Esophageal and Gastric Motility Disorders: A case based approach

Gokul Balasubramanian, MD
Assistant Professor
Director of Gastrointestinal Motility Lab
Division of Gastroenterology, Hepatology and Nutrition
The Ohio State University Wexner Medical Center

Conflicts of Interest:

• None
Overview

- Esophageal anatomy
- Dysphagia-case based approach
- Reflux disease-case based approach
- Gastric physiology
- Gastroparesis-case based approach

Dysphagia-Case based approach
Esophagus: Anatomy

- 25 cm muscular tube.
- Extends from upper esophageal sphincter to stomach.
- Proximal 1/3rd consist of striated muscles while distal 2/3rd is formed by smooth muscles.
- Lined squamous epithelium.

Terminology

- Dysphagia: derived from the Greek word dys (difficulty, disordered) and phagia (to eat).
- Odynophagia: painful swallowing.
- Globus Sensation: Sensation of lump in throat between meals.
# History

## Oropharyngeal
- **Oral:**
  - Drooling of saliva
  - Food spillage
  - Sialorrhea
  - Piecemeal swallows
  - Associated dysarthria
- **Pharyngeal:**
  - Choking/cough during swallow
  - Associated dysphonia

## Esophageal
- **Food stuck in suprasternal notch or retrosternal region**
- **Motility:**
  - Dysphagia to solids and liquids
  - Associated with heartburn or chest pain.
- **Mechanical:**
  - Progressive dysphagia to solids; may involve liquids at later stages

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## Dysphagia Assessment

- **Fluoroscopic examination**
- **Endoscopic examination**
- **Manometric examination**
Case Study 1:

78-year-old female with no significant medical history presenting with:
- Dysphagia to both solids and liquids
- Chest pain
- Denies any heartburn
- 50 lb weight loss

- Epiphrenic diverticulum
- Resistance at GEJ

- Epiphrenic diverticulum
- Beaking at GEJ

Case Study 1:

- Mean DCI: 2380
- Mean LES IRP: 32 mm Hg
- Mean DL: 3.8 sec
Case Study 1:

- Post extended myotomy and diverticulectomy
- Fairly doing

Achalasia

- Rare esophageal motility disorder
- Esophageal aperistalsis
- Impaired LES relaxation

Loss of inhibitory neurons secreting VIP and NO leads to unopposed excitatory activity and failure of LES relaxation

Achalasia: Subtypes

Type I is characterized by a quiescent esophageal body, type II has pan-esophageal pressurization, and type III is characterized by simultaneous contractions.


Achalasia: Treatment Algorithm

### Achalasia: Treatment Options

<table>
<thead>
<tr>
<th>Treatment Options</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications (CaCB/Nitrates)</td>
<td>• On Demand</td>
<td>• Least effective</td>
</tr>
<tr>
<td></td>
<td>• Minimal risk</td>
<td>• Not durable</td>
</tr>
<tr>
<td></td>
<td>• For non-operative candidates</td>
<td></td>
</tr>
<tr>
<td>Botulinum toxin injection</td>
<td>• Good option for nonoperative candidates</td>
<td>• Durability of 6–12 months</td>
</tr>
<tr>
<td></td>
<td>• Short procedure time</td>
<td></td>
</tr>
<tr>
<td>Pneumatic dilation</td>
<td>• Most effective nonsurgical option</td>
<td>• Perforation (1%–5%)</td>
</tr>
<tr>
<td></td>
<td>• Short recovery time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Durability 2–5 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Procedure time &lt;30 minutes</td>
<td></td>
</tr>
<tr>
<td>Surgical myotomy</td>
<td>• Durability 5–7 years</td>
<td>• General anesthesia required</td>
</tr>
<tr>
<td></td>
<td>• Procedure time ~90 minutes</td>
<td>• Hospital stay of 1–2 days</td>
</tr>
<tr>
<td>Esophagectomy</td>
<td>• For end-stage disease</td>
<td>• High morbidity and mortality</td>
</tr>
</tbody>
</table>

### Case Study 2:

24-year-old female presented with dysphagia to solids and liquids.

- Mean DCI: NA
- Mean LES IRP: 24 mm Hg
- Mean DL: NA

**Diagnosis??**

Type 2 Achalasia. Patient sent for myotomy
Diagnosis?? Opioid induced esophageal dysfunction

Opioid-induced esophageal dysfunction

Opioid-induced esophageal dysfunction is often characterized by EGJ outflow obstruction and type III achalasia pattern.

# Achalasia syndromes beyond the CC v3.0

<table>
<thead>
<tr>
<th>CC v3.0 diagnosis</th>
<th>IRP &gt; ULN?</th>
<th>Oesophageal contractility</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Oesophago gastric junction outflow obstruction | Yes        | Sufficient peristalsis to exclude type I, II or III achalasia | * Heterogeneous group  
* Early or incomplete achalasia  
* Can resolve spontaneously  
* Recording artefacts          |
| Absent contractility               | No         | Absent contractility             | * Can be achalasia  
* Abnormal EUS distensibility index supports achalasia  
* Oesophageal pressurization with swallows or MRS supports achalasia |
| Distal oesophageal spasm           | Yes or no  | ≥20% premature contractions (DL <4.5s) | Might be spastic achalasia                                          |
| Jackhammer                         | Yes or no  | ≥20% of swallows with DCI >8,000 mmHg cm | Might be spastic achalasia if DL <4.5 s with ≥20% swallows           |
| Opioid effect (not in CC)          | Yes        | Normal, hypercontractile or premature | Can mimic EGJOO, type III achalasia, DES or jackhammer               |
| Mechanical obstruction             | Yes        | Absent, normal or hypercontractile | EUS, CT or MRI of the EGJ might clarify the aetiology              |

Kahrilas, P. J. et al. (2017) Advances in the management of oesophageal motility disorders, in the era of high-resolution manometry: a focus on achalasia syndromes.

## GERD-Case based approach
Gastroesophageal Reflux Disease Definition

GERD is a condition that develops when the reflux of gastric content causes troublesome symptoms or complications.

- Mild symptoms once in > 2 days/week
- Moderate/Severe once in >1 day/week


Risk factors:

- Obesity
- Family history for GERD
- Tobacco smoking
- Alcohol consumption
- Associated psychosomatic complaints

Impact of Gastroesophageal Reflux Disease

Non-erosive GERD (EGD negative)
- Impairs quality of life

Esophagitis
- Stricture
- Barrett's metaplasia & Adenocarcinoma
- Bleeding

Extra-esophageal GERD
- ENT
- Asthma
- Dental

Goals for Treatment of GERD

• Eliminate symptoms
• Heal erosive esophagitis
• Prevent the relapse of erosive esophagitis and complications from GERD

Life-Style Modifications include:

• Elevate the head of the bed on 4" to 6" blocks.
• Advise weight loss for obese patients.
• Avoid recumbency for 3 hours after meals.
• Avoid bedtime snacks.
• Avoid fatty foods, chocolate, peppermint, onions, and garlic.
• Avoid cigarettes and alcohol.
• Avoid drugs that decrease LES pressure and delay gastric emptying.
Medical treatment options:

Proton Pump Inhibitors:
- Higher healing rates in mild to moderately severe reflux esophagitis (80% to 100%).
- Improves dysphagia.
- Decreases the need for esophageal dilation in patients who have peptic esophageal strictures.
- About 70% may have nocturnal acid breakthrough that requires H2RA.

Maintenance of Healing Erosive Esophagitis

**GERD Is a Chronic Condition Likely to Relapse**

![Graph showing patients in symptomatic remission over time after cessation of therapy.]


**Healing of esophagitis**

**Proton-pump inhibitor**

- Superior to placebo (83% vs. 18%) at 8 wk; NNTB, 1.722
- Superior to H2-blocker (83% vs. 18%); relative risk, 0.5122
- Superior to H2-blocker (84% vs. 52%); relative risk, 0.512
- Significant dose–response effect at 4 wk
  - Low dose vs. standard dose once daily: NNTB, 10
  - Standard dose vs. high dose once daily: NNTB, 25

**H2-blocker**

- Superior to placebo (41% vs. 20%) at 6 wk; NNTB, 522
- No significant dose–response effect (standard dose vs. high dose twice daily) 22

*Best practice recommendations for proven GERD consist of long-term therapy with the lowest dose of PPI that provides symptom control and/or healing of esophagitis.*
### Resolution of heartburn†

**Esophagitis**
- Proton-pump inhibitor superior to placebo (56% vs. 8%) at 4 wk; NNTB, 2 to 323
- Proton-pump inhibitor superior to H2-blocker (77% vs. 48%) at 4 to 12 wk
- H2-blocker superior to placebo (56% vs. 45%) at 12 wk
- No significant dose–response effect for proton-pump inhibitor at 4 wk
  - Low dose vs. standard dose once daily: 75% vs. 79%
  - Standard dose vs. high dose once daily: 73% vs. 76%

**Patients without known esophagitis**
- Proton-pump inhibitor superior to placebo (36.7% vs. 9.5%); NNTB, 3 to 423
- Proton-pump inhibitor superior to H2-blocker (61% vs. 40%); NNTB, 526
- H2-blocker superior to placebo (relative risk, 0.77; 95% CI, 0.60 to 0.99)
- No significant dose–response effect for H2-blocker at 8 wk
  - Standard dose vs. high dose twice daily: 45.8% vs. 44.8%

### Maintenance therapy‡

**Remission of esophagitis**
- Proton-pump inhibitor superior to placebo (93% vs. 29%)
- Low dose of proton-pump inhibitor sufficient in 35 to 95% of patients

**Remission of heartburn**
- Acceptable symptom control with low-dose, intermittent therapy with proton-pump inhibitor in 83 to 92% of patients without esophagitis

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*Best practice recommendations for proven GERD consist of long-term therapy with the lowest dose of PPI that provides symptom control and/or healing of esophagitis.*
Decisions to start, properly dose, continue, or discontinue PPI therapy should be personalized based on indication, effectiveness, patient preferences, and risk assessment.
Medical treatment options:

- Antacids and Alginic Acid:
  - Temporarily relieve episodic heartburn
  - Useful add on therapy

- Histamine H2-Receptor Blocking Agents:
  - Safe and effective in mild esophagitis
  - Not useful in severe esophagitis
  - Useful for breakthrough symptoms
  - Concern for tachyphylaxis

- Prokinetic Agents:
  - Limited efficacy and side effects in up to 30%

- TLESR Inhibitors:
  - As addon for non-acid reflux/post prandial reflux

Indications for anti-reflux surgery

- Unwillingness to remain on medical therapy
- Intolerance of medical therapy
- Medically refractory symptoms with objective evidence of GERD
- GERD in the setting of a large hiatal hernia

Case Study 4:

42-year-old female with prior history of scleroderma is presenting with persistent reflux inspite of twice daily PPI, referred for fundoplication.

- Mean DCI: NA
- Mean LES IRP: 2mm Hg
- Mean DL: NA

Acid exposure:
- Total AET: 14.5%
- Reflux events: 112

Reflux symptom analysis:
- SI: 54
- SAP: 98

What would be the next step?
Case Study 4:

- Educated on lifestyle measures.
- Added H2B at bedtime.
- Was doing much better.

Case Study 5:

- 28 yr old female with anxiety presenting with persistent heartburn inspite of PPI twice daily
- EGD: normal esophagus with biopsy
Case Study 5:

- Acid exposure:
  - Total AET: 10.5%
  - Reflux events: 119
- Reflux symptom analysis:
  - SI: 50
  - SAP: 96

What would be the next step?

DDx to PPI-Refractory GERD

- Refractory reflux symptoms with esophagitis
- Eosinophilic esophagitis
- Pill induced esophagitis
- Skin disorders like Lichen planus
- Hypersecretory condition like ZES
- Genotypic differences in CYP450 2C19

- Refractory reflux symptoms with normal esophagus
- Eosinophilic esophagitis
- Achalasia
- Gastroparesis
- Aerophagia and Belching disorder
- Rumination syndrome
- Functional heartburn
Effect of DBT on belching and GERD


Case Study 5:

- **Continued PPI,**
- **Started on behavioral therapy and anti-anxiety medication,**
- **Educated on DBT**
Gastroparesis-Case based approach

Physiology of stomach
Normal Velocities of emptying of solid and liquid chyme.

**Definition:**

_Gastroparesis is defined as a delay in the emptying of ingested food in the absence of mechanical obstruction of the stomach or duodenum._

Etiology of Gastroparesis

Gastroparesis

- Idiopathic gastroparesis
- Diabetic gastroparesis (30-35%)
- Post-surgical gastroparesis
  - Cholecystectomy
  - Vagotomy
  - Nissen fundoplication
  - Partial gastrectomy
  - Obesity related surgeries
  - Pancreatectomy (5-10%)

Pathophysiology

Clinical Presentation:

- Nausea
- Vomiting
- Early satiety
- Bloating
- Postprandial fullness
- Abdominal pain
- Weight loss/weight gain
- Constipation and/or diarrhea
- Wide glycemic fluctuations

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IG (n 254) N (% or mean)</th>
<th>T1DM (n 78) N (% or mean)</th>
<th>T2DM (n 59) N (% or mean)</th>
<th>IG vs all DM</th>
<th>IG vs T1DM</th>
<th>IG vs T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms prompting evaluation for gastroparesis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>214 (84.3)</td>
<td>66 (84.6)</td>
<td>56 (94.9)</td>
<td>.19</td>
<td>.94</td>
<td>.03</td>
</tr>
<tr>
<td>Vomiting</td>
<td>152 (59.8)</td>
<td>69 (88.5)</td>
<td>54 (91.5)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Bloating</td>
<td>146 (57.5)</td>
<td>44 (56.4)</td>
<td>37 (62.7)</td>
<td>.75</td>
<td>.87</td>
<td>.46</td>
</tr>
<tr>
<td>Early satiety</td>
<td>146 (57.5)</td>
<td>37 (47.4)</td>
<td>44 (74.6)</td>
<td>.75</td>
<td>.12</td>
<td>.02</td>
</tr>
<tr>
<td>Postprandial fullness</td>
<td>136 (53.5)</td>
<td>44 (56.4)</td>
<td>39 (66.1)</td>
<td>.18</td>
<td>.66</td>
<td>.08</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>193 (76.0)</td>
<td>47 (59.3)</td>
<td>41 (59.5)</td>
<td>.01</td>
<td>.907</td>
<td>.03</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>98 (35.6)</td>
<td>35 (44.9)</td>
<td>30 (50.8)</td>
<td>.09</td>
<td>.32</td>
<td>.08</td>
</tr>
<tr>
<td>Constipation</td>
<td>112 (44.1)</td>
<td>32 (41.0)</td>
<td>34 (57.6)</td>
<td>.44</td>
<td>.63</td>
<td>.06</td>
</tr>
<tr>
<td>Anorexia</td>
<td>32 (12.6)</td>
<td>12 (15.4)</td>
<td>17 (28.8)</td>
<td>.03</td>
<td>.53</td>
<td>.02</td>
</tr>
<tr>
<td>Weight loss</td>
<td>118 (46.5)</td>
<td>41 (52.6)</td>
<td>31 (52.5)</td>
<td>.25</td>
<td>.35</td>
<td>.40</td>
</tr>
<tr>
<td>Weight gain</td>
<td>45 (17.7)</td>
<td>14 (18.0)</td>
<td>14 (23.7)</td>
<td>.57</td>
<td>.96</td>
<td>.24</td>
</tr>
<tr>
<td>Gastroesophageal reflux</td>
<td>137 (53.9)</td>
<td>43 (55.1)</td>
<td>35 (59.3)</td>
<td>.57</td>
<td>.85</td>
<td>.45</td>
</tr>
<tr>
<td>Problems with diabetes control</td>
<td>0 (0.0)</td>
<td>39 (50.0)</td>
<td>27 (45.8)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Pair-wise P value*

In 416 patients from the NIH Gastroparesis Registry, symptoms prompting evaluation more often included vomiting for diabetic gastroparesis and abdominal pain for idiopathic gastroparesis.

Treatment Algorithm for Suspected Gastroparesis

1. Suspected Gastroparesis
2. Confirm Diagnosis Testing for Cause
   - Restoration of Fluids and Electrolytes Dietary Modifications Glucose Control
   - Prokinetic Therapy qac Anti-emetics prn
3. Consider Feeding Jejunostomy, Decompressive Gastrostomy, Gastric Electrical Stimulation OR Surgical Therapy

Diagnostic Testing for Gastroparesis:

**TABLE 2. Diagnostic Testing for Gastroparesis**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric scintigraphy</td>
<td>Widely available</td>
<td>Radiation exposure</td>
</tr>
<tr>
<td>4-hour solid phase</td>
<td>Considered the &quot;gold standard&quot; for diagnosis</td>
<td>False positives with liquid phase only studies</td>
</tr>
<tr>
<td>Wireless motility capsule</td>
<td>Avoids radiation exposure</td>
<td>Less validated than scintigraphy</td>
</tr>
<tr>
<td>Smart Pill, given imaging</td>
<td>FDA approved for diagnosis</td>
<td>Cannot be used in those with pacemaker or defibrillator</td>
</tr>
<tr>
<td>Radiolabeled carbon breath test</td>
<td>Low cost</td>
<td>Lack of standardization</td>
</tr>
<tr>
<td>$^{13}$C-labeled octanoic acid or Spirulina platensis</td>
<td>Has primarily been used as a research tool</td>
<td></td>
</tr>
</tbody>
</table>
Radionuclide Gastric Emptying Scintigraphy

- Best current test for measuring gastric emptying because it is sensitive, quantitative, and physiological.
- $^{99m}$Tc sulfur colloid-labeled low-fat egg white meal as a test meal.
- Imaging is performed in the anterior and posterior projections at least at four time points (0, 1, 2, and 4 h).
- The 1 h image is used to help detect rapid gastric emptying.
- The 2 and 4 h images are used to evaluate for delayed gastric emptying.
- Hyperglycemia (glucose level > 270 mg/dL) delays gastric emptying in diabetic patients.


Radionuclide Gastric Emptying Scintigraphy


<table>
<thead>
<tr>
<th>Medications</th>
<th>Mechanism</th>
<th>Pros</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domperidone</td>
<td>D2 Antagonist</td>
<td>Improvement in symptoms (54% to 79%). Drug interaction.</td>
<td>Less CNS effects. Associated with QTc interval. Increases Prolactin levels. Requires IND for approval.</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Motilin agonist</td>
<td>Usefulness during acute exacerbation. IV better than PO.</td>
<td>Tachyphylaxis. Associated with QTc prolongation.</td>
</tr>
<tr>
<td>Cisapride</td>
<td>5-HT4 agonist</td>
<td>Significant improvement in symptoms.</td>
<td>Cardiac arrhythmias and death. Requires IND.</td>
</tr>
<tr>
<td>Prucalopride</td>
<td>5-HT4 agonist</td>
<td>Improves gastric emptying and colon transit times. FDA approved for chronic constipation.</td>
<td>Diarrhea and suicidal ideations. Avoidance in ESRD. No cardiac toxicity document.</td>
</tr>
</tbody>
</table>
### Anti-emetics:

<table>
<thead>
<tr>
<th>Medications</th>
<th>MOA</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenhydramine</td>
<td>Antihistamines</td>
<td>Useful in mild nausea/vomiting.</td>
<td>• Sedative effect.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Anticholinergic S/E.</td>
</tr>
<tr>
<td>Hyoscine</td>
<td>Anti-cholinergics</td>
<td>Cheap and widely available. Useful in mild cases.</td>
<td>• Anti-cholinergic side effects (dry mouth, glaucoma, etc).</td>
</tr>
<tr>
<td>Phenothiazines/ prochlorperazine</td>
<td>D1/D2 Antagonist</td>
<td>Useful in severe nausea and vomiting.</td>
<td>• EKG changes.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Psychomotor issues in elderly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Dystonia/Parkinsonism</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>5HT3 antagonists</td>
<td>Widely available. Useful in mild vomiting.</td>
<td>• QT prolongation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Serotonin syndrome.</td>
</tr>
<tr>
<td>Transdermal granisetron</td>
<td>5HT3 antagonists</td>
<td>Not widely available/cost. Useful in those who cannot tolerate oral meds.</td>
<td>• QT prolongation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Serotonin syndrome.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Constipation.</td>
</tr>
<tr>
<td>Aprepitant</td>
<td>NK1 receptor antagonists</td>
<td>Not widely available/cost. Useful in reducing N/V.</td>
<td>• Fatigue.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Neutropenia.</td>
</tr>
<tr>
<td>Dronabinol</td>
<td>Agonist of CB1 and CB2</td>
<td>Helpful for N/V when other therapies have failed.</td>
<td>• Delays gastric emptying.</td>
</tr>
</tbody>
</table>

### Neuromodulators:

<table>
<thead>
<tr>
<th>Medications</th>
<th>MOA</th>
<th>Pros</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline/ Amitriptyline</td>
<td>TCA</td>
<td>Modest improvement in N/V and abdominal pain</td>
<td>Worsens gastric emptying. Anti-cholinergic side effects. Constipation.</td>
</tr>
</tbody>
</table>
Gastric electric stimulation

- **Patient Selection:** *Diabetic gastroparesis with refractory N/V even after 1 year of pro-kinetics.*
- **Response to therapy:**
  - Diabetics.
  - Not on narcotics.
  - Predominant nausea/vomiting.
- **Response was modest with 43% over a period of a year and half.


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**Final Case Study**

- **42-year-old gentleman with type 2 diabetes (HgbA1c: 9) on exenatide presenting with recurrent vomiting and nausea for the last 6 months?**

What would be the next step?

Normal upper endoscopy with moderate food retention in the stomach. Bx: negative for H. pylori.

4-hour GES: 43%. What do we do next?

Switch exenatide to insulin+CGM.
Nutrition consult for gastroparesis.