Gastroparesis Evaluation

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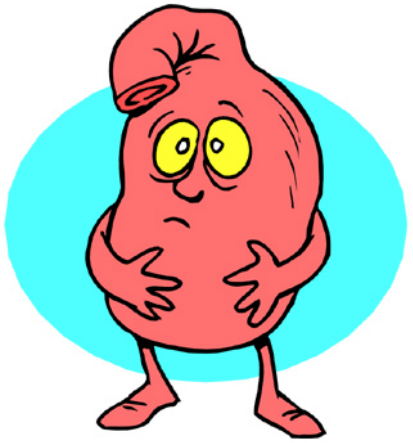

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CanMEDS Roles Covered

X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
	Communicator (as *Communicators*, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
X	**Collaborator** (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
	Health Advocate (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
X	**Scholar** (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Conflict of Interest Disclosure

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(Over the past 24 months)
Name: Adriana Lazarescu

Commercial or Non-Profit Interest	Relationship
Allergan	Speaker, Educational grant

I will not discuss the off-label use of medications

Objectives

To review normal gastric motility and what goes wrong in patients with gastroparesis

To describe the role of various diagnostic tests in the evaluation of a patient with suspected gastroparesis

To formulate an approach to managing a patient with gastroparesis

Case 1

- 31yo man with type 1 DM x 18 years
- Daily nausea and vomiting with every meal x 3 years
- Near constant epigastric discomfort, becomes painful during meals
- Bloated, especially in upper half of abdomen

- Having trouble keeping up with diabetic meals and snacks due to symptoms
- Has lost 15 pounds in past year

Case 1

- No hematemesis, heartburn or dysphagia
- Slightly constipated, no change recently

- HbA1C 12.5%
- Retinopathy, albuminuria

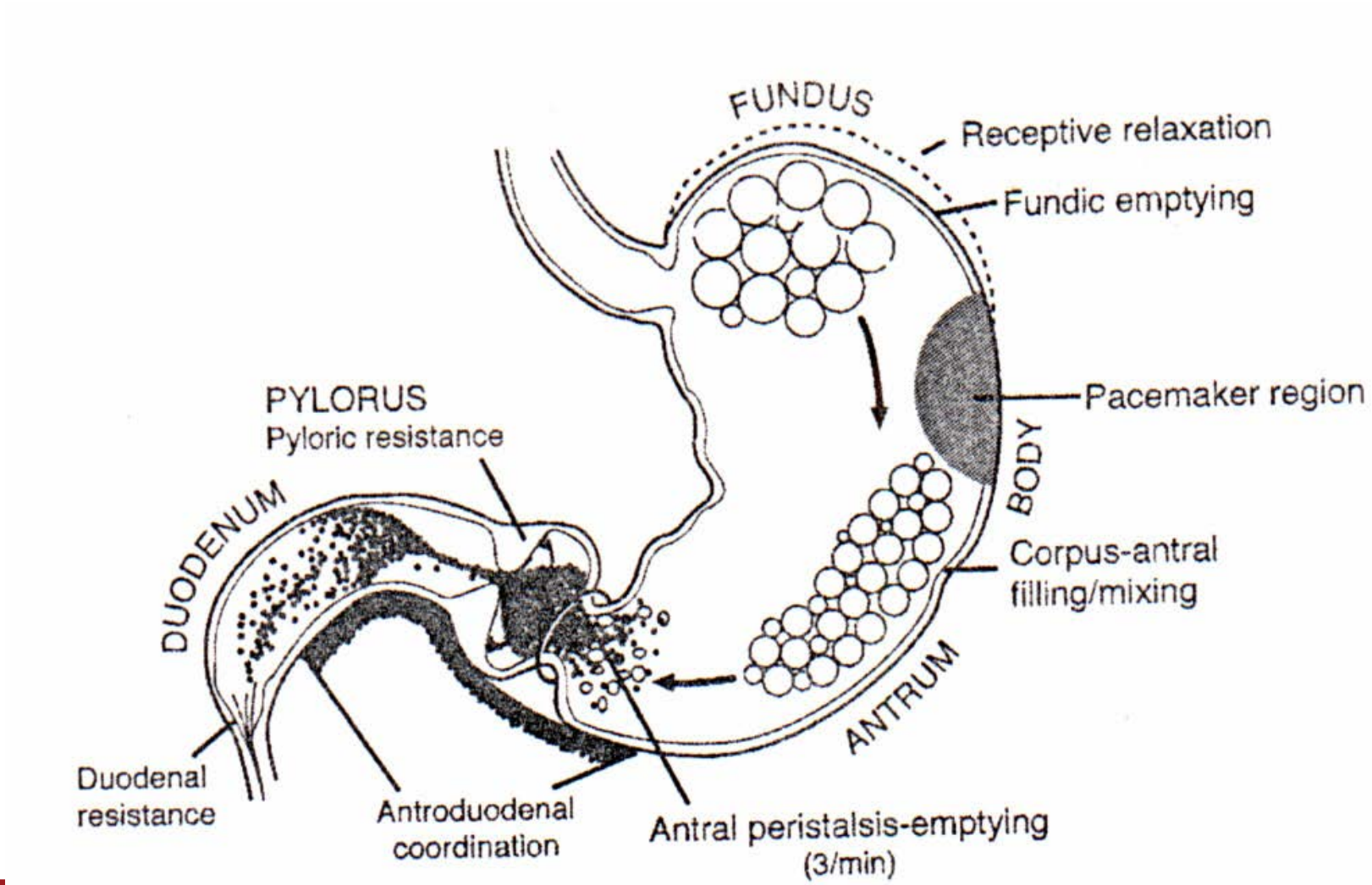
- Gastroscopy shows LA grade A esophagitis

Case 2

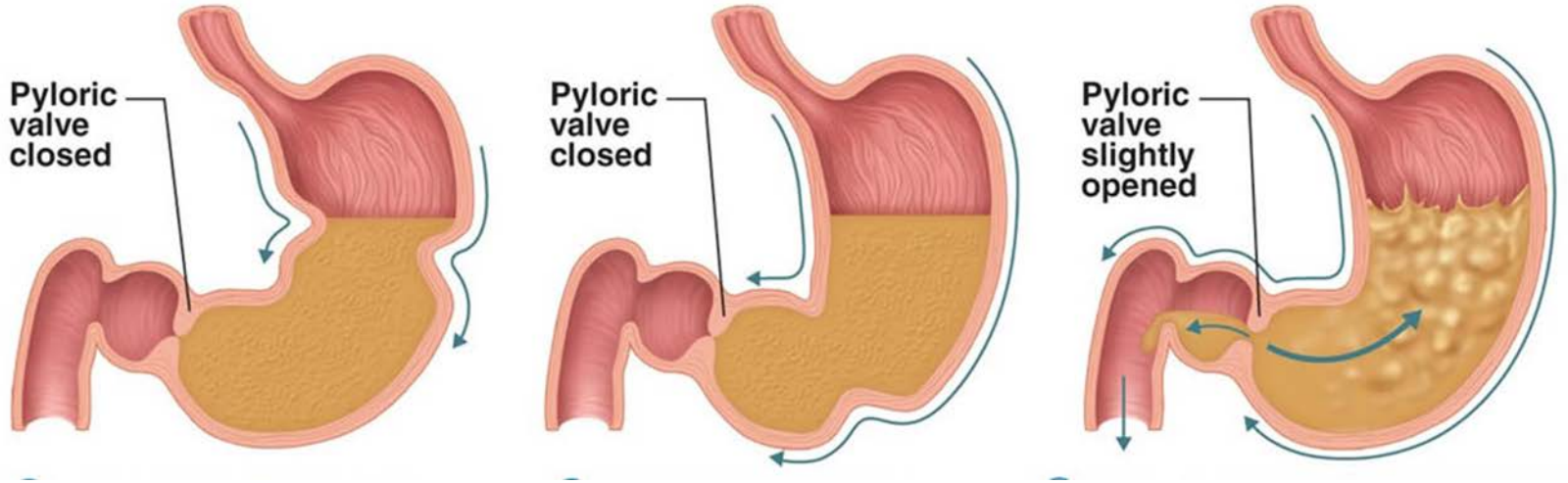
- 59yo woman 7 days post bilateral lung transplant for COPD
- Nauseated since OR
- Vomits any time she tries to eat
- No abdominal pain
- Normal BMs

- No prior history of any GI symptoms
- Gastroscopy shows a stomach full of food

The stomach during a meal



Gastric mixing and emptying



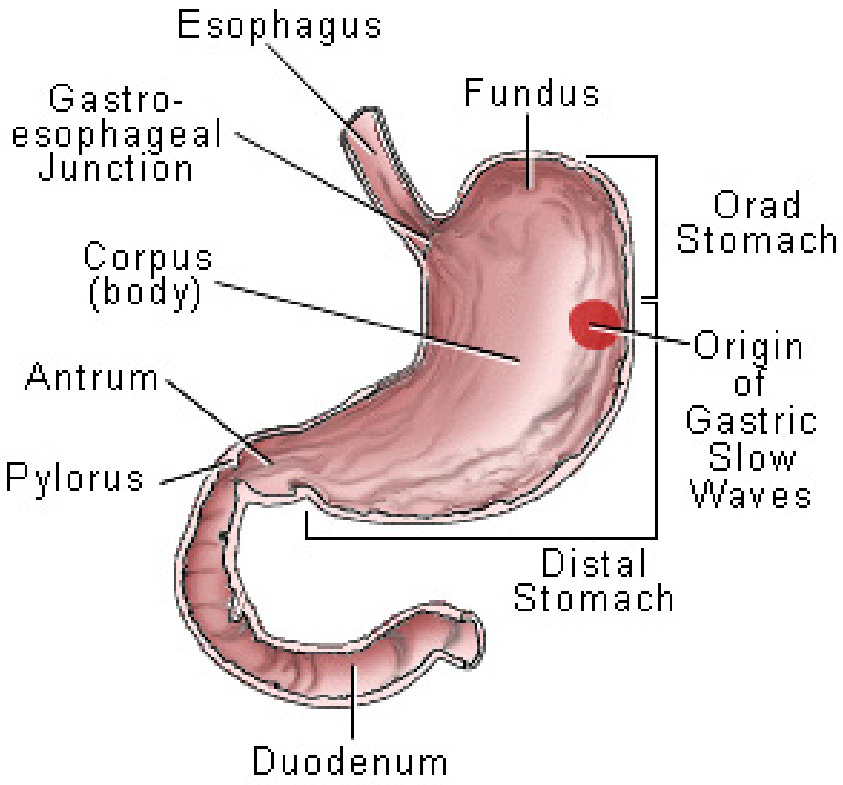
① **Propulsion:** Peristaltic waves move from the fundus toward the pylorus.

② **Grinding:** The most vigorous peristalsis and mixing action occur close to the pylorus.

③ **Retropulsion:** The pyloric end of the stomach acts as a pump that delivers small amounts of chyme into the duodenum, simultaneously forcing most of its contained material backward into the stomach.

Basic electrical rhythm (BER)

- Basic electrical rhythm (BER) set by gastric pacemaker
- Rhythmic depolarization results in slow wave potentials that sweep down stomach at ~ 3/per minute
- The **rate does not change**, but **the force of contraction is increased** by gastric distention, vagal activity, and gastrin.



Gastric mixing and emptying

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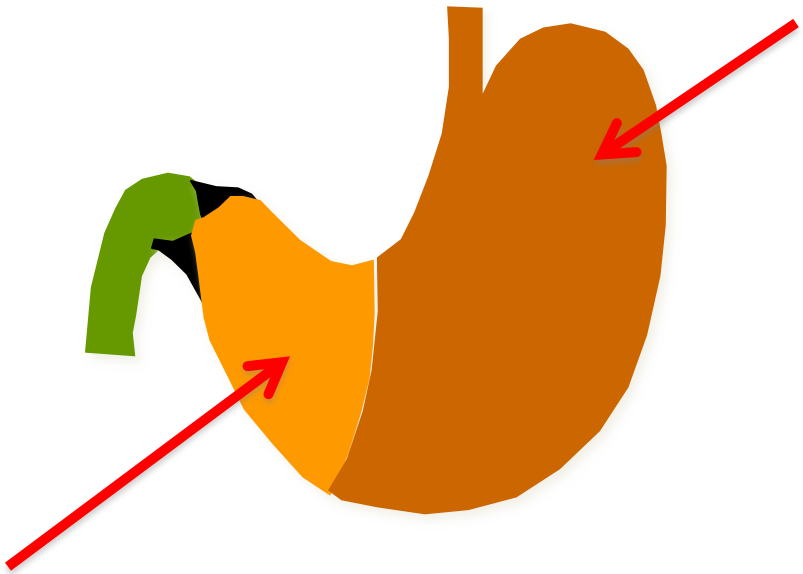
Fundus regulates emptying of liquids



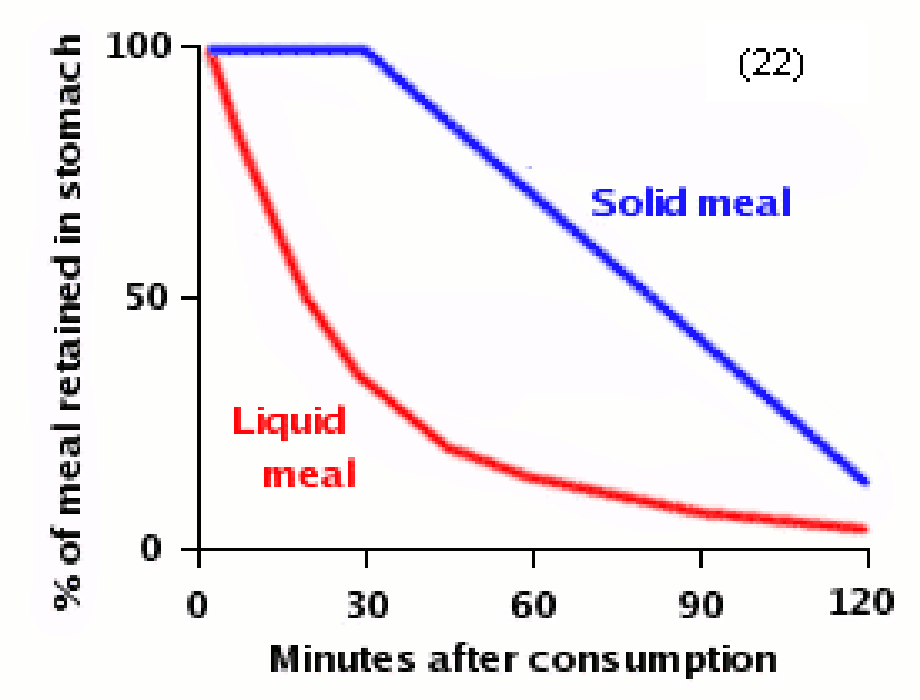
Antrum regulates emptying of solids

Factors that regulate gastric emptying

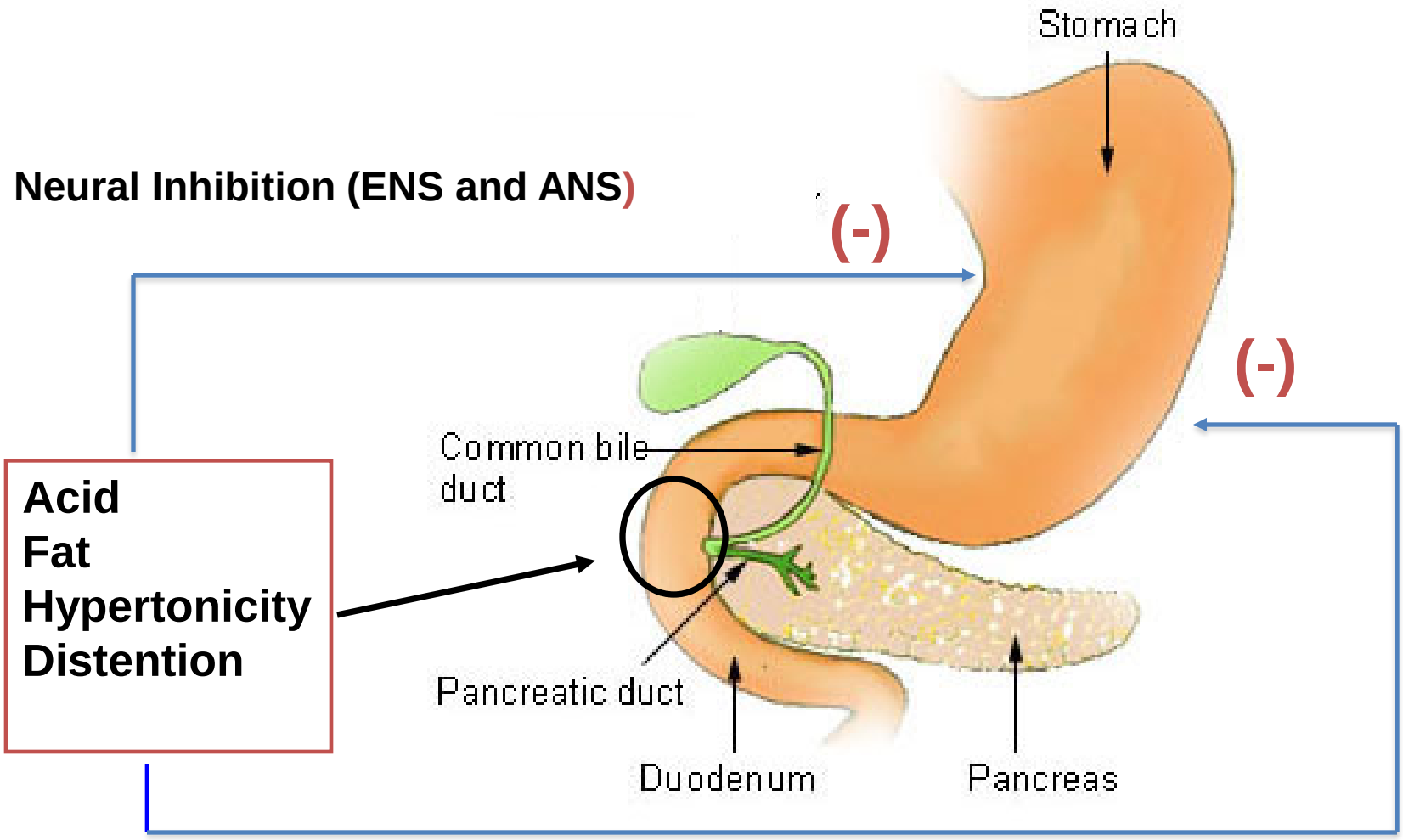
- Gastric emptying is regulated by:
  - *Physical composition* of the meal
    - Carbohydrate fastest, fat slowest
  - *Degree of fluidity*
    - Liquid empties faster than solids
  - *Amount ingested*

- Nervous and hormonal signals released from the stomach and duodenum regulate gastric emptying

Liquid vs. solid gastric emptying



Gastric emptying is inhibited by factors in the duodenum (enterogastric reflex)



Why do these factors inhibit gastric emptying?

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- **Fat**
  - Fat is digested and absorbed more slowly than other nutrients
  - Most potent inhibitory stimulus
- **Acid**
  - Acidic chyme is neutralized by sodium bicarbonate secreted into the duodenal lumen
  - Unneutralized acid irritates the mucosa and inactivates pancreatic digestive enzymes
- **Hypertonicity and distention**
  - Increased osmolarity of duodenal contents can result in circulatory disturbances due to large volumes of water entering duodenum

Hormonal control of gastric emptying

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- **ENHANCES gastric motility**
  - **Gastrin**
    - Released from G cells in the antrum of the stomach

- **INHIBITS gastric motility**
  - **Secretin**
    - Released from duodenal endocrine cells primarily in response to acid
  - **Cholecystokin (CCK)**
    - Released from duodenal endocrine cells primarily in response to fat and protein
  - **Gastric inhibitory peptide (GIP)**
    - Released from duodenal endocrine cells in response to fat, acid, hypertonicity, glucose, and distention

Causes of Gastroparesis

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- Diabetes
- Medications (opioids)
- Post-surgical (fundoplication, lung transplant)
- Idiopathic (?post viral)
- Connective tissue disorder (Scleroderma)
- Neurological disease (Parkinson, MS)
- Paraneoplastic
- Amyloidosis

Clinical presentation of gastroparesis

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- Symptoms
  - Nausea, vomiting, postprandial fullness, bloating, anorexia
  - Carefully differentiate between vomiting and regurgitation and whether self-induced
  - Ask what patient does with vomitus – spit it out or swallow it again?

- Physical exam
  - Succussion splash

Clinical presentation of gastroparesis

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- Endoscopic
  - Retained gastric contents despite fasting – not reliable
  - Bezoar
  - Refractory reflux esophagitis
  - Mallory-Weiss tear

- Complications
  - Malnutrition
  - Volume depletion
  - Electrolyte disturbances
  - Increased frequency of DKA in diabetic patients

Initial evaluation

- Endoscopy to rule out a mechanical obstruction or mucosal disease
- Gastric emptying scintigraphy

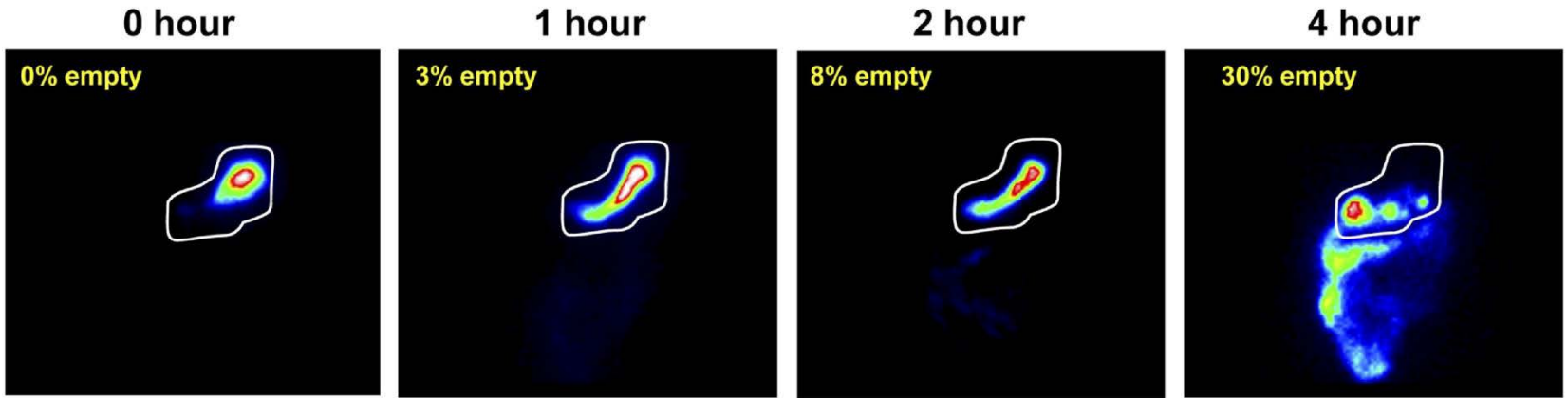
- Other options
  - CT or MR enterography to assess small bowel for contributing structural cause
  - Functional lumen imaging probe (EndoFLIP) to assess pylorus if pyloric spasm suspected
  - Wireless motility capsule (Smartpill)
  - Antroduodenal manometry
  - Gastric emptying breath test

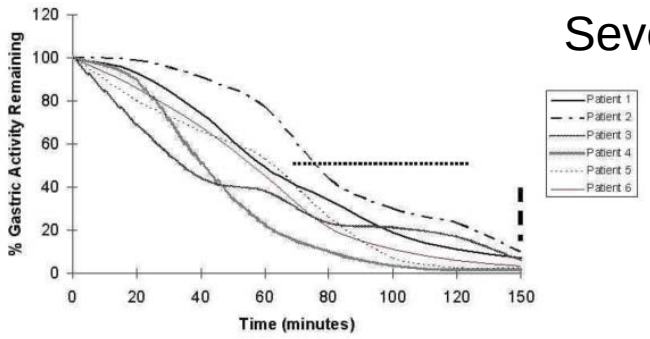
Gastric emptying scintigraphy

- Meal composition (solid only – liquid not standardized)
  - Liquid egg white, 2 slices of bread, strawberry jam
  - Technetium 99 tracer
  - Eat over 10 min
- Image acquisition
  - 0, 1,2 4 hours
  - Some centres stop at 2 hours and extrapolate – inadequate
- Medications
  - Stop medications that speed up or slow down gastric emptying 48 hours prior to test
- Blood glucose
  - Test not done if >16

Tougas G et al. Am J Gastroenterol (2000) 95(6):1456

Gastric Emptying Scintigraphy





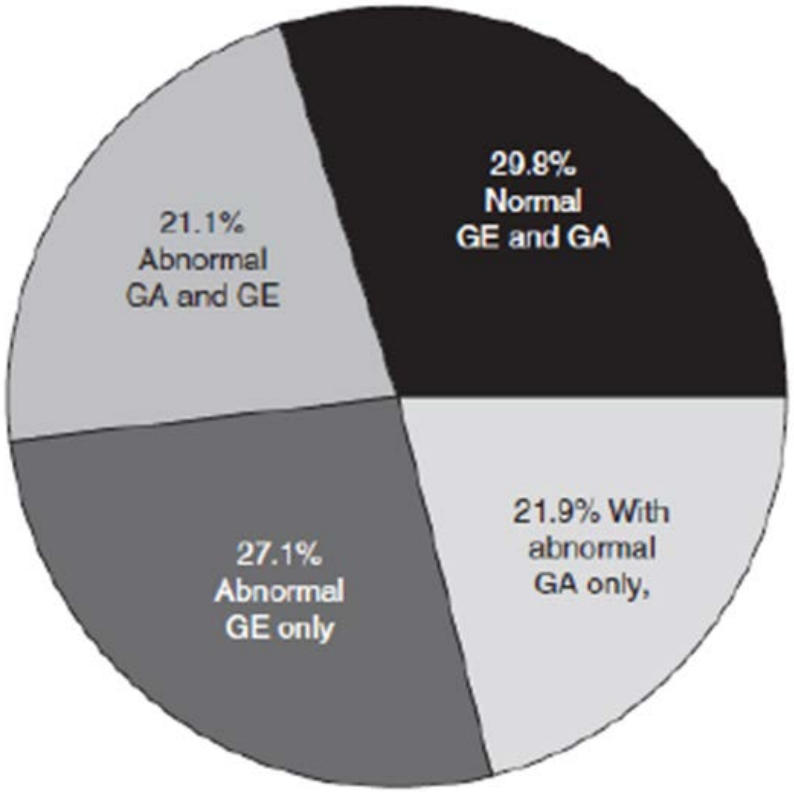
Gastroparesis >10% retention at 4 hours
Severe >35%

Clin Gastroenterol Hepatol. (2009); 7:823-7

Beware of Mimics

- Rumination syndrome
- Cyclic vomiting syndrome
- Cannabis hyperemesis syndrome
- Gastric outlet obstruction
- Linitis plastica

Overlap with functional dyspepsia



Am J Gastroenterol (2017) Sep 12. doi: 10.1038/ajg.2017.264

Differential diagnosis of nausea and vomiting is long…

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Differential diagnosis of nausea and vomiting

Medications and toxic etiologies
Cancer chemotherapy
Severe - cisplatinum, dacarbazine, nitrogen mustard
Moderate - etoposide, methotrexate, cytarabine
Mild -f luorouracil, vinblastine, tamoxifen
Analgesics
Aspirin
Nonsteroidal antiinflammatory drugs
Auranofin
Antigout drugs
Cardiovascular medications
Digoxin
Antiarrhythmics
Antihypertensives
Beta blockers
Calcium channel antagonists
Diuretics
Hormonal preparations/therapies
Oral antidiabetics
Oral contraceptives
Antibiotics/antivirals
Erythromycin
Tetracycline
Sulfonamides
Antituberculous drugs
Acyclovir
Gastrointestinal medications
Sulfasalazine
Azathioprine
Nicotine
CNS active drugs
Narcotics
Antiparkinsonian drugs
Anticonvulsants
Antiasthmatics
Theophylline
Radiation therapy
Ethanol abuse
Jamaican vomiting sickness
Hypervitaminosis

Infectious causes
Gastroenteritis
Viral
Bacterial
Nongastrointestinal infections
Otitis media
Disorders of the gut and peritoneum
Mechanical obstruction
Gastric outlet obstruction
Small bowel obstruction
Functional gastrointestinal disorders
Gastroparesis
Chronic intestinal pseudo-obstruction
Nonulcer dyspepsia
Irritable bowel syndrome
Organic gastrointestinal disorders
Pancreatic adenocarcinoma
Inflammatory intraperitoneal disease
Peptic ulcer disease
Cholecystitis
Pancreatitis
Hepatitis
Crohn disease
Mesenteric ischemia
Retroperitoneal fibrosis
Mucosal metastases

CNS causes
Migraine
Increased intracranial pressure
Malignancy
Hemorrhage
Infarction
Abscess
Meningitis
Congenital malformation
Hydrocephalus
Pseudotumor cerebri
Seizure disorders
Demyelinating disorders
Cranial radiation
Emotional responses
Psychiatric disease
Psychogenic vomiting
Anxiety disorders
Depression
Pain
Anorexia nervosa
Bulimia nervosa
Labyrinthine disorders
Motion sickness
Labyrinthitis
Tumors
Ménière disease
Iatrogenic
Fluorescein angiography
Endocrinologic and metabolic causes
Pregnancy
Other endocrine and metabolic
Uremia
Diabetic ketoacidosis
Hyperparathyroidism
Hypoparathyroidism
Hyperthyroidism
Addison's disease
Acute intermittent porphyria
Miscellaneous causes
Postoperative nausea and vomiting
Cyclic vomiting syndrome
Cardiac disease
Myocardial infarction
Heart failure
Radiofrequency ablation of the liver
Starvation
Radiation therapy to the upper abdomen and lower chest

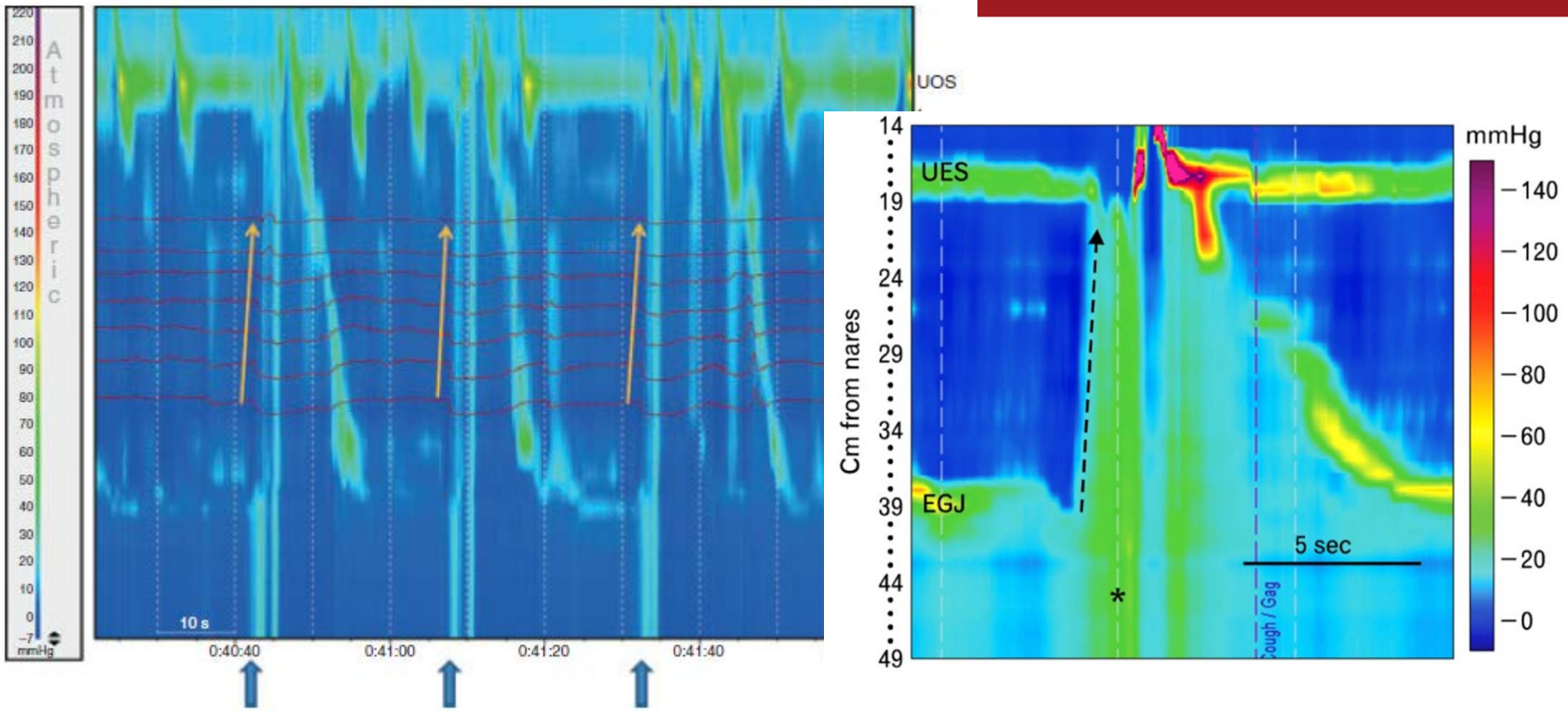
Reproduced with permission from: the American Gastroenterological Association. Gastroenterology 2001; 120:263.

UpToDate®

Rumination syndrome

- Diagnostic criteria
  - Persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spiting or remastication and swallowing
  - Regurgitation is not preceded by retching
- For the last 3 months, symptom onset at least 6 months prior to diagnosis
- Supportive criteria
  - Effortless regurgitation events are usually not preceded by nausea
  - Cessation of the process when regurgitated material becomes acidic
  - Regurgitant contains recognizable food that might have a pleasant taste

Rome IV Diagnostic Criteria for FGID. Gastroenterology (2016) 160(6):1380-92



Tack et al. Aliment Pharmacol Ther (2011) 33:782-8

Management of gastroparesis

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- Restoring nutrition and hydration
- Glycemic control (if diabetic)
- Medications
  - Prokinetics
  - Anti-emetics
- Treat pyloric spasm if present
  - Pyloromyotomy
  - G-POEM
- Gastric electric stimulation

Camilleri M et al. Am J Gastroenterol (2013) 108(1):18

Nutrition

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- Working with a dietician is very helpful

- Multiple small meals per day or graze
- Decrease fibre and fat intake
- Downgrade to whatever consistency of food is tolerated

- If oral feeding not tolerated, try postpyloric feeding
- Longterm GJ tube (with or without gastric venting)

Prokinetics

- Metoclopramide
- Domperidone
- Erythromycin - tachyphylaxis
- Prucalopride – off label use
- (Cisapride)

- Watch QT interval
- Regular use generally works better than PRN

Anti-emetics

- Do not improve gastric emptying, but can help with nausea and vomiting symptoms
- Low quality evidence

- Ondansetron
- Dimenhydrinate
- Nabilone
- Aprepitant

Other medications

- Low dose TCA can help with nausea, vomiting and abdominal pain
- Nortriptyline preferred due to lower anticholinergic effects
- SSRIs for treatment of depression in diabetic gastroparesis leads to improved glycemic control and less GI symptoms

- Mirtazapine
  - Also works in functional dyspepsia so useful if possible overlap

Kim SW et al. Psychosomatics (2006) 47:440; Sawhney MS et al. Dig Dis Sci (2007) 52:418

Treating pylorospasm

- Cause of symptoms in only a minority of patients with gastroparesis

- G-POEM
  - Promising early studies
  - Need long term data

- Botulinum toxin - NO
  - 2 double-blind placebo controlled studies showed improvement in gastric emptying, but no improvement in symptoms compared with placebo

Arts J et al. Aliment Pharmacol Ther (2007) 26:1251; Friedenberg FK et al. Am J Gastroetnerol (2008) 103:416

Gastric electrical stimulation

- For compassionate treatment for patients with refractory symptoms of gastroparesis despite trial other appropriate therapies
- Data is inconsistent
- Diabetic GP seems to respond better than other GP

- High frequency, low energy electrical stimulation to the stomach

Case 1

- Diabetic gastroparesis

- Dietary modification
  - Work with diabetic dietician
  - Multiple small meals through the day or graze

- Tighten glycemic control
- Review medications for any contributors to symptoms

Case 2

- Iatrogenic gastroparesis due to vagal nerve injury during lung transplant

- Failed all promotility agents and changes to medication
- Fed via NJ tube for first month postop
- Transitioned to GJ tube feeds

Take home messages

- A careful history can help rule out mimics of gastroparesis
- Depending on symptoms and response to initial therapy, further diagnostic modalities can help direct management
- Stepwise approach to management with a focus on nutrition is recommended