Chronic constipation

Dr foroogh Alborzi

OBJECTIVES

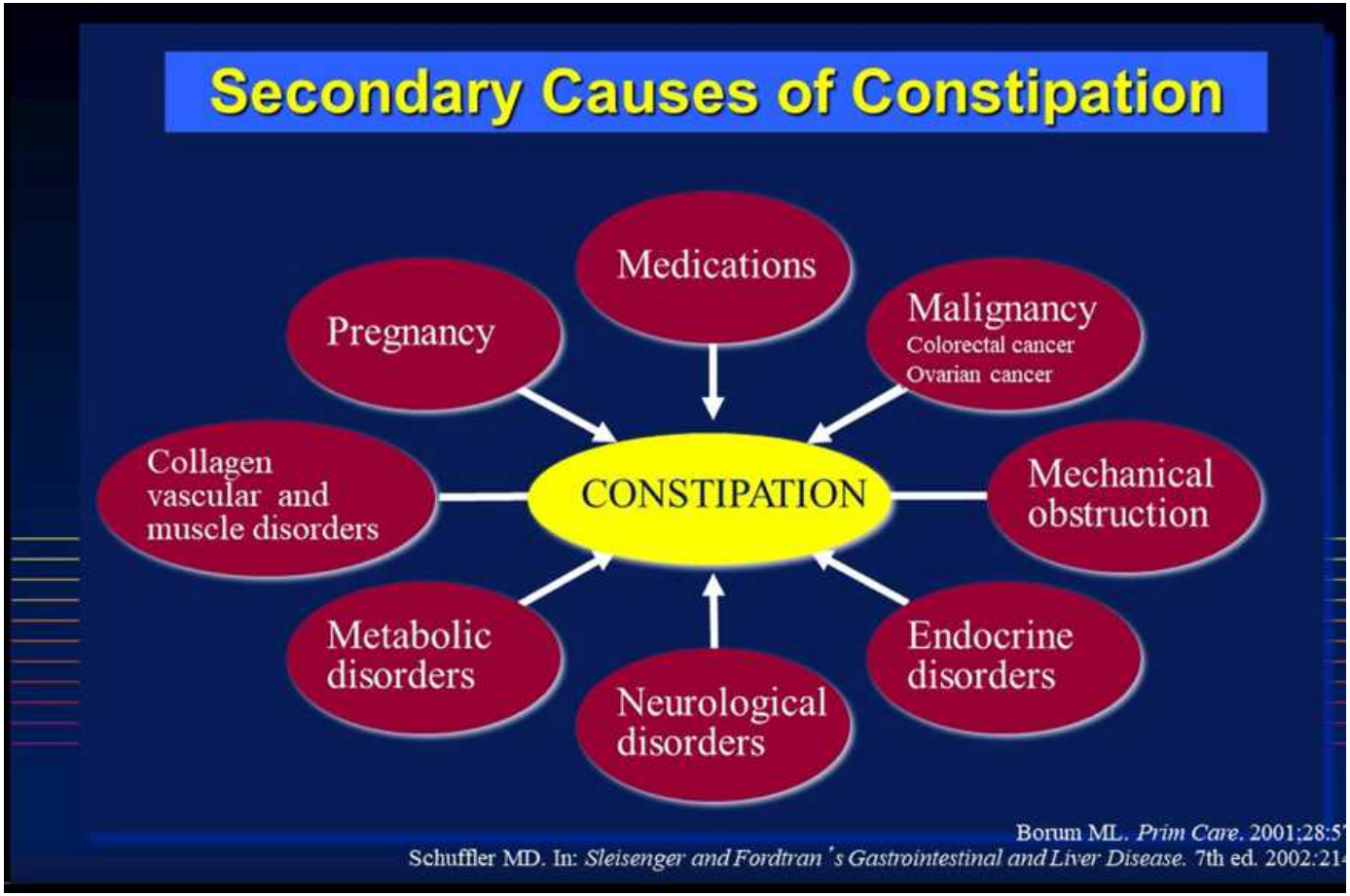
- Define constipation subtypes, and symptom patterns
- Discuss its pathophysiology
- Review novel diagnostic tests using a problem-based approach
- Explore Treatment options: One size does not fit all !!
  - Secretogogues
  - Prokinetics
  - Biofeedback therapy

Types of Constipation

1. Occasional or Travelers constipation
2. Dietary causes- Fiber deficiency
3. Chronic Constipation
   - *-Primary*
     - *-Slow transit constipation*
     - *-Dyssynergic Defecation*
     - *- IBS-C*
     - *-Pelvic floor disorders-Rectal Hyposensitivity/ Hypersensitivity*
   - *-Secondary*
   - *-Opioid induced constipation*

Rao S et al Nature Revs 2016; Rao SSC. Gastroenterol Clin N Am 36 (2007) 687-711

Camilleri M, Rao SSC, et al. Nature Rev. Dis Primers 2017;3:17095;1-19


Secondary Causes of Constipation
Medications
Pregnancy
Malignancy
Colorectal cancer
Ovarian cancer
Collagen vascular and muscle disorders
CONSTIPATION
Mechanical obstruction
Metabolic disorders
Neurological disorders
Endocrine disorders
Borum ML. Prim Care. 2001;28:5
Schuffler MD. In: Sleisenger and Fordtran's Gastrointestinal and Liver Disease. 7th ed. 2002:21

40 yr old Nurse, Severe Constipation-2 yrs

- Constipation:
  - B.M once/week, Type 1-2, Straining +++, FICE ++, No blood
  - Laxatives give diarrhea then no BM 1-2 wks, Tried Bisacodyl, PEG, Ex-lax, Senna, Lubiprostone- ? Colectomy
- Pain: RLQ, sharp, radiates RUQ, every other day, worse p.prandial and with BM, lasts few hours,
- Bloating/gas: worse after meals, avoids eating, wt loss
- QOL: Significantly affected, missed several wks. work
- Past Hx: Cholecystectomy, Benign breast tumor
- Investigations:
  - Labs, Colonoscopy, CAT scans, EGD & MRI Spine-Normal

40 yr old Nurse, Severe Constipation, pain, gas & bloating- worse 2 yrs

- Meds: Intermittent opioids, Depo Provera, laxatives
- O/E: General Exam normal, tender RUQ, stool ++ in LLQ

What would you do next?

What would you do next?

THE RED SECTION 635

HOW I APPROACH IT

Rectal Exam: Yes, it can and should be done in a busy practice!

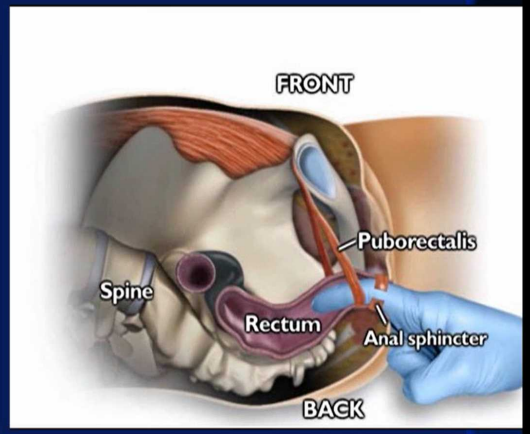
Satish S.C. Rao, MD, PhD, FRCP(LON), FACG, AGAF

Am J Gastroenterol (2018) 113:635–638. https://doi.org/10.1038/s41395-018-0006-y

"Dr, I am constipated and feel tied to the bathroom" said Mrs. Smith during an office consultation. "Let's arrange a colonoscopy to check your colon", said her gastroenterologist. At follow-up, "Mrs. Smith, good news, your colonoscopy is normal". "But Dr, I am very constipated". "Well, I suggest you take polyethylene glycol daily". And that was it! 1 year later, she was referred to another specialist, who performed a digital rectal examination (DRE), whose findings (summarized below) changed the course of her management.

Dyssynergic defecation, focal incontinence (FI), and other anorectal disorders are common problems that affect one third of the US population [1]. DRE is a key component of physical examination [2, 3], but is rarely performed, except for perhaps a cursory exam prior to colonoscopy [4]. This problem is further compounded by a lack of knowledge on how to perform a comprehensive DRE.

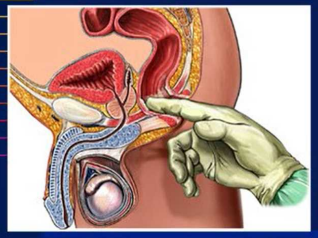
A survey of 256 final-year medical students revealed that 17% had never performed a DRE, and 48% were unsure of their find-



Rao S. Am J Gastroenterol 2018;112:635-38

3-step DRE-PROTOCOL

1) **Inspection**
2) **Perianal sensation & anocutaneous reflex:**
   - **normal, impaired, absent**
3) **Digital maneuvers: mass, tenderness, stool**
   - **Squeeze x 2: normal, weak, increased**
   - **Bearing down x 2**
     - **push effort, sphincter relaxation, perineal descent**



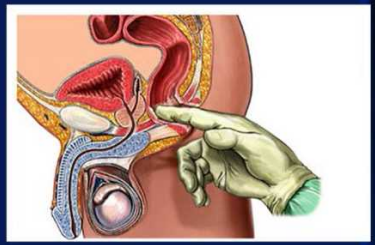
Clinically dyssynergia *if* ... any 2;

- inability to
  - •contract abdominal muscles
  - •relax anal sphincter
- paradoxical contraction of anal sphincter
- absence of perineal descent

Tantiphlachiva, Rao et al, CGH 2010

Yield of rectal exam in dyssynergia, n=209

- All patients had
  - DRE
  - Anorectal manometry
  - Balloon Expulsion Test
- Data Analyzed independently



Parameter	Sensitivity (%)	Specificity (%)
Dyssynergia from DRE	75%	87%
Balloon expulsion test	49%	90%

Tantiphlachiva K, Rao S et al, CGH 2010

40 yr old Nurse, Severe Constipation, pain, gas & bloating- worse 2 yrs

- **O/E:** General Exam normal, tender RUQ, stool ++ in LLQ
- **DRE:**
  - Anocutaneous reflex intact
  - Adequate Resting/squeeze tone, No stool, Guaiac -ve
  - Good perineal descent, incomplete relaxation
- Anoscopy- Normal

40 yr old Nurse, Severe Constipation, pain, gas & bloating- worse 2 yrs

- Does she have Colonic Inertia or severe Slow transit Constipation ?
- Does she have dyssynergic defecation ± STC?
- Does she have pseudoobstruction/generalized dysmotility?
- Does she have CHO malabsorption
- Is her constipation secondary to opiods?

Rome IV Criteria for Chronic Constipation

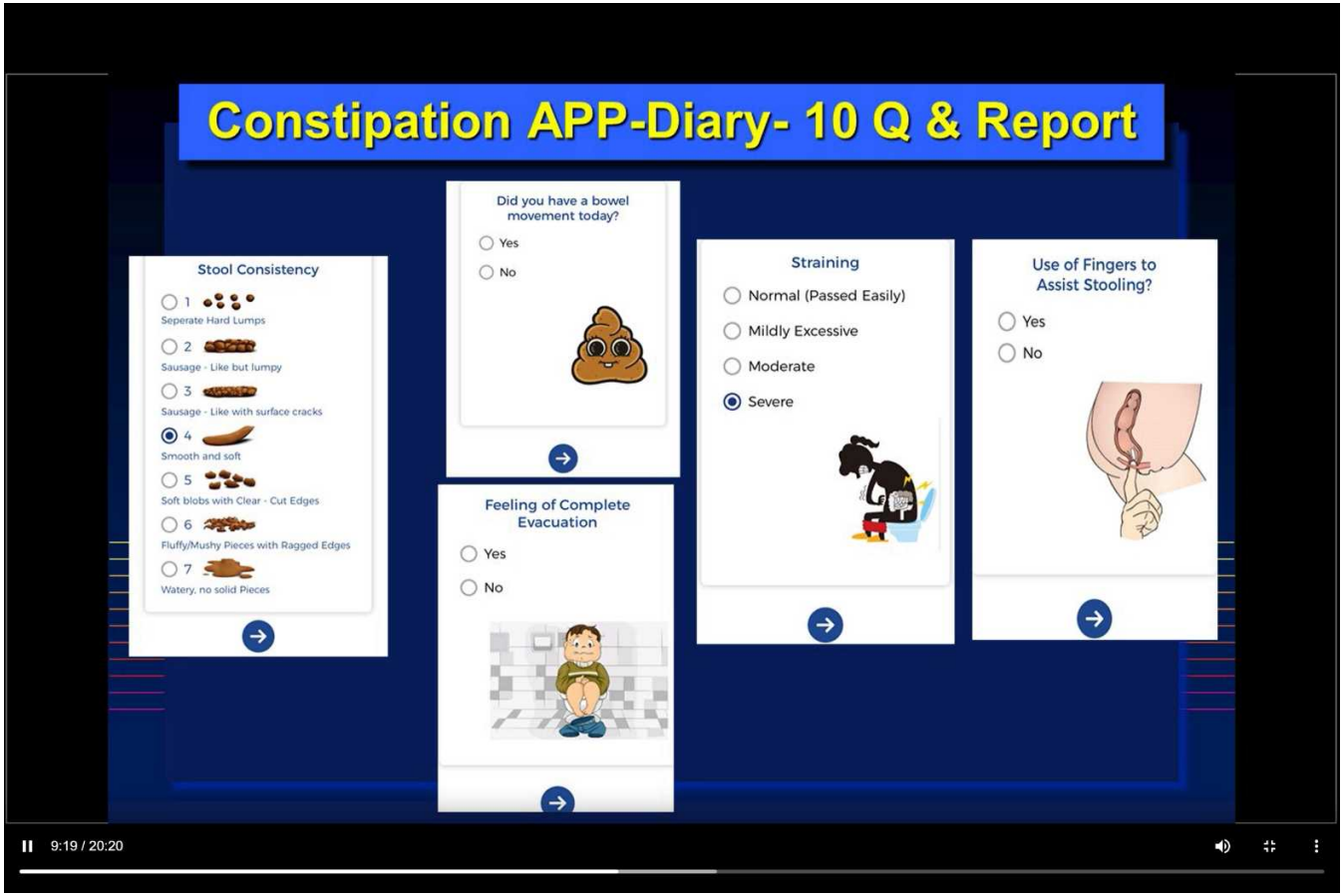
- Symptoms for 3 months and onset at least 6 months & include TWO or more of following with ≥25% of BMs:
  - Straining
  - Hard or lumpy stools
  - Feeling of incomplete Evacuation
  - Sensation of Blockage
  - Digital Maneuvers to assist BMs
  - Infrequent BMs < 3 BM/week
- Bloating/Pain may be present but not predominant

Lacy B et al Am J Gastroenterol 2015

Tools for understanding Mechanism(s)

- History
- Stool diary
- Digital Rectal Exam
- Colonoscopy (particularly if age > 50 years)
- Colonic transit study
  - Radiopaque markers
  - Scintigraphy
  - Wireless pH/Motility (SmartPill)
- Balloon expulsion test
- Defecography/MRI defecography
- Anorectal manometry
- Colonic manometry

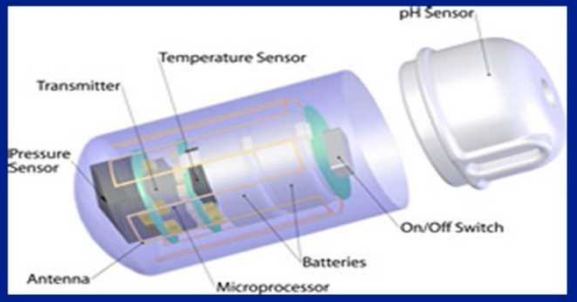
Rao SSC, et al. Nat Rev. 2018


Constipation APP-Diary- 10 Q & Report
Stool Consistency
1
Seperate Hard Lumps
2
Sausage - Like but lumpy
3
Sausage - Like with surface cracks
4
Smooth and soft
5
Soft blobs with Clear - Cut Edges
6
Fluffy/Mushy Pieces with Ragged Edges
7
Watery, no solid Pieces
Did you have a bowel movement today?
Yes
No
Feeling of Complete Evacuation
Yes
No
Straining
Normal (Passed Easily)
Mildly Excessive
Moderate
Severe
Use of Fingers to Assist Stooling?
Yes
No
9:19 / 20:20

40 yr old Nurse, Severe Constipation, pain, gas & bloating- worse 2 yrs

- **Investigations:**
- Breath Tests - Glucose/ fructose/ lactose
- Anorectal Manometry
- Defecography
- Colonic Transit – Wireless motility Capsule (SmartPill)
- Colonic Manometry

Wireless pH & Motility Capsule Test (SmartPill)



Clinical Utility of WMC in GI Dysmotility, n=324

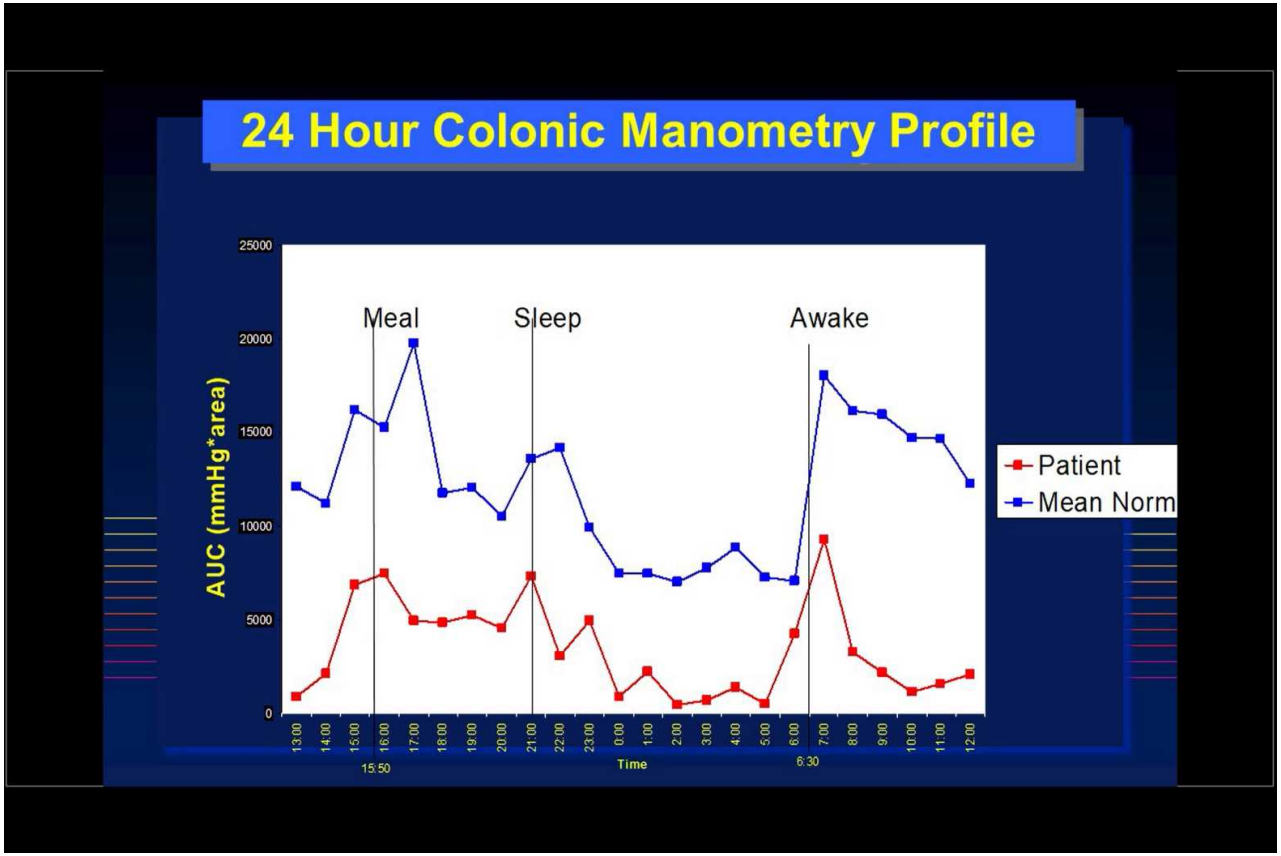
	Normal study	Confirm clinical suspicion **(Diagnostic yield)**	New diagnostic information **(Diagnostic gain)**
UGI group n=89	34 (38%)	Gastroparesis 29 pts (33%)	38 pts (42%)
LGI group n=101	43 (43%)	Slow transit constipation 42 pts (42%)	25 pts (25%)
Pan-GI group (UGI+LGI) n=124	38 (30%)	Delayed Regional transit 86 pts (70%)	N/A

Leelasinjoran P, Rao S et al, DDW. Gastroenterology 2017

Wireless Motility capsule Test
40-yr old Nurse

	Subject	Normal Range
Gastric Emptying Time	6 hrs 32 mins	2.4- 5 hours
Small Bowel Transit Time	5 hrs 23 mins	3-6 hours
Colonic Transit Time	>111hours	17-59 hours
Whole Gut Transit Time	>122 hours	26-71 hours

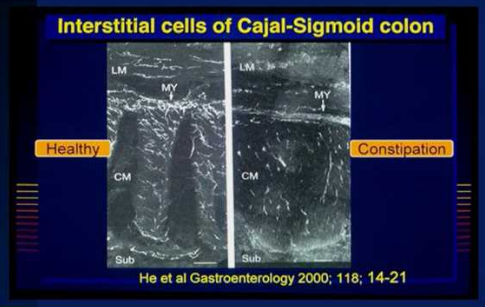
24 Hour Colonic Manometry Profile



40 yr old Nurse, Severe Constipation
INVESTIGATIONS

- Breath Tests –
  - Glucose/ fructose- Normal excluding SIBO/DFI
  - Lactose Intolerance
- Anorectal Manometry- Normal
- Defecography –Normal
- SmartPill- Delayed GET, CTT & WGTT
- Colonic Manometry-Myopathy, no neuropathy

Pathophysiology-Slow Transit Constipation



Methane & STC

- About 1/3rd of population produces CH_4
- Predominant organism is Methanobrevibacter smithii
- Increased prevalence in STC
- A genetic finger print

-Rao S & Pimentel et al Am J Gastro 2012

Altered Intestinal Microbiota

Women & Constipation

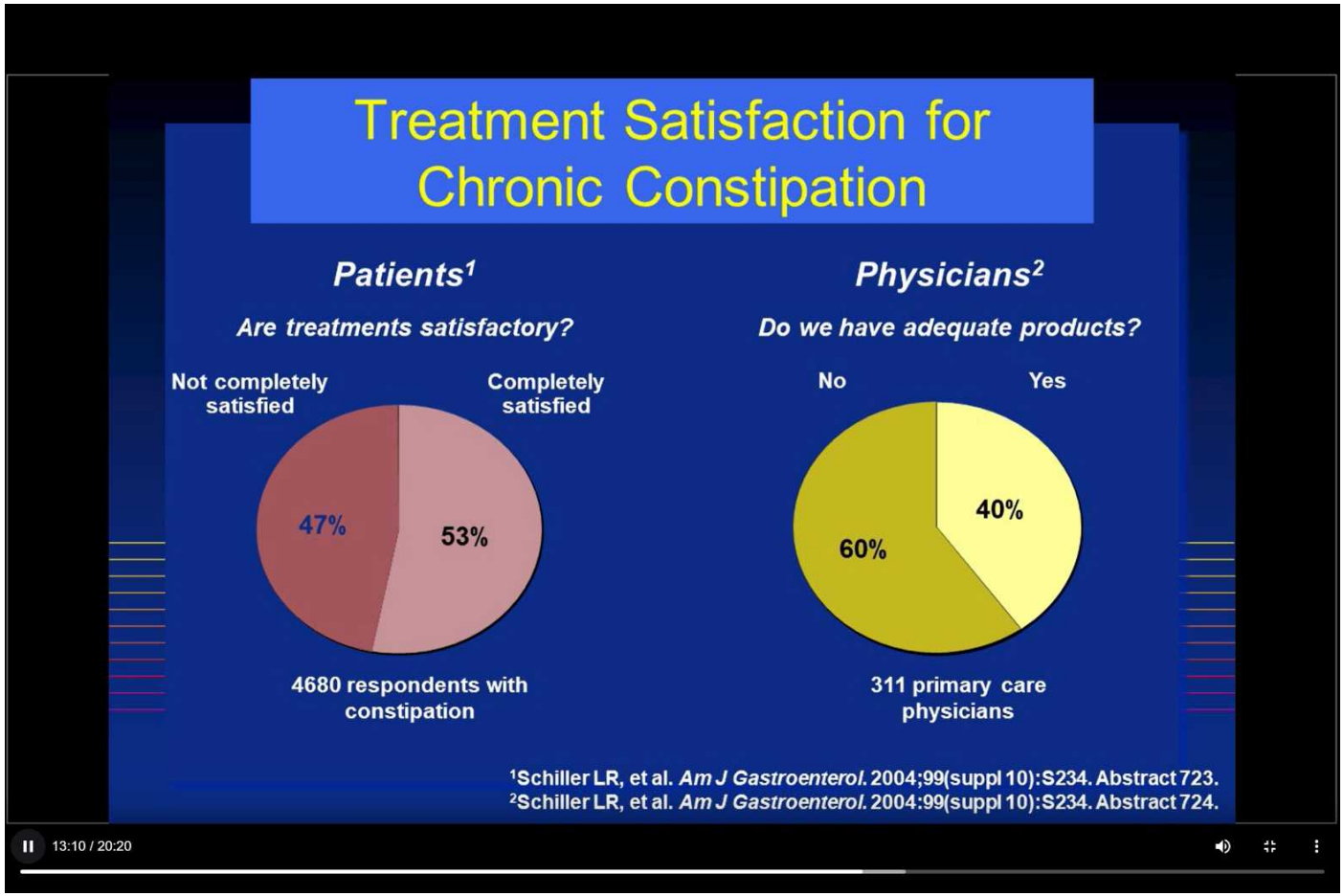
- Down-regulation of contractile proteins & Up-regulation of inhibitory G proteins caused by overexpression of progesterone receptors

- Xiao et al Gastro 2005;128:667

Colonic Manometry

- Absence of HAPC
- Loss of Gastrocolonic/Waking response
- Altered PRMA
- Sensory changes/Reflexes

-Rao et al Gastro Clin N.Am 2007


Treatment Satisfaction for Chronic Constipation
Patients[1]
Are treatments satisfactory?
Not completely satisfied
Completely satisfied
47%
53%
4680 respondents with constipation
Physicians[2]
Do we have adequate products?
No
Yes
60%
40%
311 primary care physicians
[1]Schiller LR, et al. Am J Gastroenterol. 2004;99(suppl 10):S234. Abstract 723.
[2]Schiller LR, et al. Am J Gastroenterol. 2004:99(suppl 10):S234. Abstract 724.
13:10 / 20:20

General measures in all patients

- All patients should first be treated conservatively

- Avoidance of straining,digitation
- Minimization of time on commode.
- Time spent in the toilet should be adjusted
- Consumption of a high-fiber diet and bulk laxatives.


Constipation!
You can do..
Eat fruits
Eat vegetable
Drink more water
Exercise

Life style modification

Fiber

Patient education

- Toilet training
- Exercise

مصرف فیبر

- میزان فیبر
- نوع فیبر
- عوارض فیبر
- غذاهائی که فیبر دارند، چه نانی بخوریم؟
- غذاهای ویژه دارای قیبر
- میوه با پوست یا بدون پوست، چه وقت بخوریم میوه تازه یا خشک
- میزان فیبر در هر غذا
- پسیلیوم چه فیبری است
- دادن فیبر در افراد کهنسال


برای پیشگیری از سرطانهای روده بزرگ، مقعد، پانکراس و ... مفید است.
سبوس باعث پیشگیری از یبوست می شود.
حاوی ویتامین B است.
سبوس ، کلسترول و مواد سمی را از بدن دفع می کند.
سبوس باعث فعال شدن سیستم دفاعی بدن می شود.
باعث تمرکز، دقت عمل و شادابی و می شود.
باعث کاهش بیماری های قلبی و عروقی می شود .
نان سبوس دار
Wholemeal bread
RangiRangi.com

Fiber?

	FOOD	SERVING SIZE	FIBRE CONTENT IN GRAMS
FRUIT	PASSIONFRUIT	½ cup	12
	PEAR WITH PEEL	1 medium	5.8
	APPLE WITH PEEL	1 medium	4.4
	ORANGE	1 medium	4
NUTS & SEEDS	ALMONDS WITH SKIN	½ cup	8.5
	HAZELNUTS	½ cup	6.5
	CHIA SEEDS	1 tbs	5.5
	SESAME SEEDS	¼ cup	4
	FLAXSEEDS	1 tbs	1.9
GRAINS	RAW WHEAT BRAN	½ cup	12.5
	WHOLEMEAL OR WHOLEWHEAT PASTA	1 cup	6.3
	OATMEAL	1 cup	4
	BROWN RICE	½ cup	1.8
BEANS & LEGUMES	CANNELLINI BEANS	½ cup	9
	CHICKPEAS	½ cup	6
	PEANUTS	½ cup	6
VEGETABLES	RAW SPINACH	1 bunch	7
	AVOCADO	½	6.7
	CORN	1 medium cob	5.9
	CAULIFLOWER	1 cup	5

- Prunes
- Patients reported more complete spontaneous bowel movements
- And improved stool consistency


جو دوسر پرک۱۱۱
OAT MEAL ۱۱۱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محصول آلمان
OAB
سبوس جو دوسر
(پولاف)
حاوی فیبر بالا
۱۰۰٪ خالص و طبیعی
Fortin
Germany
600 × 600

میزان فیبر به گرم	نحوه سرو	نام غذا
		میوه
۴/۴	یک عدد متوسط با پوست	سیب
۳/۱	یک عدد متوسط	موز
۳/۱	یک عدد متوسط	پرتغال
۱۲/۴	یک لیوان معمولی(۲۵۰میلی لیتر)	الوبخارا
		اب میوه
۰/٦	یک لیوان معمولی	اب سیب
		غذای پخته
۴	یک لیوان معمولی	لوبیا سبز پخته
۲/۲	نصف لیوان معمولی	هویج پخته
٤/٤	یک لیوان معمولی	نخود فرنگی پخته
۳/۸	یک عدد متوسط	سیب زمینی کباب شده
		مواد خام
۱/۵	یک عدد متوسط	خیار با پوست
۰/۵	یک لیوان معمولی	کاهو خورد شده

۱/۵	یک عدد متوسط	گوجه فرنگی
۰/۷	یک لیوان معمولی	اسفناج
		حبوبات
۱۳/۵	یک لیوان معمولی	لوبیا کشاورزی کنسرو شده
۱۱/۶	یک لیوان معمولی	باقلا و لوبیای استانبولی پخته یا کنسرو شده
۱۵/۶	یک لیوان معمولی	عدس پخته یا کنسرو شده
		نان
۰/۶	یک و نیم کف دست	نان لواش یا تافتون
۱/۹	یک کف دست	نان سبوس دار سنگگ یا بربری
		ماکارونی و برنج پخته
۲/۵	یک لیوان معمولی	ماکارونی
۳/۵	یک لیوان معمولی	برنج قهوه ای
۰/۵	یک لیوان معمولی	برنج سفید
		تنقلات
۸/۷	نصف لیوان معمولی	بادام زمینی
۷/۹	نصف لیوان معمولی	بادام ها


Unkinked colon
Kinked colon
35°

Exercise and activity

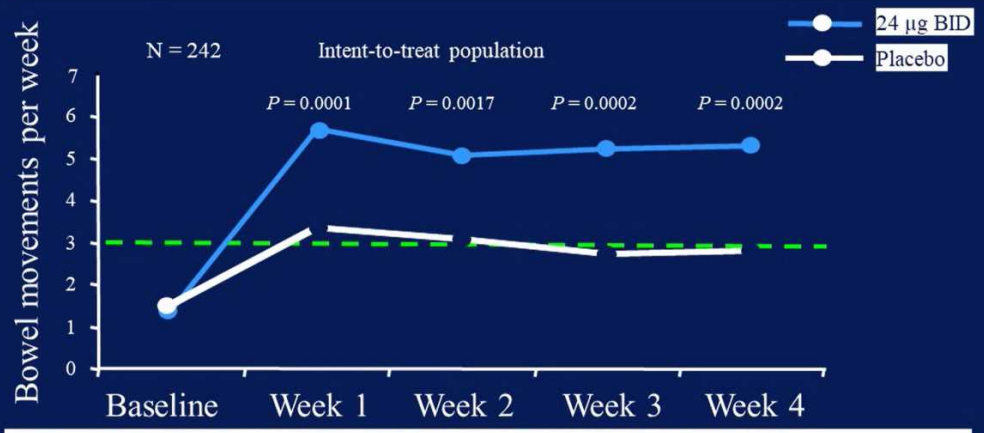
- Regular walking plan even 10 to 15 minutes several times a day can help body and digestive system work at their best.

- Aerobic exercise such as running, jogging, swimming, or dancing. Stretching and yoga may help ease constipation.


بمدت ۵ تا ۱۵ دقیقه این عمل را تکرار کن، روزی دو تا سه بار

To exit full screen, press Esc

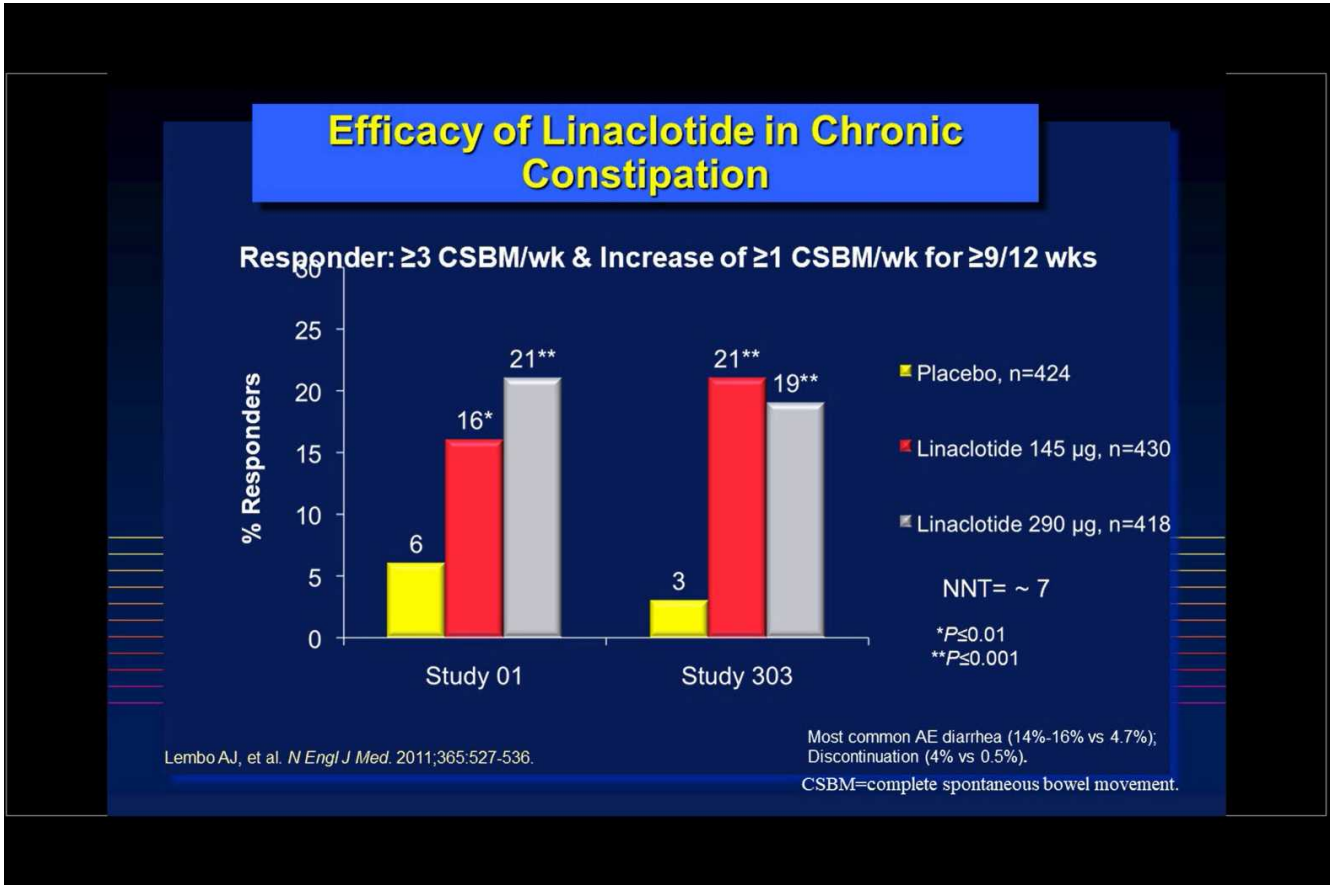
Effects of Lubiprostone on Number of Spontaneous Bowel Movements



- Onset of action was within 24 hours in the majority of subjects
- Most common adverse events were nausea, diarrhea, and headache
- 9 subjects taking lubiprostone withdrew due to adverse events

Johanssen et al Am J Gastroenterol 2008;103:170-7.

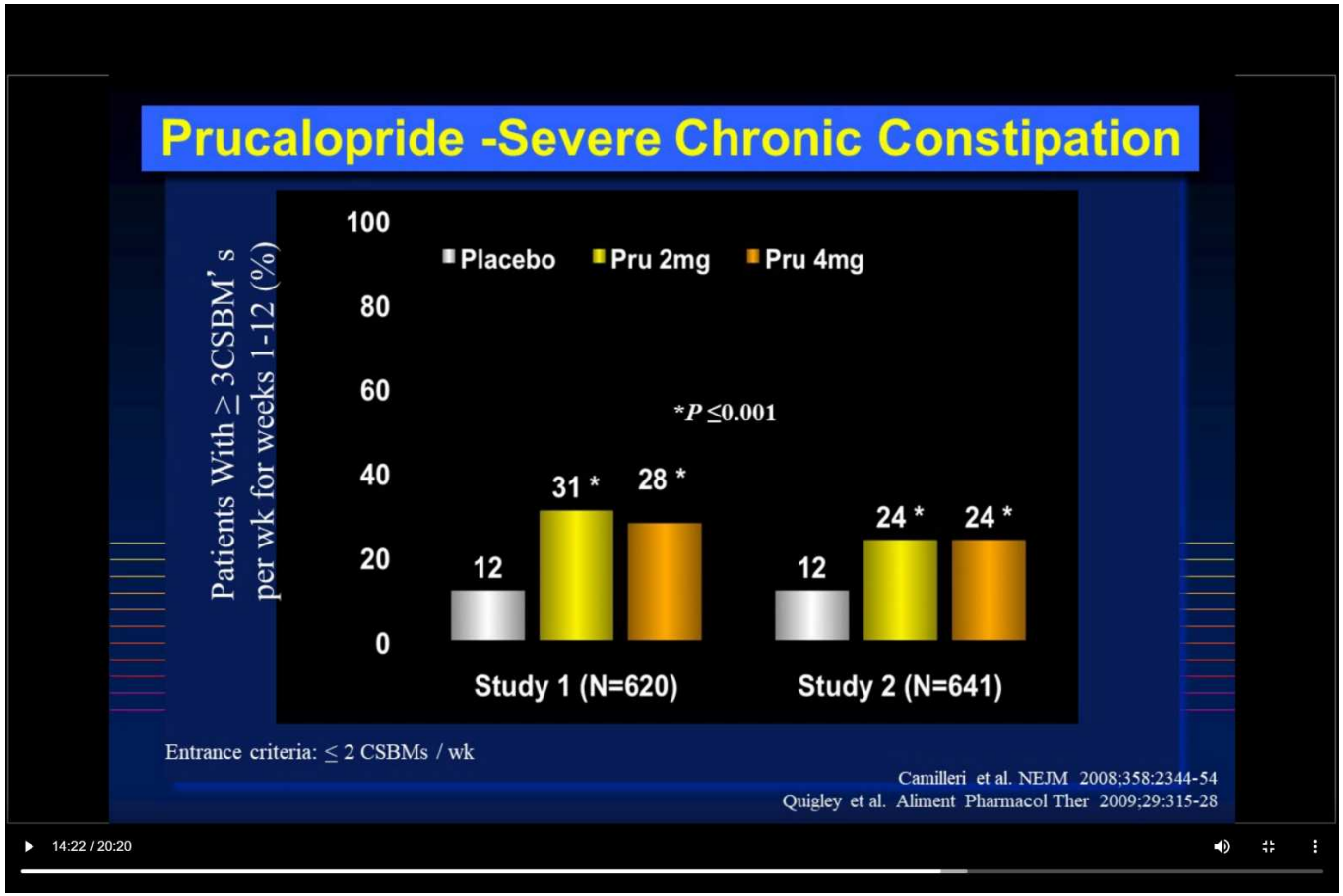
Efficacy of Linaclotide in Chronic Constipation



Lembo AJ, et al. *N Engl J Med.* 2011;365:527-536.

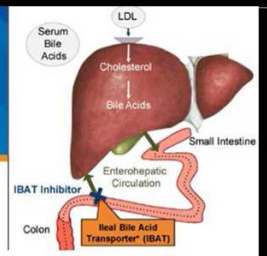
Most common AE diarrhea (14%-16% vs 4.7%); Discontinuation (4% vs 0.5%).

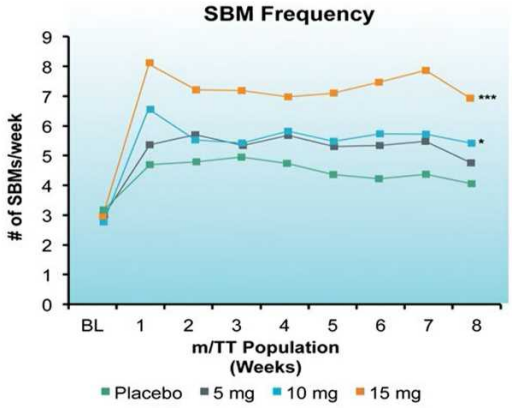
CSBM=complete spontaneous bowel movement.


Prucalopride -Severe Chronic Constipation
Patients With ≥ 3CSBM's per wk for weeks 1-12 (%)
100
80
60
40
20
0
Placebo
Pru 2mg
Pru 4mg
*P ≤0.001
12
31 *
28 *
12
24 *
24 *
Study 1 (N=620)
Study 2 (N=641)
Entrance criteria: ≤ 2 CSBMs / wk
Camilleri et al. NEJM 2008;358:2344-54
Quigley et al. Aliment Pharmacol Ther 2009;29:315-28
14:22 / 20:20

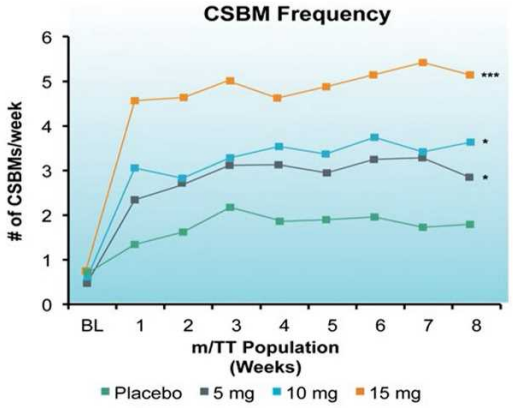
Effects of Elobixibat on Stool Frequency in CIC: Phase II, n=190

Chey WD, et al. *Am J Gastroenterol.* 2011;106:1803-1812.





Overall
5 mg vs. placebo p=0.113
10 mg vs. placebo p=0.017
15 mg vs. placebo p<0.001



Overall
5 mg vs. placebo p=0.021
10 mg vs. placebo p=0.017
15 mg vs. placebo p<0.001


40 yr old Nurse, Severe Constipation
MANAGEMENT
Lactose exclusion diet
Reassure- evidence of colonic myopathy but no neuropathy, mild generalized dysmotility
Explain Slow Transit Constipation
Life style + Behavioral + Diet
D/C opioids & Depo Provera
Linaclotide 290 micrograms daily
F.up 6 weeks- BM every 2-3 days, Type 4 stool
15:19 / 20:20

Case Study
31-yr-old school teacher

- Increasing constipation- 9 years
  - Began during college days
  - Now, B.M once every 2 weeks, hard, pellet-like stool only after Fleet's enema + Suppository and laxatives
  - Occasional digital disimpaction, but describes excessive straining, incomplete evacuation and occasional bleeding
  - Tried OTC laxatives, MOM, PEG-no relief
  - DRE: Paradoxical anal contraction, stool ++

Diagnostic Criteria-Dyssynergic Defecation

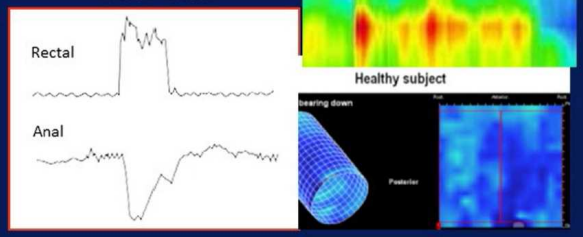
1. The patient must satisfy diagnostic criteria for functional constipation-Rome IV
2. During repeated attempts to defecate must demonstrate Dyssynergic pattern of defecation
   - Manometry
   - EMG
3. Patient must demonstrate one other abnormal test:
   a. Abnormal balloon expulsion Test (> 1 minute)
   b. Prolonged Colonic Transit Time (radioopaque markers or WMC or Scintigraphy)
   c. Abnormal Defecography (≥50% barium retention)

Rao SSC. Gastroenterol Clin N Am 36 (2007) 687-711

Rao et al, Am J Gastroenterol 2015

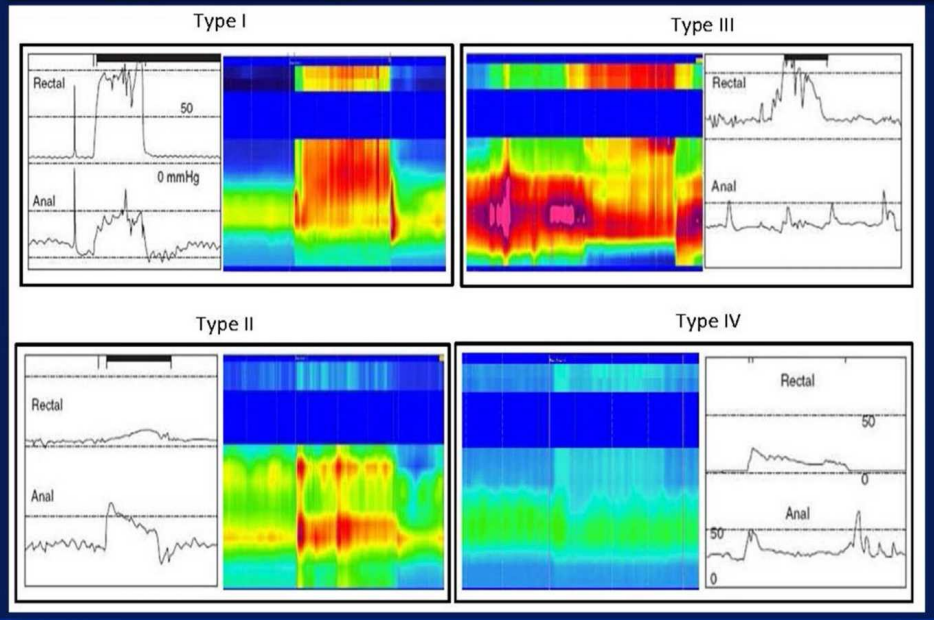
Types of Dyssynergic Defecation

Normal



Rao et al, Neurogastroenterol Motil 2004; 16: 589

Types of Dyssynergic Defecation



Rao et al, Neurogastroenterol Motil 2004; 16: 589

How to Treat Dyssynergic Defecation ?

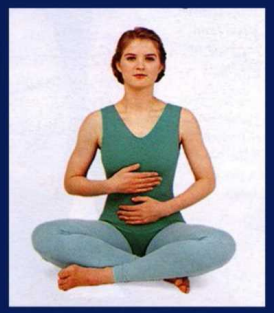
- General Measures
  - Diet, exercise, fluids & habit training
  - Laxatives/Prokinetics
- Specific Treatment
  - Botox injection
  - Biofeedback therapy
  - Cognitive Behavioral Therapy
  - Surgery
    - Myectomy- 30% improvement
    - Colostomy

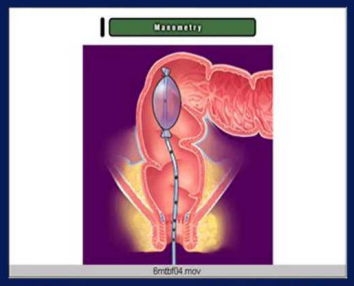
Rao et al, Gastro Clin N Am 2009

Biofeedback-Dyssynergia

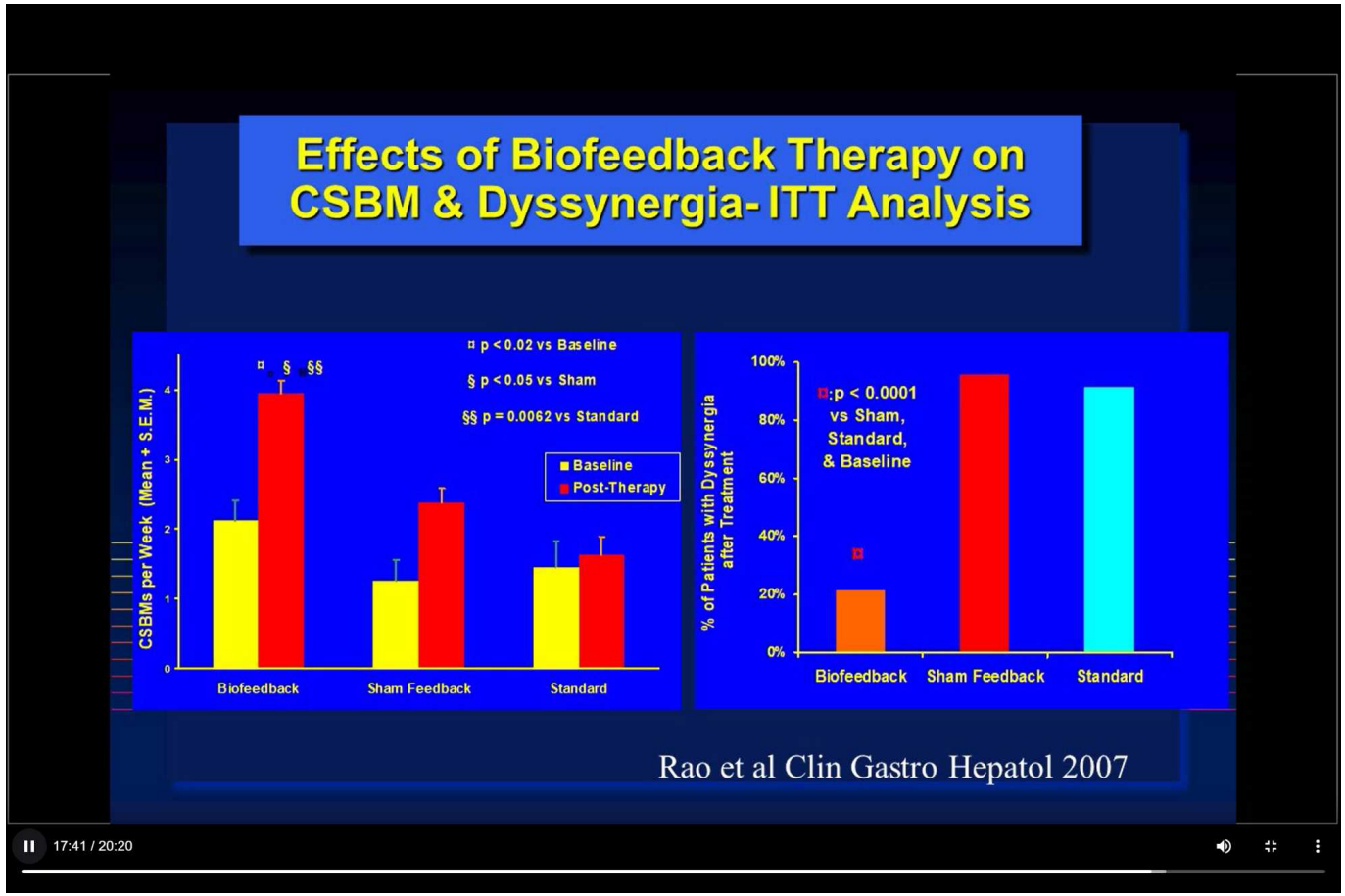
» Goals of Therapy :

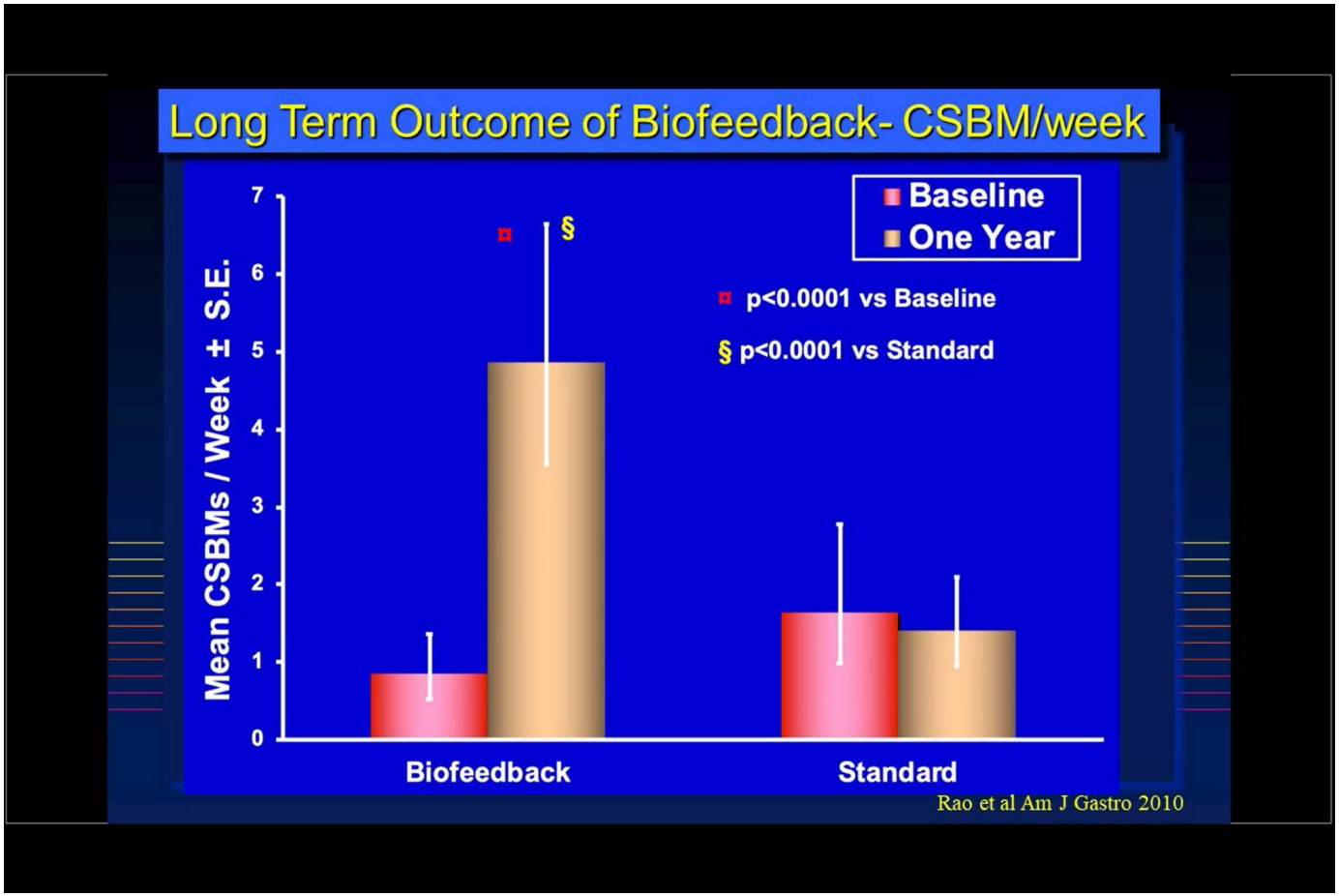
- A) Teach Diaphragmatic breathing exercise
- B) Teach anal sphincter & pelvic floor relaxation
- C) Improve Rectal Sensation
- D) Eliminate Sensory Delay
- E) Improve Recto-anal Coordination





Rao et al, Neurogastro Mot 2015


Effects of Biofeedback Therapy on CSBM & Dyssynergia- ITT Analysis
¤ p < 0.02 vs Baseline
§ p < 0.05 vs Sham
§§ p = 0.0062 vs Standard
Baseline
Post-Therapy
CSBMs per Week (Mean + S.E.M.)
Biofeedback
Sham Feedback
Standard
¤:p < 0.0001 vs Sham, Standard, & Baseline
% of Patients with Dyssynergia after Treatment
Rao et al Clin Gastro Hepatol 2007
17:41 / 20:20


Long Term Outcome of Biofeedback- CSBM/week
Baseline
One Year
p<0.0001 vs Baseline
§ p<0.0001 vs Standard
Mean CSBMs / Week ± S.E.
0
1
2
3
4
5
6
7
§
Biofeedback
Standard
Rao et al Am J Gastro 2010

Home vs Office Biofeedback- Responder Analysis, How Effective?

RESPONDER= ≥ 1 CSBM/wk + Normalization of Dyssynergia pattern

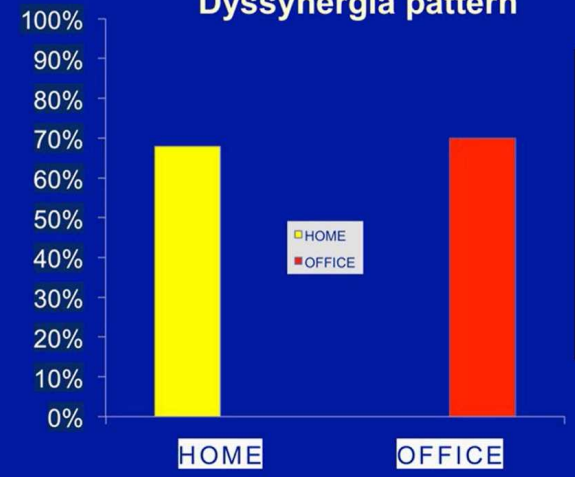
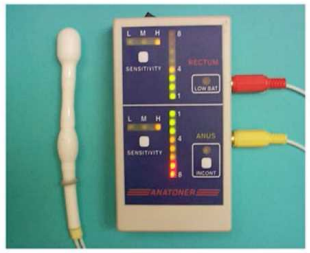


Fig 3. ANATONER-Home Trainer & Probe



Rao et al Lancet Gastro 2018

Biofeedback Therapy-RCTs

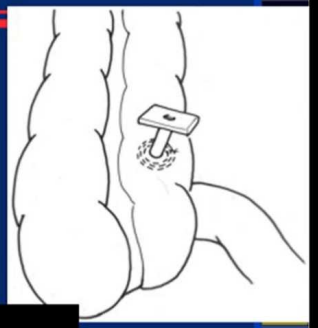
- Biofeedback Vs PEG 14.6 g for Dyssynergia
  - *Chiarioni et al, Gastroenterology 2006; 130: 657-64*
- Biofeedback vs Diazepam for Dyssynergia
  - Heymen et al, Dis Col Rectum 2007
- Biofeedback vs Sham Therapy vs Standard Therapy
  - *Rao et al CGH 2007*
- Biofeedback vs Standard Therapy-One Year outcome
  - *Rao et al Am J Gastroenterol 2010*
- *Home vs Office Biofeedback Therapy- Efficacy & Cost Effectiveness*
  - *Rao et al Lancet 2018 & Rao SS, Go J et al, Am J Gastroenterol 2019*

Evidence Level: Type 1; Recommendation Grade: A

Rao et al: American & European NGM Societies, Neurogastro Mot 2015

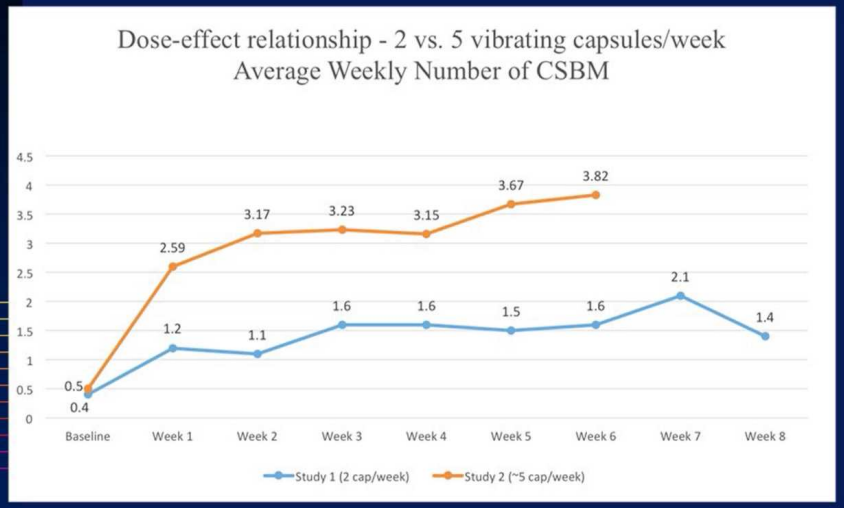
Other Therapies

- **Surgical**
  - Maloney's Procedure - Cecostomy with antegrade enemas; 1 liter-glycerin: saline, 1:1
  - Subtotal Colectomy + Ileorectal Anastomosis or Ileostomy
- **Future**
  - Sacral Nerve Stimulation
  - Pacing
  - Transplantation



Rao et al, Gastro Clin N Am 2009

Vibrating Capsule: Double Blind Study



Quigley E, Rao SS et al ACG 2017; Rao SS et al, ACG 2018

Take Home Points- 1

- Chronic constipation involves multiple overlapping subtypes
- Detailed History, Physical & DRE important
- Constipation APP - accurate stool diary
- DRE is a useful bedside clinical tool
- Dyssynergic defecation is common
- Prunes, Suprafiber effective in mild constipation

Take Home Points- 2

- Chronic Constipation: Investigation is key
  - Colonic Transit, WMC, ARM, Defecography, Colonic manometry are complementary & useful
- Recognize comorbid illnesses, Burden & QOL
- Therapeutic options will depend on a clear understanding of pathophysiology
  - STC/CIC: Linaclotide, Plecanatide, Prucalopride, Lubiprostone
  - OIC: Naloxegol, Methyl naltrexone, Naldemedine
  - Dyssynergic Defecation: Biofeedback therapy