Manifestation and Management of Gastroparesis

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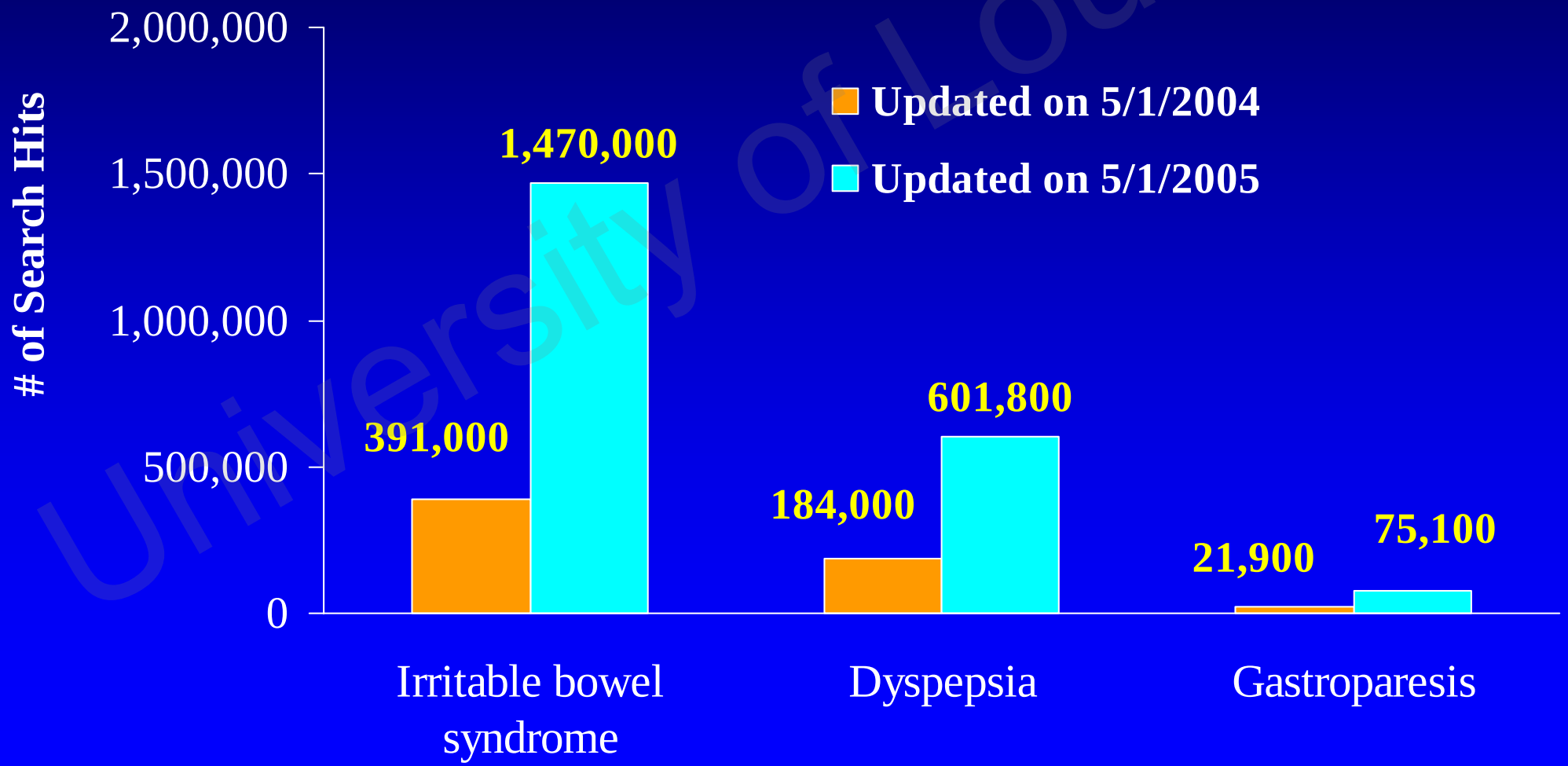
Manifestation and Management of Gastroparesis

- Etiology
- Clinical manifestation
- Evaluation
- Treatment options
- Gastric electrical stimulation

Google® Internet Search for Functional Gastrointestinal Disorders



Definition of Gastro-Paresis

- “Chronic disorder of gastric motility, defined as delayed gastric emptying of a solid meal.” *

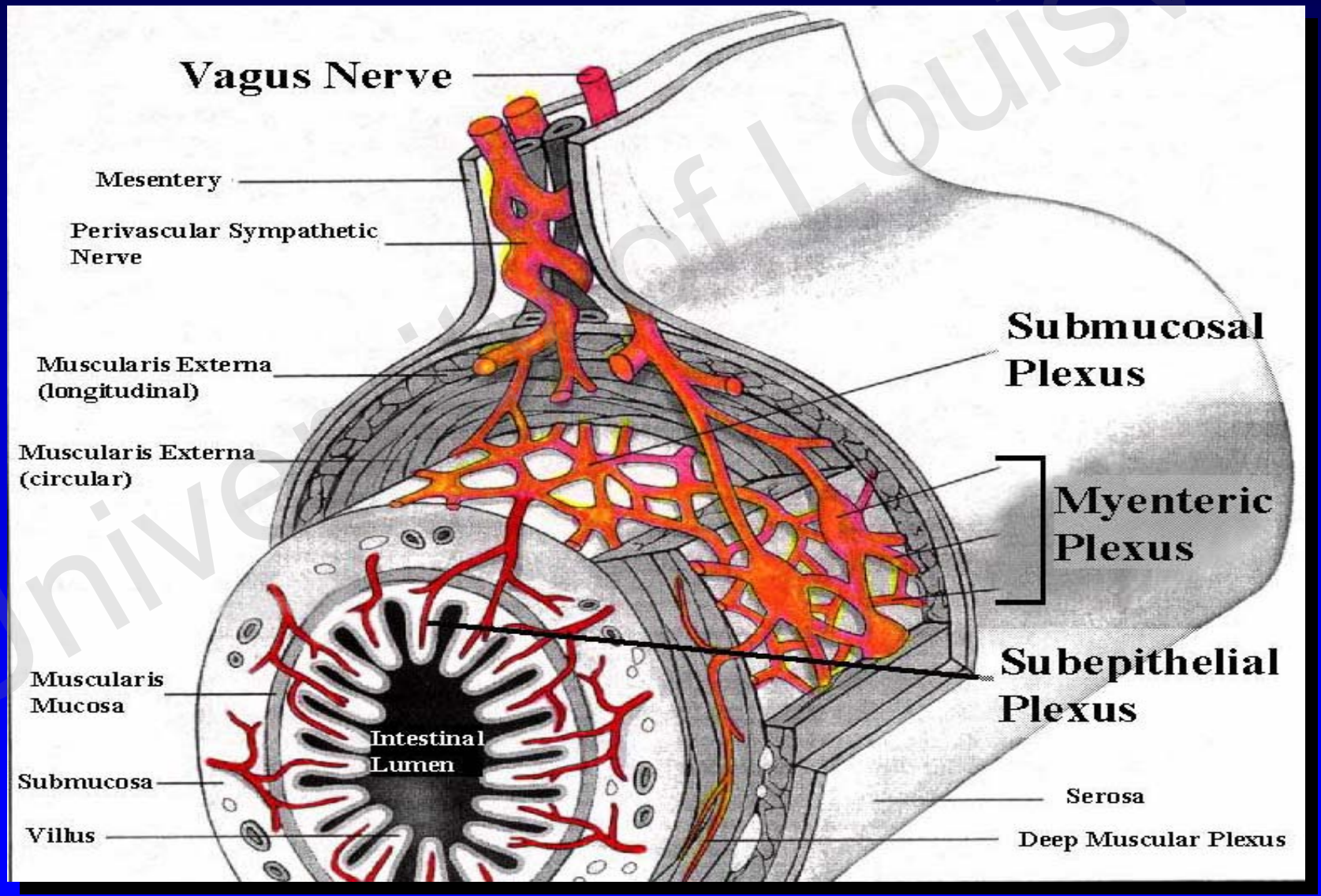
*McCallum et al. Gastroenterol 1998;114:456-61.

Prevalence of Delayed Gastric Emptying

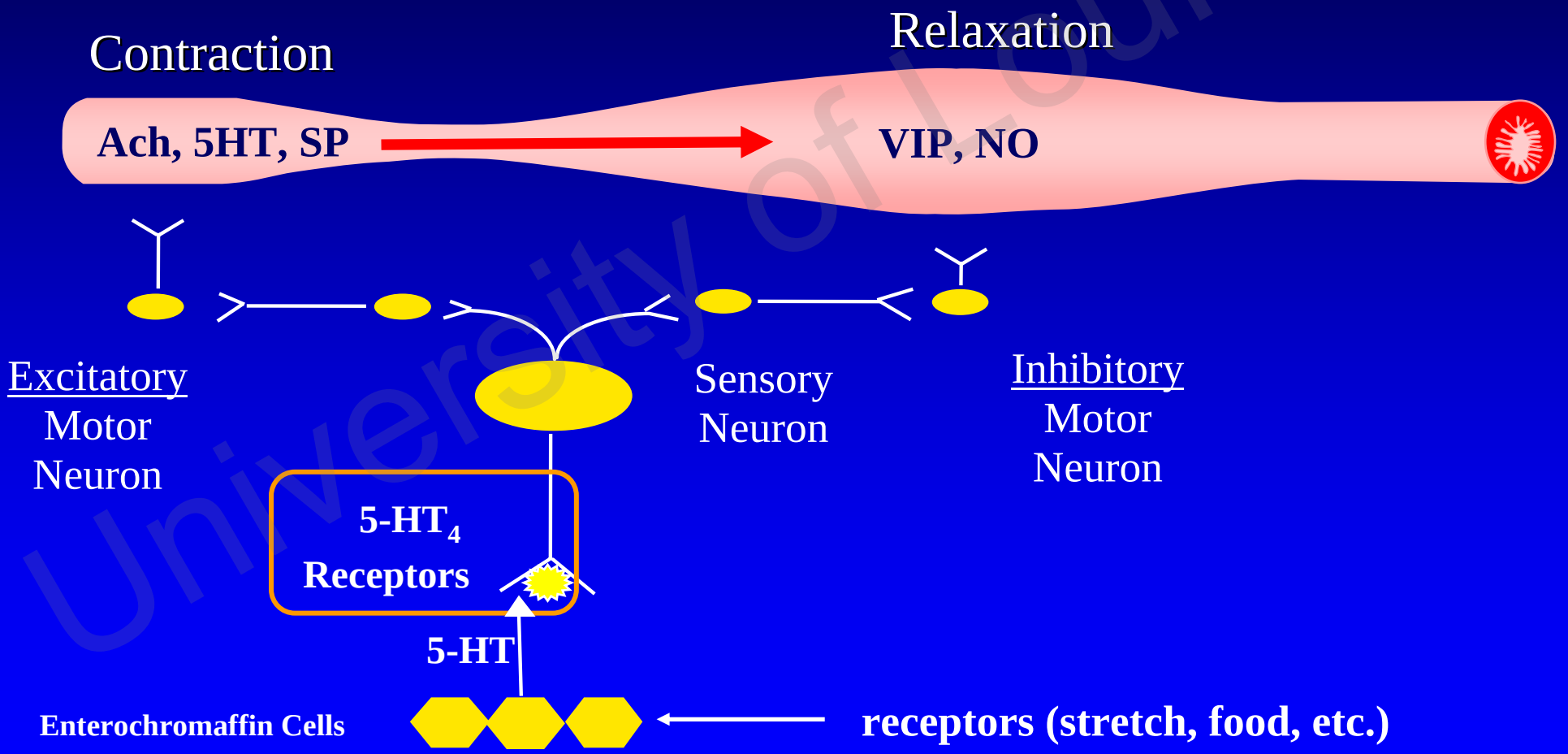
- Unselected diabetics [1,2] 40 - 65%
- Non-ulcer dyspepsia [3,4] 23 - 34%
- GERD [5,6] 30 - 33%

[1]De Block et al. *Diabetes Care*. 2002;25:912. [2]Jones et al. *Diabetes Care*. 2001;24:1264.
[3]Sarnelli et al. *Am J Gastroenterol*. 2003;98:783. [4]Stanghellini et al. *Gastroenterol*. 1996;110:1036.
[5]Soykan et al. *J Investig Med*. 1997;45:483. [6]Buckles et al. *Am J Med Sci*. 2004;327:1.

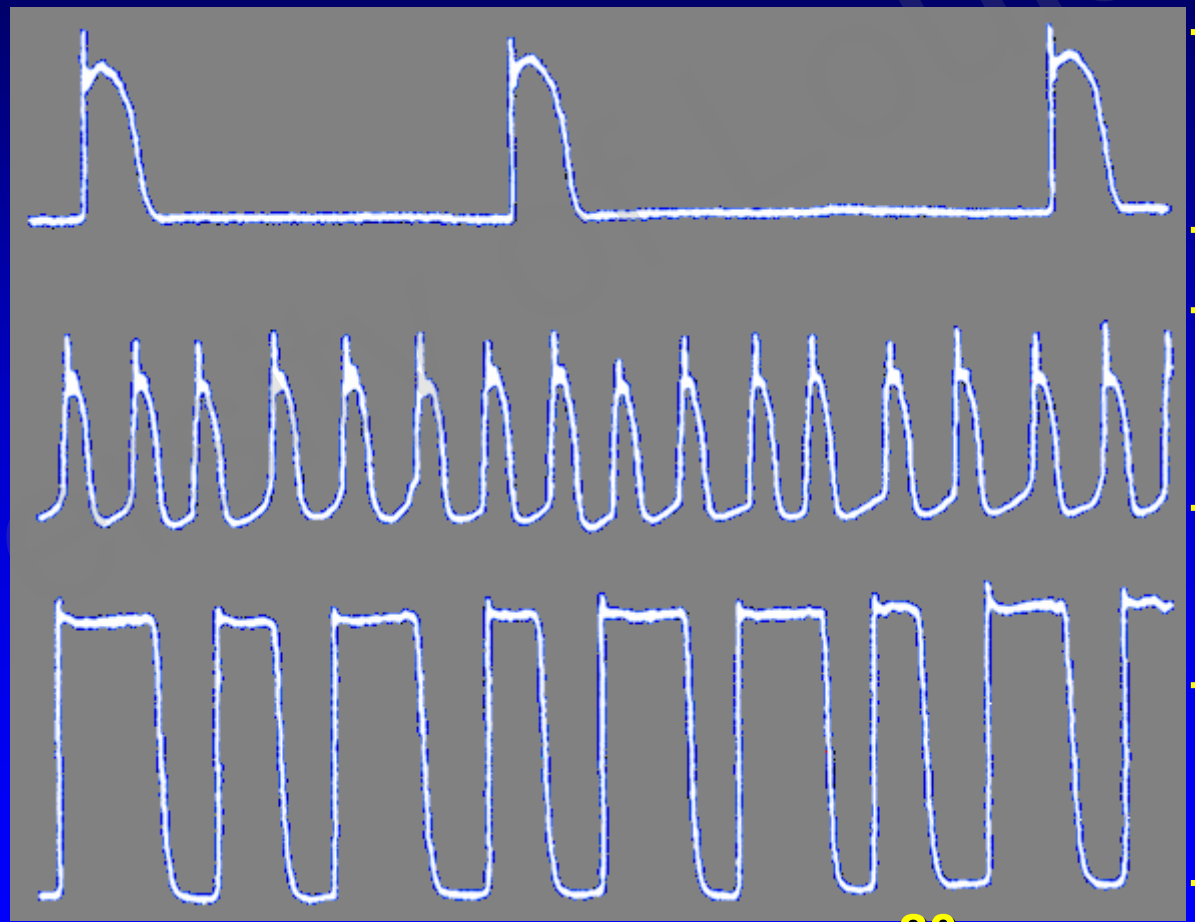
Enteric Nervous System (ENS)



Enteric Nervous System Controls GI Peristalsis



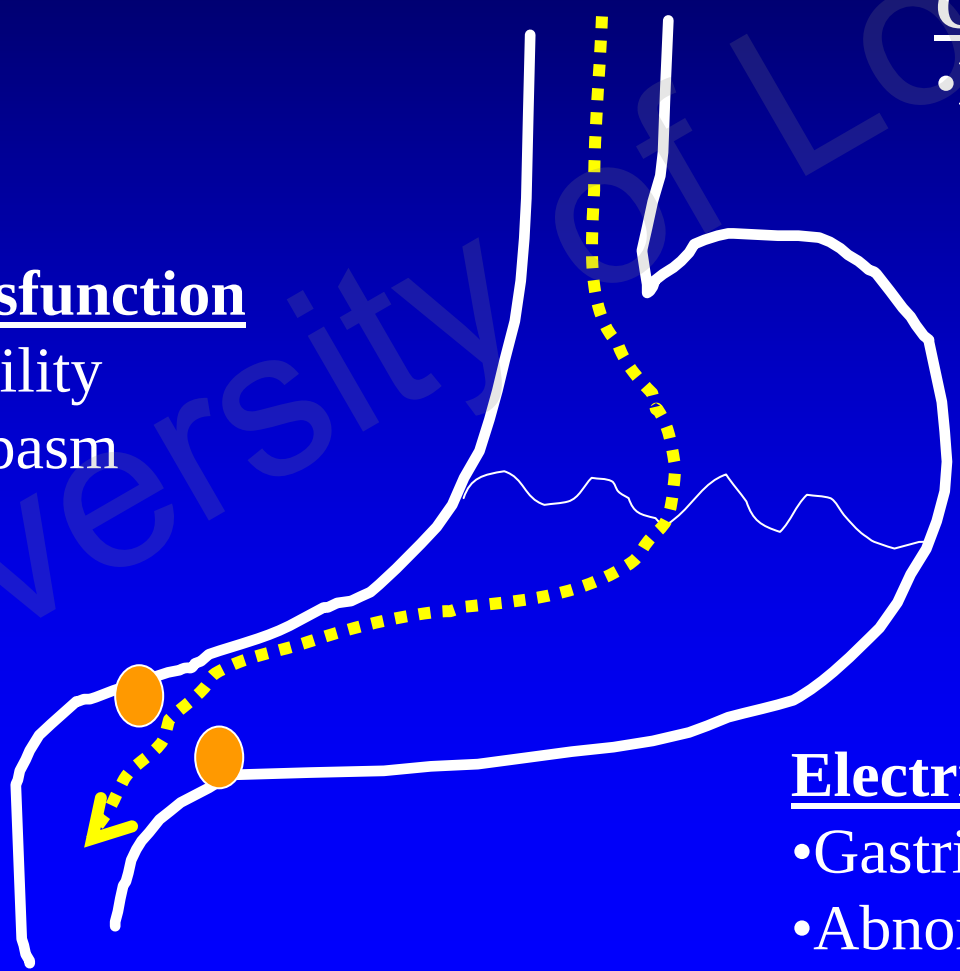
Enteric Nervous System Controls
GI Electrical Rhythm



Pathophysiology of Gastroparesis is Multifactorial and Complex

CNS
- Nausea & Vomiting

Motor dysfunction
- Hypomotility
- Pyloric spasm



Sensory dysfunction
- Impaired fundic relaxation
- Abnormal sensation

Electrical dysfunction
- Gastric arrhythmia
- Abnormal propagation

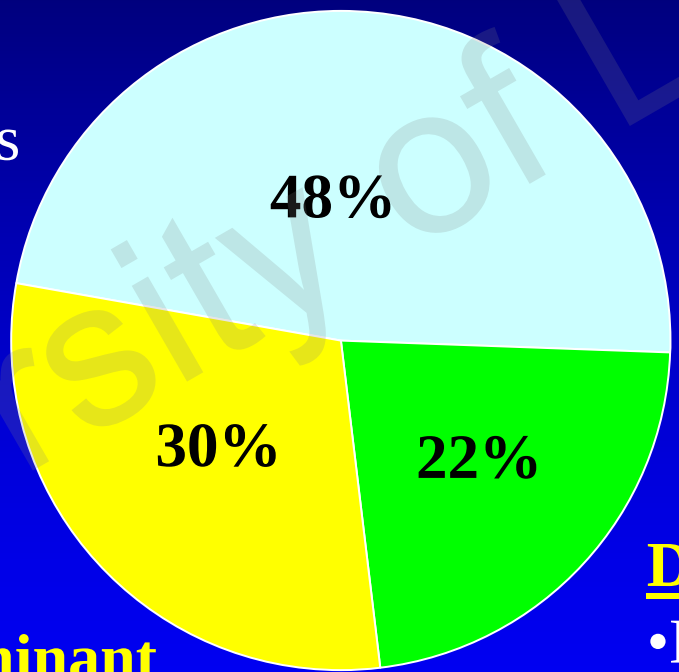
Symptoms of Gastroparesis are Diverse

- Recurrent nausea and vomiting of unclear etiology
- Others
  - Early satiety
  - Postprandial bloating
  - Dyspepsia
  - Effortless regurgitation
  - Heartburn
  - Poorly controlled glucose and reactive hypoglycemia in diabetes

Predominant Symptoms of Gastroparesis

Vomiting-Predominant
- Vomiting
- Dehydration
- Hospitalizations
- Weight loss

N=339 patients presenting to University of Louisville

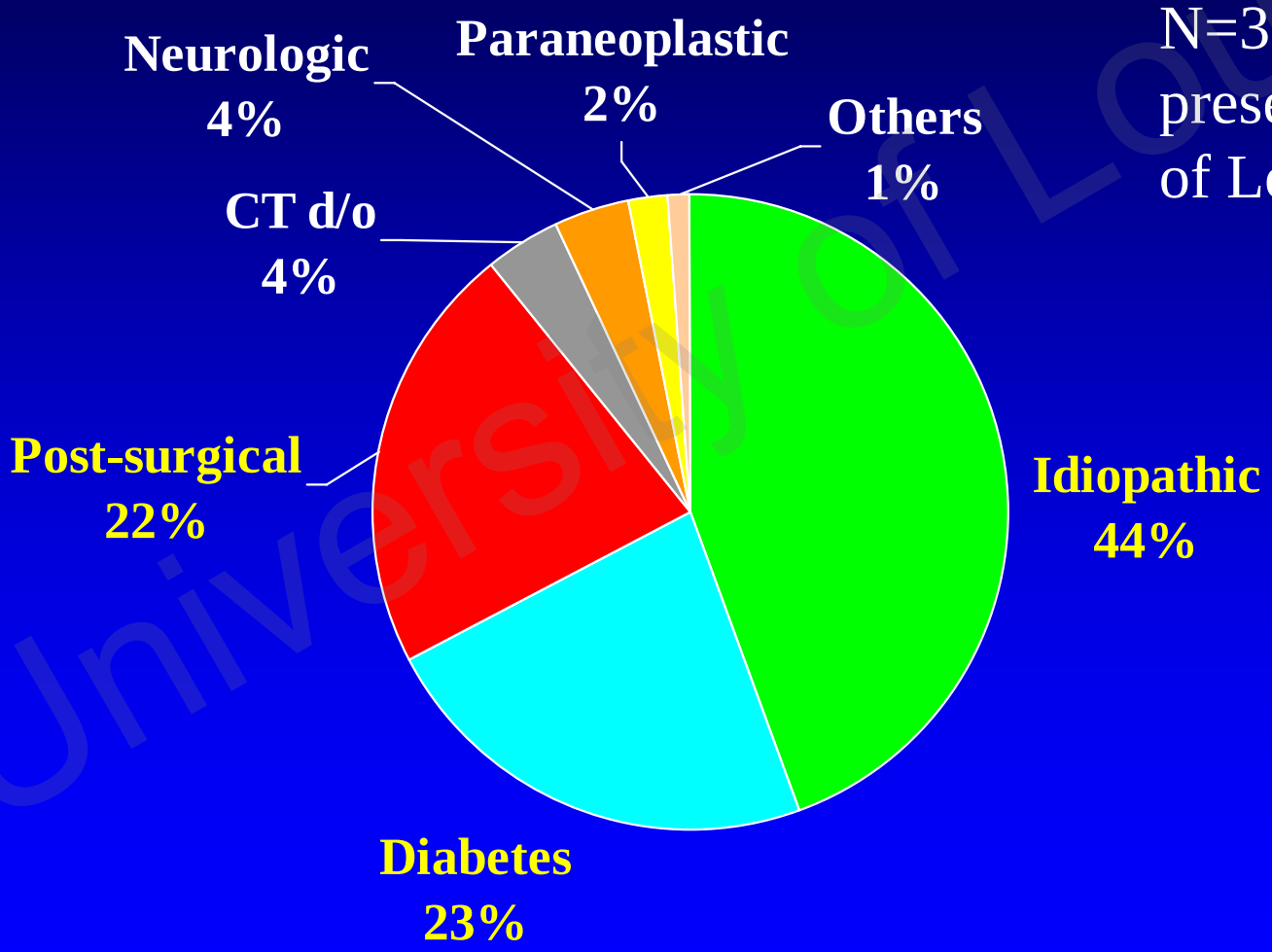


Regurgitation-Predominant
- Heartburn
- Effortless regurgitation

Dyspepsia-Predominant
- Epigastric pain
- Bloating
- Abdominal distension

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

Causes of Gastroparesis



N=339 patients presenting to University of Louisville

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

Prevalence of Diabetic Gastroparesis

	Type 1 DM	Type 2 DM
For Solids	22-56%	30%
For Liquids	0.1-44%	25-35%

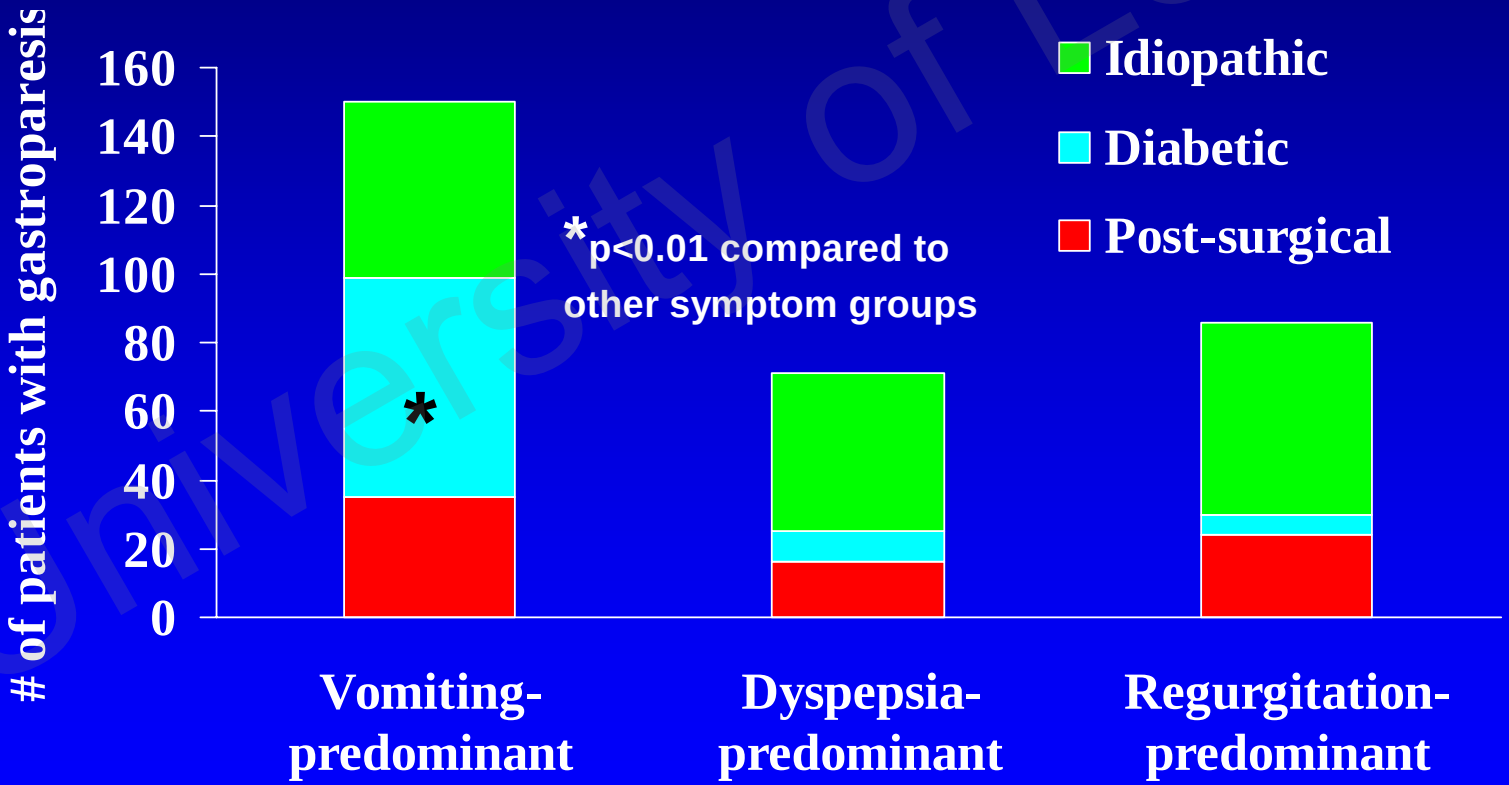
*Some patients may have minimal or no GI symptoms

Association between Gastroparesis and Diabetic Complications

	Association?
Clinical course of DM	
• age	no
• duration	no
End organ damage	
• retinopathy	no
• autonomic dysfunction	yes (type I DM), no (type II DM)
• peripheral neuropathy	yes

Presentation of Diabetic Gastroparesis is Different than Other Causes

N=339 patients presenting to University of Louisville



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

Postsurgical Gastroparesis

- Procedures with vagotomy
  - Bilroth I
  - Bilroth II
  - Roux-en-Y
  - Esophageal resection
  - Gastric resection

Postsurgical Gastroparesis

- Procedures without vagotomy
  - Fundoplication
  - Gastric bypass for obesity
  - Radiofrequency for GERD

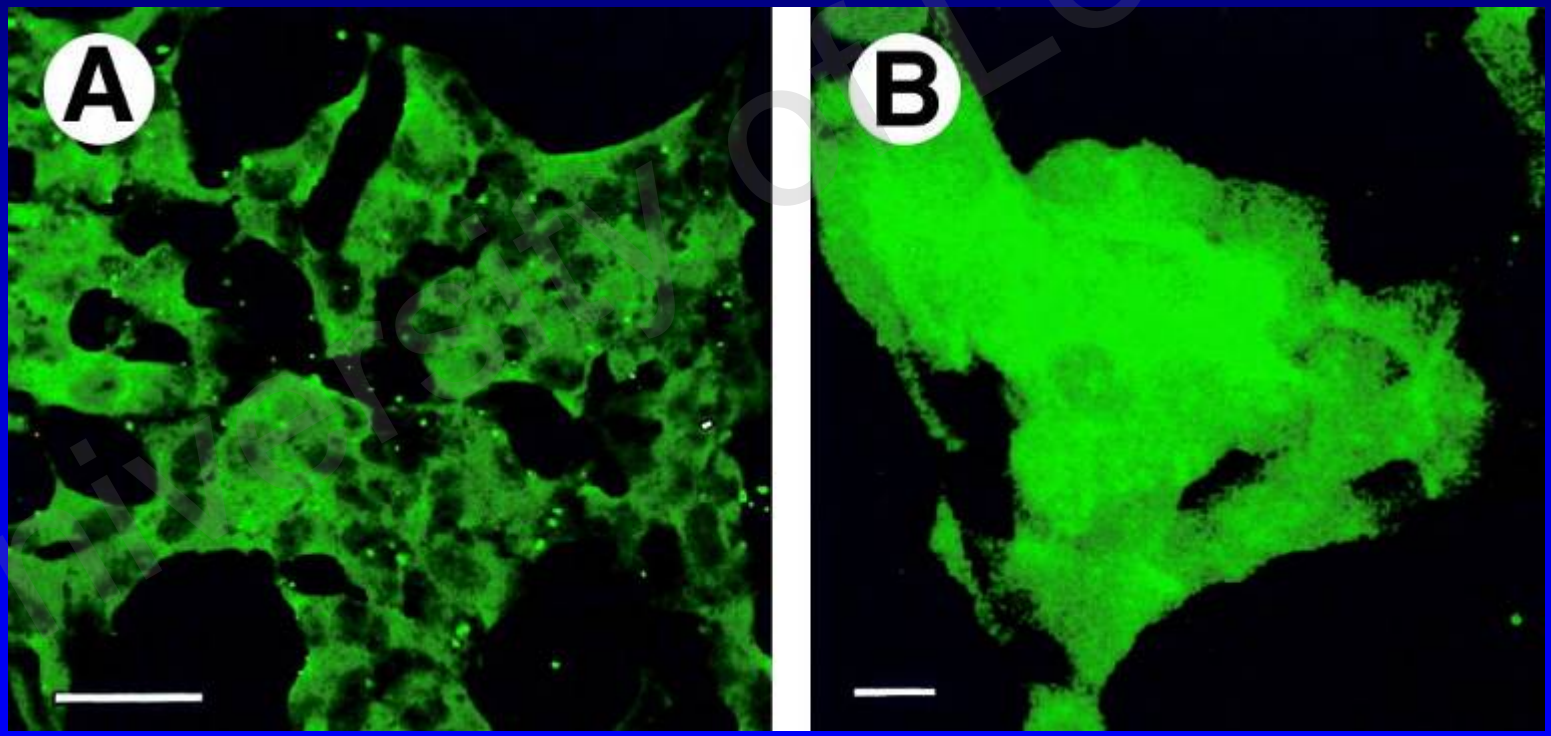
Neurologic Causes of Gastroparesis

- Central
  - Multiple sclerosis, Parkinson's, Shy-dragger syndrome, multifocal atrophy, brain stem tumor
- Peripheral and autonomic
  - CIDP (Chronic idiopathic demyelinating polyneuropathy), amyloidosis, primary dysautonomia

Paraneoplastic GI Motility Syndrome

- Cancer antigens mimicking neuronal tissues.
- Myenteric plexus infiltrated by lymphocytes and plasma cells.
- Cancers
  - Small cell lung cancer (80%), breast, ovarian, multiple myeloma, Hodgkin's lymphoma.
- GI symptoms can precede diagnosis of cancer.

Paraneoplastic GI Motility Syndrome: Anti-Hu Antibody* Against Enteric Neurons



*Antinuclear neuronal antibodies (ANNA)

Idiopathic Gastroparesis

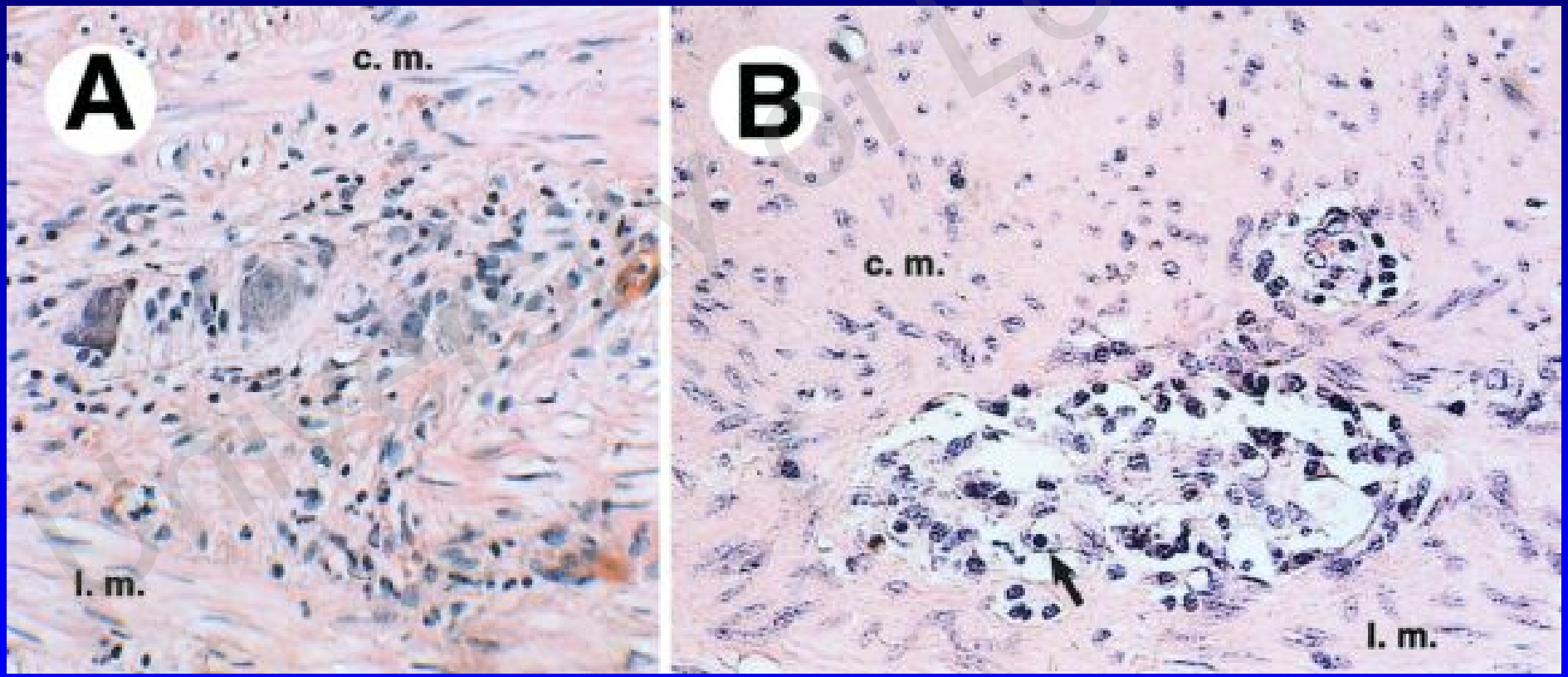
- Most common scenario: etiology of gastroparesis is unknown despite evaluation
- 70 to 80% females
- Presents equally with vomiting, dyspepsia, or regurgitation predominant symptoms
- Prognosis is unpredictable

*Soykan et al. Dig Dis Sci 1998;43:2398-404.

Post-Viral Gastroparesis

- May explain “idiopathic” gastroparesis
- Case reports only
  - Precedes by acute viral-like illness
  - CMV, herpes simplex, and rotavirus, EBV have been isolated
- May have better prognosis

Myenteric Neuritis of the Enteric Nervous System



Full-thickness antral biopsy from patient with “idiopathic gastroparesis

When to Look for Secondary Causes of Gastroparesis?

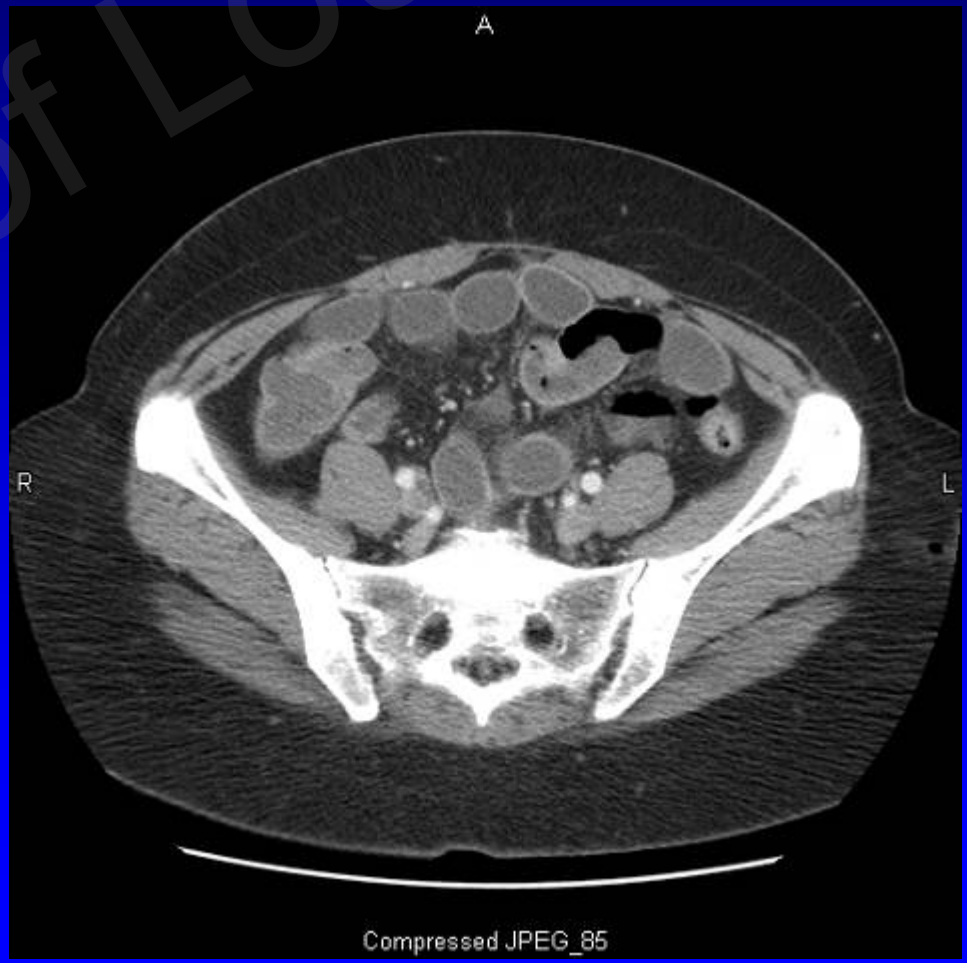
- Elderly patients
- Significant weight loss
- New onset of symptoms
- Neurologic complaints
  - Peripheral numbness, proximal muscle weakness, postural dizziness, ataxia, difficulty urination, double vision
- Associated with diffuse GI dysmotility

Diagnostic Tests in Gastroparesis

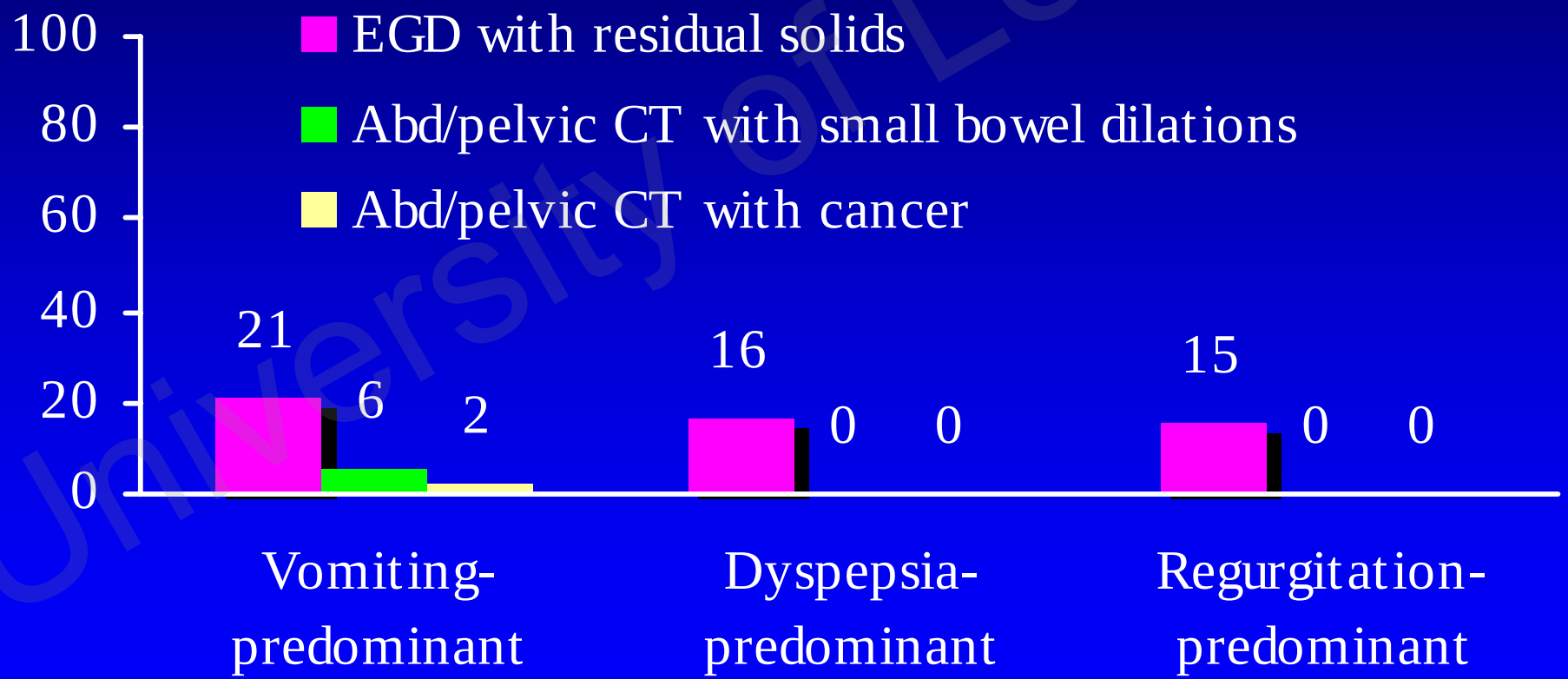
- Upper endoscopy
- Upper GI & SBFT x-ray
- Solid-phase gastric emptying test
- Antroduodenal manometry
- Electrogastrography (EGG)
- Breath test for bacteria overgrowth

Upper Endoscopy in Gastroparesis

Abdominal CT for Gastroparesis and Pseudo-Obstruction

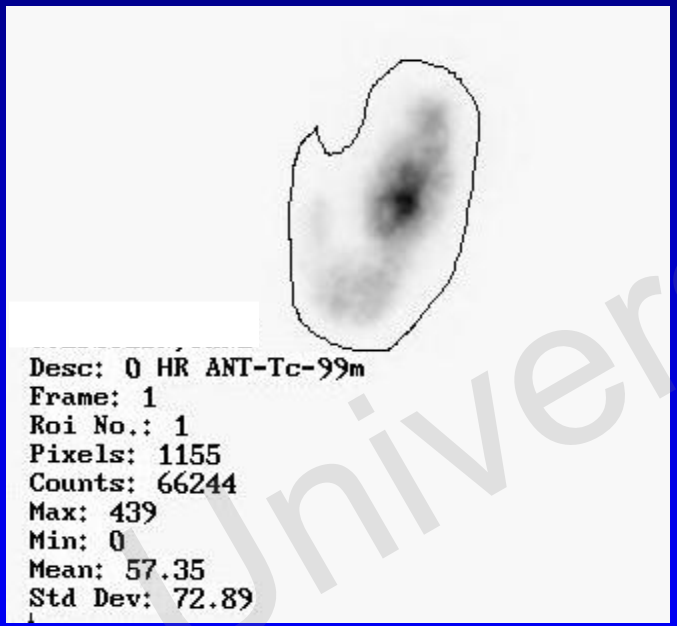


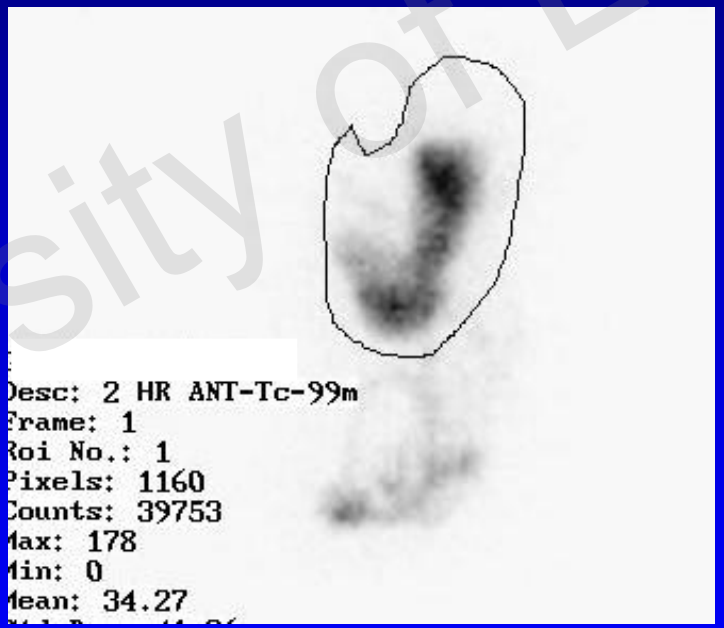
EGD and Abd CT for Gastroparesis

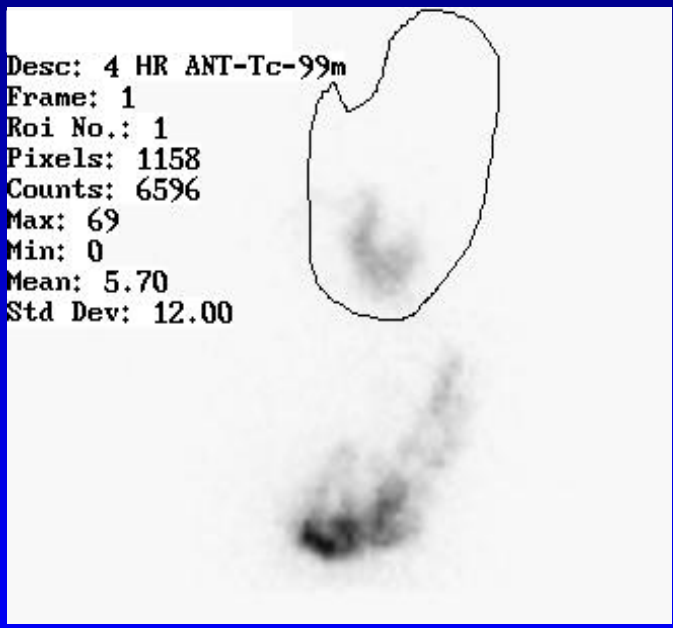


Unpublished data: N=338 patients with gastroparesis at UofL

Scintigraphy:
4-hr Gastric Emptying Test





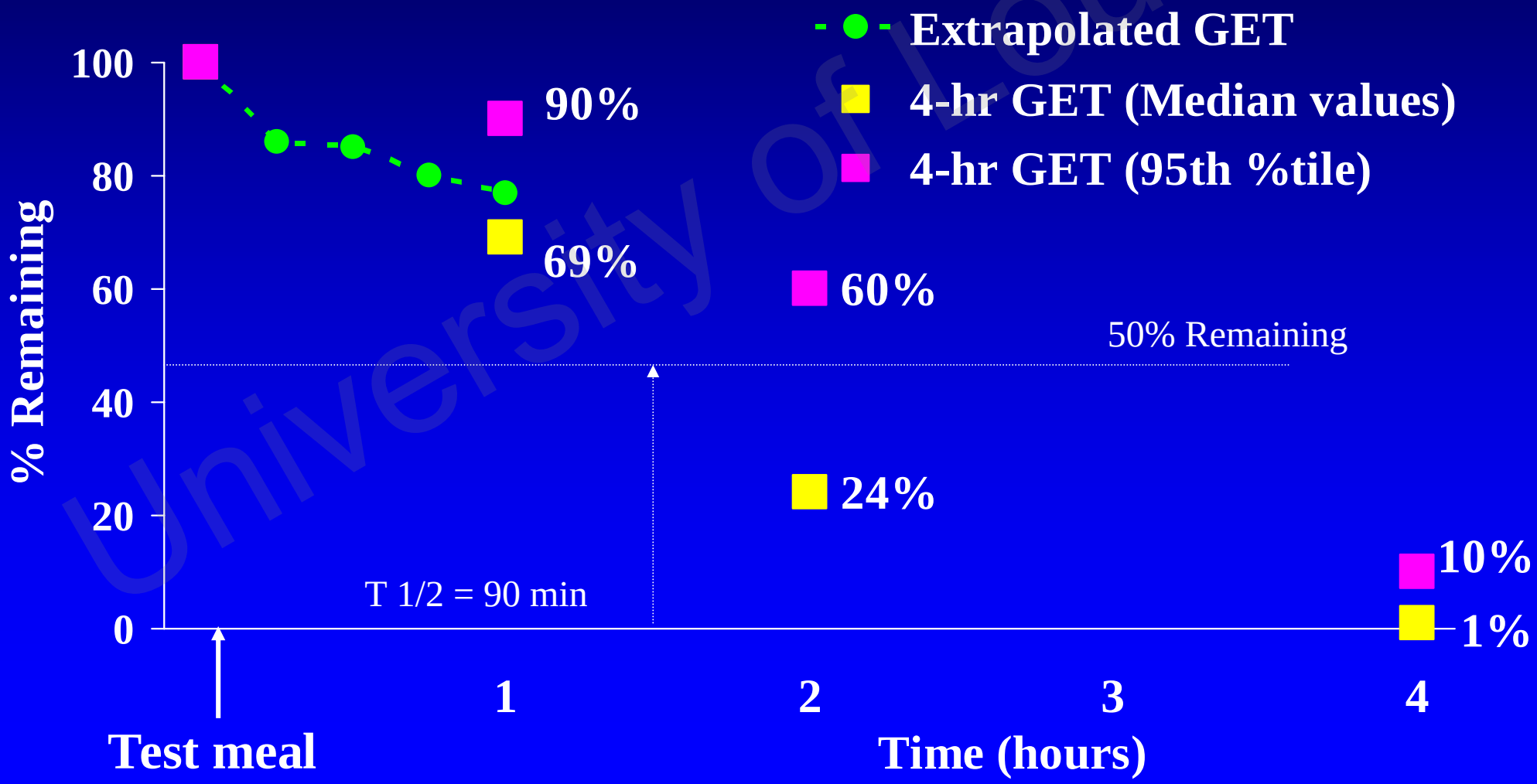


Before test meal

After 2 hours

After 4 hours

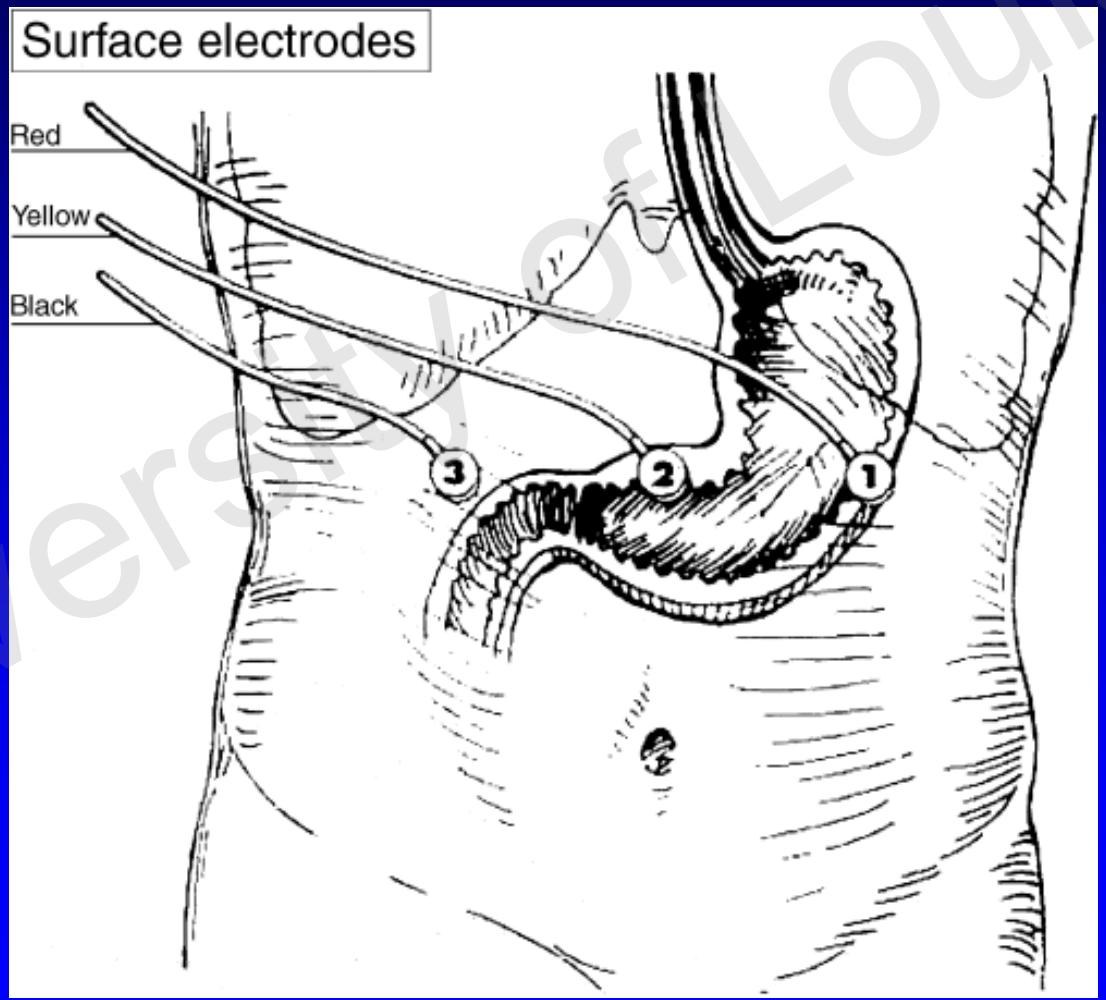
Gastric Emptying Test (GET)



Gastric Emptying Test (GET)

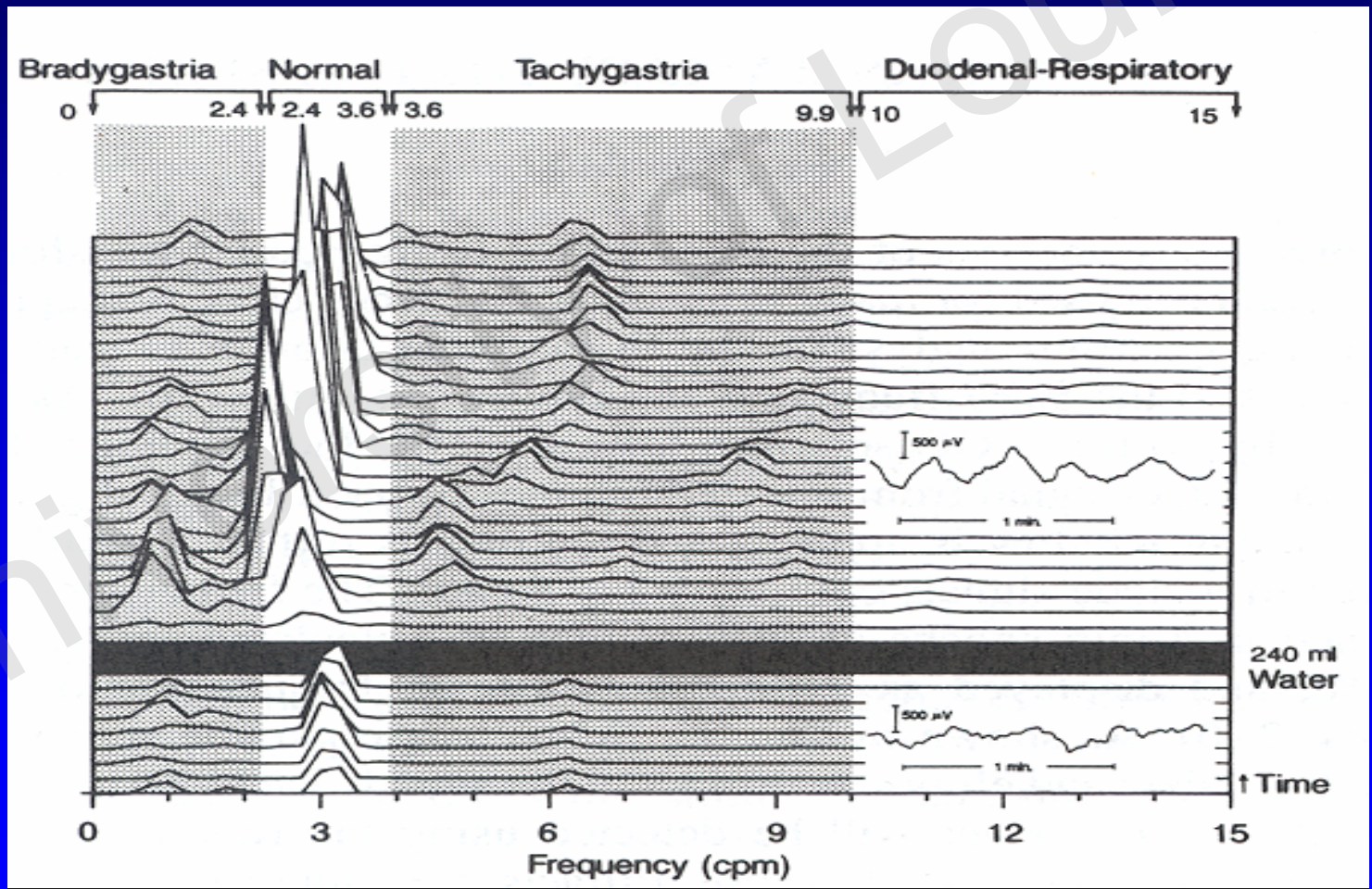
- Specific for gastroparesis but not sensitive
- Important factors
  - Standard test meal (scrambled eggs, bread, jam & juice)
  - Amount ingested
  - Emptying is not linear
- 4-hr GET is the new international standard

Cutaneous EGG

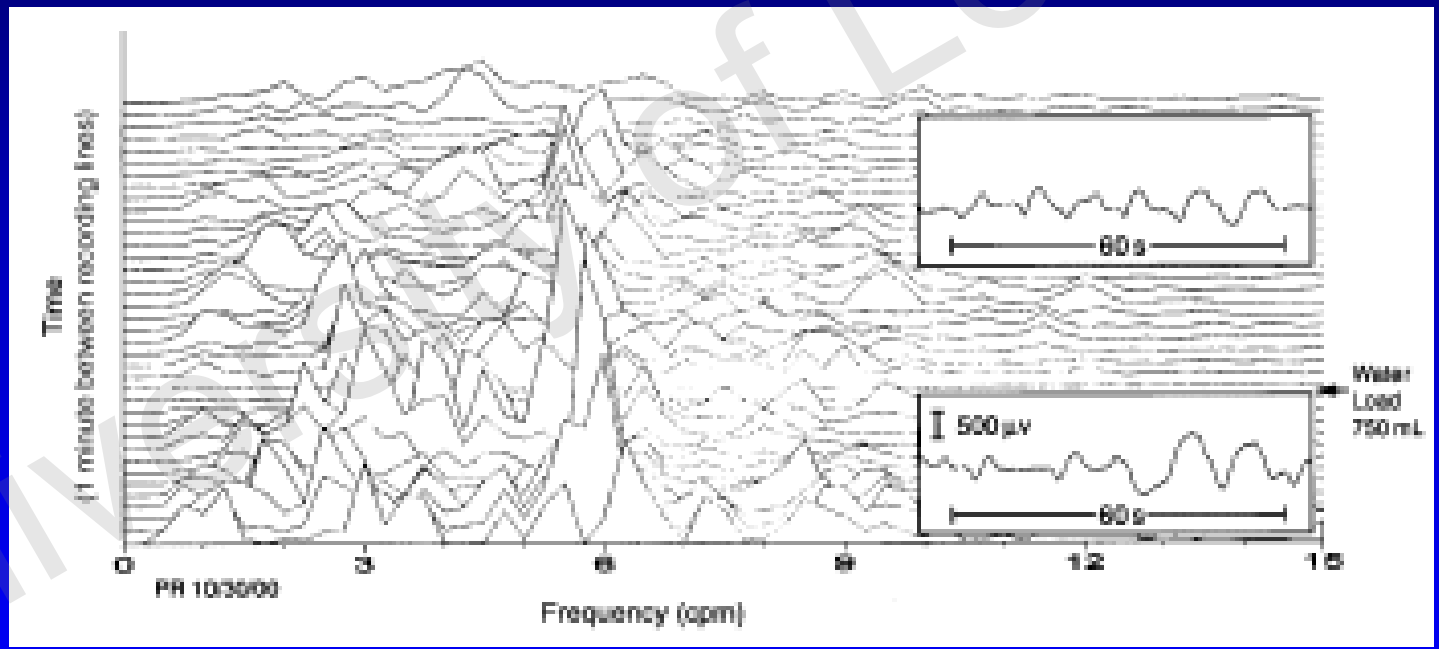


Parkman et al. Neurogastroenterol Mot 2003;15:89-102

Normal EGG:
Running Spectrum Analysis



Abnormal EGG: Tachygastria



From Koch, Electrogastrography. In Schuster Atlas of GI Motility in Health and Disease.

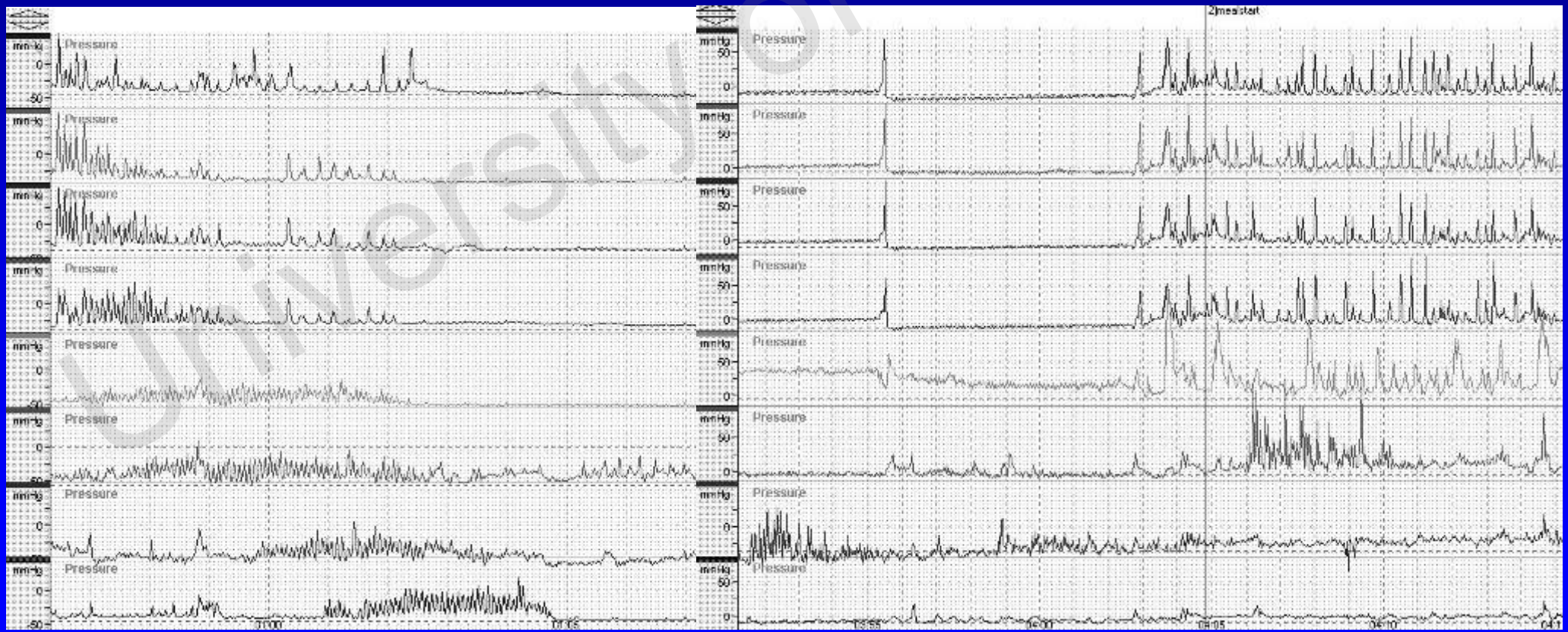
Normal Small Bowel Manometry

Fasting Pattern

Migratory motor complex

Fed Pattern

Enhanced postprandial activity



Abnormal Small Bowel Manometry

Fasting Pattern

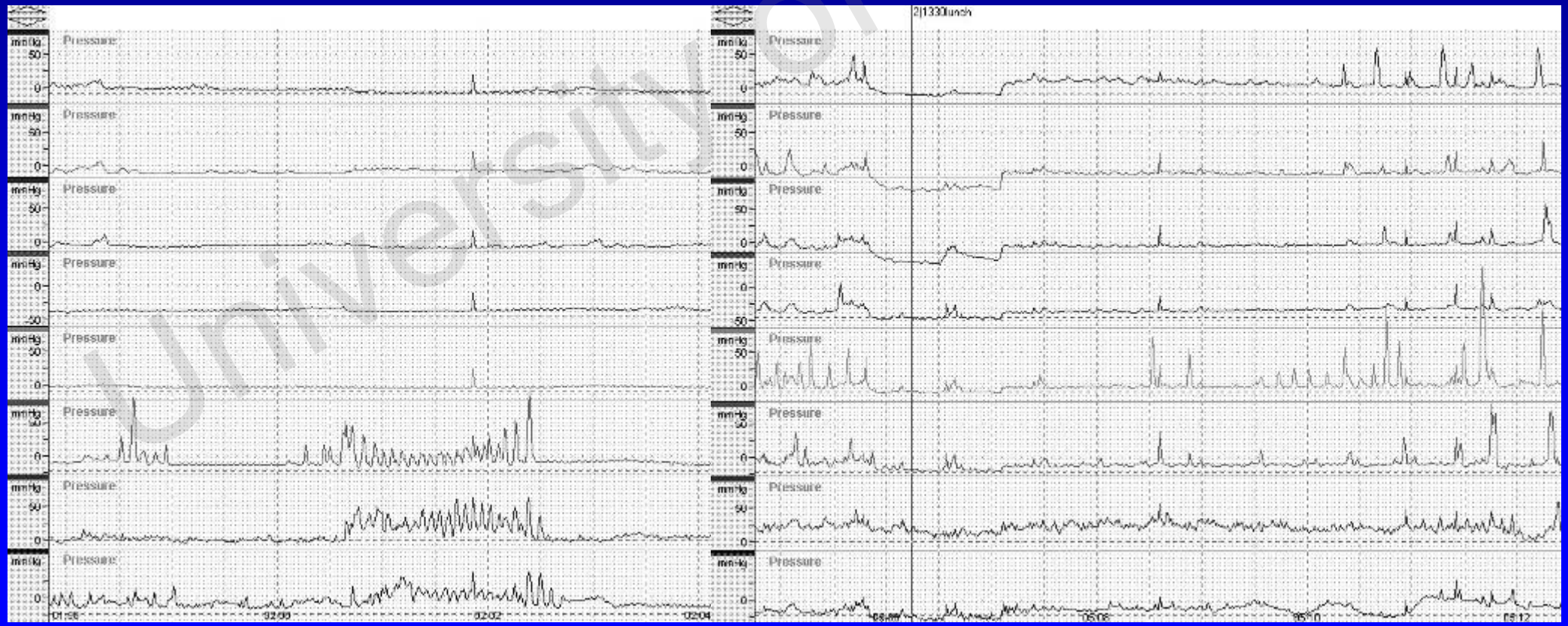
Impaired MMC:

Abnormal enteric nervous system

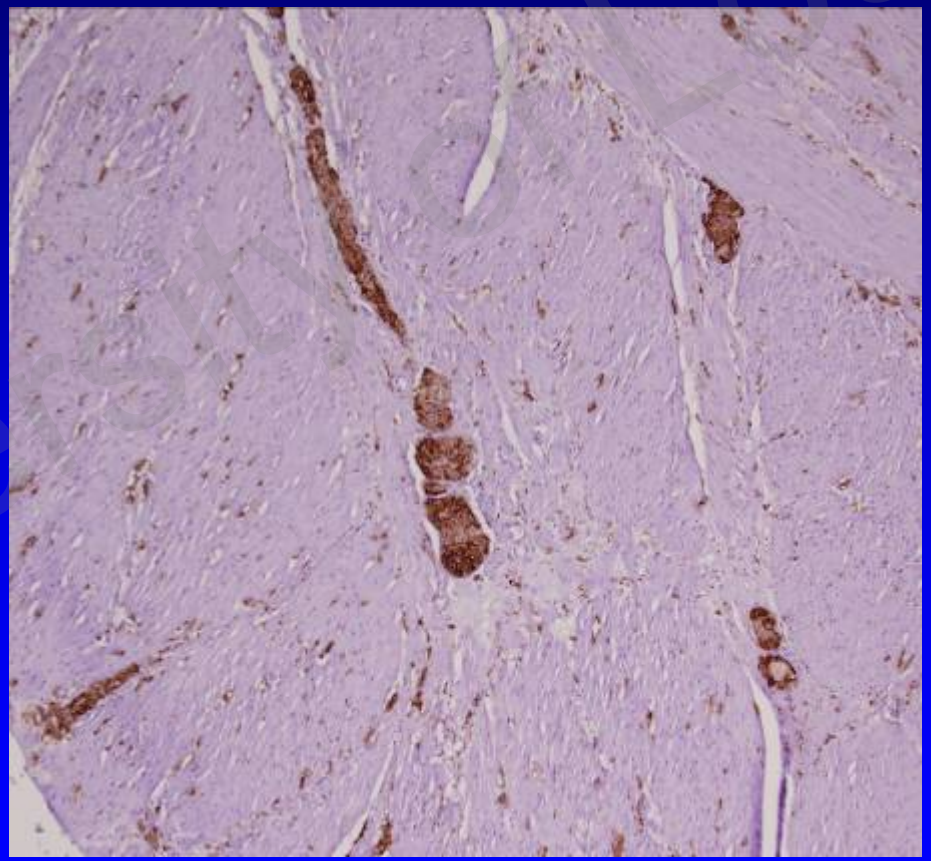
Fed Pattern

Impaired postprandial activity:

Vagal neuropathy



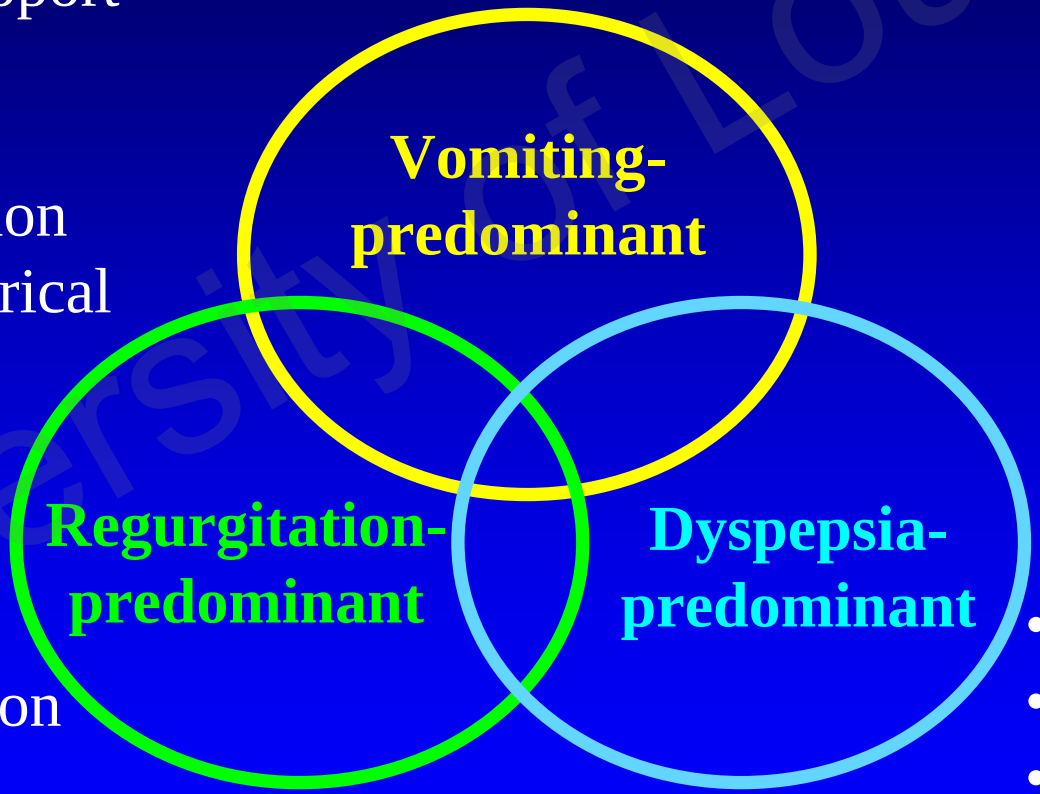
Full-Thickness Biopsy of Stomach and Small Bowel: Hyperganglionosis



Full-thickness antral biopsy from patient with “idiopathic gastroparesis

Treatment of Gastroparesis Depends on Symptom Presentation

- Nutrition support
- Prokinetics
- Anti-emetic
- Hospitalization
- Gastric electrical stimulation



- Lifestyle modification
- Acid suppression
- Prokinetics
- Avoid antireflux surgery

- Diet modification
- Prokinetics
- Antibiotics for bacteria overgrowth
- Pain control

Overall Approach to Patients Suspected with Gastroparesis

5. Consider specialized testing (EGG, manometry, etc.)

4. Treatment trial with prokinetic and/or antiemetic

3. Evaluate gastroparesis (solid-phase gastric emptying test, look for secondary causes)

2. Rule out obstruction or mucosal lesions (EGD, UGI/SBFT)

1. Initial investigation (History, PE, basic blood tests)

Parkman et al. AGA Technical Review. Gastroenterol 2004;127:1592.

Non-Pharmacologic Treatment of Gastroparesis

- Glucose control in diabetic
- Nutrition
  - Frequent smaller meals, liquids, low fat diet
  - Avoid indigestible fibers
  - Trial of nasojejunal feeding & jejunal nutrition
- Avoid G-tube
- Home health support

Metoclopramide (*Reglan*)

- Dopamine antagonist & central antiemetic
- Available in tablet, liquids and IV injection
- Only 3 small controlled trials available
- CNS side effects very common (20-30%)
- Efficacy decreases with chronic use

*Domperidone

- Peripheral dopamine-2 antagonist & antiemetic
- Do not cross blood-brain barrier
- Results dose dependent (10-30 mg qid)
- Symptoms improvement in U.S. randomized trial for diabetic gastroparesis
- Side effects
  - Increase prolactin hormone (breast tenderness)
  - Good long term safety

*Not available in U.S.

Erythromycin

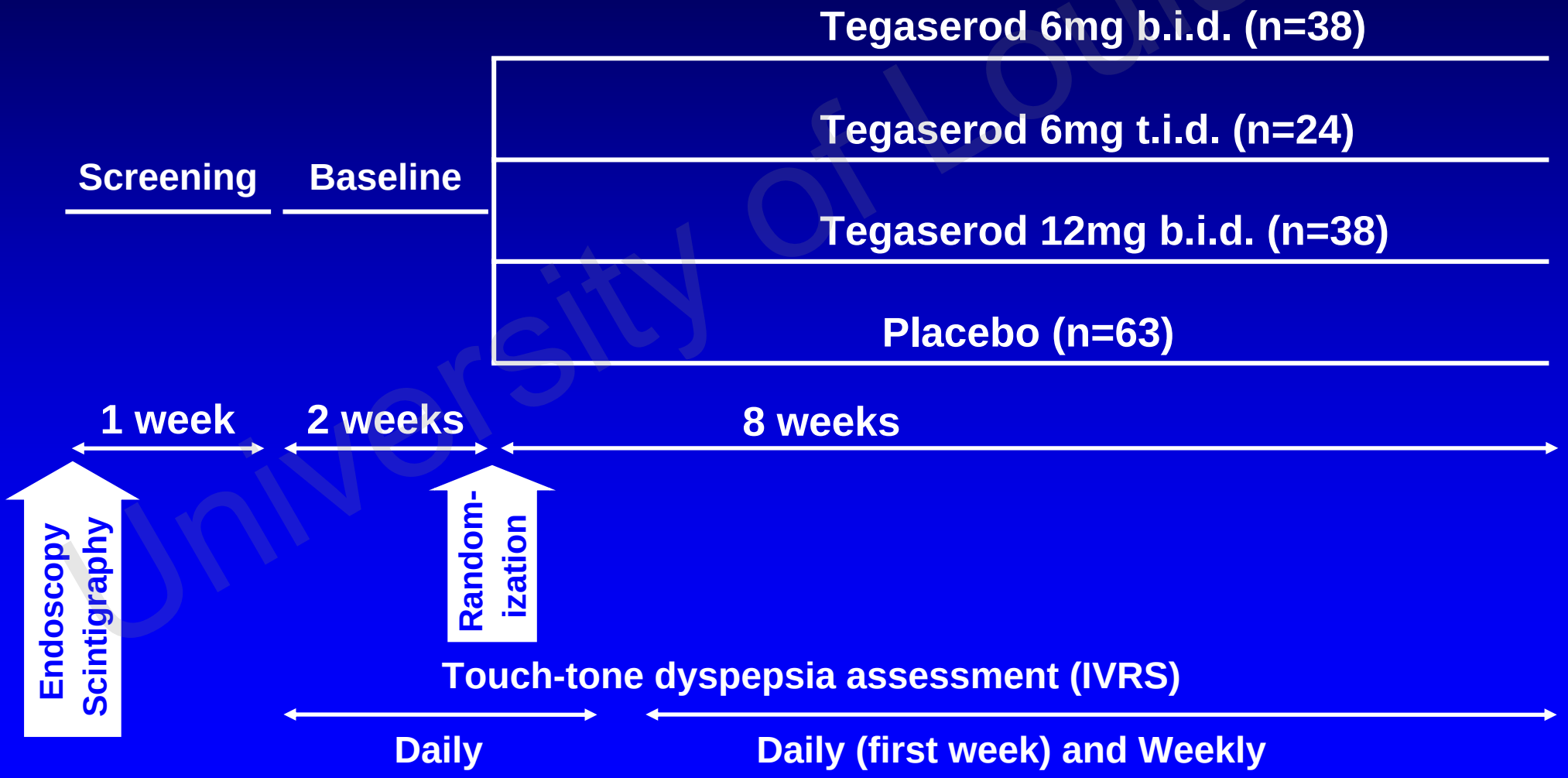
- Motilin agonist
- 35 clinical trials critically reviewed*
  - Only 1 controlled study
  - Limited data on efficacy with small sample sizes
- Narrow therapeutic dosage
  - p.o. liquids (62.5 - 125 mg po tid)

*Maganti et al. Am J Gastroenterol 2003;98:259-63.

Tegaserod: 5-HT Agonist *(Zelnorm)*

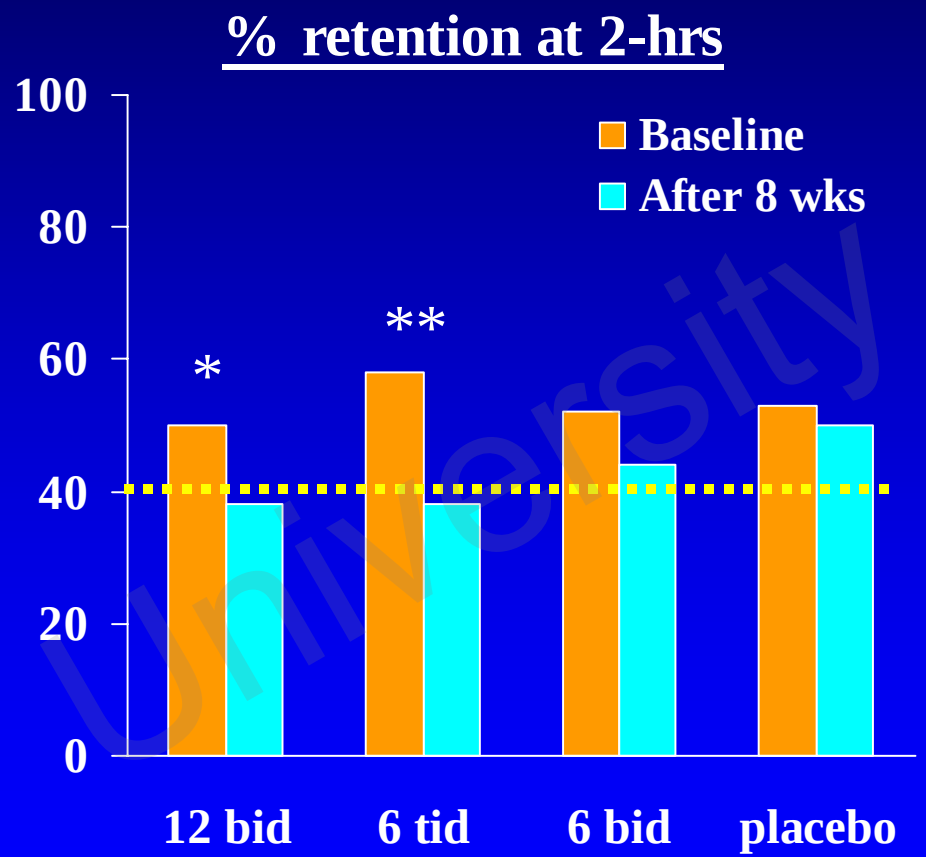
- Prokinetic indication for constipation
- Stomach contain different receptor subtypes
  - $5\text{-}HT_1$, $5\text{-}HT_3$, $5\text{-}HT_4$

Tegaserod for Dyspeptic-Predominant Gastroparesis

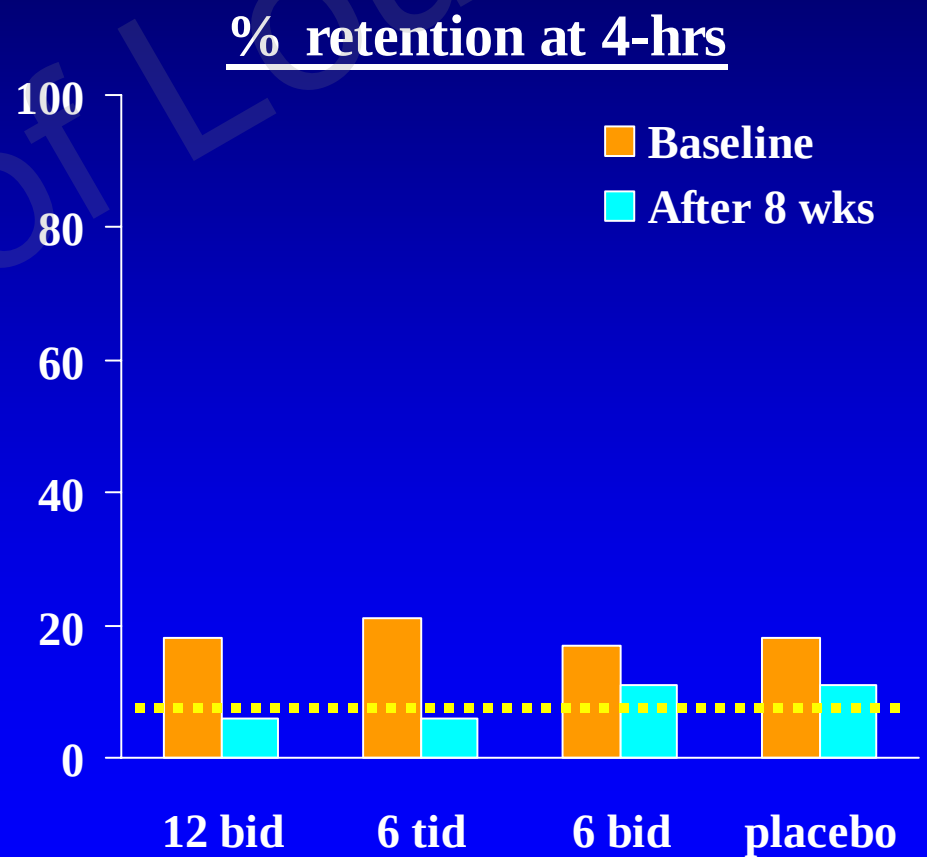


Tougas G et al. DDW 2003 (NOT FDA indication)

Tegaserod for Dyspepsia-Predominant Gastroparesis



*p=0.077 vs placebo; **p=0.003 vs placebo



Tougas et al. DDW 2003, N=163 (NOT FDA indication)

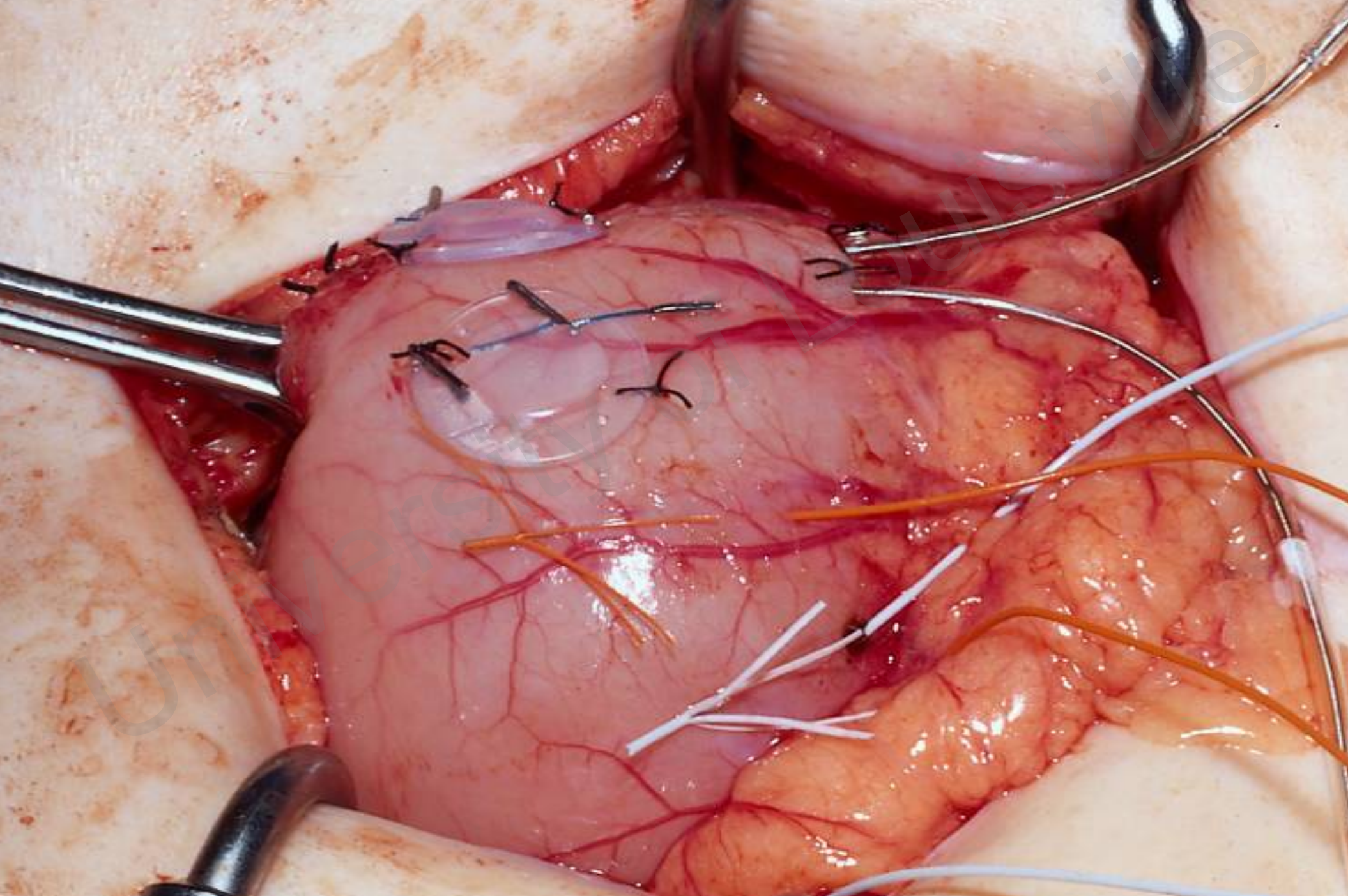
Opened-Label Trials of Botulinum Toxin Injection for Gastroparesis

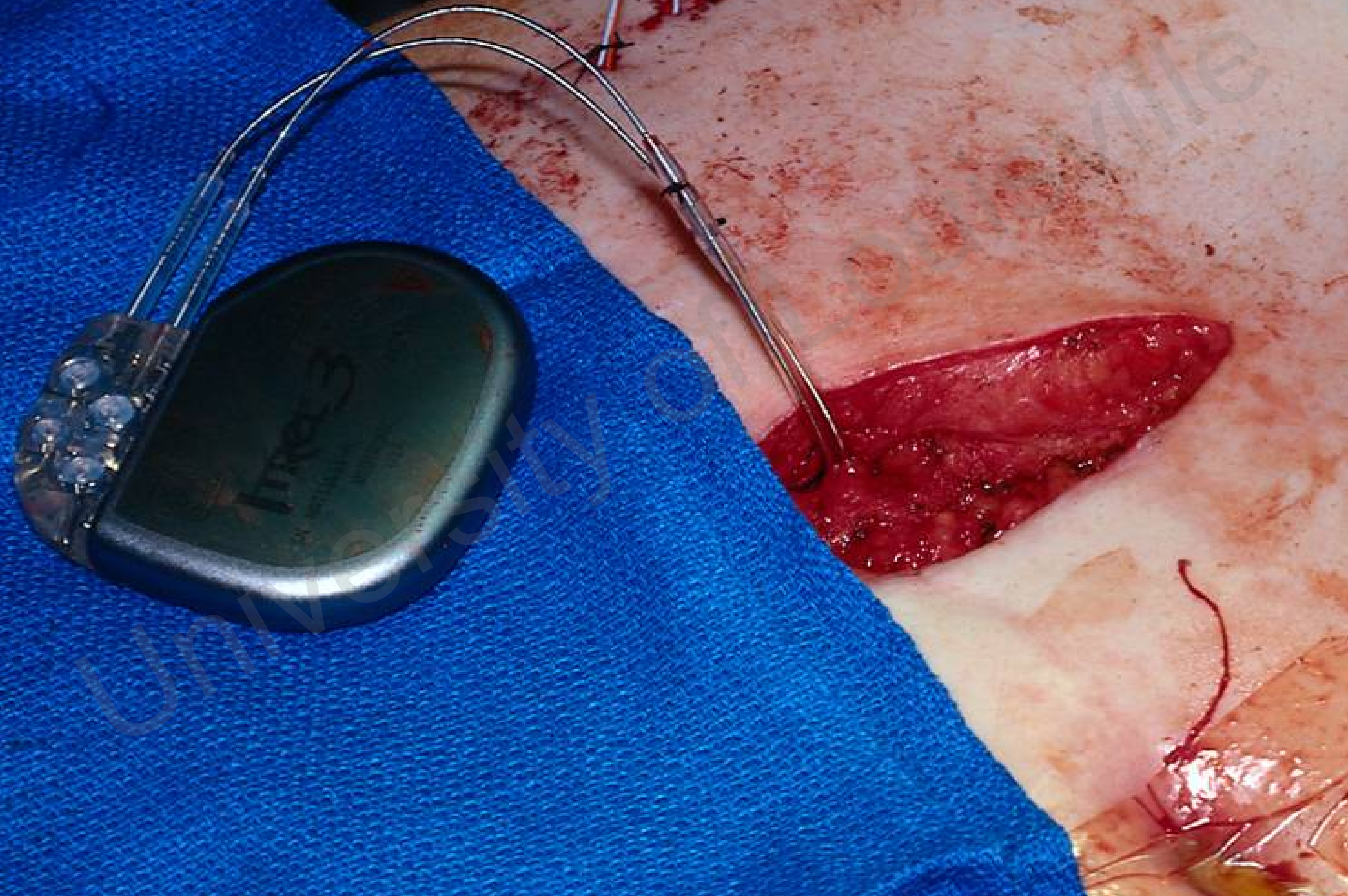
- Total 39 patients
  - Most had idiopathic gastroparesis
- 80 to 200 units botulinum toxin
- Follow-up at 4-6 weeks
  - Improve symptoms and GET
- Maybe useful in acute nausea & vomiting and in diabetics

Miller et al. Am J Gastroenterol 2002;97:1653-60.
Lacy et al. Am J Gastroenterol 2002;97:1548-52.
Ezzeddine et al. Gastroint Endosc 2002;55:920-3.
Arts et al. DDW 2003, 431A.

Gastric Electrical Stimulation for Severe Gastroparesis

- Received humanitarian device exemption in 2000
- Not a Pacemaker
- Hypothesis: increase vagal afferent to the brain and increase vagal efferent to the stomach



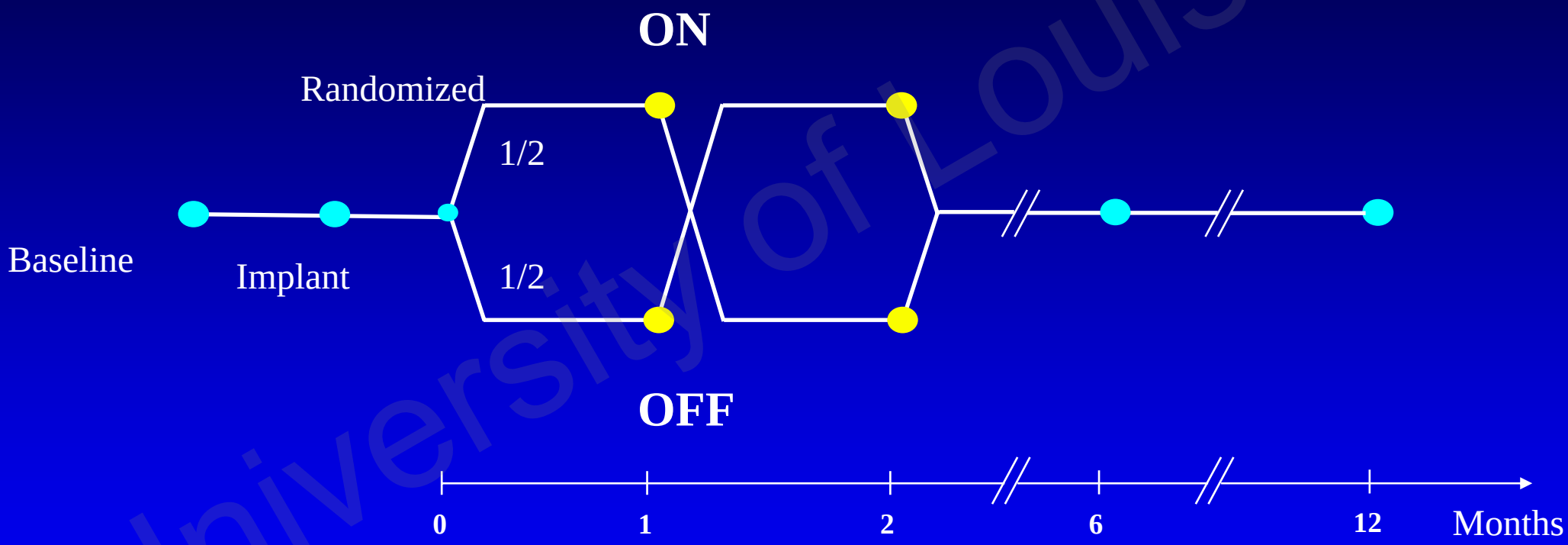


WAVESS (Worldwide Anti-Vomiting Electrical Stimulation Study)

	Diabetics	Idiopathic	All Patients
n =	17	16	33
Gender (M / F)	9/8	0/16	9/24
Age (Mean)	38.1	41.1	38.9
Vomiting/Week (Median)	25.0	26.8	26.0
GET (med, %retention):			
2 hours	80.0	76.5	78.0
4 hours	46.0	28.0	34.0

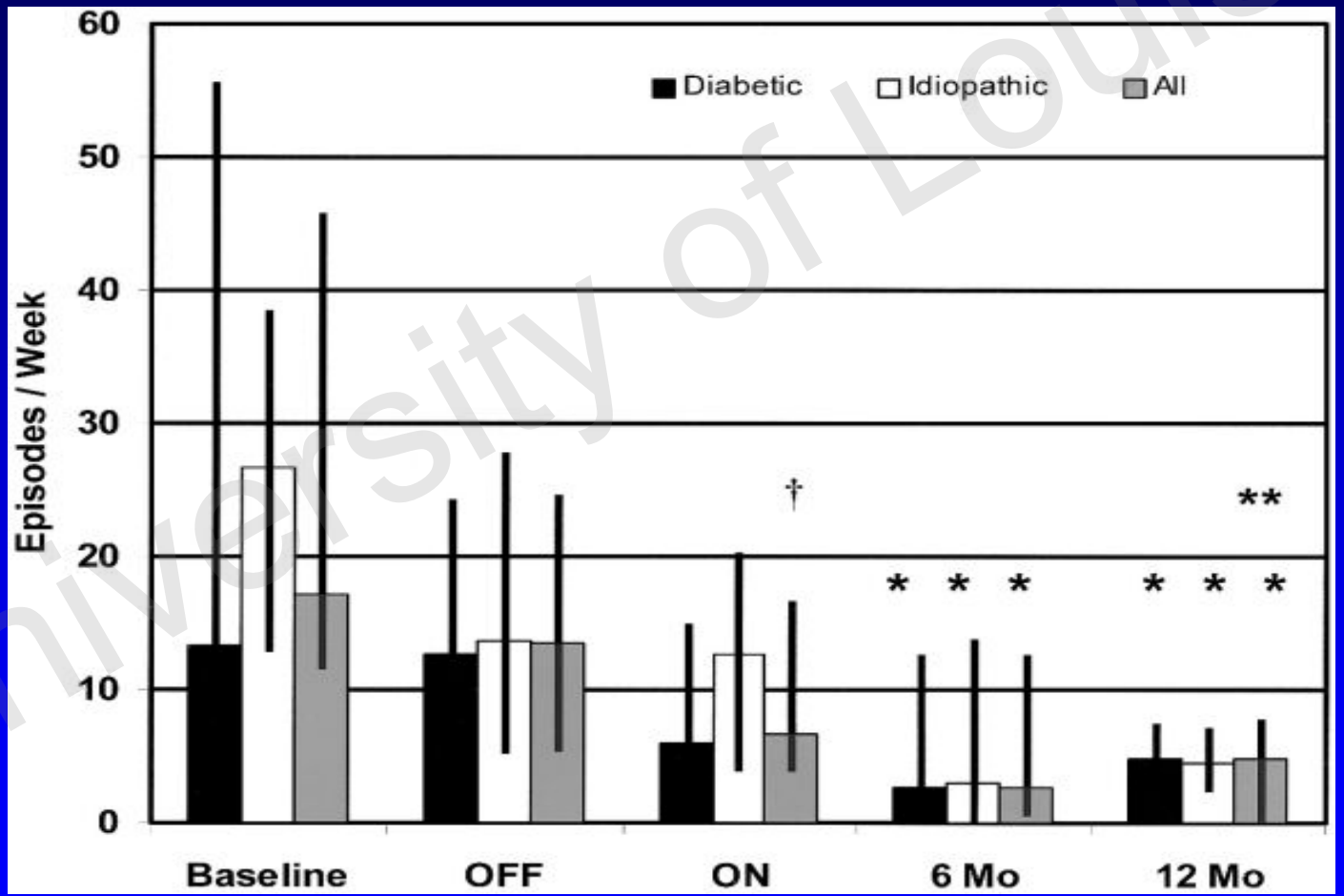
Abell et al. Gastroenterol 2003;125:421-428

WAVESS Study

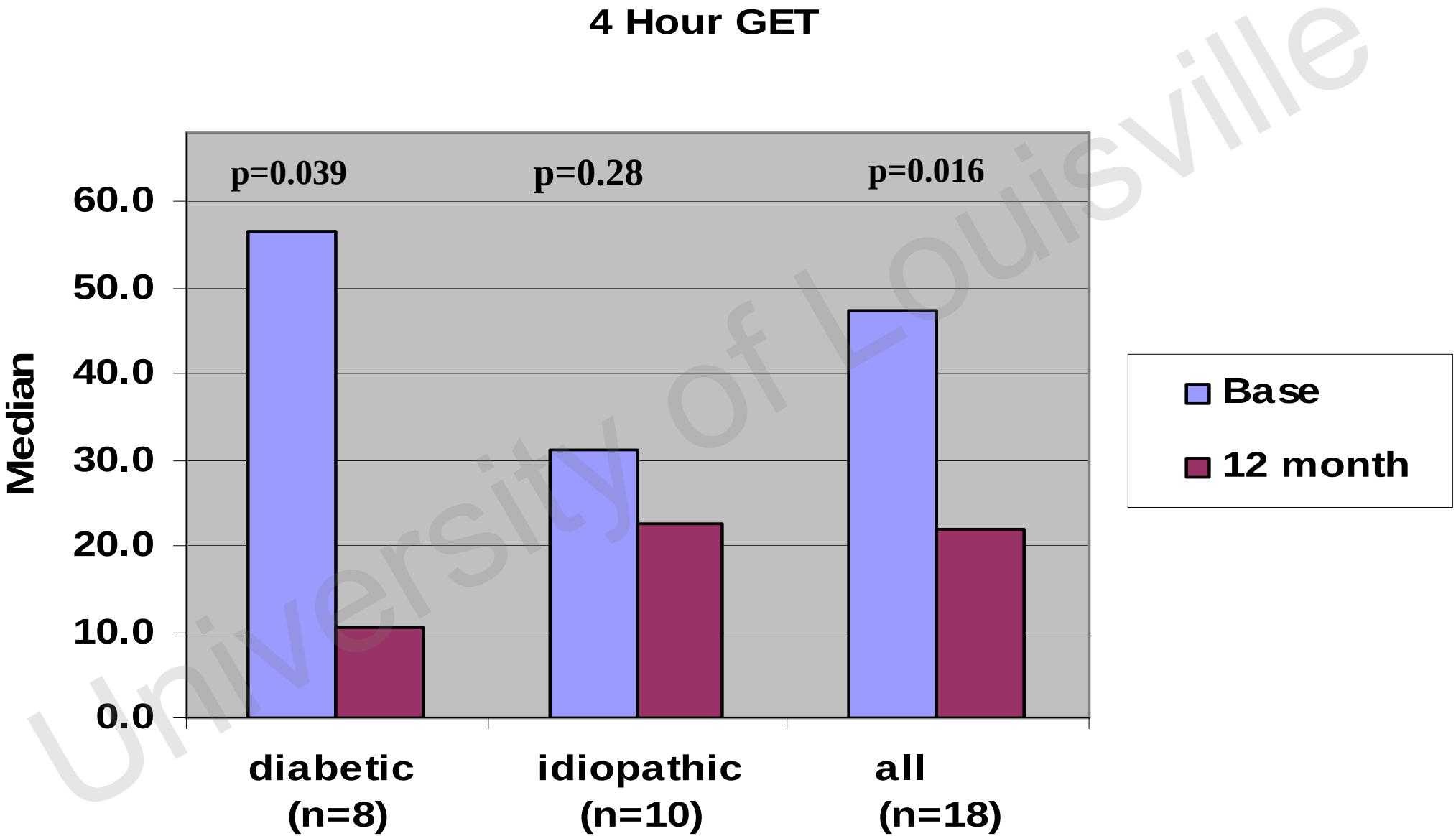


1. Cross over results
2. Longitudinal results

Weekly Vomiting Frequency

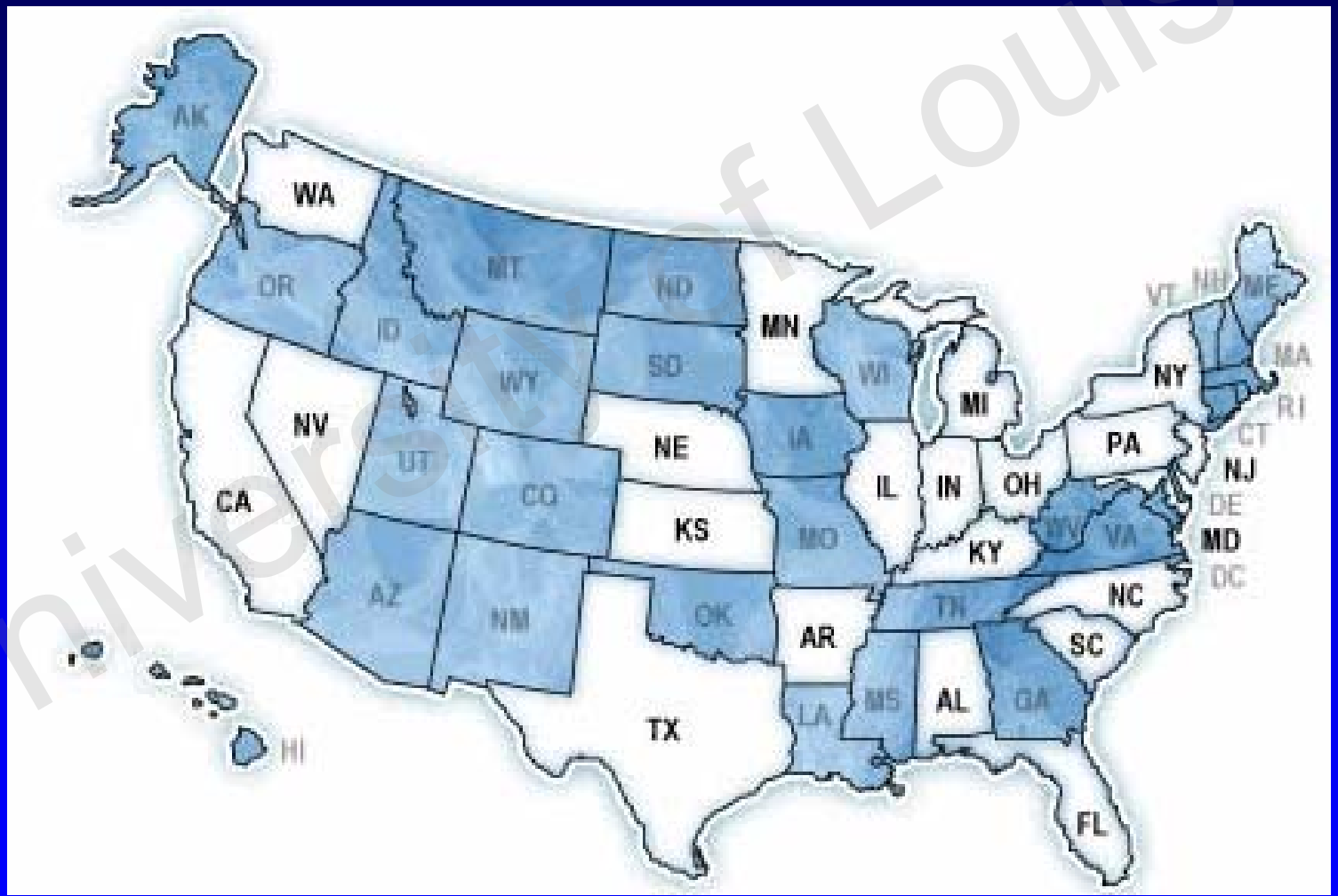


Abell et al. Gastroenterol 2003;125:421-428



Abell et al. Gastroenterol 2003;125:421-428

Gastric Enterra® Therapy in the U.S.



From Medtronic website

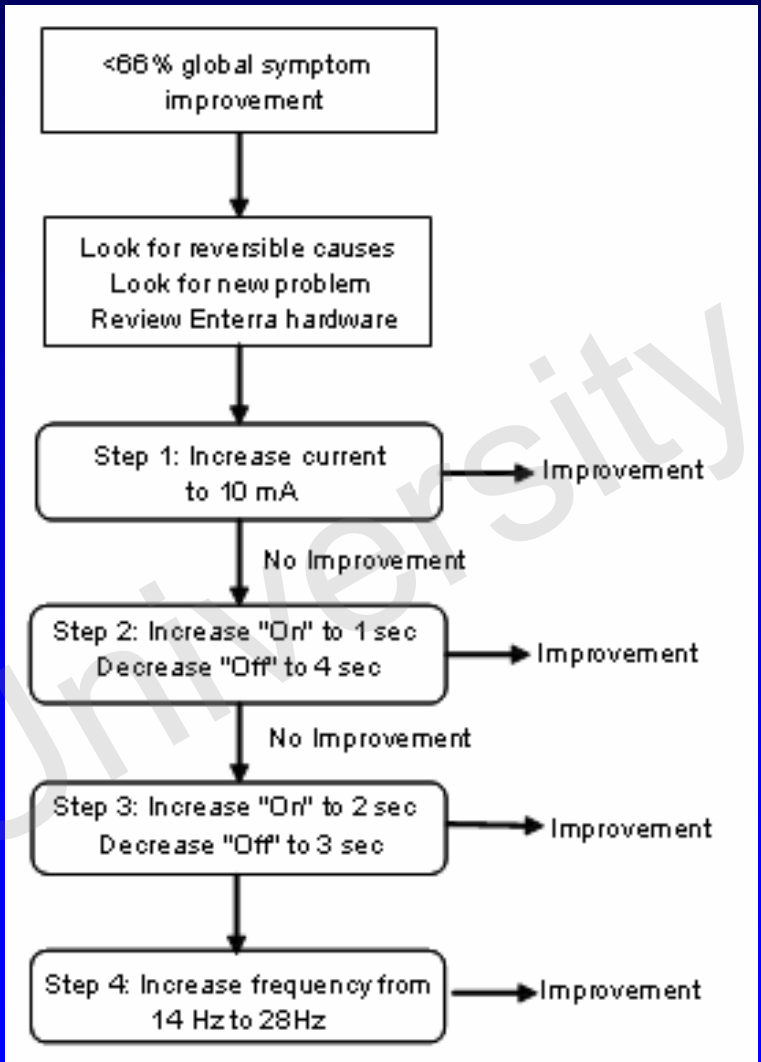
States with Enterra® therapy available

Gastric Electrical Stimulation at University of Louisville

- 50 patients implanted
  - 41 HDE and 9 randomized protocol
  - 15 M, 35 F
  - median age 43 (range 18 - 66)
  - 31 diabetic, 17 idiopathic, 2 other causes
  - 20 (40%) with J tube
  - More effective in type 1 diabetic gastroparesis

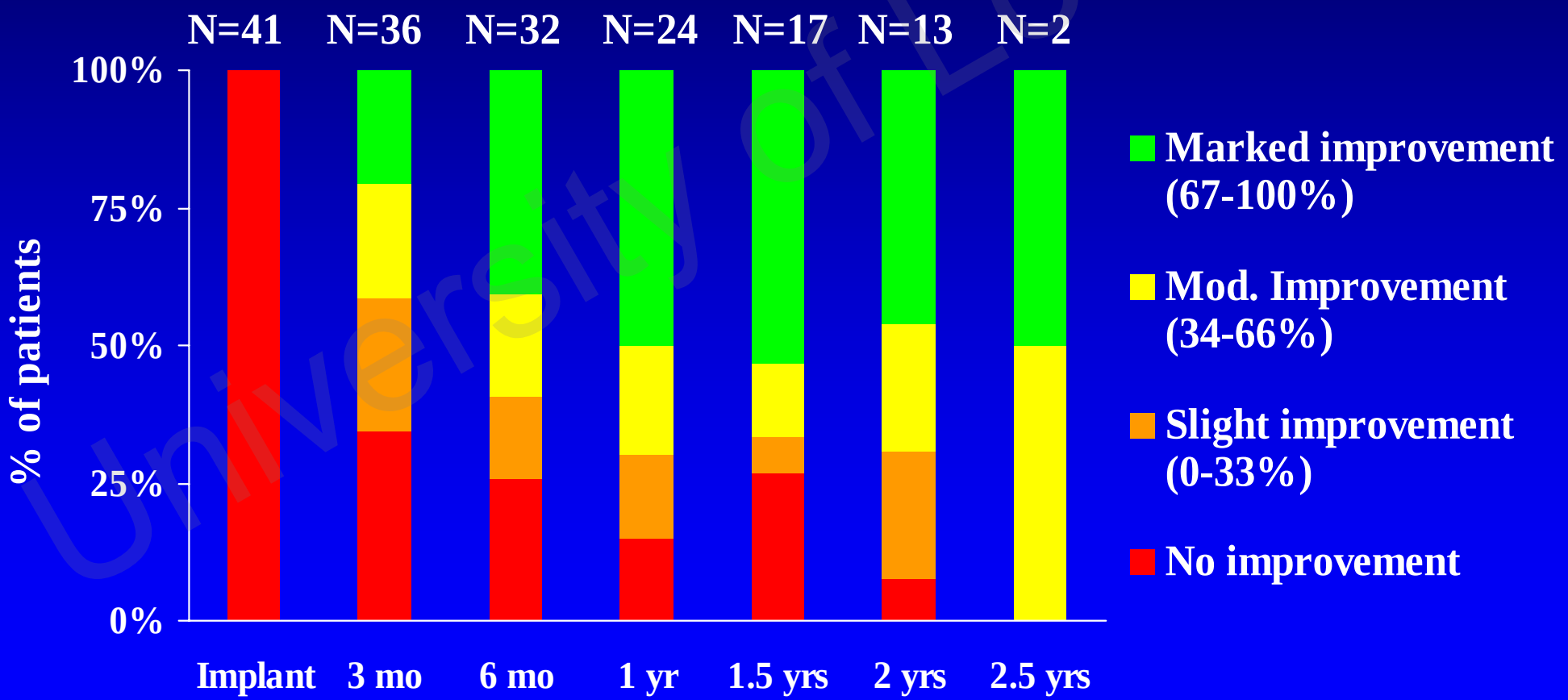
Updated on March 2005

Gastric Electrical Stimulator Setting



Power = Current x Resistance

Gastric Electrical Stimulation at University of Louisville*



Updated on March 2005

Follow-Up Period

*Humanitarian device exemption protocol

Gastric Electrical Stimulation for Gastroparesis

- Indication is vomiting-predominant gastroparesis refractory to medical therapy
- Very good option for type-1 diabetic gastroparesis
- Suboptimal in patients with multifactorial causes
- Controversial for postsurgical gastroparesis

Conclusions

- Clinical manifestation of gastroparesis is diverse
- Treatment depends on symptom presentation
- Medical therapy is suboptimal, but tegaserod and domperidone can be effective
- Electrical stimulation is good option in selected individuals with refractory nausea and vomiting