
What you really need to know about Gastroparesis?



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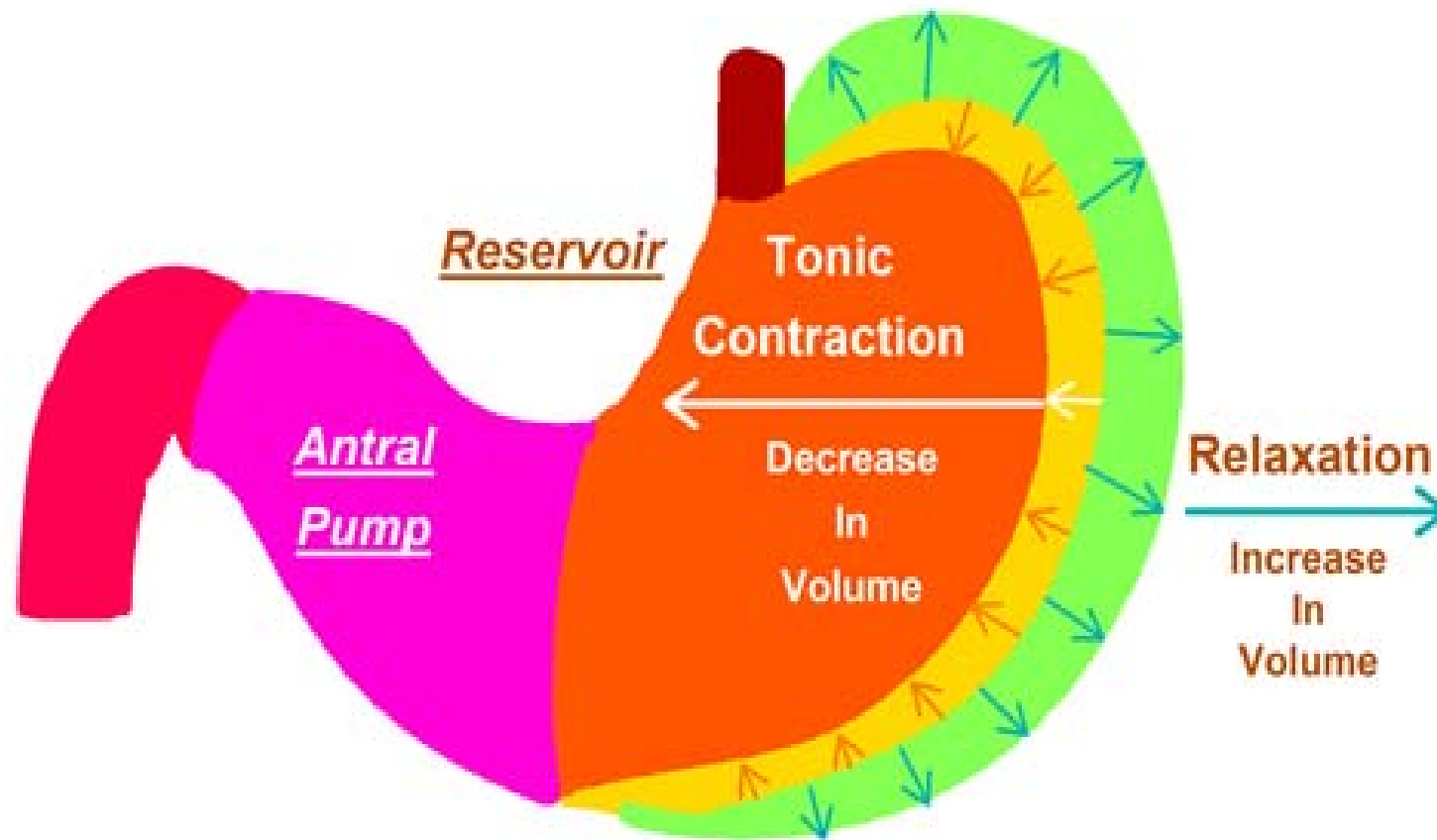
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What you really need to know about Gastroparesis?

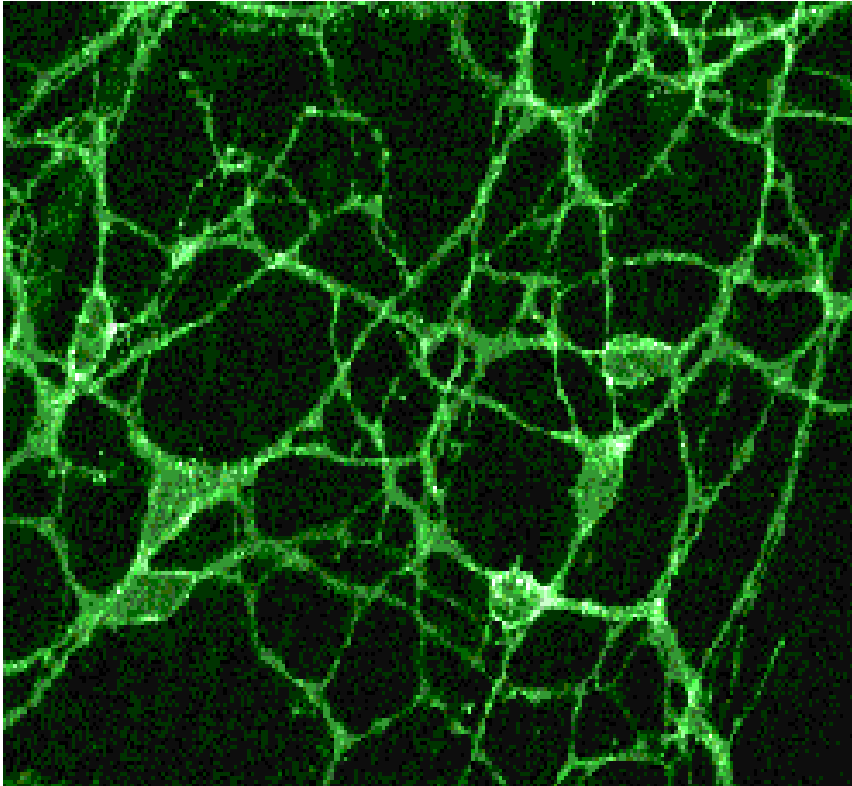
- Normal function of the stomach
- Causes of gastroparesis
- Symptom presentation
- Evaluation
- 4 most important things to know about gastroparesis
- Gastric electrical stimulation



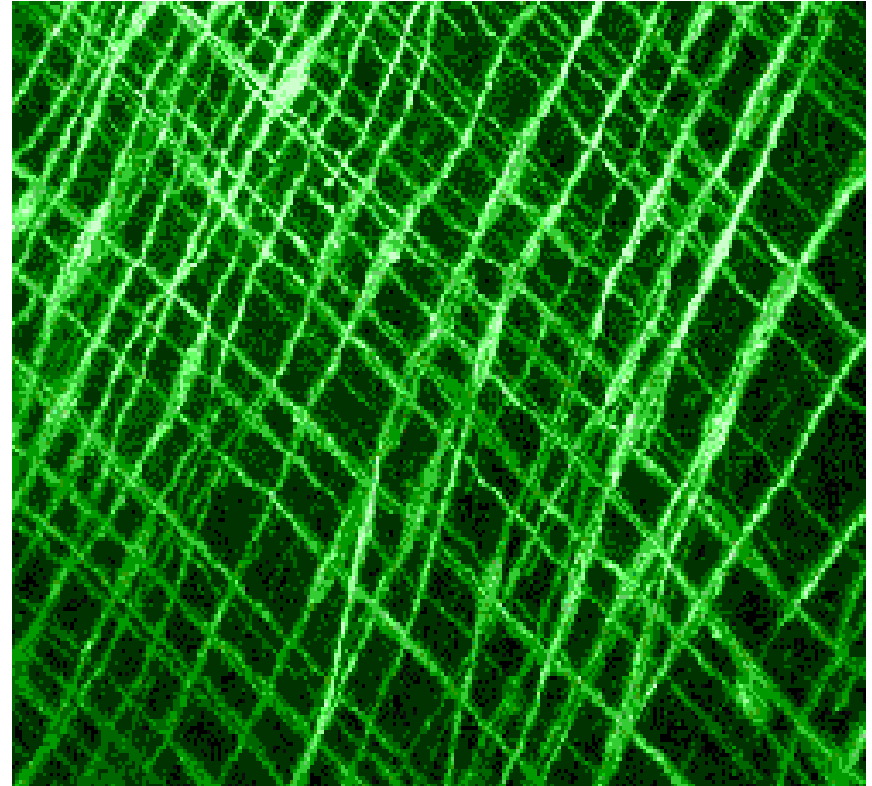
Functional Compartments of the Stomach



Interstitial Cells of Cajal: The GI Pacemakers



Small Intestines



Gastric Fundus



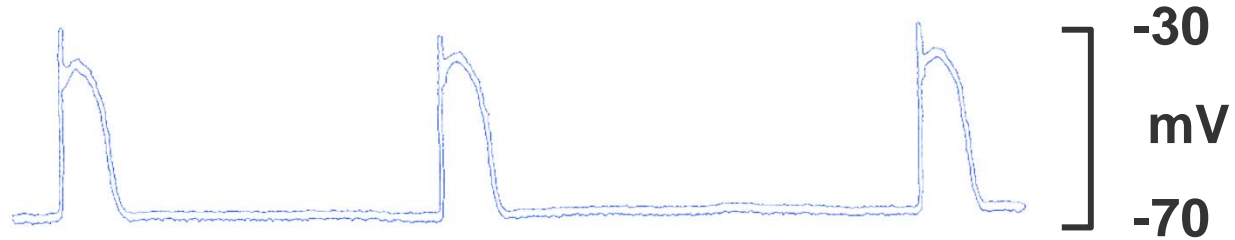
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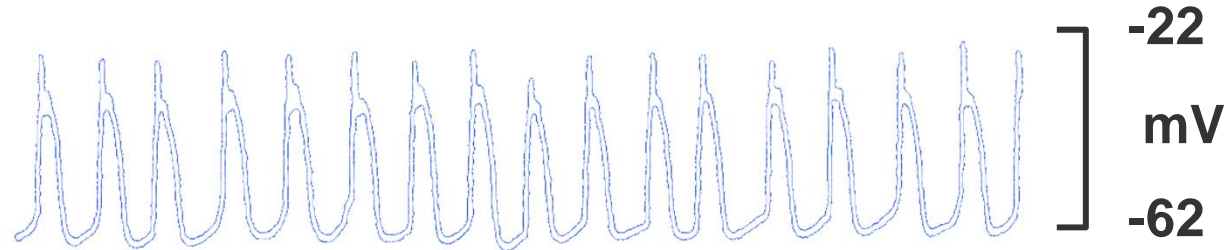
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Enteric Nervous System Controls Electrical Rhythm of GI Tract

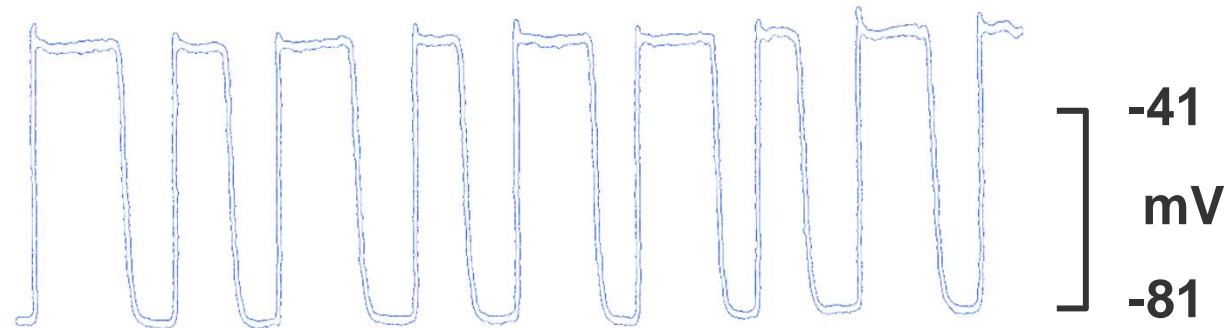
**Stomach
(3/min)**



**Small
intestine
(8-12/min)**



**Colon
(3-6/min)**

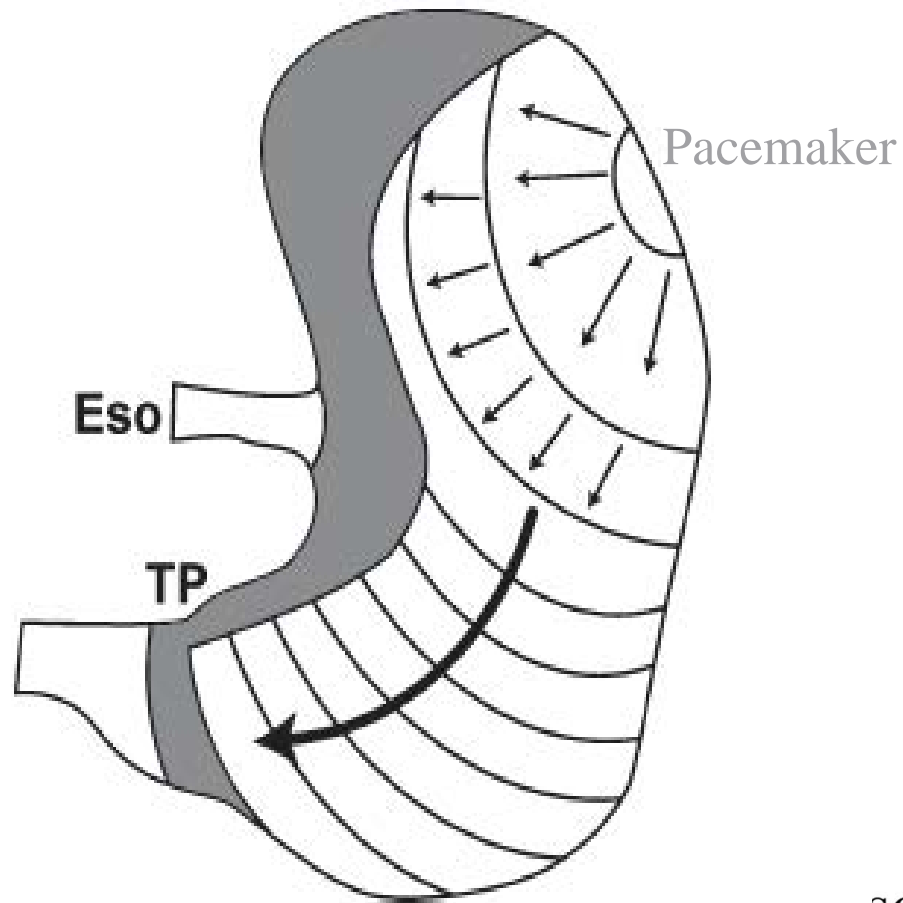


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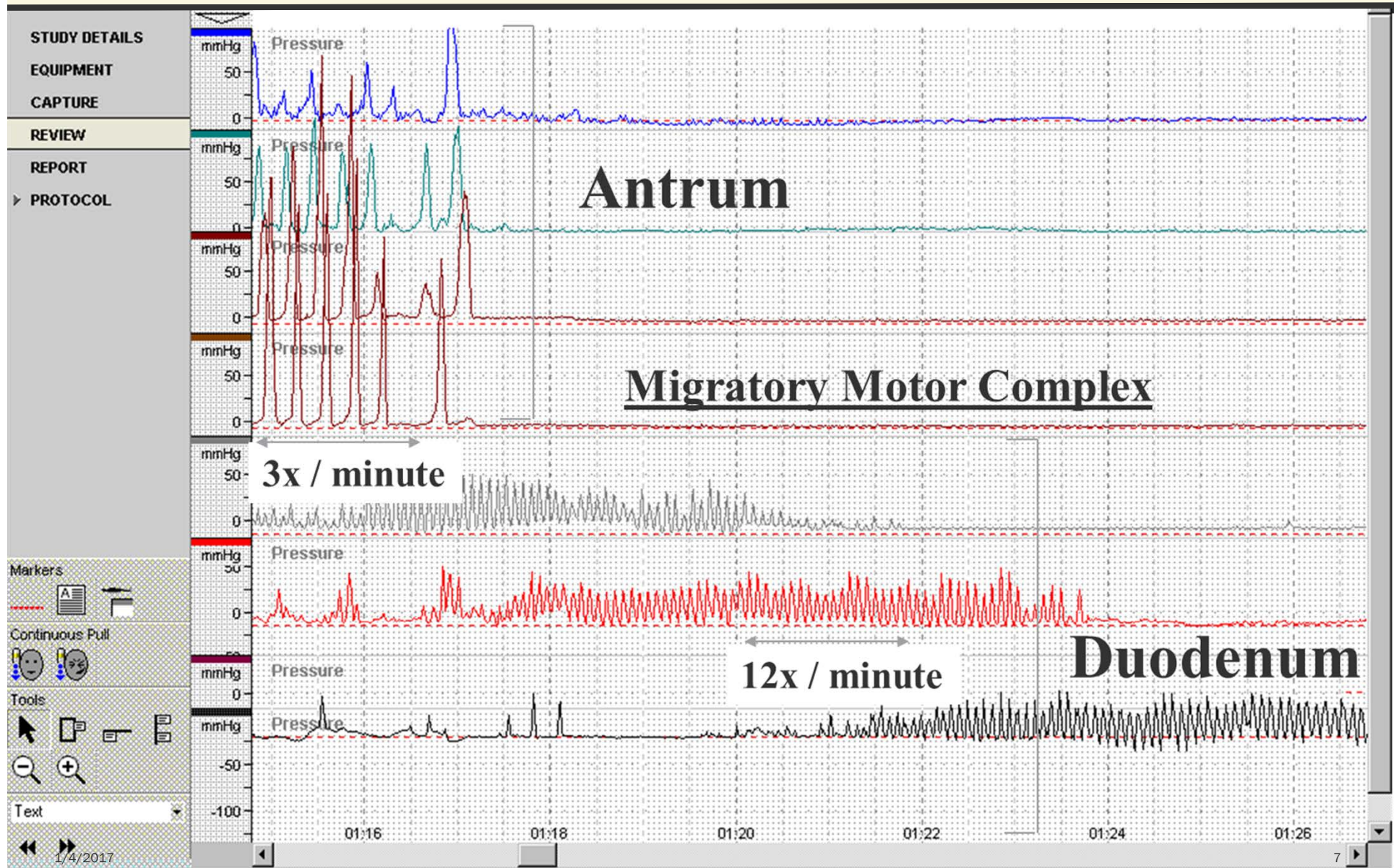
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Porcine Gastric Slow Wave Activity



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Emptying of Indigestible Solids Requires Coordinated Electrical-Mechanical Association



What is Gastroparesis?

- A symptomatic chronic “syndrome” characterized by delayed gastric emptying without a mechanical obstruction.
- Delayed gastric emptying should be contributing to patient’s symptoms
- Finding delayed gastric emptying \neq gastroparesis

Wo JM, Parkman HP. Pract Gastroenterol 2006;30:23.



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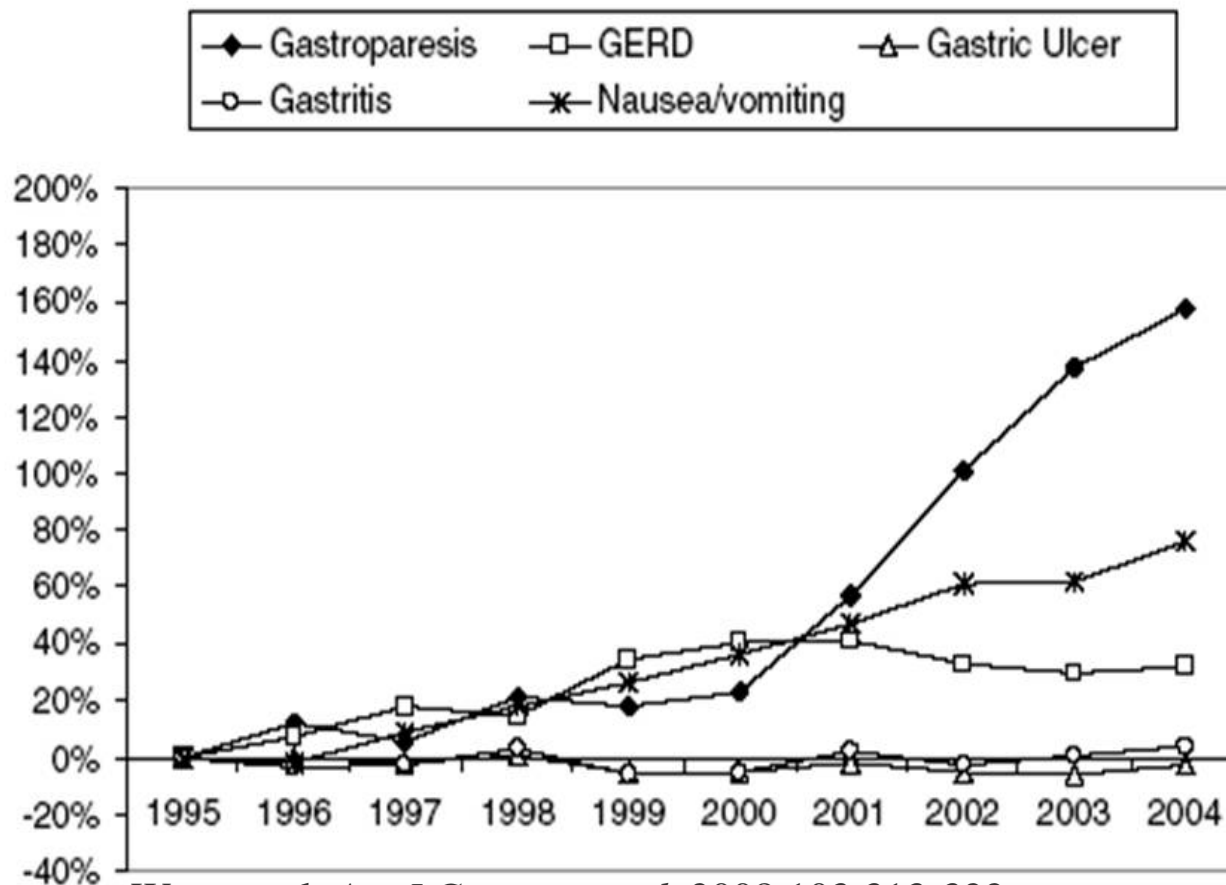
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Epidemiology

- 2 to 12% of diabetics in the general community report nausea and vomiting.
- 40-50% of unselected diabetics presenting to outpatient clinic has delayed gastric emptying of solids.
 - However, many of these diabetics have no GI symptoms.



Incidence of Gastroparesis Hospitalizations are Increasing



Wang et al. *Am J Gastroenterol.* 2008;103:313-322.

(Nationwide Inpatient Sample: Agency for Healthcare Research and Quality)



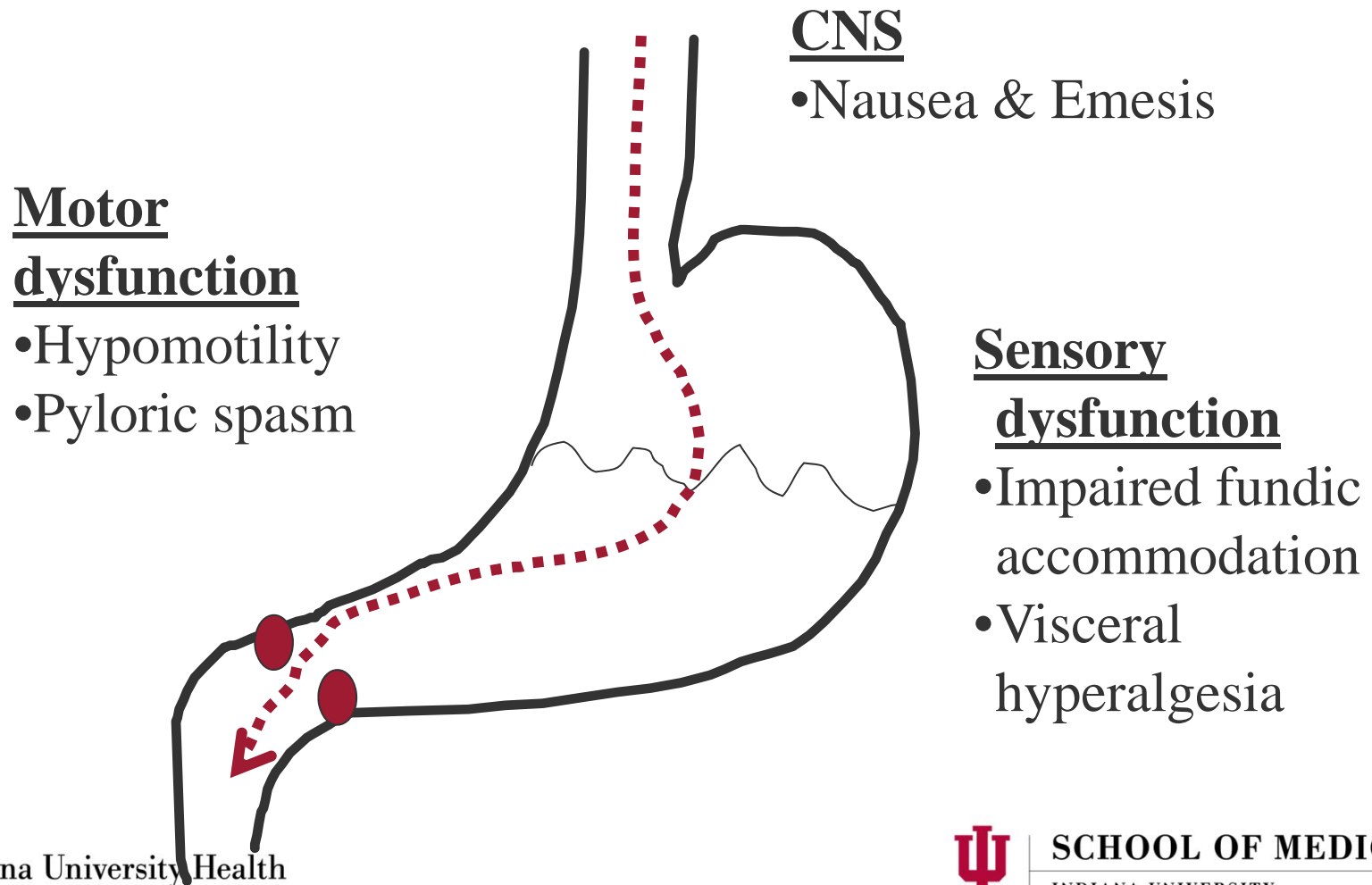
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Functional Abnormalities of Gastroparesis



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Causes of Gastroparesis



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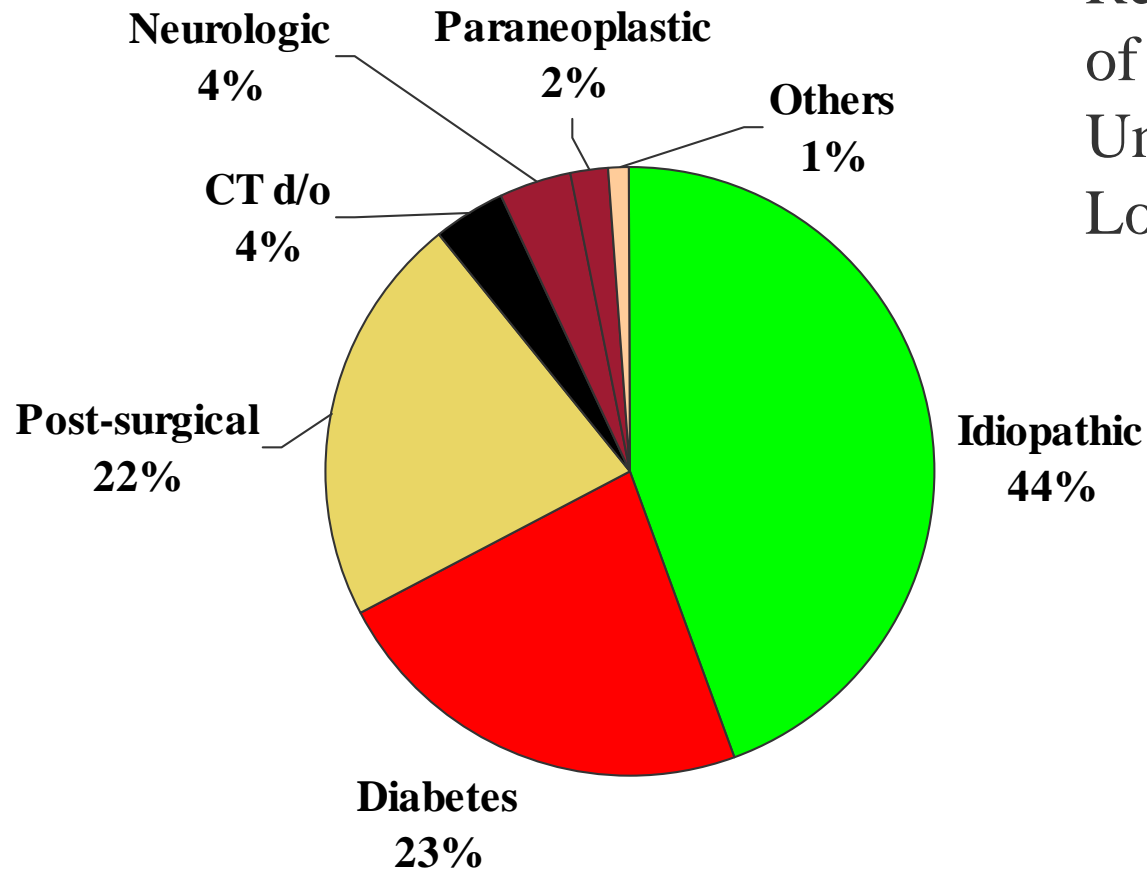


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Causes of Gastroparesis

Retrospective review
of 339 patients at
University of
Louisville

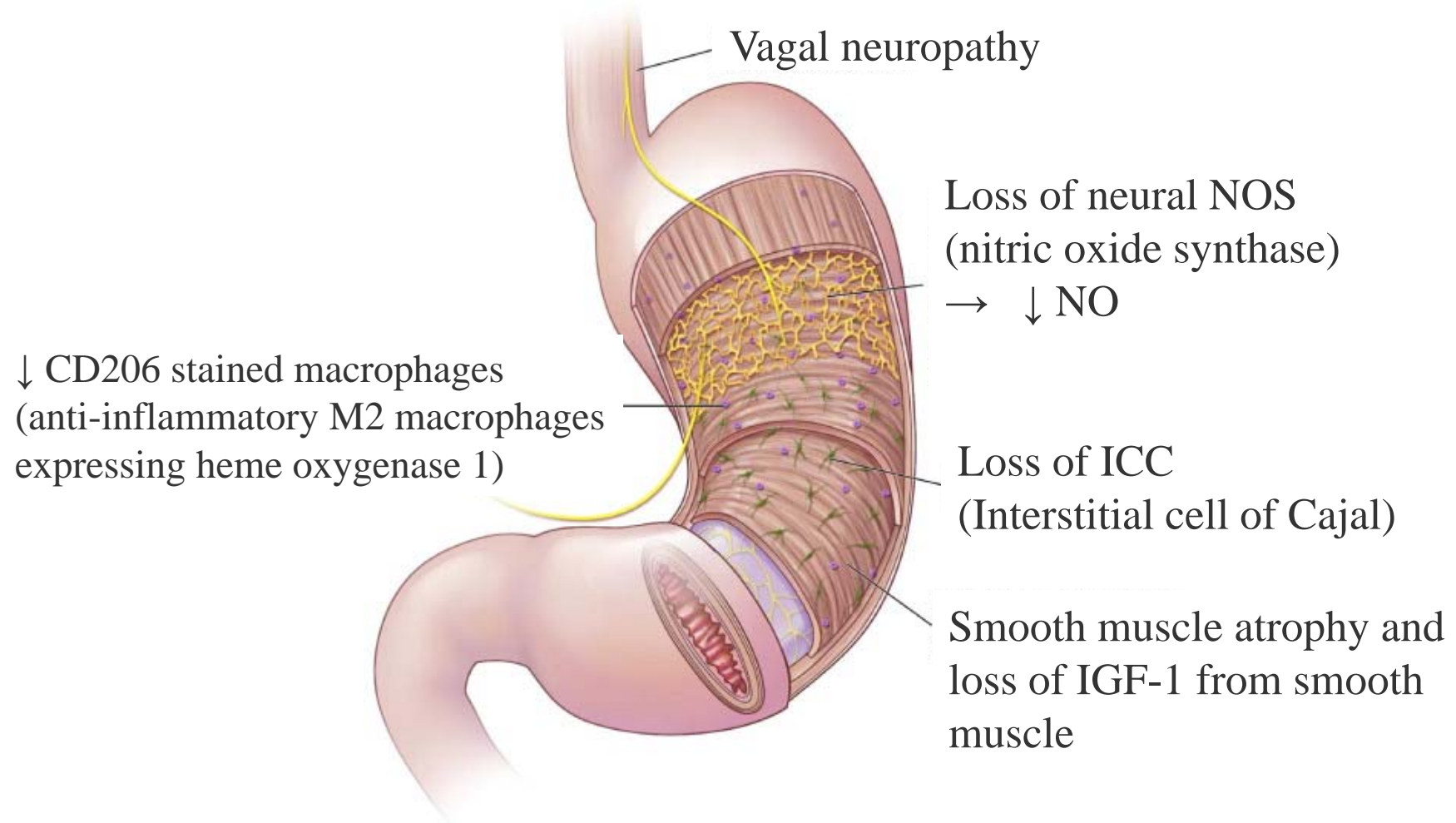


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Pathologic Findings from Animal Models of Diabetic Gastroparesis (Type 1)



Pathogenesis of Diabetes Gastroparesis (Type 1 DM)

- Oxidative stress from diabetes activates a shift of macrophages from M2 → M1
 - M2 macrophages express heme oxygenase 1 (HO1) is protective against oxidative stress
 - M1 macrophages which lack HO1 is injurious and leads to delay in injury to ICC

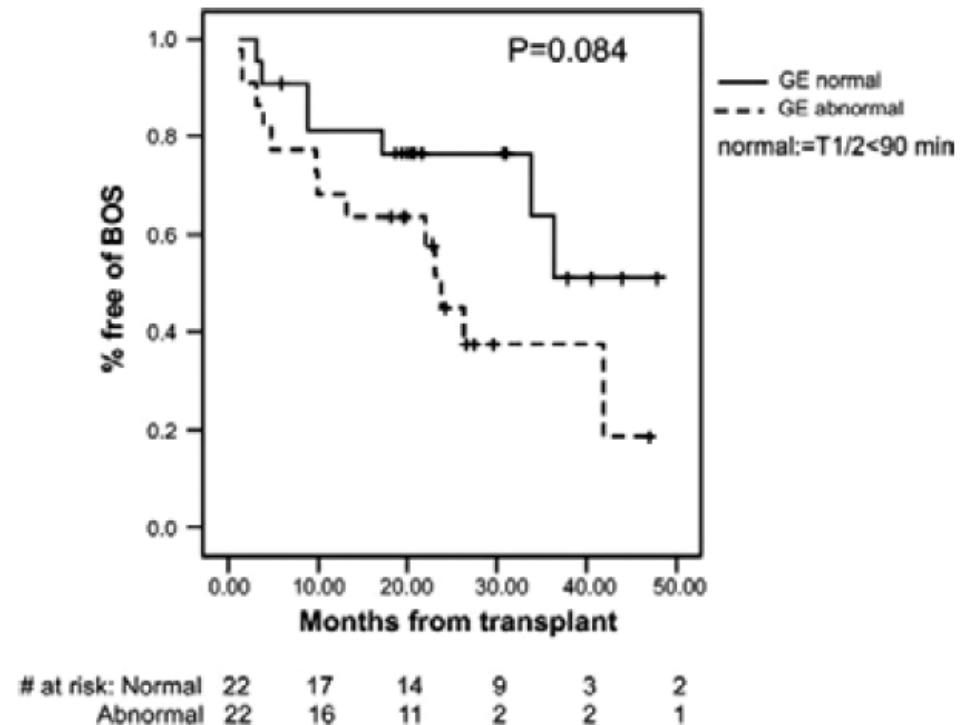
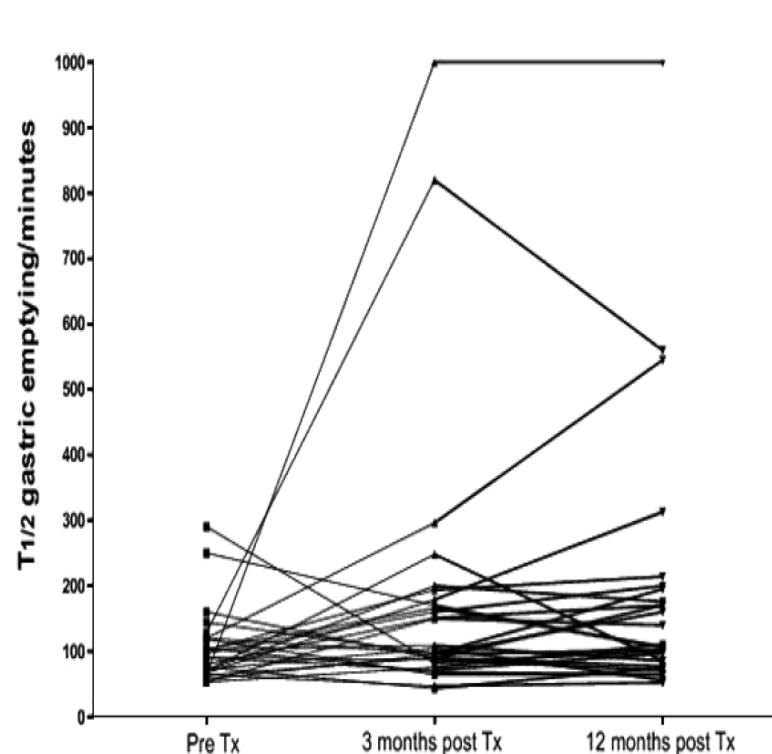


Post-Surgical Gastroparesis

- Procedures with vagotomy
 - Partial or complete gastrectomy, vagotomy/pyloroplasty, partial esophagectomy
- Procedures without intentional vagotomy
 - Fundoplication, bariatric surgery (lap band), mediastinal surgery, radiofrequency (epicardial ablation for arrhythmia and endoscopic GERD therapy)



Gastroparesis is Common after Lung Transplant and is associated with Bronchiolitis Obliterans Syndrome*



*Raviv et al. Clin Transplant. 2012;26:133-142.

(Retrospective review of 139 pts undergoing lung transplant at University of Toronto)



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“Idiopathic” Gastroparesis

- 42 to 47% of patients with gastroparesis
- 70 to 80% females
- Presents equally with vomiting, dyspepsia, or regurgitation predominant symptoms
- Prognosis is unpredictable



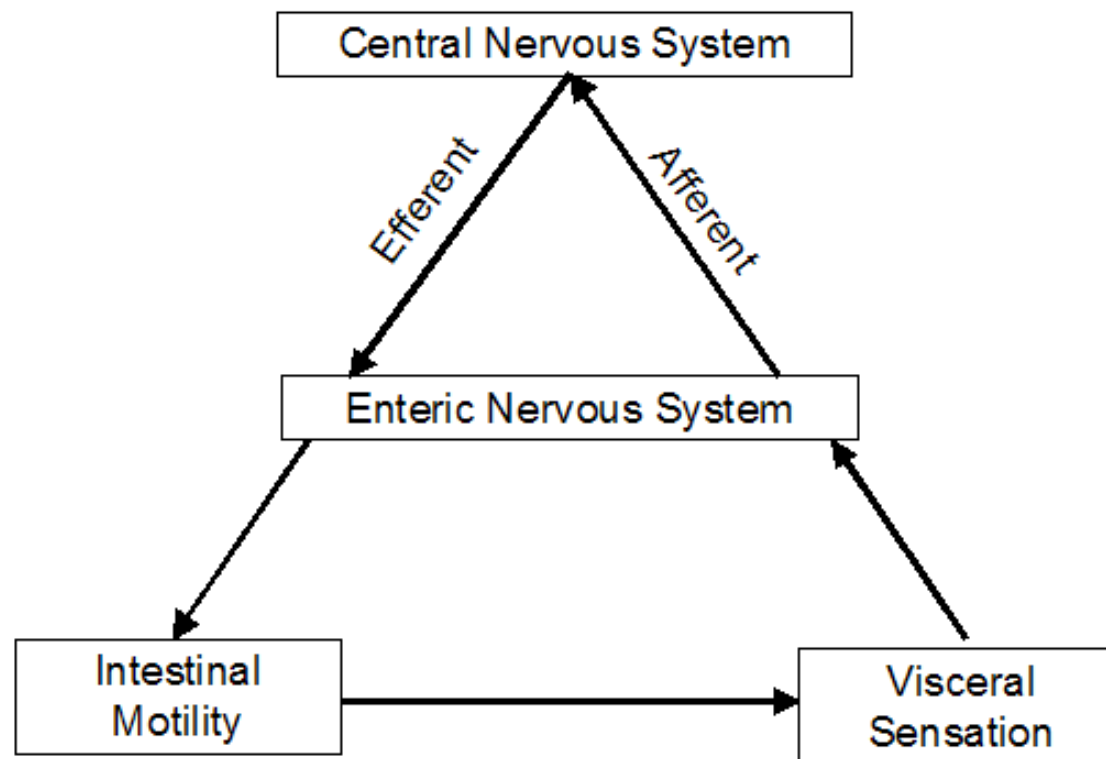
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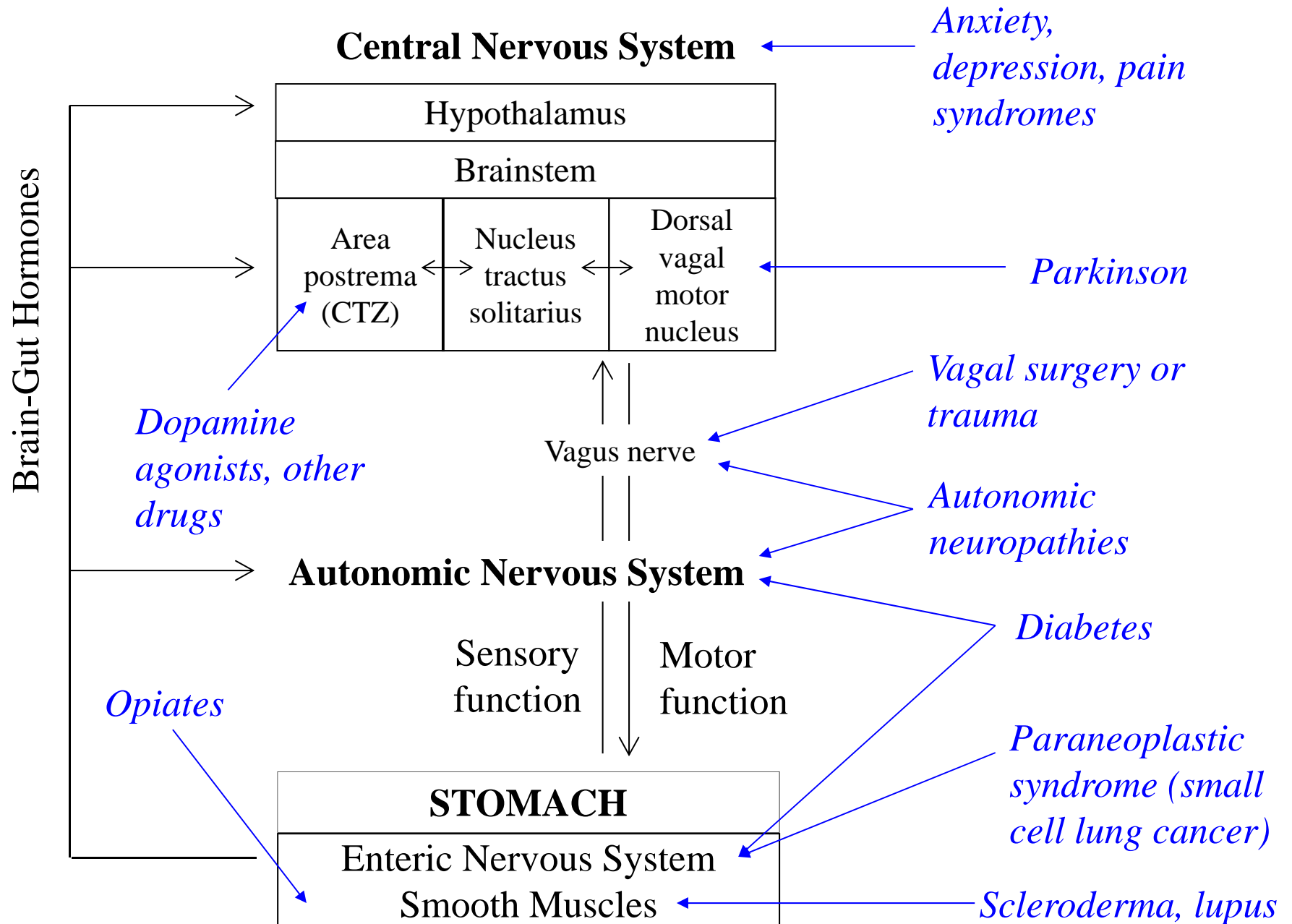
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Brain-Gut-Axis



Control of Gastric Sensory and Motor Function



Symptoms of Gastroparesis



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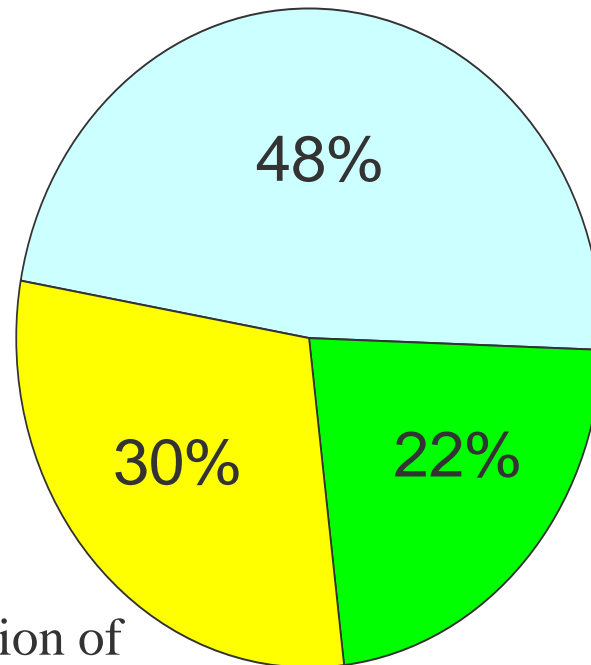
Symptoms of Gastroparesis are Highly Variable

Vomiting-Predominant

- Emesis
- Retching
- Dehydration
- Weight loss
- Hospitalizations

Regurgitation-Predominant

- Heartburn
- Effortless regurgitation of undigested foods
- Nocturnal aspiration



Retrospective review of 338 patients presenting to University of Louisville

Dyspepsia-Predominant (Functional Dyspepsia)

- Postprandial distress
- Epigastric pain
- Bloating
- Abdominal distension

Bizer, Wo et al. Gastroenterol 2005; 128 (suppl 2): abstract.



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Clinical Classification: Vomiting-Predominant Gastroparesis

- “Vomiting with retching and nausea are the most bothersome symptoms”
- Pathophysiology may represent involvement of CNS and vomiting center
- More common in type 1 diabetics

Harrell et al. J Clin Gastroenterol. 42:455-459, 2008.



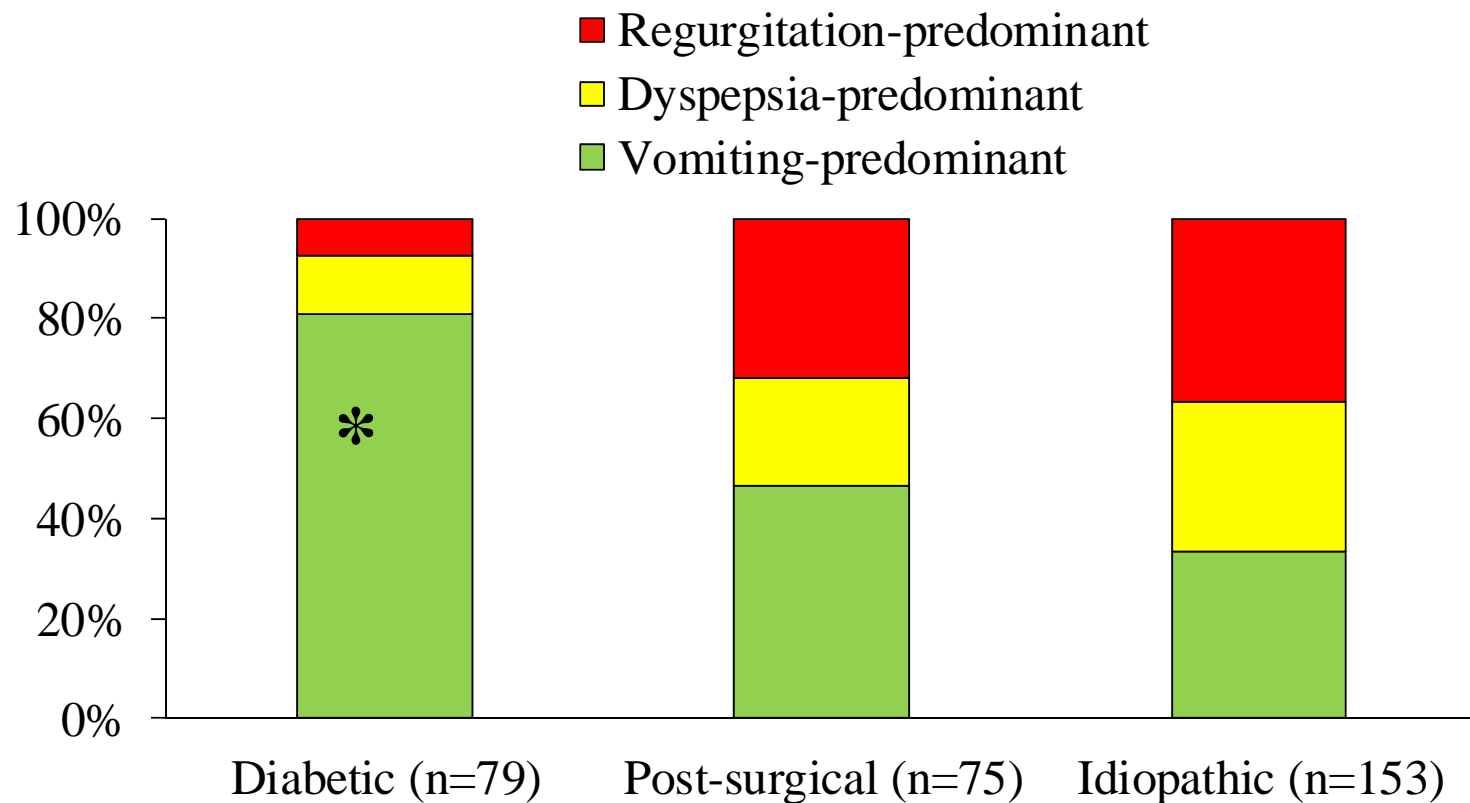
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Patients with Diabetic Gastroparesis Presents with Vomiting-Predominant Symptoms



* $p < 0.01$ compared to other symptom groups

Bizer, Wo et al. Gastroenterol 2005; 128 (suppl 2): abstract.

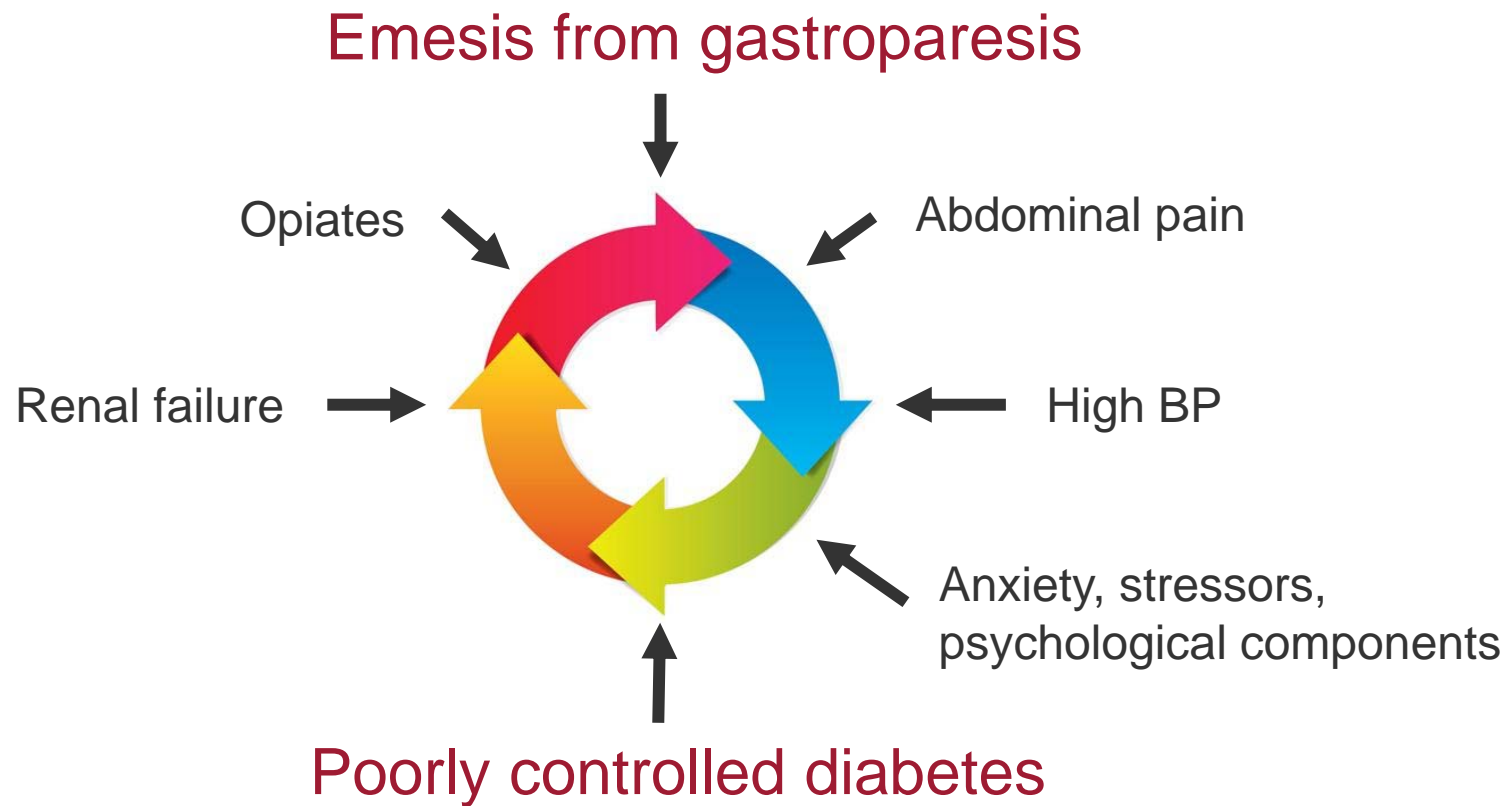


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The Dreaded Vicious Cycle for Diabetic Gastroparesis (type 1 DM)



Clinical Classification:

Dyspepsia-Predominant Gastroparesis

- “Unpleasant or troublesome sensation (discomfort or pain) centered in the upper abdomen is the most bothersome symptom; this sensation may be characterized by or associated with upper abdominal fullness, fullness after small meals, bloating, or nausea”

Harrell et al. J Clin Gastroenterol. 42:455-459, 2008.



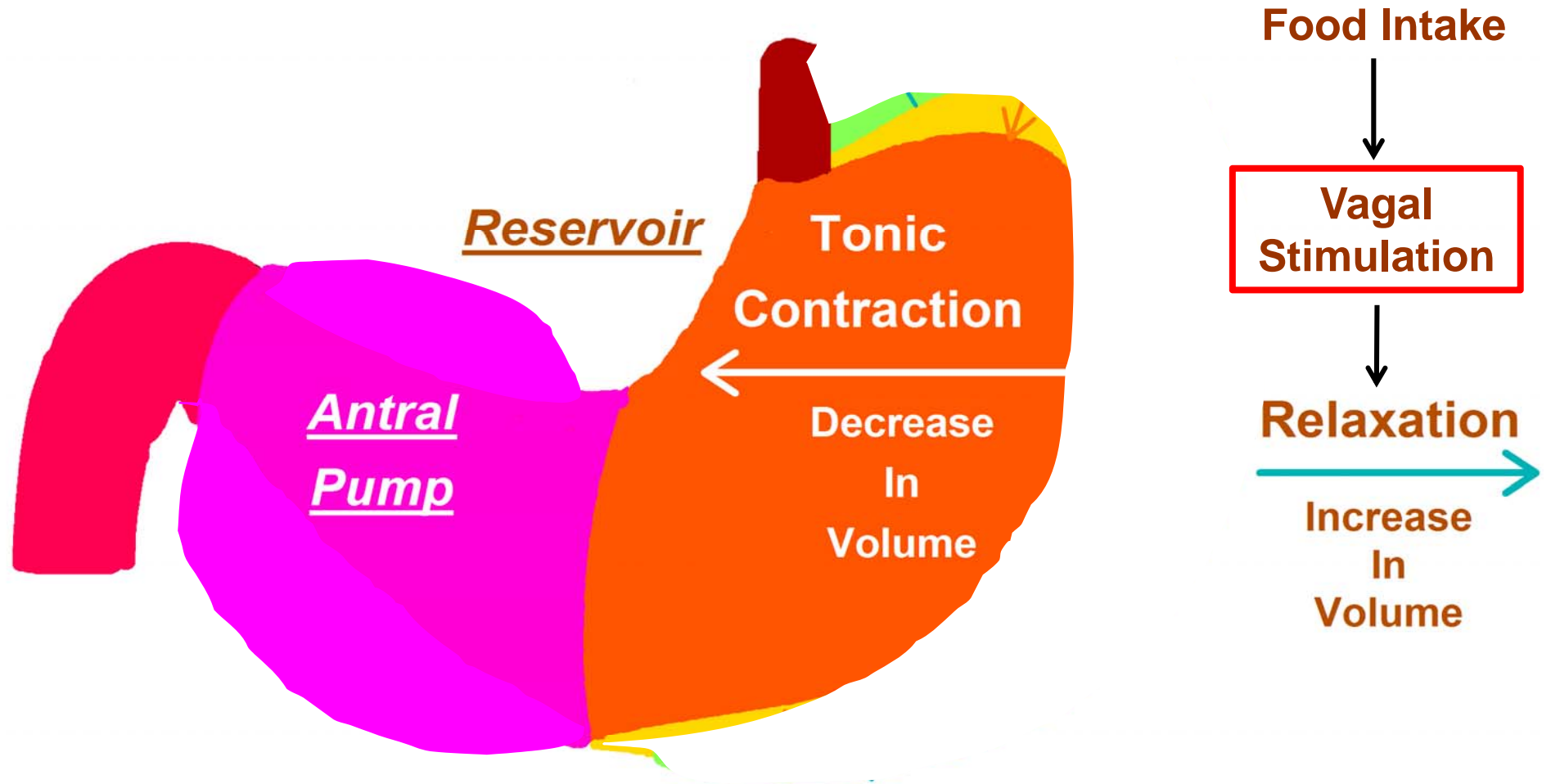
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Dyspepsia and Impaired Gastric Accommodation



Clinically Classification: Regurgitation-Predominant Gastroparesis

- “Effortless regurgitation of acid or undigested food or heartburn is the most bothersome symptom”

Harrell et al. J Clin Gastroenterol. 42:455-459, 2008.



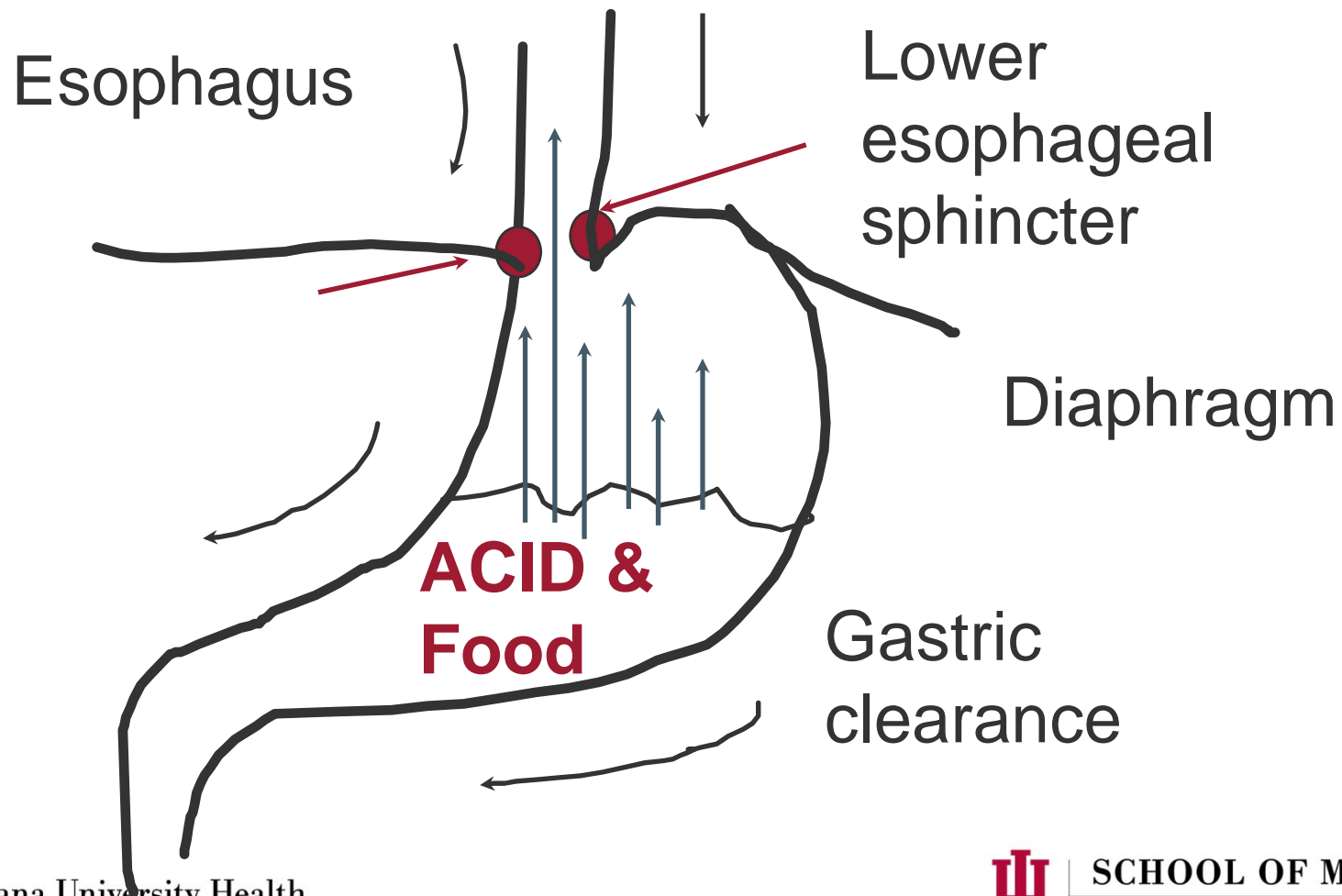
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Regurgitation-Predominant Gastroparesis: Causing GERD & Aspiration



Clinical Classification:

Regurgitation-Predominant Gastroparesis

- Typical presentation of post-surgical severe gastroparesis
 - Lack of vagal afferent
 - Lack of emesis or nausea
- Often has severely delayed gastric emptying

Harrell et al. J Clin Gastroenterol. 42:455-459, 2008.



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Bezoars in Common in Regurgitation-Predominant Gastroparesis



- Due to absence of Migratory Motor Complex (MMC)



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Diagnostic Evaluation



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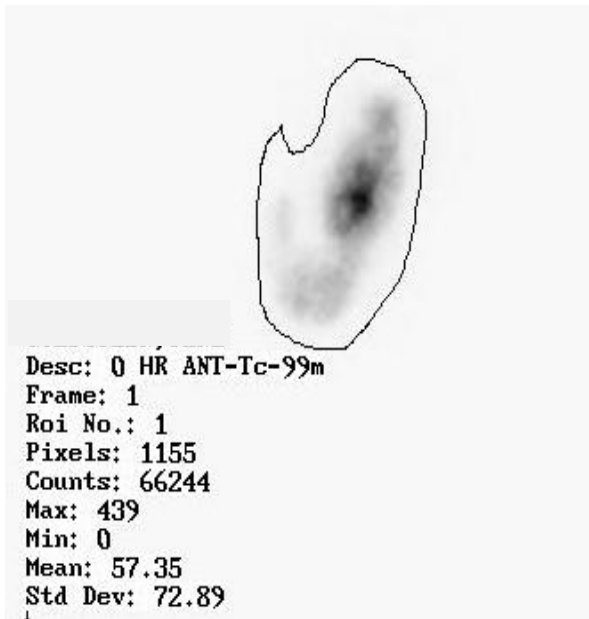
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Extent of Evaluation should be based on Severity of Disease

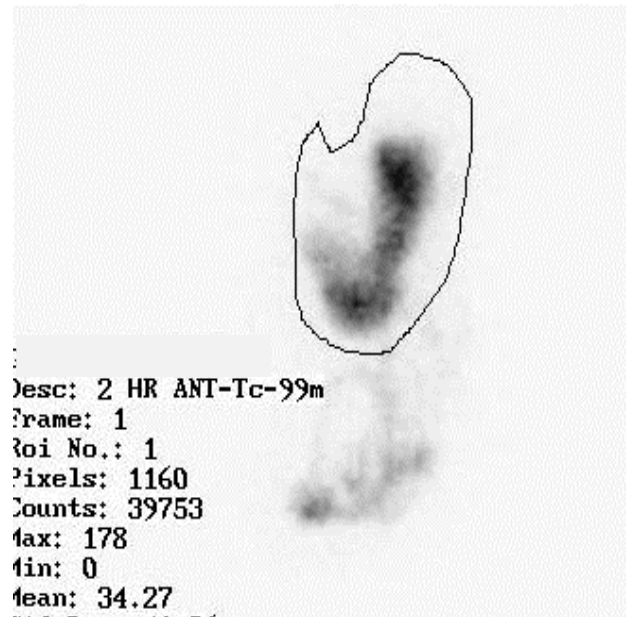
- Goal: Look for underlying cause(s) & extent of involvement
 - Review of System
 - Labs
 - Anatomical evaluation
 - EGD, small bowel enteroscopy, UGI-SBFT, abdominal CT
 - Motility testing
 - Electrogastrography, antroduodenal manometry, wireless motility testing (SmartPill), anorectal manometry
 - Peripheral & autonomic neurologic testing
 - Full-thickness biopsy



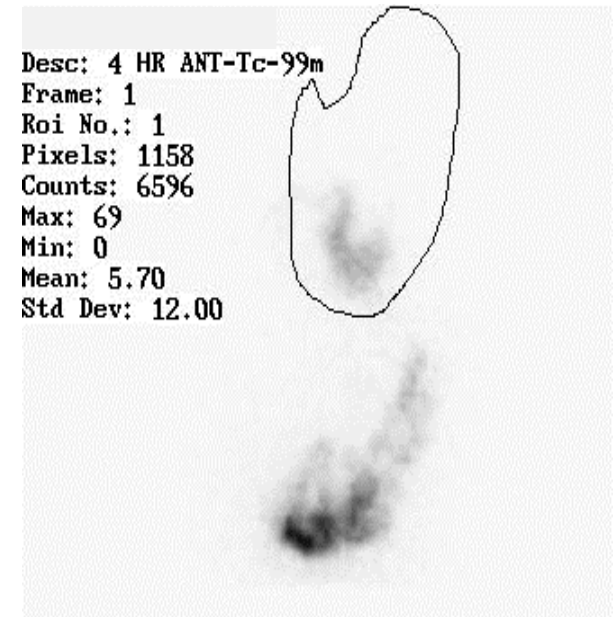
4-hr Gastric Emptying Test: New International Standard



T=0 after test meal



**After 2 hours
Normal: <60%
retention**



**After 4 hours
Normal: <10%
retention**



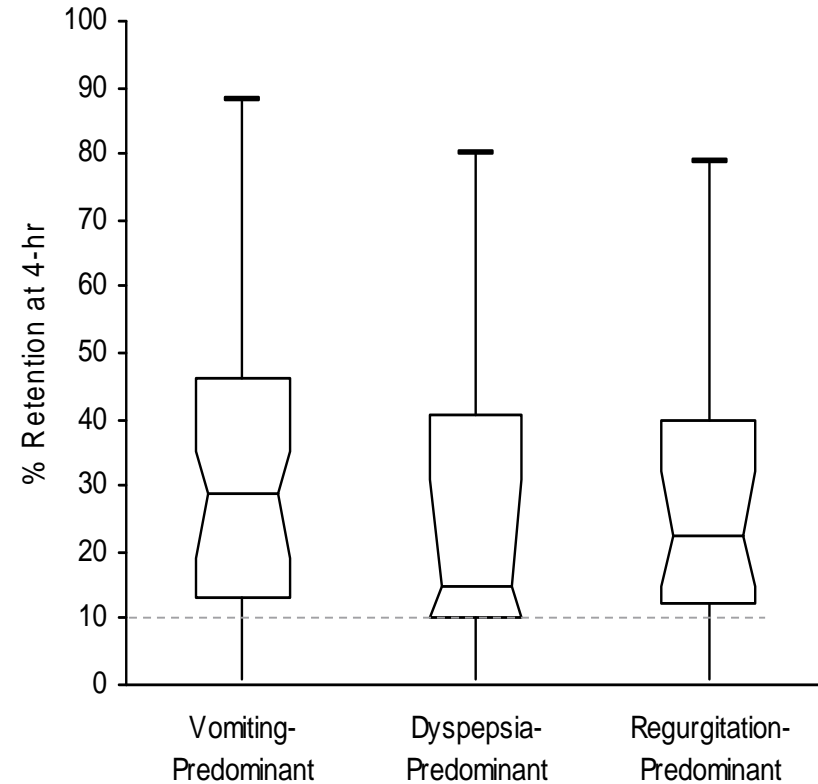
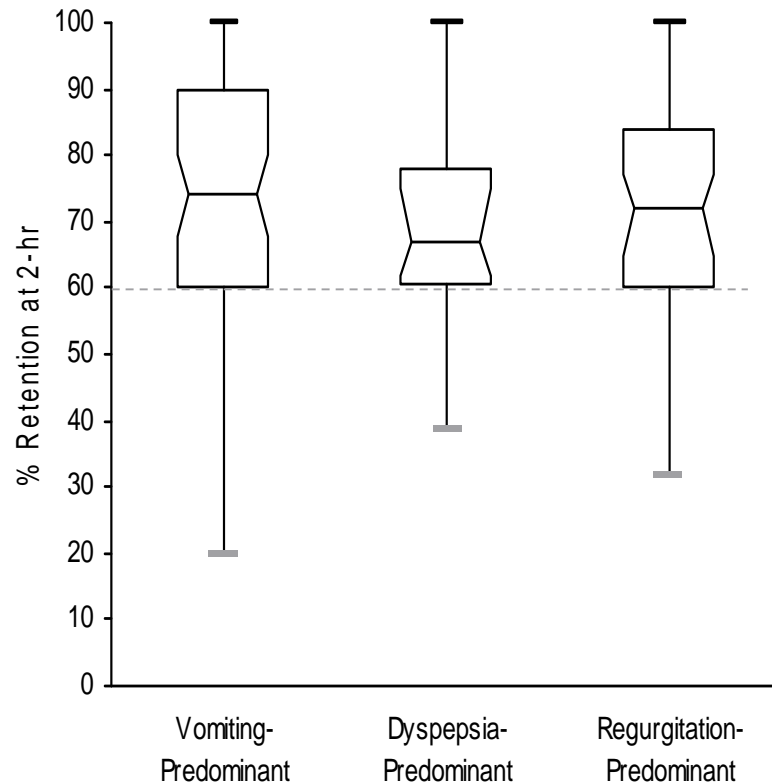
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Gastric Emptying Does Not Correlate with Symptom Presentation



Bizer et al. Gastroenterol 2005; 128 (suppl 2): abstract.

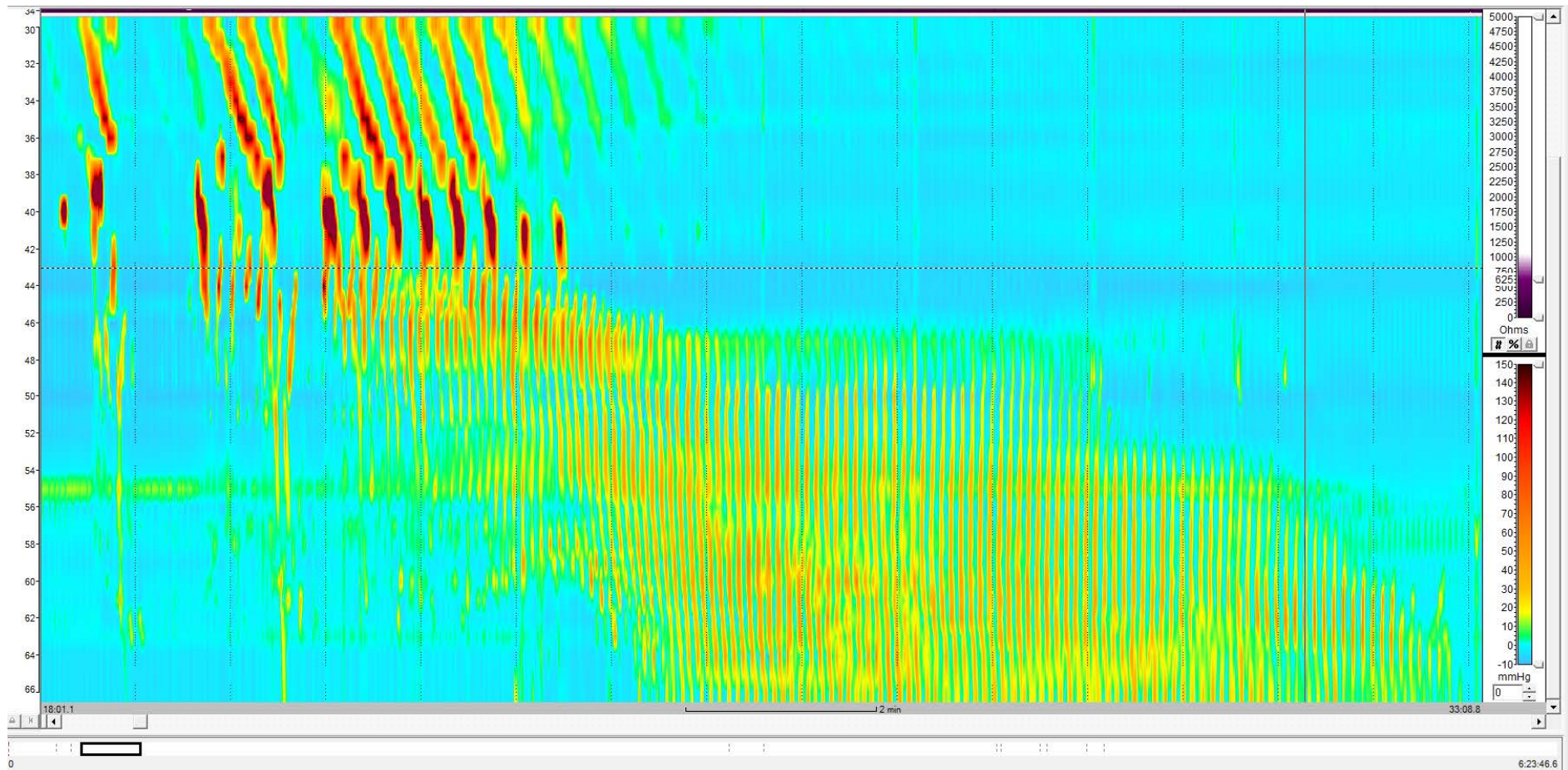


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High-Resolution Antroduodenal Manometry



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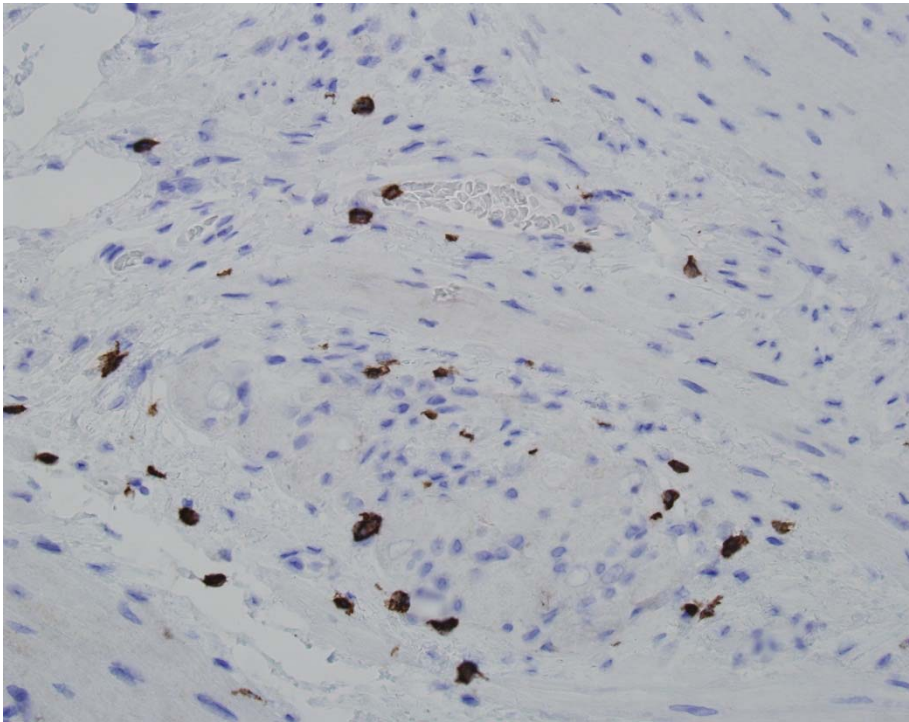
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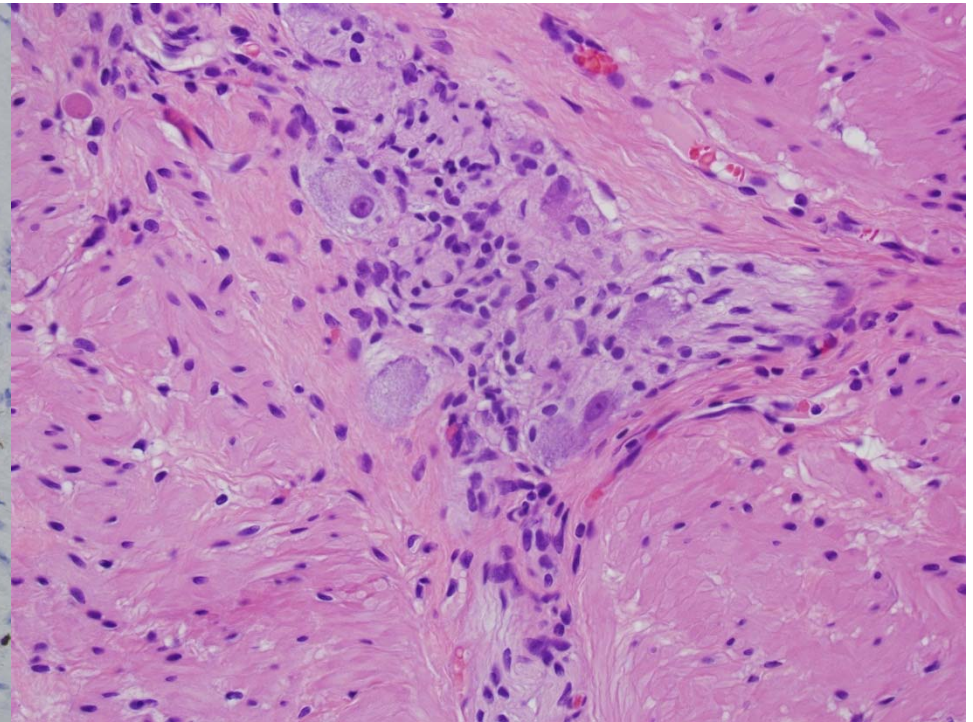
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Full-Thickness Biopsy to Look for Underlying Cause in Idiopathic Gastroparesis



Immunohistochemical stain for c-kit
(interstitial cells of Cajal)



Lymphocytic infiltration of myenteric
ganglion



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London Classification of GI Neuromuscular Pathology*

- Neuropathies
 - Absent neurons
 - Decreased numbers of neurons
 - Increased numbers of neurons
 - Degenerative neuropathy
 - Inflammatory neuropathies
 - Lymphocytic ganglionitis
 - Eosinophilic ganglionitis
 - Abnormal content in neurons
 - Abnormal neurochemical coding
 - Relative immaturity of neurons
 - Abnormal enteric glia
- Myopathies
 - Muscularis propria malformation
 - Muscle cell degeneration
 - Muscle hyperplasia/hypertrophy
 - Abnormal content in myocyte
 - Abnormal supportive tissue
- Interstitial Cell of Cajal (ICC) abnormalities

*Knowles et al. Gut. 2010;59:882-887.



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4 Most Important Things to Know about Gastroparesis



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4 Most Important Things to Know about Gastroparesis

1. What is the predominant-symptom presentation?

- a) Emesis-predominant
- b) Dyspepsia-predominant
- c) Regurgitation-predominant

2. Any alarm features?

- a) Weight loss > 10% past 6 months
- b) Emesis causing dehydration, ARF, electrolyte abnormalities
- c) Aspiration



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4 Most Important Things to Know about Gastroparesis

3. Any underlying systemic causes?

- a) Diabetes, autonomic symptoms, connective tissue, CNS, mitochondrial, etc.
- b) Take a good history and review of system

4. Extent of GI motility involvement?

- a) Involving esophagus, small bowel or colon
- b) Ask for other GI motility symptoms!



Treatment Options



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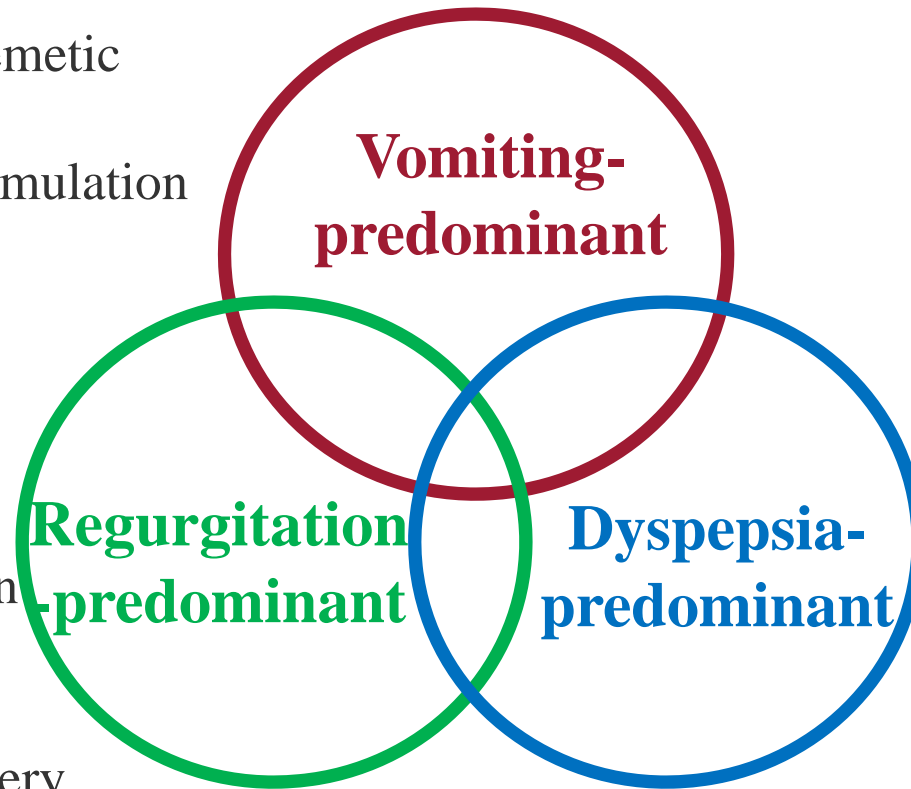


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Treatment of Gastroparesis Depends on Symptom Presentation

- Nutrition support
- Prokinetics & anti-emetic
- Hospitalization
- Gastric electrical stimulation



- Lifestyle modification
- Adjust PPI
- Prokinetics
- Avoid antireflux surgery

- Diet modification
- Prokinetics
- Set treatment goals
- Cognitive behavioral therapy



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Gastric Electrical Stimulation for Emesis-Predominant Gastroparesis



- It's a neurostimulator, NOT a pacemaker
- Hypothesis: increase vagal afferent to the brain and then increase vagal efferent to the stomach

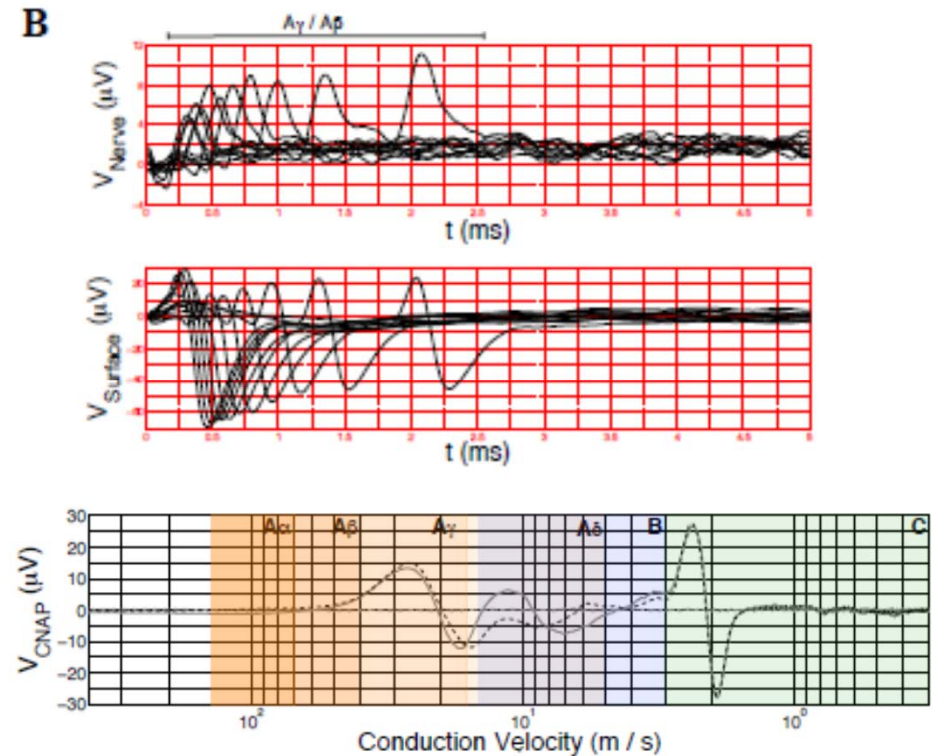
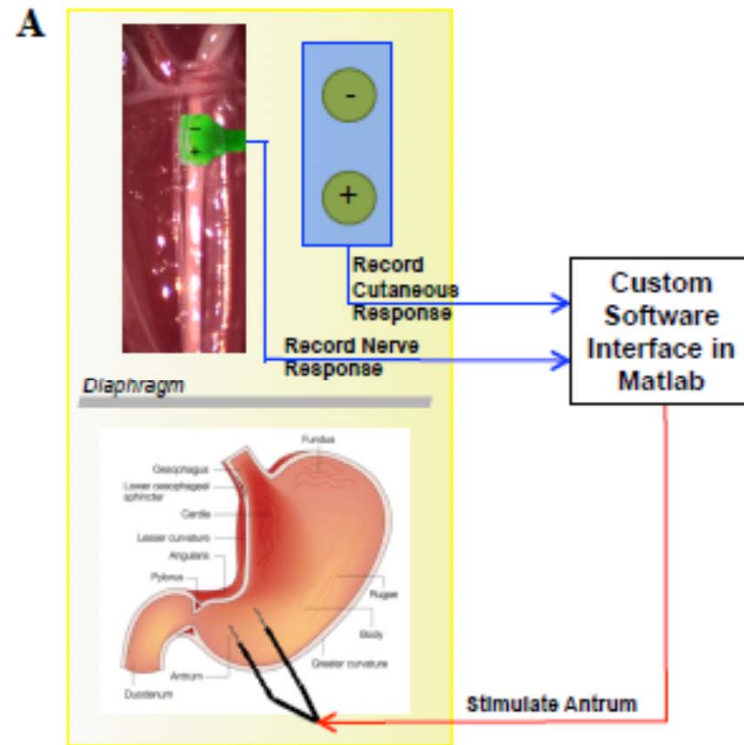


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Rodent Model of GES at Purdue Biomedical Engineering



Ward et al. DDW 2015

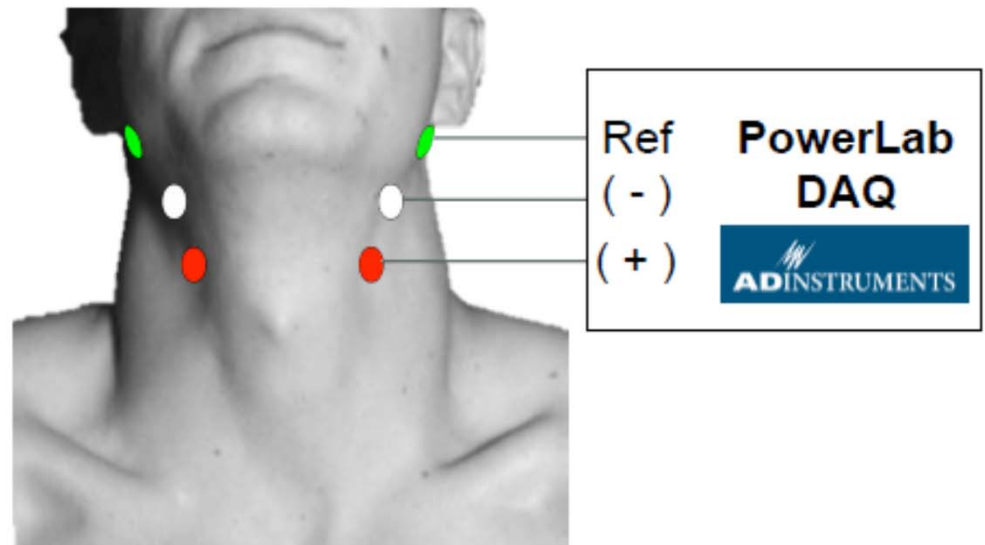
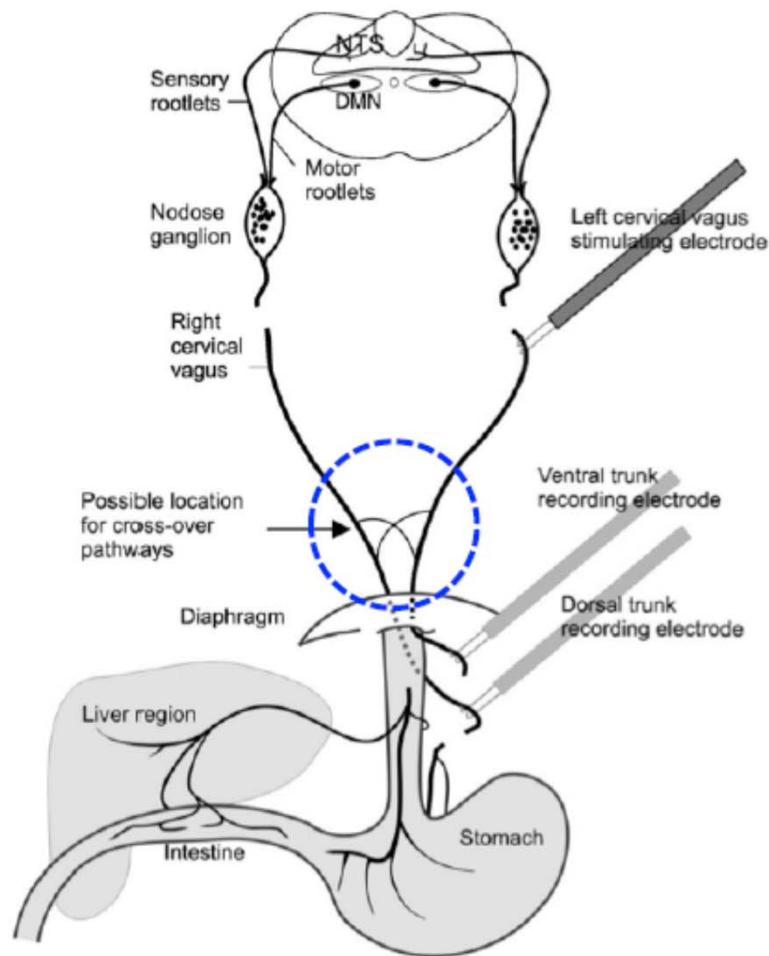


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Cutaneous Vagal Recording and Electrode Placement



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Vagal Compound Nerve Action Potential (CNAP) Features Classified by Conduction Velocity

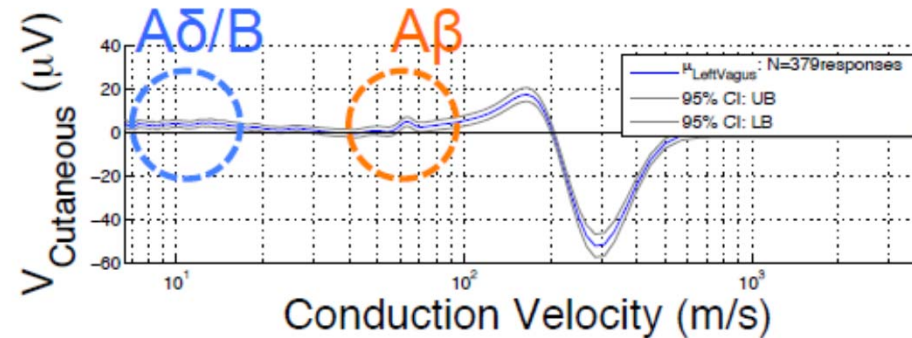
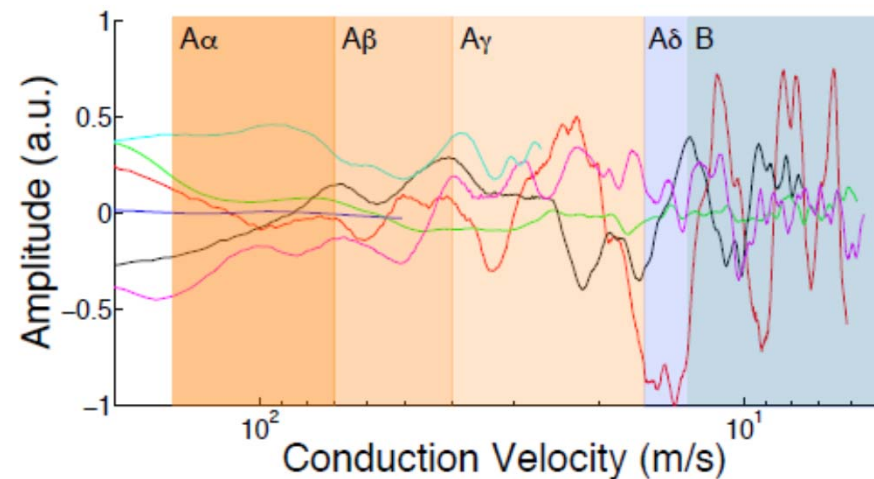
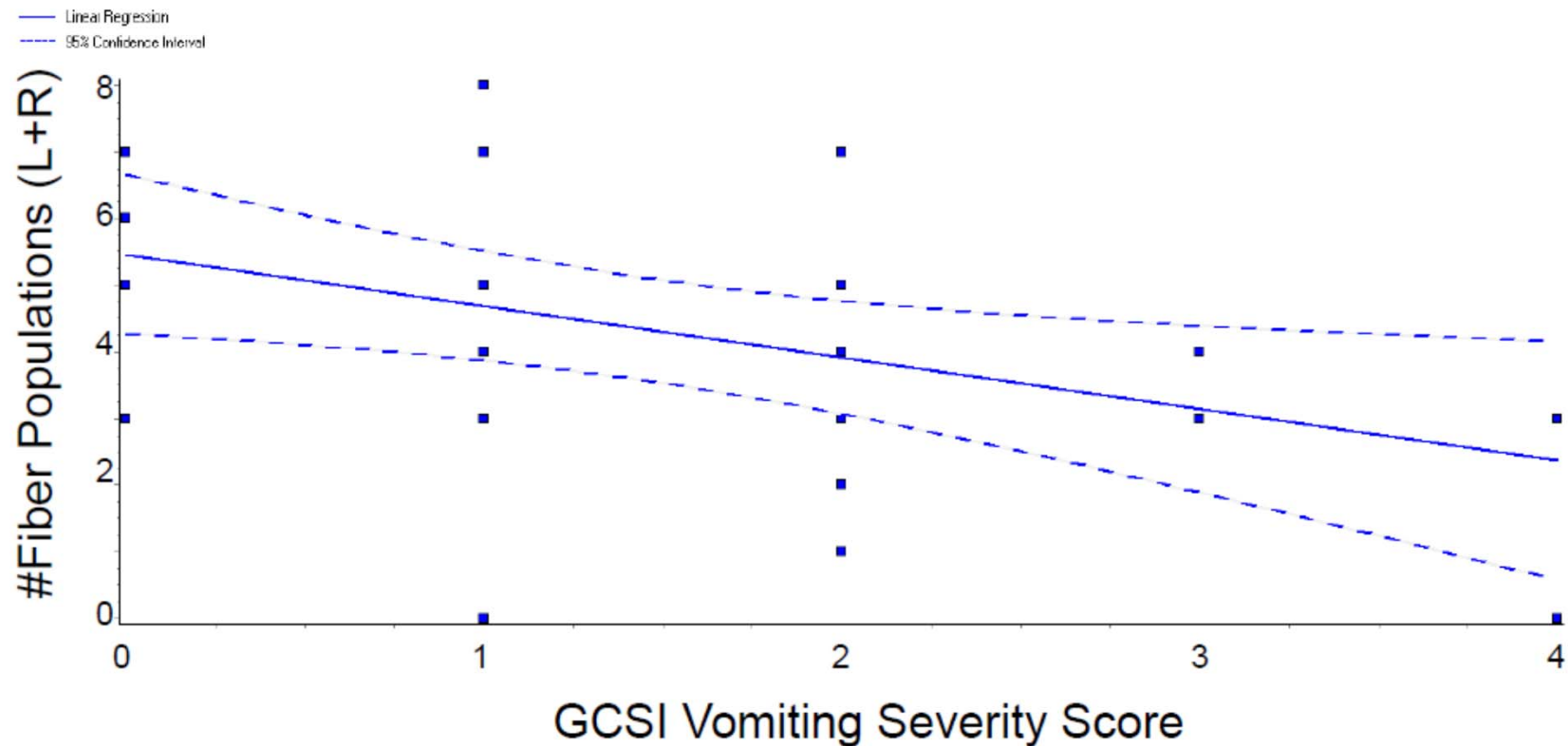


Fig 3. Sample mean left vagal response with 95% CI



Vagal Fiber Recruitment Correlates with Symptom Improvement



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Patient Selection for Gastric Electrical Stimulation

- Indication is refractory vomiting-predominant gastroparesis with alarm features
- Good option for type-1 diabetic gastroparesis
- Predictors for non-responder
 - Idiopathic gastroparesis
 - Frequent opiate use
 - Prominent abdominal pain



Patient Selection for Gastric Electrical Stimulation

- Careful evaluation of idiopathic gastroparesis is essential
 - Look for underlying cause
- Avoid PEGJ prior to GES
- Avoid abdominal surgery after GES



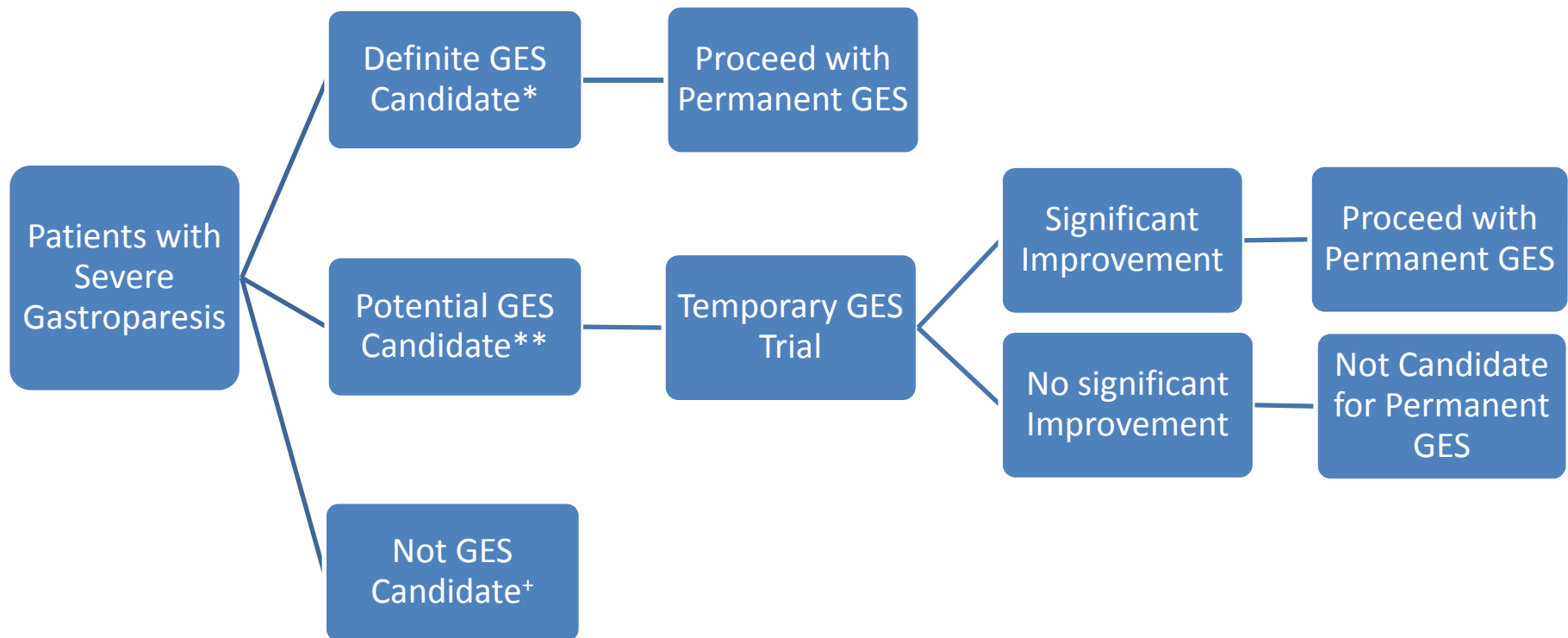
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Clinical Pathways for GES in Adult Patients with Gastroparesis at IU Hospital



*No contraindication for permanent GES and high likelihood of success

**No contraindication for permanent GES but likelihood of success unclear

+Contraindicated for permanent GES or likelihood of success is poor

Conclusions: Take-Home Points

- Not all gastroparesis patients are the same
 - Etiologies and symptoms are highly variable
- 4 Most Important Things to Know about Gastroparesis
 1. What is the predominant-symptom?
 2. Any alarm features?
 3. Any underlying systemic causes?
 4. Extent of GI motility involvement?
- Evaluation and treatment depends on above
- GES is effective in “selected” patients

