MYOTONIC DYSTROPHY FOUNDATION

Care and a Cure

2018

MDF ANNUAL CONFERENCE

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GUT INSTINCTS: GI SYMPTOM MANAGEMENT

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Stanford MEDICINE

Overview

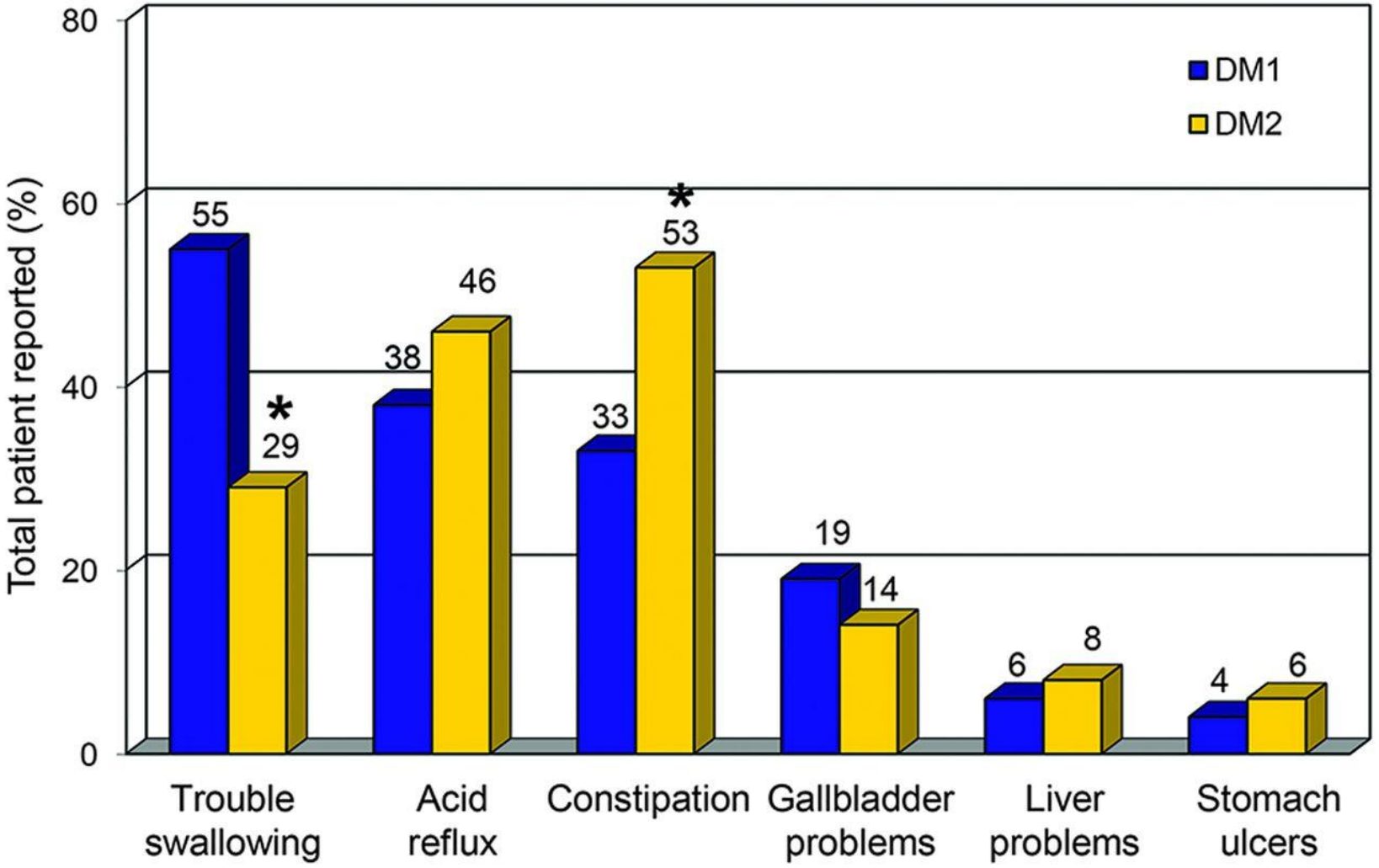
- GI symptoms in DM
- Diagnostic testing
- Treatment options
  - Symptom based management

GI Involvement in Myotonic Dystrophy

- GI symptoms are present in up to 60% of patients
  - GI symptoms may precede myotonia by >10 years
  - Severity of GI symptoms does not correlate with severity of muscle dysfunction or duration of the DM
- Different pathophysiologic abnormalities described
  - Dysfunction of smooth muscle
  - Degeneration of the myenteric neurons

James E. Hilbert et al. Neurology 2017;89:1348-1354
Ronnblom A et al. Scand J Gastroenterol 1996;31:654-647
Bellini M et al. World J Gastroenterol 2006;12:1821-1828

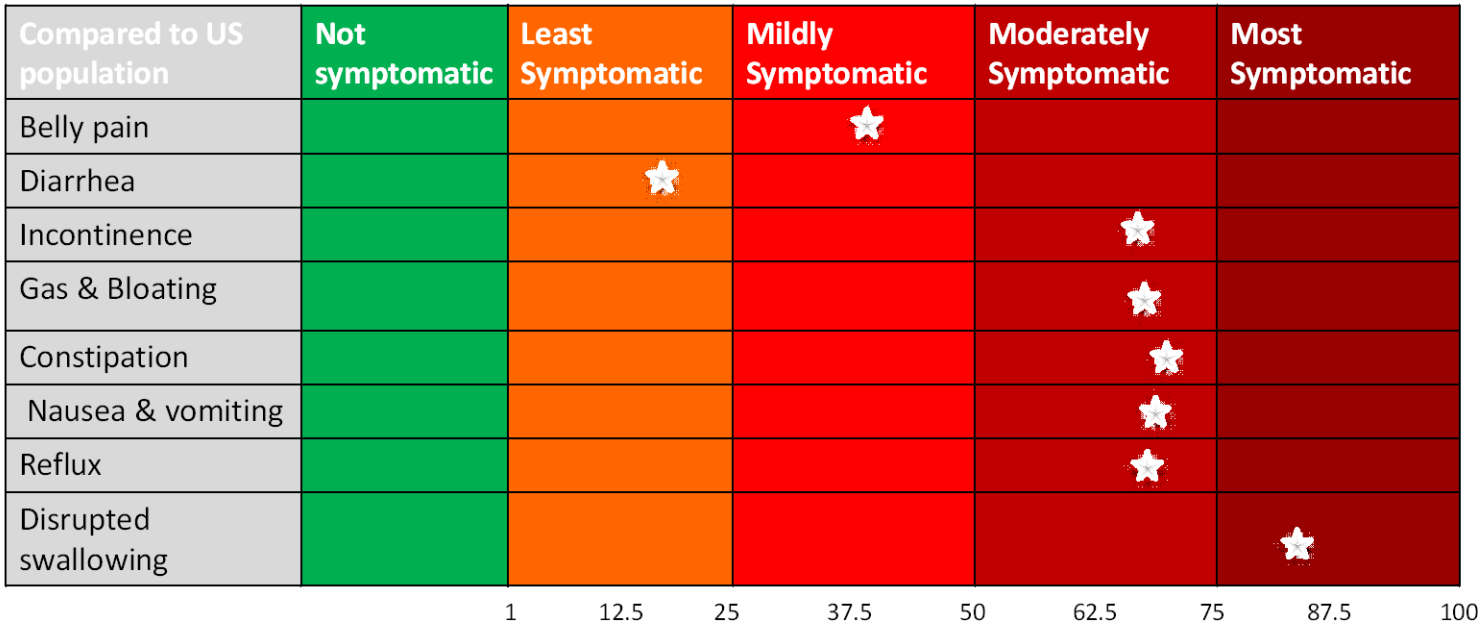
Percentage of Patients with DM1 & DM2 Who Reported GI Symptoms



James E. Hilbert et al. Neurology 2017;89:1348-1354

Prevalence of GI Symptoms in DM

Gastrointestinal symptom severity in our DM population



GI Symptoms Impair Quality of Life

- Health Related Quality of Life is impaired in patients with DM
- GI Factors associated with decreased Quality of Life:
  - Constipation
  - Difficulty swallowing
- 25% of DM patients felt GI symptoms were the most disabling problem related to DM

Peric S et al. Clinical Neurology and Neurosurgery 2013;115:270
Tieleman et al. Neuromuscular Disorder 2008;18:646–649

Dysphagia

- Difficulty swallowing/choking
  - Most commonly reported symptom
  - Decreases nutritional intake
  - Exacerbates risks of pneumonia

Ronnblom A et al. Scand J Gastroenterol 1996;31:654-647
James E. Hilbert et al. Neurology 2017;89:1348-1354

Differentiate Oropharyngeal vs. Esophageal

- Oropharyngeal = difficulty initiating swallow, coughing with swallows
  - Myotonia of the face, tongue, Pharyngeal muscle weakness (weak swallow)
- Esophageal = food difficult/slow to pass after swallow initiated
  - Weak esophageal contractions
  - Esophageal stricture/narrowing (Complication of acid reflux)

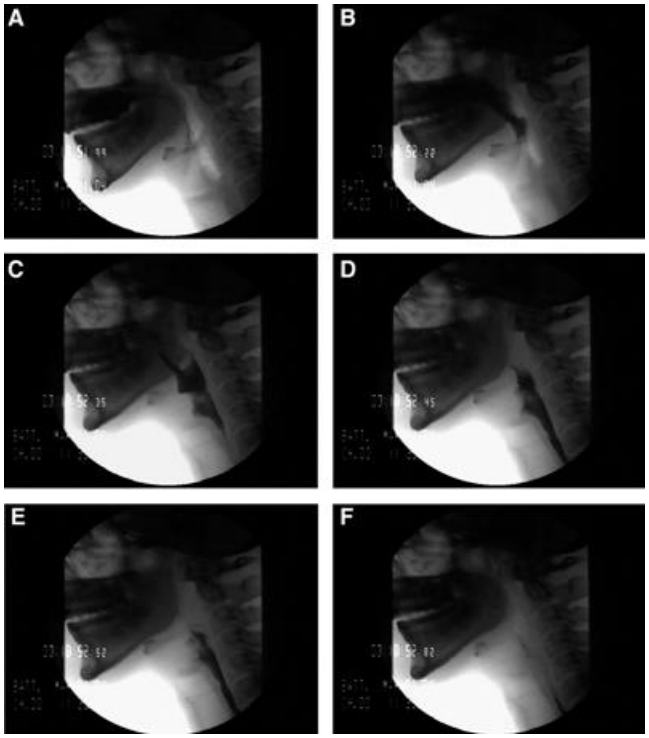
Ronnblom A et al. Scand J Gastroenterol 1996;31:654-647
James E. Hilbert et al. Neurology 2017;89:1348-1354

Other Symptoms of Pharyngeal & Esophageal Dysfunction

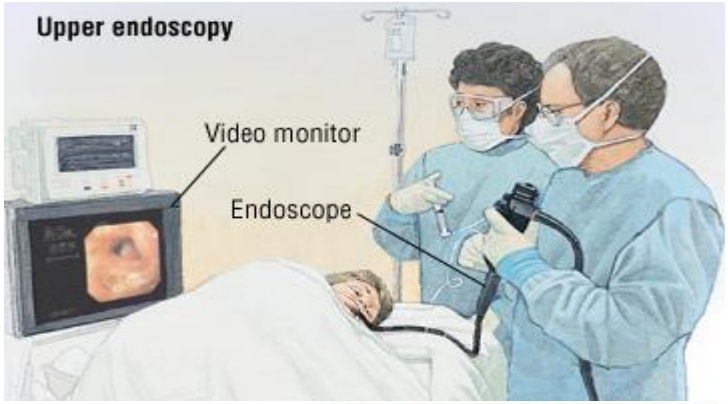
- Acid reflux
  - More common in DM patients as compared to general population
  - Abnormal lower esophageal sphincter function
  - Chest pain
- Aspiration: Coughing/Pneumonia
  - Weak upper esophageal sphincter
  - Acid reflux

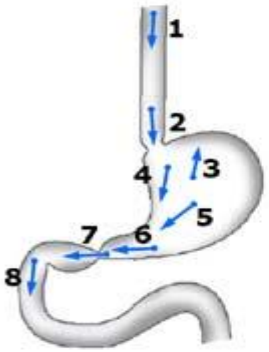
Pharyngeal & Esophageal Testing

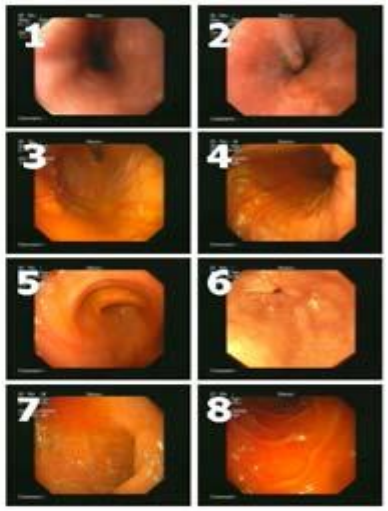
- Video Fluoroscopy (Swallow Study)



- Endoscopy

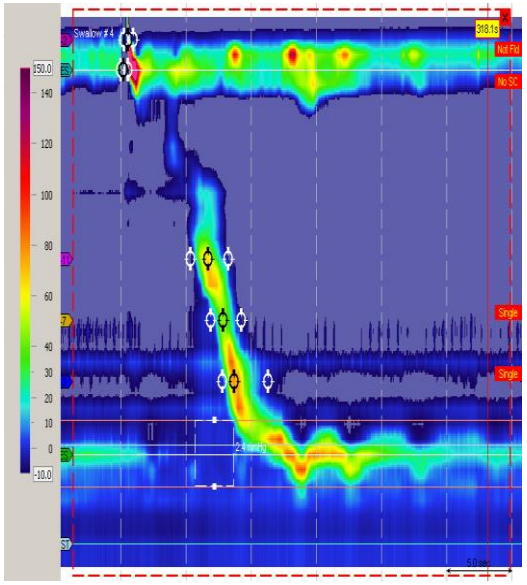






Esophageal Testing

- Esophageal Manometry (Motility Study)

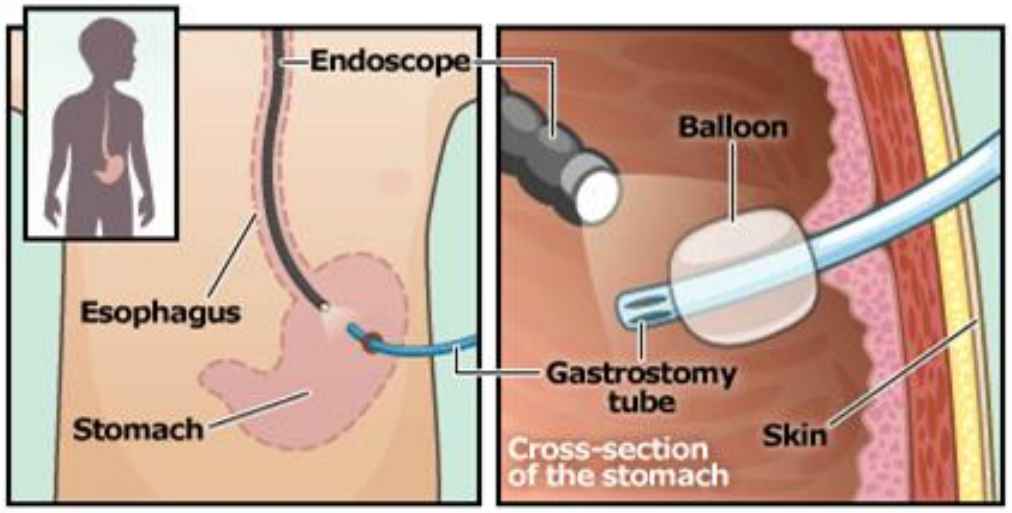


- Studies of DM patients:
  - Decreased pharyngeal contraction amplitude
  - Lower upper esophageal sphincter tone
  - Diminished esophageal contraction amplitude in all patients

Pilz W et al. Dysphagia. 2014 Jun;29(3):319-31.

Treatment of Swallowing Problems

- Speech therapy
- Dietary changes: mechanical chopped, soft, thick liquids
- Feeding tube (especially if aspirating, weight loss) ?



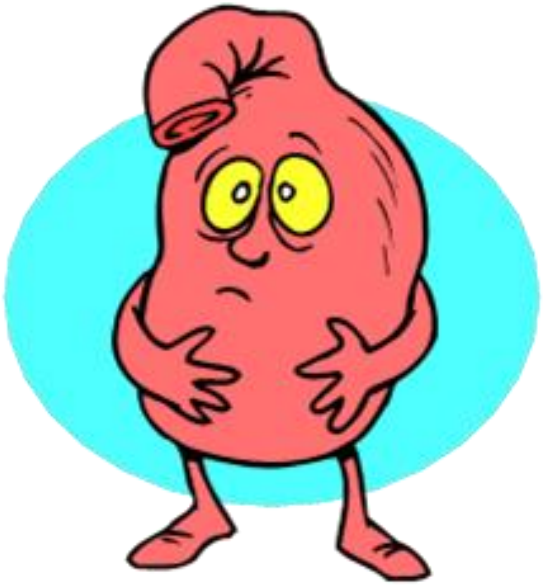
PEG Procedure

Treatment of Acid Reflux

- Dietary changes:
  - Avoid: acidic foods, spicy foods, fatty foods, caffeine, alcohol
  - Remain upright at least 3 hours after eating
- Elevate the head of the bed (> 30 degrees, wedge)
- Acid suppression therapy
  - Ranitidine, Famotidine
  - Omeprazole, Pantoprazole, Esomeprazole, …

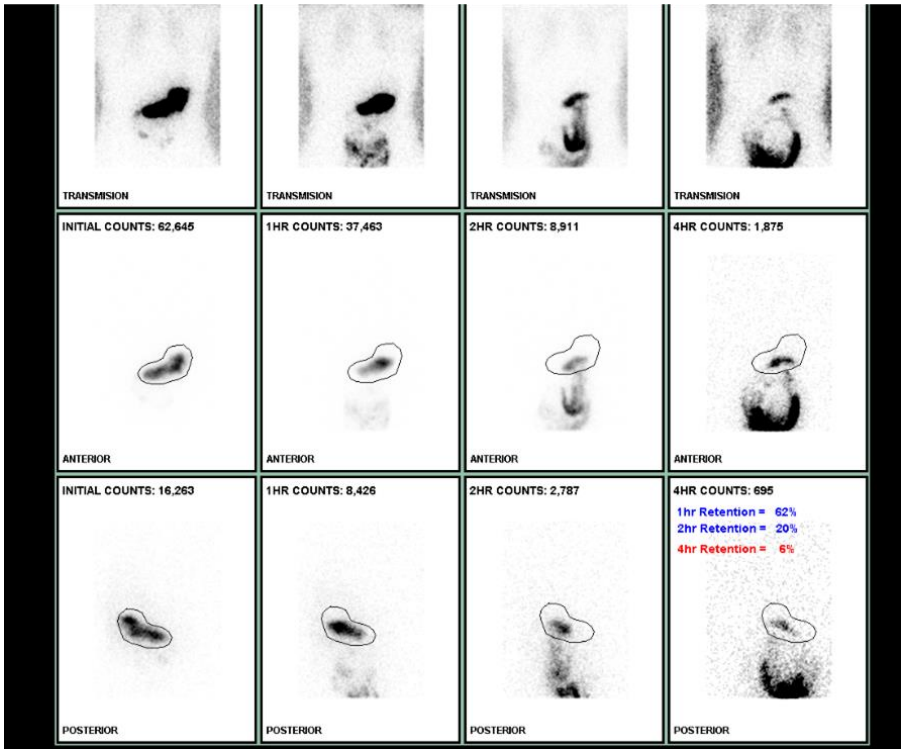
Gastroparesis

- Slow stomach emptying
- DM patient have slower gastric emptying compared to healthy controls
  - Even in the absence of symptoms
- Symptoms:
  - Nausea and/or vomiting
  - Fullness or Bloating
  - Abdominal pain (after eating)
  - Refractory acid reflux



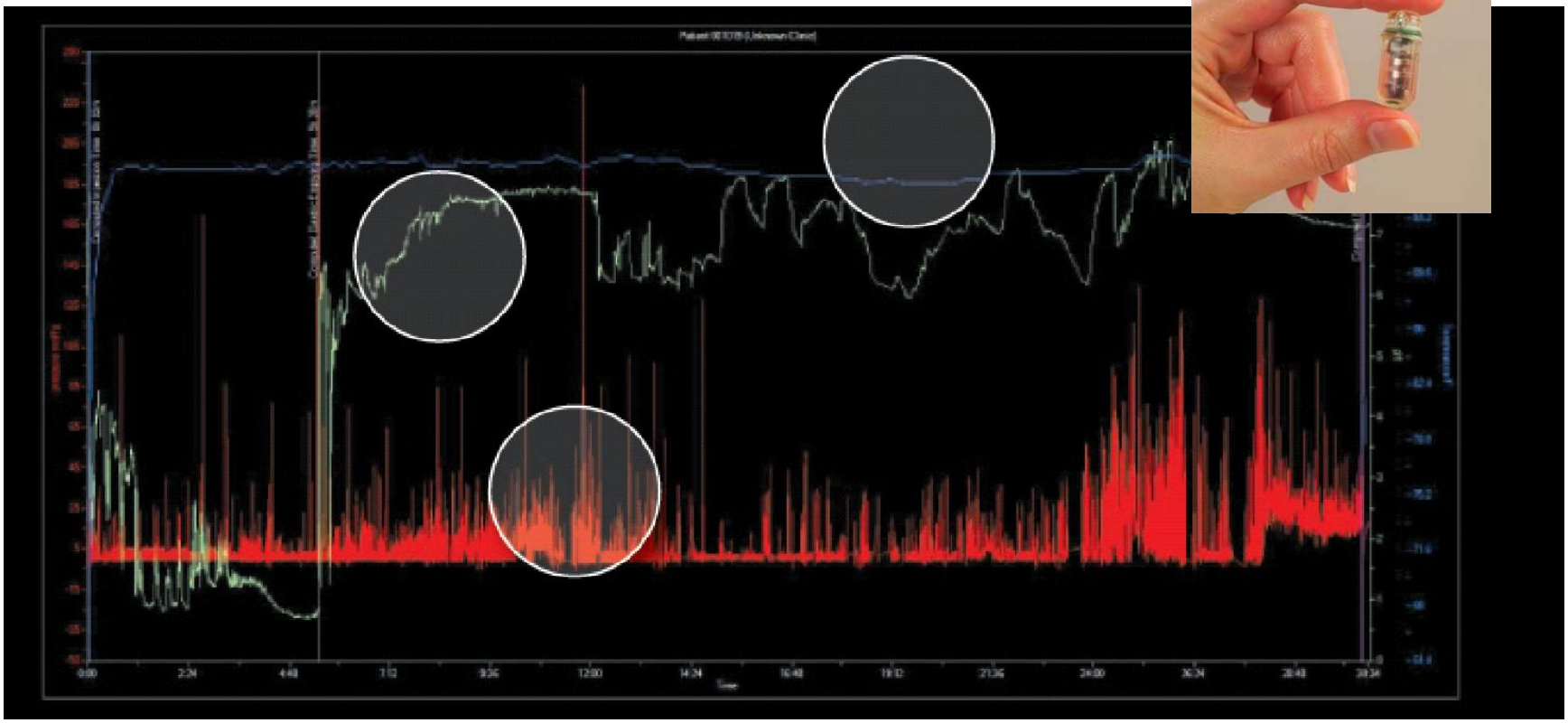
Gastric Emptying Scintigraphy

Delayed Gastric Emptying



Normal Gastric Emptying

Wireless Capsule Motility (Smart Pill)



Treatment of Gastroparesis (1)

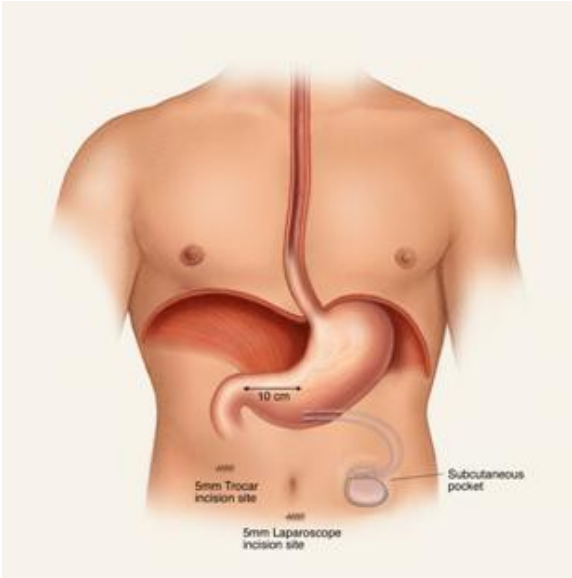
- Dietary changes
  - Low fat diet (fat slower to digest)
  - Low fiber (avoid “roughage”)
  - Small frequent meals
- Stay hydrated with electrolytes
  - Gatorade
  - Pedialyte
- If diabetic, maintain glucose control

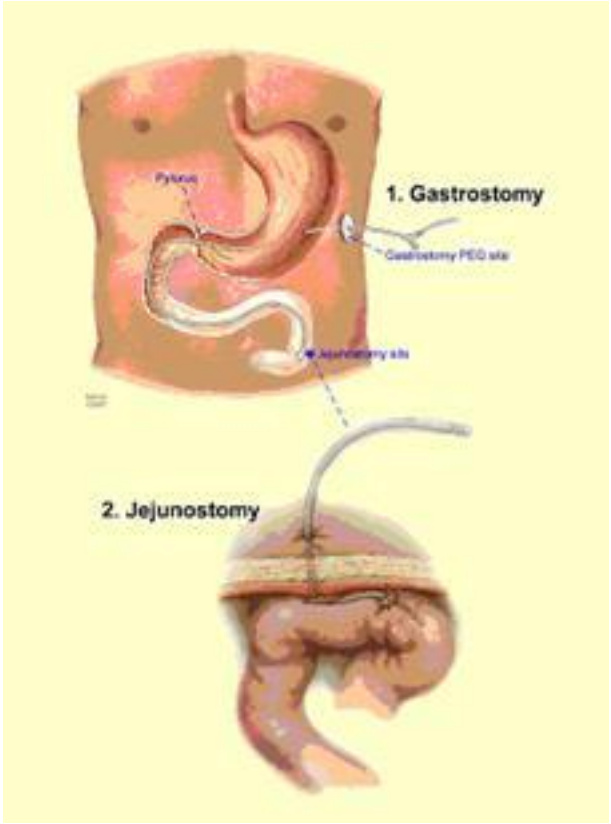
Treatment of Gastroparesis (2)

- Medical Management:
  - Promotility agents:
    - Metoclopramide, Domperidone
    - Erythromycin, Azithromycin
    - Neostigmine
  - Antiemetics:
    - Diphenhydramine (Benadryl), Cyproheptadine, Promethazine (Phenergan), Prochlorperazine (Compazine), Ondansetron (Zofran), Dronabinol (Marinol)

Treatment of Gastroparesis (3)

- Feeding tube
  - Small bowel
- Gastric electrical stimulation





Treatment of Gastroparesis (DM)

- Therapies reported/studied in DM
  - Metoclopramide (N=16): increased gastric emptying
  - Erythromycin (N=10): Modest improvement of gastric emptying and symptoms(?)

Horowitz et al. Gastroenterology 1987 Mar;92(3):570-7.
Ronnblom A et al. European Journal Clinical Investigation. 2002 Aug;32(8):570-4.

Intestinal Pseudo-obstruction

Chronic Intestinal Pseudo-obstruction

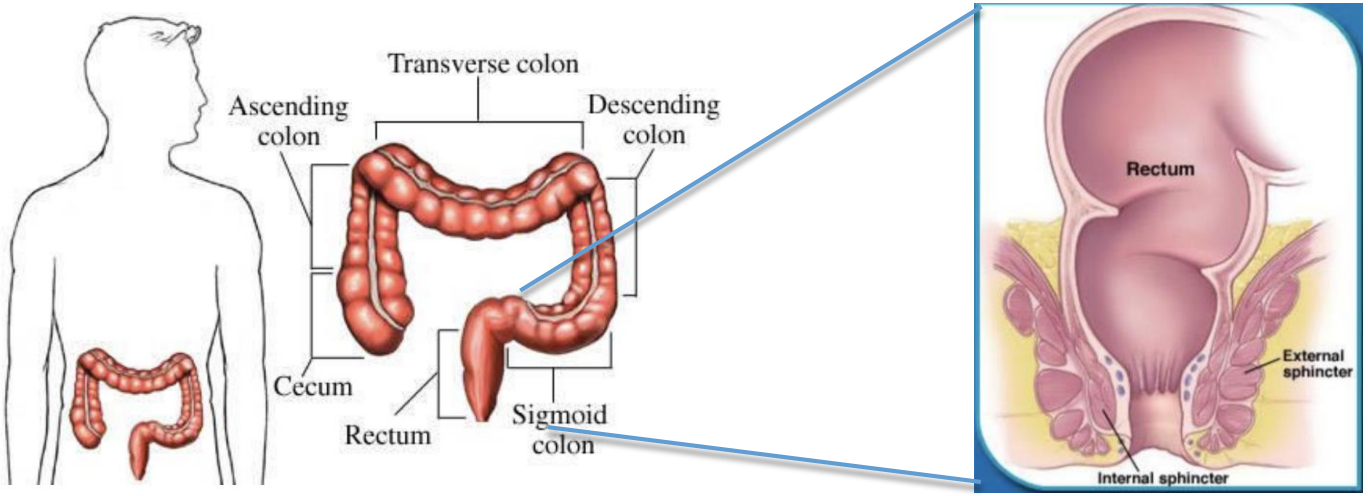
- Disordered small bowel motility (neuropathic or myopathic) leading to obstructive-like symptoms and dilated bowel
  - Distension - 75%
  - Abdominal pain - 58%
  - Nausea - 49%
  - Constipation - 48%
  - Heartburn/regurgitation - 46%
  - Fullness - 44%
  - Epigastric pain/burning - 34%
  - Early satiety - 37%
  - Vomiting - 36%

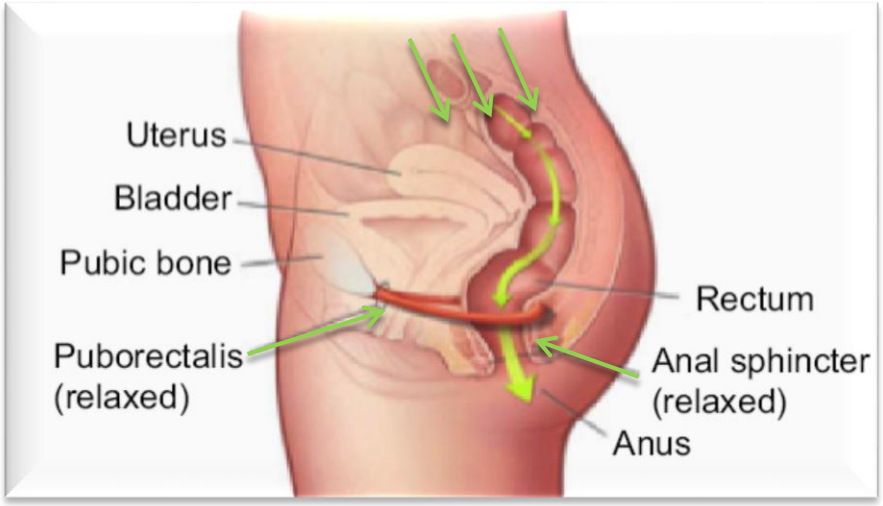
Stanghellini V et al. Gut 1987

Treatment of Chronic Intestinal Pseudo-obstruction

- **AVOID UNNECESSARY SURGERY**
- Dietary modification
- Nutritional support, IV hydration
- Treatment of bacterial overgrowth
- Promotility agents
  - Erythromycin/Azithromycin
  - Metoclopramide, Domperidone
  - Prucalopride (coming soon)
  - Neostigmine, Pyridostigmine, Bethanechol
  - Octreotide

Defecation & Continence

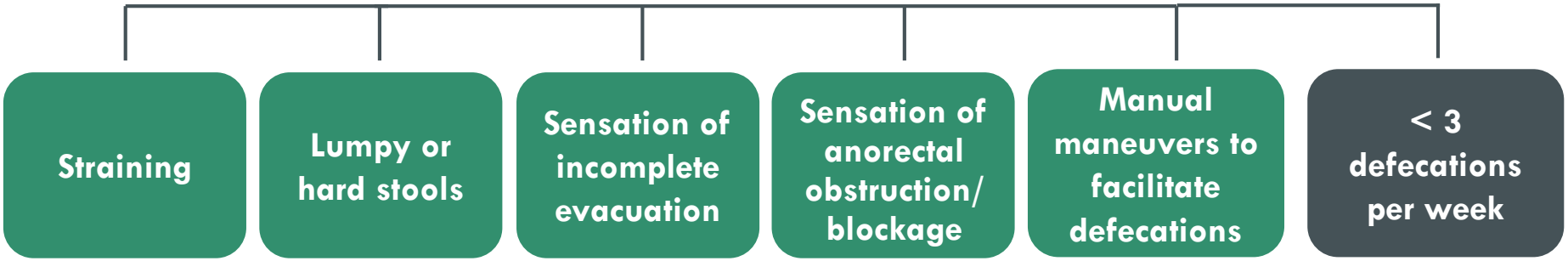




Defining Constipation

Chronic constipation must include 2 or more of the following:

During at least 25% of defecations



- Loose stools are rarely present without the use of laxatives
- Insufficient criteria for irritable bowel syndrome

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

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**

Causes of Constipation in DM

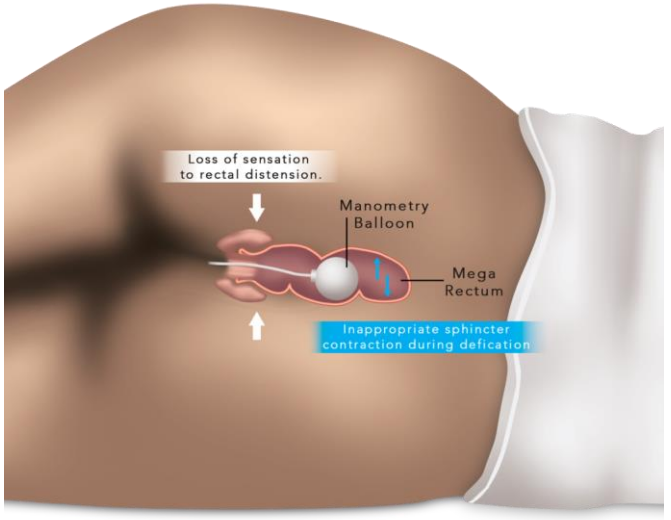
- Slow colon transit
  - Colon transit time was increased in 24% of the DM2 patients
  - Dysfunction of colonic smooth muscle
  - Loss of enteric nervous system
- Dyssynergic defecation (>90 %)
  - Inability to coordinate anal sphincter relaxation
  - Insufficient rectal pressures
- Idiopathic constipation/IBS with constipation

Tierleman et al. Neuromuscular disorders 2008 Aug;18(8):646-9.

Diagnostic Testing

- Smart-Pill
  - Evaluation of colon transit time
  - Diagnosis of slow transit vs. normal transit constipation

- Anorectal manometry
  - Evaluation of anorectal function
  - Anal sphincter strength



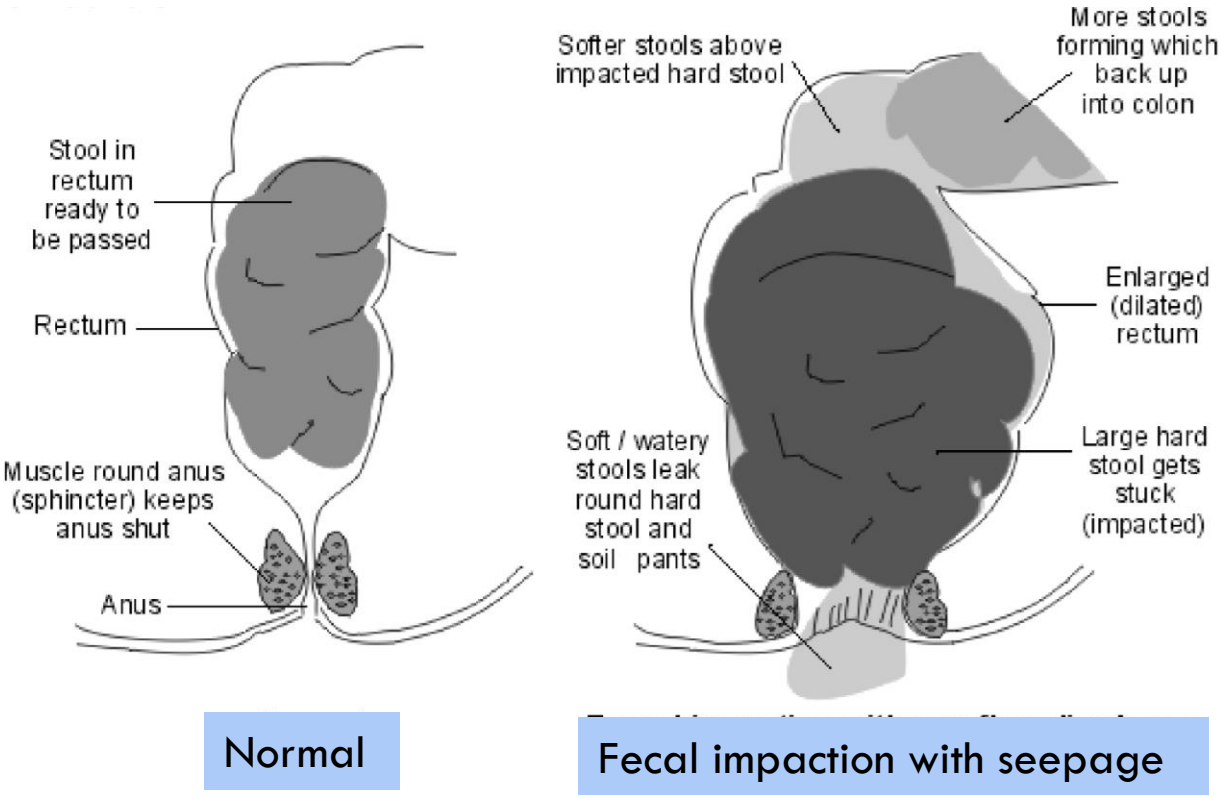
Causes of Fecal Incontinence in DM

- Anal sphincter dysfunction
  - Low resting sphincter pressure
  - Weak squeeze pressure
- Abnormal bowel habits
  - Diarrhea
  - Constipation

Lecointe-Besancon et al. Dig Dis Sci 1999;44:1090

Causes of Fecal Incontinence in DM

- Fecal impaction with overflow diarrhea



Normal

Fecal impaction with seepage

Non-medical Treatment of Constipation

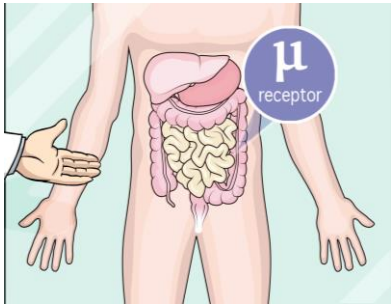
- Exercise
- Diet
  - fluids
  - fiber
- Squatting stool

Soluble vs. Insoluble Fiber

- Total Fiber intake 20-30 grams per day
  - Too much fiber can cause excessive bloating and gas
- Fiber
  - Soluble Fiber
    - Effective for treatment of constipation
  - Insoluble Fiber

Medical Treatment of Constipation

- Osmotic laxatives (lactulose, magnesium citrate, Miralax)
- Stimulant laxative (bisacodyl, senna)
- Prosecretory agents
  - Lubiprostone (Amitiza)
  - Linaclotide (Linzess)
  - Plecanatide (Trulance)
- Peripherally selective opioid antagonist
- Suppositories/Enema- help with rectal evacuation

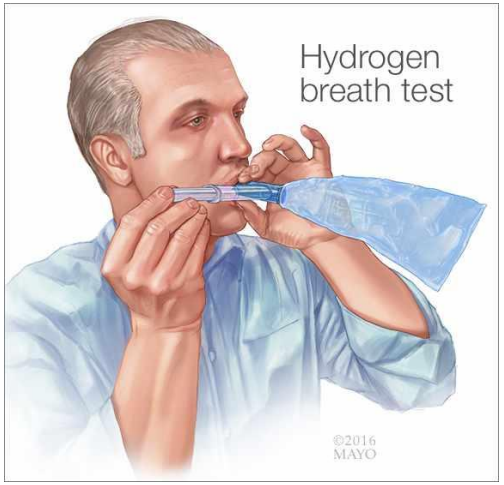


Treatment of Defecatory Disorders

- Pelvic floor dyssynergia
  - Pelvic floor rehab and Biofeedback therapy
    - Teach relaxation of pelvic floor
    - Abdominal exercises
  - Timing BMs after meals and when urge present
  - Squatting stool
  - Digital stimulation/scheduled defecation
  - Enemas/suppository
- Rectal Prolapse
  - Surgery

Diarrhea

- Small Intestinal Bacterial Overflow
  - Common (65%) in DM
  - diarrhea, bloating, cramping
  - Diagnosis: Hydrogen breath tests
  - Treatment: Antibiotics



- Bile salt malabsorption
  - Bile salt binder

Gallstones

- Present in 25-50% of DM patients
- Results from poor gallbladder function/motility
- Causes abdominal pain after eating
- Treatment
  - Surgery (cholecystectomy)

Causes of Abdominal Pain

- Gastroparesis
- Small intestinal bacterial overflow (SIBO)
- Pseudo-obstruction
- Constipation
- Gallstones

Treatment of Abdominal Pain

- Dietary
  - Low FODMAP diet for functional dyspepsia or IBS
  - Low Fiber diet for Gastroparesis
- Anti-spasmodics
  - Peppermint
  - Anti-cholinergics (use with caution, prefer shorter acting)
    - Hyoscyamine
- Anti-neuropathic agents
  - Gabapentin, lyrica
  - Tricyclic antidepressants (desipramine, nortriptyline, etc)
  - SNRIs (duloxetine, venlafaxine)
  - Mexiletine

Summary

- DM can affect the GI tract from the mouth to the anus
- GI symptoms are common in patients with DM
- A variety of motility and diagnostic tests are available for assessment of GI symptoms
- Most of the GI symptoms are amenable to treatment
- Treatment of GI symptoms will improve quality of life in patients with DM