Diabetic Gastroparesis: 
Pathophysiology, Management, & the Role of Gastric Electrical Stimulation (GES)

“…Ah… the stomach, a complex and highly regulated organ with much opportunity for dysfunction” .... Dr. Ken Koch- Jan. 1994
Disclosures:

I work in Sales & Field Training for Medtronic Neuromodulation- which is the manufacturer of the Gastric Stimulation Device.

I also work in the field to provide technical support to Dr. Glenroy Heywood for his Gastric Stimulation program.
Pathophysiology & Treatment of Gastroparesis (Learning Objectives)

- Pathophysiology of Diabetic Gastroparesis
  - Mechanical Physiology
  - Electrical Physiology
- Diagnosis of Diabetic Gastroparesis
- Treatment of Diabetic Gastroparesis
- Gastric Electrical Stimulation (GES)
  - Screening criteria
  - Outcomes data
Stomach Function

– Hollow, muscular organ
– 4 Functions:
  • Stores food during eating
  • Secretes digestive juices
  • Mixes food with these juices
  • Propels partially digested food called *chyme* into the duodenum
Mechanical Physiology-
(Accomodation)
Mechanical Physiology –
(Trituration)
Mechanical Physiology - (Emptying)

- **F**: Pyloric resistance
- **H**: Duodenal resistance
- **G**: Antroduodenal coordination
- **E**: Antral peristalsis-antral emptying (3 peristaltic waves/min)
Mechanical Physiology of the Stomach

Gastric Emptying

- Lag
- Active
Solid Gastric Emptying - Enterra

Time (min)

N = 123

60%

Q95

10%

0 10 20 30 40 50 60 70 80 90 100

0 60 120 180 240
Electrophysiology of the stomach

- Gastric fundus, body and antrum have potential for neuromuscular dysfunction.

- The early stages of neuromuscular disorders of the stomach may exhibit **gastric dysrythmias** progressing to **antral hypomotility** and **gastroparesis** with/without symptoms of functional dyspepsia.
Electrophysiology of the Stomach

- Slow waves, spike waves & motility
Electrophysiology of stomach

- Interstitial Cells of Cajal, Calcium ion Channels and the creation of slow-wave depolarizations.
Interstitial Cells of Cajal -ICC

- Pacemaker current leading to slow waves appears to originate in ICC’s
- Recording of electrical activity in a mouse (normal and deficient in ICC)
Relationship between Slow Waves and Contractions
Gastroparesis
Experimental Model of Slow wave degradation in Acute Hyperglycemia

Figure 2. Representative multichannel mucosal slow wave recordings are shown from a healthy volunteer. Under basal conditions (A), slow waves from the proximal (top), middle and distal (bottom) leads exhibit a regular oscillation with a period of approximately 20 s. The dashed lines show the close coupling between adjacent leads. With hyperglycaemic clamping to 250 mg dl⁻¹, there is loss of the stable rhythm that is most prominent in the distal lead (B). In this recording, the regular rhythm is replaced by a high frequency, chaotic waveform with a mean period of approximately 10 s and poor coupling.
Cellular effects of Hyperglycemia

We know hyperglycemia is the underlying cause of diabetic gastropathy.

2 Primary Cellular Pathways by which Hyperglycemia damages body tissue in general:

1) excessive glycosylation of hemoglobin & cell structures

2) increased activity of polyol pathway leading to reduced nerve conduction velocity & altered nerve fiber anatomy
Stomach Pathophysiology of Diabetic Gastroparesis

1) Extrinsic control via Vagus Nerve, degraded by Hyperglycemia – causing Gastroparesis

2) Oxidative Stress-Damage to ICC network Disruption of Spike Potentials And Slow waves

3) Loss of Nitric Oxide Expression - ↓ Accommodation, ↑ liquid emptying, ↓ Solid Emp.

4) Smooth muscle atrophy
Diagnosis of Diabetic Gastroparesis

• We know Diabetes is a risk factor for Gastroparesis-
  – Type 1 (Autonomic Neuropathy, Condition for 10 years(Prevalence 25-55%)
  – Type 2 (long-standing, poorly controlled) (Prevalence 30%) (Patrick, A., Aliment. & Pharmacol Therapeutics, 2008)

  – Highly fluctuating blood sugars post-prandially
  – Symptoms of Gastroparesis: (Nausea, Vomiting, Abdominal pain, Early Satiety)

1) History and Physical / Dietary regiment
2) Refer for 4 Hour Solid-Phase Nuclear Medicine Emptying Study:
3) EGD – exclude mechanical obstruction for cause of symptoms
4) Smart Pill – Lower GI Tract transit time – Small Bowel -dysmotility)
5) Autonomic Function testing – assess degree of neuropathy
Other causes of Gastroparesis

Consider:
Connective tissue disorders (scleroderma)
Post-gastric surgery (vagus nerve injury)
Idiopathic Gastroparesis (post-viral)
Neuromuscular disorders (polymyositis or dermatomyositis)
Hyperthyroidism
Infiltrative Disorders (amyloidosis)
Medication induced:
   Amylin
   Tranquilizers
   Opiates
   Anti-depressants etc..
Management of Diabetic Gastroparesis

- Restore Hydration, electrolytes, nutrition (enteral preferable to parenteral)
- Glycemic Control
- Administer Prokinetics – Reglan, Domperidone or IV erythromycin in acute cases
- Administer Anti-emetics to control nausea / vomiting
- Manage Pain without Narcotics (tramadol 50-75mg)
- Implement Gastroparesis Diet
- Consider J-tube placement if Necessary
- **Gastric Electrical Stimulation (GES)**
- TPN
- Surgical Pyloroplasty
- Gastrectomy
Gastric Electrical Stimulation (GES)

Screening Gastroparesis Patients for GES:

Inclusion Criteria:

- Must document Gastroparesis (based on nuclear Medicine Study)
  - (off prokinetics for 3 days prior to study, stable and normal as possible blood sugar prior to GET test)
- Must be refractory or intolerant to prokinetic & anti-emetic therapy
- Should have Nausea and/or Vomiting as part of symptomology
- Should be symptomatic for 6 months or longer.
- EGD to exclude mechanical obstruction of stomach/ small bowel
- Ages 18 – 70
Gastric Electrical Stimulation (GES)

- **Exclusion Criteria:**
  - Narcotic-addicted patients
  - Patients suspected of psychogenic vomiting
  - Patients with a strong need for MRI’s
  - Patients not considered a viable surgical candidate
Gastric Electrical Stimulation
FDA = Indication for Use

• “Enterra Therapy is indicated for the treatment of chronic, intractable, drug-refractory nausea & vomiting secondary to Gastroparesis of diabetic and idiopathic etiology”

• FDA approved as a Humanitarian Use Device in 2001

• Has become the largest Humanitarian Use Device in the world.
• Over 200 Hospitals performing Enterra Therapy
• 10,000 patients have received Enterra in the US since 2001
Gastric Electrical Stimulation – “Mechanism of Action”

- **Central Nervous System (Brain):**
  - Via direct stimulation of Gastric vagal afferents, there is a **neuromodulation of the nausea/vomiting signals** leading to the chemoreceptor trigger zone.

- **Local Effect (Stomach):**
  - Some evidence points to direct modulation or enhancement of the **biomechanical properties** of the stomach, including **receptive relaxation** of the fundus and some effect on **slow wave rhythmicity**.

- **Evidence:** Abell, T. showing slow wave frequency decreased from **5.66 CPM to 3.60 CPM** after 3.5 years of stimulation
Gastric Electrical Stimulation
Nausea/Vomiting Outcomes:

• **Enterra Therapy** – functions as a “potent anti-emetic” through central and local channels… Dr. Richard McCallum… 2014

• 67.8% reduction in weekly episodes of Vomiting by 12 months in Diabetics. (57% reduction at 6 weeks) (McCallum, R. Clinical Gastroenterology & Hepatology:2010)

• 87.1% reduction in weekly episodes of vomiting by 12 months in idiopathics. (McCallum, R. Neurogastroenterology & Motility, 2013)

• Meta-Analysis Review: Nausea/Vomiting Reduction was highly significant (p < .0001) (O’Grady, World Journal of Surgery, 2009)
Gastric Electrical Stimulation – (Gastric Emptying Outcomes)

Gastric Retention based on 4 hour nuclear medicine emptying study:

4 Hour Emptying was significantly reduced from 46.5% retention to 20.5% retention at 12 months post-implant.
Gastric Electrical Stimulation – Hospitalization/Cost Savings Outcomes

- Hospitalization Days significantly decreased from 40 days prior to implant to 10 days after implant (75% reduction) (WAVESS II, McCallum, R. : Clinical Gastroenterology & Hepatology: 2010)

- In 3 year comparison of GES vs. Intensive Medical Management, an average of ~ $80,000 was saved per patient over 3 years in the GES group and symptom scores were significantly better. (Cutt’s et.al. Neurogastroenterology & Motility, 2005)
Gastric Electrical Stimulation – Nutritional Status/ Quality of Life

- Meta-analysis of 13 studies showed there was a 78% reduction in the reliance on feeding J-tubes or TPN by 12 months post GES

- SF -36, widely used measure of Mental (MCS) and Physical (PCS) in measuring Health-related Quality of Life: Following Parameters all significantly improved:
  - physical functioning
  - role physical
  - bodily pain
  - general health
  - vitality
  - social functioning
Gastric Electrical Stimulation – Effects on HbA1c

HbA1c Levels

- Forster (2003): Baseline 9.8%, 6 Months 9.0%, 1 Year 8.5%, 3 Year 8.5%
- Lin (2004): Baseline 8.4%, 6 Months 8.7%, 1 Year 8.4%, 3 Year 8.4%
- Van der Voort (2005): Baseline 8.6%, 6 Months 6.2%, 1 Year 6.5%, 3 Year 6.5%
- Lin (2006): Baseline 9.5%, 6 Months 8.4%, 1 Year 7.9%, 3 Year 7.9%
Gastric Electrical Stimulation

Adverse/Events:

- Published Adverse Event Rates from various studies report an average rate of 5% to 8.5%.

- Most Common A/E- feeling stimulation at high settings

- Most serious-
  - migration of the leads in the stomach wall which require surgical replacement
  - Infection of the device at the pocket site – requiring removal of the device.
Gastric Electrical Stimulation

Thank You!