



CONSTIPATION OR STYPSIS

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How Do We Define Constipation?

• The American College of Gastroenterology (ACG) definition of constipation:

Unsatisfactory defecation characterized by infrequent stools, difficult stool passage or both. Difficult stool passage includes straining, a sense of difficulty passing stool, incomplete evacuation, hard/lumpy stools, prolonged time to pass stool or need for manual maneuvers to pass stool

• The ACG Chronic Constipation Task Force also clarified what is meant by *chronic:*

Chronic constipation is defined as the presence of these symptoms for at least 3 months

Table 1. Rome II Criteria for Constipation.

Adults

Two or more of the following for at least 12 weeks (not necessarily consecutive) in the preceding 12 months:

Straining during >25% of bowel movements

Lumpy or hard stools for >25% of bowel movements

Sensation of incomplete evacuation for >25% of bowel movements

Sensation of an orectal blockage for >25% of bowel movements

Manual maneuvers to facilitate >25% of bowel movements (e.g., digital evacuation or support of the pelvic floor)

<3 Bowel movements per week

Loose stools not present, and insufficient criteria for irritable bowel syndrome met¹⁰

Infants and children

Pebble-like, hard stools for a majority of bowel movements for at least 2 weeks

Firm stools ≤2 times per week for at least 2 weeks

No evidence of structural, endocrine, or metabolic disease

Definition

- Patients describe:
 - Hard stools, infrequent stools, excessive straining, a sense of incomplete bowel evacuation, and excessive time spent on the toilet or in unsuccessful defecation
- Rome II (1999) describes:
 - Inability to evacuate stool completely and spontaneously three or more times per week
- Rome III (2006):
 - Symptoms currently active 3 months
 - Use *Bristol stool classification* to define "constipation"

Stewart WF et al. Epidemiology of constipation (EPOC) study in the United States: relation of clinical subtypes to sociodemographic features. Am J Gastroenterol 1999;94:3530-3540.

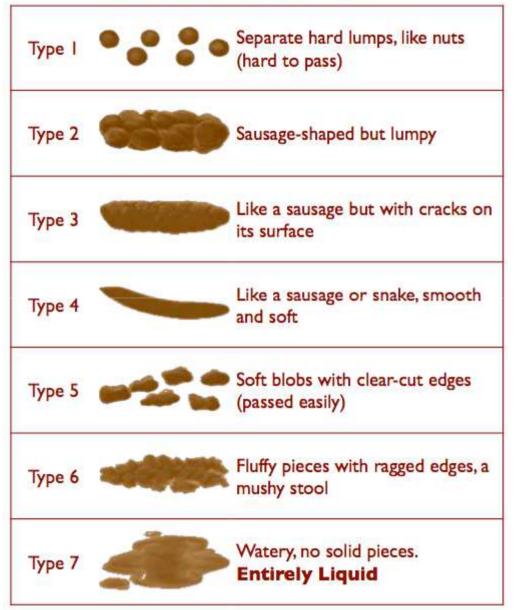
Sandler RS, Drossman DA. Bowel habits in young adults not seeking health care. Dig Dis Sci 1987;32:841-845. Koch A et al. Symptoms in chronic constipation. Dis Colon Rectum 1997;40:902-906.

Drossman DA. The functional gastrointestinal disorders and the Rome III process. Gastroenterol 2006 130:1377-90.

Stool form correlates with the intestinal transit time

The Bristol Stool Form Scale						
Slow Transit Type 1		• • • •	Separate hard lumps			
		Type 2		Sausage-like but lumpy		
		Туре 3		Sausage-like but with cracks in the surface		
		Туре 4		Smooth and soft		
		Type 5		Soft blobs with clear-cut edges		
		Туре 6		Fluffy pieces with ragged edges, a mushy stool		
Fast Transit		Type 7		Watery, no solid pieces		

Bristol Stool Chart



Correlates with symptoms of straining and difficult evacuation

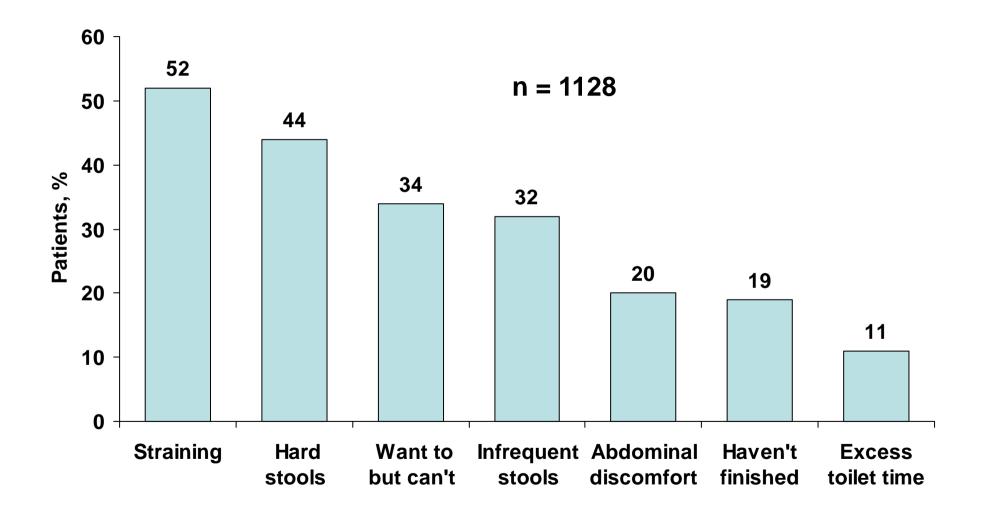
Also correlates with colonic transit (Type 1 or Type 7 stool is correlated with slow or rapid colonic transit Degen LP, Phillips SF. How well

does stool form reflect colonic transit? Gut

Majority of "constipated" patients have stools that are Type 1-3

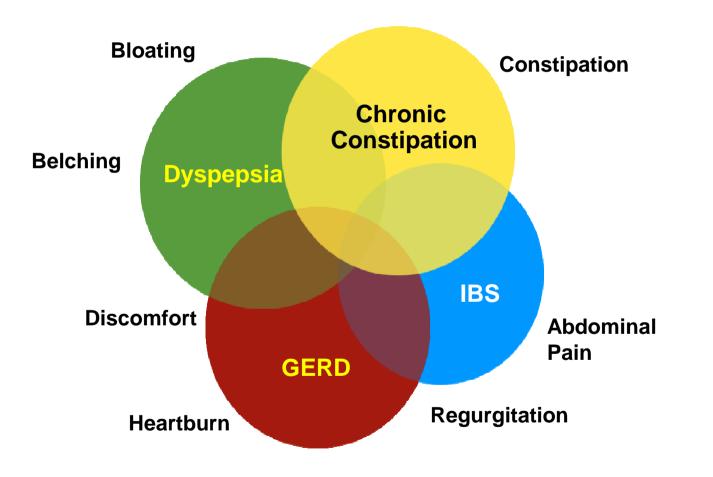
University of Bristol, Scand J Gastroenterol

Most often reported Constipation symptoms



Sandler RS et al. Dig Dis Sci.

Overlap Between Common Disorders

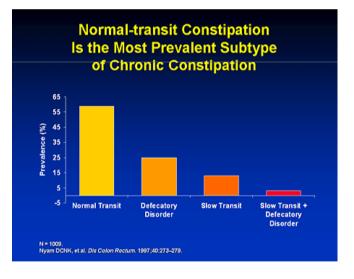


Brandt L, et al. Am J Gastroenterol. 2005

Primary Causes of Chronic Constipation

- 1. Normal-transit constipation
- 2. Defecatory dysfunction
- 3. Slow-transit constipation





1. Normal-Transit Constipation

- Frequent type of constipation
- Intestinal transit and stool frequency are within the normal range
- Misperception of bowel habit ...
- Often psychosocial stresses are present

Bosshard W, et al. *Drugs Aging*. 2004 Gallagher P, et al. *Drugs Aging*. 2008

2. Defecatory Dysfunction (30%)

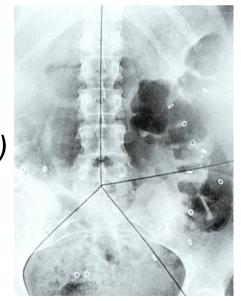
- More common in older women: child-birth trauma
- Pelvic floor dysynergia
- Excessive perineal descent
- Contributing factors include: anal fissures, hemorrhoids, rectocele, rectal prolapse, posterior rectal herniation
 - Abnormal anorectal manometry and/or defecography



Bosshard W, et al. *Drugs Aging*. 2004 Hadley S.K, et al. *Journal of Am Fam Physician*. 2005

3. Slow-transit Constipation (60%)

- Characterized by prolonged intestinal transit time
- Altered regulation of enteric nervous system
- Serotonin metabolism alteration
- Decreased nitric oxide production
- Impaired gastrocolic reflex
- Alteration of neuropeptides (VIP, substance P)
- Decreased number of interstitial cells
- of Cajal in the colon



Lembo A, Camilleri M. N Eng J Med

4. Irritable Bowel Syndrome (IBS) with Constipation

- Alterations in brain-gut axis
- Stress-related condition
- Visceral hypersensitivity
- Abnormal brain activation
- Altered gastrointestinal motility
- Role for neurotransmitters, hormones
- Presence of non-GI symptoms: Headache, back pain, fatigue, myalgia, dyspareunia, urinary symptoms, dizziness



Rome III Criteria for IBS-Constipation

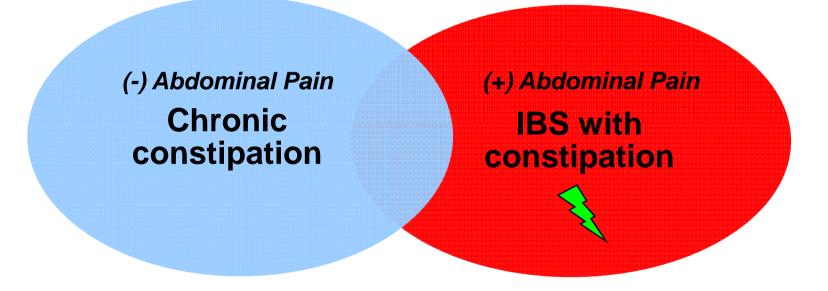
Recurrent abdominal pain or discomfort (an uncomfortable sensation not described as pain) at least 3 days per month in the last 3 months associated with 2 or more of the following:

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

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

Note: In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening for patient eligibility

Abdominal pain: a salient feature absent in chronic constipation



Presence or absence of abdominal pain seems to be the major differentiating feature

Brandt LJ, et al. Am J Gastroenterol. 2005

Risk factors for Constipation

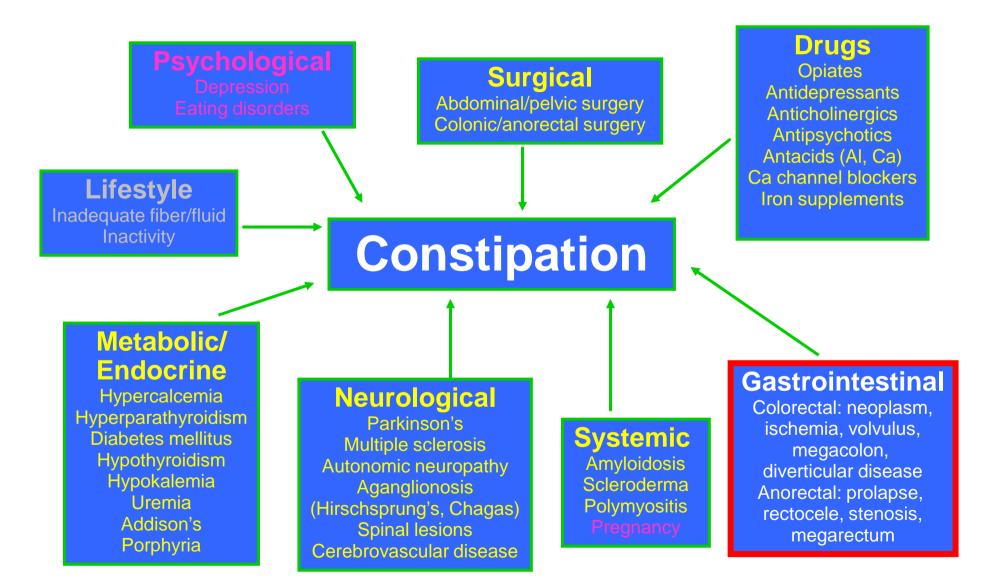
- Inherited or aquired neuromuscular disorders
- Metabolic diseases
- Pathophysiologic changes with **Ageing**
- Medications
- Gender: female (hormonal and structural causes)
- Physical inactivity
- Low income
- Limited education
- History of sexual abuse
- Symptoms of depression
- Low dietary fiber

Risk Factors for Constipation in older Population

- Reduced fiber and liquid intake
- Reduced mobility associated with functional decline
- Decreased functional independence
- Pelvic floor dysfunction
- Chronic conditions
 - Parkinson's disease
 - Dementia
 - Diabetes mellitus
 - Depression
- **Polypharmacy**: both OTC and prescription medications, such as NSAIDs, antacids, antihistamines, iron supplements, anticholinergics, opiates, Ca.C blockers, diuretics, antipsychotics, anxiolytics, antidepressants.

Secondary Constipation

Secondary Constipation



Candelli M, et al. *Hepatogastroenterology*. 2001;48:1050-1057. Locke GR, et al. *Gastroenterology*.

Table 1

Common causes of constipation.

Multiple environmental, biological, and pharmaceutical precipitants Endocrine/metabolic disorders (hypothyroidism) Colon disease (IBS, diverticulitis) Chronic idiopathic constipation Primary colorectal dysfunction Ignoring urge to defecate Lack of regular exercise Primary cause (Idiopathic) Inadequate fluid intake Dyssnerygic defecation Overuse of laxatives Changes in routine Sedentary lifestyle Myogenic disorders Low-fiber diet Secondary cause Immobility Pregnancy Slow transit Medications Obstruction Neurologic Stress Subtypes BS

Medicine (2018) 97:20(e10631)



Table 2

Medications associated with constipation.

Medications

Medicine (2018) 97:20(e10631)

5-HT₃ receptor antagonists (ondansetron) Calcium channel blockers (nifedipine, verapamil)

Antidepressants, tricyclic antidepressants (Amitriptyline > nortriptyline), other antidepressants (monoamine oxidase inhibitors).

Opiates (morphine)

Anticholinergic agents: anticonvulsants (carbamazepine), antipsychotics (phenothiazine

derivatives, chlorpromazine, clozapine, haloperidol, risperidone), antispasmodics,

(dicyclomine, mebeverine, peppermint oil)

Analgesics (opiates, tramadol, NSAIDS)

Antiparkinsonian drugs, dopaminergic agent, (benztropine, dopamine agonists) Diuretics (thiazides, loop diuretics, furosemide, hydrochlorothiazide) Antacids (calcium and aluminum)

Antidiarrheals (oveuse) (bile acid resins)

Chemotherapy agents (vincristine, cyclophosphamide

Miscellaneous compounds (oral contraceptives, polystyrene resins, barium sulfate. Endocrine medications (pamidronate and alendronic acid)

Sympathomimetics (ephedrine, terbutaline)



NSAIDS = nonsteroidal anti-inflammatory drugs.

Remember OTC Medications

- Sympatho-mimetics (for cold and flu)
- NSAIDS
- Antacids: aluminum, calcium
- Ca supplements
- Iron supplements



• Antidiarrheals: loperamide; bismuth

In Hospital causes constipation

- Decreased exercise/mobility
- Hospital food (not eating enough fibers)
- Not drinking enough fluid
- Lack of privacy
- Limited toilet access
- Depression / grief / anxiety



ALARM Signs and Symptoms

- Hematochezia
- Family history of colon cancer
- Family history of inflammatory bowel disease
- Anemia
- Positive fecal occult blood test (RSO)
- "Unexplained" weight loss ≥ 5 Kg
- Severe, persistent constipation that is unresponsive to treatment
- New-onset constipation in elderly patient

Locke GR III, et al. *Gastroenterology*. 2000 Brandt LJ, et al. *Am J Gastroenterol*. 2005

Physical Examination

"Intelligent Rectal Exam" (M Camilleri, Mayo clinic)

- Inspection
 - Anal pathology: hemorrhoids, prolapse
 - Check for sensation
 - Ask patient to strain: anus moves laterally, ballooning of perineum (rectocele)
- Palpation
 - Increased anal tone and pressure, anal fissure
 - mucosal prolapse or anterior rectal wall defect
 - Ask to strain: perineum descends on finger <1.0 or
 > 3.5cm

Laboratory Tests

- Thyroid function tests
- Electrolytes
- Calcium
- CBC
- Urine analysis



 Screen for colorectal cancer if none in last 5 years

Indications for Endoscopy

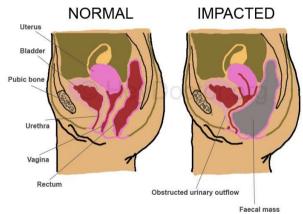
• New onset constipation:

- Weight loss, macroscopic or microscopic blood, family h/o colon Ca, anemia, undiagnosed abdominal pain
- Chronic constipation:
 - Anemia, weight loss, change in stool pattern, undiagnosed abdominal pain
- Failure of multiple laxatives
- Undiagnosed fecal incontinence

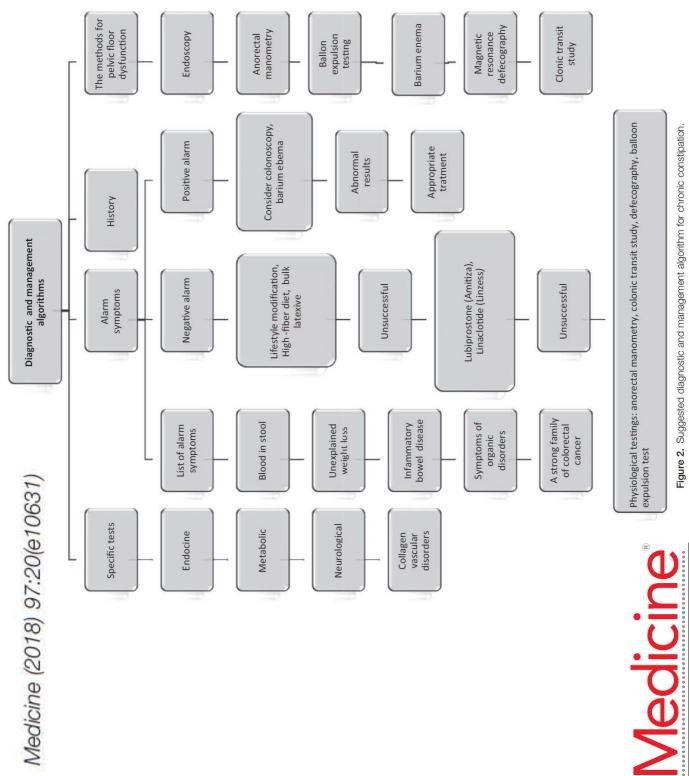


Complications of Chronic Constipation

- Fecal impaction
 - Identified in up to 40% of elderly adults hospitalized in United Kingdom
- Intestinal volvulus/<u>obstruction</u>
- Urinary and fecal incontinence
- Stercoral ulceration/ischemia
- Bowel perforation
- Possible increased risk of colorectal cancer (but it is really controversial)



Read NW, et al. J Clin Gastroenterol. 1995
 De Lillo AR, Rose S. Am J Gastroenterol. 2000
 Roberts MC, et al. Am J Gastroenterol. 2003
 Dukas L, et al. Am J Epidemiol. 2000



Treatment of Chronic Constipation

Lifestyle Modifications ... ?

Modification	Targeted Mechanism	Efficacy		
Increase fluid intake	Increase stool volume by augmenting luminal fluid	<i>Limited;</i> majority of fluid is absorbed before reaching the colon and is expelled via urine		
Increase exercise	Improve motility by decreasing transit time through the GI tract	<i>Moderate;</i> some evidence suggests this is beneficial; however, not sufficient to treat		
Increase dietary fiber	Increase water and bulk stool volume	<i>Limited benefit</i> compared with placebo		

Chung BD, et al. *J Clin Gastroenterol*. 1999 Dukas L, et al. *Am J Gastroenterol*. 2003 ACG Chronic Constipation Task Force. *Am J Gastroenterol*. 2005

Treating Constipation With Laxatives

Laxative	Description				
Bulking Agents	Absorbs liquids in the intestines and swells to form a soft, bulky stool; the increase in fecal bulk is associated with accelerated luminal propulsion				
Osmotic Laxatives	Draws water into the bowel from surrounding body tissues providing a soft stool mass and improved propulsion [saline, poorly absorbed mono-disaccharides) (polyethylene glycol)				
Stimulant Laxatives	Cause rhythmic muscle contractions in the intestines, increase intestinal motility and secretions (senna, cascara, etc,)				
Lubricants	Coats the bowel and the stool mass with a waterproof film; stool remains soft and its passage is made easier				
Stool Softeners	Helps liquids mix into the stool and prevent dry, hard stool mass has been said not to cause a bowel movement but instead allow the patient to have a bowel movement without straining (polyethylene glycol)				
Combinations	Combinations containing more than 1 type of laxative; for example, a product may contain both a stool softener and a stimulant laxative Gallagher P, et al. Drugs Aging. 20				

Treating Constipation With Laxatives

Table 4. Summary of Medications Commonly Used for Constipation

Туре	Generic name	Trade name	Dosage	Side effects	Time to onset of action (<i>h</i>)	Mechanism of action
Fiber	Bran	a - 1	1 cup/day	Bloating, flatulence, iron and calcium malabsorption	10-20	Stool bulk increases, colonic transit time decreases, gastrointestinal motility increases
	Psyllium	Metamucil Konsyl	1 tsp up to 3 times daily	Bloating, flatulence	17 <u>13</u>	
	Methylcellulose	Citrucel	1 tsp up to 3 times daily	Less bloating	0	
	Calcium polycarbophil	FiberCon	2-4 tablets once daily	Bloating, flatulence	3 <u></u>	
Stool softener	Docusate sodium	Colace	100 mg twice daily		12-72	
Hyperosmolar agents	Sorbitol	_	15–30 mL once daily or twice daily	Sweet tasting, transient abdominal cramps, flatulence	24–48	Nonabsorbable disaccharides metabolized by colonic bacteria into acetic acid and other short-chain fatty acids
	Lactulose	Chronulac	15–30 mL once daily or twice daily	Same as sorbitol	24-48	
	PEG	Golytely Colyte Miralax	8-32 oz once daily	Incontinence due to potency	0.5–1	Osmotically increases intraluminal fluids
Stimulant	Glycerin		Suppository; up to once daily	Rectal irritation	0.25-1	Evacuation induced by local rectal stimulation
	Bisacodyl Picosulfate	Dulcolax	10-mg suppositories or 5–10 mg by mouth up to 3 times/wk	Incontinence, hyperkalemia, abdominal cramps, rectal burning with daily use of suppository form	0.25-1	Bisacodyl and sodium picosulfate are prodrugs that are hydrolyzed by colonic bacteria (sodium picosulfate) or intestinal and colonic brush border enzymes (bisacodyl) to the active metabolite (bis-(p- hydroxyphenyl)-pyridyl-2-methane, which has anti-absorptive/secretory and prokinetic effects Similar to bisacodyl
	Anthraquinones (senna,	Senokot	2 tablets once daily to 4	Degeneration of Meissner's and	8-12	Electrolyte transport altered by increased
	cascara)	Perdiem (plain)	tablets twice daily	Auerbach's plexus (unproven),	8-12	intraluminal fluids; myenteric plexus
		Peri-Colace	1-2 tsp once daily 1-2 tablets once daily	malabsorption, abdominal cramps, dehydration, melanosis coli	8-12	stimulated; motility increases
Saline laxative	Magnesium	Milk of magnesia	15-30 mL once daily or	Magnesium toxicity, dehydration,	1-3	Fluid osmotically drawn into small bowel
			twice daily	abdominal cramps, incontinence	1-3	lumen; cholecystokinin stimulated; colon
		Hailey's M-O (with mineral oil)	15–30 mL once daily or twice daily			transit time decreases
Lubricant	Mineral oil		15–45 mL	Lipid pneumonia, malabsorption of fat-soluble vitamins, dehydration, incontinence	6–8	Stool lubricated
Enemas	Mineral oil retention enema		199–250 mL once daily per rectum	Incontinence, mechanical trauma	6–8	Stool softened and lubricated
	Tap water enema		500 mL per rectum	Mechanical trauma	5-15 min	Evacuation induced by distended colon; mechanical lavage
	Phosphate enema	Fleet	1 unit per rectum	Accumulated damage to rectal mucosa, hyperphosphatemia, mechanical trauma	5-15 min	
	Soapsuds enema		1500 mL per rectum	Accumulated damage to rectal mucosa, mechanical trauma	2-15 min	

Adapted from Locke GR, Pemberton JH, and Phillips SF. AGA technical review on constipation. Gastroenterology 2000;119:1766–1778, with permission from the American Gastroenterological Association.

BULKING AGENTS

- Add bulk to the stool
- Absorb water and increase faecal mass
- Soften stool and increase frequency
 - Ispaghula (Fybogel)
 - Psyllium (Psyllogel, Metamucil)
 - Guar gum (Benefibre)
 - Sterculia (Normafibe)
 - Methylcellulose
 - Calcium polycarbophil
- Not helpful in opioid induced, may worsen incipient constipation





- Osmosis keeps water within the intestinal lumen
- Attract also water into the bowel depending on dilution ...
- Improve stool consistency and frequency
 - Lactulose (Actilax, Duphalac, Genlac, Lac-dol)
 - Sorbitol (Sorbilax)
 - Magnesium sulfate ("Epsom English salt")
 - Glycerol (Glycerol / Glycerin suppositories)
 - (PEG o MACROGOL: Movicol, Selg, Isocolan)
- Lactulose can take up to 3 days
- Can get bloating and colic wind



STIMULANTS

- Increase intestinal motor activity
- Alter mucosal electrolyte,fluid transport
 - Senna, Cascara
 - Aloe, Rabarbaro
 - Castor oil, picosulfate
 - Bisacodyl
- 6-12 hour latency
- Good in opioid with stool softener
- Excessive use may cause hypokalemia, protein losing enteropathy, salt overload





Patients Treated With Opiates

Special Considerations

- Constipation is a common and troubling side effect
- Opioids inhibit GI propulsive motility and secretion: GI effects of opioids are mediated primarily by µ-opioid receptors within the bowel
- Patients do not develop tolerance to the effects of opiates on the bowel

Treatment Strategy

- 1. Laxative therapy should be initiated proactively with start of opiate use
- 2. Magnesium hydroxide, senna, lactulose, bisacodyl, stool softener
- 3. A combination of a stimulant and stool softener is often required
- 4. Laxative doses may need to be increased along with increased doses of opioids
- 5. Titrate doses of laxatives according to response prior to changing to an alternative laxative. When laxative therapy is inadequate, consider methylnaltrexone

Tamayo A, Diaz-Zuluaga P. *Support Care Cancer*. 2004 Shaiova L, et al. *Palliat Supp Care*. 2007

Patient With Dementia

Contributing Factors

- Immobility
- Dehydration
- Inadequate food intake
- Depression
- Cannot find the bathroom
- Inability to undress
- Cannot ask for help
- Cannot sense the urge to defecate
- Use of psychotropic drugs

Treatment Strategy

- 1. Appropriate assessment of bowel function
- 2. Establish a bowel routine, regular toileting program
- 3. Suppositories, stool softeners, bulking agents
- 4. Careful documentation (bowel diary, effectiveness of treatments, etc.)
- 5. Involve family or health care team (in a nursing facility)
- 6. Address nutritional/fluid needs



New Laxatives

Table 5. Newer Pharmacologic Approaches for Constipation

Generic name (chemisty)	Mechanism of action	Metabolism, bioavailability	Pharmacodynamic effects	Clinical trials	Common side effects	Cardiovascular safety#
Secretagiog) and						
Lubiprostone (prostone) ^p	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	Diaintica, nausea	No anhythmic effects
Limidolide	Stimulate intestimat chloride and fluid secretion by activating CFTR	Intestmat degradation, minimat oral bioavailability	Dowo-retailed acceleration of colonic transit in IBS C	Phones 2 and 3 in CC. IBS C	Diantica	No anti-thmic effects
Scrutorim 5-HI e receptor agonists						
Prucalopride ² (benzofuran cerhoosmide)	High selectivity and affinity for SHIT ₄ exceptions; much weaker affinity for human 04 and s1 and mouse SHIT ₄ receptors	Limited hepatic, not CYP3A4	Accelerated colonic transit in health and CC	Phases 2 and 3 in OC	Diarthea. headache	No amhythmic activity in atrial cells: inhibits ht BS all very high µmol/ L concentration; no christally relevant adverse cardiac effects in bage trials (>-1000 subjects)

Myths and Misconceptions About Chronic Constipation

Misconception

Reality

Diseases may arise from autointoxication by retained stools

Fluctuations in hormones contribute to constipation

A diet poor in fiber causes constipation

Increasing fluid intake is a successful treatment for constipation

- NO serious evidence to support this theory
- Fluctuations in sex hormones during menstrual cycle have little impact on constipation, although are associated with changes in other GI symptoms
- Changes in hormones during *Pregnancy* may play a role in slowing gut transit
- A low fiber diet may be a *contributory factor* in a subgroup of patients with constipation
- Some patients may be helped by an increase in dietary fiber, others with more severe constipation may get worse symptoms with increased dietary fiber intake!
- No evidence that constipation can be treated successfully by increasing fluid intake, unless there is a clear evidence of *Dehydration*

Myths and Misconceptions About Chronic Constipation

Misconception

Reality

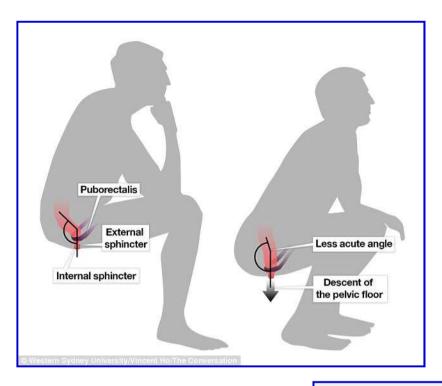
Stimulant laxatives damage the enteric nervous system and increase the risk of cancer

Laxatives cause electrolyte disturbances

Laxatives induce tolerance

Laxatives are addictive

- Unlikely that stimulant laxatives at recommended doses are harmful to the colon
- No data support the idea that stimulant laxatives are an independent risk factor for colorectal cancer
- Laxatives can cause electrolyte disturbances, but appropriate drug and dose selection can minimize such effects
- Tolerance *is uncommon* in most laxative users, however tolerance to stimulant laxatives can occur in patients with severe constipation and slow colonic transit
- No potential for addiction to laxatives, but laxatives may be misused



The right position ...

It seems that squatting widens the anorectal angle more than sitting and allows a clearer and straighter passage for stools to pass through the anal canal



