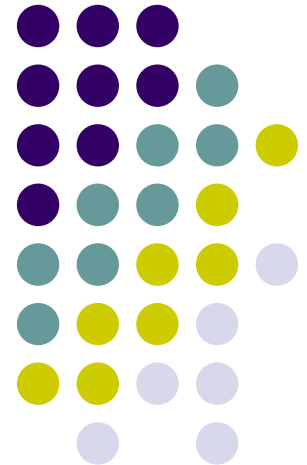


IBS:Constipation

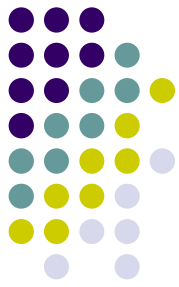
Richard N. Redinger, M.D.
Professor of Medicine





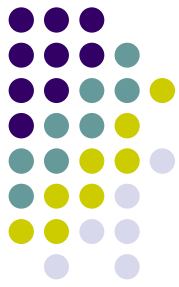
Functional Bowel Disorders

- Functional bowel disorders are best understood as a biopsychosocial model of the pathophysiology of illness or disease
- Rather than having a structural organic basis, they represent altered gut physiology via the brain/gut axis that translates neurotransmitter function into clinical symptoms



Functional Bowel Disorders

- Psychosocial factors include life stresses particularly early life experiences with psychologic stress that affect coping capability and inadequate social support
- Physiologic alterations with genetic and environmental influences impact gut motility and its sensation, inflammation and altered bacterial flora causing immune modulation that are associated with enhanced visceral sensitivity. CNS modulation of gut function also have linkages to emotional and cognitive areas that have behavioral consequences.



Rome III Functional Gastrointestinal Disorders *(Gastroenterology 2006;130:1377-1556)*

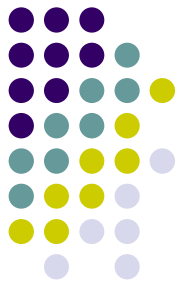
A. Functional esophageal disorders

- A1. Functional heartburn
- A2. Functional chest pain of presumed esophageal origin
- A3. Functional dysphagia
- A4. Globus

B. Functional gastroduodenal disorders

- B1. Functional dyspepsia
 - B1a. Postprandial distress syndrome
 - B1b. Epigastric pain syndrome
- B2. Belching disorders
 - B2a. Aerophagia
 - B2b. Unspecified excessive belching
- B3. Nausea and vomiting disorders
 - B3a. Chronic idiopathic nausea
 - B3b. Functional vomiting
 - B3c. Cyclic vomiting syndrome
- B4. Rumination syndrome in adults

Rome III Functional Gastrointestinal Disorders



C. Functional bowel disorders

- C1. Irritable bowel syndrome
- C2. Functional bloating
- C3. Functional constipation
- C4. Functional diarrhea
- C5. Unspecified functional bowel disorder

D. Functional abdominal pain syndrome

E. Functional gallbladder and Sphincter of Oddi (SO) disorders

- E1. Functional gallbladder disorder
- E2. Functional biliary SO disorder
- E3. Functional pancreatic SO disorder

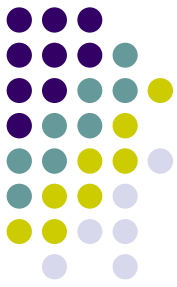
F. Functional anorectal disorders

- F1. Functional fecal incontinence
- F2. Functional anorectal pain
 - F2a. Chronic proctalgia
 - F2a1. Levator ani syndrome
 - F2a2. Unspecified functional anorectal pain
 - F2b. Proctalgia fugax
- F3. Functional defecation disorders
 - F3a. Dyssynergic defecation
 - F3b. Inadequate defecatory propulsion

Qualifications for Symptom Based Criteria



1. Coexisting disease(s) must be excluded
i.e., no evidence of inflammation, anatomy, metabolic or neoplastic abnormalities
2. Symptoms from one domain may overlap with various other GI functional bowel disorders
3. Symptoms must exist for 6 months prior to diagnosis and be active for 3 months
4. Diagnostic categories do not include psychosocial criteria but are seen more commonly in referred versus primary care practices
5. Criteria are determined by clinical consensus and existing evidence



Functional Gastrointestinal Disorders

Table 1.

C. Functional bowel disorders

C1. Irritable bowel syndrome*

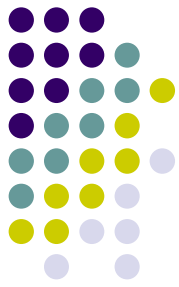
C2. Functional bloating

C3. Functional constipation*

C4. Functional diarrhea

C5. Unspecified functional bowel disorder

Irritable Bowel Syndrome



Definition:

IBS is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit, and with features of disordered defecation.

Epidemiology



Throughout the world, about 10%-20% of adults and adolescents have symptoms consistent with IBS, and most studies find a female predominance. IBS symptoms come and go over time, often overlap with other functional disorders, impair quality of life, and result in high health care costs.



Diagnostic criteria* for IBS

Recurrent abdominal pain or discomfort** at least 3 days per month in the last 3 months associated with 2 *or more* of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

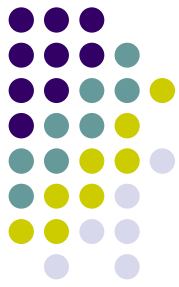
**Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.*

****Discomfort means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation for subject eligibility.**








Subtyping IBS by Predominant Stool Pattern



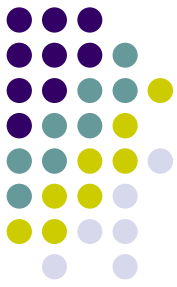
1. IBS with constipation (IBS-C) – hard or lumpy stools $\geq 25\%$ and loose (mushy) or watery stools $< 25\%$ of bowel movements.
2. IBS with diarrhea (IBS-D) – loose (mushy) or watery stools $\geq 25\%$ and hard or lumpy stool $< 25\%$ of BMs.
3. Mixed IBS (IBS-M) – hard or lumpy stools $\geq 25\%$ and loose (mushy) or watery stools $\geq 25\%$ of bowel movements.
4. Unsubtyped IBS – insufficient abnormality of stool consistency to meet criteria for IBS-C, D, or M.



The Bristol Stool Form Scale

Whole gut transit time	Type of stool	Description	Pictorial representation
Long transit (e.g., 100 hours) 	Type 1	Separate hard lumps, like nuts, hard to pass	
	Type 2	Sausage shaped but lumpy	
	Type 3	Like sausage but with cracks on its surface	
	Type 4	Like sausage or snake, smooth and soft	
	Type 5	Soft blobs with clear-cut edges (passed easily)	
	Type 6	Fluffy pieces with ragged edges, a mushy stool	
	Type 7	Watery, no solid pieces	Entirely liquid
Short transit (e.g., 10 hours)			

Bristol Stool Form Scale. Common stool forms and their consistency in relation to whole-gut transit time are shown. (From Heaton KW, Radvan J, Cripps H, et al. Defecation frequency and timing, and stool form in the general population: A prospective study. Gut 1992; 33:818-24.)



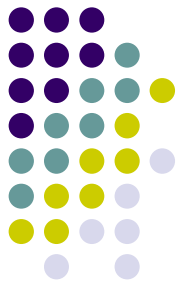
Clinical Evaluation

Diagnosis depends on careful interpretation of the temporal relationships of pain/discomfort, bowel habit, and stool characteristics. Pain/discomfort related to defecation is likely to be of bowel origin, whereas that associated with exercise, movement, urination, or menstruation usually has a different cause. Fever, gastrointestinal bleeding, weight loss, anemia, abdominal mass, and other “alarm” symptoms or signs are not due to IBS, but may accompany it.

Clinical Evaluation

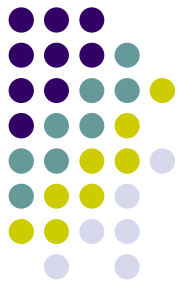


In women, so-called pelvic pain, worsening of IBS symptoms during menstruation, and dyspareunia or *other gynecologic* symptoms may obscure the diagnosis. Incorrect symptom attribution can lead to hospitalization and surgery, especially cholecystectomy, appendectomy, and hysterectomy. The recognition and evaluation of bowel dysfunction in patients with “pelvic” or abdominal pain may reduce unnecessary surgery.



Clinical Evaluation

- Heartburn, fibromyalgia, headache, backache, genitourinary symptoms, and others are often associated with IBS, but are not useful in diagnosing it.
- Few tests are required for patients who have typical IBS symptoms and no alarm features. Unnecessary investigations may be costly and even harmful.



Investigations

- Few tests are necessary for patients with typical IBS symptoms and no alarm features. Tests are based on patients age, duration and severity, psychosocial factors, alarm symptoms and FH colon cancers.
- Fiberoptic sigmoidoscopy or colonoscopy to r/o organic disease
- Stool Examination
- R/O celiac diseases based on clinical features
- Assess QOL, daily Fx, personality, life stresses.

Physiologic Features



IBS is best viewed as an interaction of important biological and psychosocial factors. Altered motility, visceral hyperalgesia, disturbance of brain-gut interaction, abnormal central processing, autonomic and hormonal events, genetic and environmental factors, postinfectious sequels, and psychosocial disturbance are variably involved, depending on the individual.



Psychosocial Features

Psychological disturbance, especially in referred patients, includes psychiatric disorders (eg, panic disorder, generalized anxiety disorder, mood disorder, and posttraumatic stress disorder), sleep disturbance, and dysfunctional coping. A history of childhood abuse is common. Although stressful life events sometimes correlate with symptom exacerbation, the nature of the link between psychosocial factors and IBS is unclear.

Treatment

Possible Drugs for a Dominant Symptom in IBS



Possible Drugs for a Dominant Symptom in IBS^a

Symptom	Drug	Dose
Diarrhea	Loperamide	2–4 mg when necessary/ maximum 12 g/d
	Cholestyramine resin	4 g with meal
	Alosetron ^b	0.5–1 mg bid (for severe IBS, women)
Constipation	Psyllium husk	3.4 g bid with meals, then adjust
	Methylcellulose	2 g bid with meals, then adjust
	Calcium polycarbophil	1 g qd to qid
	Lactulose syrup	10–20 g bid
	70% sorbitol	15 mL bid
	Polyethylene glycol 3350	17 g in 8 oz water qd
	Tegaserod ^c	6 mg bid (for IBS, women)
	Magnesium hydroxide	2–4 tbsp qd
	Smooth-muscle relaxant ^d	qd to qid ac
Abdominal pain	Tricyclic antidepressants	Start 25–50 mg hs, then adjust
	Selective serotonin reuptake inhibitors	Begin small dose, increase as needed

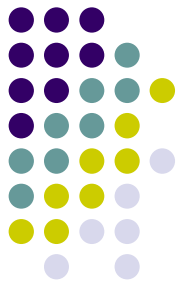
^aLocal cost should be considered in drug choice.

^bAvailable only in the U.S.

^cUnavailable in the European Union.

^dSelective antimuscarinic agents unavailable in the United States.

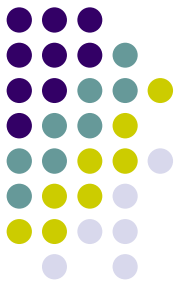
Treatment



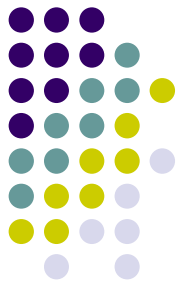
- Reassurance and Education
 - Regarding healthy lifestyles, behavioral Rx, provide counseling for psychosocial issues.
- Establish a Therapeutic Relationship
 - Develop a strong physician-patient relationship.
 - Be sympathetic, maintain patient contact, be understanding, don't overtest or advise harmful treatment.
- Discuss diet
 - Avoid nutritional depletion, diarrheal substances (sorbitol, fructose).
- Discuss use of Probiotics
 - Bifidobacterium infantis, etc
- Cognitive-Behavioral Therapy
 - Standard and Hypnotherapy.



Constipation



Functional vs. Secondary

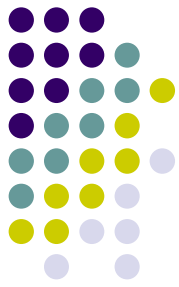


Functional Constipation

Rome III Criteria for Functional Constipation

- Two or more of the following six must be present:
 - Straining during at least 25% of defecations
 - Lumpy or hard stools in at least 25% of defecations
 - Sensation of incomplete evacuation for at least 25% of defecations
 - Sensation of anorectal obstruction/blockage for at least 25% of defecations
 - Manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)
 - Fewer than three defecations/wk

Secondary Causes



Mechanical Obstruction

Anal stenosis

Colorectal cancer

Extrinsic compression

Rectocele or sigmoidocele

Stricture

Secondary Causes



Medications

Antacids

Anticholinergic agents (e.g., antiparkinsonian drugs, antipsychotics, antispasmodics, tricyclic antidepressants)*

Anticonvulsants (e.g., carbamazepine, phenobarbital, phenytoin)*

Antineoplastic agents (e.g., vinca derivatives)

Calcium channel blockers (e.g., verapamil)*

Diuretics (e.g., furosemide)*

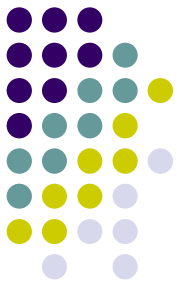
5-Hydroxytryptamine, antagonists (e.g., alosetron) – off market

Iron supplements*

Nonsteroidal anti-inflammatory drugs (e.g., ibuprofen)*

Mu-opioid agonists (e.g., fentanyl, loperamide, morphine*)

Secondary Causes



Metabolic and Endocrinologic Disorders

Diabetes mellitus*

Heavy metal poisoning (e.g., arsenic, lead, mercury)

Hypercalcemia*

Hyperthyroidism

Hypokalemia

Hypothyroidism*

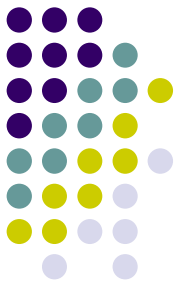
Panhypopituitarism

Pheochromocytoma

Porphyria

Pregnancy*

Secondary Causes



Neurologic and Myopathic Disorders

Amyloidosis

Autonomic neuropathy

Chagas' disease

Dermatomyositis

Hirschsprung's Disease – complete or partial

Intestinal pseudo-obstruction

Internal neural dysplasia

Multiple sclerosis

Myopathy of colon or rectum – anal sphincter genetics

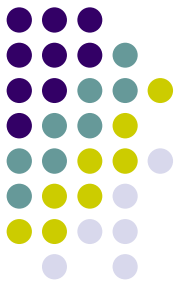
Parkinsonism

Progressive systemic sclerosis

Shy-Drager syndrome

Spinal cord injury

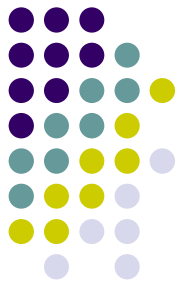
Stroke



Risk Factors

- Risk factors for Constipation
 - Advanced age
 - Female gender
 - Low level of education
 - Low level of physical activity
 - Low socioeconomic status
 - Nonwhite ethnicity
 - Use of certain medications

Epidemiology



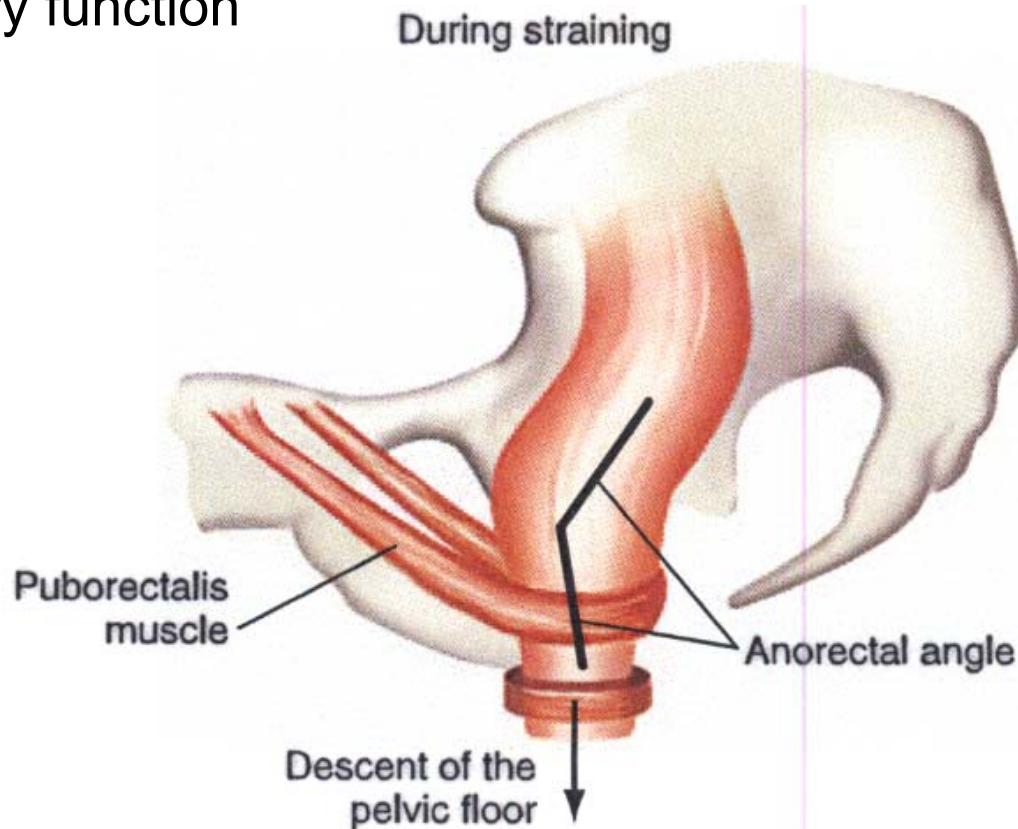
- Incidence – 15% Olmstead Study, non-elderly
- Prevalence – 2% - 28% variable methods, demographics
- Cost - \$6.9 billion/yr, medical eval \$2,252 (colonoscopy)
 - Only 4% get to gastroenterologists

A decorative graphic in the top right corner consisting of a grid of colored dots. The dots are arranged in a roughly triangular shape, with colors including dark purple, teal, yellow, and light purple. The colors transition from dark purple on the left to light purple on the right.

- Luminal content
 - Bacteria 55%
 - Fiber 17%
 - Food residue, H₂O, gas
- Absorption
 - H₂O Na, 1.5L-200/100 ml
 - Bowel diameter 6-5 cm
- Motor function
 - 1. Delays passage
 - 2. Mixes contents
 - 3. Storage (distal bowel)
 - 4. Propulsion:transit 35-72 hrs
- LAPCs Low amplitude propagated contractions
 - HAPCs High amplitude propagated contractions
- Innervation
 - involuntary, ENS, Proximal colon
 - Voluntary defecation
- Myenteric plexus – excitatory Transmitter substance P
 - inhibitory VIP (Vasoactive Intestinal Polypeptide)
 - Interstitial cells of Cajal (ICCS)
 - Intestinal pacemaker cells – provide slow wave propagation
 - Neural signaling between ENS and muscle

Colonic Function - Physiology

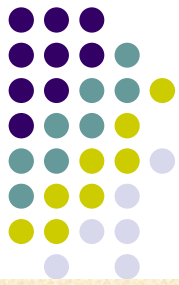
- Defecatory function



Physiology of defecation. Defecation requires relaxation of the puborectalis muscle with descent of the pelvic floor and straightening of the anorectal angle during straining, as well as relaxation of the internal anal sphincter. (From Lembo A, Camilleri M. Chronic constipation. N Engl J Med 2003; 349:1360-8.)



Secondary Causes



Secondary Causes of Constipation

Mechanical Obstruction

- Anal stenosis
- Colorectal cancer
- Extrinsic compression
- Rectocele or sigmoidocele
- Stricture

Medications

- Antacids
- Anticholinergic agents (e.g., antiparkinsonian drugs, antipsychotics, antispasmodics, tricyclic antidepressants)
- Anticonvulsants (e.g., carbamazepine, phenobarbital, phenytoin)
- Antineoplastic agents (e.g., vinca derivatives)
- Calcium channel blockers (e.g., verapamil)
- Diuretics (e.g., furosemide)
- 5-Hydroxytryptamine₃ antagonists (e.g., alosetron)
- Iron supplements
- Nonsteroidal anti-inflammatory drugs (e.g., ibuprofen)
- Mu-opioid agonists (e.g., fentanyl, loperamide, morphine)

Metabolic and Endocrinologic Disorders

- Diabetes mellitus
- Heavy metal poisoning (e.g., arsenic, lead, mercury)
- Hypercalcemia
- Hyperthyroidism
- Hypokalemia
- Hypothyroidism
- Panhypopituitarism
- Pheochromocytoma
- Porphyria
- Pregnancy

Neurologic and Myopathic Disorders

- Amyloidosis
- Autonomic neuropathy
- Chagas' disease
- Dermatomyositis
- Intestinal pseudo-obstruction
- Multiple sclerosis
- Parkinsonism
- Progressive systemic sclerosis
- Shy-Drager syndrome
- Spinal cord injury
- Stroke

Pathophysiology

Functional Causes



Disordered function of colon or rectum

Clinical Classification of Functional Constipation

CATEGORY		FEATURES	CHARACTERISTIC FINDINGS
Normal-transit constipation	59%	Incomplete evacuation; abdominal pain may be present but not a predominant feature	Normal physiologic test results
Slow-transit constipation	13%	Infrequent stools (e.g., $\leq 1/\text{wk}$); lack of urge to defecate; poor response to fiber and laxatives; generalized symptoms, including malaise and fatigue; more prevalent in young women	Retention in colon of $>20\%$ of radiopaque markers five days after ingestion If severe, is called colonic inertia
Defecatory disorders (pelvic floor dysfunction, anismus, descending perineum syndrome, rectal prolapse)	25%	Frequent straining; incomplete evacuation; need for manual maneuvers to facilitate defecation	Abnormal balloon expulsion test and/or rectal manometry

Pathophysiology

Functional Causes



Disordered function of colon or rectum

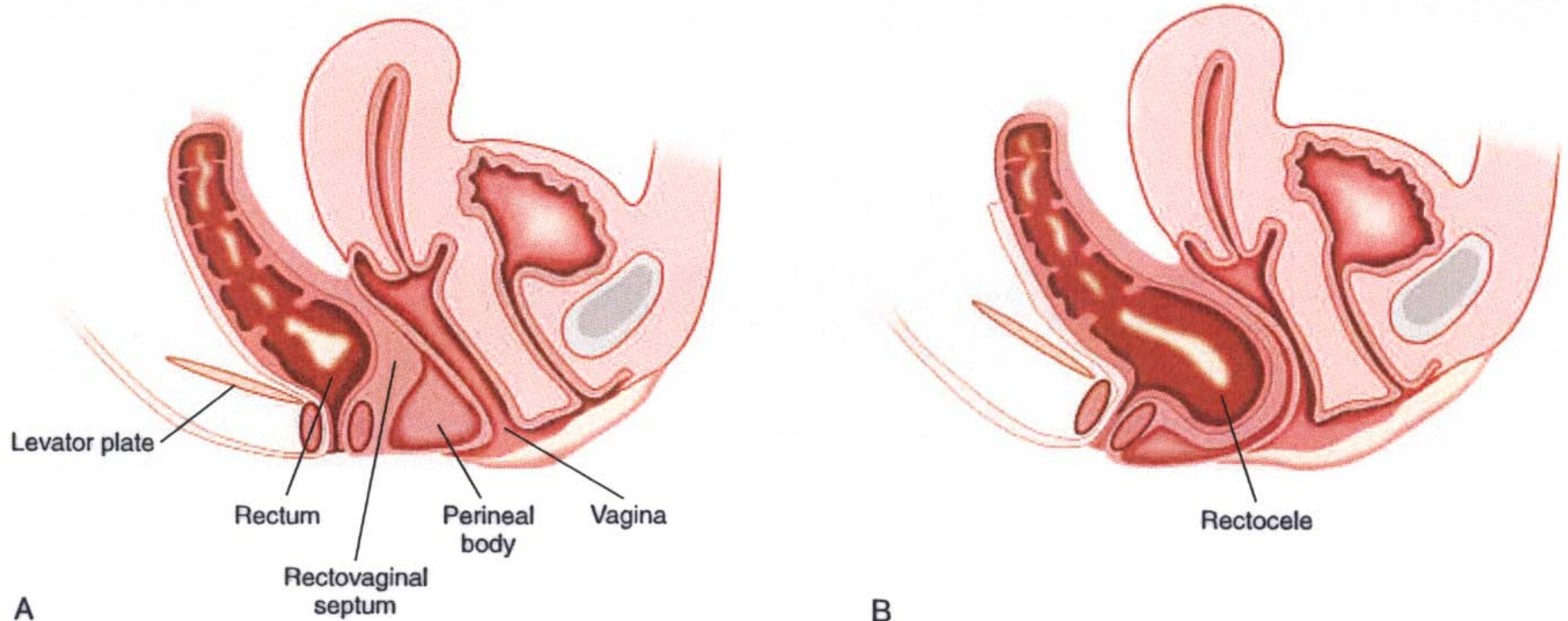
- Also called dyssynergia, obstructive defecation, outlet obstruction
 - These commonly have inappropriate contraction of anal sphincter, abnormal pelvic floor descent and deficient rectal pressure and sensation

Rome III Criteria for Functional Defecation Disorders

- The patient must satisfy diagnostic criteria for functional constipation
- During repeated attempts to defecate, the patient must have **at least two** of the following:
 - Evidence of impaired evacuation, based on balloon expulsion test or imaging
 - Inappropriate contraction of 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

Pathophysiology








Functional Causes



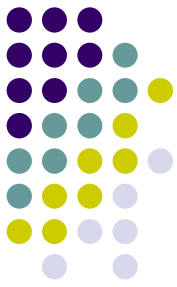
Development of a rectocele. A, Normal anatomy of the female pelvis. The levator plate is almost horizontal, supporting the rectum and vagina. The perineal body provides support for the lower posterior vaginal wall; above it lies the rectovaginal septum. B, Weakness of the pelvic floor leads to a more vertical levator plate. The perineal body is attenuated, which favors the formation of a rectocele. The laxity of the pelvic floor also favors rectal mucosal prolapse. (From Loder PB, Phillips RKS. Rectocele and pelvic floor weakness. In: Kamm MA, Lennard-Jones JE, editors. Constipation. Peterfield, England: Wrightson Biomedical; 1994. p 281.)

Bristol Stool Scale



Whole gut transit time	Type of stool	Description	Pictorial representation
Long transit (e.g., 100 hours) 	Type 1	Separate hard lumps, like nuts, hard to pass	
	Type 2	Sausage shaped but lumpy	
	Type 3	Like sausage but with cracks on its surface	
	Type 4	Like sausage or snake, smooth and soft	
	Type 5	Soft blobs with clear-cut edges (passed easily)	
	Type 6	Fluffy pieces with ragged edges, a mushy stool	
	Type 7	Watery, no solid pieces	Entirely liquid
Short transit (e.g., 10 hours)			

Bristol Stool Form Scale. Common stool forms and their consistency in relation to whole-gut transit time are shown. (From Heaton KW, Radvan J, Cripps H, et al. Defecation frequency and timing, and stool form in the general population: A prospective study. Gut 1992; 33:818-24.)



Psychosocial Disorders

- Depression
- Eating disorders
- Denied bowel movements
- Symptoms of somatization, obsessive compulsiveness and affective disorders

Clinical Assessment



History

Prolonged straining to expel stool

Assumption of unusual postures on toilet to facilitate stool expulsion

Support of perineum, digitation of rectum, or application of pressure to the posterior vaginal wall to facilitate rectal emptying

Inability to expel enema fluid

Constipation after subtotal colectomy for constipation

Rectal Examination (with patient in left lateral position)

Inspection

Anus “pulled” forward during attempts to simulate strain during defecation

Anal verge descends <1 cm or >4 cm (or beyond ischial tuberosities) during attempts to simulate straining at defecation

Perineum balloons down during straining; rectal mucosa partially prolapses through anal canal

Palpation

High anal sphincter tone at rest precludes easy entry of examining finger (in absence of a painful perianal condition such as an anal fissure)

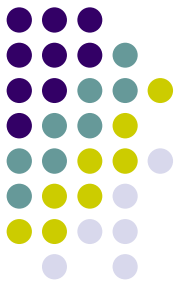
Anal sphincter pressure during voluntary squeeze only minimally higher than anal tone at rest

Perineum and examining finger descend <1 cm or >4 cm during simulated straining at defecation

Puborectalis muscle tender to palpation through rectal wall posteriorly, or palpation reproduces pain

Palpable mucosal prolapse during straining

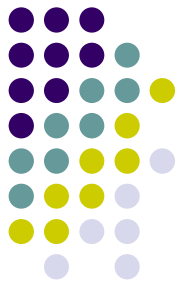
“Defect” in anterior wall of the rectum, suggestive of rectocele



Diagnostic Tests

1. To exclude systemic illness or structural disorders.
2. To elucidate the underlying pathophysiology process

Diagnostic Tests



- Tests to exclude systemic disease are Hb, ESR, biochemical screening tests for thyroid, Ca, glucose and to r/o inflammation, neoplasia, metabolic or other systemic disorders.
- To exclude structure disease
 - Do Ba enema, SBFT
 - Endoscopy for Δ BM, blood in stool, weight loss, fever
 - Age > 50y
 - C-Scope or flexsign

Diagnostic Tests



- Physiologic measures aided by symptom diaries
 - Do transit studies – radiopaque markers
 - Anorectal manometry
 - Pressure measures relaxation of sphincter
 - Sensation
 - EMG
 - Defecating proctogram
 - Balloon Expansion Test

Diagnostic Tests



Anal Sphincter Pressures

Max. Resting sphincter pressure: 62 mm Hg
 Max. Squeeze sphincter pressure: 81 mm Hg
 Cough Reflex:

Normal Values (Mean, 95% confidence interval)

Men: 72 (64-80) Women: 65 (56-74)
 193 (175-211) 143 (124-162)

Rectal pressure: 27 mm Hg
 Anal sphincter pressure: 75 mm Hg
 Attempted Defecation:
 Rectal pressure: 22 mm Hg
 Anal residual pressure: 73 mm Hg

66 (51-81) 62 (51-73)
 154 (138-170) 106 (89-123)
 68 (58-78) 63 (54-72)
 49 (35-63) 40 (32-48)

Recto-anal inhibitory reflex

Complete

Complete

Rectal Sensation

Threshold for first sensation: 10 cc
 Threshold for desire to defecate: 40 cc
 Maximum tolerable volume: 60 cc

20 (15-25) 19 (15-23)

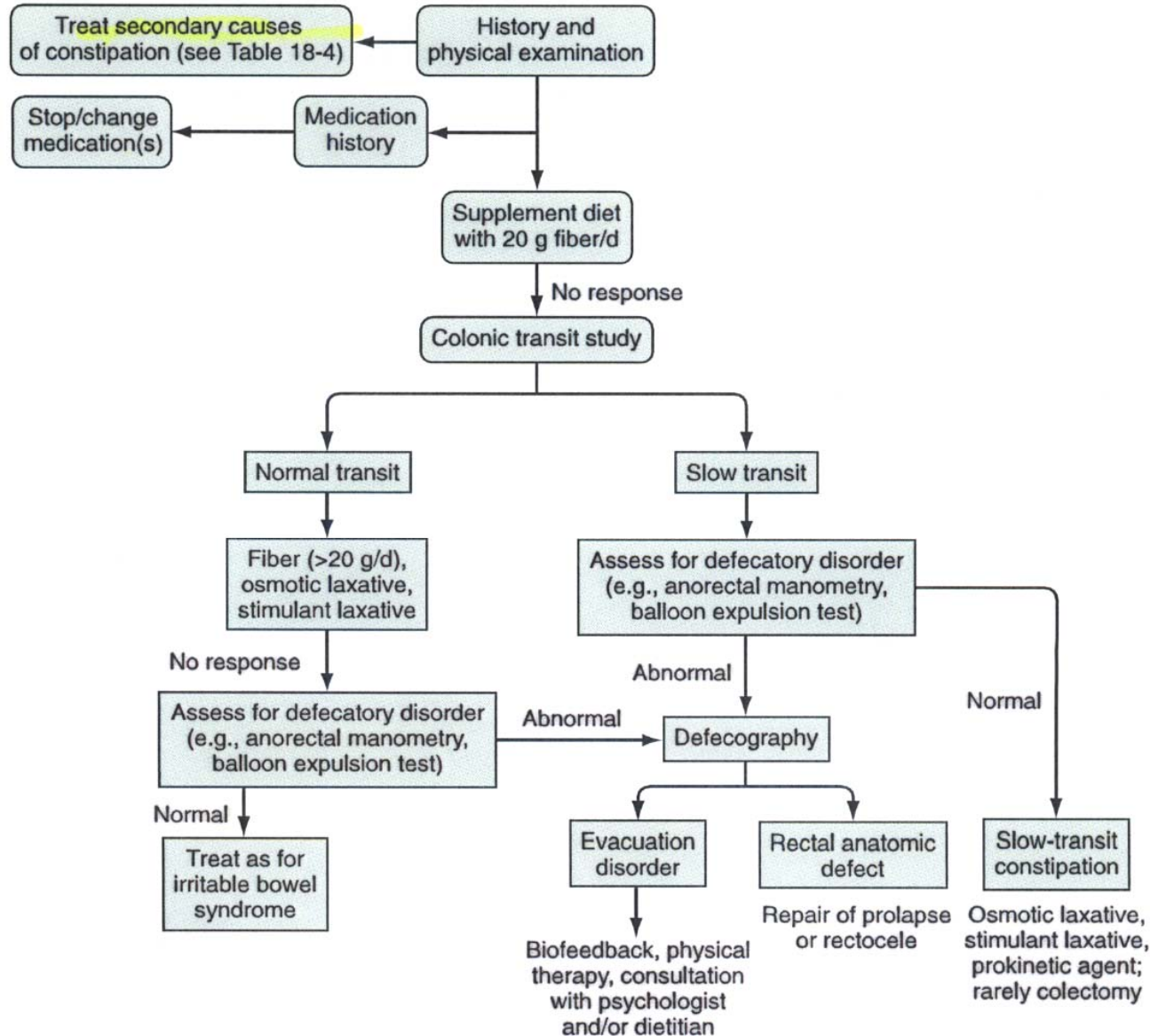
Rectal Compliance (after correcting for intrinsic balloon wall compliance)

Volume/Pressure: 20 cc / 19 mmHg 40 cc / 33 mmHg cc / mmHg
 30 cc / 29 mmHg 60 cc / 37 mmHg cc / mmHg

IMPRESSION: *Resting anal canal pressures were normal. Patient has low squeeze pressures. Cough reflex was impaired with low anal pressures. Attempted defecation was consistent with type 2 dyssynergic defecation (impaired generation of rectal pressure with paradoxical increase of anal sphincter pressure). There was normal sensation in the rectal vault but tolerance was impaired. Recto-anal inhibitory reflex was complete. Rectal compliance was diminished (less distendable). Consistent with weak external anal sphincter.*

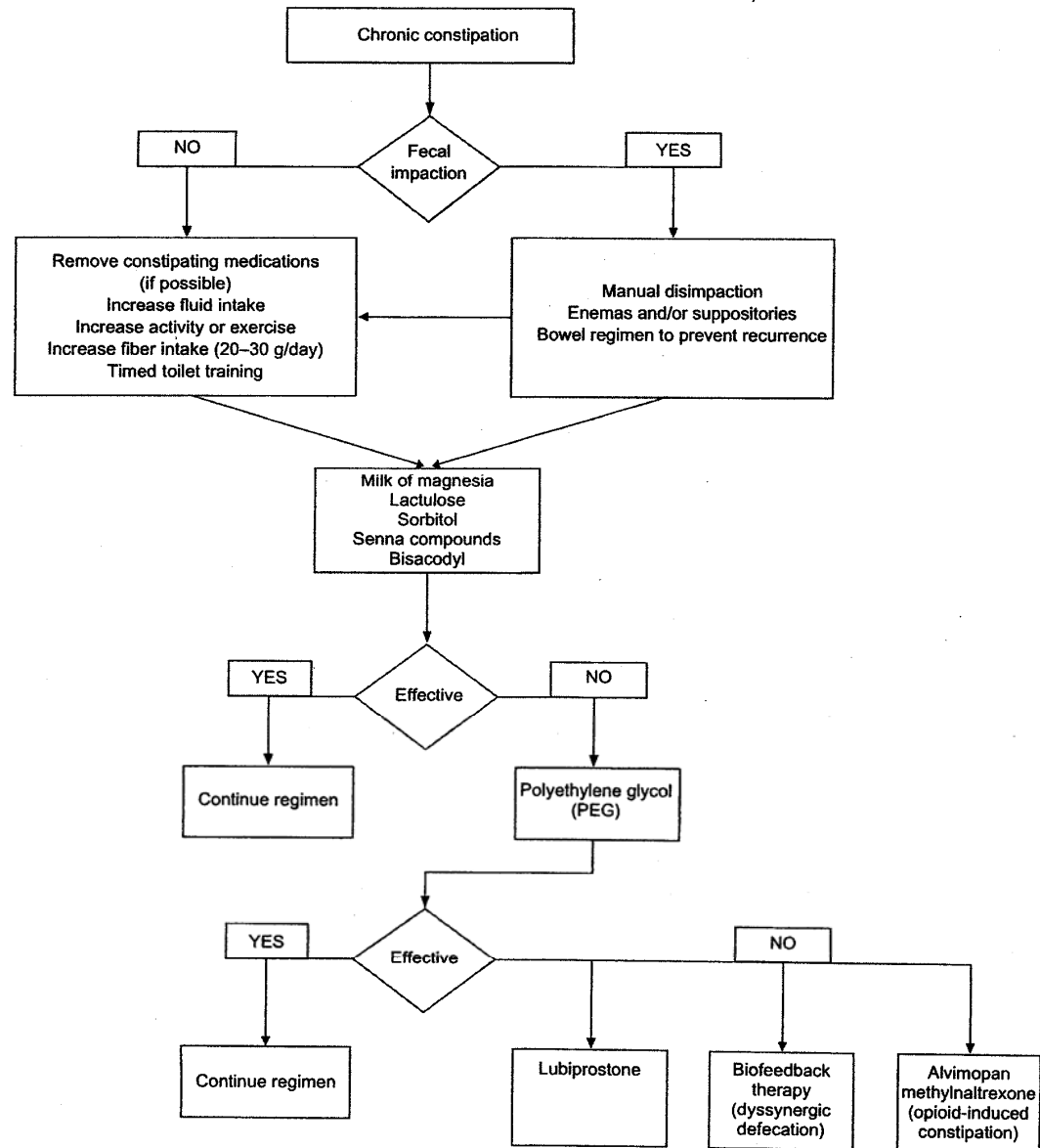
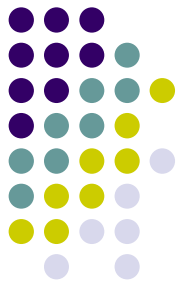
COMMENTS: *Patient was given instructions for Kegel exercises and bowel management program. Need clinical correlation for impaired tolerance to rectal distension and "stiff" rectum.*

Treatment



Algorithm for the evaluation and treatment of severe constipation.

Treatment



Treatment



General measures – Reassurance, lifestyle changes, psychological support, fluids, dietary and fiber changes.

Commercial Fiber Products

AGENT	STARTING DAILY DOSE (G)	COMMENTS
Methylcellulose	4-6	Semisynthetic cellulose fiber that is relatively resistant to colonic bacterial degradation and tends to cause less bloating and flatus than psyllium
Psyllium	4-6	Made from ground seed husk of the ispaghula plant; forms a gel when mixed with water, so an ample amount of water should be taken with psyllium to avoid intestinal obstruction; undergoes bacterial degradation, which may contribute to side effects of bloating and flatus; allergic reactions such as anaphylaxis and asthma have been reported but are rare
Polycarbophil	4-6	Synthetic fiber made of polymer of acrylic acid, which is resistant to bacterial degradation
Guar gum	3-6	Soluble fiber extracted from seeds of the leguminous shrub <i>Cyamopsis tetragonoloba</i>

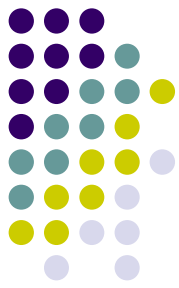
Treatment



Laxatives Commonly Used for Constipation

TYPE OF LAXATIVE	GENERIC NAME(S)	DOSE	COMMENTS
Osmotic Laxatives <i>Poorly Absorbed Ions</i>			
Magnesium	Magnesium hydroxide	15-30 mL once or twice daily	Hypermagnesemia can occur in patients with renal failure and in children.
	Magnesium citrate	150-300 mL every day	
Sulfate	Magnesium sulfate	15 g every day	Sulfate is generally not used by itself as a laxative agent.
	Sodium sulfate	5-10 g every day	
Phosphate	Sodium phosphate	0.5-10 mL with 12 oz of water	Hyperphosphatemia can occur, especially in patients with renal failure.
<i>Poorly Absorbed Sugars</i>			
Disaccharides	Lactulose	15-30 mL once or twice daily	Gas and bloating are common side effects. Sorbitol is commonly used as a sweetener in sugar-free products. In older adults, sorbitol has an effect similar to that of lactulose but has a lower cost.
Sugar alcohols	Sorbitol	15-30 mL once or twice daily	
	Mannitol	15-30 mL once or twice daily	
Polyethylene glycol	Polyethylene glycol electrolyte	17-34 g once or twice daily	Tends to cause less bloating and cramps than other agents; tasteless and odorless, can be mixed with noncarbonated beverages. Typically used to prepare colon for diagnostic examinations and surgery; also available as powder without electrolytes for regular use (MiraLax)

Treatment



Stimulant Laxatives

Anthraquinones

Cascara sagrada
Senna

325 mg (or 5 mL) at bedtime
1-2 7.5-mg tablets daily

Cause apoptosis of colonic epithelial cells phagocytosed by macrophages; result in lipofuscin-like pigmented condition known as pseudomelanosis coli; no definitive association established between anthraquinones and colon cancer or myenteric nerve damage (cathartic colon) Cramping is common.

Ricinoleic acid Diphenylmethane Derivatives

Castor oil
Bisacodyl
Phenolphthalein

15-30 mL at bedtime
5-10 mg at bedtime
30-200 mg at bedtime

Has effects in small intestine and colon
Removed from U.S. market because of teratogenicity in animals

Stool Softeners Emollients

Sodium picosulfate
Docusate sodium
Mineral oil

5-15 mg at bedtime
100 mg twice daily
5-15 mL at bedtime

Likely has effects only on colon
Efficacy in constipation not well established.
Long-term use can cause malabsorption of fat-soluble vitamins, anal seepage, and lipoid pneumonia in patients predisposed to aspiration of liquids.

Enemas, Suppositories

Phosphate enema
Mineral oil retention enema
Tap water enema
Soapsuds enema
Glycerin suppository
Bisacodyl suppository

120 mL
100 mL
500 mL
1500 mL
60 g
10 mg

Serious damage to rectal mucosa can result from extravasation of enema solution into the submucosa; hypertonic phosphate enemas and large-volume water or soapsuds enemas can lead to hyperphosphatemia and other electrolyte abnormalities if enema is retained; soapsuds enemas can cause colitis.

Chloride Channel Activator

Lubiprostone

8-24 µg twice daily

Increases secretion in the intestines

Treatment

Grade of Evidence for the Use of Laxatives
According to the American College of
Gastroenterology Task Force on Chronic
Constipation

LAXATIVE	GRADE OF EVIDENCE*
Bulking agents	
Psyllium	B
Calcium polycarbophil	B
Bran	†
Stool softeners	B
Lubricants	C
Osmotic laxatives	
PEG	A
Lactulose	A
Milk of magnesia	†
Stimulant laxatives	B
Prokinetic agent	
Tegaserod‡	A
Chloride channel activator	
Lubiprostone	§

*Grade A: Based on two or more randomized controlled trials (RCTs) with adequate sample sizes and appropriate methodology. Grade B: Based on evidence from a single RCT of high quality or conflicting results from high-quality RCTs or two or more RCTs of lesser quality. Grade C: Based on noncontrolled trials or case reports.

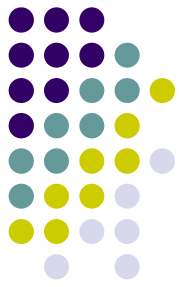
†Insufficient data.

‡Removed from the U.S. market.

§Not yet graded.

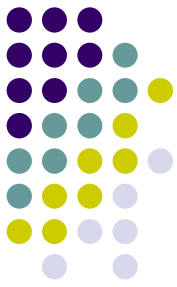
PEG, polyethylene glycol.

Data from Brandt LJ, Prather CM, Quigley EM, et al. Systematic review on the management of chronic constipation in North America. Am J Gastroenterol 2005; 100(Suppl 1):S5-21.



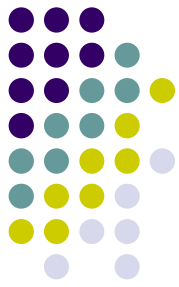
Prokinetic Agents

- Tegaserid – 5HT4 agonist – Withdrawn from market
- Prucalopride – 5HT4 agonist – in clinical trials
- Peripheral Mu – opioid antagonists – methylnaltrexone to reverse narcotic bowel syndrome
- Alvimopan – for surgical ileus recovery



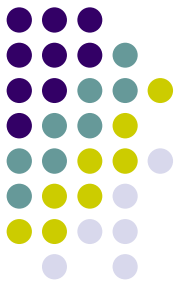
Other Agents

- Cholinergic agents
 - Bethanechol, neostigmine, botulinum toxin
- Newer neurotrophins
 - NGF, BDNF, neurotrophin 3
 - Linogliride – guanylate cyclase C agonist



Other Forms of Therapy

- Defecation training
- Anorectal biofeedback
- Complementary Alternative Medicine
- Sacral nerve stimulation
- Surgery – Colectomy with ileorectal anastomoses



PDF of Talk can be found here:

- <https://louisville.edu/medschool/gimedicine/division-education/miscellaneous-.html>