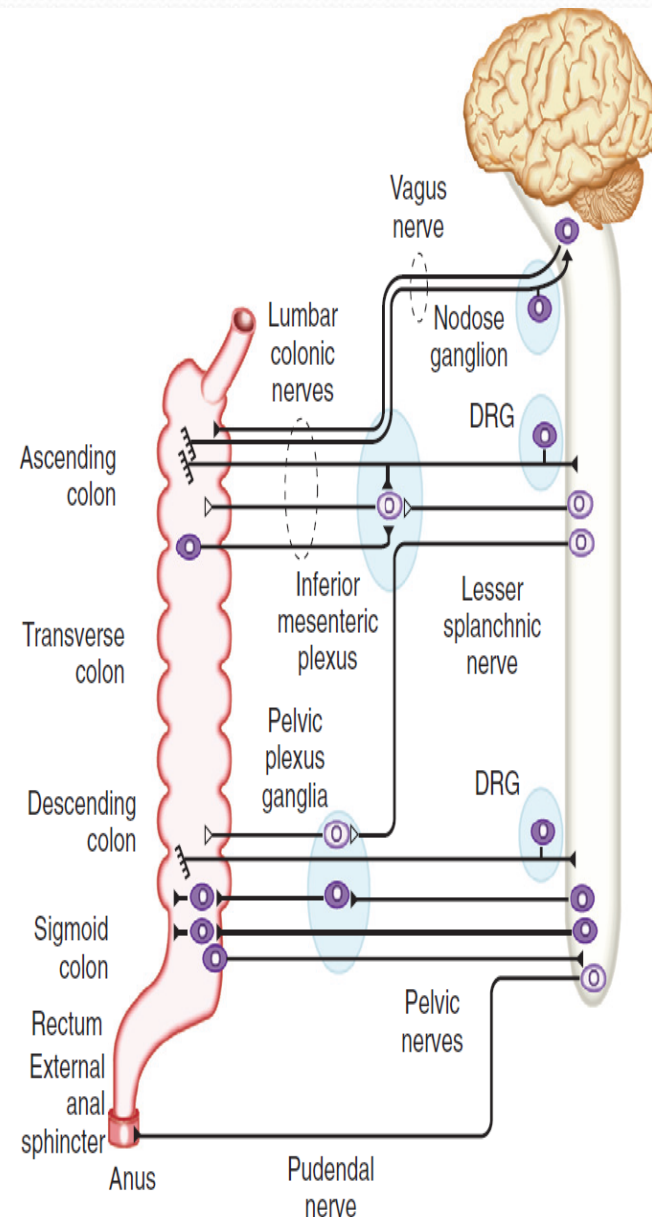


# Colonic Motility and Constipation

Hammad Liaquat

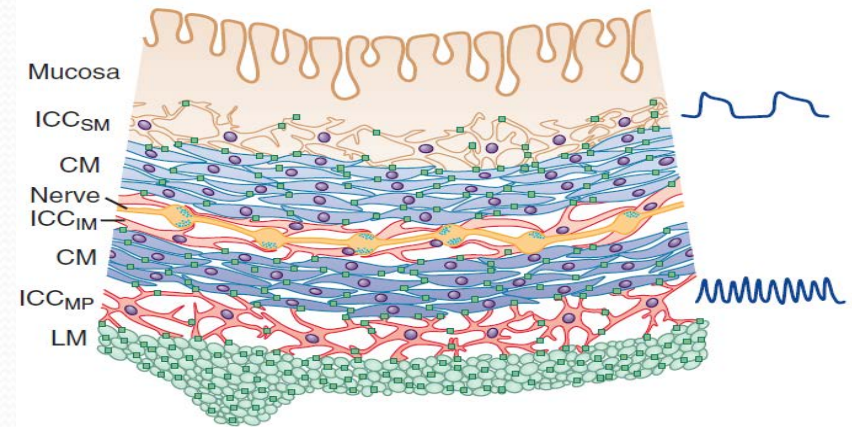
# The Colon

- Colonic innervation emanates from two sources: the extrinsic (parasympathetic/sympathetic) and the intrinsic (ENS) nerves.
- Storage of stool in AC and TV.
- Mixing of contents through phasic contractions, long. muscle contractions – formation of haustra
- Mass movements – via HAPCs over 15 cm each. Circular muscle contraction. 5-6 times/day btw 6 am to 2 pm



# Interstitial cells of Cajal (ICC)

- ICC play role of pacemaker
- Facilitate electric current conduction and neural signalling to muscles
- Ach, 5HT, Substance P (excitatory) vs VIP, NO (inhibitory)

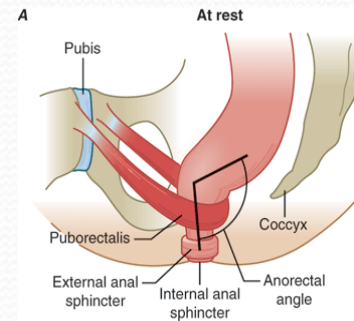


# Physiology

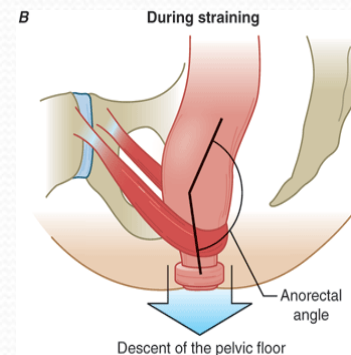
- Colon gets 1.5 l fluid daily, most of it absorbed, 100-200 ml expelled with stool.
- Na/Cl exchange and short chain fatty acid transport stimulate water absorption.
- Mean colonic transit time is 36 hours (max 74 hours)

# Defecation

- Distension of rectum and relaxation of int. anal sphincter
- coordinated relaxation of the puborectalis and external anal sphincter muscles
- increased intra-abdominal pressure
- Inhibition of colonic segmenting activity



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>  
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Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>  
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# Constipation

# Definition

- Variable amongst patients and physicians!
- Patients: Stools may be too hard or too small, too difficult or infrequent.
- Physicians: Reduced stool frequency, straining to defecate, hard stools, or inability to defecate.
- Normal bowel habits vary widely:
  - 2/day to 2/week
  - 20-250g/day
  - Formed to semi-formed

# Rome III criteria for functional constipation

- Presence of two or more of the following for at least three months (with symptom onset at least six months prior to diagnosis):
  - 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 (eg, digital evacuation, support of the pelvic floor)
  - Fewer than 3 stools/week
- Loose stools are rarely present w/o use of laxatives
- Criteria for IBS not fulfilled

# Epidemiology

**Table 18-2** Population-Based Studies of the Prevalence of Constipation

LOCATION OF STUDY (REFERENCE)	SURVEY METHOD	SAMPLE SIZE	DEFINITION OF CONSTIPATION	AGE RANGE (YR)	PREVALENCE (%)	PREVALENCE BY GENDER (%)
United States <sup>3</sup>	Face-to-face interview	15,014	SR	12-74	12.8	M, 7.0; F, 18.2
Chapel Hill, NC <sup>1</sup>	Questionnaire administered in person	563	SR	Mean, 24 (65% students)	7.3	—
United States <sup>11</sup>	Face-to-face interview	14,407	SR	25-74	—	M, 8.06; F, 20.8
United States <sup>12</sup>	Face-to-face interview	42,375	SR	<40 to >80	3.5	M, 1.3; F, 4.9
Olmsted County, Minn <sup>13</sup>	Mailed questionnaire	835	Straining and hard stools or frequency < three/wk	30-64	17.4	—
East Bristol, UK <sup>14</sup>	Face-to-face interview with questionnaire	1,897	Stool type and frequency	25-69	—	M, 0.6; F, 3.5
Olmsted County, Minn <sup>15</sup>	Mailed questionnaire	328	Straining and hard stools or frequency < three/wk	65-93	24.1	—
Olmsted County, Minn <sup>16</sup>	Mailed questionnaire	690	SR; RI, FC; RI, OD	30-64	12.5, SR; 18.3, FC; 11.0, OD	FC: M, 17; F, 16 OD: M, 6; F, 17 FC: M, 2.4 F, 4.8; D: M, 11.5; F, 16
United States <sup>17</sup>	Mailed questionnaire	5,430	RI, FC; RI, D	15 to >45 (mean, 49)	3.6, FC; 13.8, D	—
United States <sup>8</sup>	Telephone interview	10,018	RII, FC; RII, OD	18 to >70	4.6, FC; 4.6, OD	—
Canada <sup>9</sup>	Mailed questionnaire	1,149	SR	18 to >65	27.2, SR; 16.7, RI; 14.9, RII	—
Spain <sup>*</sup>	Mailed questionnaire	349	SR, RI, RII	18-65	29.5, SR; 19.2, RI; 14.0, RII	SR: M, 18.4; F, 35.4; RI: M, 12.0; F, 21.0; RII: M, 8.3; F, 21.1

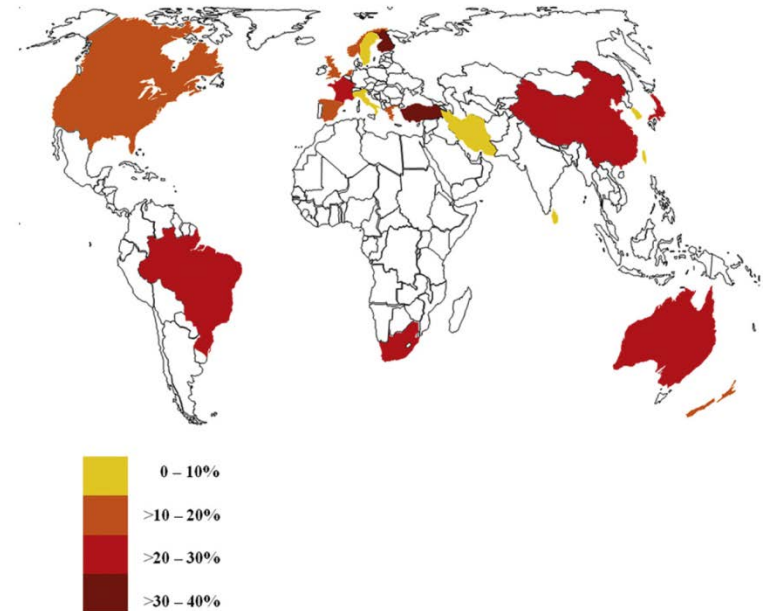
Garrigues V, Galvez C, Ortiz V, et al. Prevalence of constipation: Agreement among several criteria and evaluation of the diagnostic accuracy of qualifying symptoms and self-reported definition in a population-based survey in Spain. *Am J Epidemiol* 2004; 159:520-6.

# Epidemiology

- MEDLINE literature review, 68 studies included
- Subjects: children and adults
- median prevalence of constipation was 16% (range, 0.7%–79%) in adults overall; 33.5% in adults aged 60 to 101 years.
- More in the nonwhite population
- Median female-to-male ratio of 1.5:1
- Higher in institutionalized than community-living elderly residents
- Individuals of lower social, economic and educational level seem to have a tendency towards higher constipation rates.
  
- Lack of uniform definitions used to classify constipation, variable age groups studied, and different methods of data collection.
- Average prevalence of constipation was found to be 20.6%.
- In studies using the Rome I, II, and III criteria the prevalence rates were respectively 18%, 12.7% and 11%, respectively.

# Worldwide distribution

- Worldwide variation in prevalence rates may arise from diverse cultural, dietary, genetic, environmental and socioeconomic conditions and different health care systems.
- Lack of data in the literature about the prevalence of constipation in developing countries



# Epidemiology

- 2.5 million physician visits, 92,000 hospitalizations, and several hundred million dollars of laxative sales/year.
- The annual direct medical costs for constipation were recently estimated to exceed \$230 million
- At tertiary referral centers, the average cost of a medical evaluation was \$2,252, with the greatest cost attributed to colonoscopy.
- Patients followed by adult primary care providers (33.4%), pediatricians (20.9%), and gastroenterologists (14.1%).

# Risk Factors

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

## Causes of chronic constipation

Neurogenic disorders	Non-neurogenic disorders
Peripheral	Hypothyroidism
Diabetes mellitus	Hypokalemia
Autonomic neuropathy	Anorexia nervosa
Hirschsprung disease	Pregnancy
Chagas disease	Panhypopituitarism
Intestinal pseudoobstruction	Systemic sclerosis
Central	Myotonic dystrophy
Multiple sclerosis	<b>Idiopathic constipation</b>
Spinal cord injury	Normal colonic transit
Parkinson disease	Slow transit constipation
<b>Irritable bowel syndrome</b>	Dyssynergic defecation
<b>Drugs</b>	
See separate table	

## Drugs associated with constipation

<b>Analgesics</b>
<b>Anticholinergics</b>
Antihistamines
Antispasmodics
Antidepressants
Antipsychotics
<b>Cation-containing agents</b>
Iron supplements
Aluminum (antacids, sucralfate)
Barium
<b>Neurally active agents</b>
Opiates
Antihypertensives
Ganglionic blockers
Vinca alkaloids
Calcium channel blockers
5HT <sub>3</sub> antagonists

# Constipation and Parkinsonism

- Abnormally low GI motility is the most common autonomic symptom in patients with PD.
- Constipation reported by 80% of PD patients
- Autopsy findings in PD patients showed LB pathology in enteric neurons along the entire gastrointestinal tract.
- Constipation is recognized as the most reliable autonomic disturbance in premotor PD.
- The strongest evidence that constipation can precede PD comes from the Honolulu Heart Program.
- 6790 men aged 51 to 75 years without PD
- 24 yr follow up
- 2.7-fold risk of PD among men with < 1 BM/day vs. men having 1 or more bowel movements/day
- 4.5-fold risk of PD when compared with men with more than 2 bowel movements/day.

# Classification


- Idiopathic/Primary: disordered function of colon and rectum
  - Normal transit constipation (NTC) – 59%
  - Slow transit constipation (STC) – 13%
  - Defecatory disorders – 25 %
  - Mixed – 3%
- Secondary

# Normal transit constipation (NTC)

- Pathogenesis not well understood.
- Stool travels along the colon at a normal rate.
- Barostat measurements revealed reduced fasting, postprandial colonic tone and/or compliance in 40% of patients.
- Some patients have abnormalities of anorectal sensory and motor function indistinguishable from those in patients with STC.
- Unclear if increased rectal compliance and/or reduced rectal sensation are effects of chronic constipation or contribute to the failure of the patients to experience an urge to defecate.

# Slow transit constipation (STC)

- Most common in young women
- Infrequent bowel movements (less than one bowel movement/week)
- Arises from disordered colonic motor function – marked reduction in colonic intrinsic nerves and interstitial cells of Cajal
- Resting colonic motility that is similar to normal controls.
- Fewer high-amplitude propagated contractions & reduced phasic contractile responses to a meal and/or to pharmacologic stimuli (eg, bisacodyl or neostigmine)

- 
- Onset of symptoms is gradual and usually occurs around the time of puberty.
  - Conservative measures are usually ineffective.
  - Colonic inertia
    - symptoms at the severe end of the spectrum.
    - colonic motor activity absent or fails to increase after any stimulus

# Defecatory Disorders

- Also known as anismus, dyssynergia, pelvic floor dyssynergia, spastic pelvic floor syndrome, obstructive defecation, or outlet obstruction.
- Acquired and may start in childhood
- Can be learned behavior to avoid discomfort or pain during defecation
- The pathogenesis is not completely understood.
  - Inappropriate contraction of the ext. anal sphincter.
  - Failure of the pelvic floor to descend on straining.
  - Can also be associated with rectal hyposensitivity, delayed colonic transit, structural disturbances

# Rome III Criteria for Functional Defecation Disorders

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








# Evaluation

- History
- Physical Exam
- Diagnostic tests

# History

- Duration , frequency, stool consistency, stool size, and degree of straining during defecation.
- Red flags: unintentional weight loss, rectal bleeding, change in the caliber of the stool, severe abdominal pain and family history of colon cancer.
- Dietary history including amount of daily fiber and fluid consumed
- Co-morbidities, Obstetric and surgical histories, drug history.
- History of sexual/physical abuse

# 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)			

- 66 volunteers
- Whole-gut transit time (WGTT) measured with radiopaque marker pellets and stools weighed.
- Kept a diary of stool form on a 7-point scale and of their defecatory frequency.
- WGTT measurements correlated with defecatory frequency ( $r = 0.35$ ,  $P = 0.005$ ) and with stool output ( $r = -0.41$ ,  $P = 0.001$ ) but best with stool form ( $r = -0.54$ ,  $P < 0.001$ ).

Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997; 32:920-4.

# The rectal exam

## **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

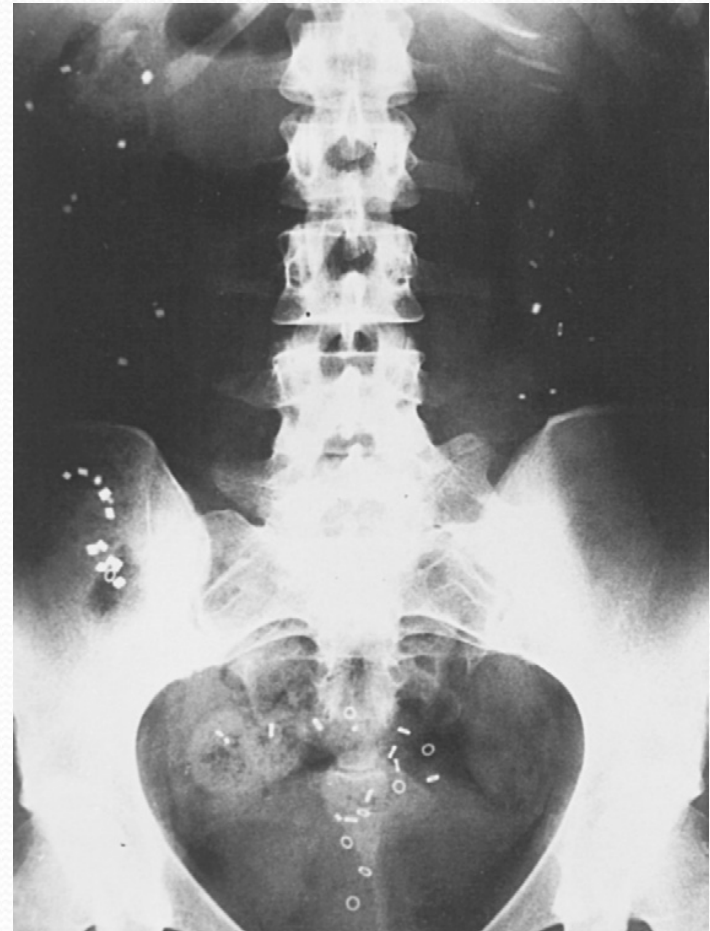
“Defect” in anterior wall of the rectum, suggestive of rectocele

# Diagnostic tests

- Labs and Imaging to exclude secondary causes
- Colonic transit study
  - Radiopaque markers
  - Wireless motility capsule
  - Colonic manometry/barostat-manometric testing
- Defecation disorder study
  - Defecography
  - Balloon expulsion test
  - Anorectal manometry
  - Electromyographic Testing of Striated Muscle Activity
  - Rectal Sensitivity and Sensation Testing

# Radiopaque markers test (ROM)

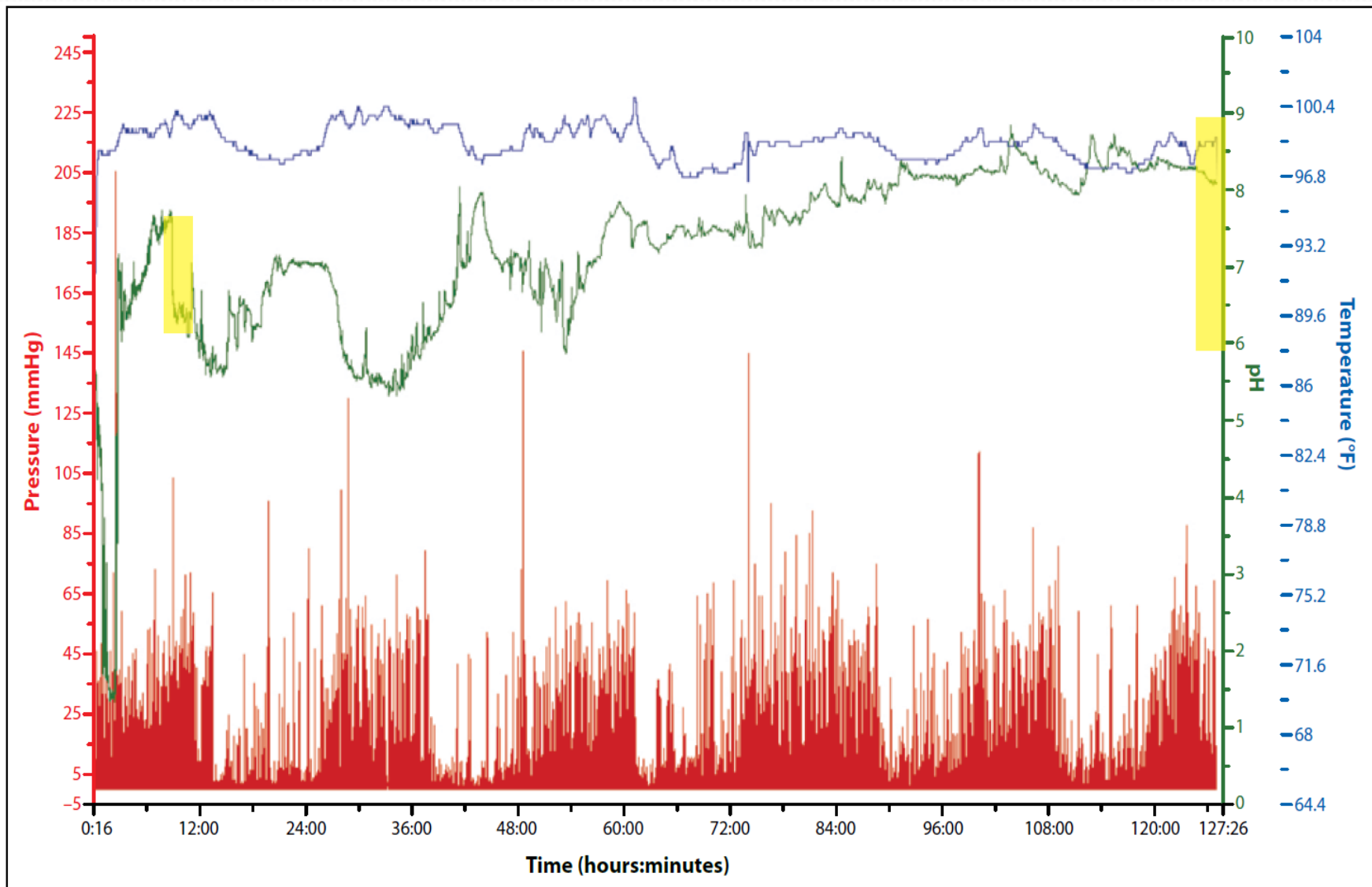
- The patient ingests a high fiber diet (20 to 30 g per day)
- Abstain from laxatives, enemas, and medications that may affect bowel function for 2-3 days prior to the test.
- A single capsule with 24 markers is administered on day 1 and followed by single x-ray on day 5 (after 120 hours).
- Retention of more than five markers on day 5 is considered abnormal
- Retention of all or most of the markers in distal sigmoid/rectum (defecation disorder)



# Wireless Motility Capsule (WMC)

- Approved by the FDA for the eval of patients with suspected delayed gastric emptying and colonic transit time in patients with chronic idiopathic constipation
- Continuously measures the temperature, pH, and pressure of its surrounding environment
- Any meds that disturb GI physiology should be discontinued prior to test
- Gives segmental transit times
- Abnormal gastric or small bowel motility can influence treatment of constipation.



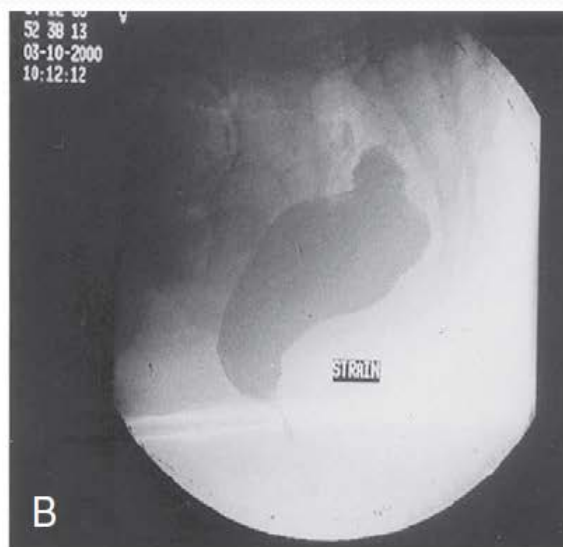
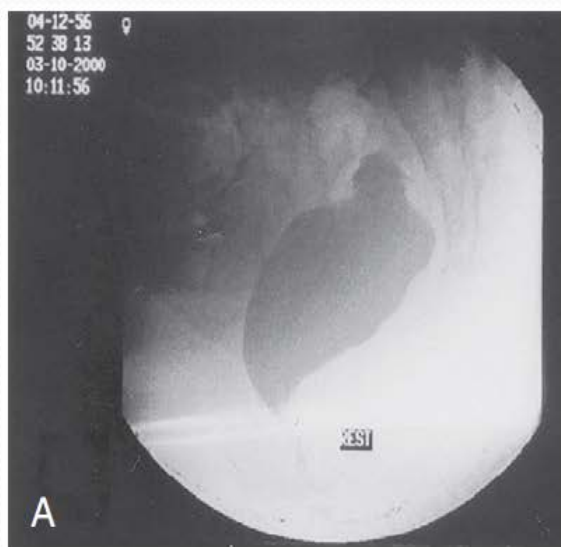


# WMC vs ROM

- 158 eligible patients underwent simultaneous measurement of colonic transit time (CT)
- ROM (Metcalf method, cut off for delay >67 h), and WMC (cutoff for delay >59 h).
- Substantial equivalence defined as diagnostic agreement > 65% for patients.
- 59/157 patients had delayed CT.
- Positive percent agreement between WMC and ROM for delayed transit was approximately 80%; agreement vs null hypothesis (65%)  $P = 0.01$ .
- Negative percent agreement (normal transit) was approximately 91%; agreement vs null hypothesis (65%),  $P = 0.00001$ .
- Overall device agreement was 87%. This validates WMC relative to ROM in differentiating slow vs normal CT.

# Defecation Proctography

- Thickened 150 mL of barium instilled into rectum
- Patient sits on a radiolucent commode.
- Films or videos are taken during fluoroscopy with the patient resting, deferring defecation, and straining to defecate.
- Limitations
  - Variability in interpretation among radiologists
  - Inhibition of normal rectal emptying
  - Differences in texture between barium paste and stool.

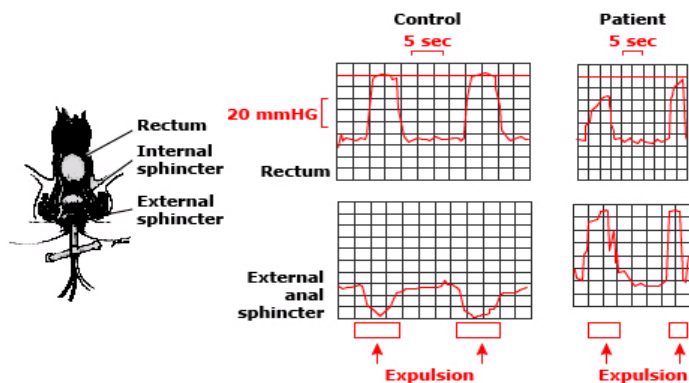


# Balloon Expulsion Test

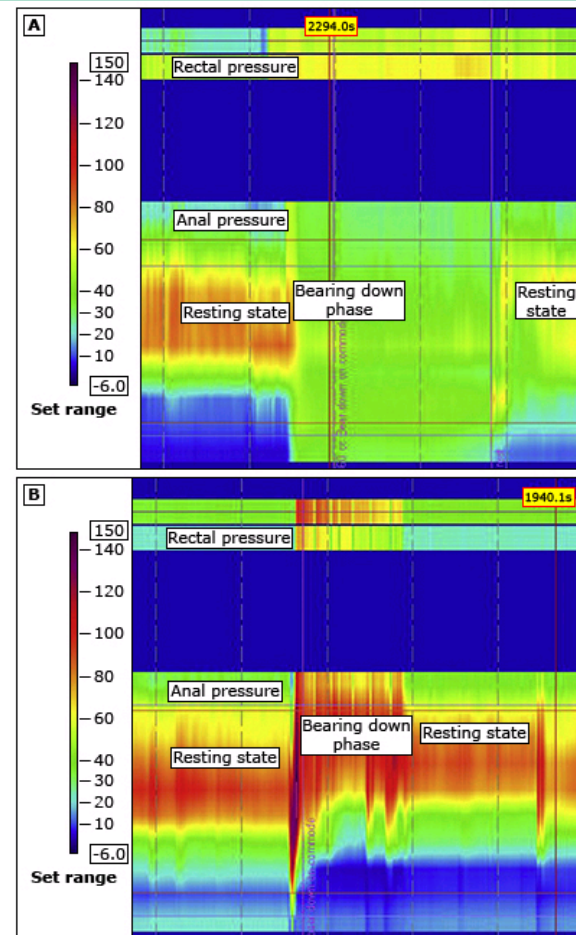
- The methodology has not been standardized.
- Requires expulsion of a 50 mL water-filled balloon in rectum with 200g weight attached at the end of balloon within 2 minutes.
- Failure to evacuate balloon in time indicated defecation disorder
- An effective and useful screening tool for identifying patients with a defecatory disorder who do not have pelvic floor dyssynergia.
- Diagnosis in 21/24 patients with DD and 12/106 w/o dyssynergia.
- Findings confirmed with manometry and defecography.

# Anorectal Manometry

- Measures rectal sensation and compliance, reflexive relaxation of the IAS, and manometric patterns produced upon attempted expulsion of the apparatus.
- Pressure recordings of the anal sphincter transducers indicate relaxation or inappropriate contraction.
- No evidence that HRM is inferior to regular procedure



High resolution manometry images showing patterns of defecation

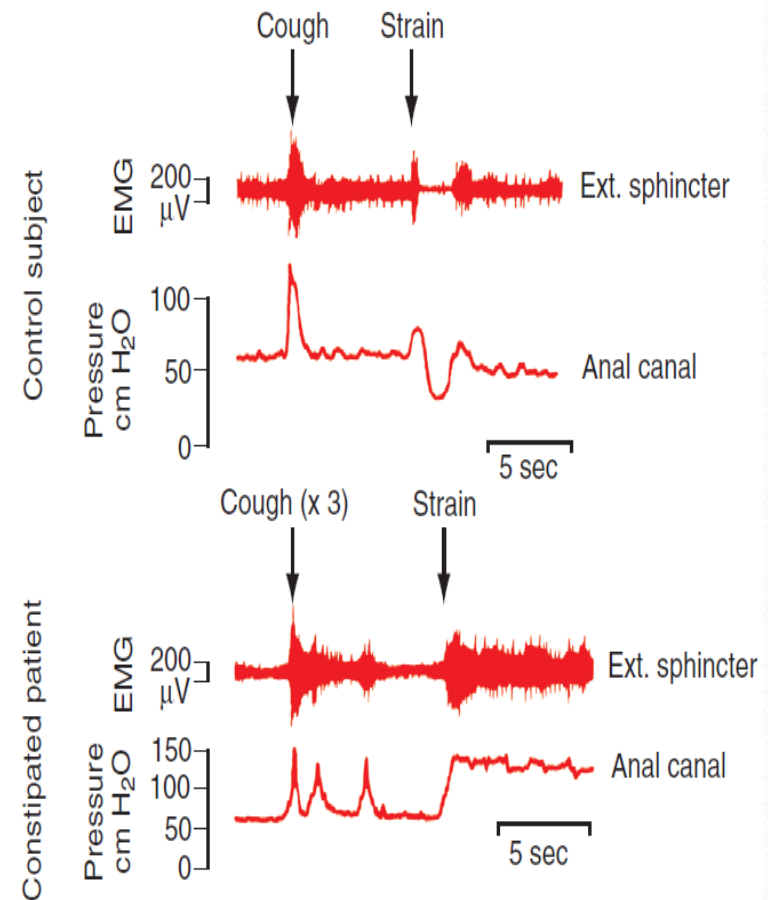


# Anorectal Manometry

	Measurement	Disease states
Resting pressure (50-100 mmHg)	<ul style="list-style-type: none"><li>•70-85% internal anal sphincter</li><li>•parasympathetic motor (S2-S4)</li></ul>	Diabetes, autonomic neuropathy, incontinence (low), fissure (high)
Squeeze pressure (50-100mmHg above resting pressure)	<ul style="list-style-type: none"><li>•70-85% external anal sphincter</li><li>•pudendal motor (S2-S4)</li></ul>	OB trauma, excessive straining, perineal descent , incontinence (low)
Rectal sensation	<ul style="list-style-type: none"><li>•central &amp; spinal sensory</li><li>•parasympathetic sensory (S2-S4)</li></ul>	Spinal cord injury, multiple sclerosis, cauda equina
Anorectal inhibitory reflex	<ul style="list-style-type: none"><li>•sphincter relaxation reflex with balloon distension (&gt;20 ml)</li><li>•myenteric plexus</li></ul>	Hirschsprung , Chagas, dermatomyositis, scleroderma

# EMG

- Small electrical sensors are placed in the anal canal to record the electrical activity of sphincter muscles when they squeeze and relax.
- Can be very useful in biofeedback therapy.
- Useful in suspected spinal cord or cauda equina lesions, in whom bilateral or unilateral dysfunction of the external anal sphincter can be demonstrated.



# Rectal Sensitivity and Sensation Testing

- Successive volumes of air is introduced into a rectal balloon
- Volume is recorded when:
  - the stimulus is first perceived
  - an urge to defecate develops
  - further addition of air is uncomfortable
- Can be useful with biofeedback therapy.

# Medical Management

- Lifestyle Changes
- Fiber Supplementation
- Bulk forming laxatives
- Osmotic agents
- Stimulant laxative
- Emollients/Stool softeners
- Enemas/Suppositories
- Newer therapies

# Fiber and Fluid

- Supplementation of 20 to 35 g/day of fiber in diet
- Low cost, are easy to use and safe
- Multiple food sources
- For some patients (eg STC) fiber increases bloating and distention leading to poor compliance

Badiali D, Corazziari E, Habib FI, et al. Effect of wheat bran in treatment of chronic nonorganic constipation. A double-blind controlled trial. *Dig Dis Sci* 1995; 40:349-56.

- NO evidence that increasing fluid intake increases colonic transit time
- Maintaining adequate intake of fluids prevents dehydration and slowing down colon transit beyond baseline.
- AI for men 13 cups (3 liters), for women is about 9 cups (2.2 liters) per day.

Lindeman RD, Romero LJ, Liang HC, et al. Do elderly persons need to be encouraged to drink more fluids? *J Gerontol A Biol Sci Med Sci* 2000; 55:M361-5.

# Medications

**Table 18-8** 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>

# Medications

**Table 18-9** Laxatives Commonly Used for Constipation

TYPE OF LAXATIVE	GENERIC NAME(S)	DOSE	COMMENTS
<b>Osmotic Laxatives</b>			
<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)

# Medications

## 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)

Ricinoleic acid  
Diphenylmethane Derivatives

Castor oil  
Bisacodyl  
Phenolphthalein

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

Cramping is common.  
Has effects in small intestine and colon  
Removed from U.S. market because of teratogenicity in animals  
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 lipid pneumonia in patients predisposed to aspiration of liquids.

### Stool Softeners Emollients

Sodium picosulfate  
Docusate sodium  
Mineral oil

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

### 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.

# Newer therapies

Generic name (chemistry)	Mechanism of action	Metabolism, bioavailability	Pharmacodynamic effects	Clinical trials	Common side effects	Cardiovascular safety <sup>a</sup>
<b>Secretagogues</b>						
Lubiprostone (prostone) <sup>b</sup>	Stimulate intestinal chloride and fluid secretion by activating chloride channels	Intestinal degradation, minimal oral bioavailability	Accelerated small bowel and colonic transit in health	Phases 2 and 3 in CC, IBS-C	Diarrhea, nausea	No arrhythmic effects
Linaclotide	Stimulate intestinal chloride and fluid secretion by activating CFTR	Intestinal degradation, minimal oral bioavailability	Dose-related acceleration of colonic transit in IBS-C	Phases 2 and 3 in CC, IBS-C	Diarrhea	No arrhythmic effects
<b>Serotonin 5-HT<sub>4</sub> receptor agonists</b>						
Prucalopride <sup>c</sup> (benzofuran carboxamide)	High selectivity and affinity for 5-HT <sub>4</sub> receptors; much weaker affinity for human D <sub>4</sub> and s1 and mouse 5-HT <sub>3</sub> receptors	Limited hepatic, not CYP3A4	Accelerated colonic transit in health and CC	Phases 2 and 3 in CC	Diarrhea, headache	No arrhythmic activity in atrial cells; inhibits hERG at very high $\mu\text{mol/L}$ concentration; no clinically relevant adverse cardiac effects in large trials (>4000 subjects)

- Prucalopride not available in US.

**Table 18-10** 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 <sup>‡</sup>	A

- Tegaserod no longer available d/t cardiovascular side effects.

**Table 6.** Comparison of Efficacy of Approved, Over-the-Counter, and Phase 3 Completed but Not Approved Pharmacologic Therapies for Relief of Chronic Constipation and IBS-C

Agent	Chronic constipation			IBS-C		
	Number needed to treat	Number of patients	Quality of evidence	Number needed to treat	Number of patients	Quality of evidence
Soluble fiber	<sup>a</sup>	368 <sup>111</sup>	Very low	4.5 <sup>114</sup>	275	Moderate
Osmotic and stimulant laxatives	3 (2–4)	1411	High	NA	NA	Moderate <sup>b</sup>
PEG	2.4 <sup>117</sup>	573	High	NA	NA	Moderate <sup>b</sup>
Lubiprostone	4 (3–7)	610	Moderate	13 <sup>206</sup>	1171	Moderate
Linaclotide	6 (5–8)	2858 <sup>207</sup>	Moderate	10 <sup>208</sup>	420	Moderate
Prucalopride	6 (5–9)	2639	Moderate	NA	NA	Very low

# Management of defecatory disorders

- Defecation training
  - 3 to 5 treatment sessions, each lasting at least 30 minutes.
  - Discussion about normal defecation process, life style changes to improve defecation.
  - Reduce dependence on laxatives.
- Anorectal biofeedback
  - Follows defecation training.
  - patients receive visual and/or auditory feedback, on the functioning of their anal sphincter and pelvic floor muscles.
  - Assisted with EMG or anorectal manometry catheter.
  - Simulated evacuation with a balloon or silicone-filled artificial stool is commonly taught.
  - Therapy can range from 6 sessions in 6 weeks to 3 sessions/day for 10 successive days.

# Success of Anorectal feedback

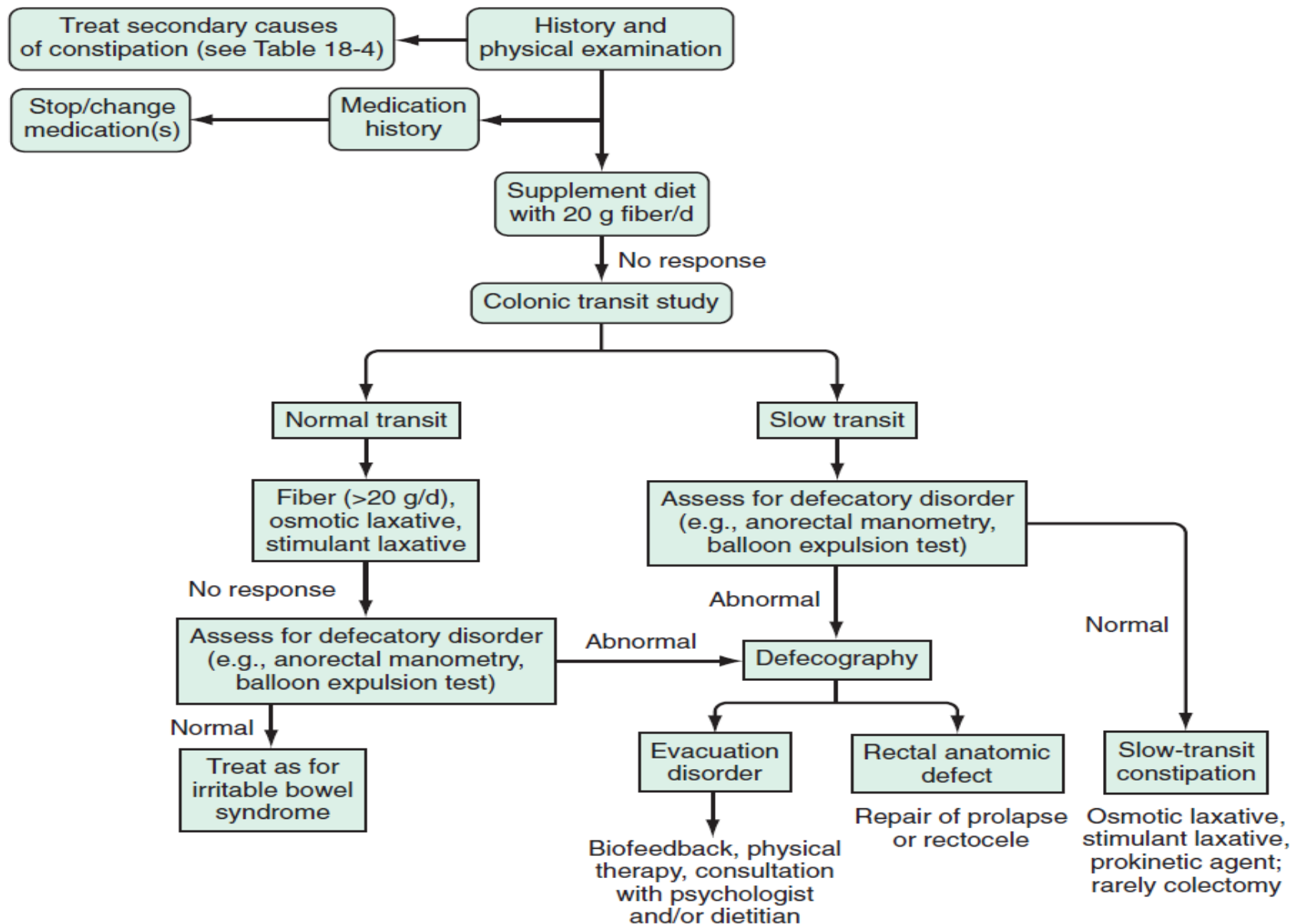
- Systemic review found 67% success rate in 1996 but no controlled studies available then.
- More recently some RCT have supported efficacy of biofeedback
- Recent study, 109 patients, 54 got biofeedback training, 55 got PEG with 5 counseling sessions
- At 6 months, greater reductions in straining, sensations of incomplete evacuation and anorectal blockage, use of enemas and suppositories, and abdominal pain was reported by 80% of patients who underwent biofeedback compared with 22% of the laxative-treated patients ( $P < 0.001$ ).
- The benefits of biofeedback were sustained at 12 and 24 months.
- Most other trials also have small sample sizes and favorable results.

# Sacral Nerve Stimulation

- Most common lower GI indication for SNS is constipation.
- 10 studies, 225 temporary neuromodulations and 125 permanent implants performed.
- Bowel diaries showed improvement more than 50% of patients on temporary neuromodulation.
- Results were maintained in approximately 90% of patients who underwent permanent implantation over medium to long-term follow-up.
- Longest follow up was 42 months in a study of 13 patients
- Largest study(N=60) with medium follow up found high rates of adverse effects related to electrode displacement
- Currently SNS is not approved for treatment of constipation in the US.

# Surgery

- Subtotal colectomy with ileorectal anastomosis can dramatically ameliorate incapacitating constipation in carefully selected patients
  - The patient has chronic, severe, and disabling symptoms from constipation that are unresponsive to medical therapy.
  - The patient has slow colonic transit of the inertia pattern.
  - The patient does **not** have intestinal pseudoobstruction, as demonstrated by radiologic or manometric studies.
  - The patient does **not** have pelvic floor dysfunction based on anorectal manometry.
  - The patient does **not** have abdominal pain as a prominent symptom.



# Fecal Incontinence (FI)

- Risk factors include diarrhea, advanced age, female gender, disease burden, obesity, decreased physical activity and smoking.
- Prior childbirth, pelvic floor anatomical disturbances are also associated
- Pathogenesis: dysfunction of the anal sphincters, abnormal rectal compliance, decreased rectal sensation, altered stool consistency, or a combination of any of these abnormalities. **Usually multifactorial.**
- Evaluation
  - Anorectal manometry
  - Anal rectal sensation testing
  - Defecography
  - Endorectal ultrasound/magnetic resonance imaging
  - Balloon expulsion test

## Causes of fecal incontinence

Structural abnormalities	
Anal sphincter muscles	Obstetrical injury, hemorrhoidectomy, anal dilation, radiation, inflammatory bowel disease
Rectum	Prolapse, hypersensitivity/hyposensitivity, neoplasms, congenital abnormalities, excessive perineal descent
Puborectalis muscle	Trauma, obstetrical injury
Pudendal nerve	Surgical injury, excessive perineal descent
Central nervous system, spinal cord, autonomic nervous system	Spinal cord injury, head injury, stroke, back surgery, diabetes mellitus, multiple sclerosis, tabes dorsalis, cauda equina injury or tumor
Functional abnormalities	
Anorectal sensation	Obstetrical injury, central nervous system/autonomic nervous system injury, diabetes mellitus
Fecal impaction	Dyssynergic defecation
Stool characteristics	
Volume and consistency	Inflammatory bowel disease, irritable bowel syndrome, medications, infections
Irritants	Bile salt malabsorption, laxatives
Hard stools and retention	Dyssynergic defecation, fecal impaction, medications
Other	
Physical mobility and cognitive function	Aging, disability, dementia, sedation
Psychosis	Willful soiling
Medications	Laxatives, anticholinergics, antidepressants, caffeine, muscle relaxants
Food intolerance	Lactose, fructose, sorbitol

# Fecal Incontinence - Management

- Conservative measures (effective in 25%)

- Fiber
- Antidiarrheals
- Scheduled toileting
- Pelvic floor exercises

- Biofeedback

- Improved quality of life in 75%
- Improved continence in 55%

- Injectable anal bulking agents

- 4 Inj, 5 ml each, 5 mm above the dentate line
- Increased resting anal pressures
- proctalgia, rectal hemorrhage, abscess

- Tibial nerve electric stimulation

- Promising but evidence is weak at this point
- Needs long term studies

- Sacral nerve stimulation

- improved resting and squeeze pressures, rectal sensation
- 120 patients, 86% achieved > 50% reduction in FI, and 40% had no fecal incontinence at 3 year follow-up
- Implant-site pain, paresthesia, change in the sensation of stimulation, and infection

Mellgren A, Wexner SD, Collier JA, et al. Long-term efficacy and safety of sacral nerve stimulation for fecal incontinence. Dis Colon Rectum 2011; 54:1065.

- Anal sphincteroplasty

- Long term (5 year) outcomes poor

- Dynamic graciloplasty

- electrical stimulation of the gracilis muscle
- implantable pulse generator
- Not available in the US

# Acute colonic pseudo-obstruction (Ogilvie's syndrome)

- Gross dilatation of the cecum and usually right hemicolon
- Absence of obstruction the flow of intestinal contents.
- Pathogenesis unclear; increased sympathetic and/or decreased parasympathetic innervation of distal colon incriminated
- Inflammation may also derange neuromuscular function
- Patients present with nausea, vomiting, abdominal pain, constipation.

## Common clinical conditions associated with Ogilvie's syndrome

Trauma, especially fractures
Obstetrical surgery, especially involving spinal anesthesia
Pelvic, abdominal, or cardiothoracic surgery
Major orthopedic surgery
Severe medical illness, such as pneumonia, myocardial infarction, or heart failure
Neurologic conditions
Retroperitoneal pathology, such as malignancy or hemorrhage
One of the above <b>plus</b> metabolic imbalance or medication administration (eg, narcotics, phenothiazines, calcium channel blockers, alpha-2-adrenergic agonists, epidural analgesics)

# Acute colonic pseudo-obstruction (Ogilvie's syndrome)

- If peritoneal signs present ~ impending perforation
- Hypokalemia, hypocalcemia, and hypomagnesemia in > 50% patients
- Conservative management for 1-2 days if colonic diameter < 12cm
- Correction of fluids, electrolytes, NG suction, rectal tube, gentle enemas, treat reversible causes, discontinue meds that can cause/worsen disease
- Serial abd exam and imaging (q12-24) hours



- Neostigmine 2.0 mg IV with cardiovascular monitoring
- Relistor – opioid induced disease

# Acute colonic pseudo-obstruction (Ogilvie's syndrome)

- Role of endoscopic decompression in patient remains controversial
- Success rates for endoscopic decompression in uncontrolled series vary from 69 to 90 percent.
- In a retrospective study of 25 patients with cancer, pseudo-obstruction, and a cecal diameter ranging from 9 to 18 cm, 23 resolved without colonoscopy, usually within 48 hours.
- Complication and death rates associated with colonoscopy for treatment of Ogilvie's syndrome are 3 and 1 percent in two recent studies.
- An attempt at colonoscopic decompression is indicated when supportive measures have failed with increasing colonic diameter (11 to 13 cm)
- Recurrence requiring repeated colonoscopic decompression occurs in approximately 40%.
- Percutaneous endoscopic colostomy can be attempted
- Percutaneous tube cecostomy reserved for patients requiring repeat c-scope
- Surgery for peritonitis/perforation

# Irritable Bowel syndrome

- Pathophysiology is evolving.
- Altered intestinal motility/secretion in response to various stimuli
- Enhanced pain perception and dysregulation of brain-gut axis.
- Diagnosis via Rome III criteria can help avoid costly and invasive testing to rule out other diseases

## Rome III diagnostic criteria\* for irritable bowel syndrome

**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.

- Treatment is sx based:
  - Pain: TCA, SSRI, antispasmodics
  - Bloating: antibiotics, probiotics
  - Diarrhea: imodium, lomotil, alosetron, **enteragam**
  - Constipation: High fiber, laxatives, lubiprostone

# Serum-derived bovine immunoglobulin (EnteraGam)

- Randomized, double-blind, placebo-controlled study
- Evaluate impact on gastrointestinal symptom scores and quality of life (QoL)
- 66 subjects diagnosed with IBS-D were enrolled : 25 in the 10 g/day SBI group, 19 in the 5 g/day SBI group, and 22 in the placebo group
- SBI at 10 g/day (N = 15) had statistically significant within-group reductions in abdominal pain ( $p < 0.01$ ), loose stools ( $p < 0.01$ ), bloating ( $p < 0.05$ ), flatulence ( $p < 0.01$ ), urgency ( $p < 0.05$ ) and any symptom ( $p < 0.01$ ) at EOT vs. baseline
- Subjects receiving 5 g/day of SBI (N = 15) realized statistically significant within-group reductions in days with flatulence ( $p < 0.035$ ), incomplete evacuation ( $p < 0.05$ ), and any symptom ( $p < 0.01$ ).
- No significant changes in QoL scores.
- Additional studies are underway with larger numbers of subjects to validate these findings.

# Hirschsprung disease (HD)

- Failure of neural crest cells (precursors of enteric ganglion cells) to migrate completely during intestinal development.
- 1 in 5000 live births with male predominance 5:1
- Mutations in RET protooncogene
- Variable length of distal colon can be involved
- Aganglionic segment fails to relax -> dilation of proximal colon
- Usually presents in neonatal period with failure to pass meconium or stool with bilious emesis, abdominal distension
- Can present in adults with chronic constipation and recurrent fecal impaction
- Eval includes barium enema, anorectal manometry and rectal biopsy

# Hirschsprung disease (HD)

- Barium enema can miss very short segment disease
- Anorectal manometry: failure of int. anal sphincter relaxation with rectal distension
- False positives on manometry when capacious rectum with chronic constipation -> balloon distension may not result in IAS relaxation
- Rectal biopsy: absence of ganglion cells and hypertrophy of nerve fibres
- Treatment: Resection of involved segment, bring the normal ganglionic bowel down close to the anus, and preserve sphincter function





THE END