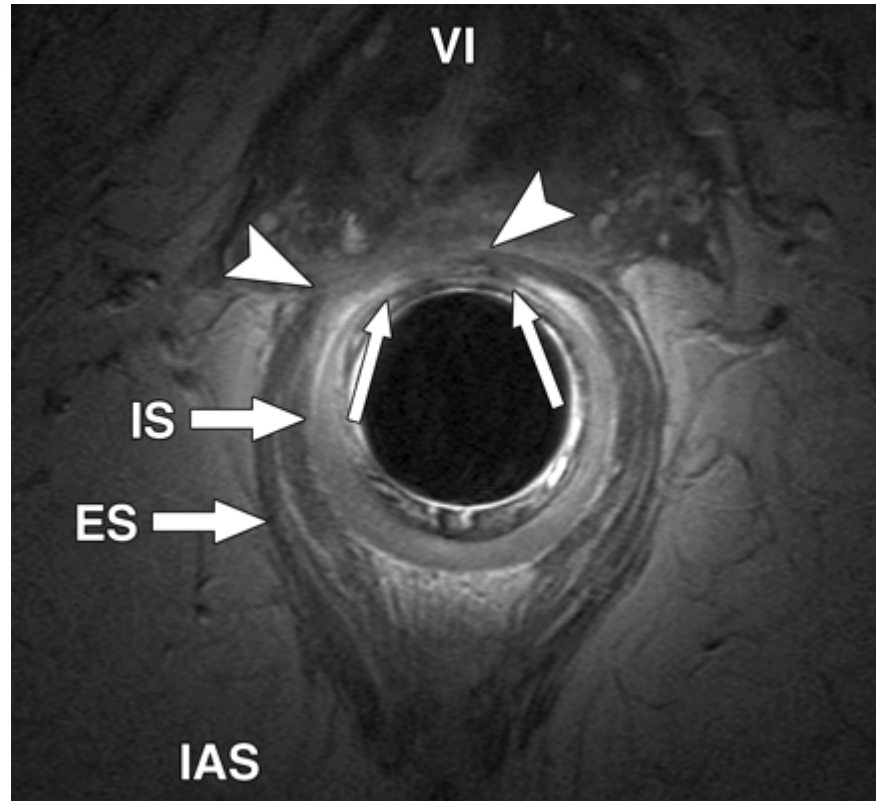


- There appears to be an increased incidence with increasing age and some studies have shown sex-related differences in prevalence
 - NIH consensus: 6% rate of FI in women <40 and increased to 15% at age >40. Men had a rate of 6-10%, with only a slight increase as they age

Fecal Incontinence

- Disruption in either structural or functional components of the anorectal system can result in FI
 - Defects in anal sphincter muscle
 - Injury to the pudendal nerve
 - Disturbance of anorectal sensation caused by obstetric injury can result in loss of stool awareness and rectal agnosia
 - Fecal impaction associated with pelvic floor dysfunction can lead to overflow incontinence
- Obstetric Risk Factors:
 - Forceps Delivery
 - Third or Fourth Degree tears
 - Length of second stage of labor
 - Fetal weight >4000g

Fecal Incontinence



- Predominant event is rupture of the anal sphincter (occurs in 0.6%-20% of the OB population), also can have damage to or stretching of the pudendal nerves and defects in anorectal sensation

Fecal Incontinence

- Perineal descent at rest and during straining was found to be similar in women with chronic straining at stool and women with incontinence
 - Women with chronic straining may be at risk for development of incontinence
- Imperative to perform detailed H&P
 - Stool loss, use of coping mechanisms, and impact on lifestyle
 - Thorough digital rectal exam
- Diagnosis should be tailored to patient's presentation

Fecal Incontinence

- Gold standard in defining sphincter function has been anorectal manometry
- Endoanal ultrasound can identify sphincter defects
- Defecography can offer functional information related to continence and defecation
- Functional pelvic MRI can use real time to assess sphincter anatomy and pelvic floor function
- Pudental nerve terminal motor latencies and EMG may be helpful

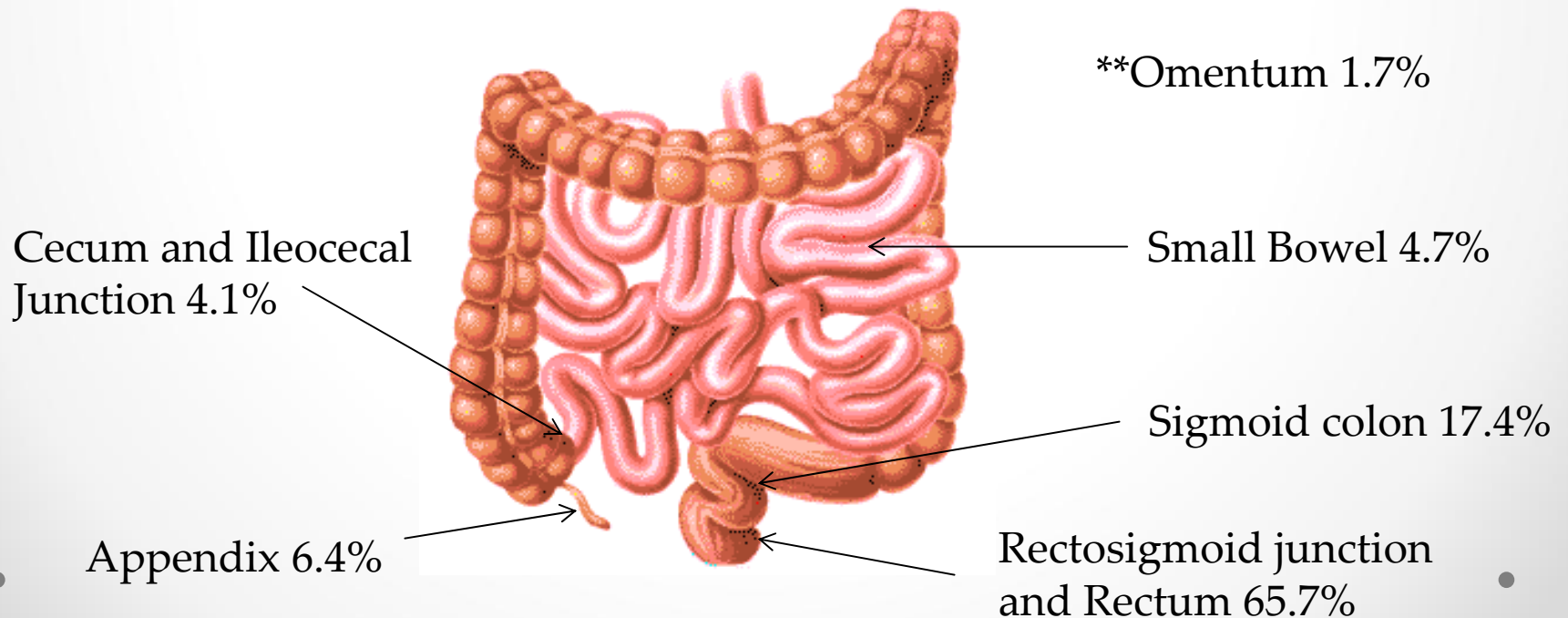
Chronic Pelvic Pain

- Defined as noncyclic pain lasting \geq 6 months, localized to the pelvic region, causing functional disability
- Approx. 15-20% of women (ages 18-50) experience pain lasting \geq 1 year
- Many different etiologies – gynecological, GI, urinary, and musculoskeletal
 - Four most common diagnoses determined for the cause of chronic pelvic pain:
 - 1) Endometriosis
 - 2) Adhesions
 - 3) Irritable Bowel Syndrome
 - 4) Interstitial Cystitis



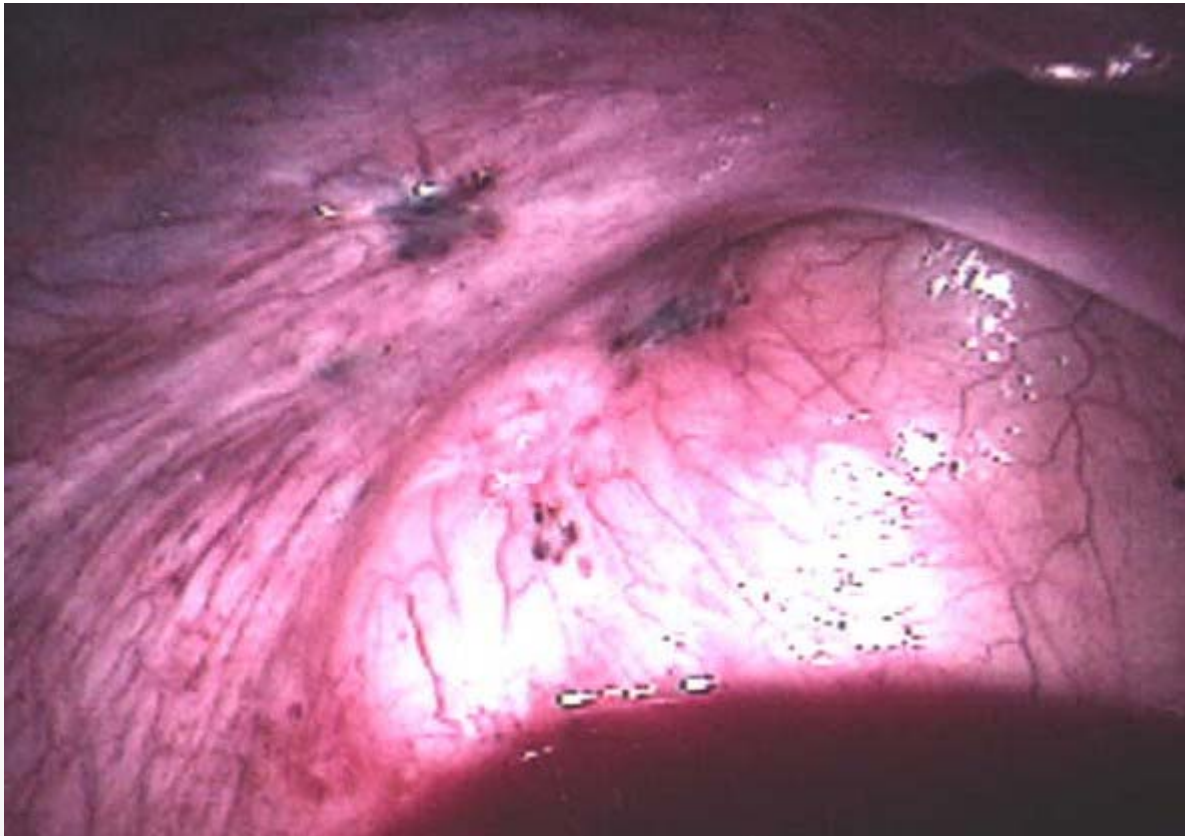
Endometriosis

- Frequent symptoms: dysmenorrhea, chronic pelvic or back pain, premenstrual straining, painful defecation, proctalgia
- Bowel involvement occurs in up to 37% of patients
 - Sigmoid colon, rectosigmoid junction, and rectum account for 82% of deep infiltrating endometriosis of the intestine



Endometriosis

- When intestinal symptoms occur – usually associated with abdominal pain or diarrhea
- Intestinal bleeding and ascites may occur



Endometriosis

- Consider in woman of reproductive age who presents with abdominal pain, especially in lower abdomen or pelvis
- Diagnosis is by direct visualization
- Rarely seen on colonoscopy (may have fixation or distortion of the colon, extrinsic compression, localized extra-mucosal mass, or stricture)
- Imaging is not very helpful. MRI, barium enema, and endorectal ultrasound can be used to determine extent
- Treatment include medication and surgery

Inflammatory Bowel Disease and Women

- UC patients who are managed without surgery have a high (97%) rate of achieving pregnancy
 - This rate falls to 56% after ileal pouch anal anastomosis
- Majority of studies from referral populations showed decreased fertility in women with Crohn's disease
- Menstrual cycle may be disrupted by disease activity or medications
- Women with IBD have a higher incidence of abnormal cervical cytology compared to the normal population

Liver Disease and Women

- Alcoholic Liver Disease
 - Women are at higher risk of developing more serious liver disease than men (after adjustment of body weight)
 - Women are more likely to develop liver disease, even with less consumption of alcohol than men
- Autoimmune Hepatitis
 - Female predominance with female-male ratio of >3:1 (initially described as a disease of young girls)
 - Young women in remission on therapy may have successful pregnancies
 - Modest increase risk of prematurity and fetal loss
 - ALH flares are more common after delivery (maternal responses are enhanced)

Liver Disease and Women

- Primary Biliary Cirrhosis
 - 95% of patients with PBC are women
 - Increased risk for osteopenia and osteoporosis – DEXA should be performed at diagnosis and every 2 years thereafter
- Gallstones
 - Estrogens decrease the concentration of bile acids and increases cholesterol secretion, resulting in supersaturated bile prone to form sludge and stones
 - Female gender increases the incidence 3-4 times up to the age of 50
 - 7-fold increase in obese female patients

Liver Disease and Women

- Liver Lesions
 - Hemangiomas - insufficient evidence to link estrogens to either development or growth. Recommend routine u/s follow up in women who are receiving hormone therapy.
 - Focal Nodular Hyperplasia – linked to female hormones and use of OCPs.
 - Discontinuation of OCPs is not necessary, but should follow-up with imaging
 - Hepatic Adenomas – predominantly seen in young women with prolonged OCP use.
 - Controversy in managing patients who are taking OCPs (discontinue OCPs vs. surgical resection)
 - Advise patients against pregnancy, since behavior of adenoma during pregnancy is unpredictable. Resection prior to pregnancy may be the best option
 - Hepatocellular Cancer – no association between OCPs and HCC

Abuse and GI Disorders

- Increased incidence of GI symptoms in women with a history of abuse
- Intimate partner violence (IPV) may affect GI health. Women who had experienced physical or psychological IPV were more likely to have GI complaints, including:
 - Pelvic pain
 - Spastic colon
 - Indigestion
 - Diarrhea
 - Constipation



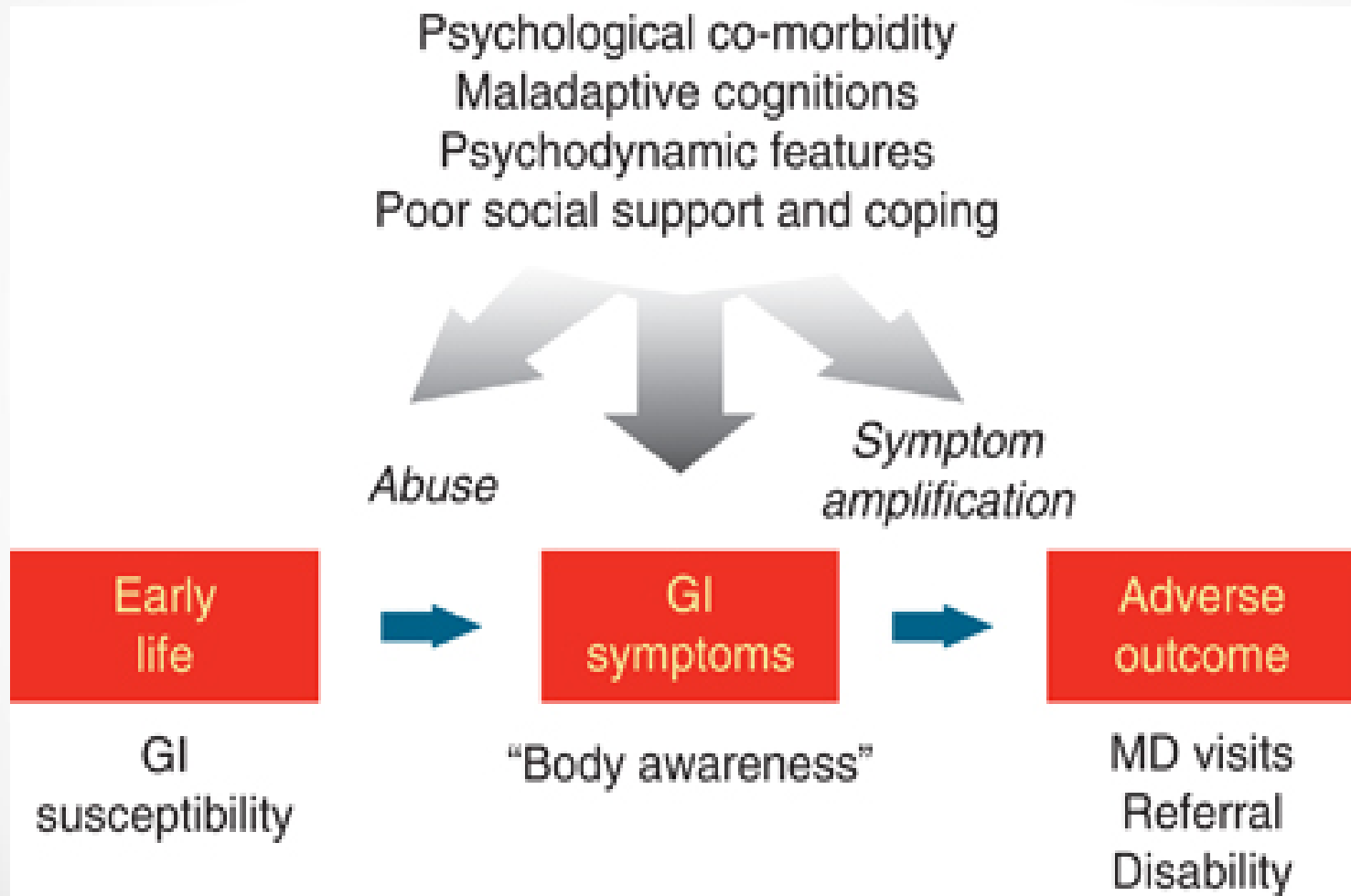
Abuse and GI Disorders

- In one year-long retrospective cohort study of women in WA, women who filed for protective orders against their partners were twice as likely to have been hospitalized for gastrointestinal illness when compared to non-abused, age-matched controls
- In a multicenter study, sexual abuse was found in higher rates in patients with IBS (31.6%) vs. patients with organic gastrointestinal diseases (14%) and healthy controls (7.6%)

Abuse and GI Disorders

- It's hypothesized that those who suffer from abuse experience increased autonomic reactivity in the gut in response to physical and psychological stressors
- Obtaining an abuse history from patients with GI complaints is key (women are usually reluctant to initiate this discussion and physicians often feel uncomfortable eliciting this information) – there must be an integrated team approach in place in order to address the issue of abuse once this history is elicited

Biopsychosocial Conceptual Model



Colorectal Cancer

- Cancer Related Deaths in Women:
 - #1 Lung Cancer
 - #2 Breast Cancer
 - **#3 Colorectal Cancer** (AA women have the highest rate)
- Screening rates have increased since 2000 for both men and women, but the rate of increase has been higher in men

Colorectal Cancer

- Estrogen seems to have a protective role in the development of colorectal cancer
- ER β is an estrogen receptor present in the colon. Expression of this receptor is diminished in colon neoplasms in general, most especially is noted to be decreased in advanced Duke stages of colorectal cancer

Colorectal Cancer

- The Women's Health Initiative found that colorectal cancer rates were reduced by 37% among women taking combined hormone replacement therapy
 - Not to be used as a method to decrease risk of developing colorectal cancer
- CONCeRN study (2005 study of the VA population) showed that overall, age-matched men (after adjusting for family history and FOB testing) were to be nearly twice as likely to have advanced neoplasia at colonoscopy as were women

CONCeRN Study

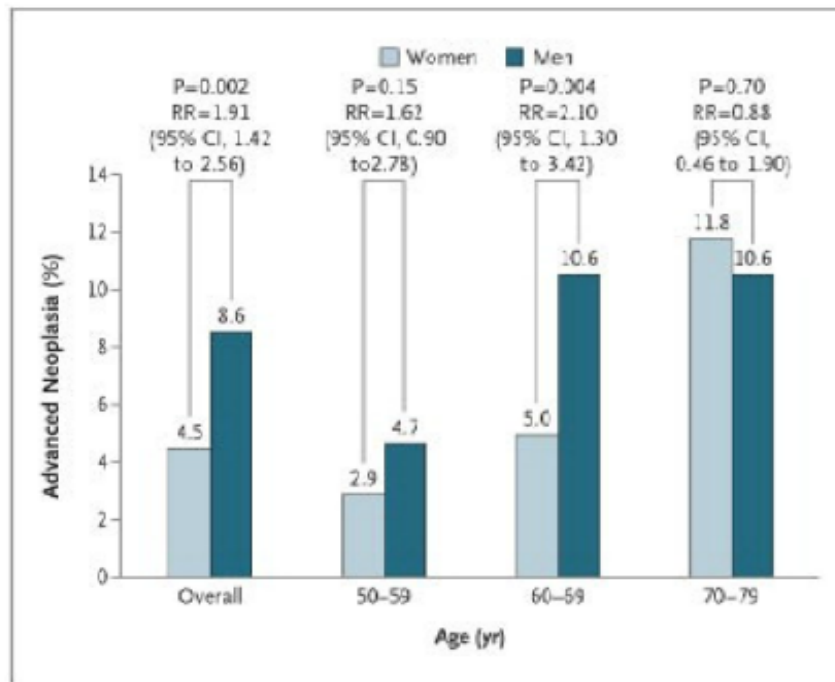
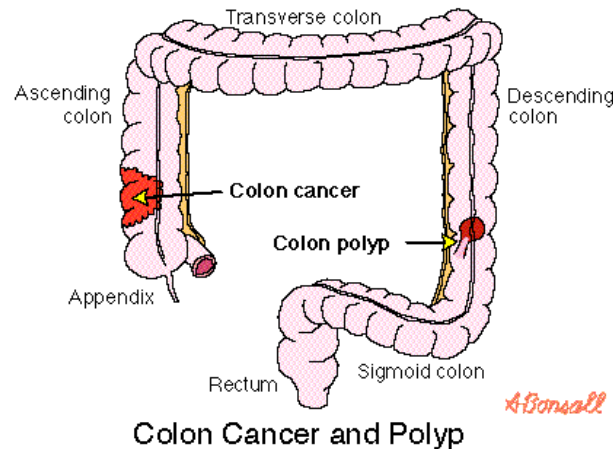


Figure 1. Prevalence of Advanced Neoplasia among Men and Women with a Negative Fecal Occult-Blood Test and No Family History of Colon Cancer, According to Age.

The women were from the current study, and the men were from VA Cooperative Study 380. The relative risk (RR) is for men as compared with women. CI denotes confidence interval.

Colorectal Cancer

- In women, there seems to be a rightward shift of advanced neoplasia



- CONCeRN study also indicated that the diagnostic yield of a flexible sigmoidoscopy is significantly lower in women (therefore more advanced cases of neoplasia would be missed in women vs. men if flex sigs alone were used as a screening tool)

Colorectal Cancer

- Completion rates to the cecum are lower in women than in men
 - Particularly true in women who have had previous pelvic surgery
 - Also less successful in thin women, suggesting less visceral fat may affect the success of the procedure
 - Diverticulosis is associated with a greater time to reach the cecum in women, but interestingly this association is not seen in men



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Colorectal Cancer

- In one study, 202 female patients were surveyed in a primary care office –
 - 43% preferred a woman endoscopist and of these, 87% would be willing to wait >30 days for a woman endoscopist
 - 14% would be willing to pay more for one
- 5% stated that would not undergo a colonoscopy unless guaranteed a woman endoscopist

