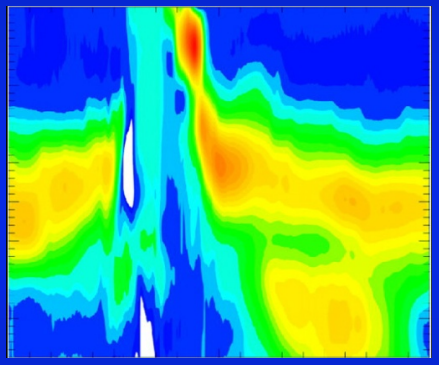
Autonomic Functions of the Gut: Motility Disorders, IBS, Diarrhea & Constipation



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Objectives & Disclosures

- Objective
  - To review basic physiology of GI motility & how dysfunction can cause symptoms
  - To discuss key motility disorders present from the stomach to anus including gastroparesis, functional dyspepsia, IBS, constipation & diarrhea
  - To discuss options for treatment, focusing on non-medical therapy
- Disclosure
  - Consultant: Pfizer, Regeneron, Sanofi

GI Function in a Picture

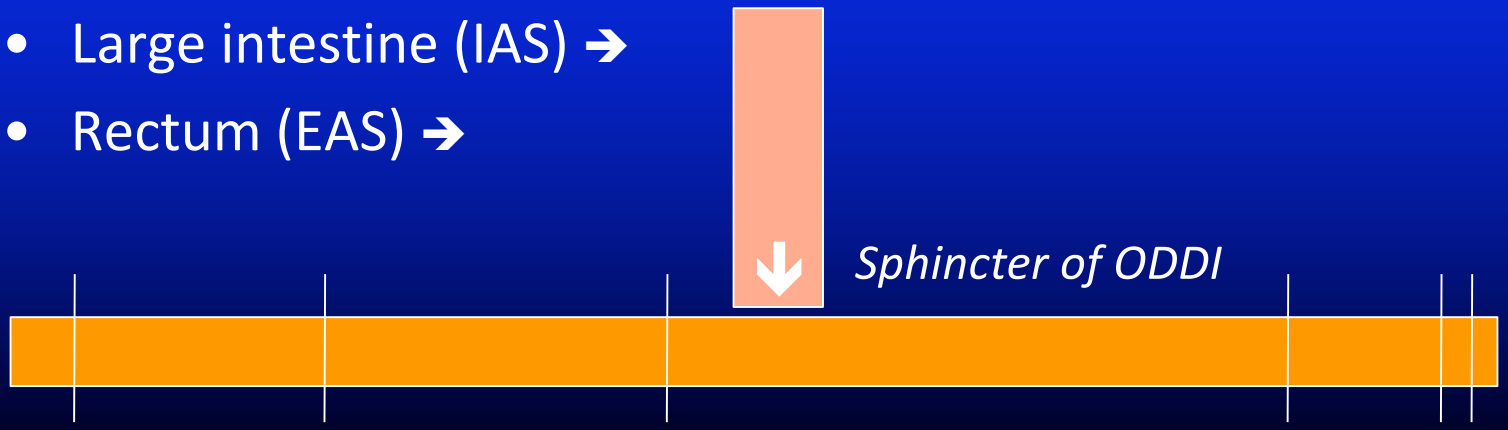
The GI Tract – What is it?

Organs in Series

- Oropharynx (UES) ➔
- Esophagus (LES) ➔
- Stomach (PYL) ➔
- Small Intestine (ILEO) ➔
- Large intestine (IAS) ➔
- Rectum (EAS) ➔

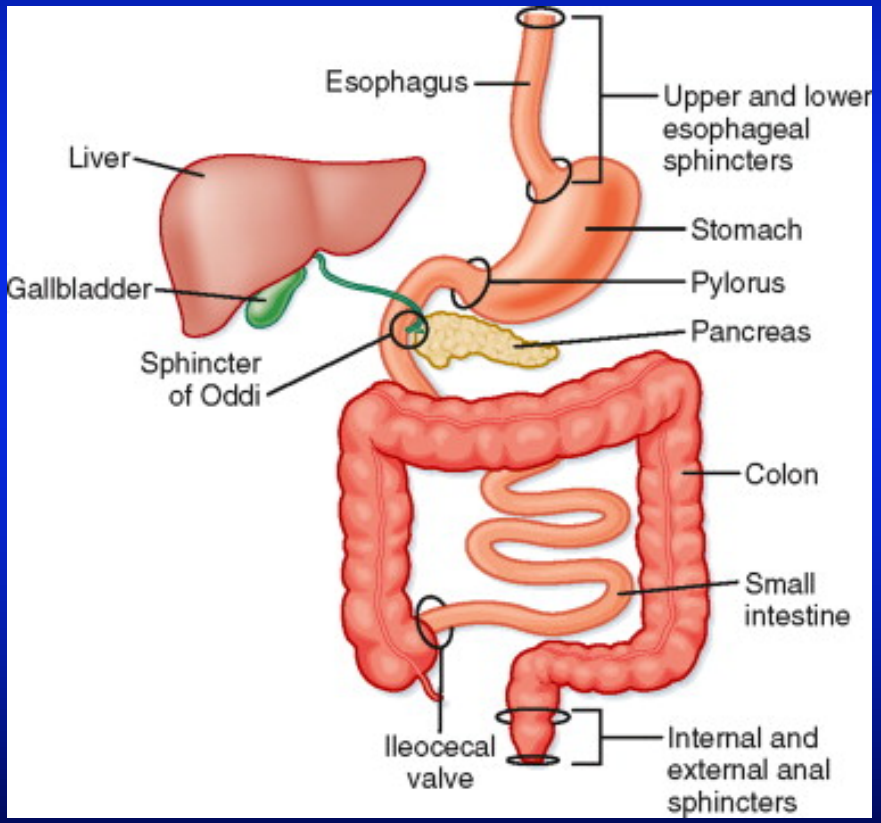
Organs in Parallel

- Liver
- Gall Bladder
- Exocrine Pancreas (acini)
- Pancreatic Duct



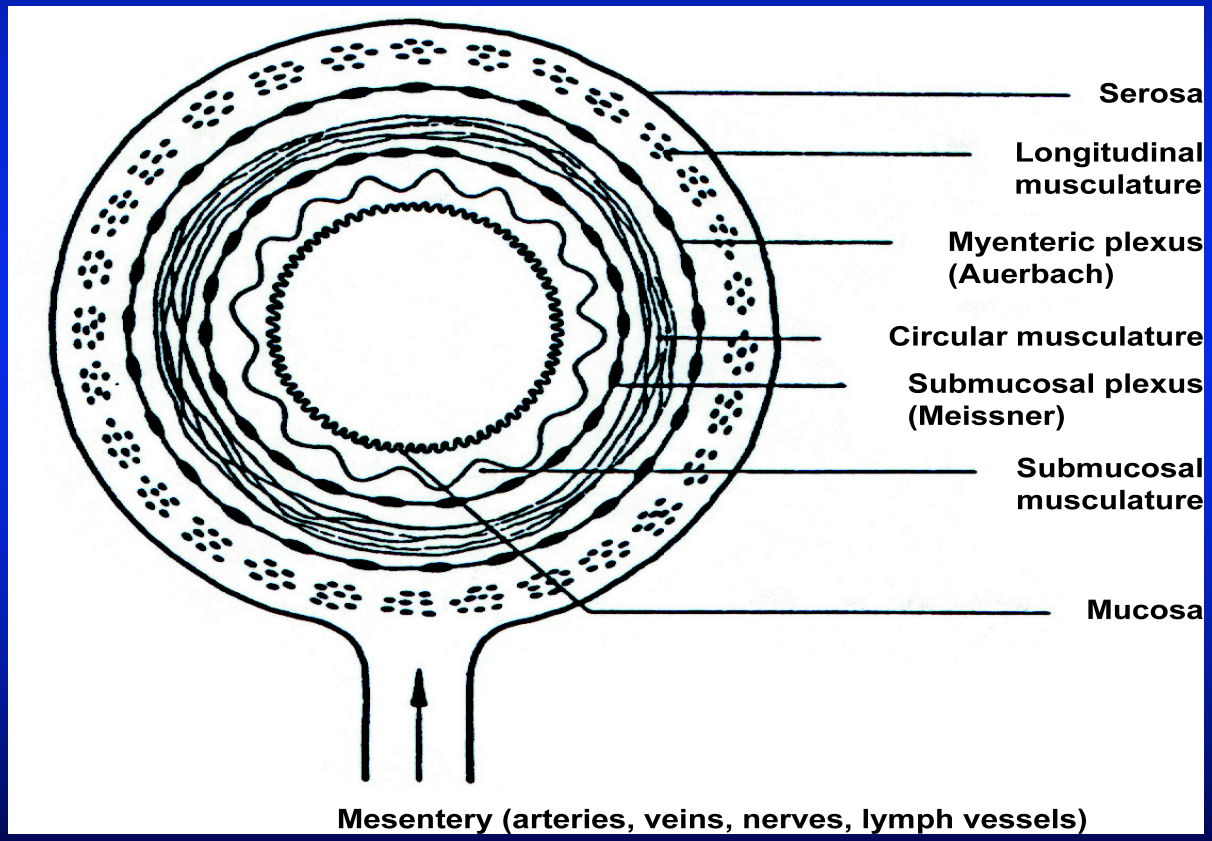
Anatomy of the GI Tract

- Sphincters
  - Upper esophageal
  - Lower esophageal
  - Pylorus
  - Sphincter of Oddi
  - Ileocecal valve
  - Internal and external anal sphincters



Berne & Levy Physiology , Sixth Edition. Bruce M. Koeppen, and Bruce A. Stanton, CHAPTER 26 , 487-495

Organization of the GI Tract



Overview

- GI motility is a tightly integrated system
- Regulated by enteric nervous system
- Responsible for
  - Mixing & propulsive movements
  - Organized patterns of movements
- Dysfunction results in symptoms & disease

Regulation of GI Motility

- Esophagus
- Stomach
- Small intestine
- Colon
- Anorectum

Stomach

- Proximal (fundus, body)
  - Accommodation & storage
  - Regulates intragastric pressure
  - Tonic movement of chyme
  - No phasic motor activity
- Distal (antrum)
  - Grinding of food
  - Responsible for emptying
  - Motor activity is phasic
  - Rate of contraction is 3/min

Small intestine

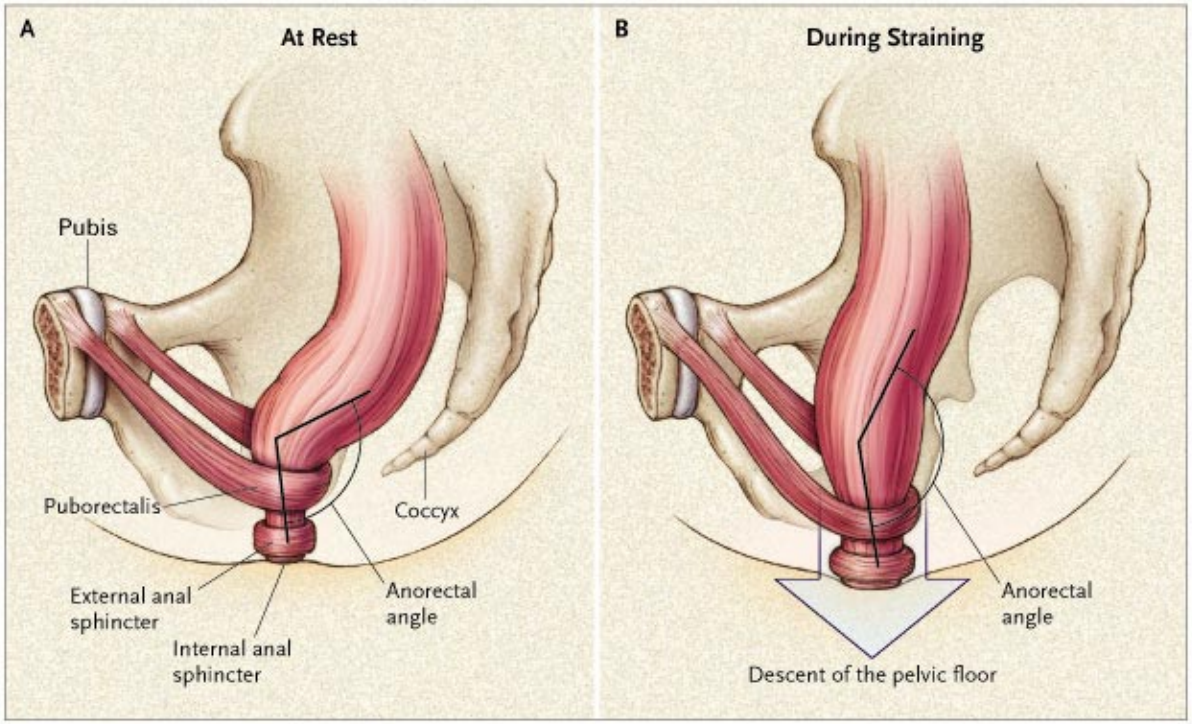
- Fed state
  - Digesting & absorbing nutrients
  - Motility aimed towards mixing & absorption
- Fasting state
  - Motility geared towards propelling non-absorbed residue
  - Keeps intestine swept clean of bacteria & other residue
- Motor activity is phasic (12/min)

Colon

- Function
  - Absorb excess fluid
  - Salvage unabsorbed nutrients via bacteria
  - Permit defecation to occur
- Motility
  - Intermittent short segmental to-and-fro patterns to induce mixing
  - Followed by relative quiescent periods for storage
  - Intermittent high amplitude peristaltic contractions (HAPC) to promote defecation (on average 5 per day)
  - Colon transit time 36 hours

Anorectum

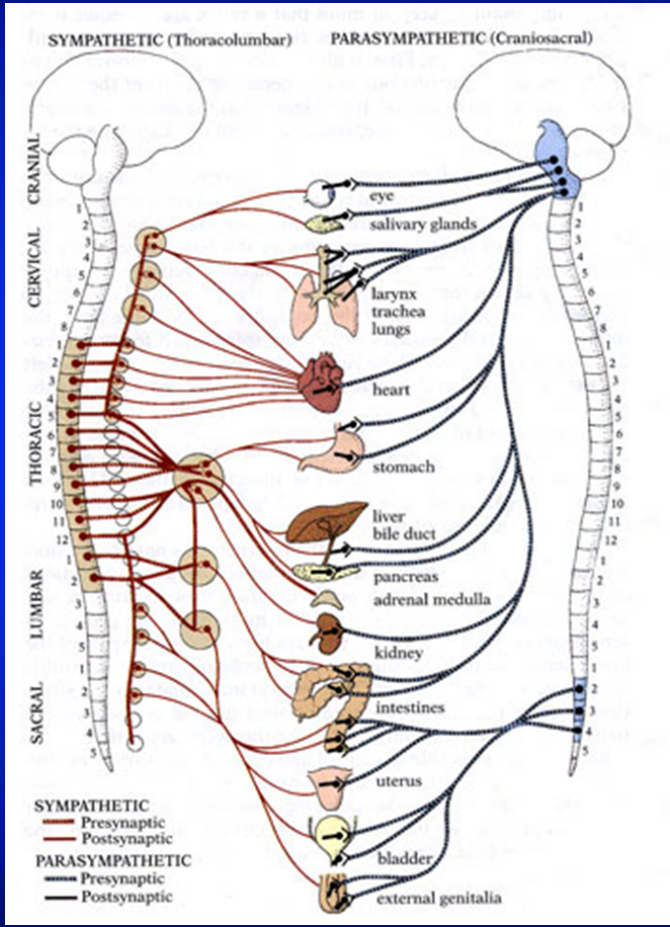
- Functions to store & eliminate feces
- Storage
  - Rectum acts as storage reservoir
  - Tonic contraction of puborectalis, internal & external anal sphincters
- Defecation
  - Puborectalis relaxation with opening of internal & external anal sphincters
  - Response to voluntary defecation or increased rectal pressure

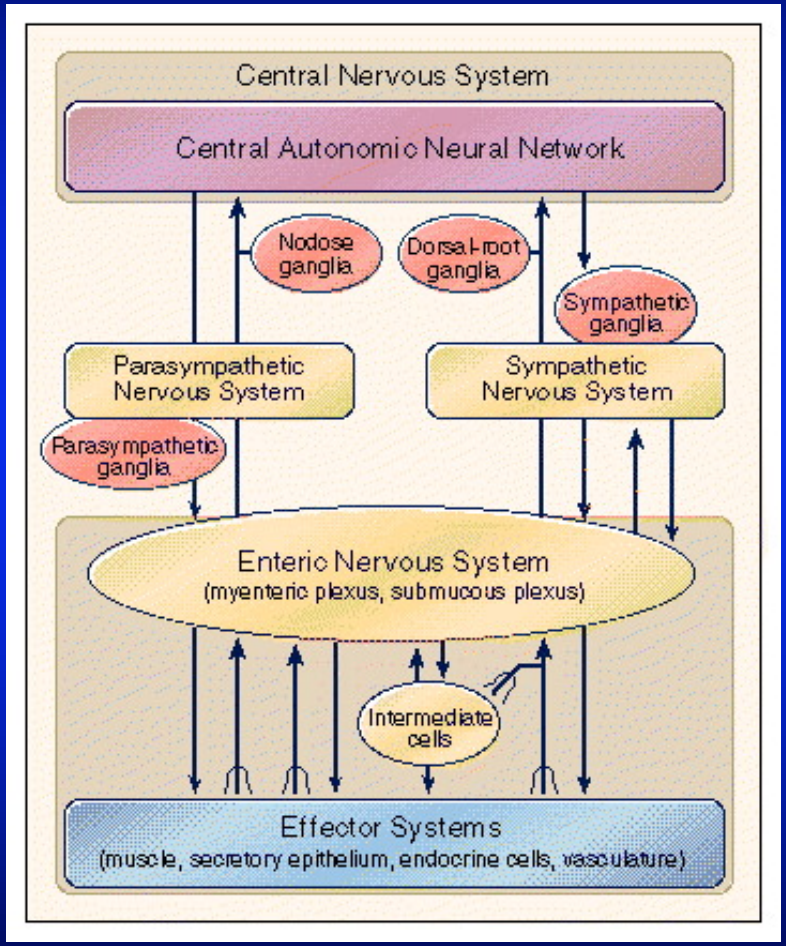

A
At Rest
Pubis
Puborectalis
Coccyx
External anal sphincter
Internal anal sphincter
Anorectal angle
B
During Straining
Anorectal angle
Descent of the pelvic floor

Enteric Nervous System

- Extrinsic
  - Parasympathetic
  - Sympathetic
- Intrinsic (500 million neurons)
  - Myenteric (Auerbach's) plexus
  - Submucosal (Meissner's) plexus
- Reflexes can occur in the absence of CNS input

Innervation of the GI Tract





Goyal RK, Hirano I. N Engl J Med 1996;334:1106-1115.

Enteric Nervous System

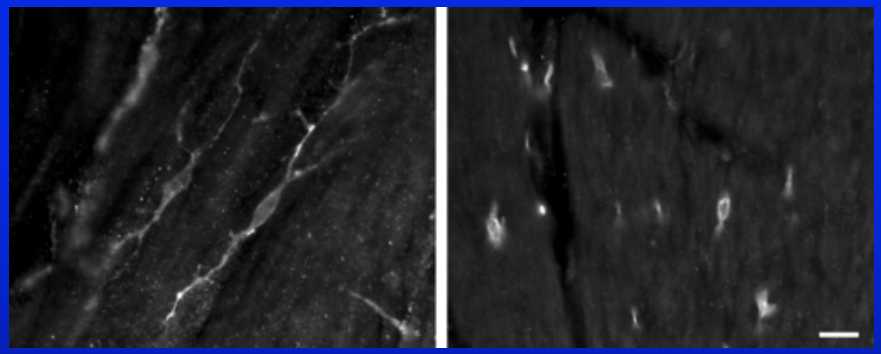
- Composed of the following 5 groups
  - Smooth muscle
  - Enteroendocrine cells
  - Nervous tissue cells (neurons & glia)
  - Inflammatory cells (mast cells, lymphocytes, macrophages, granulocytes)
  - Interstitial cells of Cajal

Interstitial Cells of Cajal

- Non-neural elements
- Communicate with neurons and smooth muscle
- Intrinsic myoelectric frequencies
- Control frequency and propagation of contractions
- While a key part of GI motility, also found outside of GI tract (urinary system)
- First described in theory in 1911 by Cajal

Interstitial Cells of Cajal

- At least 4 key functions:
  - Generate slow wave that is propagated to smooth muscle cells
  - Help mediate neurotransmission
  - Set smooth muscle membrane potential & membrane gradient
  - Involved in mechanotransduction



Farrugia. Neurogastroenterol Motil 2008

Signaling molecules

- Most are still unclear
- Serotonin believed to be the major stimulatory neurotransmitter and main component of gut sensation
- Other key transmitters include acetylcholine, substance P, nitric oxide and dopamine
- Area of rapidly emerging data

Signaling molecules

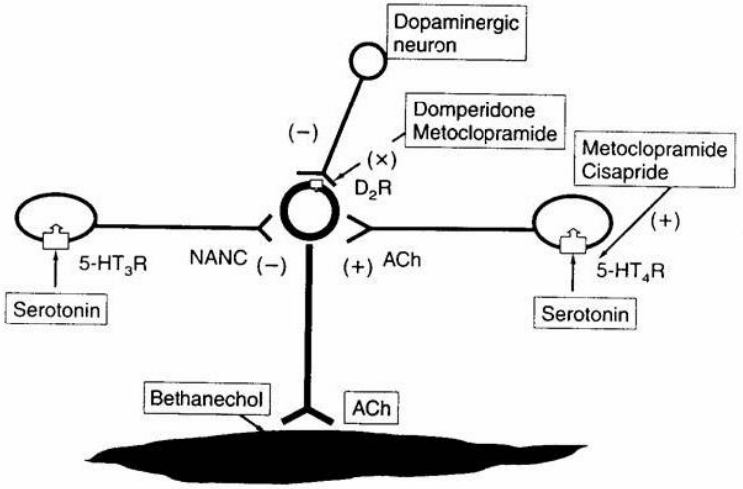
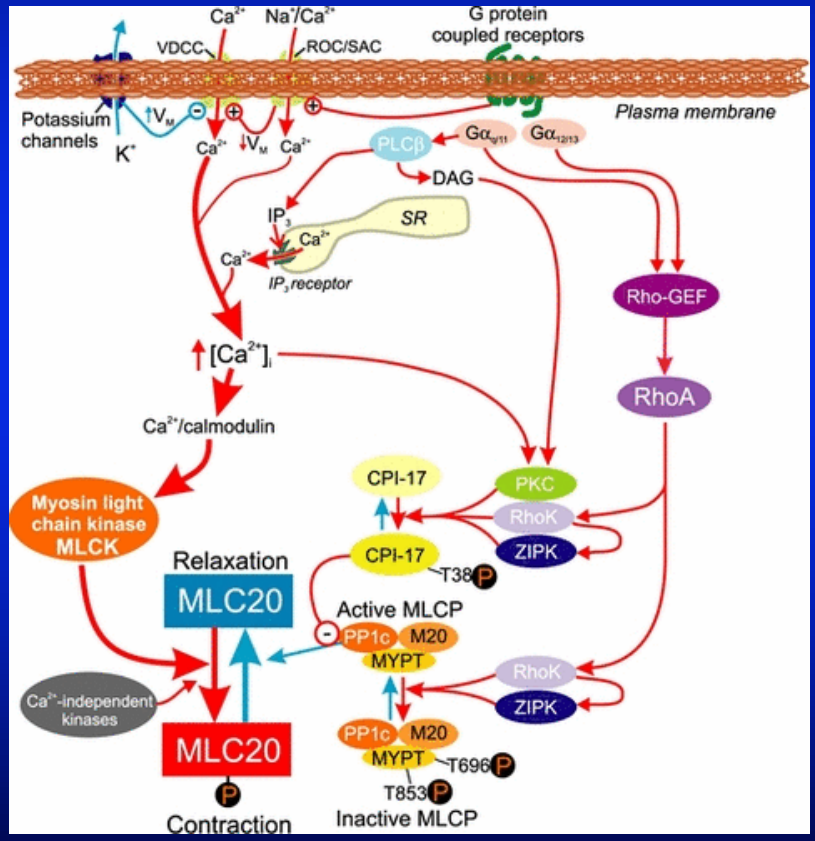


Figure 38–2. Conceptual model to explain the action of prokinetic agents.

Smooth Muscle Contraction

- Complicated
- Smooth muscles are the end-result of ICC slow wave generation and signaling molecules
- End-result is calcium-mediated



Sanders. Neurogastroenterol Motil 2008

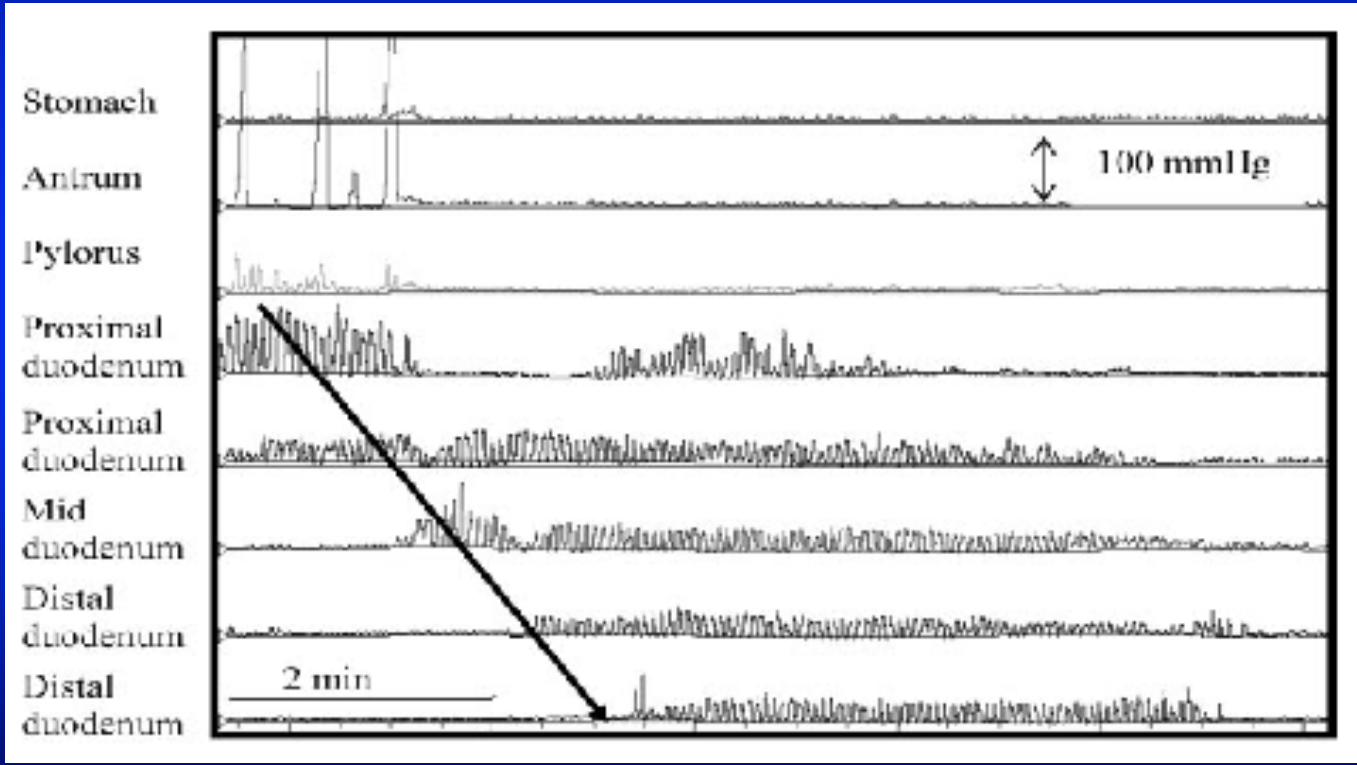
Electrical Activity & Motor Patterns

- GI motility characterized by rhythmic electrical activity
- Induced by membrane depolarization followed by repolarization
- Triggered by Interstitial Cells of Cajal
- Motor patterns can be separated into fasting & fed states

Fasting State

- Migratory Motor Complex (MMC)
- Acts to clear stomach & intestine of residual food & debris
- Occurs approximately once per 90 minutes
- Triggered by motilin (erythromycin)
- Blocked by infusion of gastrin
- Less pronounced in colon
- Loss of this pattern associated with bloating, distention & small intestinal bacterial overgrowth

Migratory Motor Complex



Fed State

- Slow contractions in stomach & small intestine
- Rate of contractions
  - Stomach - 3/min
  - Small intestine - 12/min
  - Colon – disorganized but stronger contractions
- Duration of fed state increases with caloric & fat intake
- Disrupted with opiates

Disorders of GI Motility

- Disorders of gastric motility
  - Gastroparesis
  - Functional dyspepsia
- Disorders of small intestinal motility
  - Small intestinal bacterial overgrowth
  - Chronic intestinal pseudo-obstruction
- Disorders of colon and anorectal motility
  - Constipation
  - Diarrhea
  - Fecal incontinence
- Irritable bowel may transcend geographic boundaries

Specific Disorders of Motility

- Disorders
  - Gastroparesis
  - Functional dyspepsia
  - Irritable bowel syndrome
  - Constipation
  - Diarrhea
- Goals to cover
  - Definitions
  - Mechanisms
  - Diagnosis
  - Medical/surgical options
  - Integrative approaches

Gastroparesis

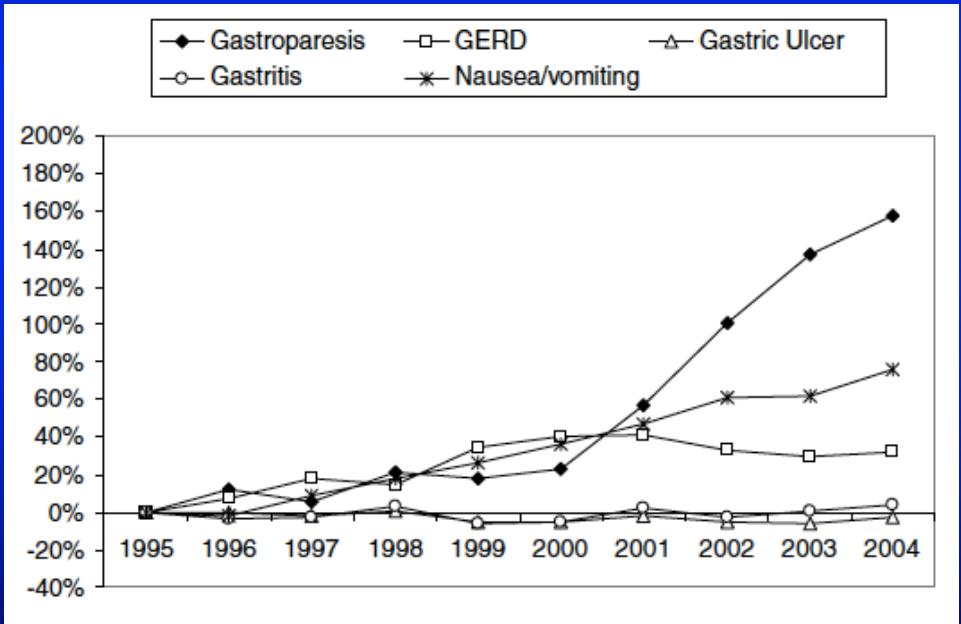
Courtesy of Bill Ravich

Gastroparesis

- Definition: delayed emptying of the stomach in the absence of mechanical obstruction
- Derived from Greek “gastro” and “pa’resis” meaning partial paralysis of stomach
- Symptoms
  - Most common
    - Nausea (93%)
    - Abdominal pain (90%)
    - Early satiety (86%)
    - Vomiting (68%)
  - Symptom severity is variable
  - Symptoms may be intermittent
- Prevalence estimates < 2%
- Increasing hospital admissions over past decade

Burden of gastroparesis

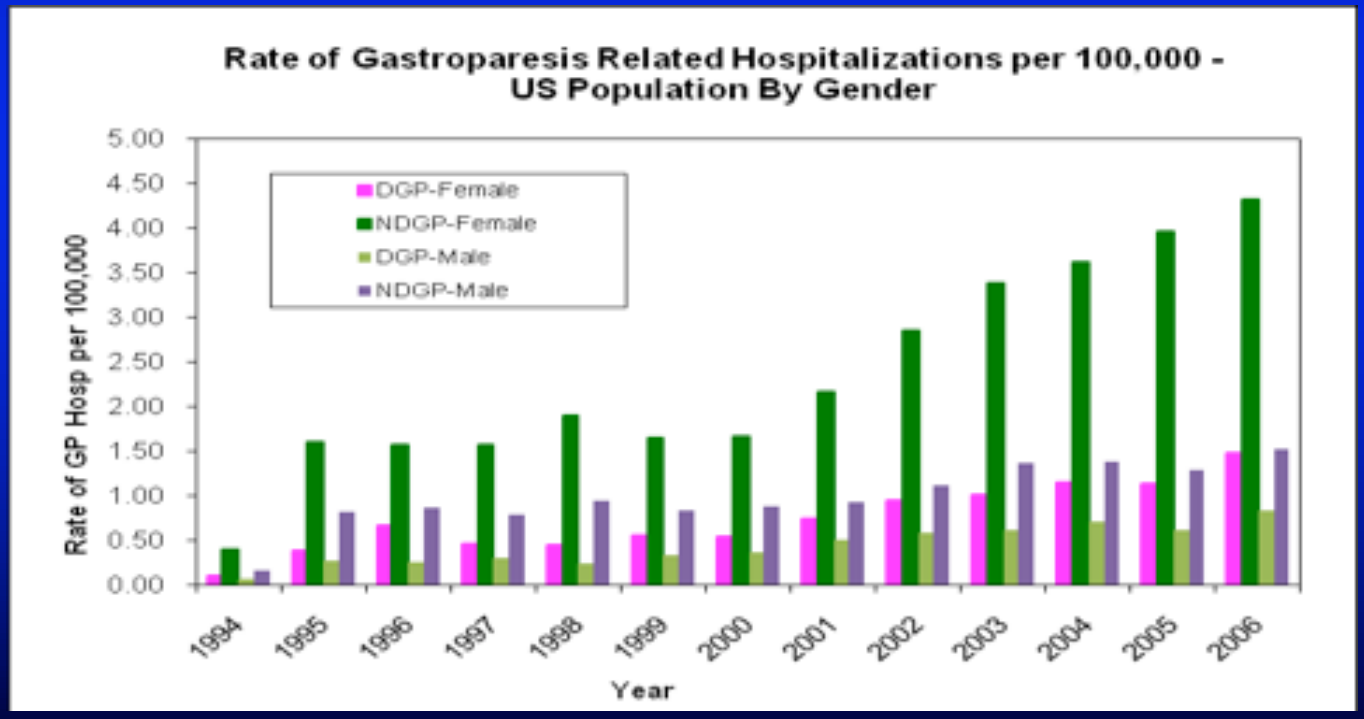
Gastroparesis-related hospitalizations increased 138% from 1995-2004



Wang YR et al. Am J Gastroenterol 2008;103:313-22.

Burden of gastroparesis

Greatest increase in women with nondiabetic gastroparesis

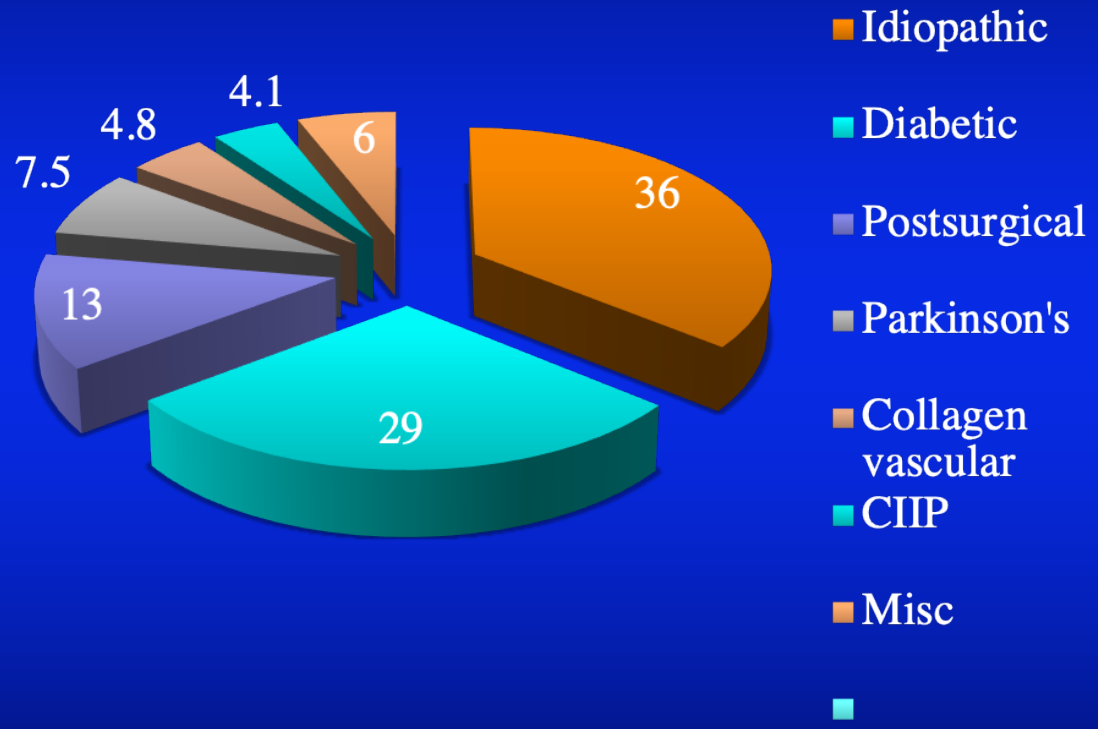


Nguyen LB et al. Abstract DDW 2009, manuscript in preparation

Etiology of Gastroparesis

- Idiopathic
- Systemic disease
  - Diabetes mellitus (29%)
  - Paraneoplastic syndromes
  - Connective tissue disorders
  - Ehlers Danlos Syndrome
- Neurologic and psychiatric disorders
  - Autonomic dysfunction
  - Spinal cord injury
  - Parkinson's disease
  - Anorexia Nervosa
- Iatrogenic
  - Vagotomy & partial gastrectomy (13%)
  - Drugs
    - Anticholinergics
    - Tricyclic agents
    - Dopamine agonists
    - Opiates
  - Radiation injury

Causes of Gastroparesis

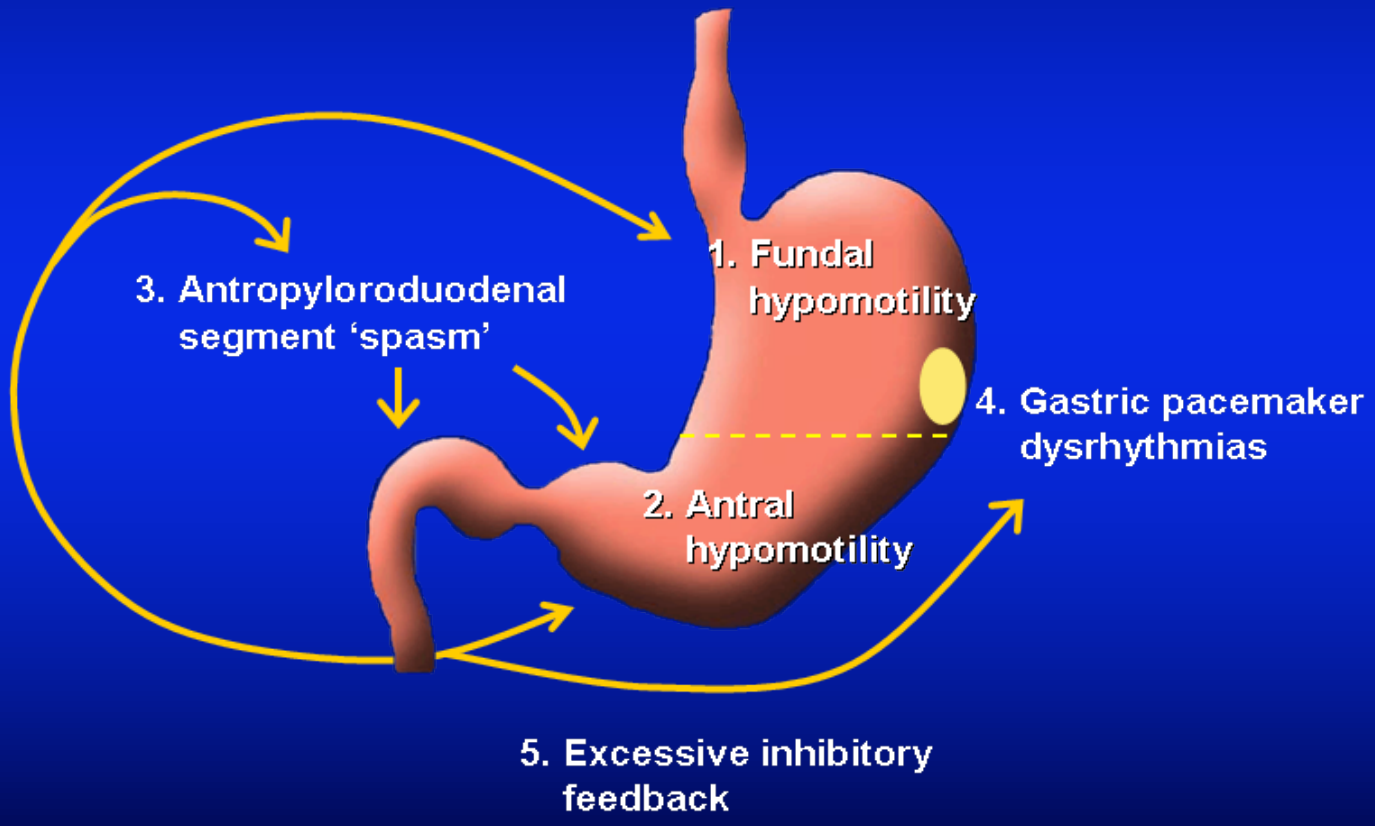


Soykan I et al. Dig Dis Sci 1998

Physiology of Gastroparesis

- Normal
  - Proximal stomach expands to accommodate
  - Intragastric pressure maintained
  - Solids broken down into 1-2 mm particles with contractions
  - Gastric emptying: 50% in 2 hours, 90% in 4 hours
- Gastroparesis
  - Loss of fundic accommodation (bloating, early satiety)
  - Altered or absent antral phasic contractions (delayed emptying)
  - Visceral hypersensitivity (pain)

Mechanisms



Courtesy of Brian Lacy

Gastric Neuromuscular Dysfunction: Looking Beyond Gastric Emptying

Anatomic Location	Physiologic Abnormality	Symptoms
Fundus	Impaired Gastric Accommodation	Diastolic Dysfunction: - Fullness - Early Satiety
Antrum	Antral hypomotility	Systolic Dysfunction: - Delayed gastric emptying - N/V
Pylorus	Pylorospasm	Functional Outlet Obstruction
Duodenum	Duodenal dysmotility	Functional Outlet obstruction
Interstitial Cells of Cajal	Tachygastria, Bradygastria, dysrhythmia	Gastric Arrhythmias - Nausea - Gastric motor dysfunction

** Any dysfunction can give rise to GI symptoms without causing a delay in gastric emptying

Diagnosis

- Symptoms consistent with gastroparesis
- Documented impairment of gastric emptying
  - Scintigraphy
  - Wireless motility capsule
  - Breath test
  - Food retention on endoscopy

Diagnosis: scintigraphy

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doi: 10.1111/j.1572-0241.2007.01636.x

Consensus Recommendations for Gastric Emptying Scintigraphy: A Joint Report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine

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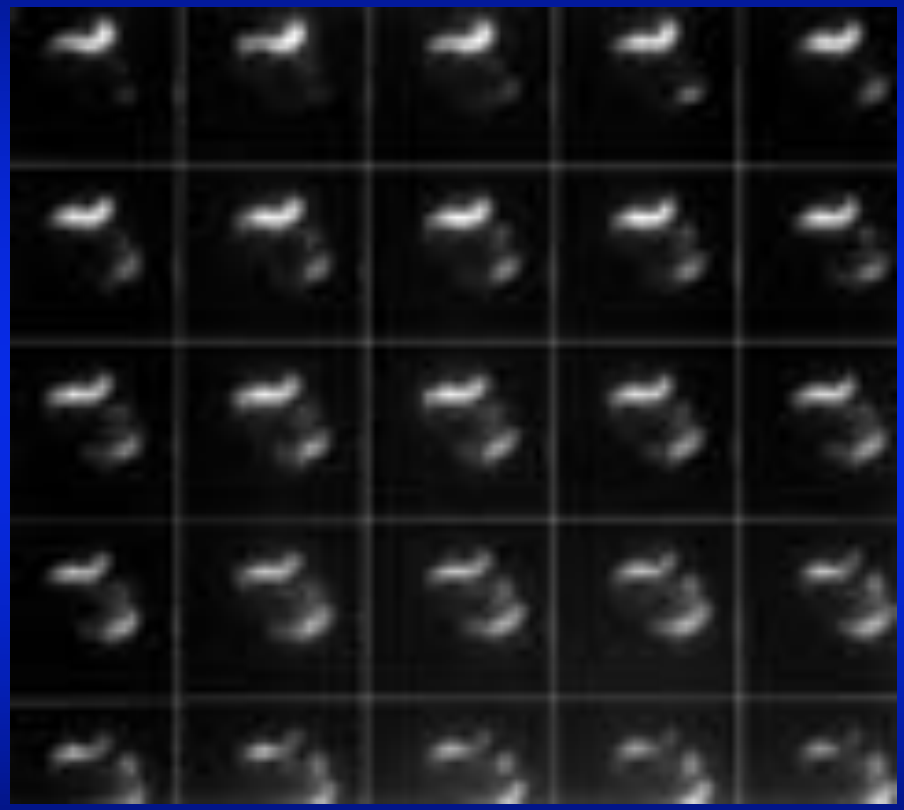
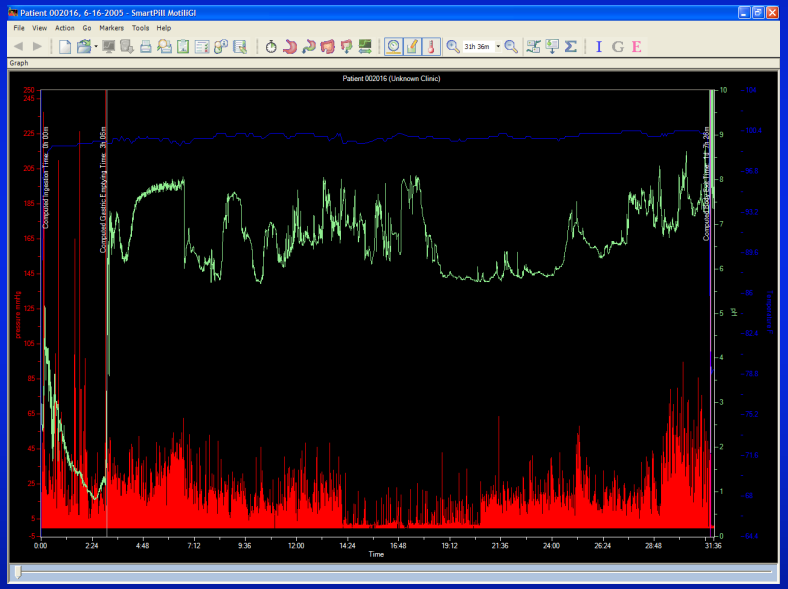
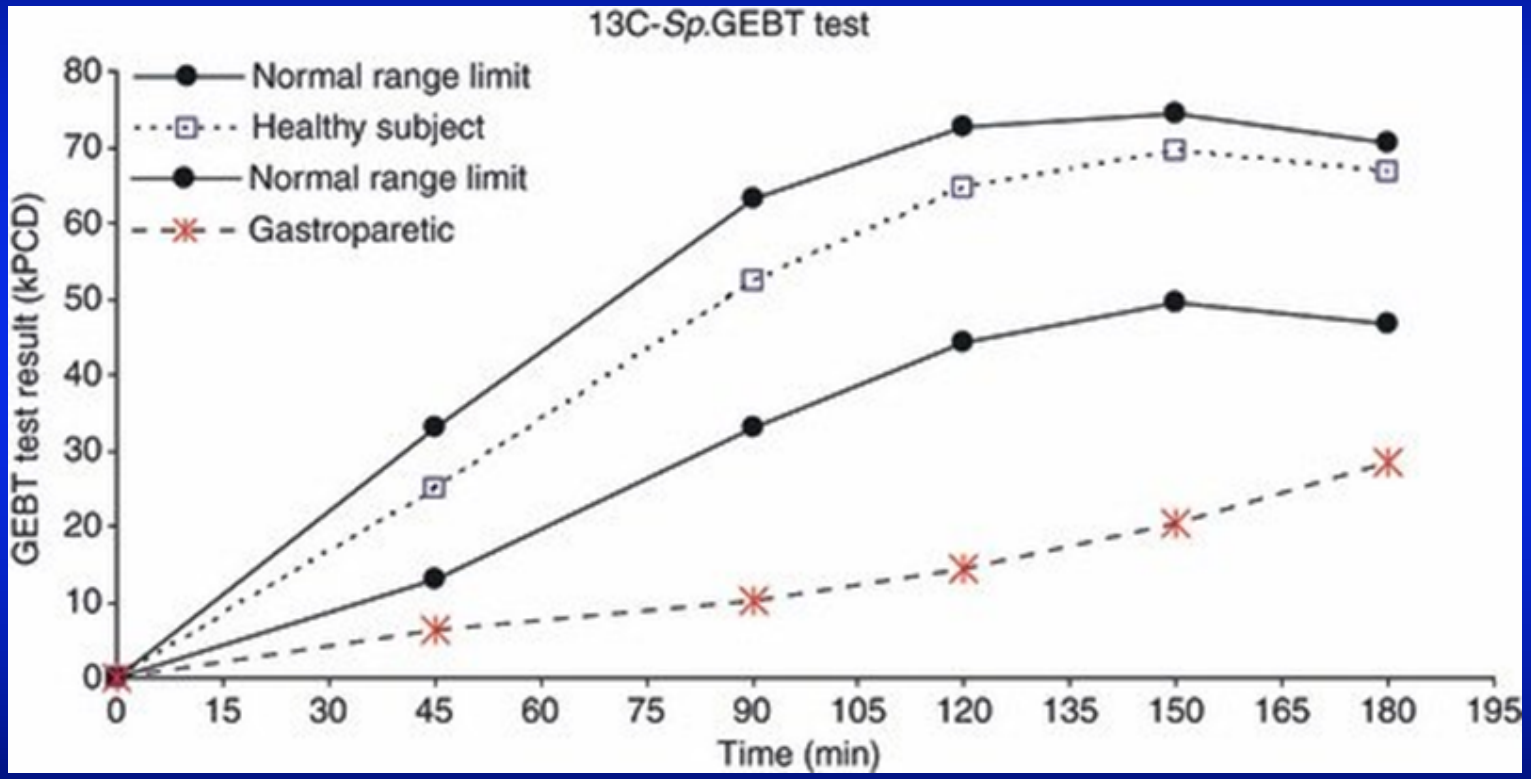


Diagnosis: wireless motility capsule

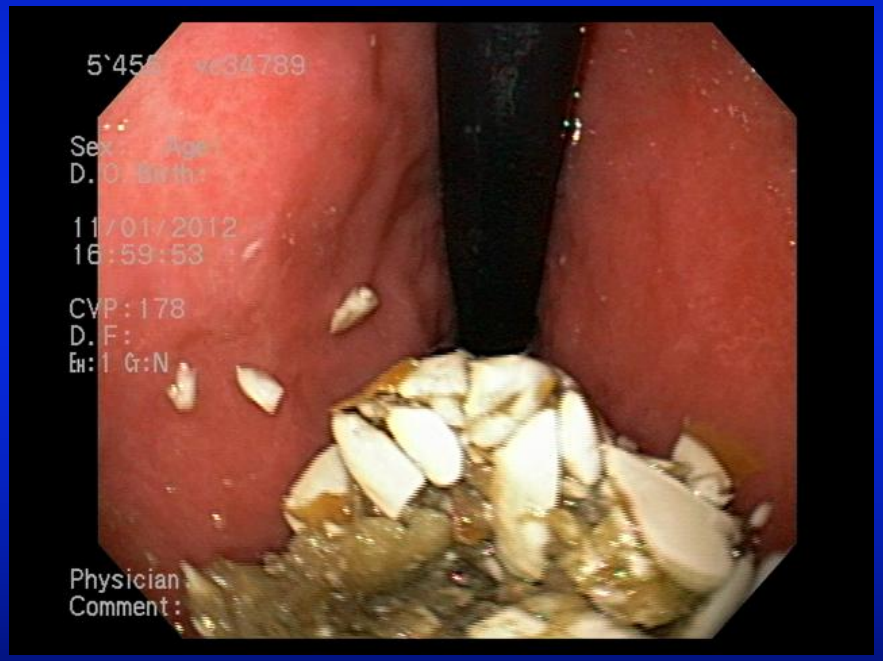


Diagnosis: C13 breath test



Endoscopy

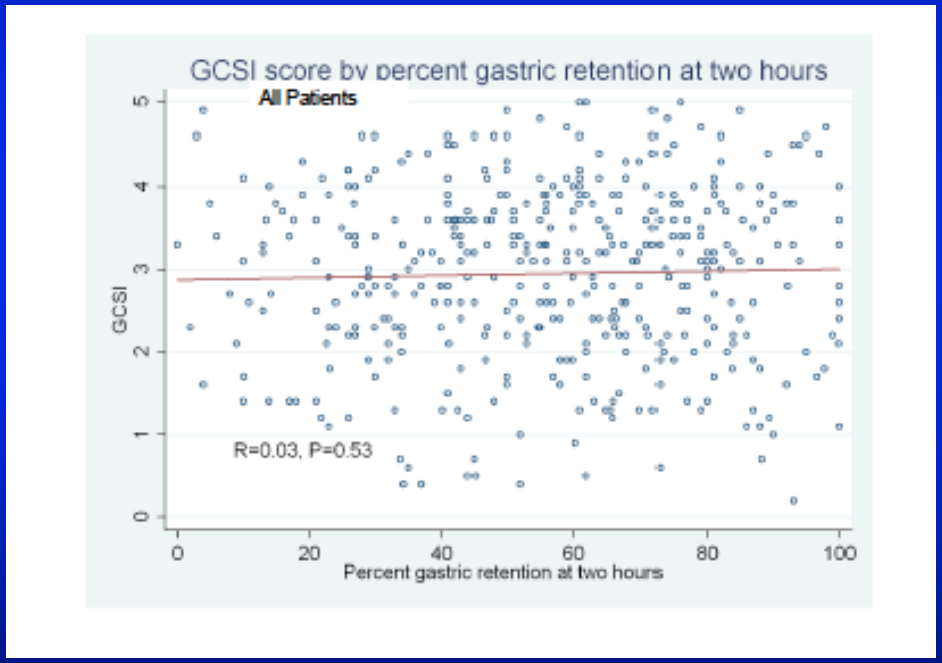
- Not a good test for motility disorders
- While not sensitive can be specific
- Helpful if food retention seen despite fasting
- Allows acquisition of biopsies and exclusion of other mimicking conditions



Controversies

- Functional dyspepsia versus gastroparesis
- Functional nausea versus gastroparesis
- Importance of gastric emptying
- Role of the microbiome
- Importance of pain
- Heterogeneity

Gastric emptying compared to symptoms



Pasricha PJ. Clin Gastroenterol Hepatol 2011; 9: 567-76

Causes of Nausea and Vomiting

Toxin Mediated

- Medications
  - Opiates
- Chemotherapy
- Infection
  - Gastroenteritis
  - Otitis media

Vestibular

- Motion sickness
- Laryrinthitis
- Meniere's disease
- Tumors

CNS Causes

- Migraines
- Seizure
- Increased ICP

GI Causes

•Functional GI Causes

- Gastroparesis
- Functional dyspepsia
- Chronic unexplained n/v (CUNV)
- PONV
- CVS
- Cannabinoid hyperemesis

- Structural Abnormalities
  - PUD
  - SBO
  - Pancreatitis

Psychogenic

•Anxiety

•Eating Disorder

Treatment of Gastroparesis

- Lifestyle modification
- Medical therapy
  - Anti-emetics
  - Prokinetics
    - Metoclopramide
    - Erythromycin/Azithromycin
    - Domperidone
    - Cisapride
    - Prucalopride
    - Bethanechol
    - Pyridostigmine
  - Accommodation agents: buspirone
  - Neuromodulators
    - Tricyclic antidepressants
    - Mirtazapine
    - Olanzapine
    - SSRI/SNRI
- Alternative & complementary
- Endoscopic
  - G-tube
  - J-tube
  - Botulinum toxin
  - Trans-pyloric stent
  - Pyloromyotomy
- Surgical
  - Gastric stimulation
  - Pyloromyotomy
  - Gastrectomy

Lifestyle modification

- Dietary modification
  - Small frequent meals (5-6/day)
  - Reduced fat intake
  - Reduced fiber
  - Liquid supplements
  - Low-residue (low-particulate) diet
- Glycemic control

Integrative approaches to consider

Herbal Therapies

Herbals

- Ginger (NK1)
- Ginseng (5HT3)
- Artichoke Leaf
- D-Limonene

Herbal blends

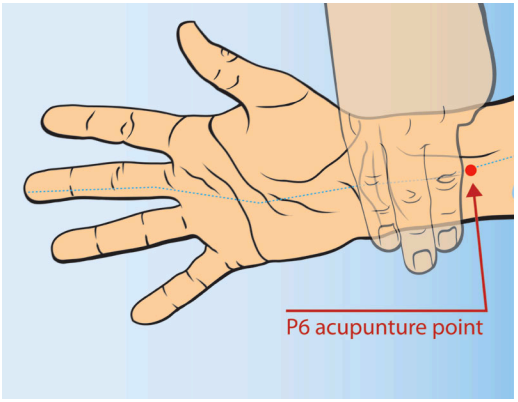
- Rikkunshito (5HT3, ghrelin)
  - Bitter orange, Ginseng root, Zingiberis Rhizoma, Jujubae fruit, Crow-dipper, Atractylodis rhisoma, Licorice root, Porio cocos
- STW5 (Iberogast)
  - Bitter candytuft, Angelica root, milk thistle fruit, caraway fruit, celandine herb, licorice root (5HT3), chamomile flower (5HT4), lemon balm leaf, and peppermint leaf
- Padma Digestin
  - Pomegranate seed, lesser galangal, long pepper, cardamom fruit, and cassia bark
  - Increases contractility of the antrum

Slide courtesy of Linda Nguyen

Acupuncture and Acupressure

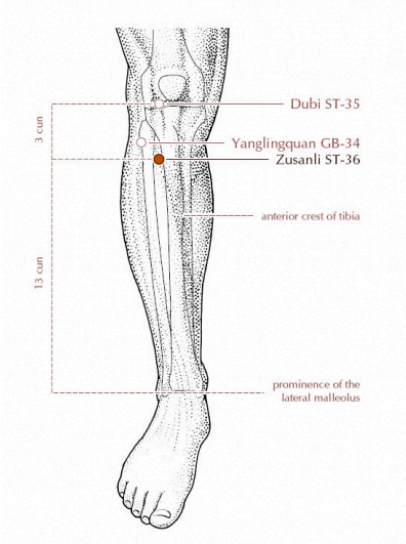
P6

- Improves N/V



ST36

- Increases gastric accommodation
- Increases antral contractions
- Decreases visceral hypersensitivity
- Decreased gastric dysrhythmias
- Increases colonic contractions
- Decreases tLESR



Slide Courtesy of Linda Nguyen

Other potential alternative options

Dig Dis Sci (2014) 59:645–652
DOI 10.1007/s10620-012-2426-7

ORIGINAL ARTICLE

Small Intestinal Bacterial Overgrowth in Gastroparesis

Nina S. George · Abhinav Sankineni · Henry P. Parkman

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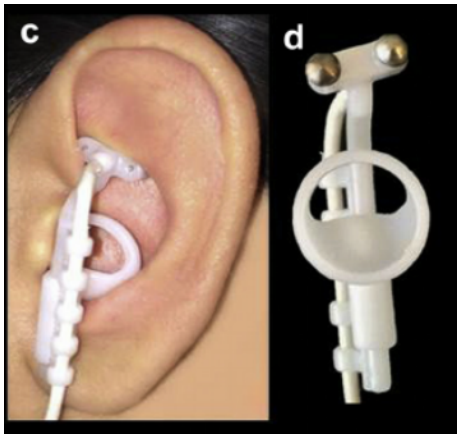
Non-invasive options for vagal nerve stimulation

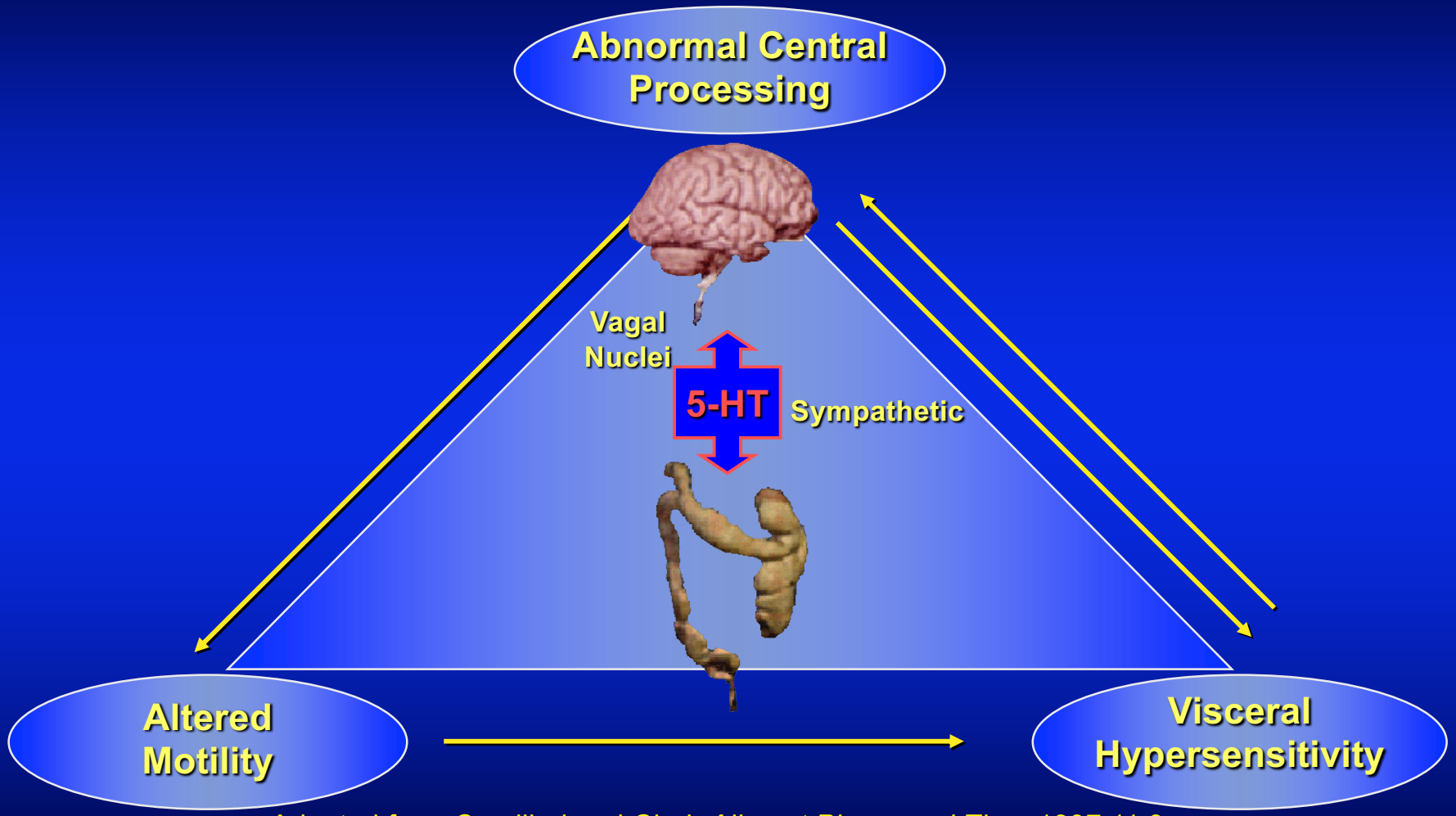


Irritable Bowel Syndrome

What is Irritable Bowel Syndrome?

- Definition
  - Functional bowel disorder
  - Chronic or recurrent abdominal pain or discomfort
  - Associated with altered bowel habits
  - Absence of organic abnormalities

IBS Pathophysiology

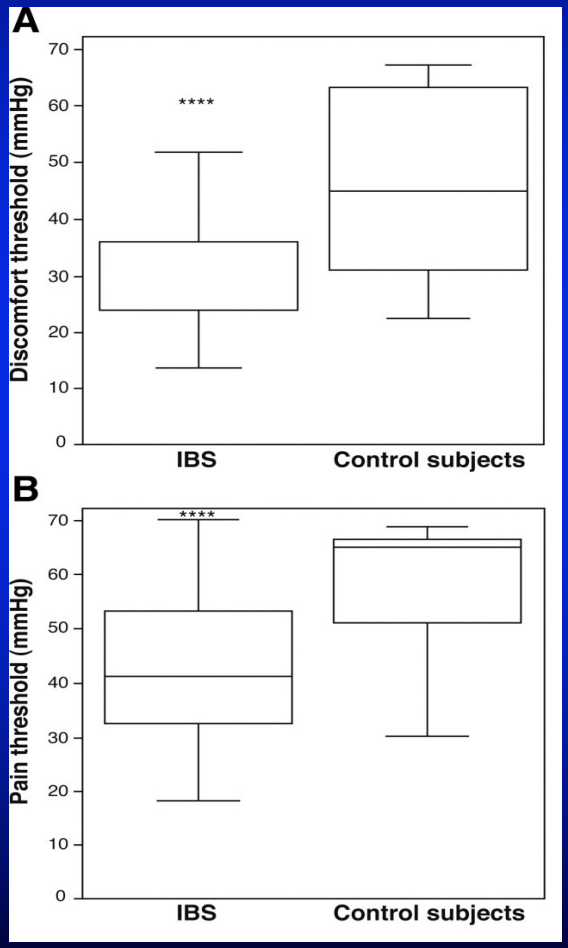


Adapted from Camilleri and Choi. *Aliment Pharmacol Ther.* 1997;11:3.

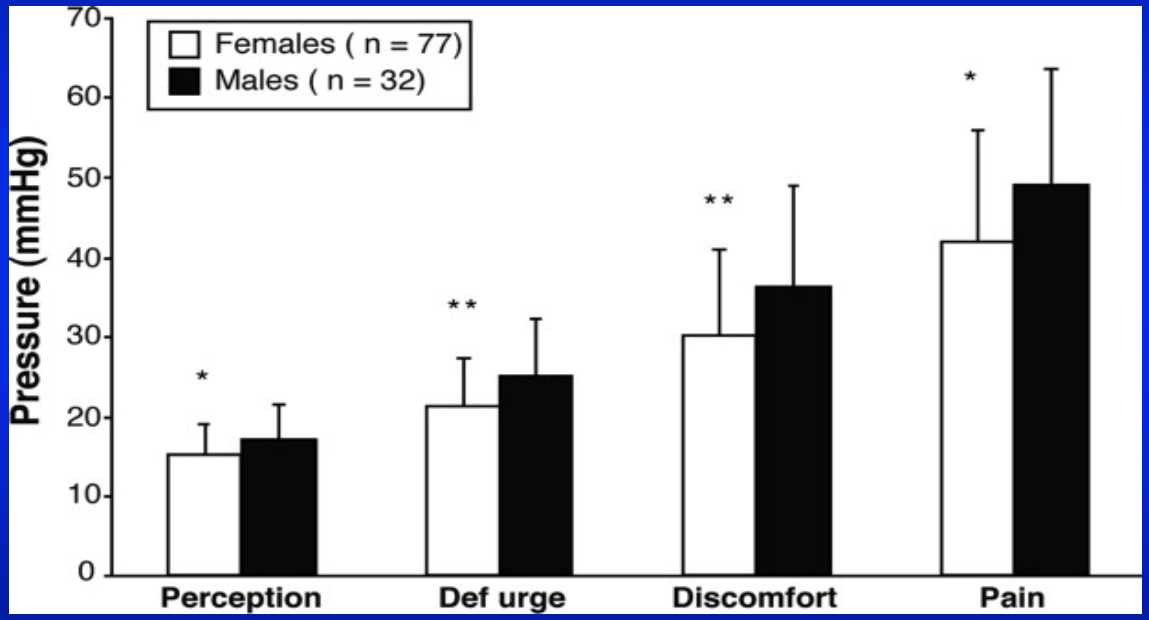
What causes IBS?

- The pathophysiology of IBS remains enigmatic.
- Proposed mechanisms of IBS
  - Visceral hypersensitivity
  - Altered GI motility
  - Abnormal central or neuroenteric processing
  - Food allergy or intolerance
  - Infection
  - Microscopic inflammation
  - Psychosocial dysfunction
  - Altered gut flora
- Syndrome is understood as a common set of symptoms rather than a disease entity

IBS: Altered visceral sensory perception correlates with symptoms



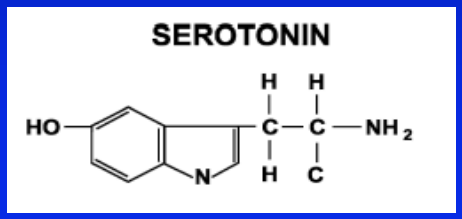
Rectal discomfort thresholds in IBS vs. controls

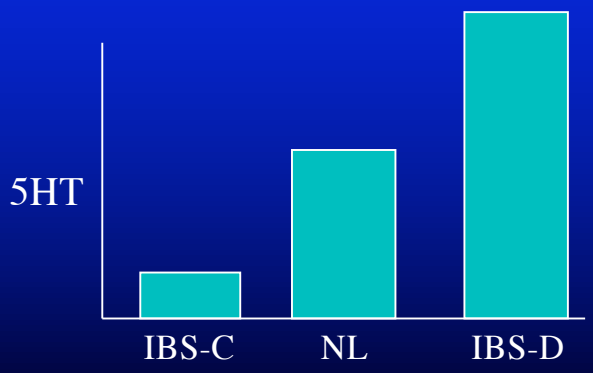


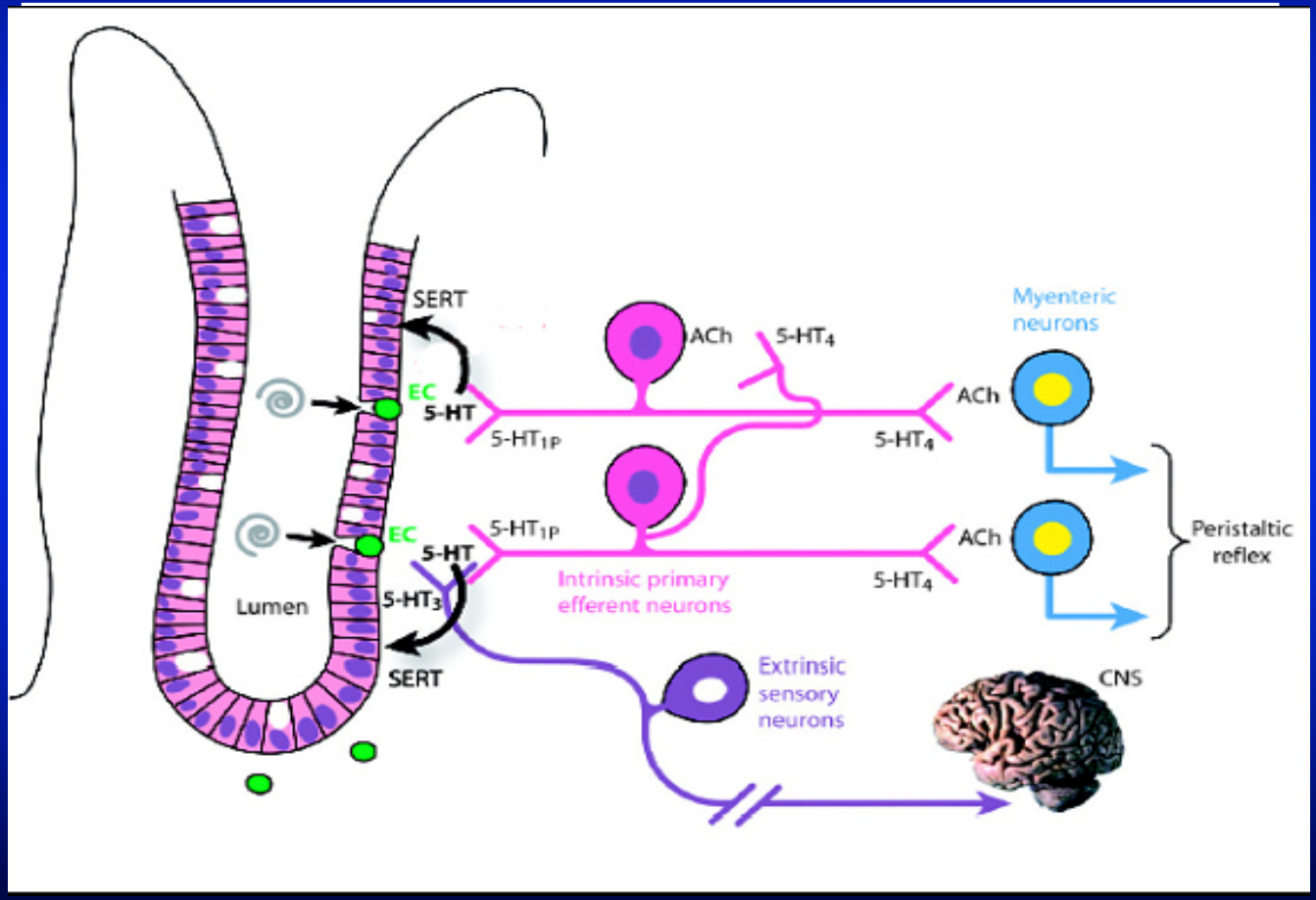
Sensory thresholds in female and male patients with IBS.
***P* < .05; ****P* < .01.**

Posserud, I et al. Gastroenterology, 2007, 133(4):1113-23

Serotonin: key mediator of visceral sensitivity and motility



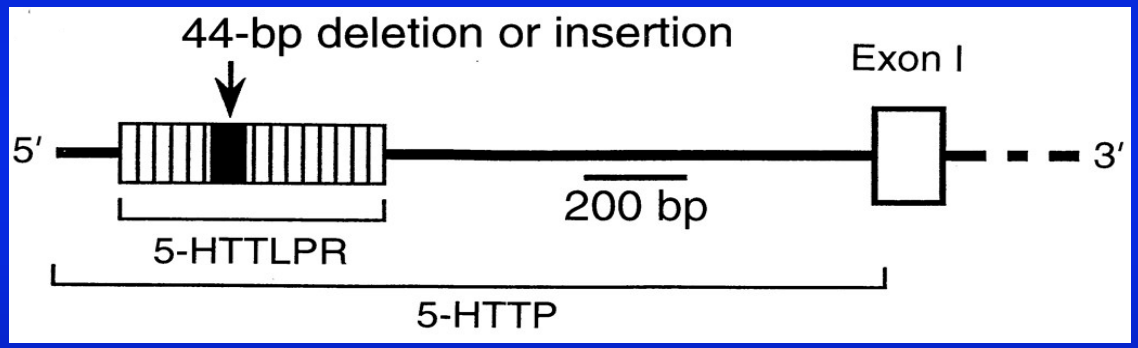




Lesurtel, M. et al. Cell. Mol. Lif. Sci. 2008, 65:940-952

IBS: A genetic etiology?

- Polymorphisms within the SERT promoter may determine SERT activity and regulate serotonin metabolism



- Serotonin-transporter-length polymorphic region *(5-HTTLPR)* LS/SS genotype is associated with increased visceral pain sensation

IBS: Disordered brain-gut axis?

→ ACTH → cortisol

Corticotrophin Releasing Factor (CRF)

Autonomic Nervous System

Visceral Hyperalgesia

Slows stomach and small intestinal emptying

Accelerates colonic motility, defecation

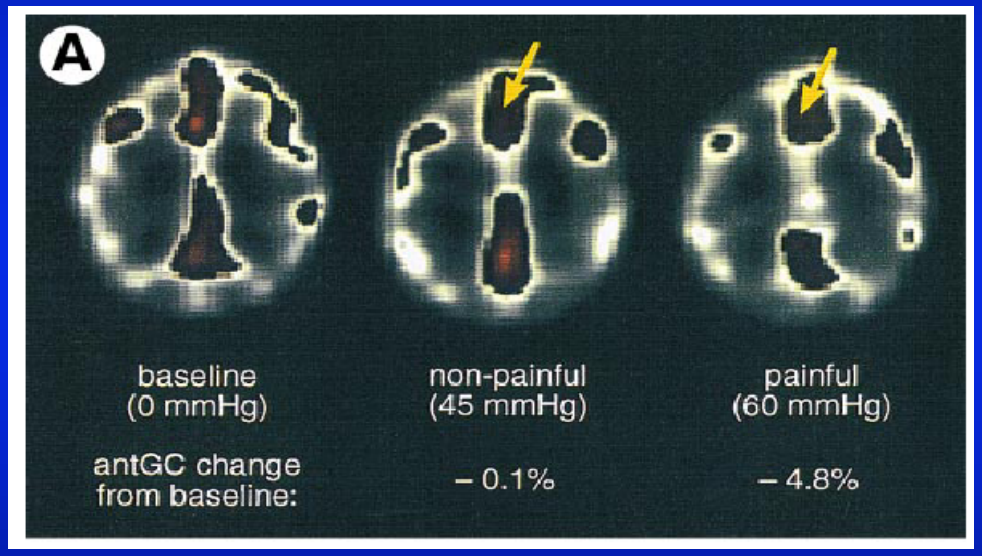
Nausea, bloating

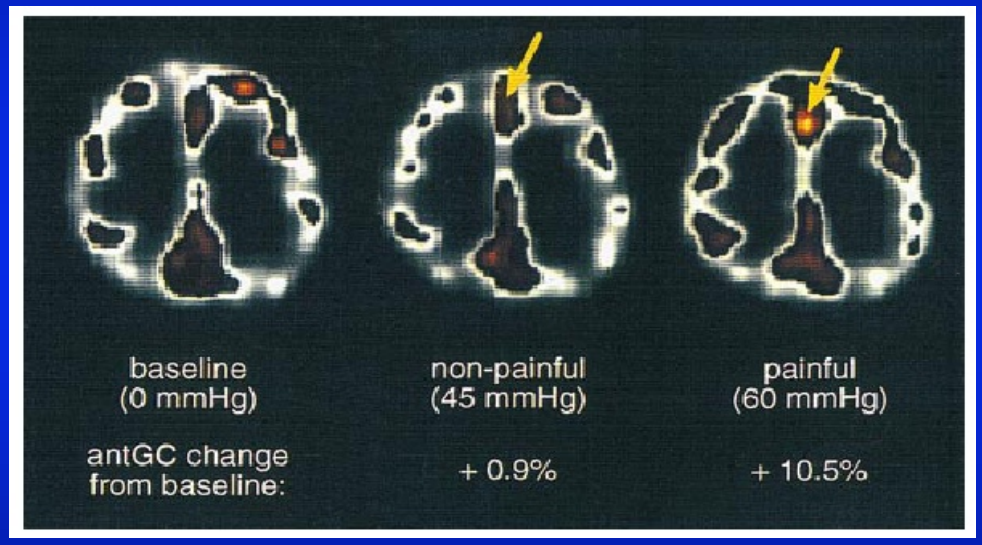
Cramping, diarrhea

IBS: Abnormal pain processing demonstrated by functional MRI

IBS

Control





Anterior cingulate cortex activated by painful rectal stimulus in controls but no
instead, IBS displayed activation of **left dorsilateral prefrontal cortex** (involv
complex cognitive behaviors and in the expression of personality)

Silverman, D et al. Gastroenterology, 1997; 112: 62-72.

Small Intestinal Bacterial Overgrowth and IBS

- Original study: 78% of IBS pts had SIBO using Lactose hydrogen breath test
- Three subsequent studies using same criteria found incidence < 17%
- Studies do not demonstrate a strong correlation between symptom improvement and normalization of the hydrogen breath test
- The evidence that SIBO is responsible for IBS symptoms remains highly controversial

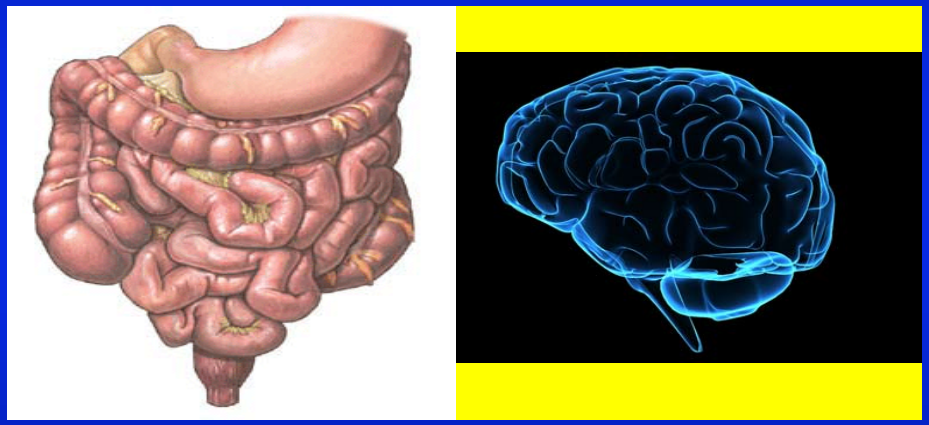
Pimental, M et al. Am J Gastroenterol 2000
Posserud, I et al. Gut, 2007

IBS in 2020

Mucosal inflammation

Altered serotonin signaling

Genetics



Psychosocial stress

CRF

Central Processing

Pain Perception

IBS

Why is IBS important?

- Most common diagnosis in gastroenterology
- Affects 20% of the general population
- Annual direct healthcare cost of $8 billion
- Annual indirect costs of up to $30 billion
- Second-highest cause of work absenteeism after the common cold
- May account for up to 50% of GI appointments

How do you establish a diagnosis of IBS?

- Identification of symptoms consistent with the disorder
- Exclusion of other conditions with similar symptoms in a cost-effective manner

Supportive diagnoses

- Association with other non-gastrointestinal diseases
  - Fibromyalgia (between 20% and 50%; lifetime 77%)
  - Chronic fatigue syndrome (51%; lifetime 92%)
  - Chronic pelvic pain (50%)
- Frequent non-gastrointestinal symptoms
  - Lethargy (36% - 63%)
  - Headache (23% - 45%)
  - Backache (27% - 81%)
  - Myalgia (29% - 36%)
  - Urinary symptoms (21% - 61%)

Sperber AD. Am J Gastroenterol 2000; 95: 995-8.
Whitehead WE. Gastroenterology 2002; 122: 1140-56.
Walker EA. J Psychosom Obstet Gynaecol 1996; 17: 39-46.

Supportive diagnoses

- Psychiatric diagnoses
  - Approximately 70% of IBS patients have an associated psychiatric disorder
    - Anxiety
    - Depression
  - Not just in patients referred to tertiary centers (where prevalence may be as high as 94% lifetime)
  - Hypochondriasis & somatisation also reported

Locke GR. Aliment Pharmacol Ther 2004; 19: 1025-31.
Whitehead WE. Gastroenterology 2002; 122: 114-56.
Spiller R. Gut 2007; 56: 1770-98.

Alarm Features in IBS

- Age > 50 years
- Short history of symptoms
- Documented weight loss
- Nocturnal symptoms
- Fevers, chills, recent travel to endemic regions
- Severe unrelenting large-volume diarrhea
- Family history of colon cancer
- Bleeding
- Recent antibiotic use
- Abnormal physical exam findings

What investigation is necessary?

- Laboratory analysis:
  - Complete blood count with differential
  - Routine chemistry panel
  - Sedimentation rate and C-reactive protein
  - Antibody testing for celiac disease (total IgA, TTG Ab)
  - Stool for occult blood (AGA recommendations only)
  - Things to consider for diarrhea predominant:
    - Colon biopsies if doing a colonoscopy for other reasons
    - Breath tests to exclude lactose/fructose intolerance

Drossman DA. Gastroenterology 2002; 123: 2108-31.
Brandt LJ. Am J Gastroenterol 2002; 97: S7-26.
Spiller R. Gut 2007; 56: 1770-98.
National Institute for Health and Clinical Excellence. 2008. www.nice.org.uk/CG061

What investigation is not necessary?

- According to the guidelines:
  - Flexible sigmoidoscopy/colonoscopy (unless over age 50)
  - Barium enema
  - Fecal occult blood tests (except AGA)
  - Stool tests for ova/parasites (AGA&BSG ambivalent)
  - Thyroid function tests
- In the absence of alarm features . . .

Drossman DA. Gastroenterology 2002; 123: 2108-31.
Brandt LJ. Am J Gastroenterol 2002; 97: S7-26.
Spiller R. Gut 2007; 56: 1770-98.
National Institute for Health and Clinical Excellence. 2008. www.nice.org.uk/CG061

Recommendations from the ACG Task Force on IBS

- CBC, chemistries, thyroid studies, stool for ova/parasites, abdominal imaging not recommended
- Celiac serologies should be pursued if diarrhea-predominant or mixed subtypes
- Colonoscopy if over 50; if colonoscopy done and pt has diarrhea-predominance, then biopsies should be taken
- Consider breath tests if diarrhea-predominant
- In the absence of alarm features . . .

Alarm Features in IBS

- How frequent do we see alarm features?
  - In a study of 1434 patients with a clinical diagnosis of IBS
    - 84% had at least 1 alarm feature
    - The average patient had 1.7 alarm features
    - Positive predictive value of alarm features was 9%
  - Guidelines of the British Society of Gastroenterology also list male sex as an alarm feature

Whitehead WE. Aliment Pharmacol Ther 2006; 24: 137-146.
Spiller R. Gut 2007; 56: 1770-98.

How do I diagnose IBS?

- Abdominal pain or discomfort with altered defecation
- Prominent bloating
- Association with stress or comorbid conditions
- Absence of alarm signs or (more often) negative diagnostic work-up

Treatment of IBS

- IBS is a chronic condition with no known cure but most patients can significantly improve their quality of life with treatment
- Treatment should be directed to
  - Relief of symptoms
  - Addressing the patient's concerns

Principles of Treatment

- Therapeutic relationship
- Patient education
- Dietary modification
- Psychosocial therapies
- Alternative & complementary therapies
- Medications

Therapeutic Relationship

- Establishing a therapeutic provider-patient relationship may be the most important principle of treatment
- Goals
  - Non-judgmental
  - Establish limits
  - Involve patient in decision-making process
- Patient with an established therapeutic relationship have fewer IBS-related follow-up visits

Owens DM. Ann Intern Med 1995; 122: 107-112.

Patient Education

- Validates the patient's illness
- Sets the basis for therapeutic interventions
- Goals of education
  - Chronic and benign nature
  - Diagnosis once established is unlikely to change
  - Normal life-span
- In a 29-year follow-up study done by Mayo only 10 of 112 patients developed an organic GI disease and patient survival was identical to expected survival

Owens DM. Ann Intern Med 1995; 122: 107-112.

Dietary Management of IBS

- Caffeine is a colonic stimulant
- Physiologic gas production may induce symptoms
  - Carbohydrate malabsorption
    - Lactose, fructose, raffinose, sorbitol, etc.
  - Foods rich in fiber
  - Fat-laden foods

Lactose malabsorption: A Common IBS Symptom Trigger

- 70% of adults worldwide have lactase deficiency
- Lactase deficiency before ages 2-3 is very uncommon, regardless of ethnicity
- Consider lactose hydrogen breath test to diagnose

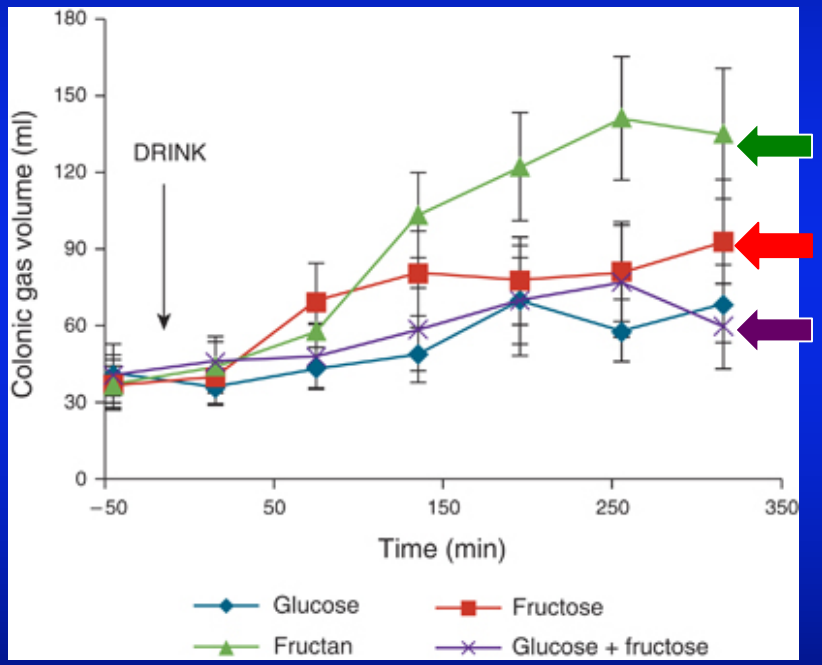
Heyman, MB, et al. Pediatrics, 2006. 118:1279 -1286

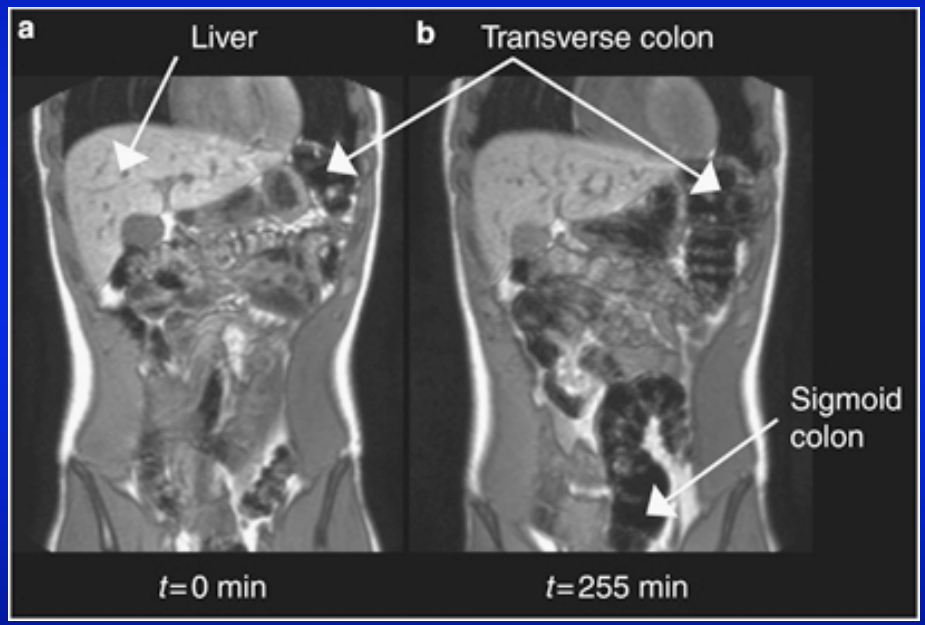
Fructose malabsorption: an IBS symptom exacerbator

- Typical American Diet contains > 100 gms fructose
- Malabsorption of 50 gms of fructose can be detected in up to 80% of healthy adults
- Malabsorbed fructose is fermented by colonic flora to produce gas

Choi YK, et al. J. Clin Gastroenterol. 2008, 42:233-238.

40 gms fructose or fructan increase colonic gas and distention





Murray, K, et al. Am J Gastroenterol 2014; 109:110–11

The low FODMAPs diet

- **F**ermentable **O**ligo-, **D**i- and **M**onosacharides **A**nd **P**olyols (FODMAPs)
- FODMAPs include: fructose, lactose, sugar alcohols (sorbitol, maltitol, mannitol, xylitol and isomaltose), fructans and galactans
- Restriction of FODMAP-rich food items should be individualized

El-Salhy, M. et al. Int J Mol Med. 2012;29:723-31

Low FODMAPs diet for IBS

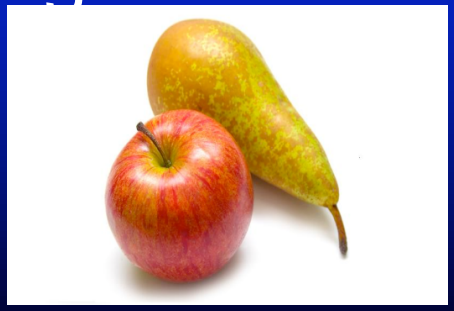
Fermentable, Oligo-, Di-, Mono-saccharides and Polyols

Table 3
Foods rich in FODMAPs by category

FODMAP	Fructose	Polyols	Lactose	Fructans and Galactans
High FODMAP food sources	Apples, pears, watermelon, honey, fruit juices, dried fruits, high-fructose corn syrup	Sugar alcohols (sorbitol, maltitol, mannitol, xylitol, and isomalt), stone fruits, avocado, mushrooms, cauliflower	Milk (cow, goat, sheep), yogurt, soft cheeses (ricotta, cottage)	Wheat, rye, garlic, onions, artichokes, asparagus, inulin, soy, leeks, legumes, lentils, cabbage, Brussels sprouts, broccoli
Alternative lower FODMAP food sources	Citrus, berries, bananas, grapes, honeydew, cantaloupe, kiwifruit	Sweeteners, such as sugar, glucose, other artificial sweeteners not ending in "-ol" (sucralose, aspartame)	Lactose-free dairy products, rice milk, hard cheeses	Starches, such as rice, corn, potato, quinoa. Vegetables, such as winter squash, lettuce, spinach, cucumbers, bell peppers, green beans, tomato, eggplant

All nonprocessed meats are generally low in FODMAPs.

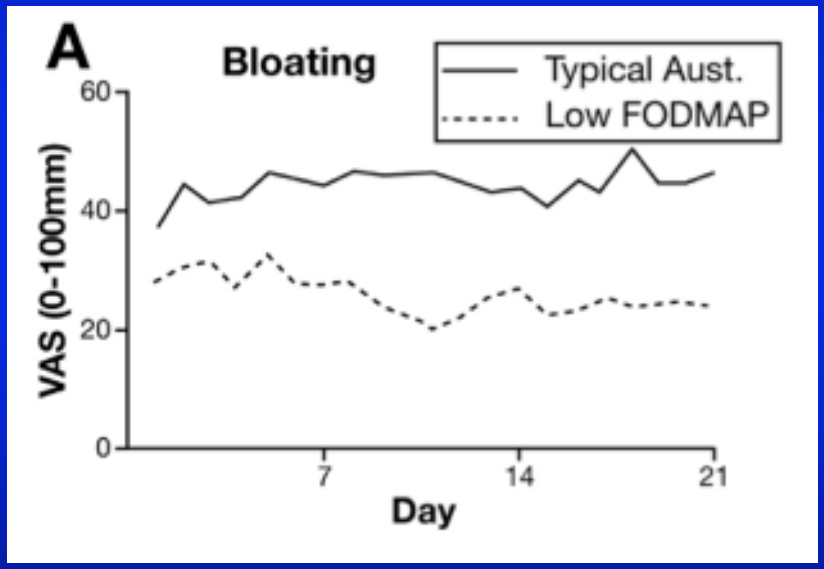
High FODMAPs

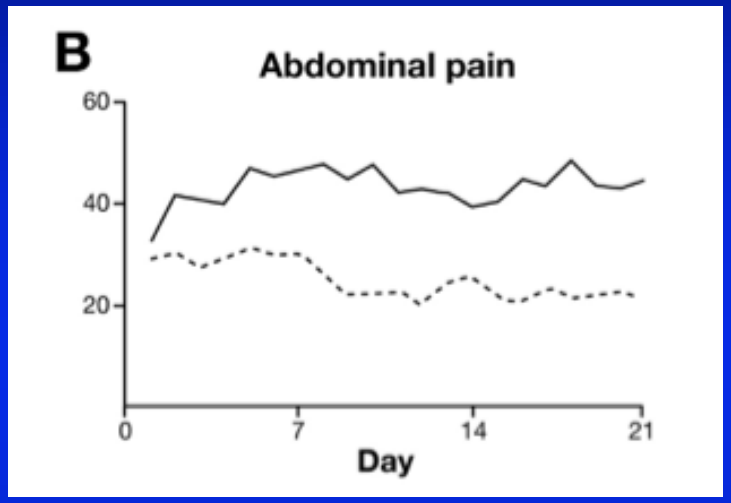


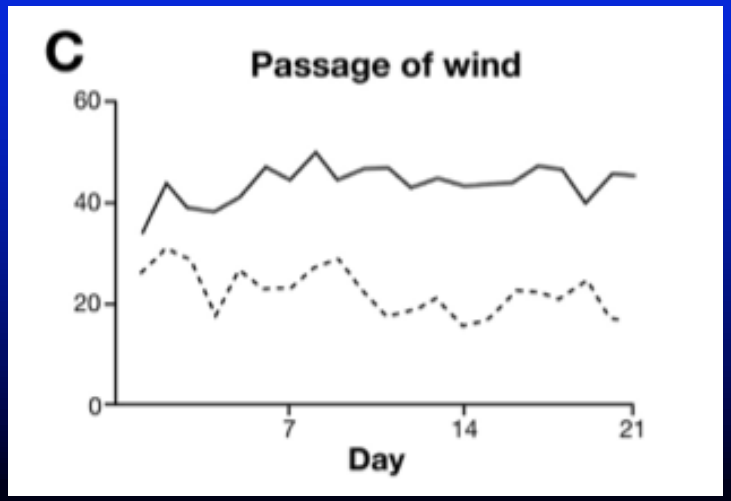
Low FODMAPs

Eswaran, S et al. Gastroenterol Clin N Am 40 (2011) 141–162.

Low FODMAPs diet improves IBS symptoms







Halmos, EP, et al. Gastroenterology, 2014;146(1):67-75

Psychosocial Therapies

- Behavioral therapies may work for selected, motivated patients who associated symptoms with particular stressors
  - Hypnosis
  - Biofeedback
  - Psychotherapy
  - Exercise
- A systematic review of 16 studies found this approach more effective than placebo

Brandt LJ. Am J Gastroenterol 2002; 97: S7-26.

Physical Activity Improves Symptoms in Irritable Bowel Syndrome: A Randomized Controlled Trial

Elisabet Johannesson[1], Magnus Simrén[1], Hans Strid, MD, PhD[1], Antal Bajor, MD, PhD[1] and Riadh Sadik, MD, PhD[1]

Am J Gastroenterol 2011

Medications

- Adjunct to therapy
- Choice of drugs tailored to symptoms
- Chronic use of medications should be minimized
  - Unclear long-term data regarding benefits
  - Lifelong nature of illness

IBS: Pharmacotherapy

FDA Approved for IBS

- Alosetron (IBS-D) 2000
  - relieves pain, improves bowel function, and provides global symptom improvement in women
- Tegaserod (IBS-C) 2002
  - modestly improves global relief of symptoms score, may not improve pain or discomfort; requires IND, emergency use only
- Lubiprostone(IBS-C) 2006
  - Improves global relief of symptoms score
- Linaclotide (IBS-C) 2012
  - Guanylate cyclase agonist
  - Improves abdominal pain and the number of spontaneous bowel movements
- Rifaximin (IBS-D/M) 2015
  - Antibiotic
  - Improves diarrhea and global symptom scores

Not FDA APPROVED FOR IBS

- Antispasmodics
- Laxatives
- Anti-diarrheals
- Anti-depressants

Complementary Therapies

- Melatonin
- Herbal therapy
- Probiotics
- Elimination diets
- Peppermint

Melatonin

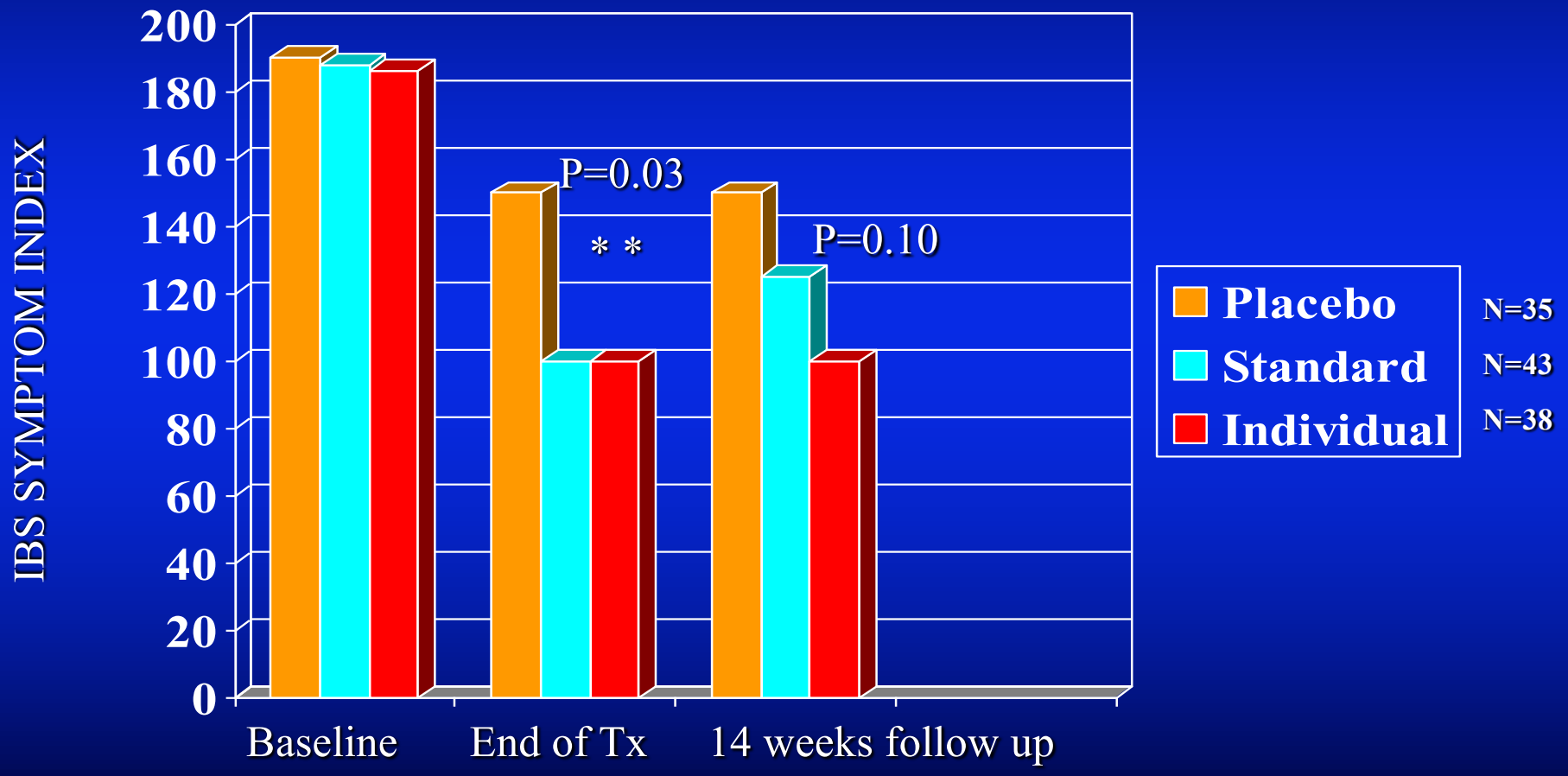
- Implicated in regulation of gut motility and sensation
- Promising results in small randomized placebo-controlled trials
- Given at a dose of 3mg at bedtime for 2-8 weeks
- Improved global IBS scores, abdominal pain
- Too little data to recommend for routine use

Song GH. Gut 2005; 54: 1402-7.

Lu WZ. Aliment Pharmacol Ther 2005; 22: 927-34.

Saha L. J Clin Gastroenterol 2007; 41: 29-32.

Treatment of irritable bowel syndrome with Chinese herbal medicine.



Bensoussan A. JAMA 1998 280: 1585-1589

What is Chinese herbal medicine?

Table 2.—Standard Formula (Capsule Ingredients)*

Chinese Name	Pharmaceutical Name	Powdered Herb, %
Dang Shen	*Codonopsis pilosulae*, radix	7
Huo Xiang	*Agastaches seu pogostemi*, herba	4.5
Fang Feng	*Ledebouriellae sesloidis*, radix	3
Yi Yi Ren	*Coicis lachryma-jobi*, semen	7
Chai Hu	*Bupleurum chinense*	4.5
Yin Chen	*Artemesiae capillaris*, herba	13
Bai Zhu	*Atractylodis macrocephalae*, rhizoma	9
Hou Po	*Magnoliae officinalis*, cortex	4.5
Chen Pi	*Citri reticulatae*, pericarpium	3
Pao Jiang	*Zingiberis offinicinalis*, rhizoma	4.5
Qin Pi	*Fraxini*, cortex	4.5
Fu Ling	*Poriae cocos*, sclerotium (Hoelen)	4.5
Bai Zhi	*Angelicae dahuricae*, radix	2
Che Qian Zi	*Plantaginis*, semen	4.5
Huang Bai	*Phellodendri*, cortex	4.5
Zhi Gan Cao	*Glycyrrhizae uralensis*, radix	4.5
Bai Shao	*Paeoniae lactiflorae*, radix	3
Mu Xiang	*Saussureae seu vladimirae*, radix	3
Huang Lian	*Coptidis*, rhizoma	3
Wu Wei Zi	*Schisandrae*, fructus	7

*Pharmaceutical terminology from Hsu.[18]

Table 2.—Standard Formula (Capsule Ingredients)*

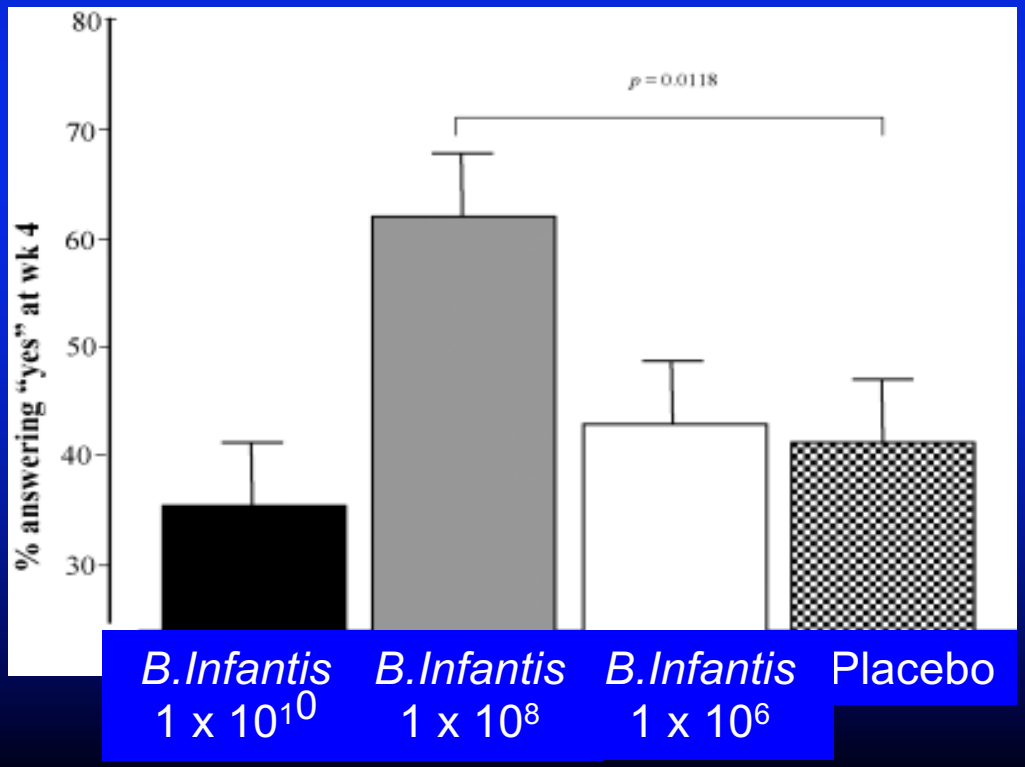
Bensoussan A. JAMA 1998 280: 1585-1589

Probiotics

- Hypothesis
  - Gut flora produce gas and malabsorption
  - Replacement of bad bacteria with good bacteria that produces less gas will result in less symptoms

Probiotics and IBS

- Largest study: 362 women with IBS randomized to
  1×10^6, 1×10^8, and 1×10^{10} CFU/ml of *Bifidobacterium infantis 35624* or placebo x 4 weeks



Elimination Diets

- Hypothesis: Antibody response to certain foods may be trigger for IBS symptoms
- Elimination diet for 2 weeks
  - Dairy (lactose)
  - Wheat (gluten)
  - High-fructose corn syrup
  - Sorbitol (chewing gum)
  - Eggs
  - Nuts
  - Shellfish
  - Soybeans
  - Beef
  - Pork
  - Lamb
- Data: One study suggested 26% greater improvement with elimination diet versus control elimination diet

Atkinson W. Gut 2004; 53: 1459-64.

Peppermint

- Hypothesis: smooth muscle relaxant that may reduce cramping and pain associated with IBS
- Three systematic reviews:
  - #1: Reviewed 5 double-blind trials, trend towards benefit.
  - #2: Modest benefit of peppermint oil over placebo
  - #3: Reviewed 16 trials, 58% response rate for peppermint versus 29% for placebo
- Enteric-coated formulations recommended because it dissolves in the lower GI tract and may reduce the risk fo reflux
- Common dosage: 0.2-0.4 mL 0.3 times daily
- Over-the-counter

My Approach To Treatment

- Build a provider-patient relationship
- Educate the patient regarding IBS
- Dietary avoidance and stress relief measures
- Fiber trial if bloating is not prominent
- Alternative agents in selected patients
- Medications only when pushed

Constipation

Constipation

- The most common GI complaint
- Affects 20% of adults in North America
- Prevalence increases with age, especially > 65
- Over 2.5 million people consult a physician in North America annually
- Over $800 million per year are spent on laxatives in the U.S. alone

Constipation

- Symptom not a disease
- Unsatisfactory defecation characterized by
  - Infrequent stool
  - Difficult stool passage
- Formal criteria established by international working committee (Rome IV)

Rome Criteria for Constipation

- Must include 2 or more of the following in at least 25% of bowel movements:
  - Straining
  - Lumpy or hard stools
  - Sensation of incomplete evacuation
  - Sensation of anorectal obstruction
  - Manual maneuvers
  - Fewer than 3 BM per week
- Loose stools are rarely present without laxatives
- Insufficient criteria for IBS

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a 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**

Constipation

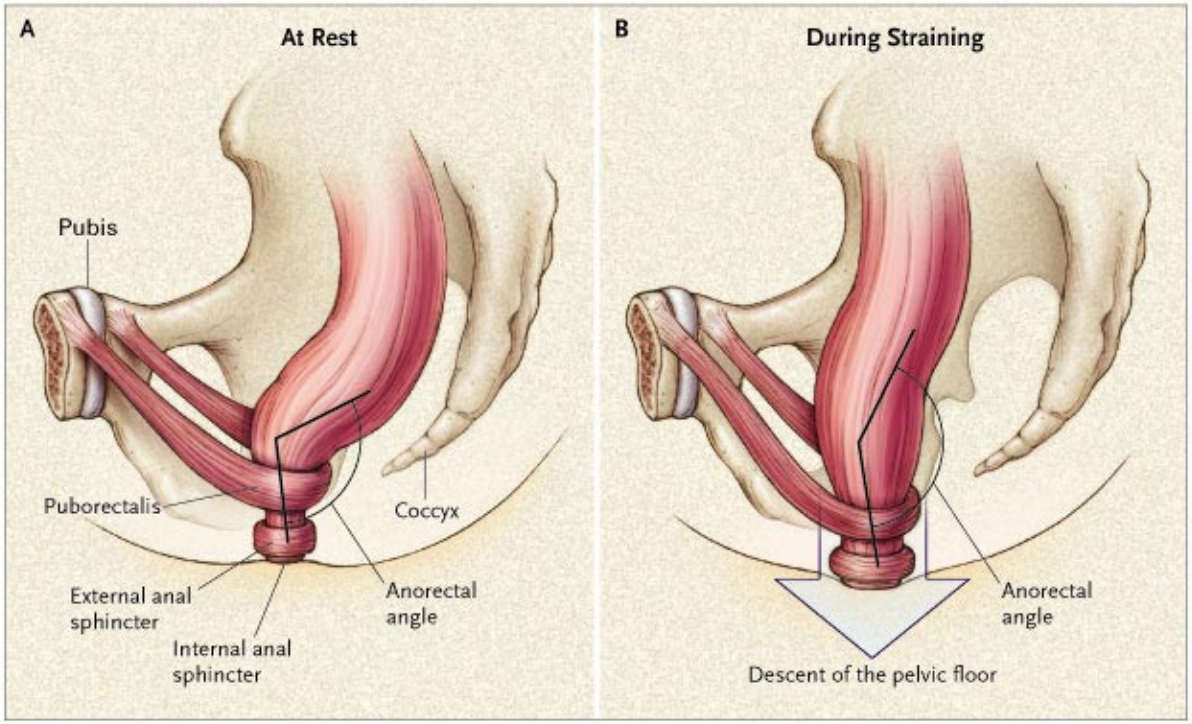
- Key points with classification
  - Symptom not disease
  - Not based entirely on frequency of bowel movements

Colon

- Function
  - Absorb excess fluid
  - Salvage unabsorbed nutrients via bacteria
  - Permit defecation to occur
- Motility
  - Intermittent short segmental to-and-fro patterns to induce mixing
  - Followed by relative quiescent periods for storage
  - Intermittent high amplitude peristaltic contractions (HAPC) to promote defecation (on average 5 per day)
  - Colon transit time 36 hours

Anorectum

- Functions to store & eliminate feces
- Storage
  - Rectum acts as storage reservoir
  - Tonic contraction of puborectalis, internal & external anal sphincters
- Defecation
  - Puborectalis relaxation with opening of internal & external anal sphincters
  - Response to voluntary defecation or increased rectal pressure


A
At Rest
Pubis
Puborectalis
Coccyx
External anal sphincter
Internal anal sphincter
Anorectal angle
B
During Straining
Anorectal angle
Descent of the pelvic floor

Etiology of constipation

- Common causes
  - Drugs
  - Neurologic
  - Irritable Bowel Syndrome
  - Non-neurologic disorders
  - Idiopathic

Clinical subcategories

- Normal transit (IBS-C)
- Slow transit
- Functional outlet obstruction

Normal transit constipation

- Synonymous with IBS-C
- Most common subcategory
- Also referred to as functional constipation
  - May misperceive bowel frequency
  - Exhibit increased psychosocial distress

Slow transit constipation

- Small subset (10%)
- Infrequent bowel movements
- Delayed transit on testing
- Motility testing
  - Alterations in numbers of neurons and ICC
  - Delayed emptying of proximal colon and fewer HAPCs
- Important to separate as this group may respond to certain medications, decreased fiber and colectomy

Functional outlet obstruction

- Inability to extrude formed stool from the rectum
  - Failure to coordinate relaxation of striated muscles
  - Weak expulsive forces
  - Misdirection of expulsive forces (such as with a large rectocele)
- Seen in approximately 15% of patients with chronic constipation
- Up to 50% of referrals to tertiary facilities
- Important to separate as will not respond to laxatives & responds to:
  - Biofeedback
  - Botox
  - Surgery

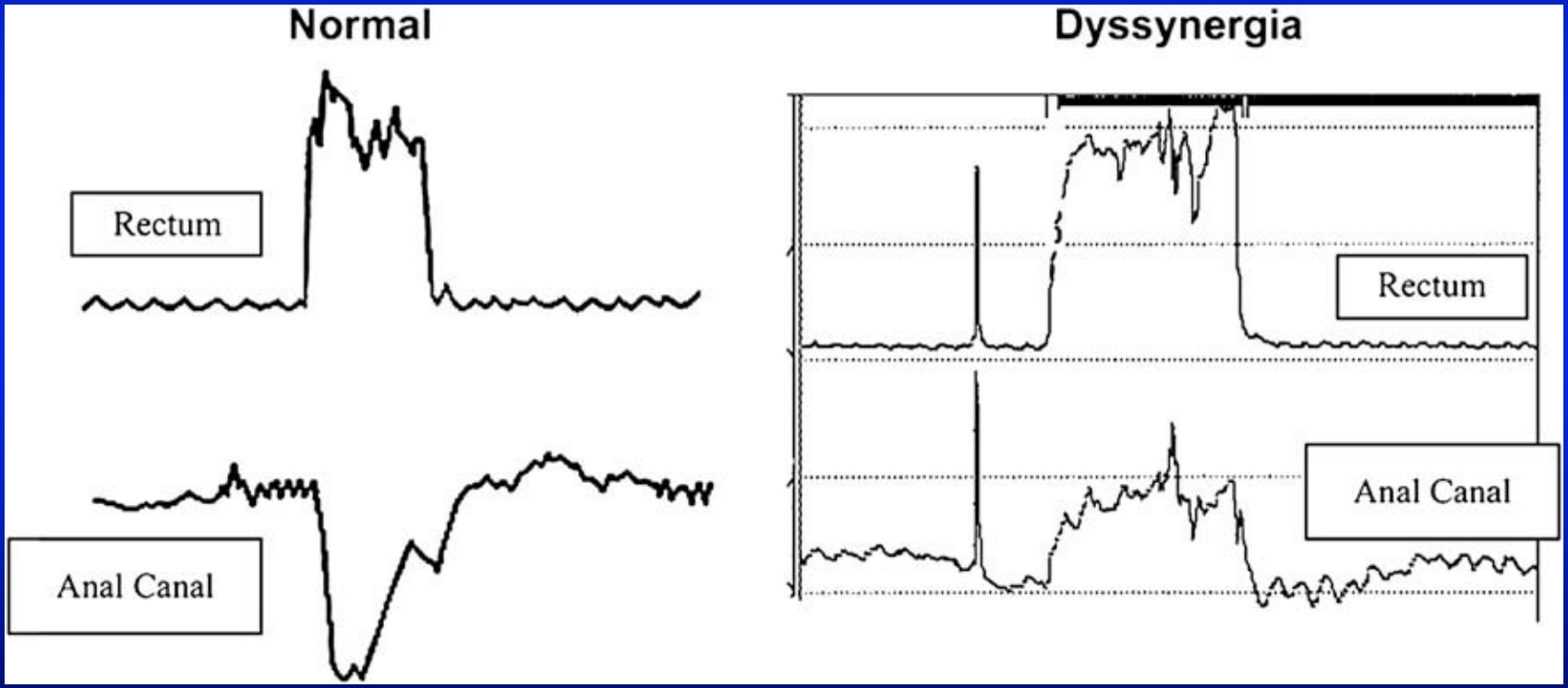
Clinical Approach to Constipation

- History & physical exam (with rectal) first
- Empiric treatment reasonable if no alarm symptoms
- If alarm symptoms or age > 50, colonoscopy
- If no improvement with treatment, recommend
  - Anorectal manometry with balloon expulsion
  - Sitz marker study or Smartpill

Anorectal Manometry

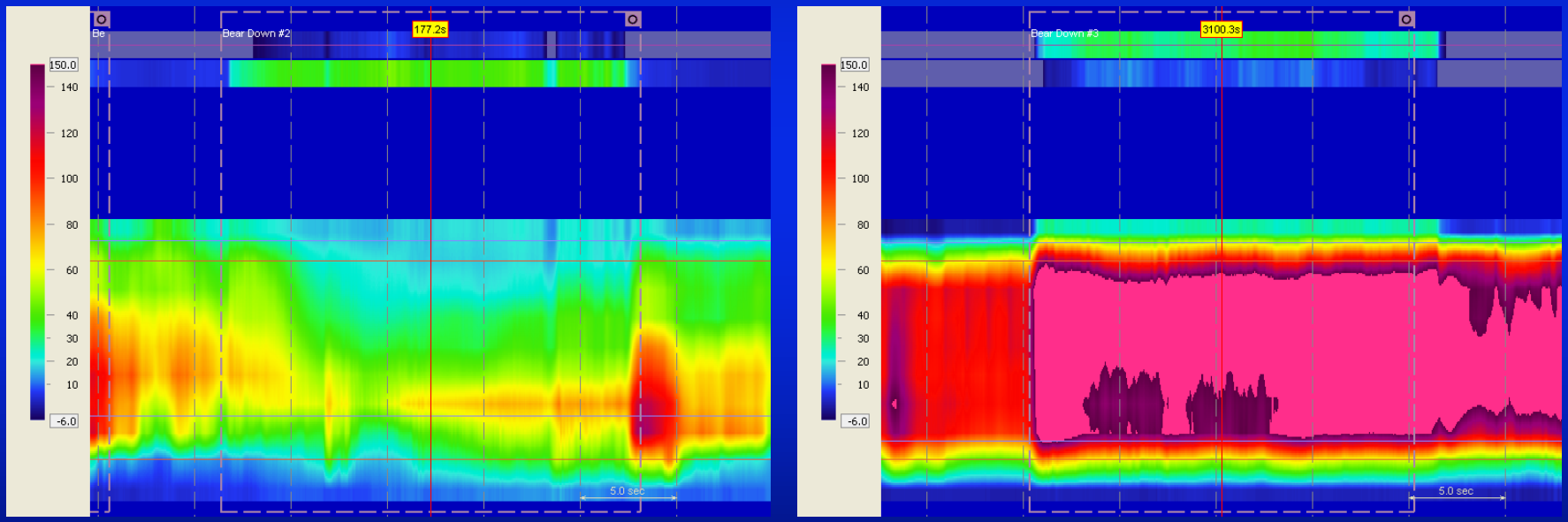
- Catheter inserted in rectum with sensors across sphincter and in rectum
- Allows assessment of:
  - Resting sphincter dynamics
  - Augmentation of sphincter pressure with squeezing
  - Sphincter relaxation with bearing down
  - Intrarectal sensation
  - Rectoanal inhibitory reflex

Anorectal Manometry



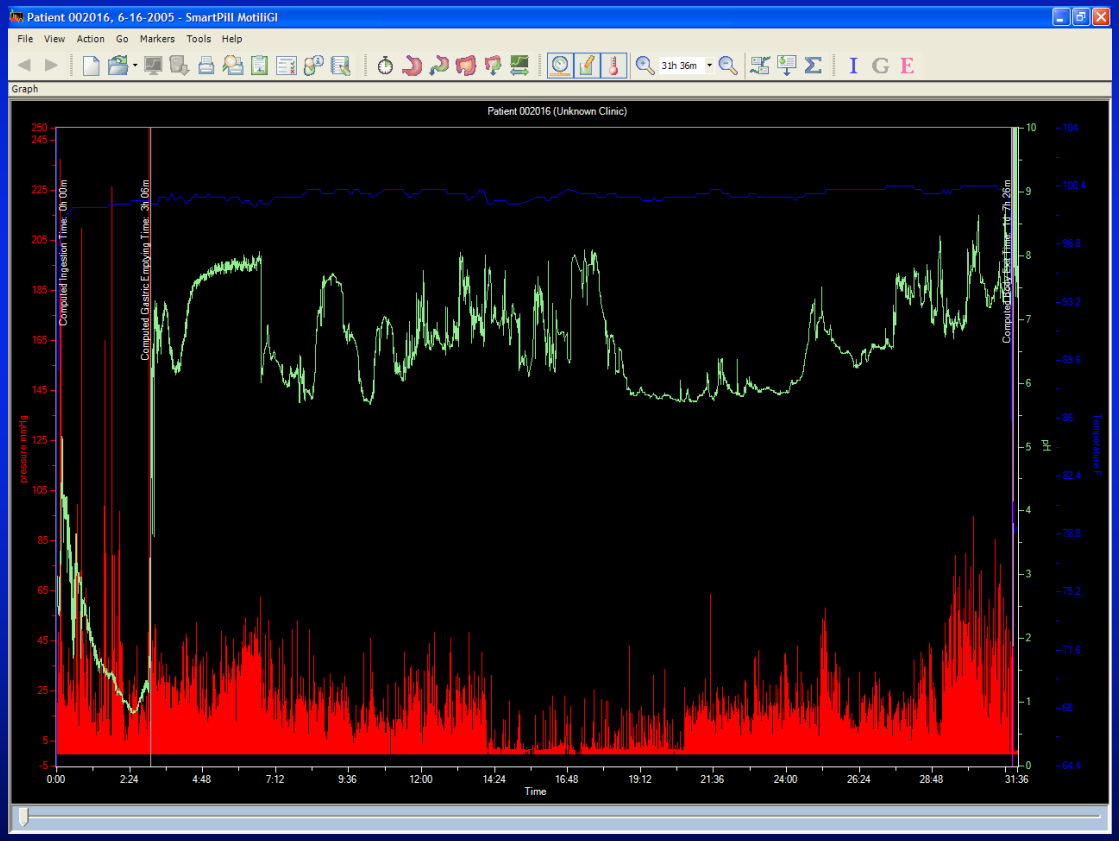
Rao SS. Gastrointest Endosc Clin N Am. 2009

Anorectal Manometry



Sitz markers

Wireless capsule motility

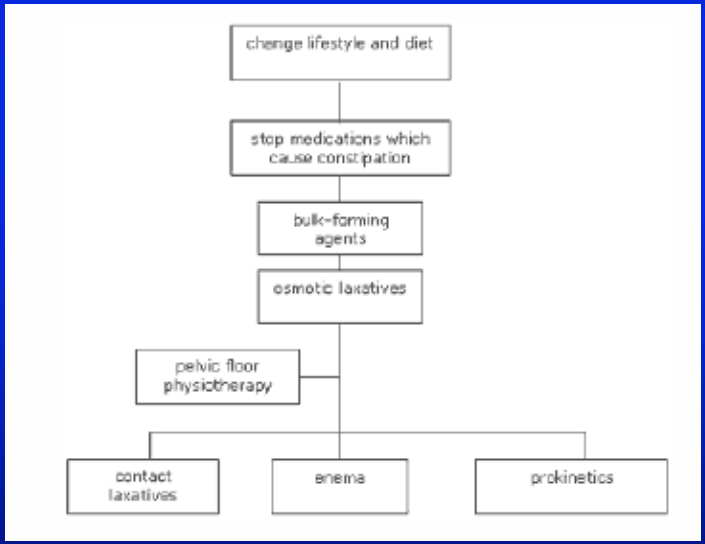


Smartpill

Treatment of constipation

- Initial management
  - Patient education
  - Dietary changes
  - Bulk-forming laxatives
  - Non-bulk forming laxatives or enemas
- Most of these agents are available over the counter

Overview of treatment



World Gastroenterology Organisation Practice Guidelines 2007

Patient education

- Increase fluid intake
- Increase fiber intake
- Defecation early in morning or after meals
- Reduce dependency on laxatives

Fiber

- Increased fiber intake is the initial treatment
  - Available in a large variety of supplements and foods
  - Low cost/easy to use/safe
  - Fiber consists of cell walls that resist digestion and maintain water – increasing stool mass/bulk
  - Important to consume water with fiber
  - Can be associated with bloating
  - Recommended daily amount is 20-35 g/day

Other specific foods

- Prunes (dried plums)
  - Used traditionally for constipation
  - No good medical trials until this decade
  - Recent study by Rao and colleagues compared prunes to psyllium
    - 50grams twice daily with meals x 3 weeks (about 12 dried plums)
    - Increase from 1.8 to 3.5 BM per week
    - Prunes were more effective than psyllium & more palatable

Attaluri A. Aliment Pharmacol Ther 2011

Bulk-forming laxatives

- Concept: fiber to bulk up fecal mass
- Types:
  - Psyllium (up to 1 tbsp TID, onset 12-72h)
  - Methylcellulose (up to 1 tbsp or 4 caps TID, onset 12-72h)
  - Polycarbophil (up to 2-4 tabs per day, onset 24-48h)
  - Wheat dextrin (up to 1-3 caps or 2 tsp TID, onset 24-48h)
- Side effects: gas/bloating, impaction above stricture, fluid overload
- Recommended as first-line therapy and anecdotal data; however, objective data is very limited

Non-bulk forming laxatives

- Surfactants
- Osmostic agents
- Stimulant laxatives

Surfactants

- Docusate (Colace)
  - Lower surface tension of stool allowing more water to enter
  - Few side effects
  - Little evidence to support use
  - Recent systematic review concluded docusate inferior to psyllium

Osmotic agents

- Concept: increase intestinal water secretion and stool frequency
- Commonly used agents
  - Polyethylene glycol (PEG/Miralax/Glycolax)
  - Poorly absorbed or nonabsorbable sugars (lactulose)
  - Saline laxatives (Natural Calm, magnesium citrate)

Polyethylene Glycol

- Available as electrolyte solutions (GoLytely) and powdered preparations without electrolytes (MiraLax)
- Systematic review found evidence that PEG is effective in improving both stool frequency and consistency
- Start with 17g dissolved in 8oz of water daily and titrated up or down (max dose 68g/day)
- No need to do more than once daily unless patient cannot drink associated volume
- If not successful, would continue 17g daily and add stimulant laxative every 2-3 days as needed

ACG Chronic Constipation Task Force. Am J Gastroenterol 2005

Nonabsorbable sugars

- Lactulose most commonly used
  - Not metabolized by digestive enzymes, keeping water/electrolytes within lumen due to osmotic effect
  - Requires 24-48 hrs
- Sorbitol is equally effective/less expensive
- Both found to be effective in systematic review
- Both associated with abdominal pain/bloating
- Per 2010 Cochrane review, PEG is more effective than lactulose

Saline laxatives

- Poorly absorbed agents that act as hyperosmolar solutions, leading to intestinal fluid secretion
- Milk of magnesia & magnesium citrate are most commonly used
- Renal failure is major complication
- Natural Calm is a favorite among my patients

Stimulant laxatives

- Effects:
  - Increase intestinal motor activity
  - Alteration of electrolyte transport by intestinal mucosa
- Common examples:
  - Bisacodyl (some forms of Dulcolax)
  - Senna (Senokot)
  - Sodium picosulfate (Dulcolax drops)
- Shown to be effective in recent RCT versus placebo
- Daily ingestion can be associated with hypokalemia, protein-losing enteropathy & salt overload – should be used cautiously
- No convincing evidence that chronic use leads to either structural/functional colon impairment or tumors

Mueller-Lissner S. Am J Gastroenterol 2010

Prescription therapy

- If initial attempts fail and there is no evidence of dyssynergy, other agents in use:
  - Lubiprostone (Amitiza)
  - Linaclotide (Linzess)
  - Methylnaltrexone (Relistor)
  - Plecanatide (Trulance)
  - Prucalopride (Motegrity)

Biofeedback

- Studied extensively in dyssynergy
- Goals:
  - Improve coordination of pelvic muscles
  - Enhance rectal sensation
- Duration: 4-6 sessions every 2 weeks
- Data:
  - 5 randomized controlled trials
  - All show improvement between 70-80%
  - Recently looked at patients referred for community biofeedback – results 60%

Acupuncture

Table 1: Articles of acupuncture or EA for CC.

Reference	Study design (participants)	Acupoints	Implementation of acupuncture	Key efficacy results	Adverse reactions
Wu et al., 2014 [14]	RCT (n = 104) adult	ST25, BL25, LI11, ST37	EA1: ST25, BL25 EA2: LI11, ST37 EA3: ST25, BL25, LI11, ST37 C: Mosapride citrate	Weekly frequency of defecation, defecation difficulty life, and quality score were all improved significantly in the four groups; in follow-up, weekly frequency of defecation of LI11 and ST37 (EA2) was superior to the other three groups	NA
Zhang et al., 2013 [15]	RCT (n = 553) adult	ST25, ST37, ST36, BL25, TE6	EA: 2 Hz/200 Hz D: Fuzhengliqi mixture EA + D: both of above C: Mosapride and Macrogol 4000	All groups decreased the defecation interval, stool property, constipation symptom grade, accompanying symptom grade, and GITT; EA + D was better than others; EA could keep long-term effect	No
Peng et al., 2013 [16]	RCT (n = 128) adult	ST25	EA-deep: 20 to 65 mm in depth EA-shallow: 5–8 mm depth D: lactulose oral liquid	All groups increased the weekly defecation frequency, EA-deep could keep long-term effect	No
Chen et al., 2013 [17]	RCT (n = NA) adult female	ST36, ST37, ST25, ST28, CV4, CV6	EA Sham-EA	EA improved constipation symptoms and increased autonomic nervous system activities, sham-EA not	NA
Zhou et al., 2012 [18]	RCT (n = 200) elder	AT3, 4i, AT3, AT4, CO7, CO7, AH8, CO18, Constipation Point	AT: according to the pattern/syndrome differentiation C: solid points	The effective rate: AT 92.0%, C 76.0%	NA
Xu et al., 2012 [19]	RCT (n = 64) adult	TE6, ST25, ST36, ST37	EA: Hwato neuro and muscle stimulator C: regular electronic stimulator	The effective rate of short term: EA 54.6%, C 29.0%	NA
Anders et al., 2012 [20]	Retrospective case series study (n = 10) children	Quchi (LI11)	Fixed indwelling acupuncture needles (0.9 mm in length)	After a median of 3 days of HIC, all children defecated within 2 h. Local constipation therapy was not required	No
L.-J. Wang and L.-L. Wang, 2011 [21]	RCT (n = 100) adult	Group 1: ST25, SP15, CV6, CV4, ST36, ST37, SP6. Group 2: BL33, BL34, BL5, BL23, BL20 Alternatively	HA: punctured by hands HA + moxibustion: grain-shaped moxibustion was given at CV6, ST36, BL25, BL20, and others with puncture	The total effective rate HA + moxibustion as 74.0% (37/50) versus 52.0% (26/50)	NA
Guo et al., 2011 [22]	RCT (n = 378) adult	ST25, ST37, ST36, BL25, TE6	EA: 2 Hz/100 Hz D: Plantain and Senna Granule EA + D: both of the above	All groups decreased the scores of defecation cycle, stool property, constipation symptom grade, accompanying symptom grade, and GITT; EA + D was better than others; EA and EA + D could keep long-term effect	No
Wang et al., 2010 [23]	RCT (n = 95) adult	ST25	EA-deep: 45 mm in depth EA-shallow: 5 mm in depth D: lactulose oral liquid	EA-deep and EA-shadow were significantly superior to D group in increasing number up to 4 and improved CCS. EA-deep worked faster than EA-shadow	NA
Wang et al., 2010 [24]	RCT (n = 95) adult	ST25	EA-deep EA-shallow D: Duphalac	EA-deep was similar to EA- shallow in number up to 4 and CCS, and its efficacy remained much longer	NA
Jin et al., 2010 [25]	Before-after study (n = 90) adult	Group 1: ST25, CV6, ST37; Group 2: BL33, BL34, BL25 Alternatively	EA: BL33, BL34, ST25, T37	The scores of defecation frequency, difficulty degree of defecation, defecation time, endless sensation of defecation, stool quality, awareness of defecation, and QoL were obviously improved after treatment. The total effective rate was 67.7% (61/90)	NA
Ding et al., 2009 [26]	Before-after study (n = 30) adult	Group 1: ST25, SP15, SP14, CV6, CV 4, ST36, ST37; Group 2: BL25, BL23, BL31, BL32, BL33, BL34, Ex-HN1 Alternatively	Deep needling was applied on acupoints of abdominal and back region and moxibustion was put on Ex-HN1	Reduced laxative, scores for awareness, and QoL. Increased frequency of defecation	No

Wang X . Evidence-Based Complementary and Alternative Medicine 2015

Other Non-Medical Options

- Massage
- Herbal remedies:
  - Bulk (fiber)
  - Stimulant (senna, aloe, rheum officinale, cascara)
  - Herb combinations (Agiolax)
  - Chinese herbal medicine
- SIBO-directed therapy

Conclusion

- Constipation is diagnosed based on symptoms, not a disease per se
- First steps are generally diet & lifestyle modification
- Stimulant & osmotic laxatives generally are the next step
- Multiple non-medical options exist & the number of patients who truly need prescription therapy is likely low

Diarrhea

Diarrhea

- Diarrhea is defined as a stool volume of > 200 ml/24 hours
- It is not medically defined by frequency or consistency of bowel movements, but it is to many patients
- Physiologically, diarrhea occurs when the balance between secretion and absorption in the gut is disrupted

Daily Intestinal Water Balance

Input / 24h	Water (ml)
Oral Intake	2000
Salivary glands	1500
Stomach	2500
Biliary Tract	500
Pancreas	1500
Small Intestine	1000
Total Presented to Intestine	9000
Absorbed	8800
Stool	200
% Absorbed	98

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a 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**

Acute Diarrhea

- 2nd leading cause of death for children < 5 years old worldwide
- 760,000 deaths/annually
- 1.7 billion cases/year globally

Acute Diarrheal Diseases in the US

Illness	Incidence	Direct Costs
Acute gastroenteritis (Non-foodborne)	135,000,000	$2,125,000,000
Foodborne illnesses	76,000,000	$ 886,000,000
TOTAL	211,000,000	$3,011,000,000

Burden of Selected Digestive Diseases in the United States, Gastroenterology 122:1500-1511, 2002

Chronic Diarrheal Disease in the U.S.A.*

	INCIDENCE	DIRECT COSTS
Chronic Diarrhea	3,080,000	$3,507,000,000
Diarrhea associated with Functional GI Disorder (eg IBS)	1,232,000	$ 197,000,000

Burden of Selected Digestive Diseases in the United States, Gastroenterology 122:1500-1511, 2002.

Diarrhea: Categories

Secretory

- Infections
- Inflammatory mediators (prostaglandins)
- GI hormone producing tumors

Osmotic

- Excessive luminal osmotic load leading to retention of water in the intestinal lumen
- Examples:
  - Celiac Disease
  - Lactase deficiency
  - Osmotic laxatives

Disordered Motility

- Leads to accelerated transit and reduced ability of the GI tract to absorb water and nutrients
- Examples:
  - Hyperthyroidism
  - IBS

Chronic diarrhea

- Defined as diarrheal symptoms > 6 weeks
- Secretory vs. Osmotic
- Inflammatory vs. non-inflammatory causes

Differential Diagnosis of Chronic Diarrhea

- **Osmotic**
  - Osmotic laxatives (magnesium, phosphate, sulfate)
  - Carbohydrate malabsorption
- **Inflammatory**
  - Inflammatory bowel disease
  - Infectious diseases
  - Ischemic colitis
  - Radiation colitis
- **Steatorrhea**
- **Small intestinal bacterial overgrowth/dysbiosis**
- **Secretory**
  - Congenital syndromes
  - Bacterial toxins
  - Inflammatory bowel disease
  - Vasculitis
  - Drugs and poisons
  - Laxative abuse
  - Disordered motility or regulation
  - Endocrine diarrhea (hyperthyroidism, hypothyroidism, Addison's disease, gastrinoma, vasoactive intestinal peptide–secreting tumor, somatostatinoma, carcinoid syndrome, medullary thyroid carcinoma, mastocytosis)
  - Other tumors (colon carcinoma, lymphoma, villous adenoma)
  - Bile salt malabsorption

The History: What You Should Ask

- Travel history
- Recent antibiotic use
- Change in medication or dosage
- Stool consistency and volume
  - Since the diarrhea began, have you ever had a formed stool?
- Relationship with eating specific foods, or eating in general?
- History of abdominal trauma
- Is there anything in the history to suggest risk for being immuno-compromised?
- Risk factors for SIBO

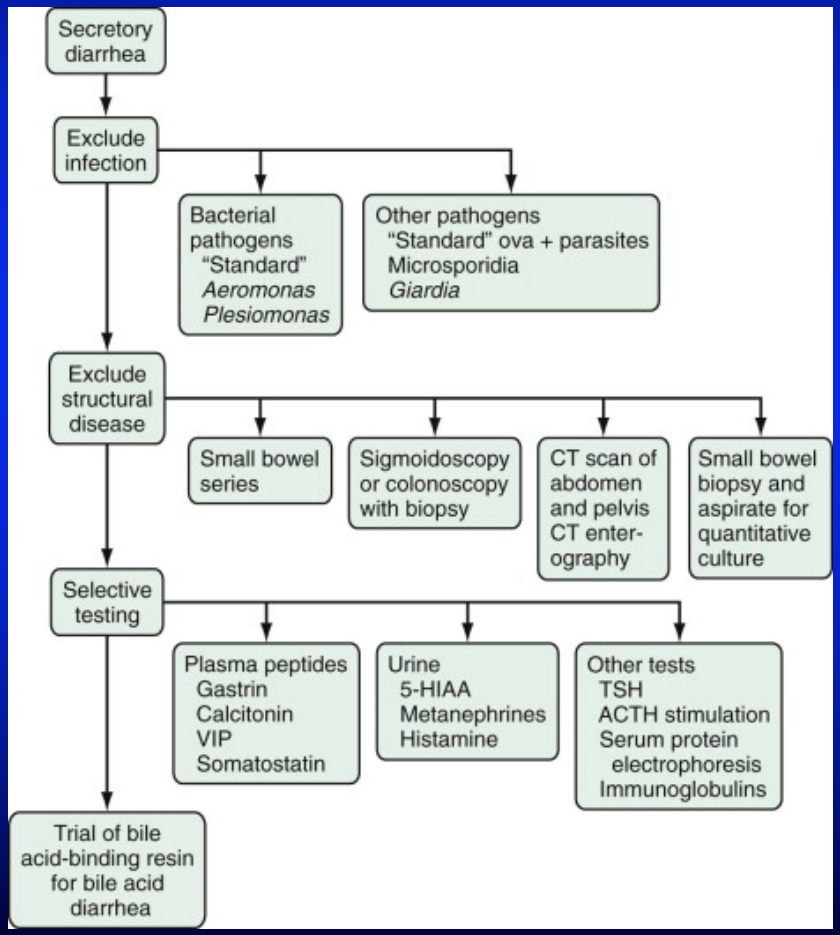
Considerations for Initial Testing

- Stool cultures
- Blood tests
  - CBC
  - Metabolic panel
  - Celiac screen (TTG IgA, Total IgA)
  - Serum amylase/lipase
  - Vitamin B12, methylmalonic acid (malabsorption)
  - Thyroid function tests
- Other tests
  - Fecal pancreatic elastase
  - Fecal leukocytes
- SIBO evaluation

Further Stool Studies if Needed

- Measure stool electrolytes, stool osmolality and stool pH
- Osmotic gap is calculated as follows:
  - Stool osmolality (290 mOsm/kg) - 2 x [Na + K]
    - If < 50 mosm/kg -> secretory diarrhea
    - If > 50 mosm/kg -> osmotic diarrhea
- Measure the actual stool osmolality if you suspect factitious diarrhea: if it is very low, this is suggestive of factitious diarrhea
- Stool pH can help suggest carbohydrate malabsorption if < 6
- Sudan stain/72 hour fecal fat collection can help document steatorrhea
- 24-hour stool collection while fasting may help quantify stool volume while also separating secretory & osmotic causes

Evaluation of Secretory Diarrhea



Courtesy of Linda Lee, MD

Stool pH and carbohydrate malabsorption

- Carbohydrate that reaches the colon is promptly fermented by the bacterial flora, with release of CO_2 and H_2 gases and short-chain fatty acids
- As a result of fermentation, the pH is acidic, usually dropping to less than 6, a finding that indirectly indicates excess carbohydrate fermentation in the colon

Causes of osmotic diarrhea

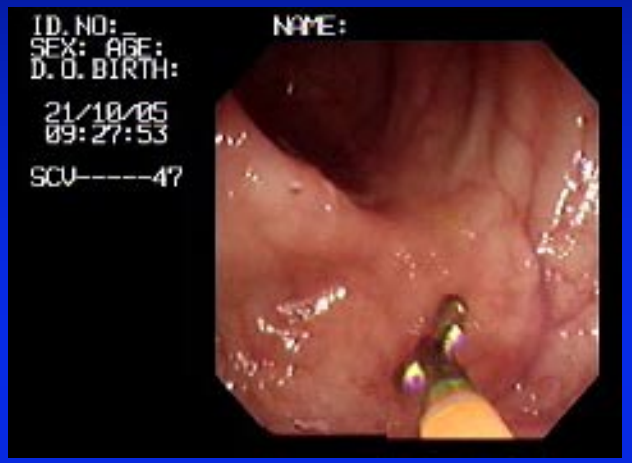
- Carbohydrate malabsorption
- Consumption of poorly absorbed carbohydrates
- Magnesium compounds (e.g. laxative)

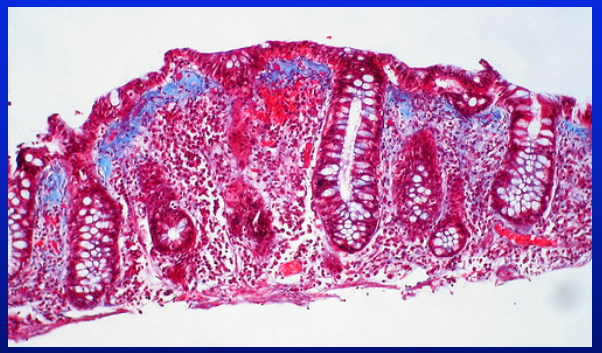
Tests for carbohydrate malabsorption

- Lactose hydrogen breath test
- Fructose hydrogen breath test
- Response to dietary restriction

Endoscopic evaluation for structural disease

- To rule out inflammatory causes of diarrhea when non-invasive testing have not revealed a diagnosis
- Allows the sampling of tissue for histologic analysis





H&E stain, colon biopsy.
Collagenous colitis

Radiologic and Motility Studies for Evaluating Chronic Diarrhea

- Do not allow tissue sampling, but structural findings may be found that reflect active inflammation (eg IBD) or severe dysmotility of intestinal segments

Barium, small bowel series. Jejunal diverticulum (arrow). This may be associated with bacterial overgrowth, leading to malabsorption.

Initial Treatment Options

- Treat underlying cause if known
- Correct underlying fluid/electrolyte imbalances
- If infection is excluded, can start anti-diarrheals

Pharmacologic Therapy for Diarrhea

- Hygroscopic agents
  - Mechanism: absorb excess water
  - Examples: fiber, Kaolin clay and pectin (the original Kaopectate)
- Bile salt binders
  - Mechanism: bind excess bile to avoid colon secretion
  - Example: cholestyramine
- Bismuth compounds
  - Mechanism: unknown but has anti-secretory, anti-inflammatory and anti-microbial properties
  - Example: Peptobismol
- Opioids
  - Mechanism: increase fluid absorption, decrease fluid secretion, decrease motility
  - Examples: loperamide (Imodium), tincture of Opium
- SIBO treatment (probiotics, herbal therapy, antibiotics)

Other Non-Medical Options to Consider

- Zinc
- Glutamine
- Partially hydrolyzed guar gum (PHGG)
- Probiotics/SIBO therapy
- Chinese herbs
- Acupuncture

Mittra D. Pediatr Rev 2008

Thank you!