# Dyspepsia

ERWIN BUDI CAHYONO

# Start ……

# Doa minta ilmu bermanfaat

اللَّهُمَّ إِنِّى أَسْأَلُكَ عِلْمًا نَافِعًا
وَرِزْقًا طَيِّبًا وَعَمَلاً مُتَقَبَّلاً

"Ya Allah, aku memohon pada-Mu ilmu yang bermanfaat, rezeki yang thoyyib dan amalan yang diterima."

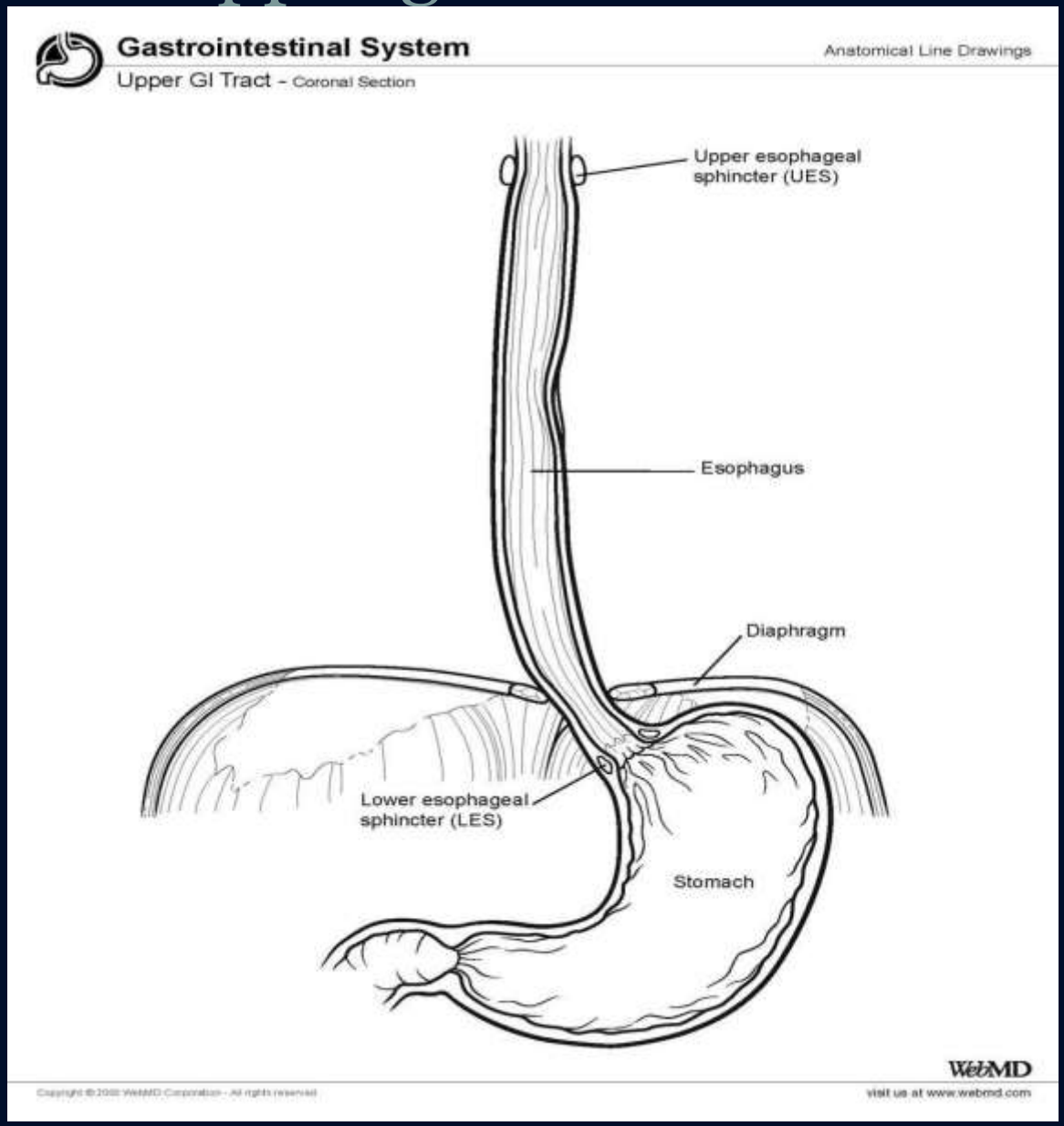
(HR. Ibnu Majah no. 925, shahih)

# DYSPEPSIA

- DEFINITION :

  Symptoms like pain or nausea in epigastrium accompanied by disgust, vomit, bloat, easy to full, fullness or nitre, which is suspected come from the abnormality of  upper gastro-intestinal tractus.

# Anatomi upper gastrointestinal tractus



# Definition

An international committee of clinical investigators developed the following revised definition (Rome III criteria) of functional dyspepsia for research purposes, which can also be applied to clinical practice :

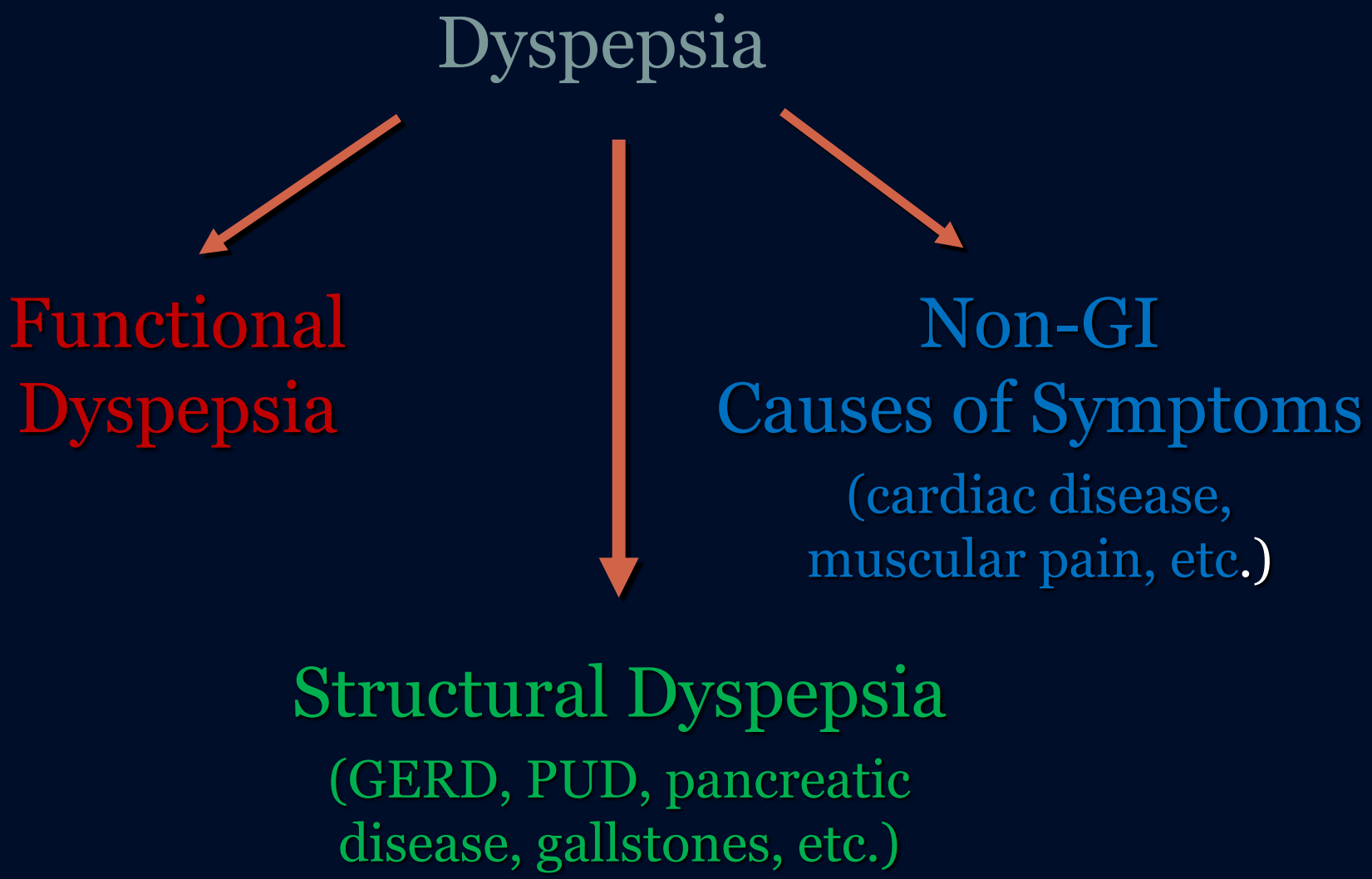
One or more of:

- Bothersome postprandial fullness
- Early satiation
- Epigastric pain
- Epigastric burning

AND

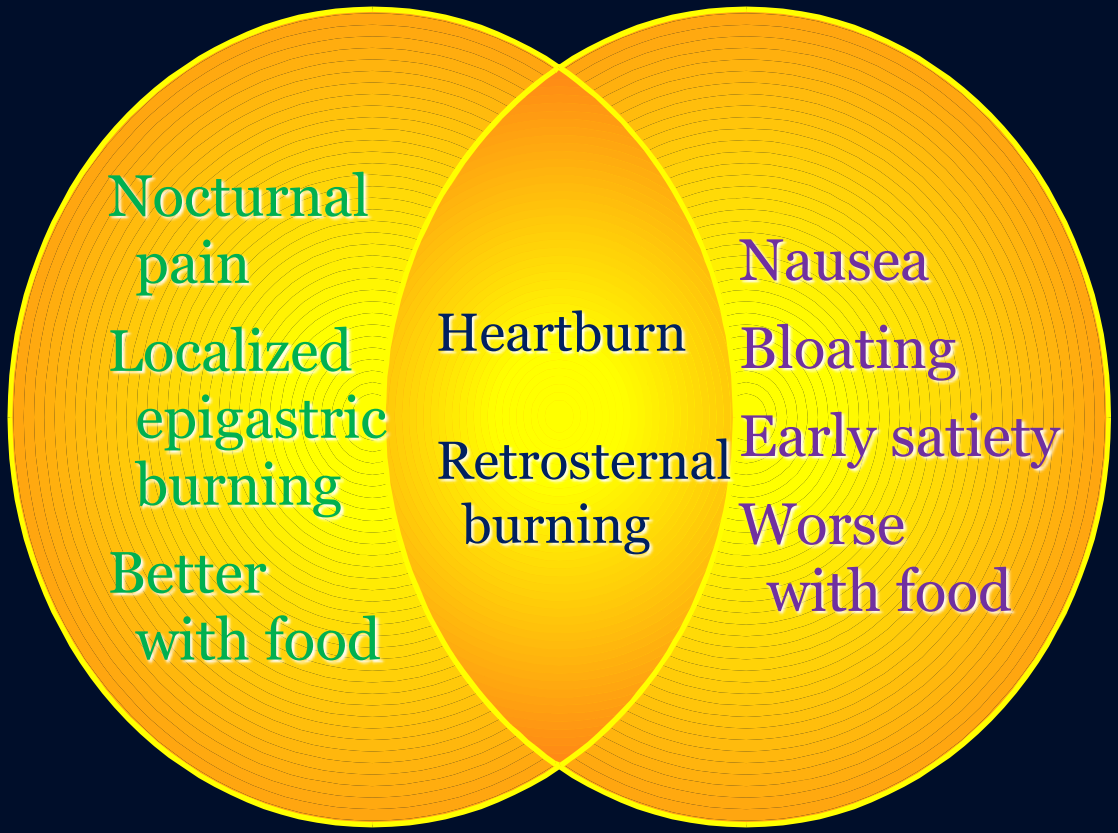
- No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms.

- These criteria should be fulfilled for the last three months with symptom onset at least six months before diagnosis.
- Two subcategories (postprandial distress syndrome and epigastric pain syndrome) were also recognized but their main value lies currently in research.

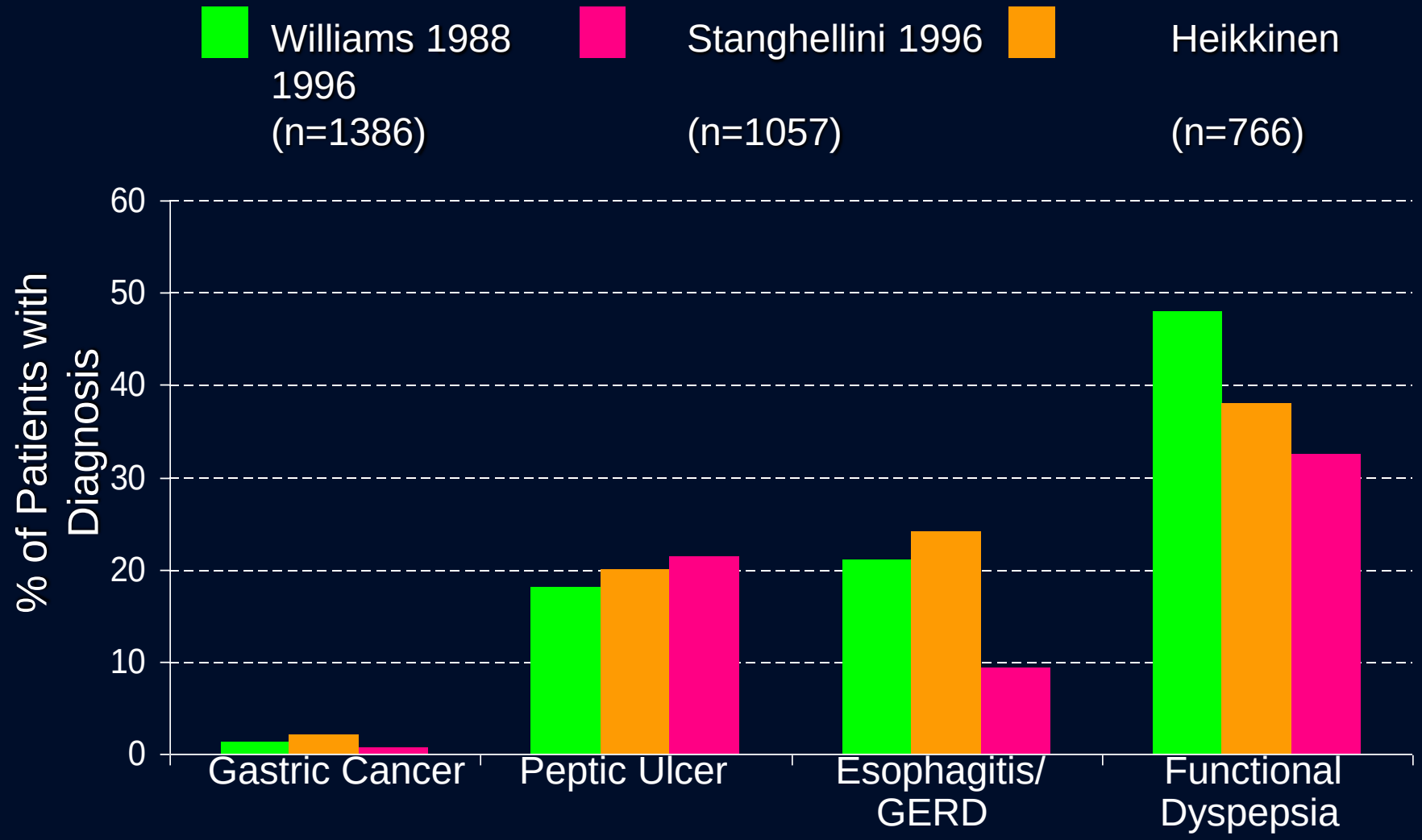

Dyspepsia
Functional Dyspepsia
Non-GI Causes of Symptoms
(cardiac disease, muscular pain, etc.)
Structural Dyspepsia
(GERD, PUD, pancreatic disease, gallstones, etc.)

# Symptoms of Functional Dyspepsia

Ulcer-like Dominant ⟷ Dysmotility-like Dominant



# Major Causes of Dyspepsia



In addition to age, the following "alarm symptoms" raise the suspicion of gastric malignancy:

- Unintended weight loss
- Persistent vomiting
- Progressive dysphagia
- Odynophagia
- Anemia with/or Hematemesis
- Palpable abdominal mass or lymphadenopathy
- Unexplained iron deficiency anemia
- Persistent vomiting Family history of upper gastrointestinal cancer Previous gastric surgery Jaundice

# Rome III
# B. Functional Gastroduodenal Disorders

- B1 Functional Dyspepsia
  - B1a: postprandial distress syndrome (PDS)
  - B1b: epigastric pain syndrome (EPS)

- Dyspepsia has been classified according to the characteristics of symptoms that predominate. However, such classification systems do not reliably correlate with underlying pathophysiologic mechanisms .

# Pathophysiology

- The pathophysiology of functional dyspepsia is unclear. Research has focused upon the following factors:
- Gastric motor function
- Visceral sensitivity
- Helicobacter pylori infection
- Psychosocial factors

# Gastric motor function

- Normal gastrointestinal motor function is a complex series of events that requires coordination of the sympathetic and parasympathetic nervous systems, neurons within the stomach and intestine, and the smooth muscle cells of the gut.
- Abnormalities in this process can lead to a delay in gastric emptying (gastroparesis), a disorder that is characterized by complaints of nausea, vomiting, early or easy satiety, bloating, and weight loss.

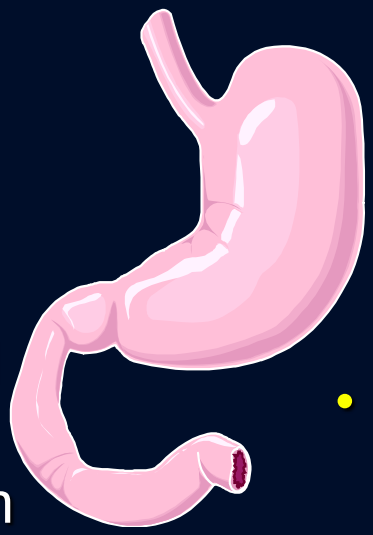
# Gastric motor function

- Delayed gastric emptying has been found in approximately 30 percent of patients complaining of dyspepsia. However, there is generally a poor correlation between these entities.
- Antral hypomotility has been found in a similar proportion of patients, but its relationship to symptoms is also uncertain.
- Up to 10 percent of patients have fast gastric emptying, which may also be associated with dyspepsia.

- The relationship between gastric motor function and gastric volumes may be important.

- A study of 57 adults suggested that symptoms were associated with low fasting gastric volume and faster gastric emptying.

# Pathogenesis & Pathophysiology of Dyspepsia



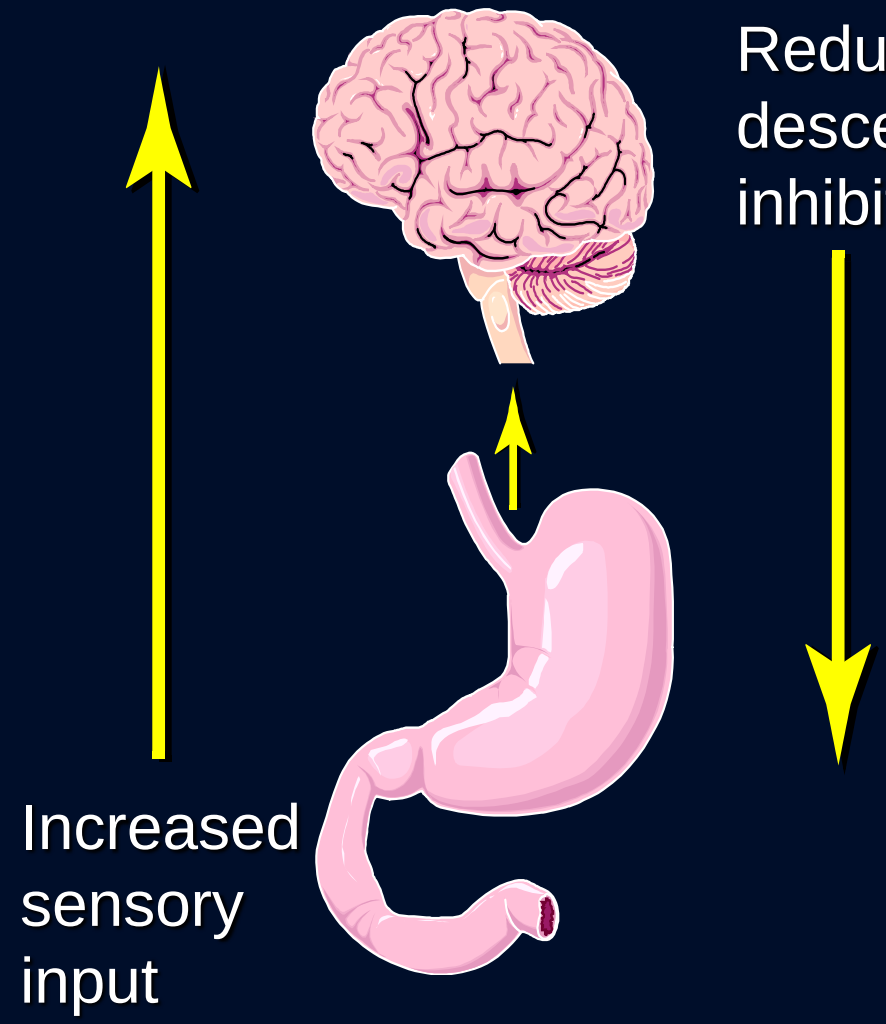
- Increased visceral perception
- Altered motility

- Behavioural factors
- Gastritis
- *H. pylori* infection

# Gastric motor function

- Gastric compliance is lower in patients with functional dyspepsia than in healthy controls .
- In one study, for example, postprandial gastric accommodation was evaluated in 40 patients with functional dyspepsia and 35 healthy controls .
- Impaired gastric accommodation was found in 40 percent of patients with functional dyspepsia (compared to the lower range observed in controls), and was associated with early satiety and weight loss.
- Treatment with sumatriptan (a 5-hydroxytryptamine agonist that causes fundus relaxation) restored gastric accommodation and improved meal-induced satiety.

# Mechanisms Underlying Increased Sensory Perception



# Visceral sensitivity

- Enhanced visceral sensitivity or visceral hyperalgesia refers to a lowered threshold for induction of pain by gastric distension in the presence of normal gastric compliance. Visceral hypersensitivity has been consistently demonstrated in patients with functional dyspepsia .

# Visceral sensitivity

- In a representative study, for example, the sensorial responses (on a 0 to 10 perception score) and the gastric tone responses (by electronic barostat) to either gastric accommodation or to cold stress were measured in 20 patients with functional dyspepsia and 20 healthy controls.
- The mechanical accommodation of the stomach to gastric distention (compliance) was similar in patients and controls (52 versus 57 mL/mmHg).

# Visceral sensitivity

- However, isobaric gastric distention elicited more upper abdominal discomfort in the patients with dyspepsia (perception scores 4.7 versus 1.1).

- Similar findings were noted in another report in which reduced perceptual thresholds or altered pain referral were found in 20 of 23 patients (87 percent) with functional dyspepsia compared to only 2 of 10 patients (20 percent) with organic causes of dyspepsia.

# Visceral sensitivity

- Patients with dyspepsia are also more sensitive to acid infusion into the duodenal bulb (which produced nausea and fewer duodenal pressure waves) compared to controls . .
- Visceral hypersensitivity, which has also been proposed as an etiologic factor in irritable bowel syndrome, appears to occur independent of delayed gastric emptying.
- In contrast, somatic sensitivity (as measured by transcutaneous electrical stimulation of the hand) is normal in these patients.

# Visceral sensitivity

- — . Patients with dyspepsia are also more sensitive to acid infusion into the duodenal bulb (which produced nausea and fewer duodenal pressure waves) compared to controls.
- Visceral hypersensitivity, which has also been proposed as an etiologic factor in irritable bowel syndrome, appears to occur independent of delayed gastric emptying. In contrast, somatic sensitivity (as measured by transcutaneous electrical stimulation of the hand) is normal in these patients.
- Both mechanoreceptor dysfunction (peripheral mechanism) and aberrant processing of afferent input in the spinal cord or brain (central mechanism) may play a role in the pathophysiology of visceral hypersensitivity. The latter mechanism is supported by the observation that sympathetic autonomic activity enhances the perception of gut distension in normal subjects.

# Helicobacter pylori infection

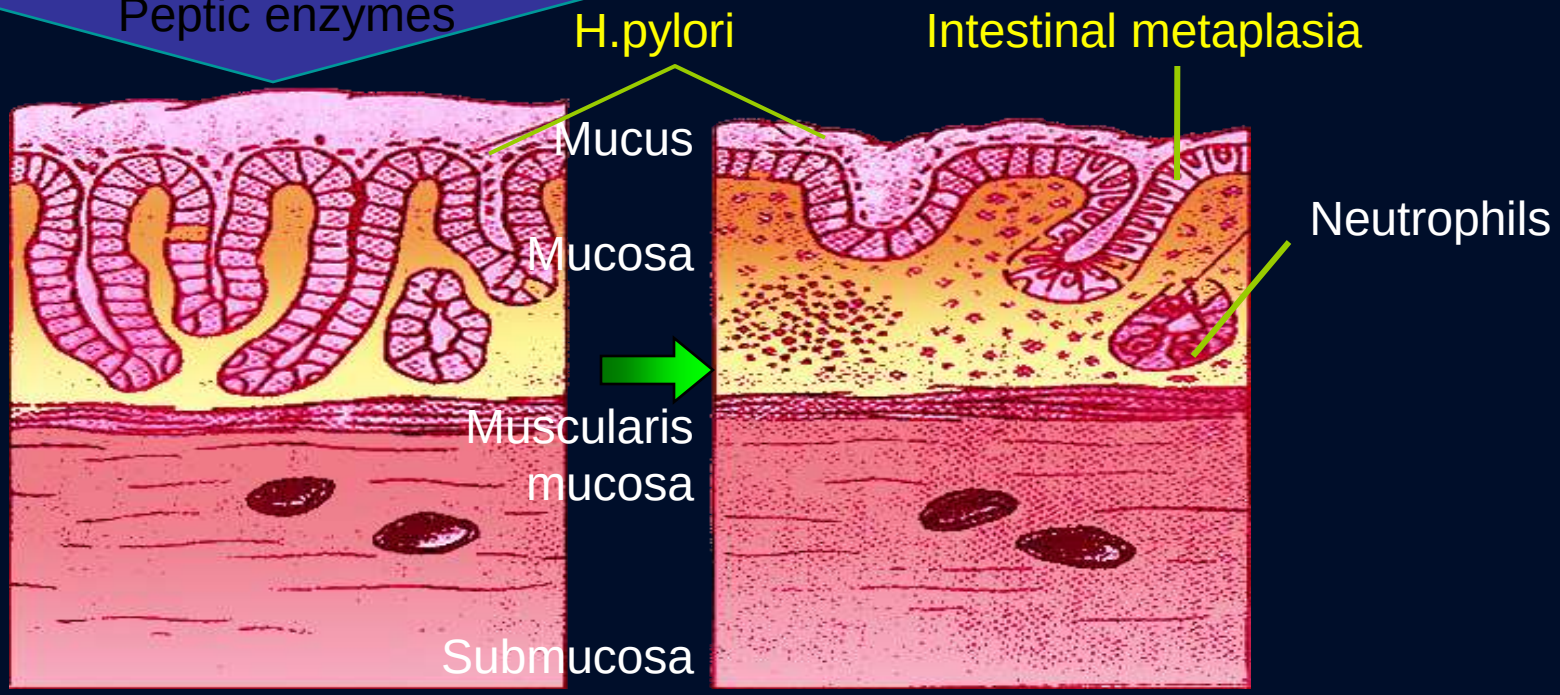
- Although a possible role for H. pylori infection in functional dyspepsia is suggested by several potential pathogenic mechanisms, a clear association among these factors, H. pylori, and functional dyspepsia has not been established.
- H. pylori is a well known cause of chronic active gastritis. However, gastritis is probably not the cause of symptoms in most patients with functional dyspepsia. A consistent link between findings on endoscopy and dyspepsia has not been found.
- H. pylori may cause altered smooth muscle dysfunction due to the induction of an inflammatory response or by the initiation of an antibody response.
- The inflammatory response induced by H. pylori may lower the discomfort threshold to gastric distension by causing alterations in the enteric or central nervous system. However, visceral hypersensitivity did not appear to be important in at least one study which found that H. pylori positive and negative patients with functional dyspepsia had no difference in the perception of mechanically-induced gastric distension.

# Gastric mucous layer in normal gaster and gastritis

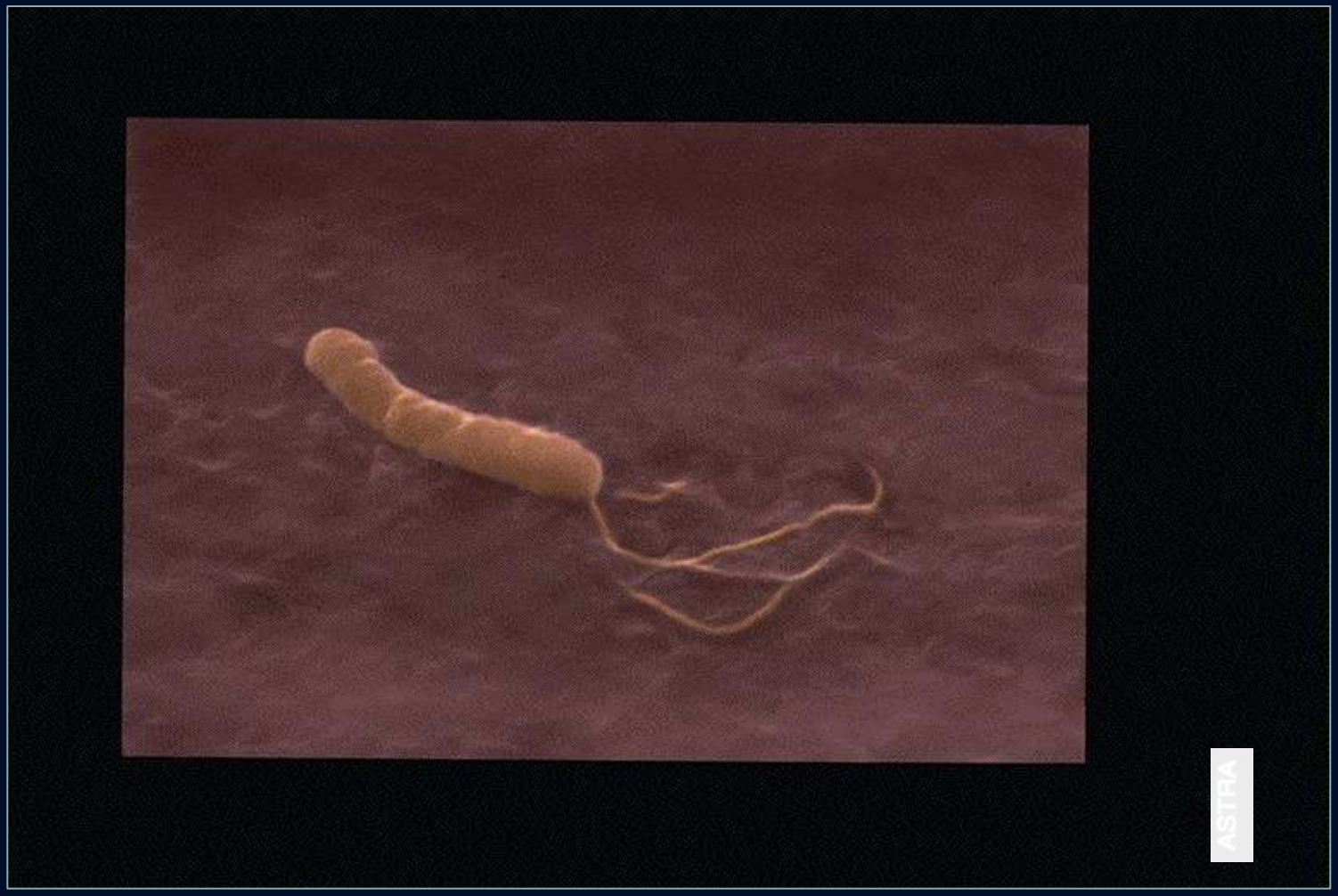
INFECTION

Damaging influences :
Helicobacter pylori
urease
toxins
Gastric acidity
Peptic enzymes

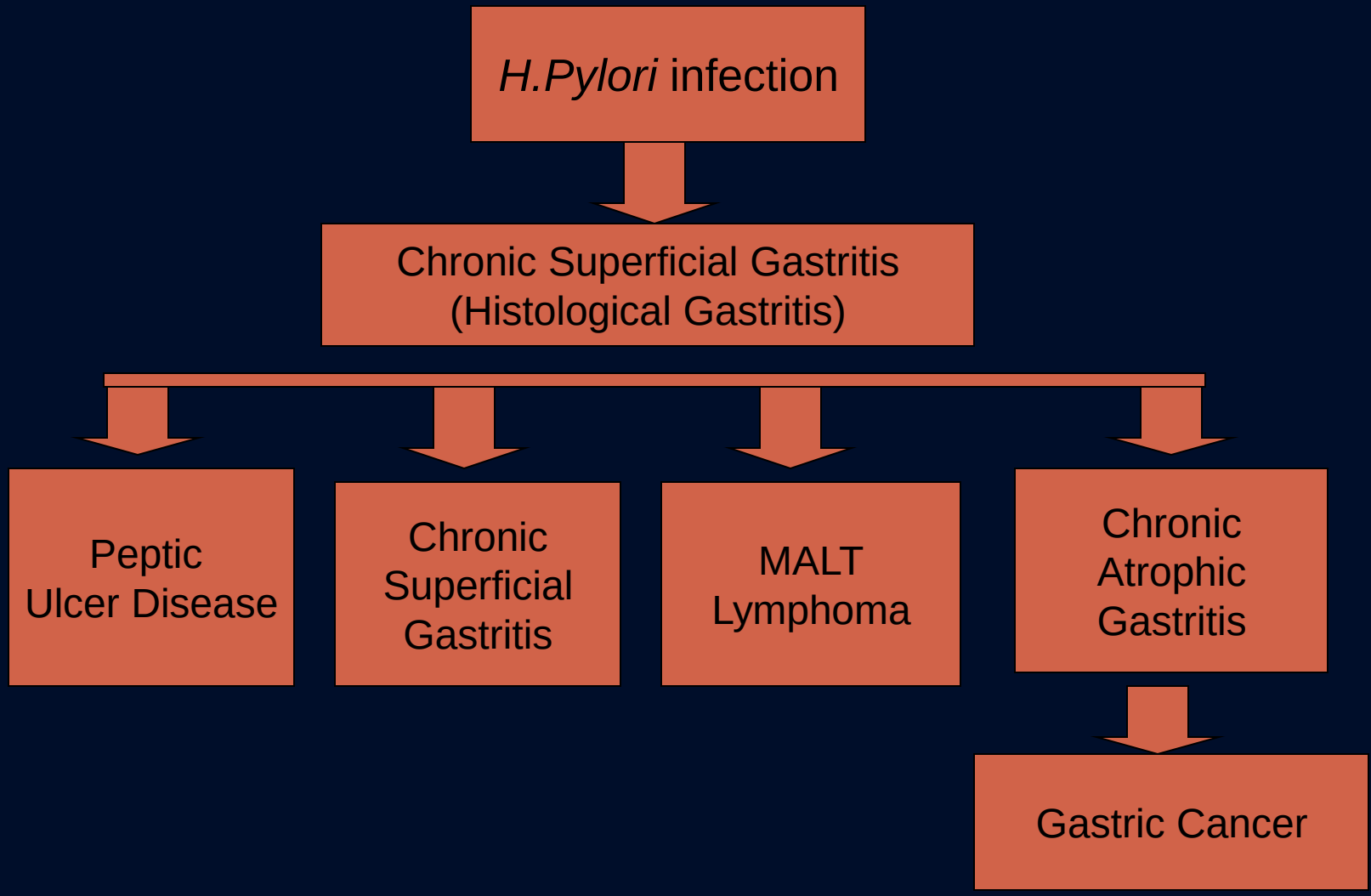
CHRONIC GASTRITIS
Atrophy
Intestinal metaplasia
Lymphoid aggregates
Neutrophil infiltrates



# Gambar *H. pylori*



# Natural History of *H.Pylori* Infection



# TREATMENT

- — Treatment of patients with functional dyspepsia is controversial and often disappointing, a sharp contrast to the therapy of peptic ulcer disease. The goal is to help patients accept, diminish, and cope with symptoms rather then eliminate them.
- Similar to patients with irritable bowel syndrome, the most important aspects of the therapy of functional dyspepsia include explanation, validation that the symptoms are not imaginary, evaluation and management of relevant psychosocial factors, and dietary advice

- . Medications that might contribute to symptoms (such as NSAIDs) should be substituted or discontinued whenever possible.
- Drug therapy, which is based upon the putative pathogenetic mechanisms described above, may help some patients. Several systematic reviews

- Prokinetic agents were more effective than placebo (relative risk reduction (RRR) of 50 percent, 95% CI 30 to 65 percent).
- H2 receptor antagonists were more effective than placebo (RRR of 30 percent, 95% CI 4 to 48 percent).
- Proton pump inhibitors and bismuth salts were more effective than placebo, but the benefits were of marginal statistical significance.
- There was no statistically significant benefit from antacids, bismuth, or sucralfate.

- **Proton pump inhibitors —** Several studies have evaluated the efficacy of proton pump inhibitors (PPIs) in nonulcer dyspepsia and at least two meta-analyses have been performed that reached similar conclusions. A meta-analysis of seven studies (with a total of 3725 patients) found that PPIs were significantly more effective than placebo for reducing symptoms (relative risk reduction of about 10 percent, 95% CI 2.7-17.3 percent).
- The largest study, included 1262 patients who were randomly assigned to receive omeprazole (20 or 10 mg daily) or placebo for four weeks. Complete symptom relief was observed significantly more often with both doses of omeprazole compared with placebo (38 and 36 versus 28 percent, respectively). The benefit was greatest in those with ulcer-like or reflux-like symptoms; there was no significant benefit in patients with dysmotility-like symptoms.

# SUMMARY AND RECOMMENDATIONS

- The following summarizes an approach in patients who have been diagnosed as having functional dyspepsia.
- There is no drug that has consistently been proven to be effective for functional dyspepsia.
- We suggest patients be reassured and given dietary and psychosocial advice as needed ( **Grade 2C**).
- We suggest that patients who do not respond to the above be given a trial of acid suppression ( **Grade 2B**).
- The benefit of acid suppression may be greatest in those who have reflux-like symptoms. We suggest a four- to eight-week trial of a proton pump inhibitor.

# SUMMARY AND RECOMMENDATIONS

- H. pylori eradication benefits only a minority of patients. Guidelines issued by the American College of Gastroenterology and Canadian Association of Gastroenterology recommend H. pylori eradication in patients with functional dyspepsia

ACG and CAG Clinical Guideline: Management of Dyspepsia

Paul M. Moayyedi, MB, ChB, PhD, MPH, FACG[1], Brian E. Lacy, MD, PhD, FACG[2], Christopher N. Andrews, MD[3], Robert A. Enns, MD[4], Colin W. Howden, MD, FACG[5] and Nimish Vakil, MD, FACG[6]

*Am J Gastroenterol* advance online publication, 20 June 2017; doi:10.1038/ajg.2017.154

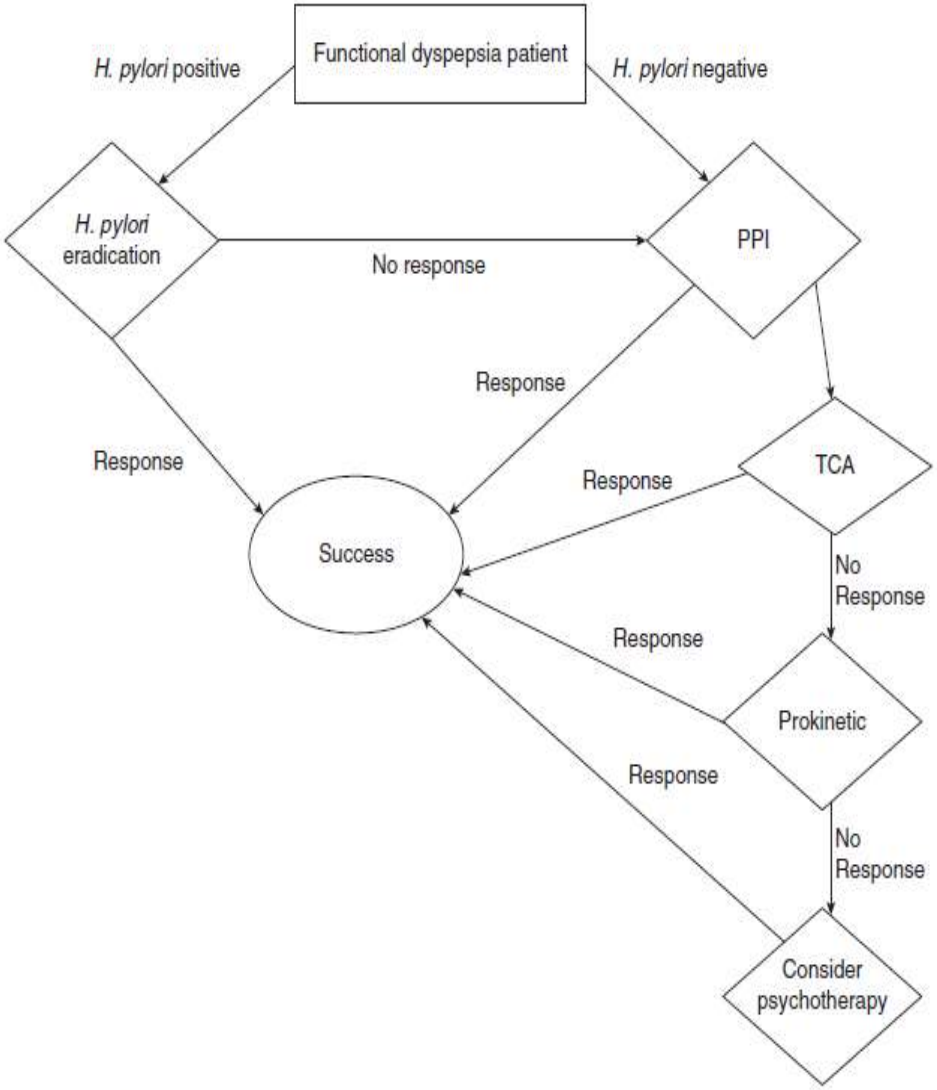



Figure 2. Algorithm for the treatment of functional dyspepsia.

- Prokinetics can occasionally help, for example cisapride, domperidone and metoclopramide.
- We generally limit a trial of metoclopramide (5 to 10 mg three times daily one-half an hour before meals and at night for about four weeks) to young patients in whom other therapies have failed.


DYSPEPSIA MANAGEMENT

$H_2$ receptor antagonists and prokinetics in dyspepsia: a critical review

P Bytzer

*Gut* 2002;**50**(Suppl IV):iv58–iv62

- However, because of potential side effects of therapy, we suggest the decision to eradicate H. pylori consider the individual patient's clinical features, including response to other therapy and psychological factors ( **Grade 2B**).

- Some patients may respond to an antidepressant drug. We suggest an antidepressant trial for patients in whom PPI therapy has failed, especially if there is insomnia, which might also respond ( **Grade 2C**).
- We generally use a tricyclic antidepressant drug or trazadone, starting with a low dose (eg, amitriptyline 10 mg at bedtime, desipramine 25 mg at bedtime, or trazadone 25 mg at bedtime) and increasing after a few days, usually to only two or three times these doses.

TERIMA KASIH