

Gastroparesis

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Objectives

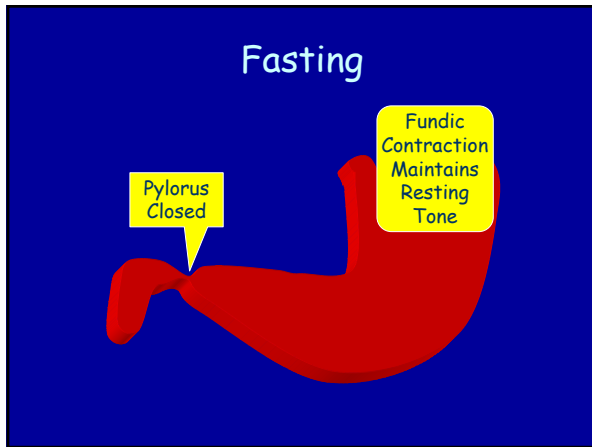
- Provide a **clinically relevant** overview of gastric and foregut motor function
- Review the **clinical definition, presenting features** and **causes** of gastroparesis
- Describe the clinical features of **other foregut motor disorders** of clinical importance
- Outline a **practical approach to the assessment** of these disorders
- Critically review **available treatment options**

Foregut Motor Physiology: the Relevant Basics

The Functions Sub-served by Gastric Motility

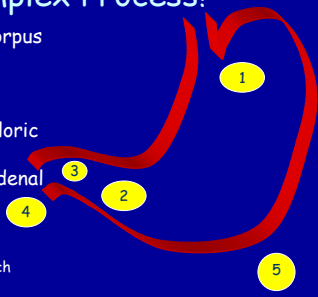
- Receive the meal
- Accommodate the meal until it is ready to be emptied
- Mix with acid and enzymes
- Triturate (grind down to particles \leq 1mm diam.)
- Empty in a regulated fashion (2-3 kcal/min)
- Prevent reflux

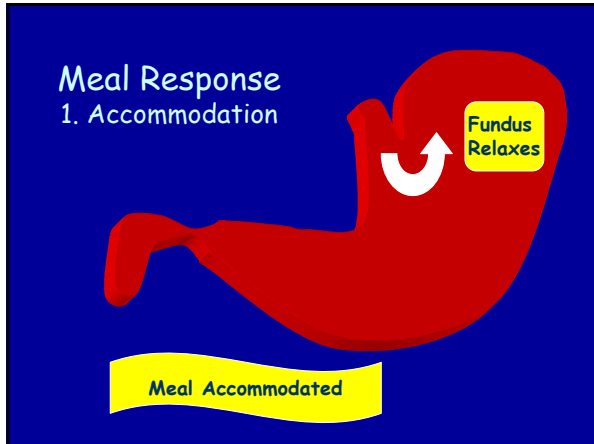
Fasting

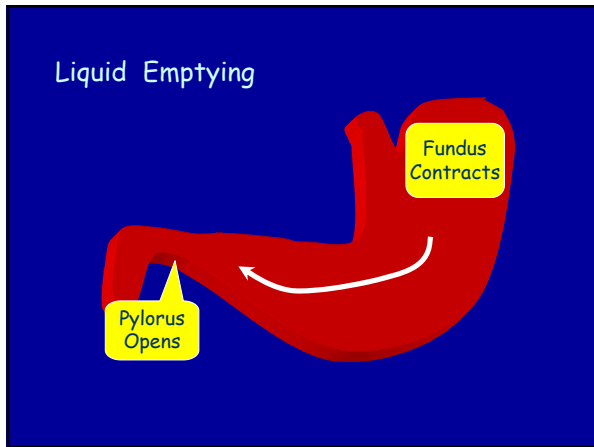


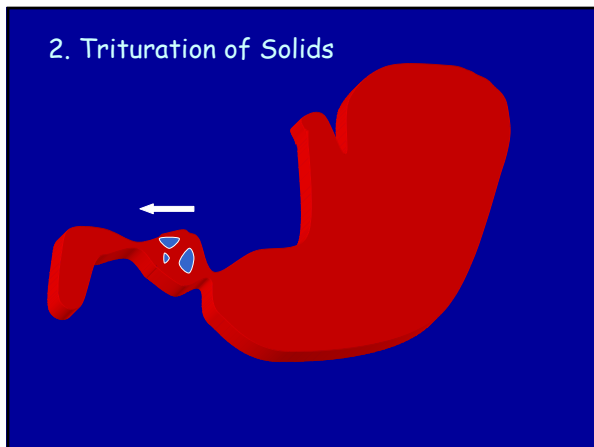
Gastric Emptying: a Complex Process!

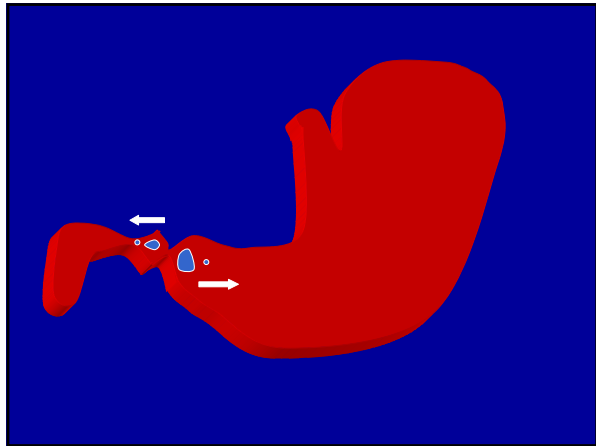
1. Fundic / Upper Corpus relaxation (accommodation)
2. Antral trituration
3. Fluctuations in pyloric tone
4. Antro-pyloro-duodenal coordination
5. Sensory input:
 - From the CNS
 - From the stomach
 - From the small intestine

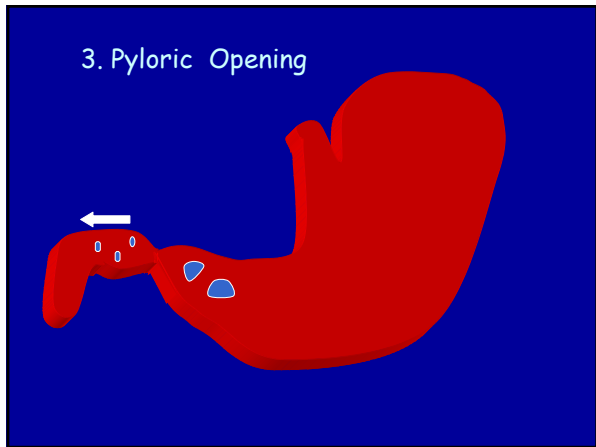


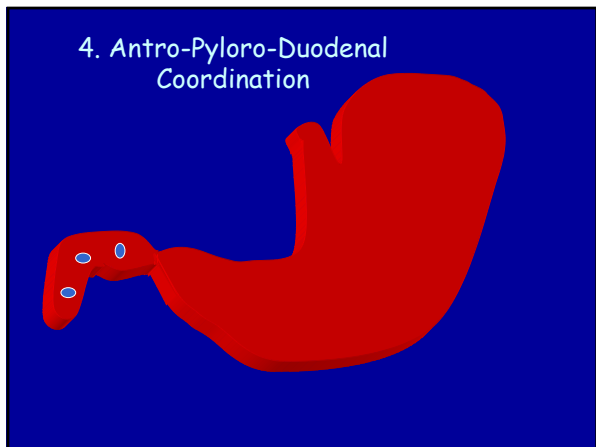












Clinical Definitions and Presentations

Definitions

Syndromes

- Dysmotility
- Gastropathy
- Gastroparesis
- Functional dyspepsia

- How do we distinguish between these terms!

Definitions

Syndromes

- **Dysmotility** Disturbed Sensory-Motor Function of the Stomach

Definitions
Syndromes

Nausea
Vomiting
Early satiety
Fullness
Bloating
Pain
Weight loss

±
• **Functional dyspepsia** Delayed Gastric Emptying
-
Obstruction

Definitions
Syndromes

Mild Delay the Rule!
Not Severe Delay

• **Functional dyspepsia** Delayed Gastric Emptying
-
Obstruction

Stanghellini et al. Dig Liver Dis 2003

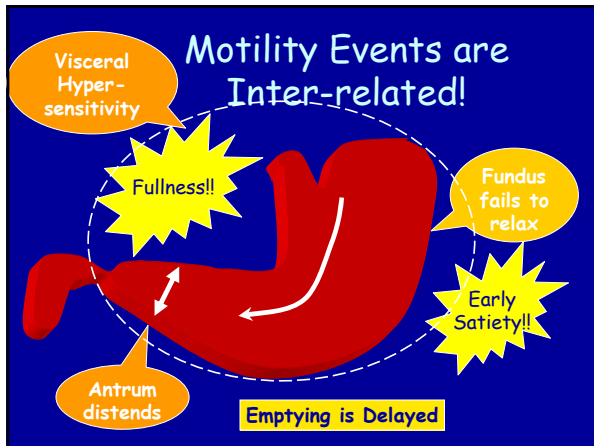
Several Factors may be Relevant to Symptom Generation

- Emptying rate:
 - Accelerated
 - Delayed
- Accommodation:
 - Impaired
- Sensation
 - Enhanced
 - Impaired
- Antrum
 - Distended
 - Dilated

ALL have been described in DM and "Idiopathic Gastroparesis!"

In severe Idiopathic Gastroparesis, symptoms do not correlate with GET or accommodation but with response to distension

Karamanolis et al. Gut 2007



Causes

- ### Gastroparesis
- Causes
- Idiopathic - 39%
 - Post-viral
 - GERD
 - FD
 - Diabetic - 29%
 - Post-gastric surgery - 13%
 - Parkinson's disease - 4.8%
 - Collagen vascular diseases - 4.8%
 - CTIP - 4.1%
- Soykan et al. DDS 1998

Miscellaneous

- Celiac sprue
- Liver disease
- Paraneoplastic syndrome
- Other CNS
- Superior mesenteric artery syndrome
- Median arcuate ligament syndrome

Post-Surgical

- Vagotomy
- Fundoplication
- Bariatric surgery
- Lung and heart-lung transplantation

Drug-Induced Gastroparesis

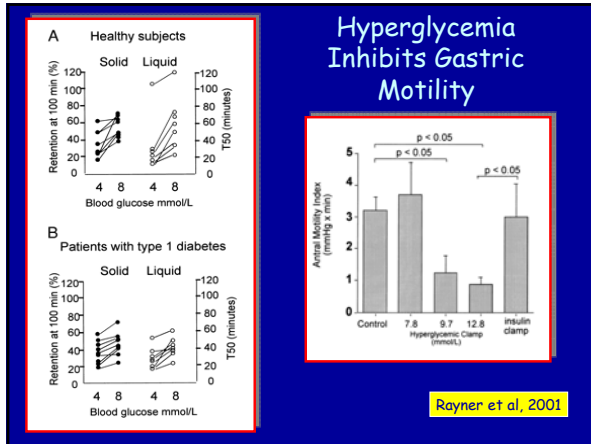
- Opioids
- Calcium channel blockers
- Clonidine
- Anticholinergics (including TCA's)
- Amylin analogues (pramlintide)
- GLP 1 (exenatide)
- Octreotide
- Dopaminergics

Prevalence of GI Symptoms in DM

- New South Wales
- N= 8657
- DM = 423
- Risk factors:
 - Poor glycemic control
 - NOT
 - Duration
 - Type
 - Therapy

Symptom	Adjusted OR
PC Fullness	2.07
Nausea	2.31
Vomiting	2.51
Dysphagia	2.71
D or C	2.04
Loose stools	2.34
Urgency	2.22
Incontinence	2.74

Bytzer et al, 2001



Diabetic Gastropathy

Differentiate between:

1. Delayed GE + dyspeptic symptoms
 - Multifactorial
 - Chance association
2. Gastroparesis
 - Significant symptoms
 - Nausea
 - Vomiting
 - Pain
 - Disturbed control

} COMMON

} RARE

The Classical Scenario

- Type 1 diabetic
- Neuropathy, retinopathy, nephropathy
- Late post-prandial vomiting of undigested food
- Bezoar

But this is rare!

The Rest

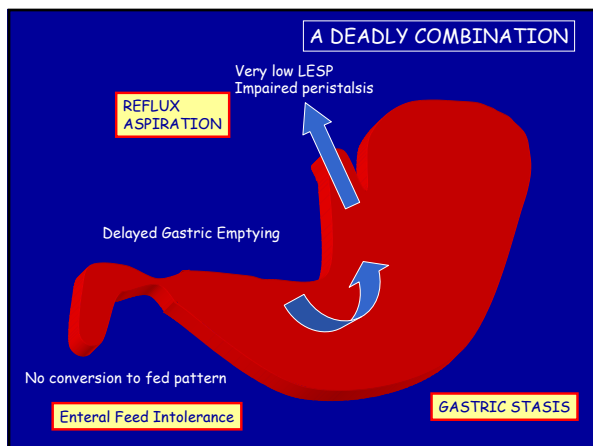
- Upper GI symptoms
 - **Recurrent** vomiting episodes
 - Rapid dehydration leading to hospitalization
- Normal EGD, ultrasound
- Delayed or normal GE on scintigraphy

LOOK FOR PRECIPITATING CAUSES

- Poor control
- Infection e.g. UTI

Other Syndromes

- Accelerated gastric emptying
 - Dumping syndrome
 - Diabetes, especially type 2
 - Idiopathic
 - Symptoms similar to "gastroparesis"
- Cyclic vomiting syndrome
- Rumination syndrome
- GERD with regurgitation
- Achalasia with regurgitation
- Sensori-motor dysfunction in FD
- ICU syndromes
 - Gastroparesis in 50% of ventilated patients



Assessment

Must Differentiate

Vomiting

Regurgitation

Rumination

What symptoms Predict Delayed Emptying and Gastroparesis?

Delayed Emptying	Gastroparesis
<ul style="list-style-type: none">• Female gender• Low body weight• Post-prandial fullness• Epigastric bloating	<ul style="list-style-type: none">• Female gender• Post-prandial fullness

Stanghellini et al. Dig Liver Dis 2004.
Jones et al. Diabetes Care 2001.
Talley et al. Gut 2006.

Initial assessment

- CNS?
 - Should have CNS symptoms or signs
- Iatrogenic
 - Rx, OTC and "alternative"!
- Mucosal disease/ gastric outlet obstruction/Encasement
 - EGD
 - Ultrasound/CT
 - Linitis
 - Metastatic:
 - Ovarian
 - Breast
- Low-grade or intermittent small bowel obstruction
 - Good quality CT and/or barium

What can we measure?

- Myoelectrical Activity
- Emptying
- Regional function
 - Fundic accommodation and receptive relaxation
 - Antral tone and relaxation
- Contractile Activity
 - At a point
 - Organised patterns
- Sensation and perception

What can we measure?

Myoelectrical Activity - EGG

- Non-invasive
- Records gastric slow wave
- Tachygastria and Bradygastria described
- Arrhythmias associated with a variety of symptoms
- Clinical role being defined:
 - pregnancy
 - ICU

What can we measure?

- Emptying
 - Scintigraphy
 - Radiopaque markers
 - Acetaminophen absorption test
 - $^{13,14}\text{C}$ -Octanoic acid breath test
 - Ultrasonography
 - Impedance
 - MRI

Scintigraphy

- ^{111}In for liquids, $^{99\text{m}}\text{Tc}$ for solids
- Mixed liquid-solid meal best for clinical purposes
- Can be simplified:
 - Low-fat, egg-beaters meal
 - Scan at 0, 60, 120, 240 mins only
 - Validated between centers

Tougas et al. Am J Gastro 2000

What can we measure?

- Regional function No clinical role
 - Fundic accommodation and receptive relaxation
 - Antral tone and relaxation

What can we measure?

- Contractile Activity
 - At a point
 - Organised patterns

- Perfused Tube vs Solid State
- Must be of sufficient duration
- Normal patterns defined
- Pathological correlations few
- Major limitations in stomach

What can we measure?

- Sensation and perception

No clinical role

Management: General Principles

- Dietary
 - Small, frequent, low-fat of complex CHO's
 - Homogenized meals
- Nutrition
 - Oral supplements
 - PEJ tube
- Diabetic control
- Correct electrolyte abnormalities
- Identify and correct underlying causes

Management: Pharmacologic

- Anti-emetics
 - Anti-histamines
 - Phenothiazines
 - 5-HT₃ antagonists
 - NK₁ antagonist
- Anti-emetics and pro-kinetics:
 - Metoclopramide
 - Domperidone
- Prokinetics:
 - Erythromycin
 - Anti-cholinesterases
 - (Tegaserod)
 - (Cisapride)
 - (Itopride)
 - (Levosulpiride)
 - (Other motilides)

Management: Pharmacologic

- Anti-emetics and pro-kinetics:
 - Metoclopramide
 - p.o. or s.c.
 - 25% incidence of adverse events; Black Box
 - Domperidone
 - May cause hyper-prolactinemia
- Prokinetics:
 - Erythromycin
 - Useful i.v., limited use p.o.
 - 3mg.kg q8 i.v.
 - 62.5-250 mg q8 p.o.

Non-Pharmacologic

- PEG decompression
- Botox
- Pacing, stimulation
- Surgery

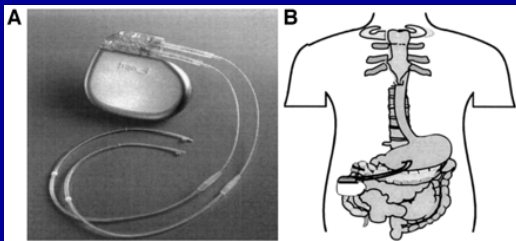
Botox to the Pylorus

- Four quadrant injections; 100 units
- Several small, uncontrolled series
- Improves solid GE and meal-related symptoms
- One controlled study: negative

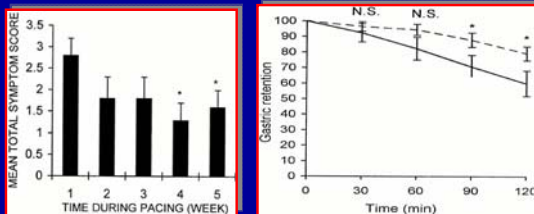


Arts et al. APT 2006
Arts et al. DDW 2005

Gastric Electrical Stimulation "Pacing"

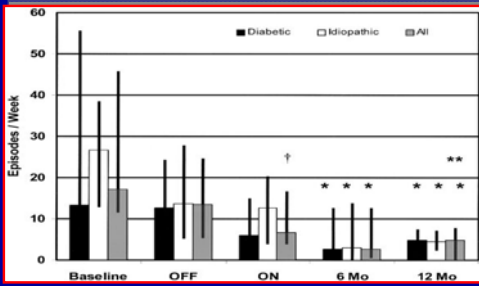


GES Improves Symptoms; no Effect on GE!



McCallum et al., 1998

Randomized Controlled Trial



Abell et al, 2003

GES

- In uncontrolled studies, benefits reported on:
 - Symptoms for up to 3 years
 - Nutritional status
 - Diabetic control
 - Pancreatic function
- Not free of complications
- Mechanism of action
 - ? Activation of vagal afferents
 - Modulation of ICC activity

Meta-analysis
 13 studies, only 1 controlled
Benefits:
 • Vomiting severity score
 • Nausea severity score
 • SF-36 physical and mental
 • Nutritional status
 • GE at 4 hours
 No weight gain

O'Grady et al, World J Surg 2009

Surgery

- Near-total gastrectomy and Roux-en-Y anastomosis
 - Significant short-term mortality from renal failure

Take Home Messages

- Great caution in the interpretation of upper GI symptoms
- Gastroparesis
 - A rare syndrome characterised by markedly delayed emptying in an appropriate clinical scenario
- Gastropathy/Dysmotility
 - Relatively common disorder in which disruption of a variety of sensori-motor functions contribute to symptoms
- Lack of available prokinetics emphasises role of supportive and symptomatic therapies
- Roles of non-pharmacological therapies continue to be assessed
