GHAPP
Gastroenterology & Hepatology Advanced Practice Providers

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Jointly provided by the Annenberg Center for Health Sciences at Eisenhower and Gastroenterology and Hepatology Advanced Practice Providers.
Gastroesophageal Reflux Disease

versus

Functional Dyspepsia

versus

Gastroparesis

Monica Nandwani, DNP, RN, FNP-BC
Disclosures

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Disclosures

Monica Nandwani, DNP, RN, FNP-BC

Advisory Board: Phathom Pharmaceuticals, Clinical Area- H. pylori
Objectives

Define gastroesophageal reflux disease (GERD), functional dyspepsia (FD), and gastroparesis (GP)

Discuss the overlap of symptoms and pathophysiology of GERD, FD, and GP

Review treatment options for GERD, FD, and GP
### Definitions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>GERD</strong></td>
<td>Reflux of stomach contents causing <em>troublesome</em> symptoms and/or complications&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td><strong>FD</strong></td>
<td>One or more of the following: a. Bothersome postprandial fullness b. Bothersome early satiation c. Bothersome epigastric pain d. Bothersome epigastric burning AND <em>no evidence of structural disease</em> (including at upper endoscopy) that is likely to explain the symptoms</td>
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<tr>
<td><strong>GP</strong></td>
<td>Delayed <em>gastric emptying</em> of solid food in the <em>absence of</em> a mechanical <em>obstruction</em> of the stomach&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Is It GERD, FD, or GP?

- Epigastric burning
- Epigastric pain
- Post-prandial fullness
- Early satiety
- Belching
- Upper abdominal bloating
- Heartburn
- Nausea and/or Vomiting

GERD

Gastroparesis

Functional Dyspepsia

References:
Pathophysiology

GERD
- Esophageal dysmotility
- Lower esophageal sphincter dysfunction
- Increased gastric pressure
- Xerostomia

Gastroparesis
- Neuromuscular dysfunction
- Pylorospasm
- Gastric pacemaker dysrhythmia

Functional dyspepsia
- Impaired duodenal mucosal integrity
- Altered central processing
- H. Pylori infection

Delayed gastric emptying
Visceral hypersensitivity
Impaired gastric accommodation
Antroduodenal discoordination

GERD

1 in 5 Americans experience GERD ≥1x/week\(^1\)

One of the most common diseases encountered by gastroenterologists\(^2\)

US annual direct cost estimated at over $10 billion\(^3\)

Up to 40% of patients with suspected GERD have inadequate symptom relief despite PPI therapy\(^4\)

GERD – The Lyon Consensus

CONCLUSIVE EVIDENCE FOR PATHOLOGIC REFLUX
LA grades C&D esophagitis
Long segment Barrett’s mucosa (≥3 cm)
Peptic esophageal stricture
AET >6%

BORDERLINE OR INCONCLUSIVE EVIDENCE
LA grades A & B esophagitis
AET 4 – 6%
Reflux episodes 40 – 80

EVIDENCE AGAINST PATHOLOGIC REFLUX
AET <4%
Reflux episodes <40

ENDOSCOPY

pH or pH-IMPEDEANCE

HIGH RESOLUTION ESOPHAGEAL MANOMETRY

ADJUNCTIVE OR SUPPORTIVE EVIDENCE
Hypotensive EGJ
Hiatal hernia
Esophageal hypomotility

Defining GERD Symptoms

Unproven GERD
Symptoms not responding to stable PPI therapy over 12 weeks
Symptoms may or may not be from GERD

Proven GERD
Symptoms caused by reflux not responding to stable PPI therapy over 12 weeks
Symptoms are from inadequate management of GERD

No GERD

Adapted from ACG Virtual Grand Rounds by C. Prakash Gyawali on 7.29.2021.
Testing ON Versus OFF PPI Therapy

**Endoscopy** to evaluate for mucosal or mechanical processes

- **Reflux suspected**
  - Esophageal
    - Heartburn
    - Regurgitation
    - Chest pain
    - PPI trial*
  - Extraesophageal
    - Cough
    - Hoarseness
    - Sore throat

**REFLUX MONITORING**
- To determine abnormal reflux burden
- To assess reflux-symptom association

**Unproven GERD**
- Test **off** PPI
- pH Impedance
- Wireless pH

**Proven GERD**
- Test **on** PPI
- pH Impedance

*If not performed earlier

Mucosal Impedance

Novel balloon catheter with 36 channels that measures esophageal mucosal integrity via impedance

May predict GERD and EoE

FDA Approved in December 2019

GERD Phenotypes

NERD
Reflux hypersensitivity
Functional heartburn

Erosive esophagitis, low grade (LA A or B)
Erosive esophagitis, high grade (LA C or D)
Barrett's esophagus

Reflux chest pain syndrome
Regurgitation-dominant reflux disease
Laryngopharyngeal reflux

Chronic cough

Not all GERD is the same

## Treatment of GERD

<table>
<thead>
<tr>
<th>Lifestyle Modification</th>
<th>Pharmacologic Therapy</th>
<th>Endoscopic Management</th>
<th>Surgical Management</th>
<th>Alternative Therapies</th>
</tr>
</thead>
</table>
| • Selective dietary avoidance | • Acid suppression  
  – H2RAs  
  – PPIs  
  – PCABs  
  • Reflux inhibition  
  – Baclofen*  
  – Prokinetics*  
  • Neuromodulators*  
  • Alginates and surface acting compounds | • Transoral incisionless fundoplication (TIF)  
• Radiofrequency ablation (RFA)  
• Anti-reflux Mucosectomy (ARMS)  
• Injectables | • Magnetic sphincter augmentation (MSA)  
• Roux-en-Y Gastric bypass  
• Fundoplication (Nissen, Toupet, Dor) | • Melatonin  
• Herbal Therapies (STW5, Rikkunshito)  
• Acupuncture  
• Diaphragmatic breathing |
| • Small meal size  
• Weight loss  
• Smoking Cessation  
• Alcohol avoidance  
• HOB elevation  
• Avoiding post-prandial recumbency | | | | |

*Denotes off-label use

Functional Dyspepsia
Dyspepsia

~20% of global population has symptoms of dyspepsia

More common in women, smokers and on NSAIDs

Estimated cost of >$18B per annum

**Functional Dyspepsia**

**Rome IV Criteria PDS**

*Must include one or both of the following at least 3 days a week*:  
1. Bothersome post-prandial fullness  
2. Bothersome early satiation  

**Supportive Criteria:**  
- Postprandial epigastric pain or burning, epigastric bloating, excessive belching, and nausea can also be present  
- Vomiting warrants consideration of another disorder  
- Heartburn is not a dyspeptic symptom but may often co-exist  
- Symptoms that are relieved by evacuation of feces or gas should generally not be considered as part of dyspepsia  

Other individual digestive symptoms or groups of symptoms (from GERD and IBS) may co-exist with PDS

**Rome IV Criteria EPS**

*Must include one or both of the following at least 1 day a week*:  
1. Bothersome epigastric pain  
2. Bothersome epigastric burning  

**Supportive Criteria:**  
1. Pain may be induced by ingestion of a meal, relieved by ingestion of a meal, or may occur while fasting  
2. Postprandial epigastric bloating, belching, and nausea can also be present  
3. Persistent vomiting likely suggests another disorder  
4. Heartburn is not a dyspeptic symptom but may often coexist  
5. The pain does not fulfill biliary pain criteria  
6. Symptoms that are relieved by evacuation of feces or gas should not be considered as part of dyspepsia  

Other individual digestive symptoms or groups of symptoms (from GERD and IBS) may co-exist with PDS

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.  
Dyspepsia Management Algorithm
Based on American College of Gastroenterology (ACG) And Canadian Association of Gastroenterology (CAG) Guidelines

≥60 years of age
Endoscopy

Adult dyspepsia patient
H. Pylori (non-invasive test)

<60 years of age

Manage based on findings

Organic Pathology
Normal
Positive
Negative

Manage as below

1. PPI
2. TCA
3. Prokinetic
4. Consider psychotherapy

Discontinue if no response after 8 weeks of once daily therapy
Can be associated with side effects such as constipation, dry mouth, somnolence
Adverse effects can include tardive dyskinesia or QT prolongation

TCA = Tricyclic antidepressant.
United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) Consensus on Functional Dyspepsia

Drink Tests Used In Functional Dyspepsia

a) Rapid water drink test or water load test
b) Rapid nutrient drink test
c) Satiety drinking test
d) Slow nutrient drink test

Gastroparesis
Gastroparesis

Epidemiology

**Incidence**
- 2.4 per 100,000 in men
- 9.8 per 100,000 in women

**Prevalence**
- 9.8 per 100,000 men
- 37.8 per 100,000 women

Etiology

- Idiopathic
- Diabetes
- Iatrogenic
- Neurologic disorders
- Post-viral infection
- Autoimmune

Tests for Gastric Emptying

- Gastric emptying scintigraphy (GES)
- Wireless motility capsule (WMC)
- Gastric emptying breath test

Endoscopic Functional Lumen Imaging Probe

EndoFLIP

• Measures the stiffness or compliance at the pylorus
• May help guide selection of patients for pyloric interventions

## Gastroparesis Treatment Options

### Dietary Modification
- Low fat, low (insoluble) fiber diet
- Small, frequent meals
- Homogenized meals if unable to tolerate solids
- Avoid carbonated beverages, smoking, and alcohol
- Enteral and parenteral supplementation for refractory symptoms

### Medication Therapy
- **Glycemic control**
- **Prokinetics**
  - Metoclopramide
  - Domperidone
  - Cisapride
  - Prucalopride*
  - Bethanechol*
  - Pyridostigmine*
- **Macrolide antibiotics**
  - Erythromycin*
  - Azithromycin*
- **Antiemetics**
- **Neuromodulators**
  - Nortriptyline*
  - Mirtazapine*
  - Buspirone

### Endoscopic Therapy
- Intrapyloric botulinum toxin injection
- Feeding tubes
- Transpyloric stenting
- Gastric per-oral endoscopy myotomy (G-POEM)

*Denotes off-label use

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# Gastroparesis Treatment Options

<table>
<thead>
<tr>
<th>Surgical Therapy</th>
<th>Alternative Therapy</th>
<th>Future Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric electrical stimulation (GES)</td>
<td>Ginger</td>
<td>Relamorelin (ghrelin agonist)</td>
</tr>
<tr>
<td>Pyloroplasty</td>
<td>Herbal preparations (STW5, peppermint)</td>
<td>Acotiamide (acetylcholinesterase inhibitor)</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>Acupuncture</td>
<td>Tradipitant (NK-1R antagonist)</td>
</tr>
<tr>
<td></td>
<td>Non-invasive Vagal Nerve Stimulator (nVNS)</td>
<td>TAK-906 (D2/D3 antagonist)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Velusetrag (5-HT4 agonist)</td>
</tr>
</tbody>
</table>

United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) Consensus on Gastroparesis

The highlights depict the percentage of agreement:

- **green color** for ≥80% consensus
- **light orange** for consensus between 70% and 80%
- **dark orange** for lower levels of consensus

**Gastroparesis**

- **Diet**: 85%
- **Proton pump inhibitor**: 10%
- **Anti-emetic**: 43%
- **Prokinetic**: 75%
- **Neuromodulators**:
  - 8% Tricyclic
  - 10% SSRI
  - 0% SNRI
  - 35% Mirtazapine

**Chronic nausea or vomiting, with or without Postprandial Distress Syndrome symptoms**

- **93% Endoscopy**
- **95% Gastric emptying test**
- **88% Radiology as needed**
- **98% Scintigraphy**
- **95% Breath test**
- **33% Mobility capsule**
- **18% Ultrasound**

**Diabetes**: 98%

**Drugs**: 100%

**Neurological disorders**: 90%

**Connective tissue disorders**: 98%

**Surgeries**: 85%

Functional Dyspepsia and Gastroparesis in Tertiary Care are Interchangeable Syndromes With Common Clinical and Pathologic Features

Pankaj J. Pasricha,1 Madhusudan Grover,2 Katherine P. Yates,1 Thomas L. Abell,3 Cheryl E. Bernard,2 Kenneth L. Koch,4 Richard W. McCallum,5 Irene Sarosiek,5 Braden Kuo,6 Robert Bulat,1 Jiande Chen,7 Robert J. Shulman,8 Linda Lee,9 James Tonascia,9 Laura A. Miriel,9 Frank Hamilton,10 Gianrico Farrugia,2 and Henry P. Parkman,11 for the National Institute of Diabetes and Digestive and Kidney Diseases/National Institutes of Health Gastroparesis Clinical Research Consortium

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Functional Dyspepsia and Gastroparesis in Tertiary Care Are Interchangeable Syndromes With Common Clinical And Pathologic Features

944 patients enrolled during a 12-year period

76% gastroparesis

24% functional dyspepsia

Functional Dyspepsia and Gastroparesis in Tertiary Care Are Interchangeable Syndromes With Common Clinical And Pathologic Features

- 944 patients enrolled during a 12-year period
- 76% gastroparesis
- 24% functional dyspepsia
- 48-week clinical outcome similar
- 42% of patients with GP were reclassified as FD
- 37% of patients with FD were reclassified as GP

“Future improvements in diagnostic ability may reveal subtle differences between these 2 syndromes but for now it is reasonable to conclude that FD and GP are part of the same spectrum…”

Take Home Points

GERD, functional dyspepsia, and gastroparesis symptoms and pathophysiology can overlap. A good clinical history is critical and can direct diagnostic investigation and treatment.

Therapy should be patient specific based on symptoms and underlying mechanisms. Research continues to explore pathophysiologic mechanisms, diagnostic testing, and novel therapeutic options.

Don’t make me upset. You wouldn’t like me when I’m upset.
References

- Camilleri, M. Pathogenesis of delayed gastric emptying. In: UpToDate, Talley, NJ (Ed), UpToDate, Waltham, MA, 2021.
References


