

DIABETIC ENTEROPATHY: TWO DIFFICULT PROBLEMS

DIAGNOSIS AND TREATMENT



Gary L. Cornette, D.O., F.A.C.O.I
Medical Director Gastroenterology

Diabetic Enteropathy: What is it?



- Motility Disorders
 - Esophageal
 - Gastric
 - Small Bowel
 - Colon

Signs & Symptoms



- Dysphagia
- Chest Pain
- Reflux
- Abdominal Pain
- Nausea/Vomiting
- Abdominal Bloating
- Malabsorption
- Malnutrition
- Bacterial Overgrowth
- Chronic Diarrhea
- Chronic Constipation

Diabetic Gastroparesis

Prevalence

- 27% - 58% Type 1 Diabetes
- 30% Type 2 Diabetes
- Majority of cases are women

Symptoms

Symptom	Percentage
Nausea	90% +
Early Satiety	80% +
Vomiting	68%
Abdominal Pain	50% - 80%
Bloating	60%

Symptom Characteristics

Characteristic	Percentage
Localized	76%
Upper Abdominal Location	36%
Constant	28%
Burning, Vague, or Crampy	64%
Nocturnal	80%
Exacerbated by Meals	60%
Relief by Meals	15%

Unpredictable Food Delivery

Affects Glycemic Control



Both Hypoglycemia and Hyperglycemia

Pathogenesis

Complicated

- ❑ Autonomic Neuropathy
- ❑ Central Effects
- ❑ Local Myopathy

Aggravating Factors

- ❑ Hyperglycemia
- ❑ Hypoglycemia
- ❑ Anticholinergic Meds
- ❑ Narcotics
- ❑ Autoimmune Disorders
- ❑ Parkinson's Disease

Gastroparesis Severity Classification

Grade I – Mild

- Intermittent, easily controlled symptoms with maintenance of weight and nutrition, treated with dietary modification and avoidance of medications that slow gastric emptying

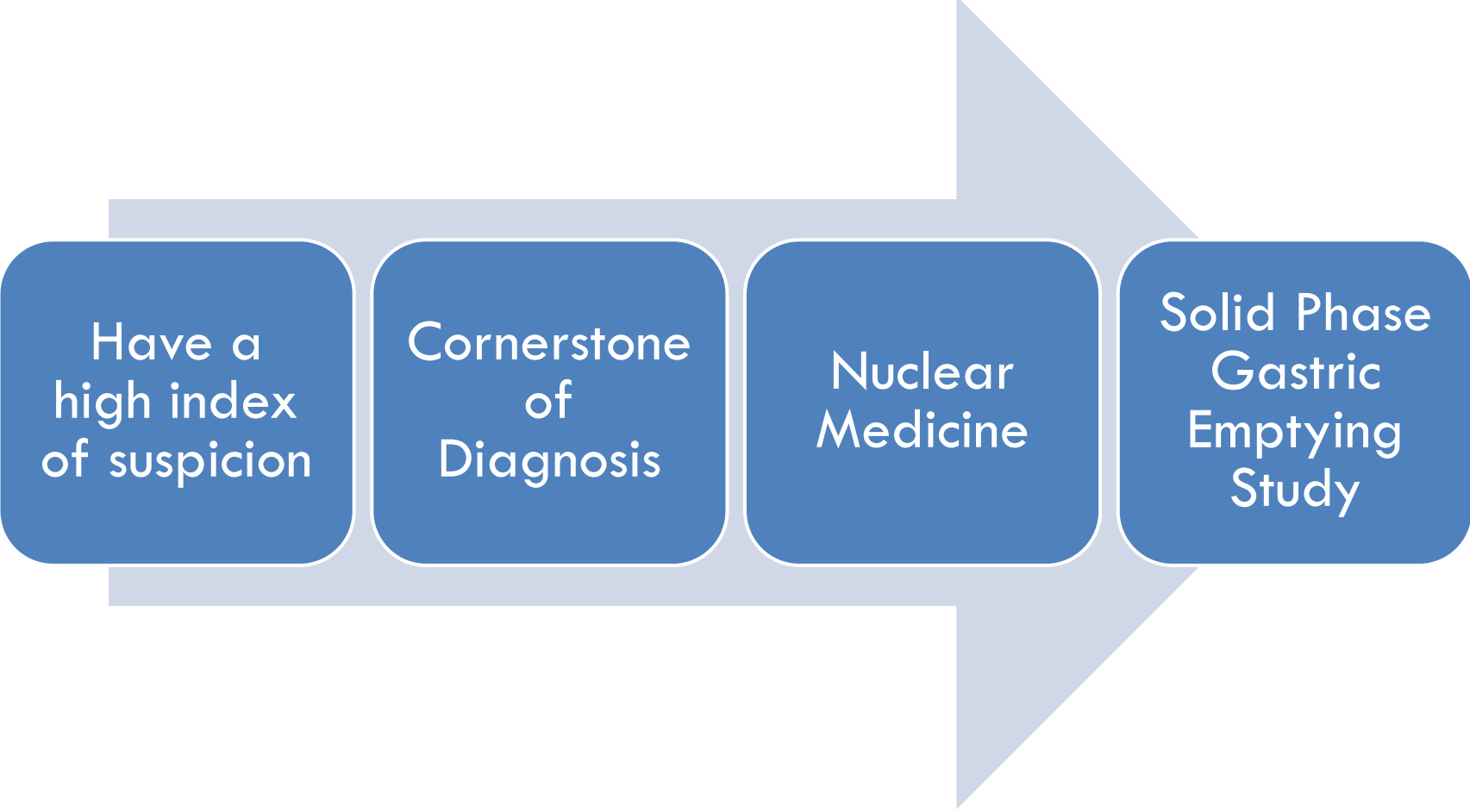
Grade II – Compensated

- Moderate symptoms, rare hospitalizations, treated by prokinetic and antiemetic agents

Grade III – Gastric Failure

- Medication unresponsive, cannot maintain nutrition, frequent E.D. visits and hospitalizations

Diagnosis and Evaluation



Have a
high index
of suspicion

Cornerstone
of
Diagnosis

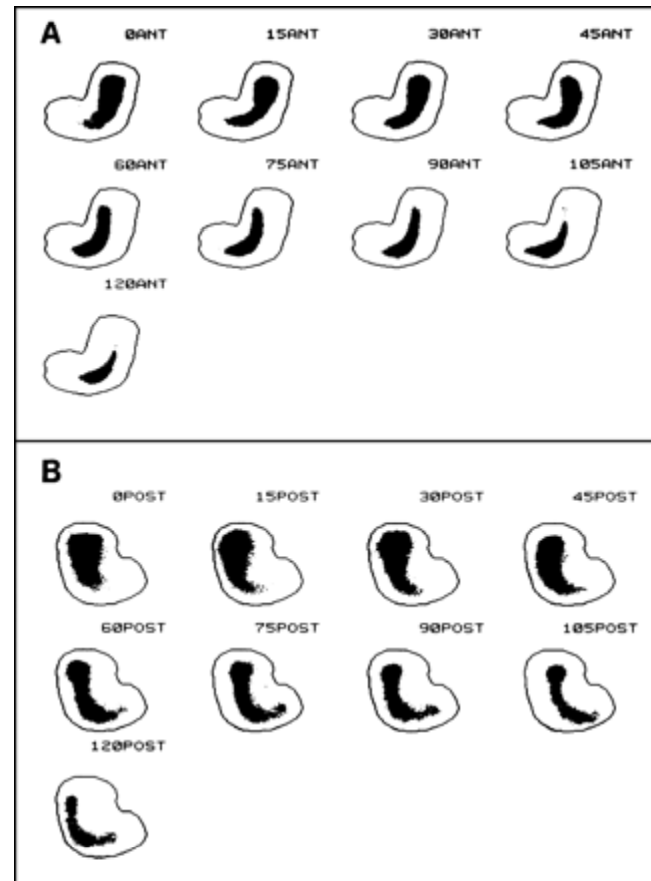
Nuclear
Medicine

Solid Phase
Gastric
Emptying
Study

The Study

Recommended Meal: Toast, jam and egg whites (eggbeaters) with Tc-Sulfur

**All medications that could delay gastric emptying must be stopped 24 hours before test



Gastroparesis – Gastric Retention

Greater
than 60%
at 2 hours

Greater
than 10%
at 4 hours

Positive
Test

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graph TD; A[Greater than 60% at 2 hours] --> B((Positive Test)); C[Greater than 10% at 4 hours] --> B;
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Reasons for Upper Endoscopy

High incidence of GERD in Gastroparesis may be relatively asymptomatic in Type I Diabetes – Screen for Barrett's



Biopsy for H. Pylori

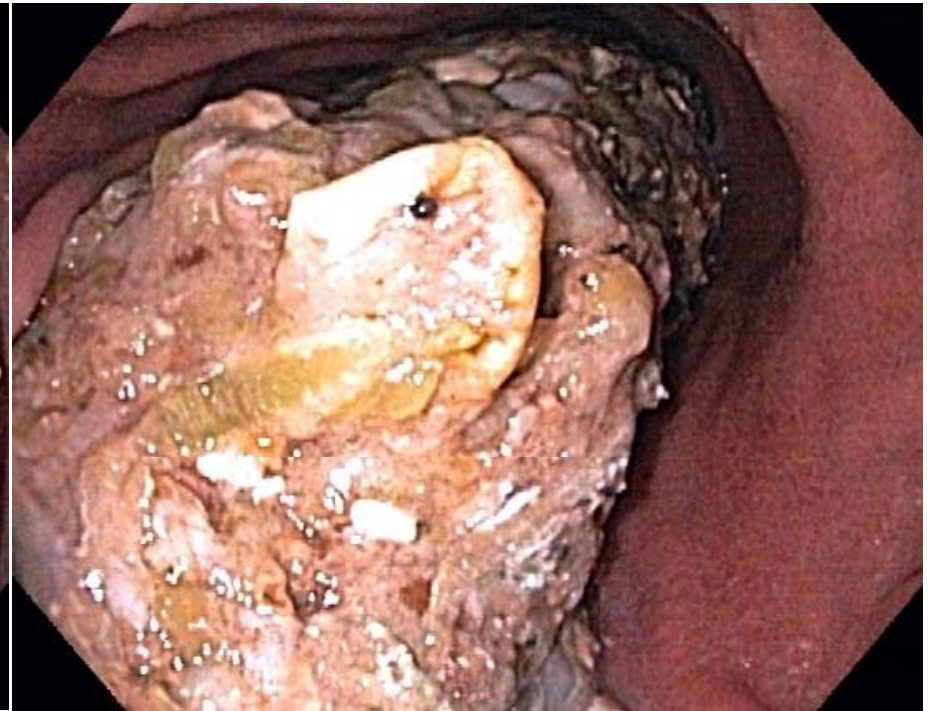


Rule out gastric outlet obstruction, ulcer disease, and infiltrative diseases



Rule out gastric bezoars

IMAGES (Food in Stomach)



Type I Diabetes: Screen for Celiac Disease with Serologic Testing

- Anti-tissue transglutaminase antibody (TTG) IgA
- Anti-endomysial antibody (EMA) IgA
- Total IgA
- Patients with IgA deficiency:
 - Deamidated gliadin peptide (DGP) IgG
 - Positive test should have small bowel biopsies

Treatment

Difficult and
Disappointing

- Discontinue medications that inhibit gastrointestinal motility
- Dietary Modification (Dietician referral)
 - ▣ Smaller, more frequent meals
 - ▣ Reduced fat meals
 - ▣ Reduced bulk meals-remove hard to digest foods like seeds, nuts, corn, popcorn, and fiber

Treatment Cont...

Prokinetic Medications

Medication	Mechanism(s) of Action	Dosing
Metoclopramide	Dopamine D ₂ receptor antagonist	5-20 mg qid
	5-HT ₄ receptor facilitation of acetylcholine release from enteric nerves	
Erythromycin	Motilin receptor agonist	50-250 mg qid
Domperidone	Peripheral dopamine D ₂ receptor antagonist	10-30 mg qid
Bethanechol	Muscarinic receptor agonist	25 mg qid
Pyridostigmine	Acetylcholinesterase inhibitor	30-60 mg tid

Metaclopramide

Is it worth a trial of metaclopramide in moderate to severe Gastroparesis?

“Black Box Warning”

- Side effects (30% of patients experience side effects)
 - ▣ Fatigue
 - ▣ Agitation
 - ▣ Sleep disturbances
 - ▣ Hyper prolactinemia
 - ▣ Dystonia
 - ▣ Irreversible Tardive Dyskinesia

Erythromycin



- Beneficial for short term use only
- Tachyphylaxis occurs in almost all patients – relates to motilin receptors down regulation

Domperidone



- ❑ Not approved by FDA
- ❑ Available from Europe, Canada, and the internet
- ❑ Antiemetic effects are stronger than prokinetic effects
- ❑ Can prolong QTc interval (same as Cisapride)

Antiemetic Medications

Drug Class	Examples	Effects on Gastric Emptying
Dopamine antagonists	Prochlorperazine, thiethylperazine	Variable
Muscarinic antagonists	Scopolamine	Delay
Histamine H ₁ antagonists	Dimenhydrinate, Meclizine	Delay
Serotonin 5-HT ₃ antagonists	Ondansetron, Granisetron	Variable
Neurokinin NK ₁ antagonists	Aprepitant	Delay
Cannabinoids	Dronabinol	Delay
Tricyclic antidepressants	Amitriptyline, Nortriptyline	Delay
Other antidepressants	Mirtazapine	?
Benzodiazepines	Lorazepam	?
Corticosteroids	Prednisone	?

Severe Gastroparesis



Symptoms



- ❑ Unrelenting symptoms
- ❑ Failed medical therapy

Gastric Electrical Stimulation



Gastric Electrical Stimulation Cont...



- Enterra Brand

- FDA approved for “Humanitarian use device exemption”

- Use restricted to clinical trials in institutions with IRB and physician trained in use and implantation

Gastric Electrical Stimulation Cont...

Case Study

- 35 to 38 patients with severe gastroparesis experienced an 80% reduction in nausea and vomiting

Complications

- Infection
- Lead dislodgement
- Bowel obstruction
- 10%-20% lead to device removal

Conclusion



- ❑ Gastroparesis common in Type I and Type II Diabetes
- ❑ Can adversely affect glycemic control
- ❑ Solid phase gastric emptying study and upper endoscopy are cornerstones of diagnosis and evaluation
- ❑ Non-medication and medication treatment is disappointing
- ❑ For severe gastroparesis, gastric stimulation may hold promise