Definitions and Diagnosis

AGA Medical Position Statement

“The diagnosis of gastroparesis is based on the presence of appropriate symptoms/signs, delayed gastric emptying, and the absence of an obstructing structural lesion in the stomach or small intestine”

Parkman et al Gastro 2004; 127(5): 1589-1591
Food Ingestion

Abnormalities can occur:

- Extrinsic Nervous System
- Intrinsic Nervous System (Interstitial Cells of Cajal)
- Smooth Muscle

Relaxation of Proximal Stomach

Liquids: <20 min
Solids: retained until broken to 2 mm particles
Abnormalities in Gastroparesis

• Physiologic
  – Impaired gastric accommodation
  – Visceral hypersensitivity
  – Gastric dysrhythmia
  – Antral hypomotility
  – Delayed gastric emptying

• Symptomatic
  – Early satiety
  – Fullness
  – Bloating
  – Nausea and vomiting
  – Abdominal pain
  – Dehydration, nutritional deficiency & poor glycemic control
Causes

- Diabetes: 32%
- Idiopathic: 38%
- Collagen Vascular Disease: 6%
- Amyloidosis: 6%
- Hereditary Disorders: 6%
- Paraneoplastic Syndromes: 6%
- Post-Surgical: 6%

Epidemiology & Natural History

• Prevalence: 5% in community, 20%-40% of diabetics in referral centers; 0.2% in general population

• Female (4) : Males (1)
  – Non-organic differences:
    • Mimics the ratio in functional GI disorders
    • 62% of patients with idiopathic GP revealed past history of physical or sexual abuse
  – Organic differences:
    • gender difference in solid and liquid emptying between men and women, possibly hormonally related

• Median age of onset = 34
DIAGNOSIS
Diagnosis

• What symptoms will the typical patient have?
  – Early satiety
  – Fullness
  – Bloating
  – Nausea and vomiting
  – Abdominal pain
  – Dehydration, nutritional deficiency & poor glycemic control

• Differential Diagnosis
  – Bacterial overgrowth, lactose/fructose intolerance, medication adverse effects, gallbladder dysfunction, uncontrolled constipation, central nervous system disorders, peptic ulcer disease/dyspepsia, Crohn’s disease, celiac disease, ovarian cancer, thyroid dysfunction, rumination, anorexia/eating disorders, cyclic vomiting, cannabis hyperemesis
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Gastric Emptying Scintigraphy

• Prior to procedure: no promotility agents, narcotics, antispasmodics, anticholinergics
• Women measured in first 10 days of menstrual cycle, avoid hyperglycemia, no smoking
• 6 hours fasting, performed first thing in the morning
• 4 oz. Egg Beaters or generic equivalent, 2 slices of white bread, strawberry jam, water
  – 255 kcal, 72% carbohydrate, 24% protein, 2% fat, and 2% fiber
  – Radiolabeled with 0.5–1 mCi 99mTechnetium
• “Abnormal” Value is > 10% at 4 hours (>60% at 2 hours)
• Alternate meals involve oatmeal, pancakes, nutritional supplements in those with egg allergies or celiac disease

Abell et al. Am J Gastro 2008;103:753–763
Other diagnostic modalities

- Non-radioactive breath tests using $^{13}$C substrates
- Wireless Motility Capsule
- Antro-duodenal manometry
- EGD (bezoar, food retention), Barium studies (UGI series, small bowel series)
TREATMENT
Clinical Grades

• Grade 1: Mild
  – Mild symptoms controlled by medications
  – Able to maintain nutrition on a regular diet
  – Grade 1 dysfunction on GES: 11–20% retention at 4 h
• Grade 2: Compensated
  – Moderate symptoms with partial control despite daily medications
  – Able to maintain oral nutrition
  – Grade 2 dysfunction on GES: 21–35% retention at 4 h
• Grade 3: Gastroparesis with gastric failure
  – Severe symptoms despite medical therapy
  – Repeated physician visits and hospitalizations
  – Inability to maintain oral nutrition/weight loss
  – Grade 3 dysfunction on GES: 36–50% retention at 4 h
Treatment

• Dietary Modification/Tx complications
• Minimizing offending medications
• Promotility/anti-emetic agents
• Complimentary & alternative therapies
• Devices/Procedures
Dietary Modification/Complications

• Avoidance of fats, fiber, smoking, drinking, hyperglycemia
  – Fats and fiber take longer to digest
  – Hyperglycemia alone delays GE

• Multiple, small meals daily
  – 5-6 small meals vs 3 big meals with snacks
  – Liquid meals are better-tolerated as liquid emptying is generally preserved

• Other Complications
  – Micronutrient supplementation, particularly iron and Vitamin B12
  – Bacterial Overgrowth
Medication Review

• Potential Offenders
  – GI Drugs
    • Ondansetron (Zofran), PPIs, sucralfate, Aluminum laxatives,
  – Neuro/Psych Drugs
    • Tricyclic Antidepressants (TCA’s), Parkinson’s medications (L-Dopa), lithium, tizanidine (Zanaflex)
  – Antihypertensives
    • Calcium Channel Blockers, Alpha-2 adrenergic agonists (clonidine, guanfacine)
  – Endocrine Drugs
    • exenatide (Byetta) & pramlintide (Symlin)
    • Calcitonin
  – Narcotics
  – Other (vincristine, cyclosporine)
Medical Therapy

• Prokinetics
  – Dopamine Antagonists
  – Motilin Agonists

• Anti-Emetics
  – Antihistamines, Anticholinergics, Dopamine & Serotonin Antagonists
  – Antineurokininergics
  – Cannabinoids
  – Benzodiazepines
  – Corticosteroids

• Other
  – Antidepressants
  – Antipsychotics
Medical Therapy-Prokinetics

• Dopamine Antagonists
  – Metoclopramide (Reglan), Domperidone (Motilium)

• Motilin Agonists
  – Erythromycin, Azithromycin

• The Good:
  – Systematic review of domperidone trials shows ~60% improvement in symptoms, GET, decreased hospitalizations
  – Domperidone doesn’t cross blood brain barrier

• The Bad:
  – All are associated with arrhythmias, some with increased risk of sudden death
  – Metoclopramide: SE of parkinsonism, BBW for Tardive Dyskinesia, irreversible
  – Erythromycin: IV form is much more effective than PO, tachyphylaxis

• The Ugly:
  – Domperidone: not approved for use in US, difficult to obtain
  – Recent shortages of IV erythromycin

Sugumar Clin Gastro Hep 2008;6(7):726-33
Medical Therapy-Anti-Emetics

• Meclizine, Promethazine (Phenergan)
• Scopalamine
• Prochlorperazine (Compazine)
• Ondansetron (Zofran)*, Granisetron (Kytril)
• Aprepitant (Emend)
• Dronabinol (Marinol)
• Lorazepam (Ativan)
• Dexamethasone
Medical Therapy-Other

• Antidepressants
  – Mirtazepine (Remeron)
  – Tricyclic Antidepressants (TCA’s)
    • Median dose 50 mg daily, 88% at least moderate symptom response, 33% complete or nearly complete resolution of symptoms
    • 46% had at least one SE, 29% changed TCA, 12% decreased dose, 4% stopped (1 patient)

• Antipsychotics
  – Olanzapine (Zyprexa)
  – Quetiapine (Seroquel)
Complimentary and Alternative Therapy

• Acupuncture
  – single-blinded, randomized pilot study with sham treatment control of 19 patients with type 2 diabetes showed symptom score and GET improvement
  – Several trials in Chinese traditional medicine journals suggest symptom improvement in >90%

• Hypnosis
  – Studies in hyperemesis gravidarum, chemotherapy (mostly pediatric) have been positive
  – No trials performed in gastroparesis

DEVICES/PROCEDURES
Devices/Procedures

• Venting Gastrostomy/ Feeding Jejunostomy
  – Considered in the setting of weight loss, malnutrition, repeated hospitalizations for IV hydration
  – Improved nutrition, well being, glucose control
  – Decreased symptoms, hospitalizations

• Botulinum Toxin injection at Pylorus
  – Data is mixed; efficacy is not certain; not recommended

• Electrical Stimulation ("Pacemaker")

• Surgical Techniques
Gastric Electrical Stimulation

True Gastric “Pacemakers”

Cardiac Pacemakers

Neurostimulators

Gastric Electrical Stimulation

• (Enterra ©Therapy, Medtronic)
  – wires are laparoscopically placed directly onto gastric smooth muscle, greater curve, pacing mechanism is inserted subcutaneously
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Efficacy

• Systematic Review of trials 1992 to 2008
• 13 studies, 12 lacked controls, 1 was blinded and randomized
• Improvement in:
  – total symptom severity score
  – vomiting severity score
  – nausea severity score
  – SF-36 physical & mental composite score
  – requirement for TPN
  – 4-h gastric emptying
• Device removal or re-implantation rate was 8.3%
• Complication rate 10%
Advanced Surgical Techniques

• Sub/Near-total gastrectomy with Roux-en-Y gastrojejunostomy
• Billroth II vs Billroth I, pyloroplasty, pyloromyotomy
• Systematic Review of Surgical Techniques
  – No study directly compared surgical technique
  – Completion gastrectomy seems to provide symptom relief in postsurgical gastroparesis
  – Lung or Heart–Lung transplants where GP associated with recurrent aspiration, PNA or BOOP
    • subtotal gastrectomy, gastric bypass, and pyloroplasty with feeding jejunostomy
    • Favorable in 5 of 6 patients
    • Improving gastric drainage decreased episodes of aspiration pneumonia

SUMMARY
Take Home Points

• Symptoms overlap with many other diseases; diagnosis requires symptoms + evidence of delayed GE

• Conservative measures are a mainstay of therapy

• Medical therapeutic options abound but data on efficacy is non-existent or weak and SE are common

• Surgical techniques may provide benefit in refractory disease
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Additional References

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- Maganti et al. AJG 2003; 98(2):259
- Went et al. Surgery 2007; 142:761-8