

Managing the Challenges of Gastroparesis

Daniela Jodorkovsky M.D.

Director, Mount Sinai Center for Gastrointestinal Physiology and Motility

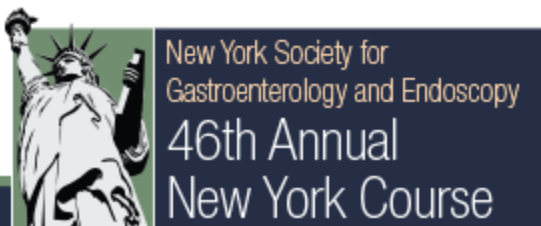
Mount Sinai West and Morningside

Associate Professor of Medicine

Icahn School of Medicine at Mount Sinai

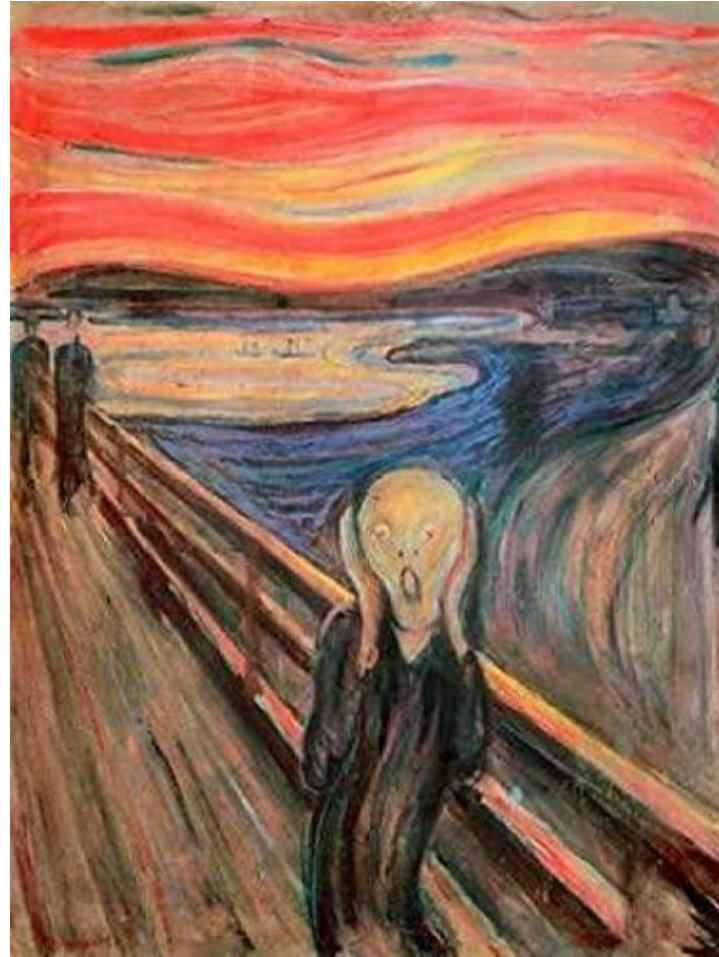


**Mount
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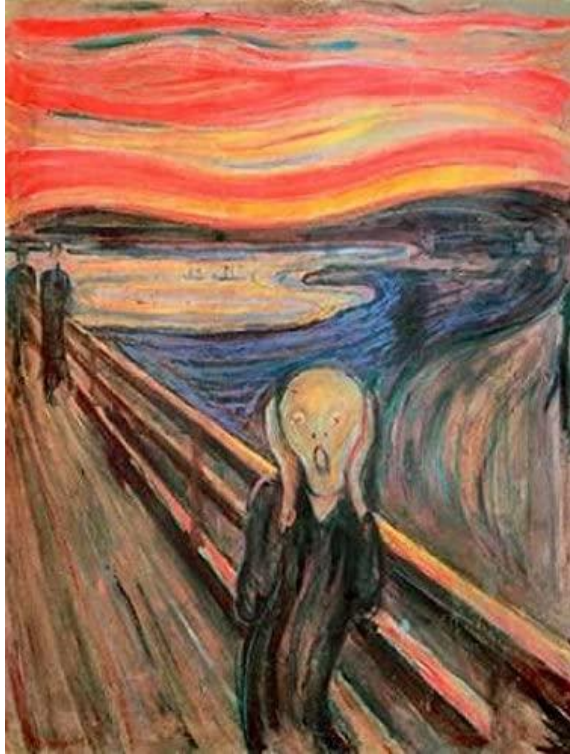
New York Society for
Gastroenterology and Endoscopy
46th Annual
New York Course

Managing Gastroparesis



Objectives

- Go from



to



Gastroparesis: a definition

- Syndrome of objective delay in gastric emptying + cardinal symptoms
 - Nausea
 - Vomiting
 - Bloating
 - Upper abdominal pain
 - Early satiety
 - Fullness
- No evidence for mechanical obstruction

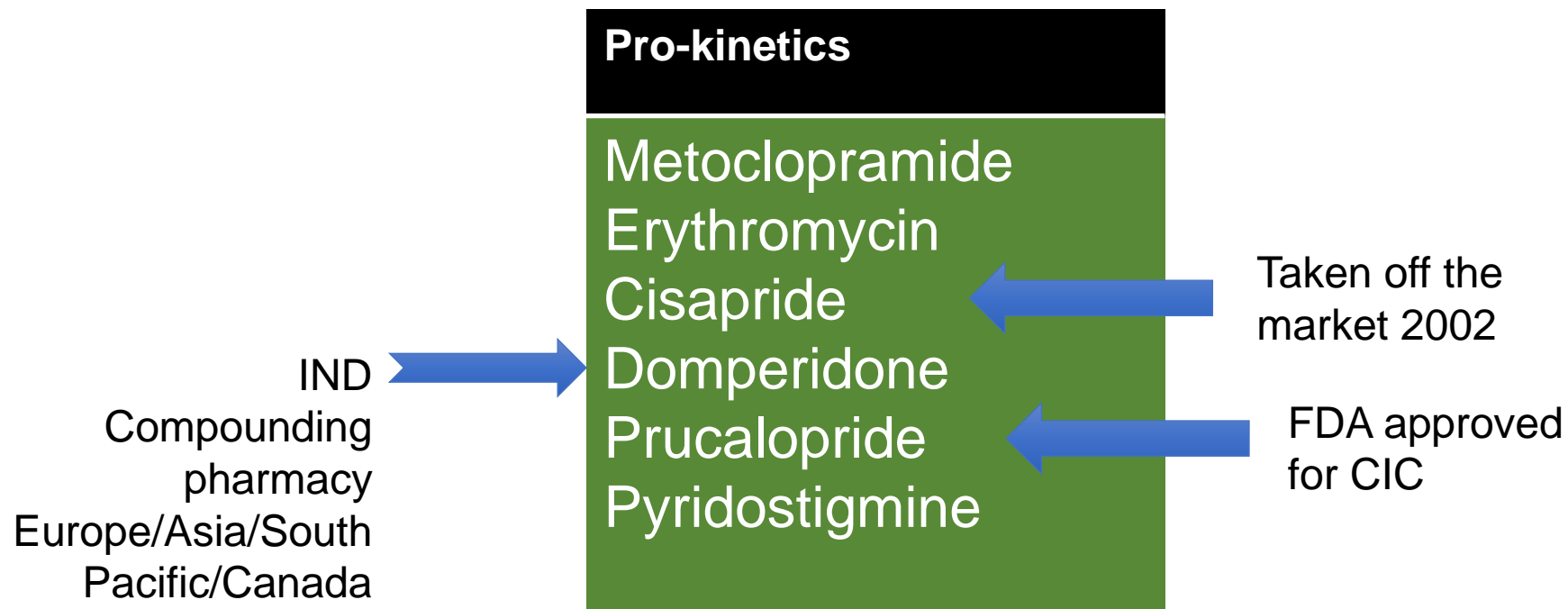
Gastroparesis: prokinetics

- If GP is due to delayed emptying, treatment with prokinetics should be effective in relieving symptoms

FDA approved meds are prokinetics

- Metoclopramide (Reglan)
 - Dopamine receptor antagonist
 - Crosses BBB- CNS side effects common
 - Black box warning TD 2009
 - Limited treatment duration to 12 weeks
- Metoclopramide nasal spray (Gimoti)
 - FDA approved 6/2020

Prokinetic Therapy: few

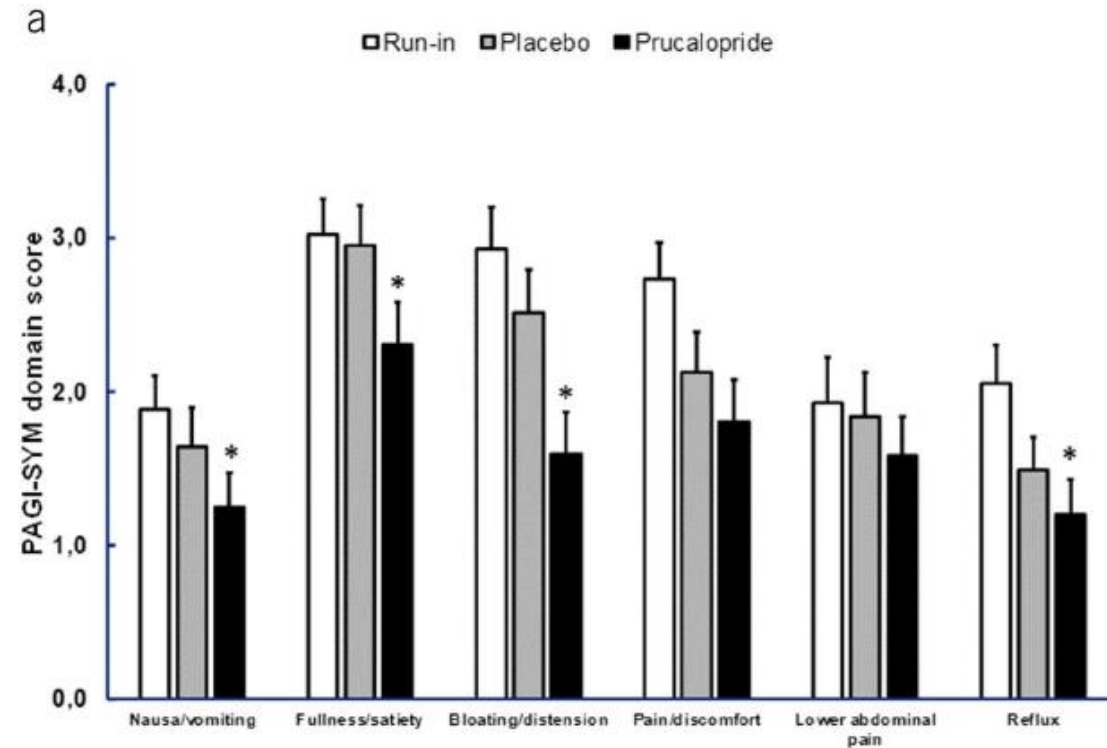


Erythromycin

- Macrolide antibiotic that agonizes motilin receptors
- Tachyphylaxis- limits long term use
- Side effects
 - Cramps
 - Nausea
 - Prolonged Qtc

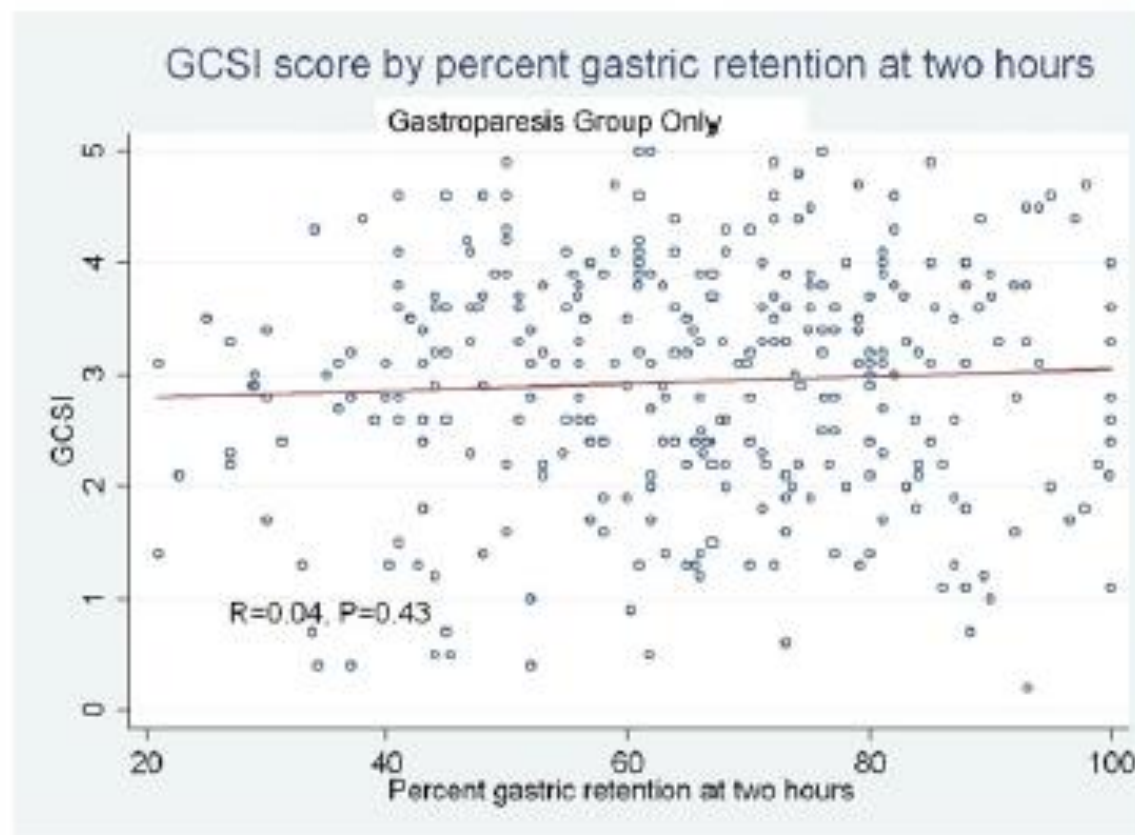
Prucalopride

- FDA approved for chronic idiopathic constipation
- Selective 5hT4 agonist (no hERG)
- RCT 34 pts (mostly idiopathic), 4 week trial
 - Improved GCSI, PAGA-SIM, and GE via BT
- S/E – diarrhea, headache



What's the problem with prokinetics?

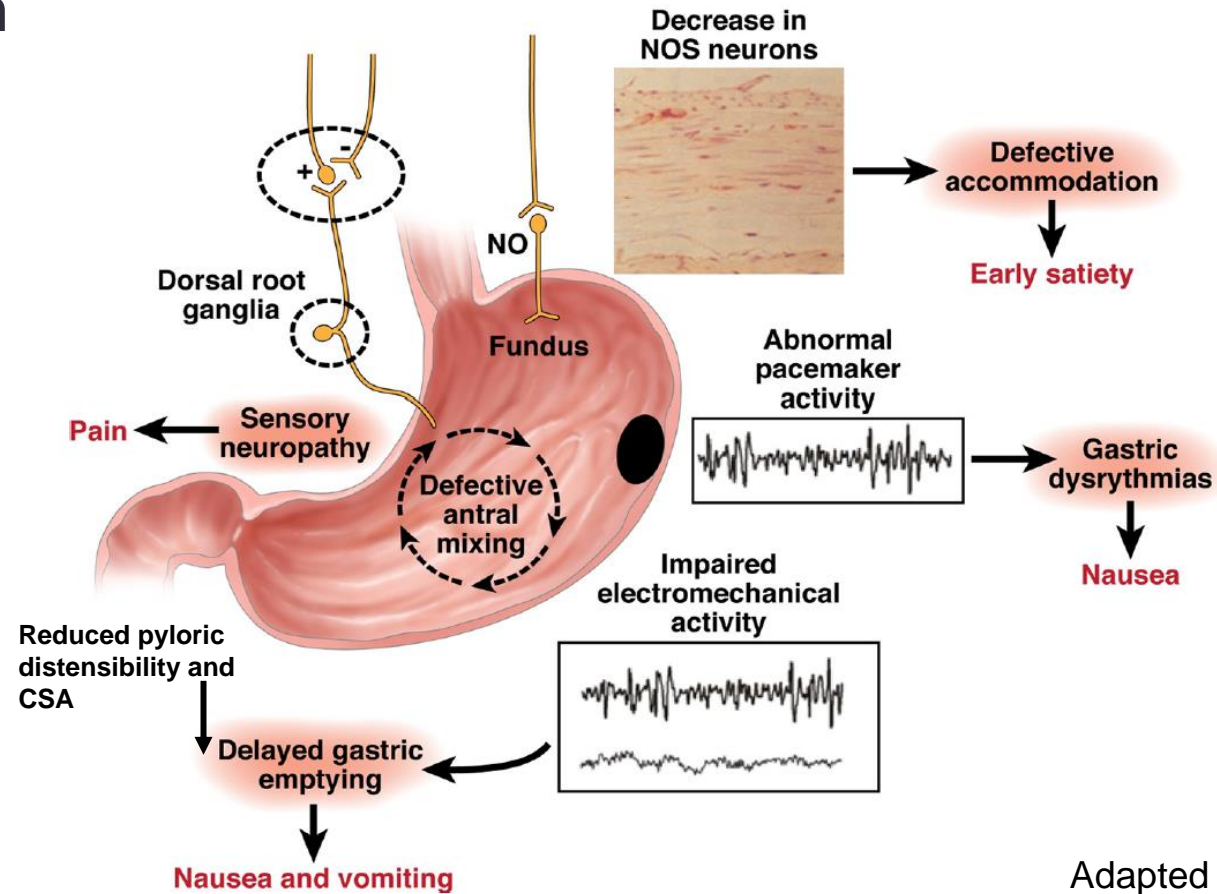
- Gastroparesis symptoms not only explained by delayed emptying, despite its definition



Pasricha PJ et al, CGH 2011; 9

Pathophysiology of symptomatology

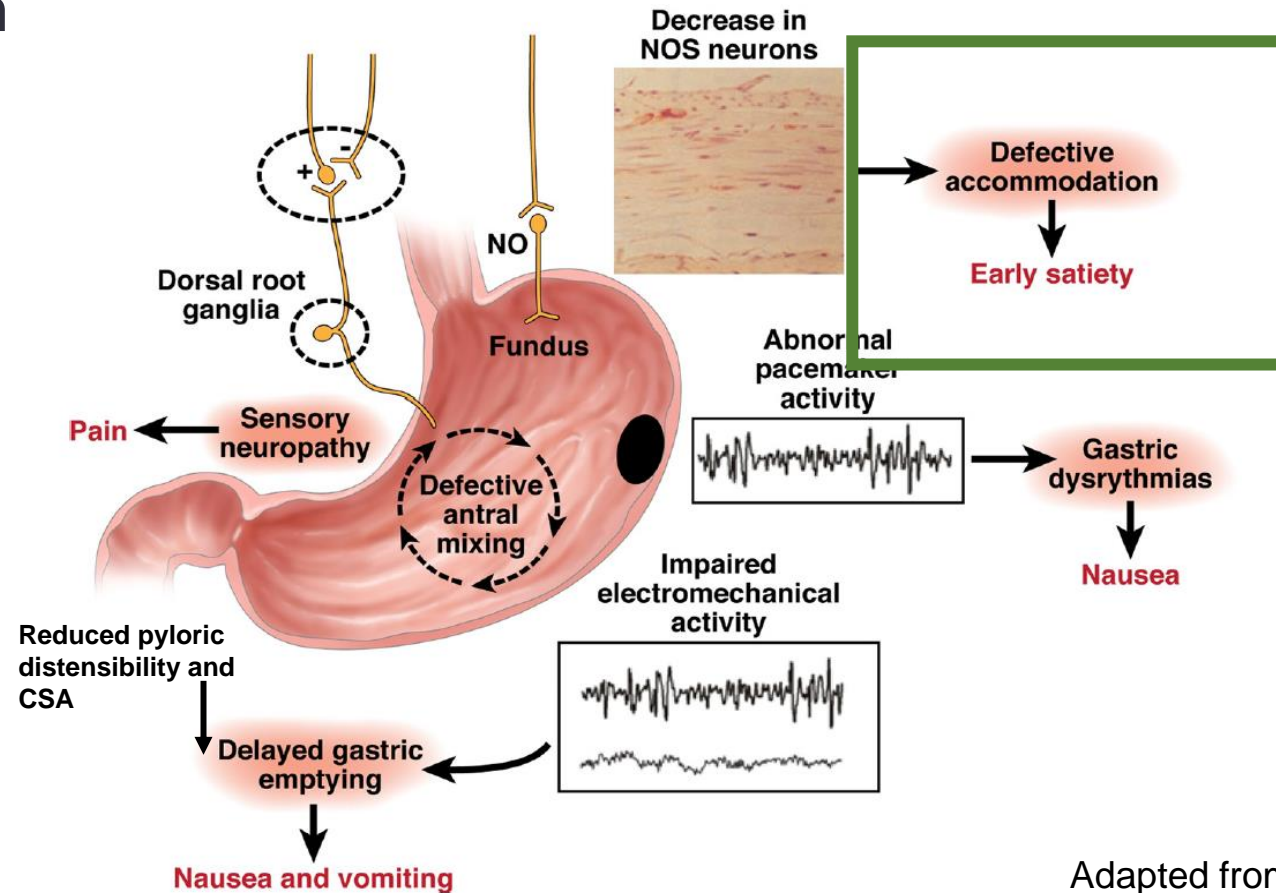
- Diverse mechanisms make treatment challenging but provide targets for therapeutic approach



Adapted from Owyang C, Gastro 2011

Pathophysiology of symptomatology

- Diverse mechanisms make treatment challenging but provide targets for therapeutic approach



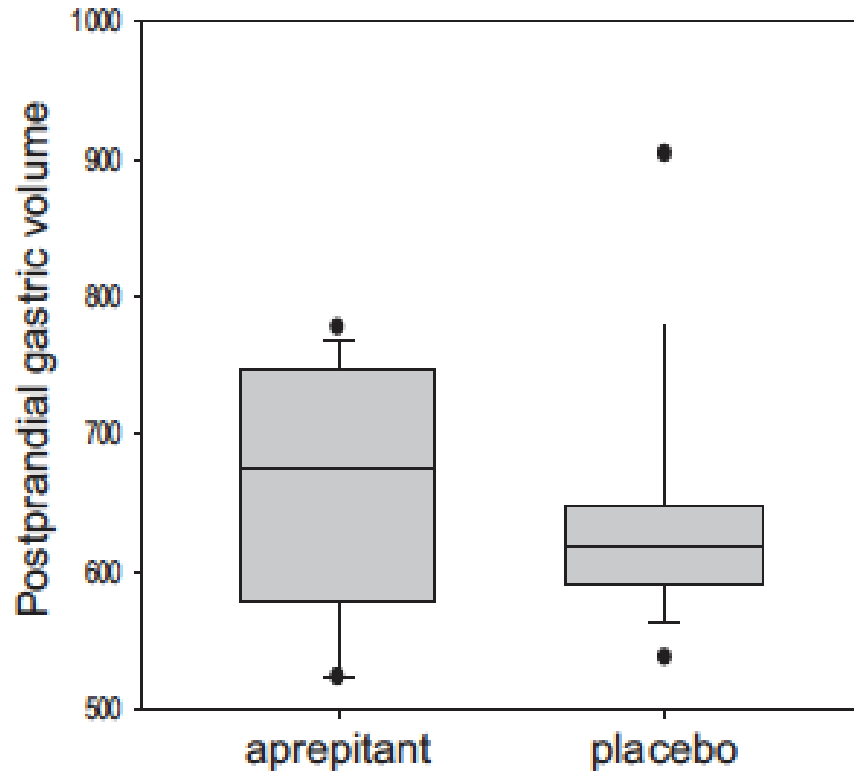
Impaired fundus accommodation

- Aprepitant
- Mirtazipine
- Buspirone

Aprepitant

- FDA approved for prevention of acute n/v 2/2 chemotherapy, post-op
- Selective neurokinin-1 antagonist
- Anti-emetic effect directly on emesis center brainstem
- But also with effects on gastric motor function

Aprepitant



P=0.004, adjusted for gender, BMI

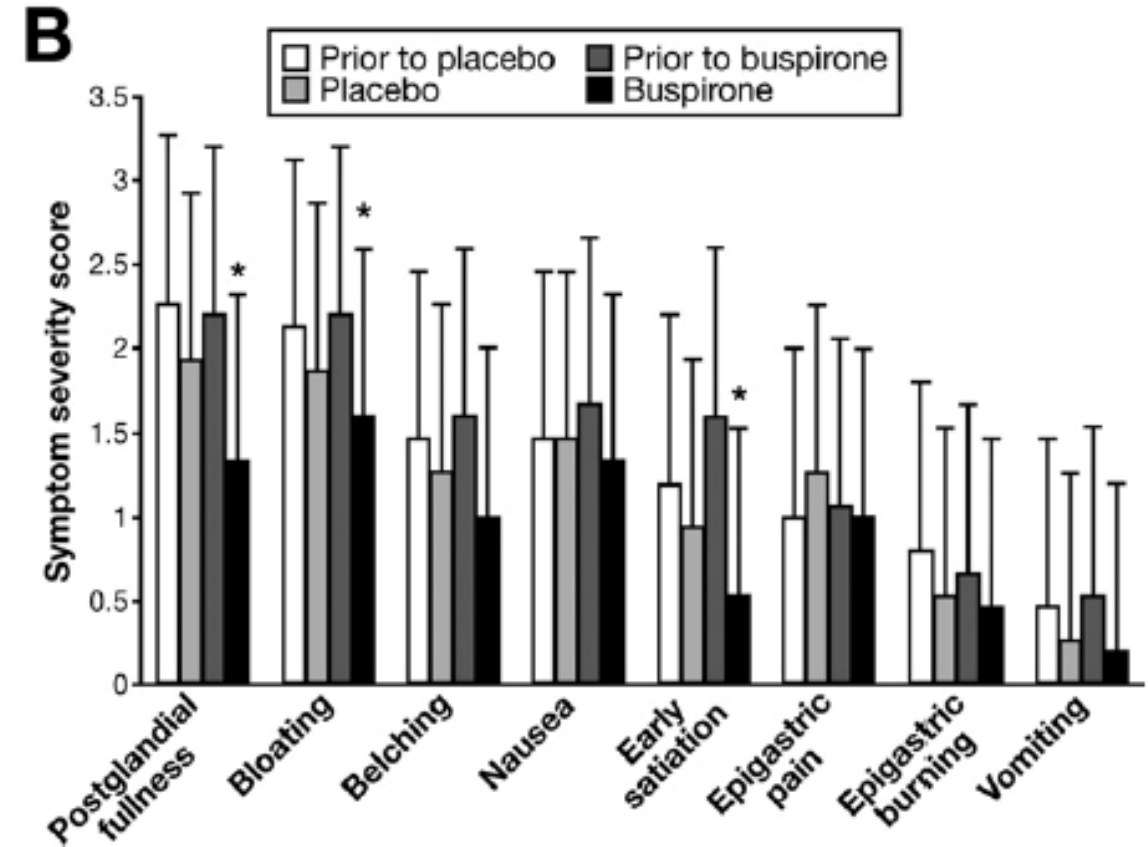
- In RCT of 24 controls, Jacob et al performed GES, nutrient satiety drink test, SPECT imaging for gastric accommodation
 - No effect on gastric emptying
 - Increased volume to fullness on nutrient drink test and gastric volume on SPECT
- Pasricha et al performed RCT 127 pts with chronic n/v (~50% had GP)
 - Improvement in GCSI and PAGI-SYM subscores but not visual analog scale (VAS) for nausea

Mirtazapine

- Anti-depressant that has mixed adrenergic and serotonin activity
 - Anti-emetic, helps gain weight
- Tack J et al: RCT mirtazapine 15mg in functional dyspepsia patients improves symptom score and nutrient volume tolerance
 - No change in gastric emptying
- Multiple case reports in Gastroparesis
- Malamood et al: Open label study 30 pts with GP
 - Statistical improvement in nausea, vomiting, and appetite scores
 - No physiologic testing performed in this 4 week study

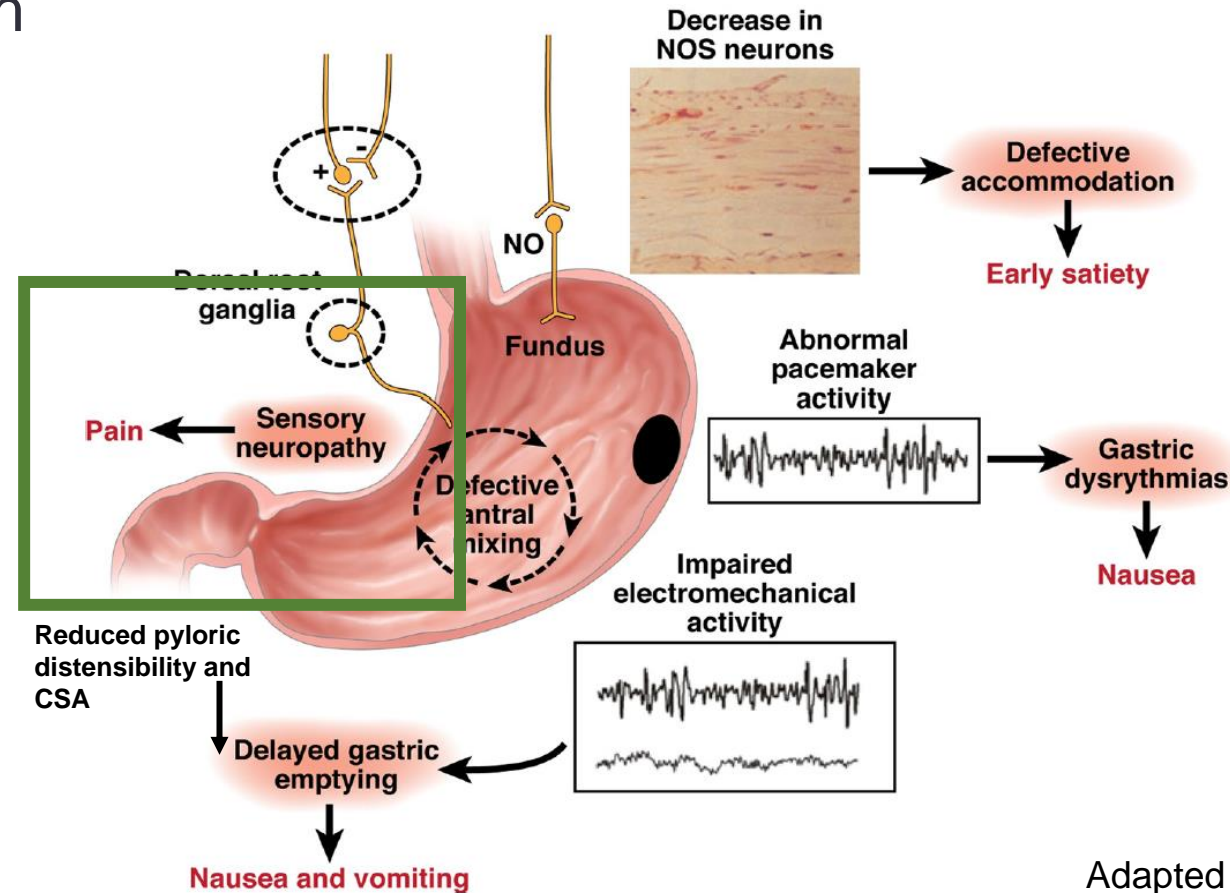
Buspirone

- 5HT_{1A} Agonist
- RCT 20 FD pts: 10mg TID vs placebo
- Improved fundus accommodation using barostat but not emptying on breath test
- Decreased symptom scores
 - Post-prandial fullness, bloating, early satiety
 - Note nausea/vomiting not significant



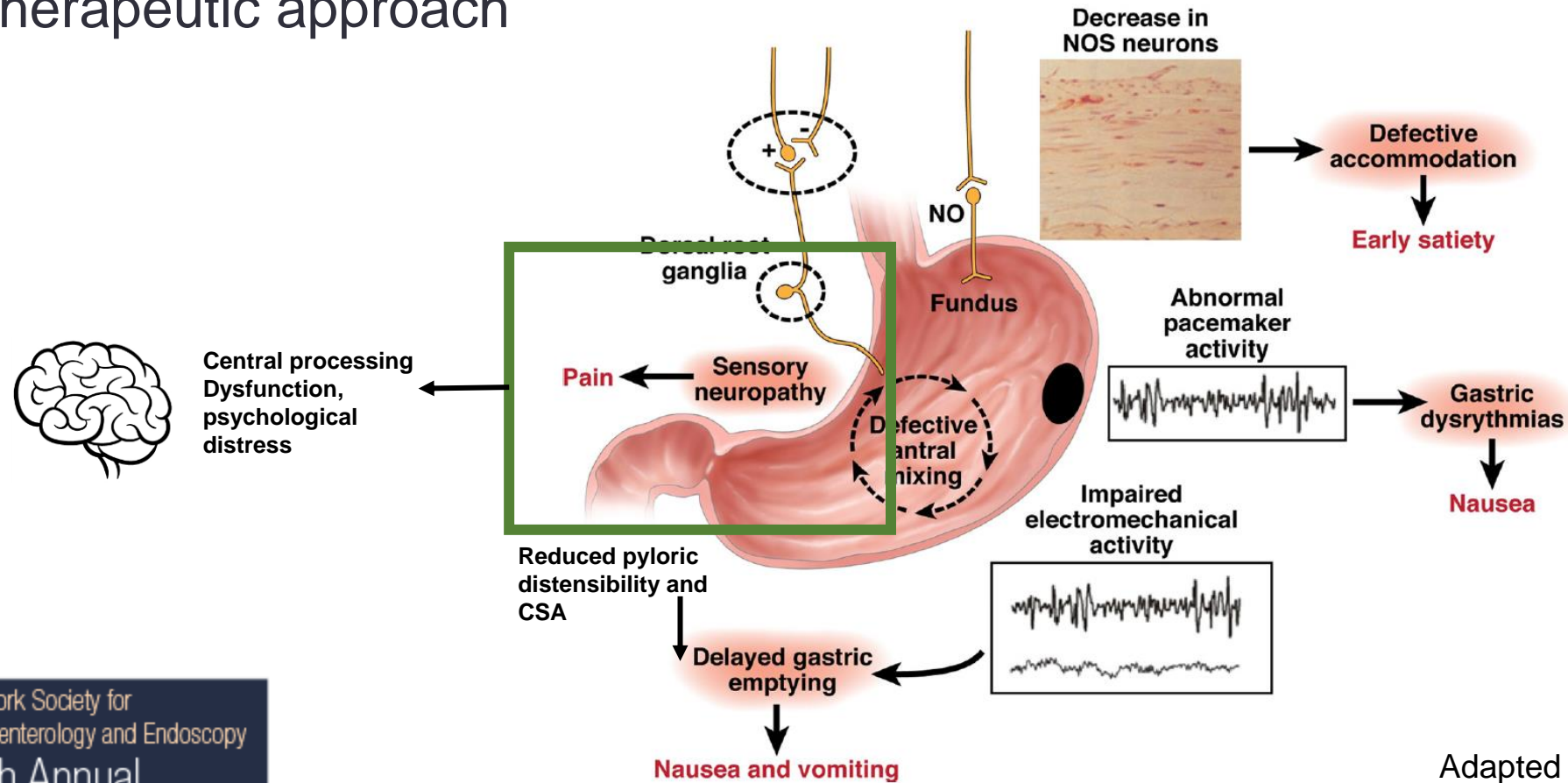
Pathophysiology of symptomatology

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Pathophysiology of symptomatology

- Diverse mechanisms make treatment challenging but provide targets for therapeutic approach

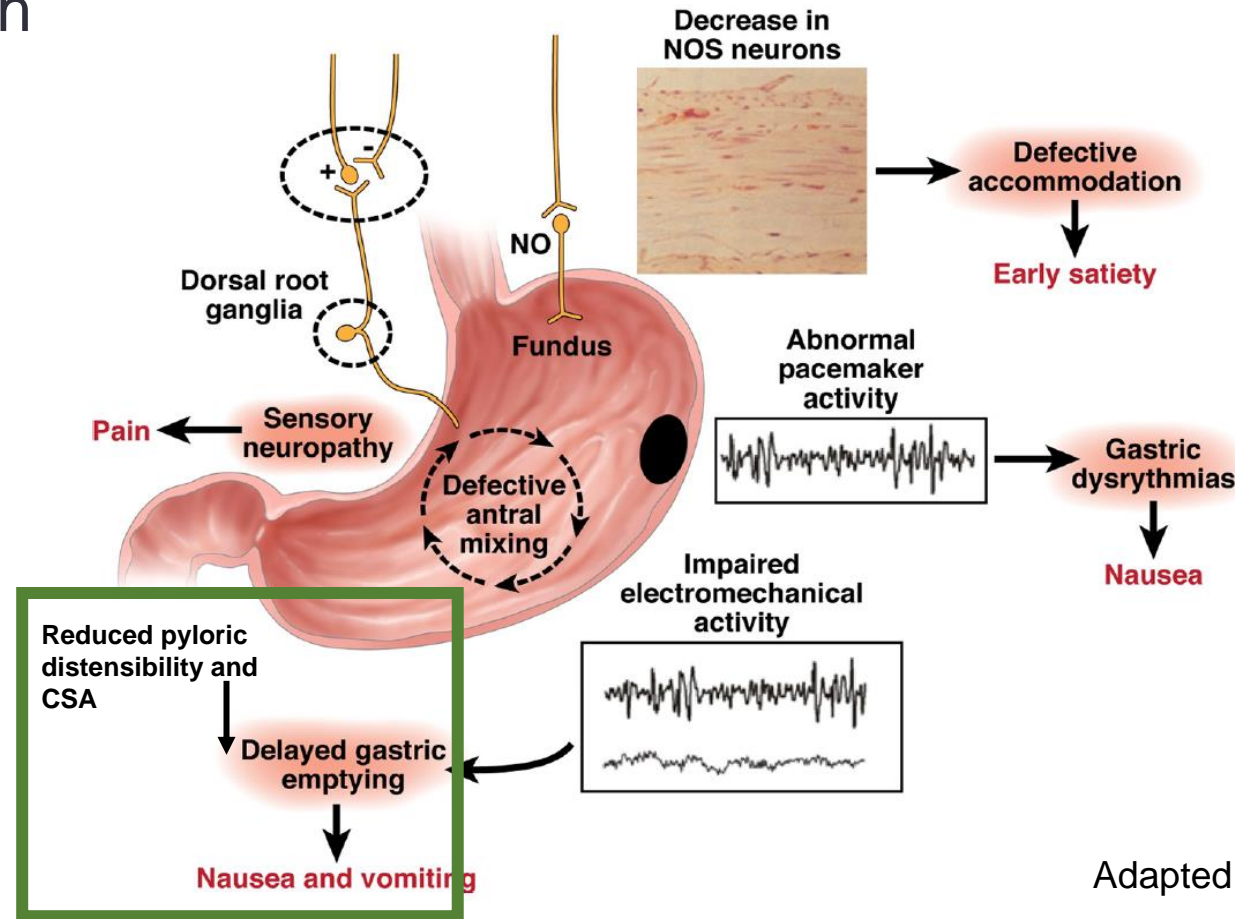


Sensory neuropathy

- Opiates not recommended
- NORIG trial: RCT 130 pts idiopathic GP
 - No difference in global score between nortriptyline and placebo arm
 - Some statistical improvement in abdominal pain score alone
 - Neuromodulators recommended by ACG guidelines
- RCTs needed for exploration of gabapentin, pregabalin, duloxetine
- CBT and hypnotherapy may target central processing
 - Gut-directed hypnotherapy reduced emptying time in open label study of 15 pts with functional dyspepsia!

Pathophysiology of symptomatology

- Diverse mechanisms make treatment challenging but provide targets for therapeutic approach



Adapted from Owyang C, Gastro 2011

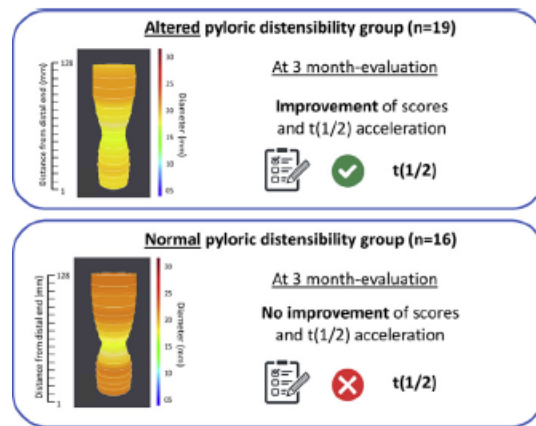
Pylorus-directed therapy: Botox

- Open label case series showed promise
- 2 RCTs, with 4 week follow up
 - 23 pts (19 IG) → no difference with placebo
 - 32 pts (19 DG, 13 IG) → no difference with placebo
- ACG guidelines: *“Intrapyloric injection of botulinum toxin is not recommended for patients with gastroparesis based on randomized controlled trials. (Strong recommendation, moderate level of evidence)”*

Freidenberg FK et al, Am J Gastro 2008:103
Arts J et al, APT 2007: 26
Camilleri M et al, Am J Gastro 202; 117

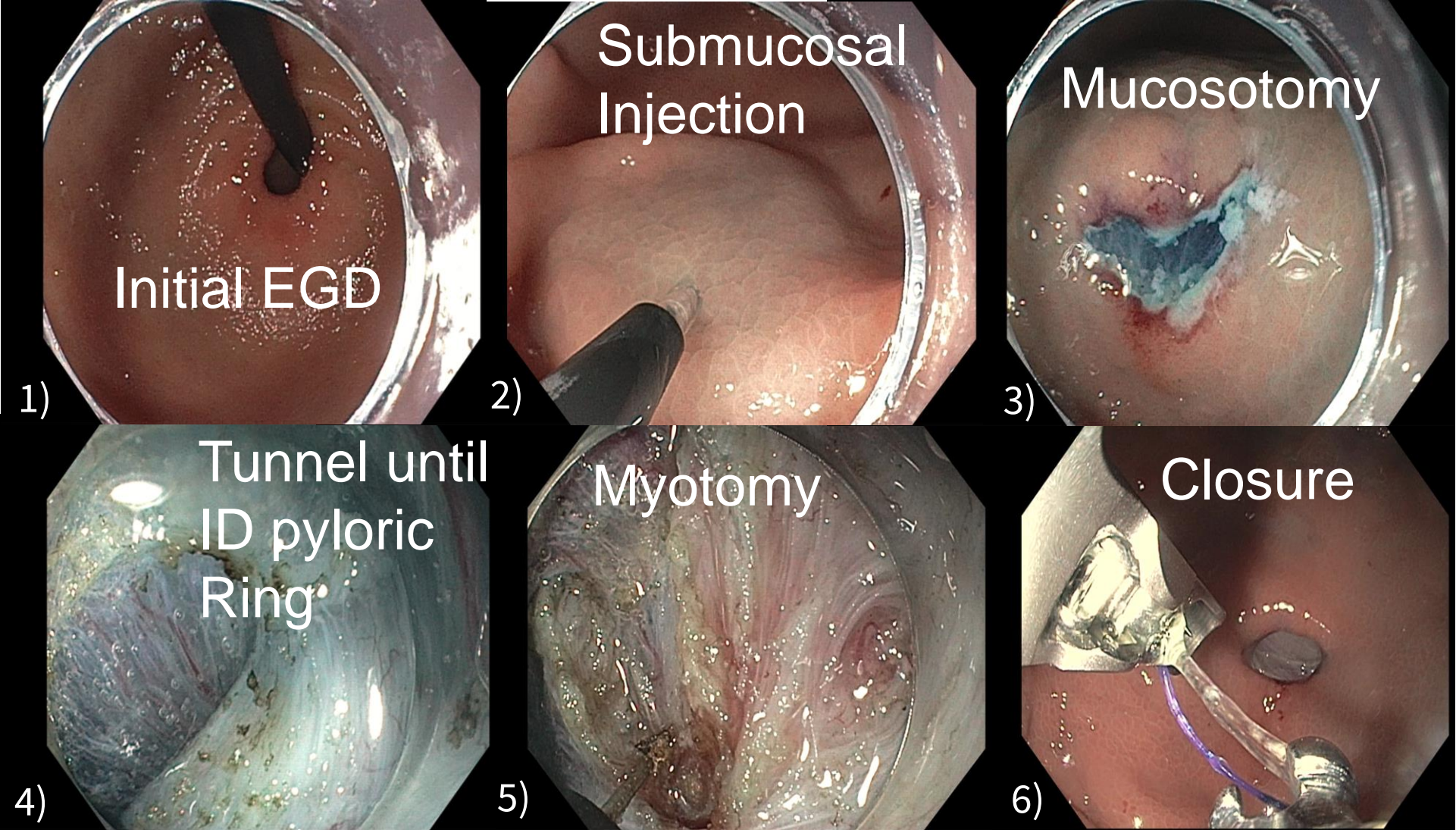
EndoFLIP may guide pylorus-directed txt

- FLIP catheter across pylorus measures distensibility and diameter
 - Symptom severity inversely correlated with DI/diameter
 - In pts with n/v, decreased DI noted in those with (+)gastric retention vs. those without retention
- In 35 patients, 19 with reduced $DI < 10$ had reduction in symptom scores following botox vs those with normal DI had no response



Malik Z et al, NGM 2015;27
Snape WJ et al, NGM 2016;28
Desprez C et al, GIE 2019;90(5)

Per-oral endoscopic myotomy (G-POEM or POP)

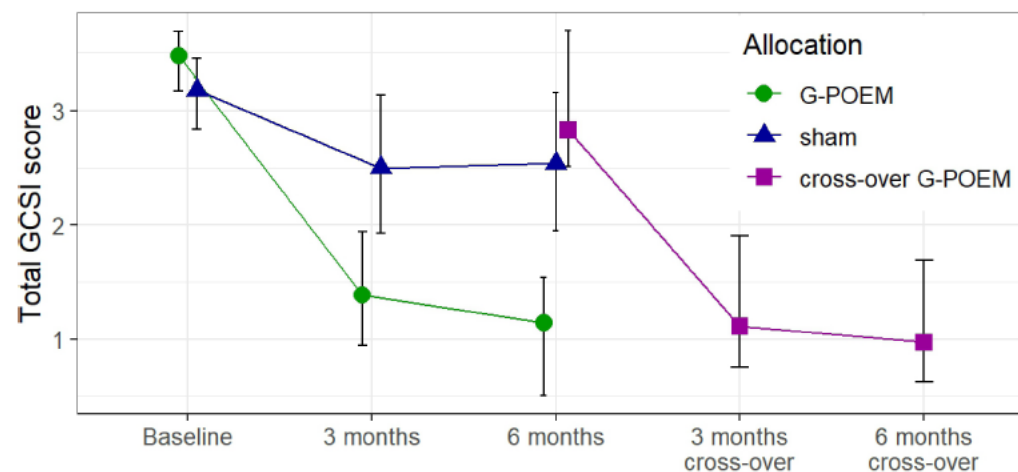


GPOEM evidence

- Systematic review of 10 studies (2 prospective)
 - Pooled clinical success 83.9%- short term follow up
 - Improvement in GES noted
- Possible predictors of success based on meta-analysis :
 - Idiopathic
 - Prior (+) txt botox
 - Stimulator
 - Results equal to surgical pyloroplasty
- Longest follow up 1 year: Retrospective review of 76 pts
 - Success at 1 year (decreased in GCSI) 65.8%
 - Increased % retention pre-op associated with failure

Randomized Sham controlled trial

- 41 pts randomized 1:1 Sham vs. GPOEM
 - Sham= EGD with general anesthesia, lasting 40 min
 - 17 diabetic, 13 post-surgical, 11 idiopathic
- Treatment outcome= 50% reduction in GCSI
- Success 71% vs 22% (p=0.005)



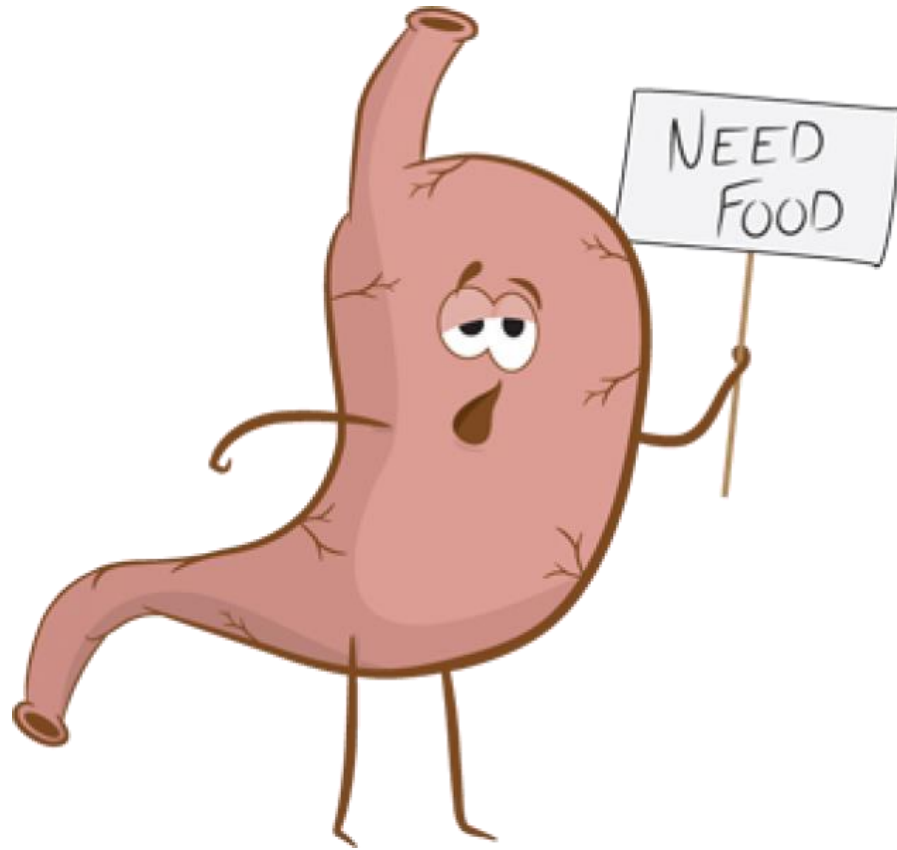
Martinek J et al, Gut 2022; 71

In summary...

- Your gastroparesis toolbox includes medications and therapies targeting ALL mechanisms of symptom generation

Nausea (central, dysrhythmia)	Enhancing emptying	Fundus accommodation	Sensory modulation
Metoclopramide	Metoclopramide	Mirtazipine	TCA's?
Domperidone	Erythromycin	Buspirone	SSRI/SNRI's
Ondansetron	Domperidone	Aprepitant	Gabapentin/Lyrica
Prochlorperazine	Prucalopride		Mirtazipine
Promethazine	Pyridostigmine		Buspirone
Scopolamine	Pylorus-directed therapies		Cognitive and hypnotherapy
Sancuso			?electronical stimulation
Dronabinol	Small particle size diet		
Aprepitant			

Thank you!



Daniela.jodorkovsky@mountsinai.org