

Approach to Nausea / Vomiting

Syndromes including Gastroparesis

Outline

- Definitions
- Pathophysiology
- Causes
- Approach
- Gastroparesis
- Other Syndromes

Definitions

Retching

Nausea

Dyspepsia

Rumination

Vomiting

Regurgitation

Pathophysiology

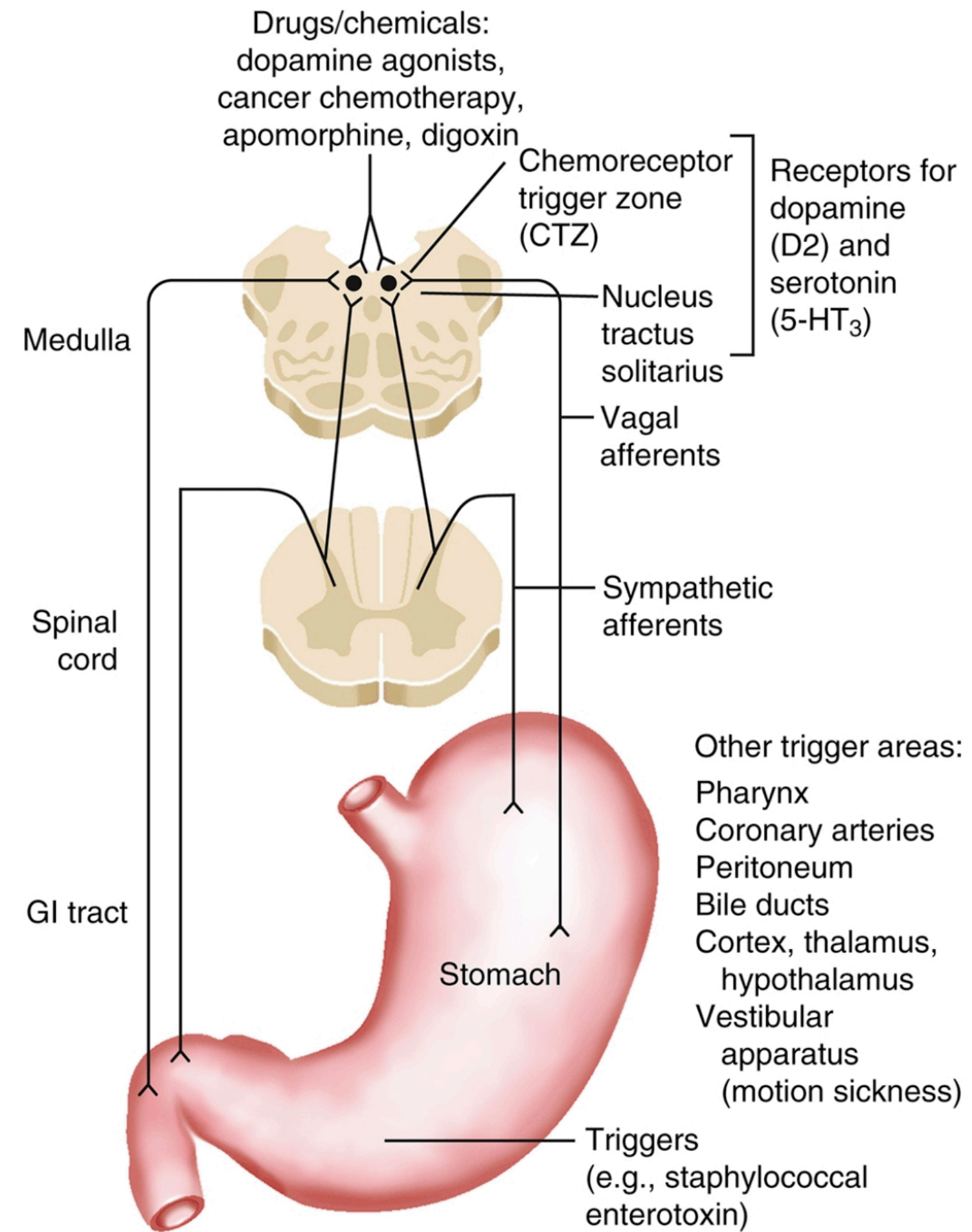


Figure 15.1 Schematic representation of the proposed neural pathways that mediate vomiting. 5-HT, 5-hydroxytryptamine.

Table 3. Anatomic Localization and Receptor Mediation of Clinical Emetic Stimuli in Humans

Anatomic site	Clinical stimuli	Receptors activated	Most common receptor-directed therapy
Area postrema	Medications (dopamine agonists, digoxin, opiates, nicotine, cytotoxics); metabolic (uremia, diabetic ketoacidosis, hypoxemia, hypercalcemia); bacterial toxins; radiation therapy	Dopamine D ₂ ; serotonergic 5-HT ₃ ; histaminergic H ₁ ; muscarinic M ₁ ; vasopressinergic	Antidopaminergics; ?5-HT ₃ antagonists
Labyrinths	Motion sickness; labyrinthine tumors or infections; Meniere disease	Histaminergic H ₁ ; muscarinic M ₁	Antihistamines, anticholinergics
Peripheral afferents	Gastric irritants (copper sulfate, <i>Staphylococcus</i> enterotoxin, salicylate, antral distention); nongastric stimuli (colonic, biliary, or intestinal distention, peritonitis, mesenteric occlusion); chemotherapy; abdominal irradiation; pharyngeal stimulation	Serotonergic 5-HT ₃	5-HT ₃ antagonists
Cerebral cortex Somatic pain	Noxious odors, visions, or tastes	Poorly characterized	

Different Causes

Table 2. Differential Diagnosis of Nausea and Vomiting

Medications and toxic etiologies

Cancer chemotherapy

Severe—cisplatin, dacarbazine, nitrogen mustard

Moderate—etoposide, methotrexate, cytarabine

Mild—fluorouracil, vinblastine, tamoxifen

Analgesics

Aspirin

Nonsteroidal anti-inflammatory drugs

Auranofin

Antigout drugs

Cardiovascular medications

Digoxin

Antiarrhythmics

Antihypertensives

β-Blockers

Calcium channel antagonists

Diuretics

Hormonal preparations/therapies

Oral antidiabetics

Oral contraceptives

Antibiotics/antivirals

Erythromycin

Tetracycline

Sulfonamides

Antituberculous drugs

Acyclovir

Gastrointestinal medications

Sulfasalazine

Azathioprine

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's disease

Mesenteric ischemia

Retroperitoneal fibrosis

Mucosal metastases

CNS causes

Migraine

Increased intracranial pressure

Malignancy

Hemorrhage

Infarction

Abscess

Meningitis

Congenital malformation

Different Causes cont.

Nicotine

CNS active

Narcotics

Antiparkinsonian drugs

Anticonvulsants

Antiasthmatics

Theophylline

Radiation therapy

Ethanol abuse

Jamaican vomiting sickness

Hypervitaminosis

Infectious causes

Gastroenteritis

Viral

Bacterial

Nongastrointestinal infections

Otitis media

Hydrocephalus

Pseudotumor cerebri

Seizure disorders

Demyelinating disorders

Emotional responses

Psychiatric disease

Psychogenic vomiting

Anxiety disorders

Depression

Pain

Anorexia nervosa

Bulimia nervosa

Labyrinthine disorders

Motion sickness

Labyrinthitis

Tumors

Meniere's 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

Postoperative nausea and vomiting

Cyclic vomiting syndrome

Miscellaneous causes

Cardiac disease

Myocardial infarction

Congestive heart failure

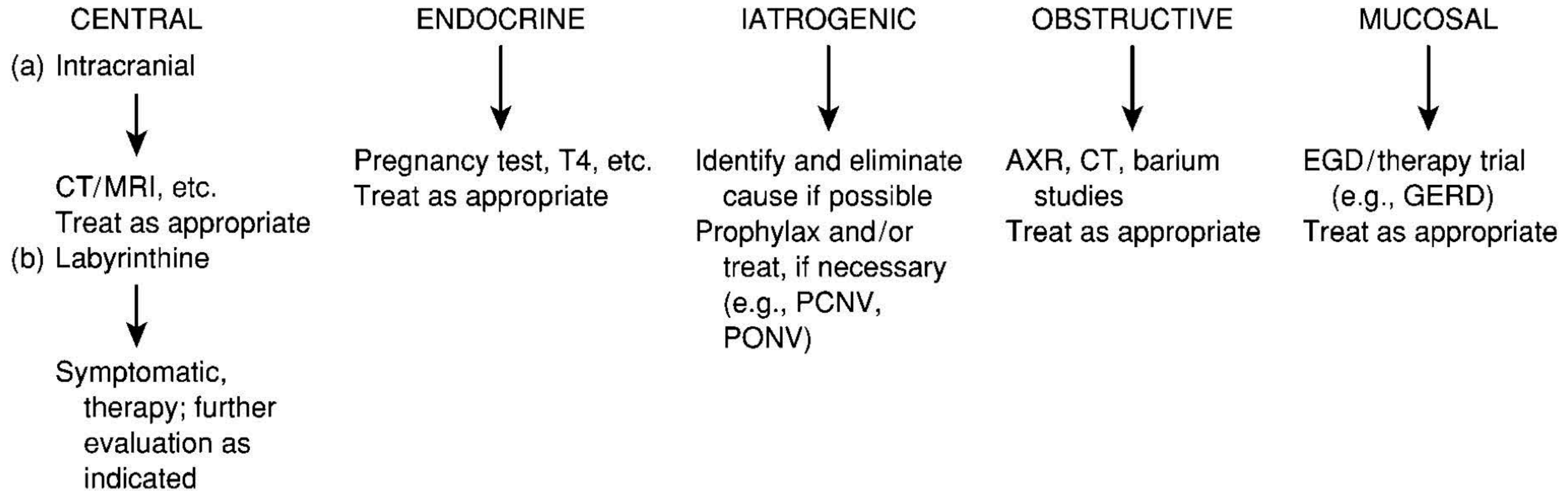
Radiofrequency ablation

Starvation

Clinical Approach

- Chronic (more than one month)
- Differentiate N/V from other symptoms
- Two objectives of history and physical exam
 - Identify signs pointing towards cause
 - Consequences / complications of vomiting
- Management
 - Fluid/electrolyte replacement
 - Symptomatic therapy

STEP 1: INITIAL ASSESSMENT
If this suggests one of the following causes:

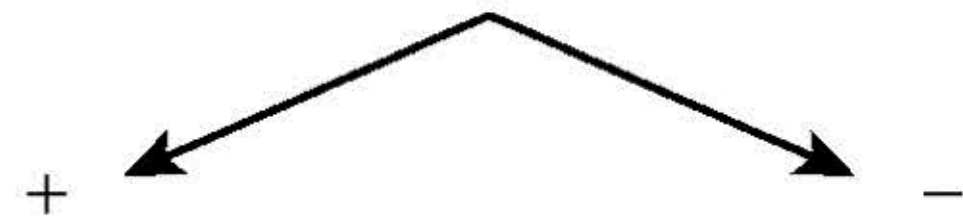


STEP 2: FURTHER ASSESSMENT

If initial assessment does not suggest a specific cause or evaluation proves unproductive.

Two options, depending on clinical context:

(i) THERAPEUTIC TRIAL
ANTIEMETIC + PROKINETIC



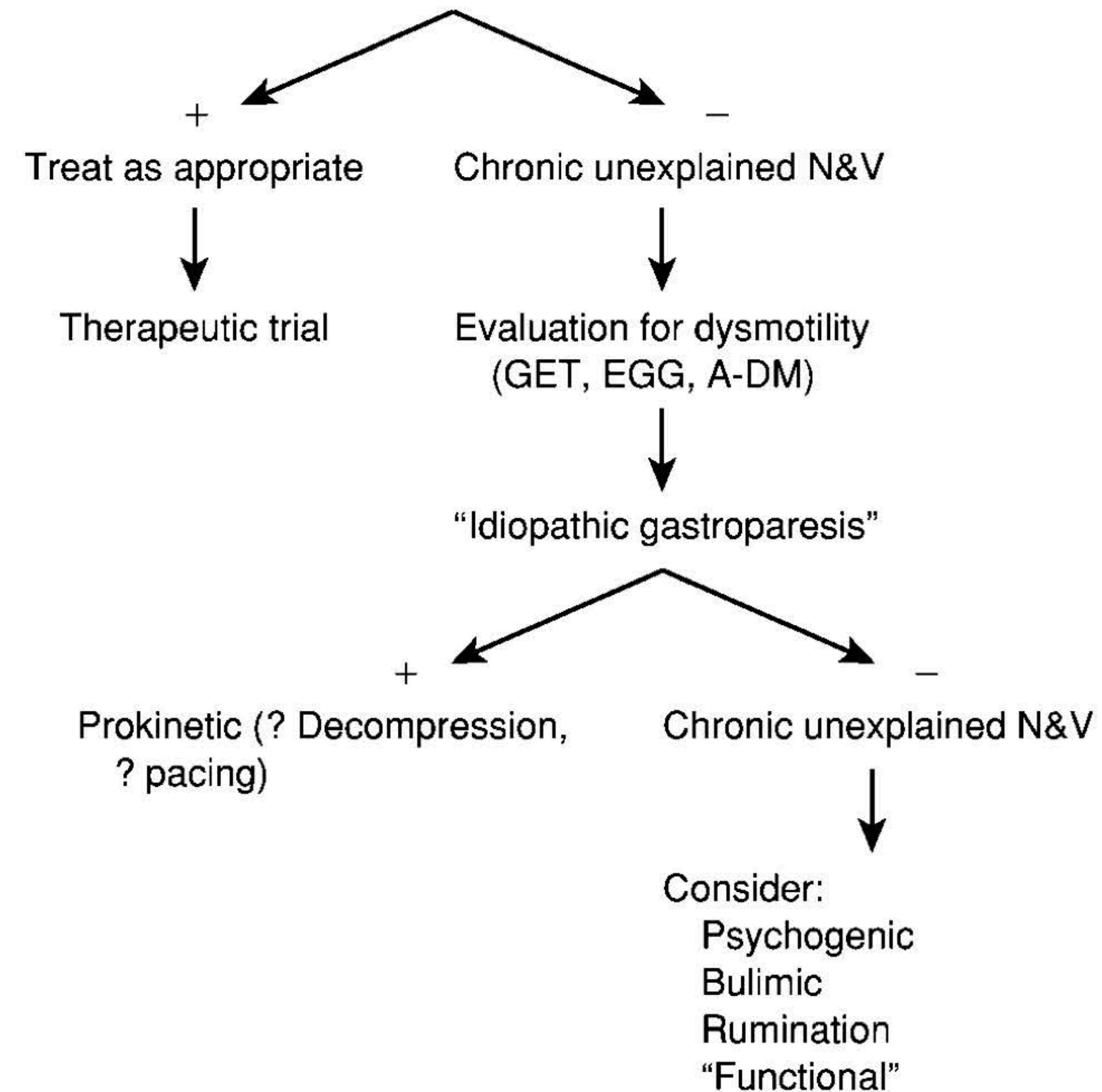
(ii) EVALUATE FOR SPECIFIC CAUSES:

Low-grade intestinal obstruction (CT, SBS)

Metabolic endocrine disease (T4, etc.)

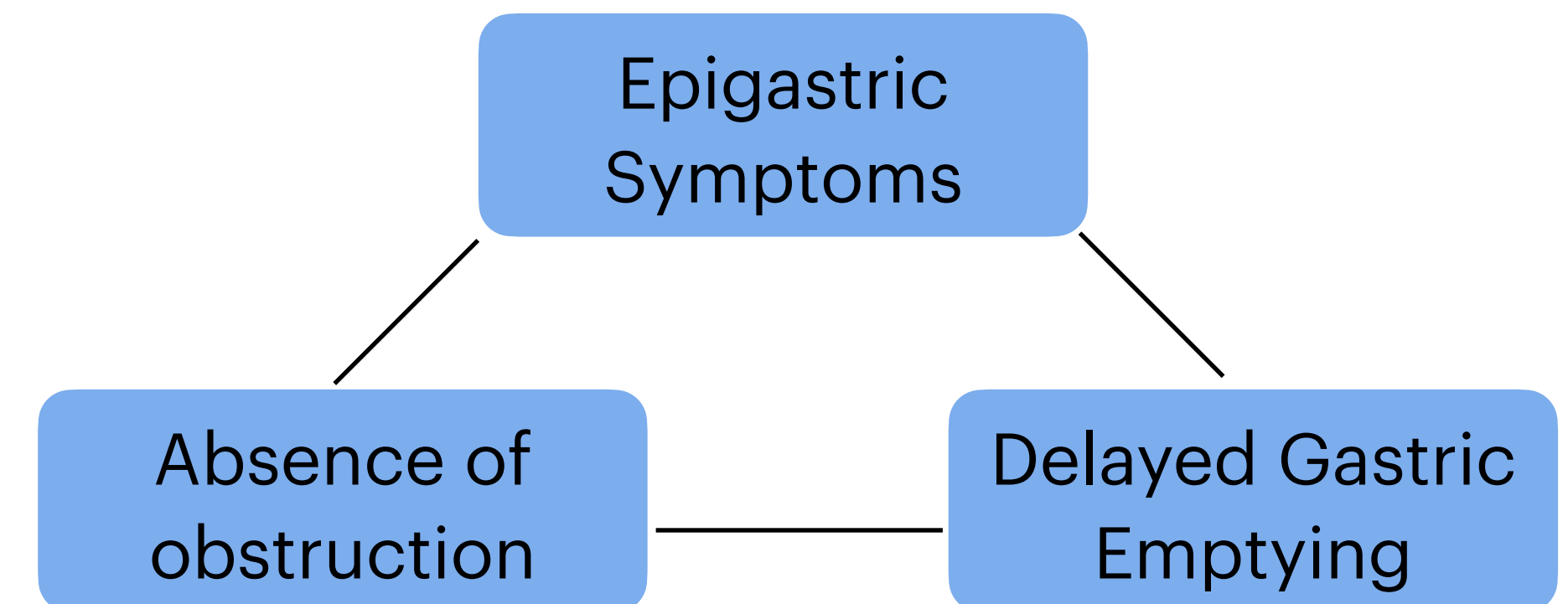
UGI mucosal disease (EGD)

Psychogenic (psychological evaluation)



Gastroparesis

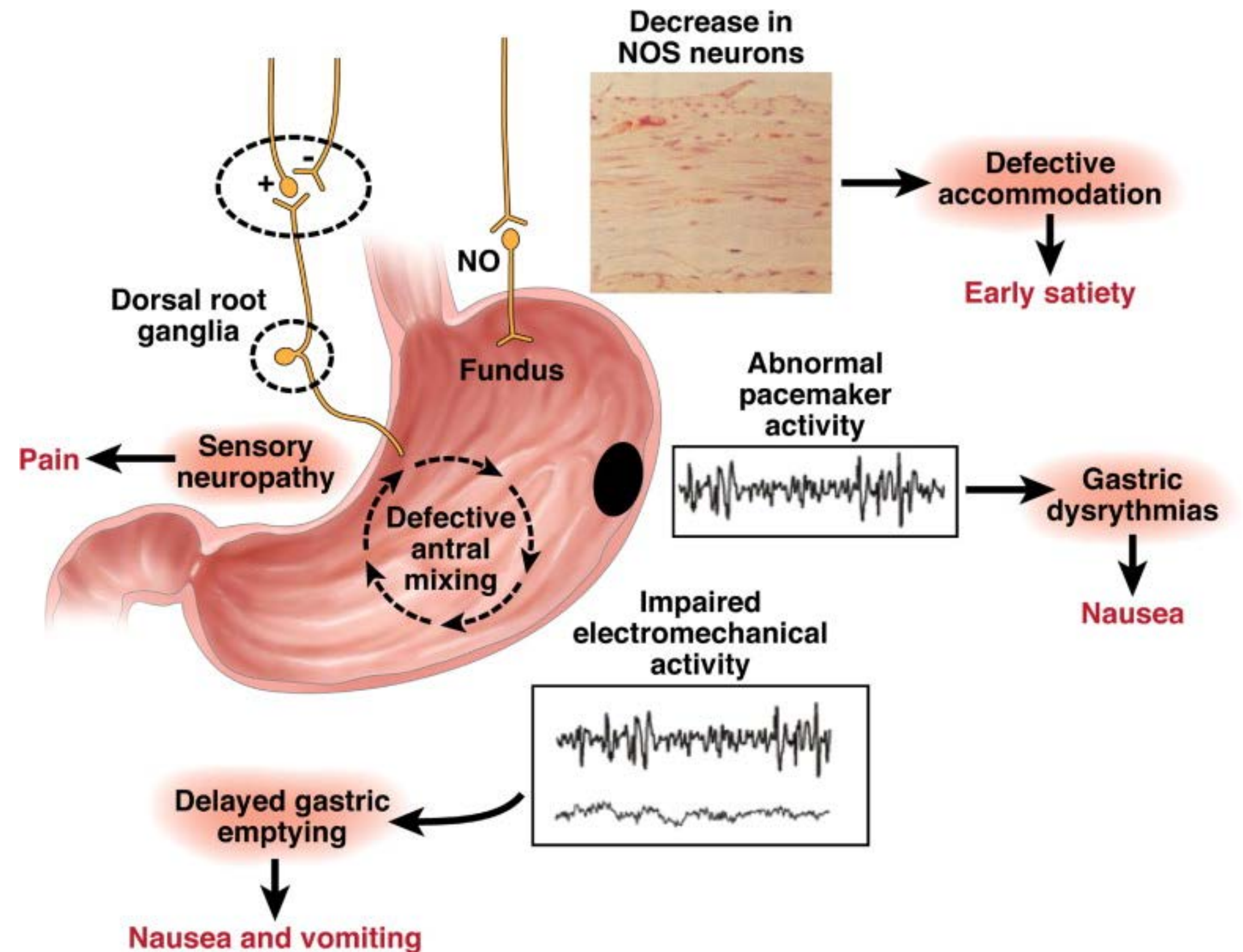
- Aetiology
 - Idiopathic (IG) - 36%
 - Diabetes (DP) - 29%
 - Post surgery (PSG) - 13%,
 - Post (viral) infectious, Thyroid, Parkinson's ..
- Symptoms:
 - **Nausea and vomiting**
 - Dyspeptic symptoms



Gastroparesis

Pathophysiology

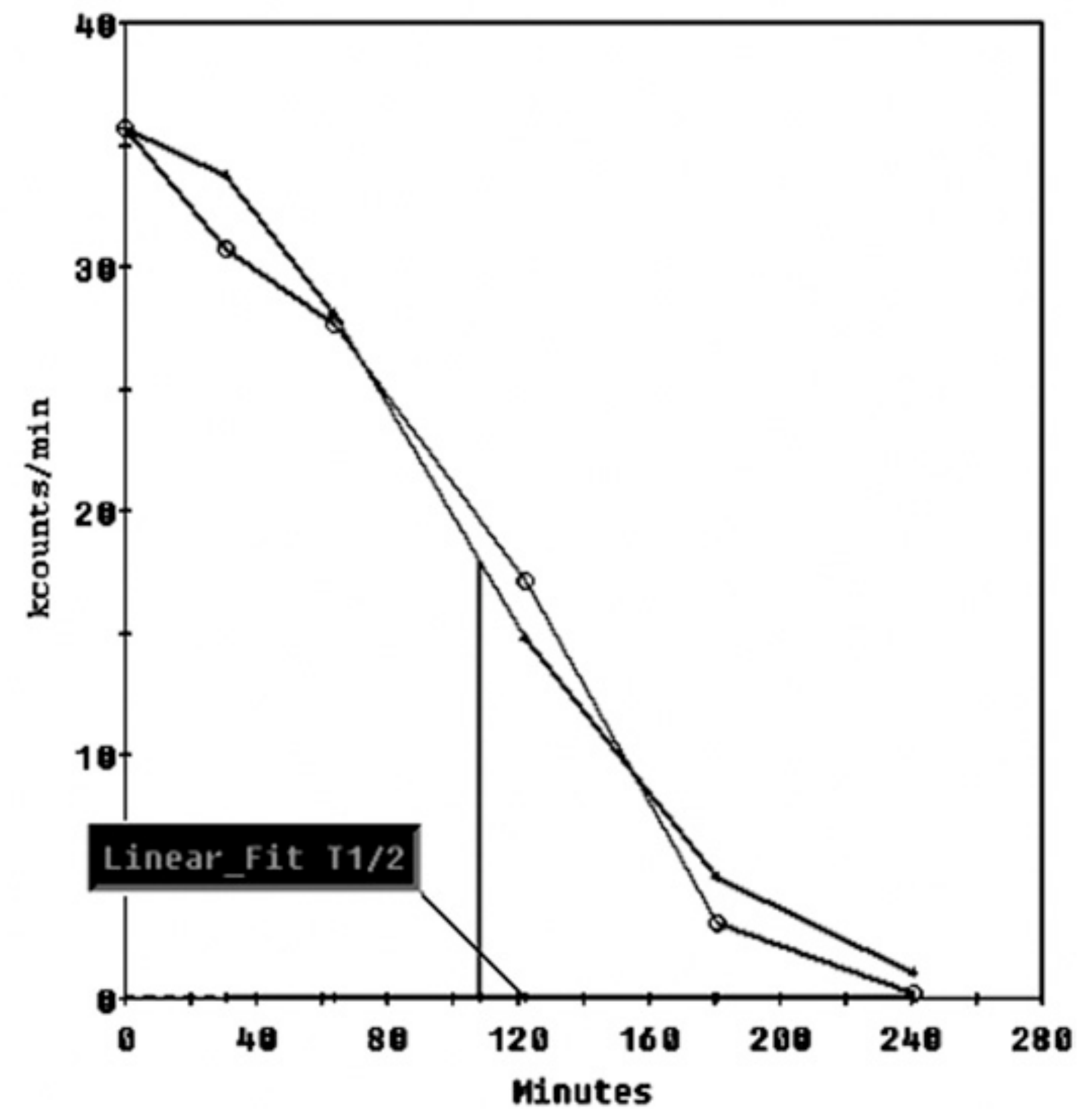
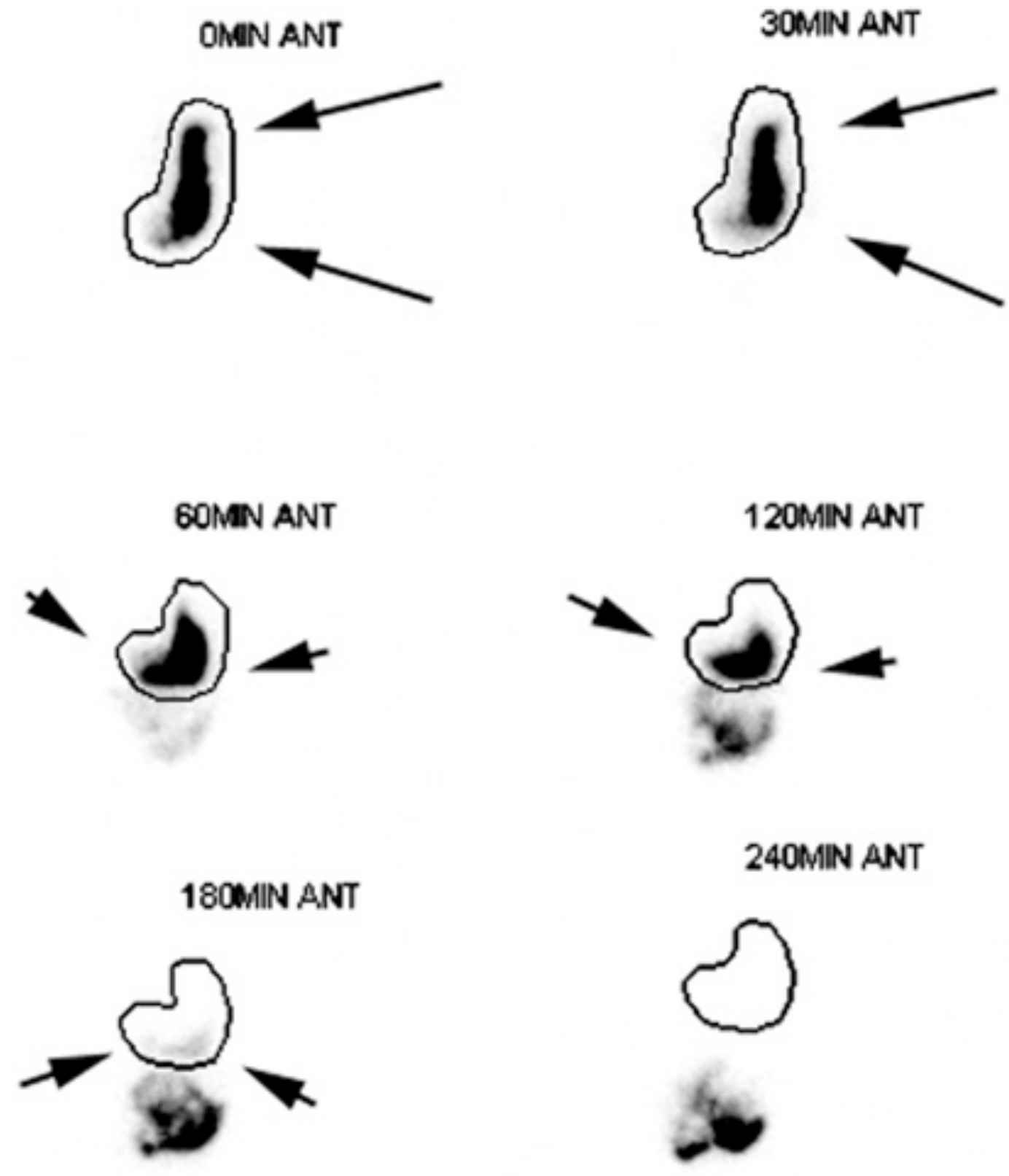
- Delayed GE
 - **Decreased accommodation**
 - **Visceral Hypersensitivity**
- Loss of intestinal cells Cajal
- Loss of enteric nerves
- Loss of vagal nerve stimulation



Gastroparesis

Diagnosis

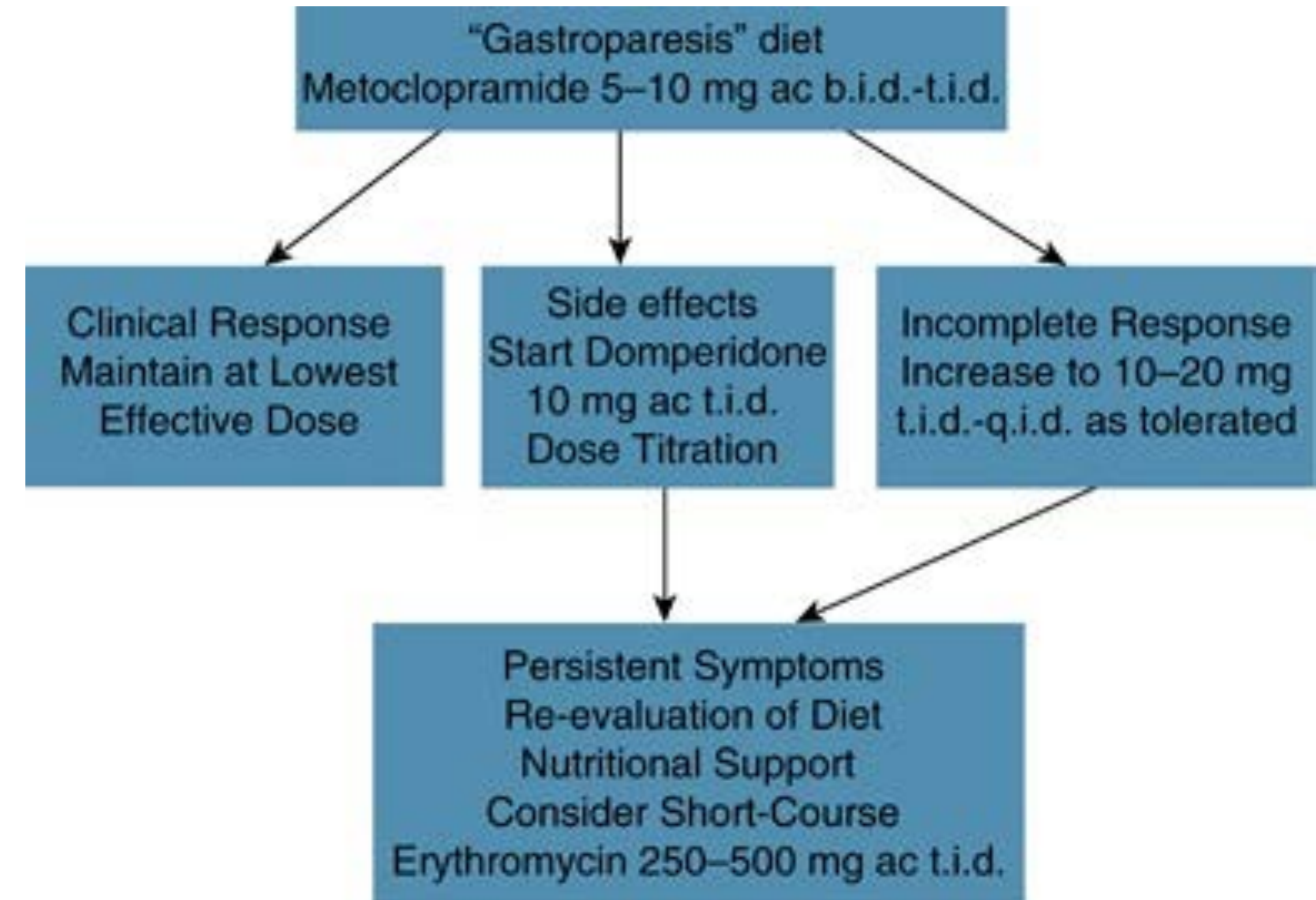
- Scintigraphy
 - Solid phase meal, **>10% retention 4hrs**
- Wireless Motility Capsule (WMC)
 - pH, pressure, temp: **gastric residence time**
- C-13 Breath testing
 - ^{13}C -Octanoate/ ^{13}C -spirulina



Gastroparesis

Medical Management

- Fluid, electrolyte, nutritional support
- Dietary advice: **low fat, low residue**
- Oral > **enteral alimentation
- Glycemic control in DG
- Pharmacotherapy: antiemetic/prokinetics



** Indications >10% weight loss
DG: Diabetic Gastroparesis

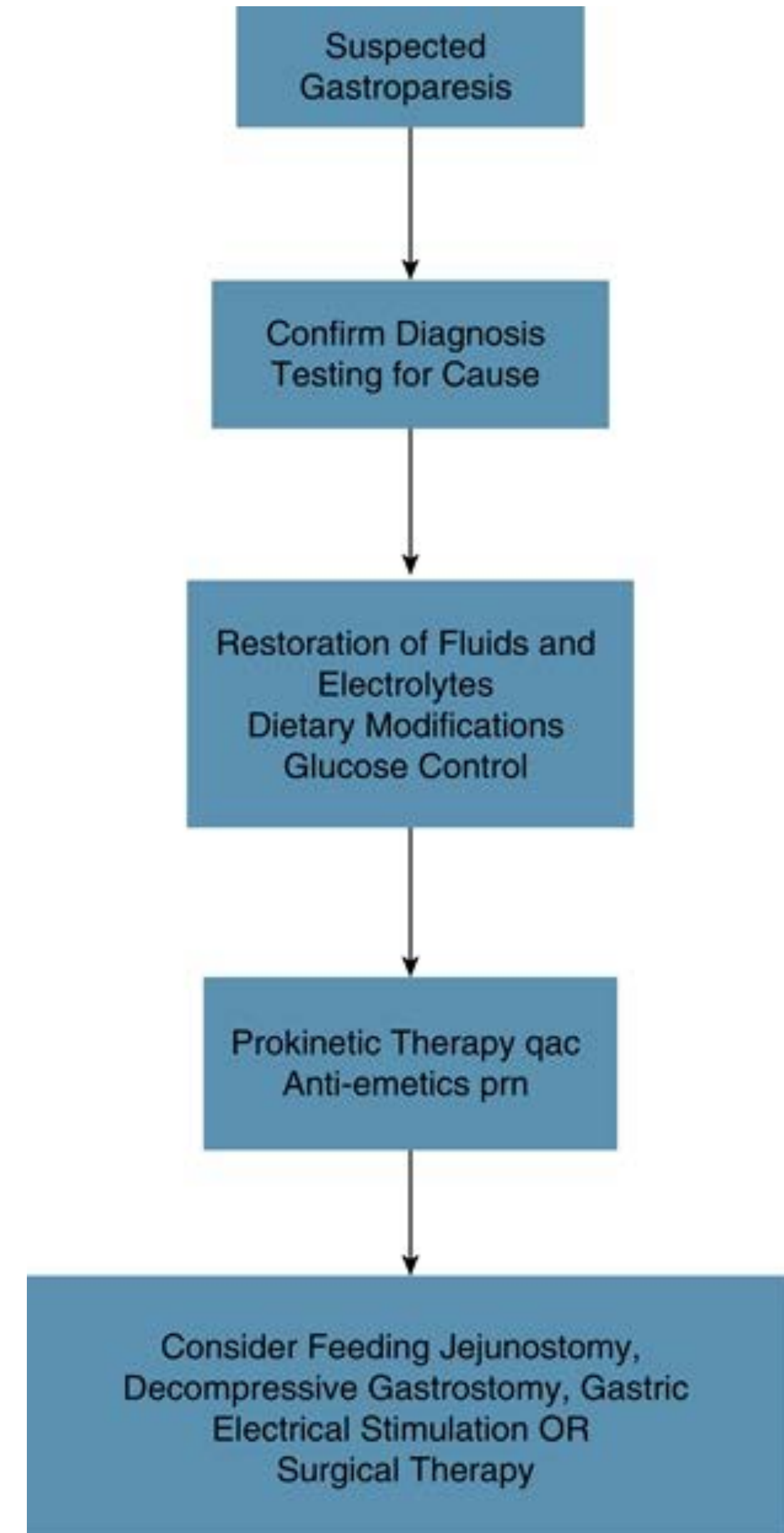
Adverse effects
Metoclopramide TD
Domperidone QT, PRL

Gastroparesis

Endoscopic/ Surgical

- Gastric electrical stimulation (GES)
- **Intrapyloric injection Botox
- Endoscopic
 - Venting gastrostomy
 - PEG-J, PEJ
 - Endoscopic pyloroplasty, stent placement
 - Gastric-POEM
- Surgical
 - Circle pyloroplasty
 - Gastrectomy

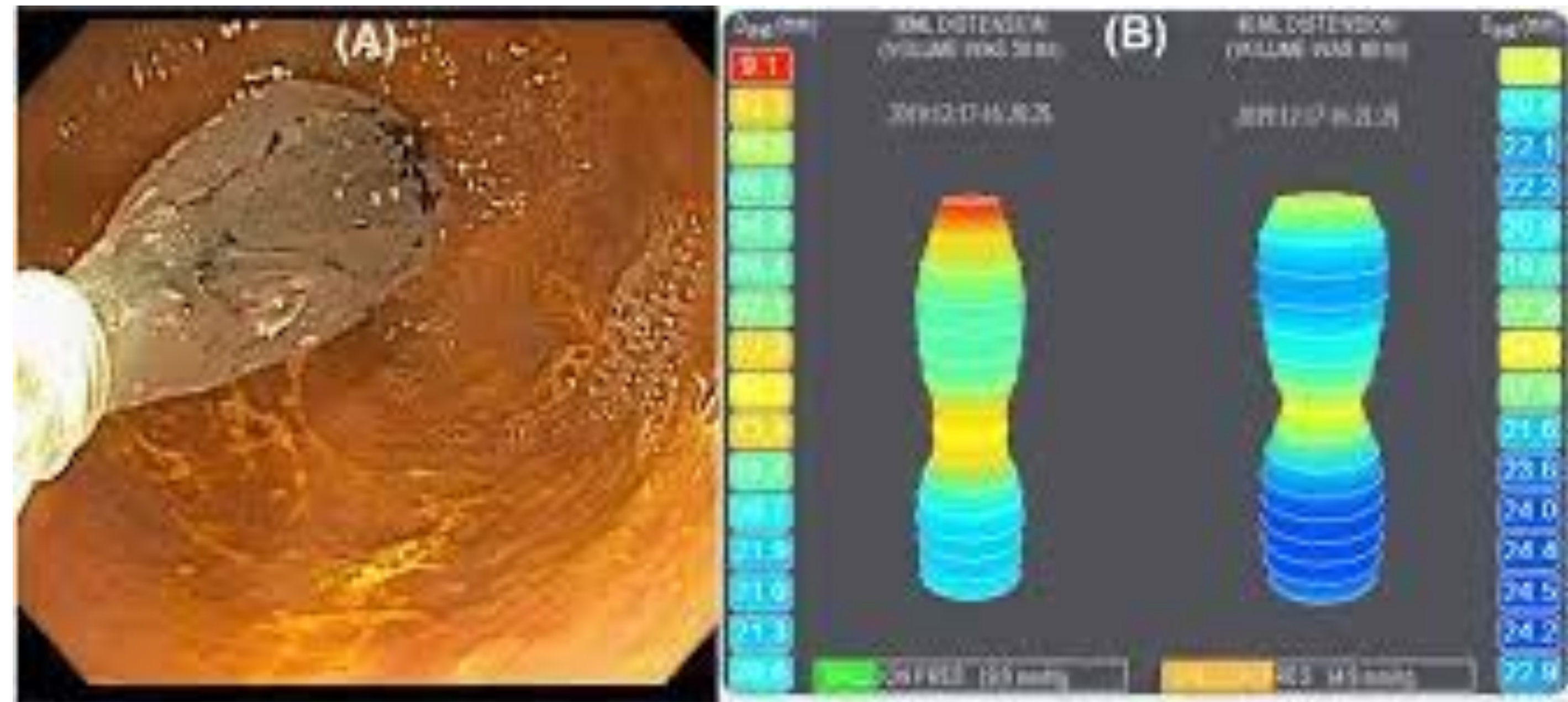
** Not enough data, functional pylorospasm
Prediction of poor response
PEG, PEG-J



Gastroparesis

Other investigations/therapies

- Antroduodenal manometry, FLIP
- Adjuncts
 - Acupuncture
 - Herbal remedies
 - Iberogast STW₅



Jehangir DDS 2021

Camilleri, AJG 2013

Functional Vomiting Syndromes

- Chronic nausea and vomiting syndrome (CNVS)
- Cyclical Vomiting Syndrome (CVS)*
 - Cannabinoid Hyperemesis Syndrome (CHS)**
- 2% Prevalence, esp younger, IBS patients
- **No delayed GE**
- Spp therapy: Antiemetics, BZD, 5HT₁ agonist *

Table 1. Rome IV Criteria for Functional Nausea and Vomiting Disorders²

CNVS	CVS ^a
Must include all of the following: <ol style="list-style-type: none"> 1) Bothersome nausea occurring at least 1 day per week and/or ≥ 1 vomiting episodes per week 2) Self-induced vomiting, eating disorders, regurgitation, or rumination are excluded 3) No evidence of organic, systemic, or metabolic diseases that is likely to explain the symptoms on routine investigations (including at upper endoscopy) 4) The symptoms have to be present for the past 3 months with onset at least 6 months prior 	Must include all of the following: <ol style="list-style-type: none"> 1) Stereotypical episodes of acute-onset vomiting lasting < 1 wk 2) At least 3 discrete episodes in the prior year and 2 episodes in the past 6 months, occurring at least 1 week apart 3) Absence of vomiting between episodes, although milder symptoms can be present 4) The symptoms have to be present for the past 3 months with onset at least 6 months prior

* “abdominal migraine” triptans

** Hot water bath during acute attacks

GE - Gastric emptying

CNVS, chronic nausea and vomiting syndrome; CVS, cyclic vomiting syndrome.

^aCannabinoid hyperemesis syndrome is a variant of CVS, in which the symptoms are attributed to chronic cannabis use and resolve after stopping cannabis.

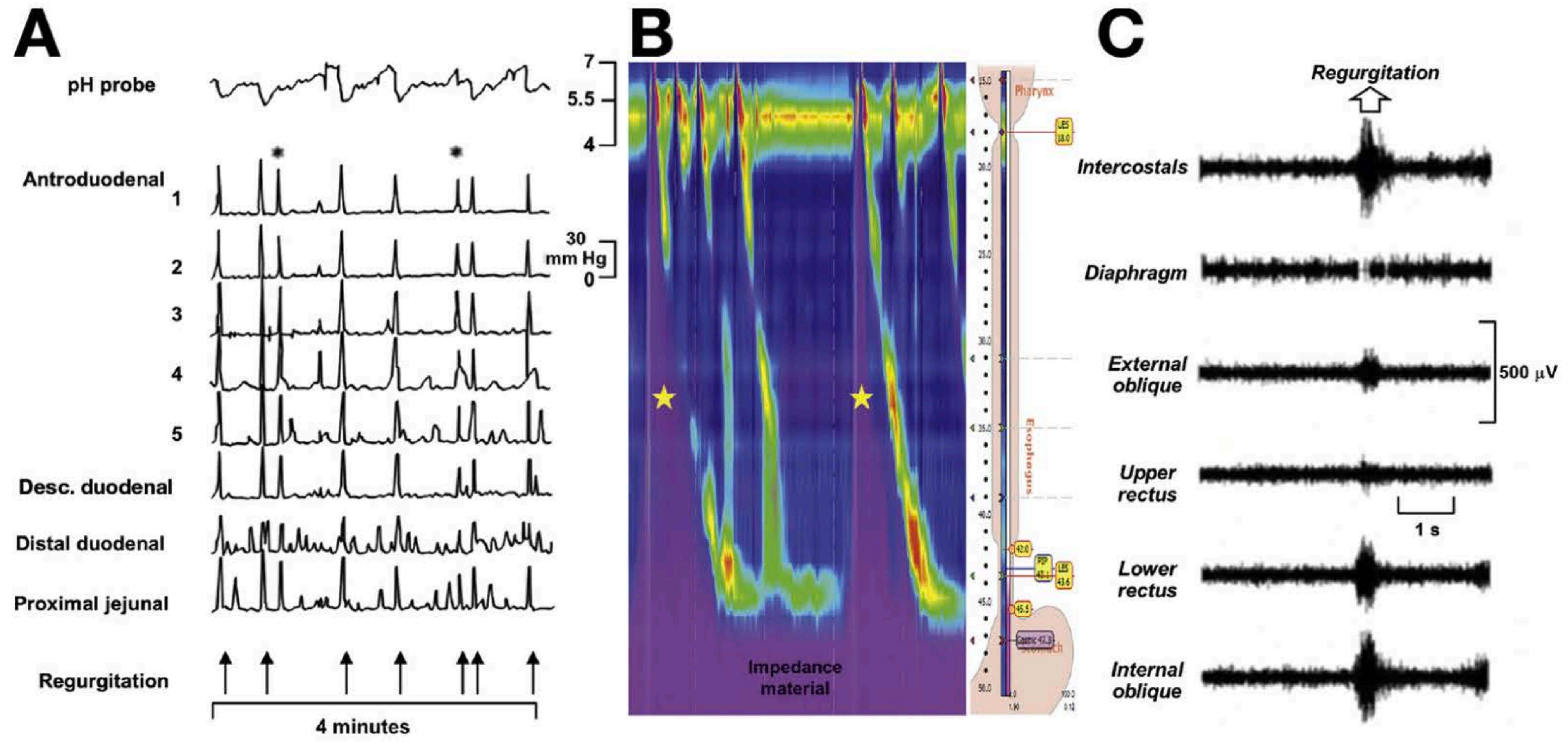
Rumination Syndrome

- Repetitive, effortless **regurgitation** of recently ingested food
- Children > adults > adolescents
- Fibromyalgia
- Pathophysiology: increased intra-abdominal pressure and negative intrathoracic gradient
- Diagnosis: clinical, gastroduodenal manometry, EMG, HRIM

EMG electromyography
HRIM High resonance
impedance manometry

Table 1. Clinical Diagnosis of Rumination in Adults

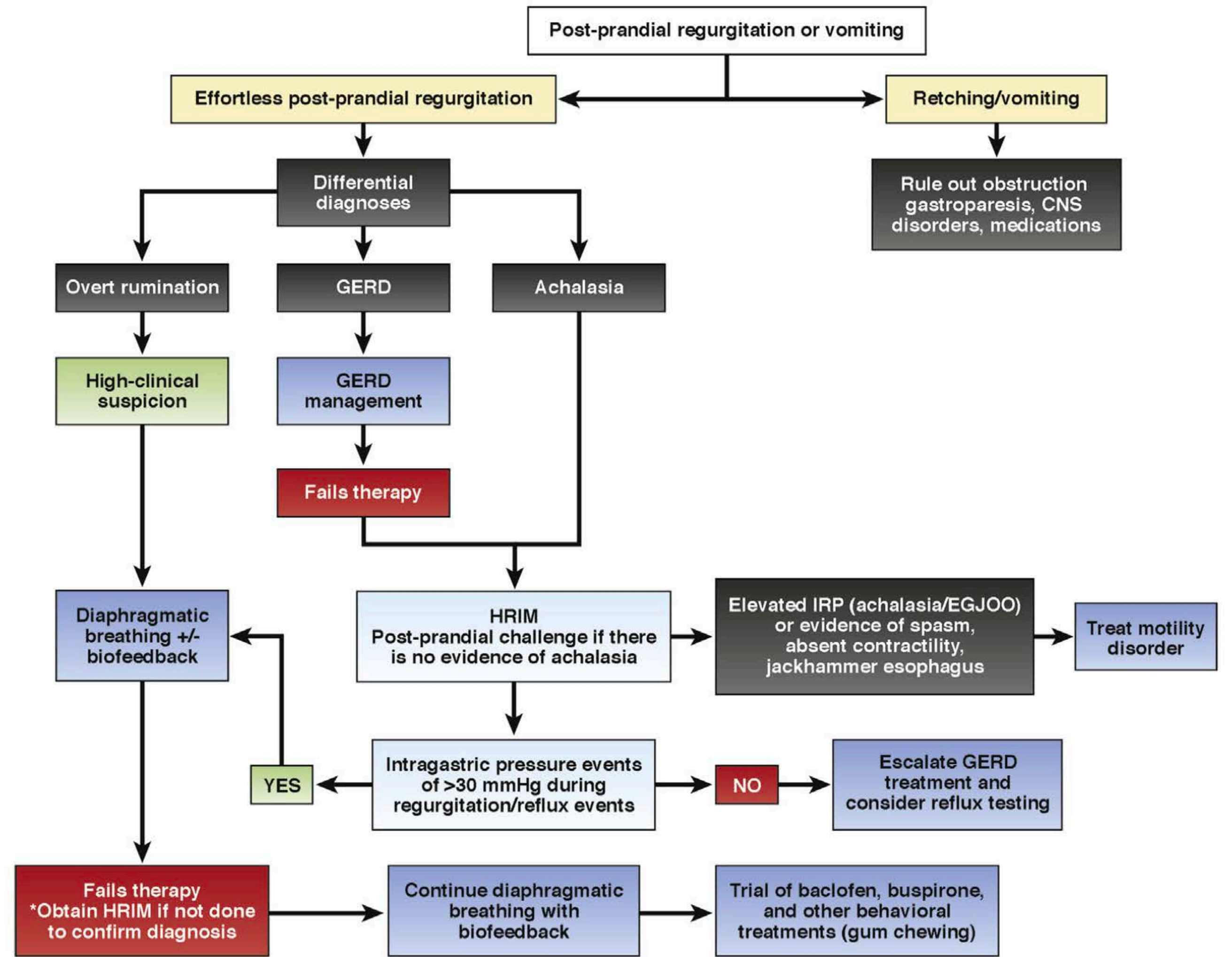
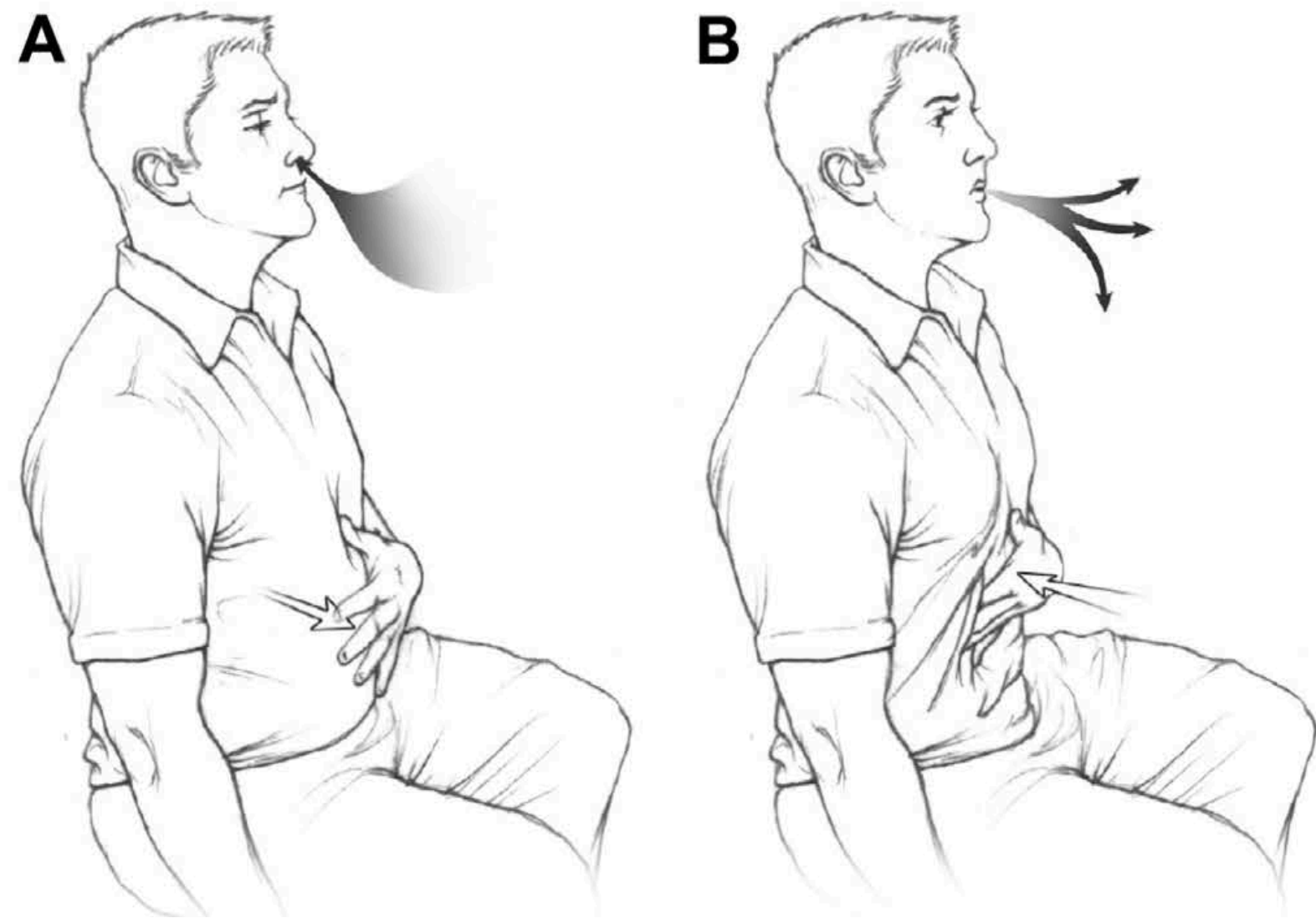
Rome IV criteria
Persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spitting or remastication and swallowing
Regurgitation is not preceded by retching
Supportive criteria
Effortless regurgitation events usually are not preceded by nausea
Regurgitant contains recognizable food that might have a pleasant taste
The process tends to cease when the regurgitated material becomes acidic
Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis



A Characteristic R waves
 B Rumination events - asterix
 C EMG activation EMG

Management

- Counselling, rule out differentials
- Diaphragmatic breathing
 - +/- Biofeedback
- Medical: Levosulpiride (D2 antagonist) Baclofen
- Surgical: Funduplication



Bulimia Nervosa

DSM V Criteria

- Recurrent episodes **binge eating**
 - Excessively large meal
 - Feeling of sense of loss of control during episode
- Recurrent inappropriate **compensatory behaviour**
 - Purging, laxatives, diuretics, enemas
- Occurring at least **once a week**, for at least **three months**
- Body **image (unduly) influenced** by weight and shape
- Episodes do not occur in concurrence with AN

Bulimia Nervosa

Cont

- High index suspicion
 - Good history, clinical signs
 - Excessive exercise, dieting despite injury/illness
- Other methods of purging
 - Coeliac disease/ diabetics
- Medical Effects of purging
 - Dental caries, cardio-/neuro-/nephrotoxicity



RDH Mag

Medications

Chemotherapy

- Chemotherapy (PCNV/CINV)
 - Acute, delayed, anticipatory
- Risk factors
 - Female, poor SE status, pre-chemo nausea,
 - pre-PCNV, highly emetogenic chemo
- Pre-emptive antiemetic therapy
- Consider Radiation - induced symptoms

PCNV Post-chemo nausea and vomiting
 CINV Chemo induced nausea and vomiting

Table 1. Emetogenic Levels of Intravenously Administered Antineoplastic Agents.*

Level 1 (minimal risk, <10%)	Level 2 (low risk, 10–30%)	Level 3 (moderate risk, 31–90%)	Level 4 (high risk, >90%)
Bevacizumab	Bortezomib	Carboplatin	Carmustine
Bleomycin	Cetuximab	Cyclophosphamide	Cisplatin
Busulfan	Cytarabine (≤ 100 mg/m ² of body-surface area)	(≤ 1.5 g/m ²)	Cyclophosphamide
Cladribine	Docetaxel	Cytarabine (>1 g/m ²)	(>1.5 g/m ²)
Fludarabine	Etoposide	Daunorubicin	Dacarbazine
Vinblastine	Fluorouracil	Doxorubicin	Mechlorethamine
Vincristine	Gemcitabine	Epirubicin	Streptozocin
Vinorelbine	Ixabepilone	Idarubicin	
	Lapatinib	Ifosfamide	
	Methotrexate	Irinotecan	
	Mitomycin	Oxaliplatin	
	Mitoxantrone		
	Paclitaxel		
	Pemetrexed		
	Temsirolimus		
	Topotecan		
	Trastuzumab		

* Percentages indicate the risk of vomiting with intravenously administered antineoplastic agents in the absence of antiemetic prophylaxis.

Table 2. Doses and Schedules of Antiemetic Agents with a High Therapeutic Index.*

Drug	Dose	
	Before Chemotherapy (day 1)	After Chemotherapy
Dolasetron (Anzemet, Sanofi-Aventis)	Intravenous dose: 100 mg or 1.8mg/kg of body weight; oral dose: 100 mg	Oral dose: 100 mg on days 2 and 3 for MEC with potential for delayed emesis
Granisetron (Kytril, Roche)	Intravenous dose: 1 mg or 0.01 mg/kg; oral dose: 2 mg	Oral dose: 1 mg twice daily on days 2 and 3 for MEC with potential for delayed emesis
Ondansetron (Zofran, GlaxoSmithKline)	Intravenous dose: 8 mg or 0.15 mg/kg; oral dose: 24 mg for HEC, 8 mg twice daily for MEC	Oral dose: 8 mg twice daily on days 2 and 3 for MEC with potential for delayed emesis
Palonosetron (Aloxi, MGI Pharma)	Intravenous dose: 0.25 mg	
Tropisetron (Navoban, Novartis)	Intravenous dose: 5 mg; oral dose: 5 mg	Oral dose: 5 mg on days 2 and 3 for MEC with potential for delayed emesis
Dexamethasone		
With aprepitant or fosaprepitant	Intravenous dose: 12 mg; oral dose: 12 mg	Oral dose: 8 mg on days 2–4 for HEC, 8 mg on days 2 and 3 for MEC with potential for delayed emesis
Without aprepitant or fosaprepitant	Intravenous dose: 20 mg for HEC, 8 mg for MEC; oral dose: 20 mg for HEC, 8 mg for MEC	Oral dose: 8 mg twice daily on days 2–4 for HEC, 8 mg on days 2 and 3 for MEC with potential for delayed emesis
Fosaprepitant (Emend [for injection], Merck)	Intravenous dose: 115 mg	Oral dose: 80 mg on days 2 and 3
Aprepitant (Emend [capsules], Merck)	Oral dose: 125 mg	Oral dose: 80 mg on days 2 and 3

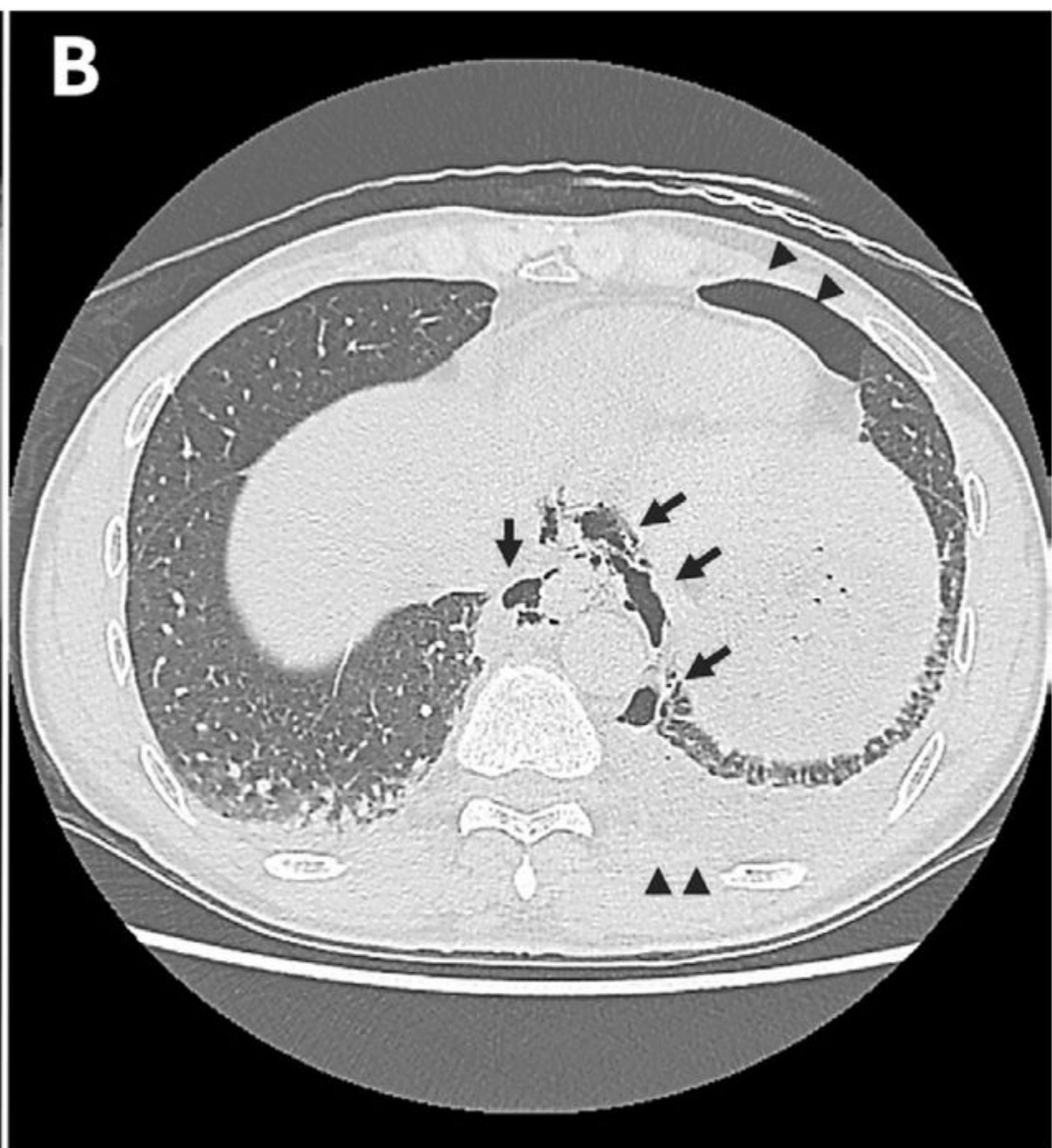
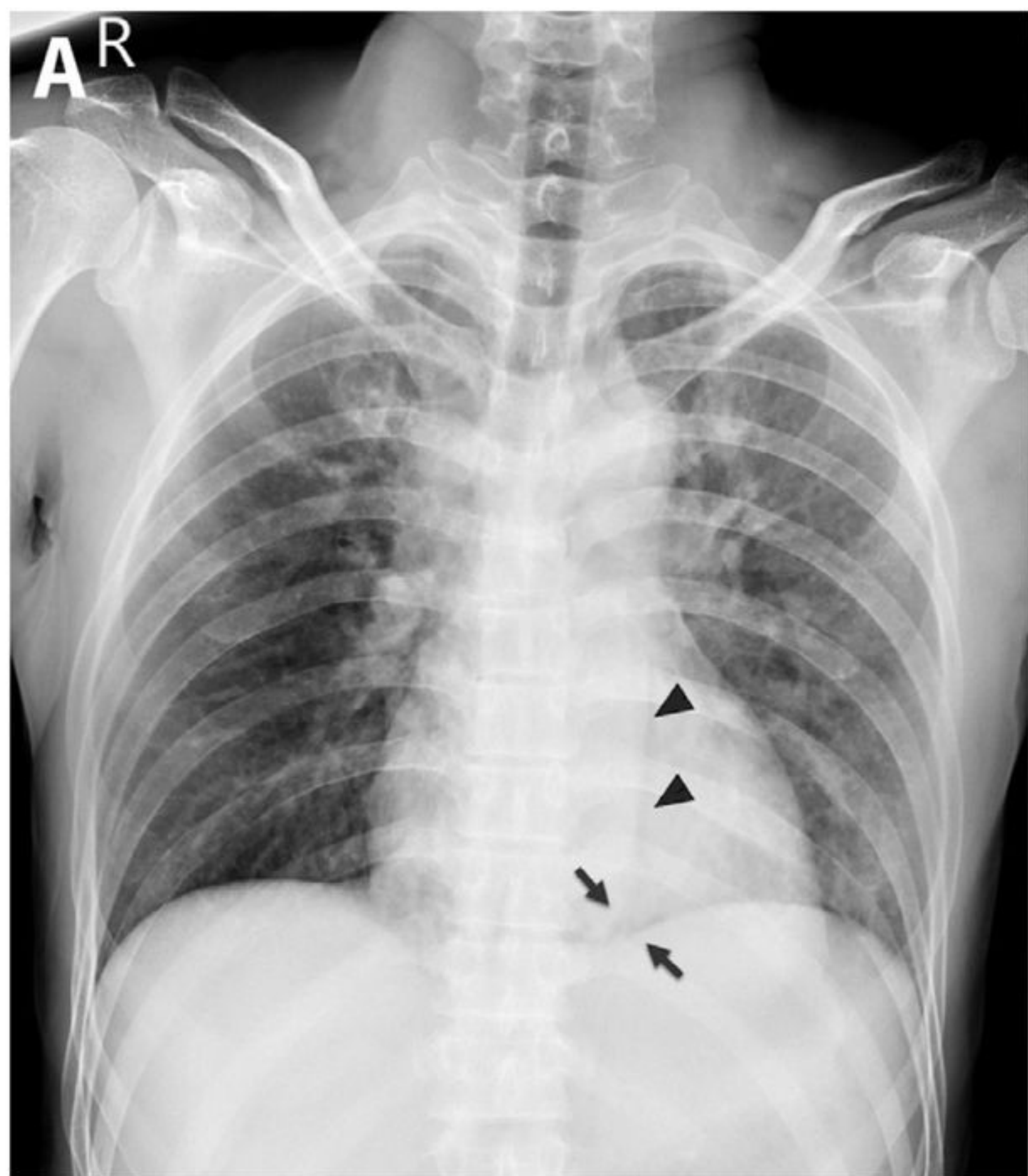
* HEC denotes highly emetogenic chemotherapy, and MEC moderately emetogenic chemotherapy.

Table 4. Recommended Antiemetic Treatment for Single-Day, Intravenously Administered Chemotherapy.

Emetogenic Level	Risk of Emesis %	Antiemetic Regimen	
		Before Chemotherapy (day 1)	After Chemotherapy
1	<10 (minimal)	None	None
2	10–30 (low)	Dexamethasone or prochlorperazine	None
3	31–90 (moderate)		
	For anthracycline plus cyclophosphamide	5-HT ₃ -receptor antagonist, dexamethasone, and aprepitant*	Aprepitant on days 2 and 3 or dexamethasone on days 2 and 3*
	For other regimens	5-HT ₃ -receptor antagonist and dexamethasone†	5-HT ₃ -receptor antagonist or dexamethasone on days 2 and 3
4	>90 (high)	5-HT ₃ -receptor antagonist, dexamethasone, and aprepitant*	Dexamethasone on days 2–4 and aprepitant on days 2 and 3*

* The recommendations for aprepitant are supported by level 1 evidence (data from at least one high-quality randomized trial).⁹¹

† The recommendation for 5-HT₃-receptor antagonist and dexamethasone administered on day 1 with emetogenic level 3 chemotherapy is supported by level 1 evidence.



Complications of vomiting

- Emetic injuries to stomach and oesophagus
 - Oesophagitis
 - Oesophageal tears - Mallory Weis
 - Boerhaave Syndrome
 - Dental caries
- Spasm of glottis, aspiration pneumonitis
- Fluid and electrolyte abnormalities

Summary

- NV common GI symptoms
- Vast differential
- Beware definitions
- High index suspicion
- Beware complications

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Thank You