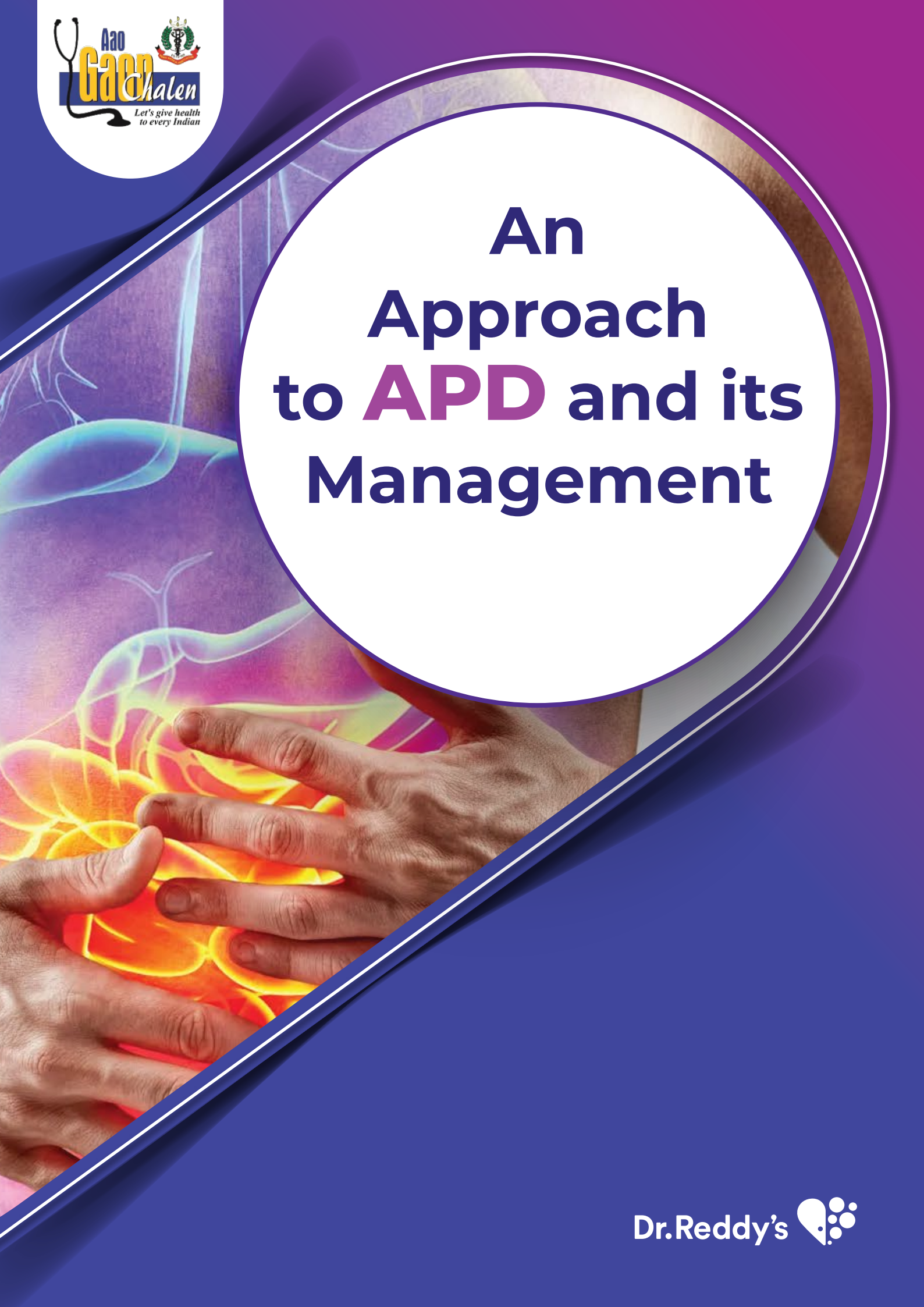
Aao Gaon Chalen
Let's give health to every Indian



# An Approach to APD and its Management

Dr.Reddy's

# Table of Contents

## Panel Members

| Doctor's Name | Specialty |
|---|---|
| Dr Ajay Gupta | Gastroenterologist |
| Dr J S Barve | Gastroenterologist |
| Dr Jayesh Lele | General Practitioner |
| Dr Jayprakash Modi | Orthopaedic Surgeon |
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| Dr Sushil Narang | Gastroenterologist |

# Message From President and Hon. Secretary-General

The Indian Medical Association (IMA) is thrilled to unveil a collaborative endeavour by a distinguished consortium of 6 revered doctors, encompassing a Gastroenterologist, Orthopaedic Surgeon, General Practitioner, Consultant Physician, General Surgeon, and Rheumatologist. This adept group has convened to craft an insightful booklet titled "Streamlining Management of Acid Peptic Disorders in India."

As the premier professional association of modern medicine practitioners in India, boasting a membership of around 4 lakhs across 1760 local branches, IMA has consistently dedicated itself to the advancement of medical and allied sciences. Our core objective remains the promotion of improved public health and medical education in India, a mission to which this project significantly contributes.

In a recent collaborative assembly, specialists in Gastroenterology, Orthopaedics, General Practice, Internal Medicine, Surgery, and Rheumatology engaged in in-depth discussions on pivotal aspects concerning the management of Acid Peptic Disorders. This publication strives to demystify the complexities of managing Acid Peptic Disorders, providing valuable insights for medical practitioners across India.

We are pleased to declare the successful completion of this joint effort, and the ultimate recommendations from the meeting have been disseminated. This resource is now available for perusal by all healthcare professionals, and we extend our heartfelt appreciation to the panel members for their substantial contributions. Crafted to function as a pragmatic guide for General Practitioners, Consultants, and specialists, these recommendations aim to facilitate effective management of Acid Peptic Disorders within the Indian healthcare landscape.

IMA remains resolute in its commitment to being the preeminent platform for the medical fraternity, fostering academic discourse, championing the cause of the medical profession, and addressing the healthcare needs of the populace. We express our gratitude to the dedicated panel members for their expertise and unwavering dedication to advancing medical knowledge and enhancing healthcare practices.

**Dr Sharad Kumar Agrawal**
National President, 2022-23
Indian Medical Association

**Dr Anilkumar J Nayak**
Hony. Secretary General (HSG), 2022-23
Indian Medical Association

# Introduction

## Definition and overview

Acid peptic disorders (APD) are the result of distinctive but overlapping pathogenic mechanisms leading to either excessive acid secretion or diminished mucosal defence. It usually includes conditions such as gastroesophageal reflux disease (GERD) and peptic ulcer disease (PUD), dyspepsia and gastritis. Acid-related disorders influence the quality of life and productivity of afflicted patients and are common and important causes of morbidity and mortality.[1]

GERD occurs when there is a frequent or chronic backflow (reflux) of stomach acid and digestive juices into the esophagus. Primary cause of GERD: weakened lower esophageal sphincter (LES), which normally acts as a barrier between the stomach and the esophagus. Symptoms of GERD: heartburn, nausea, vomiting, regurgitation, chest pain, difficulty swallowing, and chronic cough.[2]

PUD (Peptic ulcer disease): formation of ulcers, in the lining of the stomach or duodenum. usually caused by an imbalance between stomach acid and the protective factors that shield the stomach lining. The most common cause of PUD is infection with Helicobacter pylori (H. pylori) bacteria. Symptoms of PUD: abdominal pain, indigestion, bloating, nausea, and vomiting.[3]

Dyspepsia: chronic or recurrent pain or discomfort centered in the upper abdomen, mainly in or around the midline as opposed to the right or left hypochondrium (Rome III Criteria). Discomfort is characterized by or associated with fullness, early satiety, bloating, or nausea. Dyspepsia may or may not be related to eating meals.[4]

Gastritis: A general term used to describe diffuse inflammatory lesions in the mucosal layer of the stomach. can be subdivided as erosive, nonerosive, or specific types based on histological features and those found endoscopically.[5]

The management of acid peptic disorders typically involves a combination of lifestyle modifications, medications to reduce acid production or neutralize acid, mucoprotective agents, eradication of H. pylori infection, and in some cases, surgical interventions. Treatment aims to relieve symptoms, promote healing of ulcers, prevent complications, and improve the overall quality of life for individuals affected by this condition. PPIs are the main stay of treatment for APD like Esomeprazole, Rabeprazole & Omeprazole amongst others.[1]

## Epidemiology

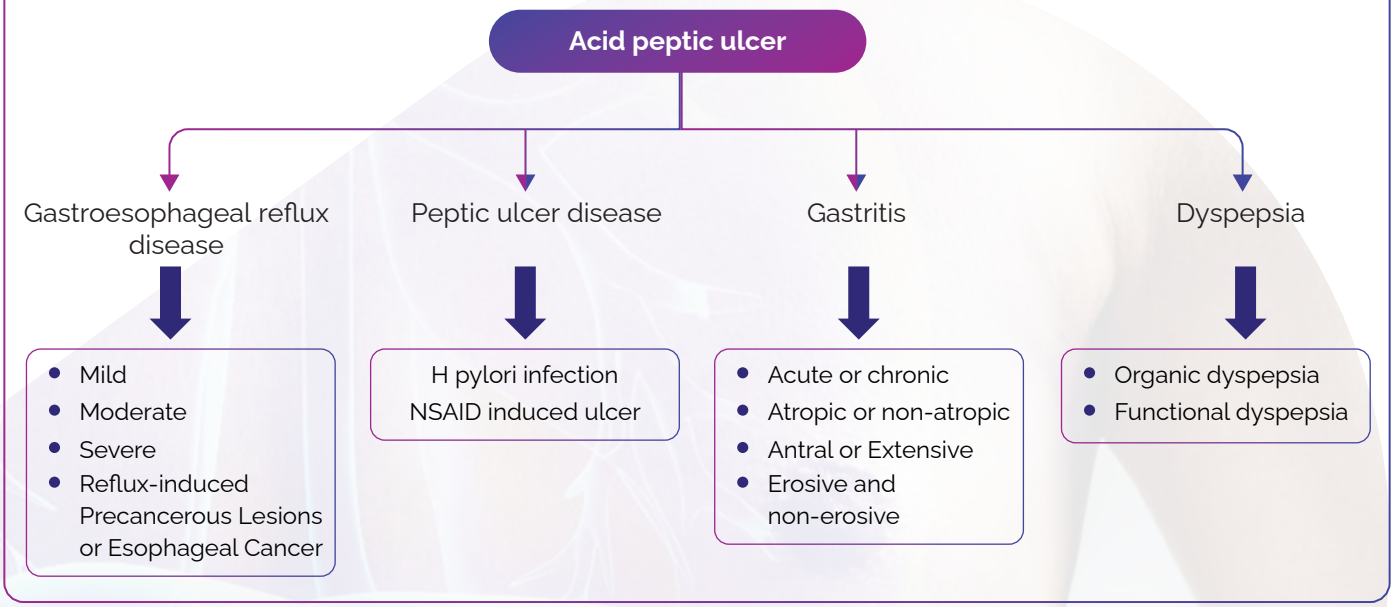
The prevalence of GERD in India ranges from 7.6% to 30%.[6] The incidence of GERD is rising in India due to shift towards poor diet, increase in weight, obesity and sedentary lifestyle. In India, NERD is severely under-diagnosed. As per in-clinic observations, 50-60% of patients with GERD in South East Asia are suffering from NERD.

Peptic ulcer disease (PUD) affects 4 million people worldwide annually with an estimated lifetime prevalence of 5–10%. Although the global prevalence of PUD has dramatically decreased in the past decades, the incidence of its complications has remained constant.[7]

The annual prevalence of recurrent dyspepsia is approximately 25% over a 3- to 12-month period. If frequent heartburn is included in dyspeptic symptoms, the prevalence exceeds 40%. Globally, 50.8% of the populations in developing countries suffer from gastritis. H. pylori infection is among the leading gastroenterological public health problems in developing countries.[5] In India, the prevalence of H pylori gastritis infection is 22%, 56%, and 87% in the 0–4 years', 5–9 years', and 10–19 years' age group, respectively.[8] Patients with H pylori and intestinal tuberculosis (ITB) may have a higher risk of gastritis.

## Types of Acid peptic disorder

**Figure 1: Types of Acid peptic disorders**




## Gastroesophageal reflux disease (GERD)

Gastroesophageal reflux disease (GERD) is defined as the condition in which the reflux of gastric contents into the esophagus results in symptoms and/or complications. GERD is objectively defined by the presence of characteristic mucosal injury seen at endoscopy and/or abnormal esophageal acid exposure demonstrated on a reflux monitoring study.[9]

### Classification of GERD[10]

**Table 1: Classification of GERD**

| Stage | Severity | Clinical presentation |
|---|---|---|
| 1 | Mild | Heartburn and regurgitation occurring infrequently (less than once a week) |
| 2 | Moderate | Heartburn and regurgitation occurring a few times a week |
| 3 | Severe | Heartburn, regurgitation, dysphagia, cough, change in voice, non-cardiac chest pain, sleep disturbance, nighttime heartburn |
| 4 | Reflux-induced Precancerous Lesions or Esophageal Cancer | Heartburn, regurgitation, dysphagia, cough, change in voice, non-cardiac chest pain, endoscopic findings of strictures, Barrett's esophagus, esophageal cancers. |

Based on endoscopic and histopathologic appearance, GERD is also classified into three different phenotypes:

- Non-erosive reflux disease (NERD),
- Erosive esophagitis (EE), and
- Severe
- Barrett esophagus (BE).

NERD mirrors the symptoms of GERD but lacks esophageal mucosal breaks. Erosive esophagitis, on the other hand, can lead to extensive erosions, ulcerations, and esophageal constriction. In severe cases, it may even prompt GI bleeding, manifesting as anemia, hematemesis, coffee-ground emesis, melena, or hematochezia. Barrett's esophagus emerges from intestinal metaplasia of the esophagus, marking a significant transformation.[11] Refractory GERD is also a type of GERD which can present as incomplete or lack of response to PPI therapy.[12]

### Simple grading of esophagitis

- Mild esophagitis: awareness of symptoms of reflux and tolerated by the patients.
- Moderate: is discomfort of reflux symptoms which are sufficient to cause interference in normal activities and are tolerable.
- Severe: persistent and unbearable symptoms that need repeat visits to the doctor and is associated with complications.

### Clinician's opinion

Burning & regurgitation are most common observed symptoms. Dysphagia & pain are uncommon symptoms that could be due to sever ulcerative disease, stricture or even maybe malignancy. Mucosal injury & activation of the afferent sensory nerves has been considered as a basic pathophysiology in GERD. Along with this visceral hypersensitivity is also an important factor for perception of the symptoms of GERD.

The incidence of complications including Barrett's Oesophagitis is lower in India compared to the Western population. Patients who complain of food particles in the mouth should be screened for GERD. A normal endoscopy does not rule out reflux disease. Symptoms and clinical history should be analysed before ruling out GERD.

### Eosinophilic esophagitis

The esophagus physiologically lacks eosinophils, and when present, the condition is considered to be pathologic. Eosinophilic esophagitis was once thought to be a component of GERD. However, it is now known to be a separate entity as we understand more about the esophagus being an active immunogenic organ. Eosinophils can be found in the esophagus in response to various stimuli or antigen. Eosinophilic esophagitis (EoE) is a chronic immune or antigen-mediated process. Clinically, it presents with various esophageal dysfunctions, and pathologically, there is mucosal inflammation predominantly with eosinophils, which is confined to the esophagus only.[13]

## Peptic ulcer disease (PUD)

Peptic ulcer disease is a mucosal defect that extends to or beyond the muscularis mucosa, reaching the submucosa, mostly occurring in the stomach (gastric ulcers) and the proximal duodenum (duodenal ulcers). The main causes of peptic ulcer disease are H. pylori infection and the use of non-steroidal anti-inflammatory drugs (NSAIDs).[14]

### Helicobacter pylori (H. pylori) infection

*Helicobacter pylori (H. pylori)* infection is the known common cause associated with the development of gastritis, noncardiac gastric cancer, gastric mucosa–associated lymphoid tissue (MALT) lymphoma, and peptic ulcer disease, affecting approximately 4.4 billion people globally. *H. Pylori* is found in 95% of patients with duodenal ulcers and in 70% of those with gastric ulcer. The risk factors include low socio-economic status, as well as contaminated water supplies. This infection is likely transmitted through faecal-oral route during early childhood and persists for decades.[15]

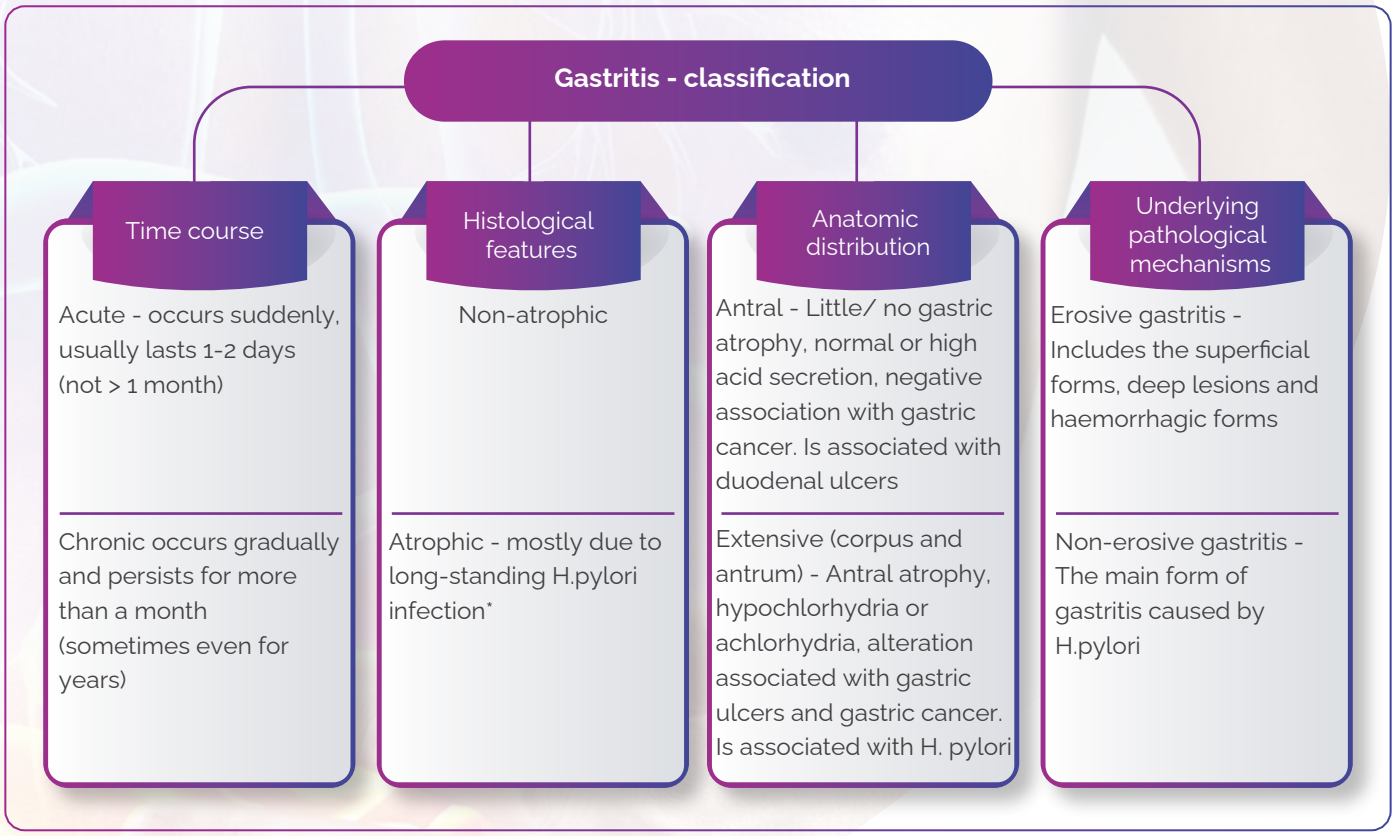
### NSAID induced ulcers

NSAIDs are second to Helicobacter pylori infection in causing peptic ulceration in the upper GI tract. NSAIDs induce mucosal injury by inhibiting cyclo-oxygenase (COX)-1, which diminishes the production of protective mucosal prostaglandins and reduces the secretion of bicarbonate mucus that forms a barrier in the stomach and small intestine. Among individuals taking NSAIDs, approximately one-third experience foregut symptoms like dyspepsia (epigastric discomfort, bloating, post-prandial nausea, early satiety, and belching) as well as gastroesophageal reflux (heartburn and regurgitation).

However, these symptoms do not reliably predict mucosal injury; around 20% of symptomatic patients show normal findings during esophagogastroduodenoscopy (OGD). Notably, up to 70% of long-term NSAID users exhibit endoscopic abnormalities such as mucosal erosions, ulcers, and subepithelial hemorrhage, even if only 10% complain of dyspeptic symptoms. This implies that severe complications of peptic ulcers, like bleeding and perforation, can arise without warning signs. The frequency of complications related to gastroduodenal peptic ulcers is amplified up to fivefold in those who use NSAIDs. Risk factors for bleeding include class, duration, and dose of NSAID, concomitant drug therapies like antiplatelet agents and presence of H pylori infection. Clinically, patients present with symptoms like melaena, hematochezia, and/or hematemesis. This is accompanied by a decline in hemoglobin levels and an elevation in urea levels due to the digestion of blood into protein and its subsequent metabolism into urea within the liver.[16, 17]

## Gastritis

Gastritis is a condition that inflames the stomach mucosal lining, causing abdominal pain, dyspepsia, bloating and nausea. Gastritis may be acute or chronic.[18]




## Dyspepsia

Dyspepsia presents with various symptoms in the upper abdomen, such as fullness, discomfort, early satiation, bloating, heartburn, belching, nausea, vomiting, or pain. Dyspepsia can be divided into 2 main categories:

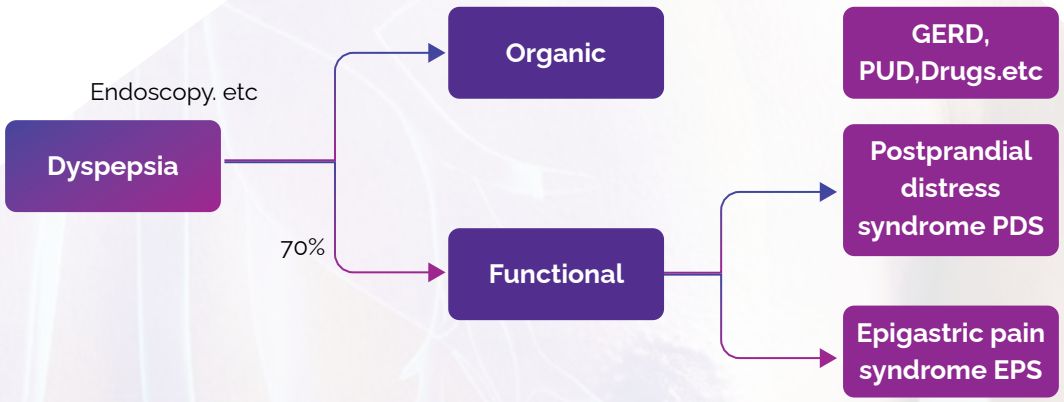
- "Organic" and
- "Functional Dyspepsia" (FD).

Organic causes of dyspepsia are peptic ulcer, gastroesophageal reflux disease, gastric or esophageal cancer, pancreatic or biliary disorders, intolerance to food or drugs, and other infectious or systemic diseases. Functional dyspepsia is one of the most common functional gastrointestinal disorders and affects more than 20% of the population. There are three different subtypes:

- Epigastric pain syndrome (EPS),
- Postprandial distress syndrome (PDS), and
- Overlapping PDS and EPS.

Functional dyspepsia is diagnosed based on the Rome IV criteria. It is defined by the presence of one or more of the following symptoms: epigastric pain or burning, early satiety, and postprandial fullness in the absence of structural disease using imaging or endoscopy.[19, 20]

**Figure 2: Causes of dyspepsia**




## Gastroparesis

Gastroparesis is a chronic disorder of delayed stomach emptying without a blockage. Symptoms include fullness after meals, pain, nausea vomiting, weight loss, belching and bloating. Certain foods like fatty foods, or carbonation may cause symptoms.[21] Diabetic Gastroparesis (DGp) is a relatively common complication of diabetes, but often goes unrecognized. About one-third of patients with gastroparesis have diabetes. DGp affects 20–50% of the diabetic population, especially those with poor early glycaemic control and long-standing (≥ 10 years) type 2 diabetes mellitus. The increasing prevalence of type 2 diabetes has resulted in larger numbers of patients with DGp. It is associated with higher morbidity, including increased hospitalizations and emergency department and hospital visits.[22]

## Causes and risk factors of acid peptic disorder:

**Table 2: Causes and risk factors of GERD[23]**

| Lifestyle | Food | Disease | Medications |
|---|---|---|---|
| Obesity<br>Pregnancy (NERD)<br>Smoking<br>Heavy lifting<br>Eating patterns:<br>• Overeating<br>• Eating right before bedtime | High-fat diet<br>Citrus<br>Tomato products<br>Carbonated beverages<br>Alcohol<br>Chocolate<br>Peppermint<br>Onion<br>Caffeine | Diabetes<br>Asthma<br>Chronic obstructive pulmonary disease (COPD)<br>Scleroderma<br>Rheumatoid arthritis<br>Oesophageal motility disorders<br>Hiatus hernia | Anticholinergics<br>SSRI antidepressant<br>Inhaled bronchodilators<br>Birth control pills<br>Corticosteroids<br>Anti-osteoporotic (Bisphosphonates) |

GERD is more common in obese patients who also have higher incidence of hiatus hernia. The first problem is the acid reflux in itself. Secondly, the acid is not able to go back into the stomach and stays longer in the oesophagus. In hiatus hernia, the acid pocket position in the stomach is above the diaphragm. Due to this there is constant irritation of the LES with acid.

**Figure 3: Possible etiologic factors involved in GERD.[24]**

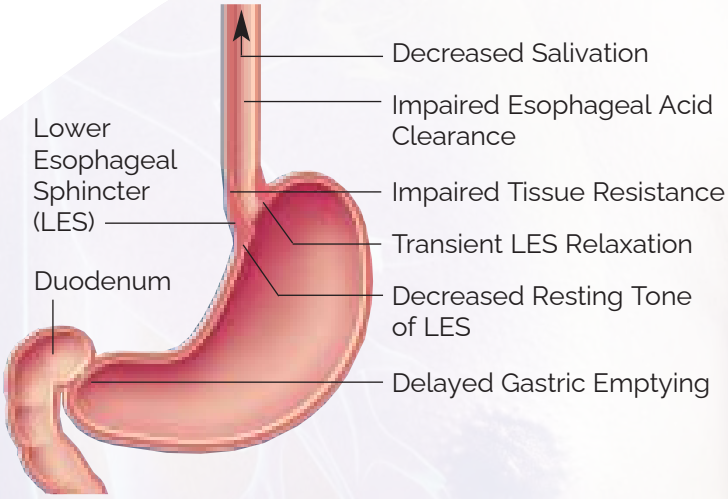
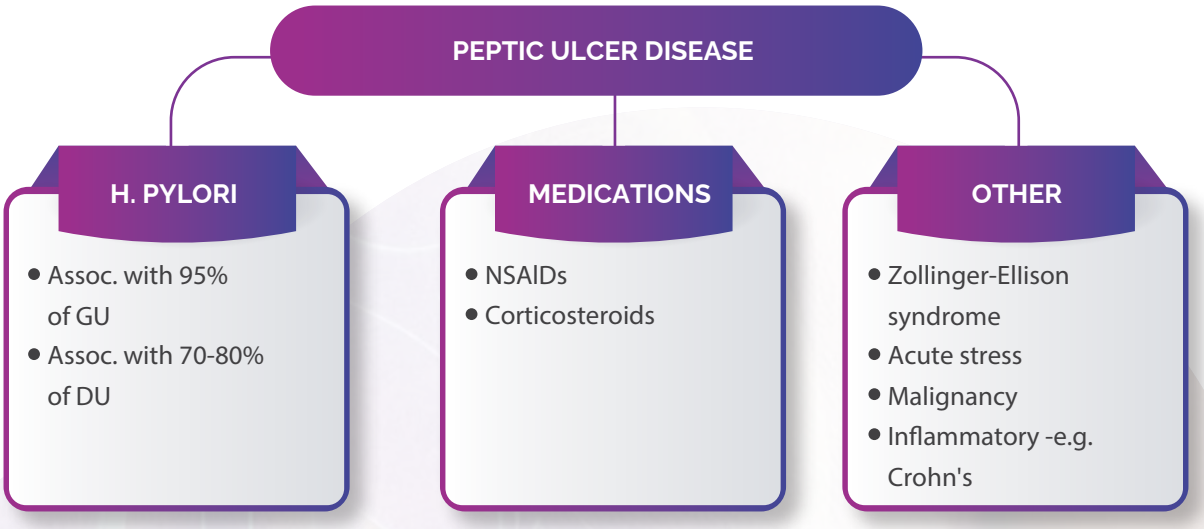



**Table 3: Causative and associated factors involved in the pathogenesis of GERD**

| Aspect | Description |
|---|---|
| Causative Factors | Direct contact of acid with larynx or trachea causing tracheobronchitis; acid reaching lungs and causing pneumonia. |
| Associated Factors | Stimulation of afferent nerves, leading to the stimulation of other nerves. |
| Reflux Mechanisms | • Defective clearance of acid from the oesophagus. |
| | • Dysfunctional LES. |
| | • Inappropriate frequency of LES relaxation. |
| | • Anatomical abnormality at the Gastroesophageal (GE) junction, such as hiatus hernia. |
| Aggravating Factors | • Obesity. |
| | • Pregnancy (increased intra-abdominal pressure). |
| | • Hyper-secretory states like Zollinger-Ellison (ZE) Syndrome. |
| | • Delayed gastric emptying (gastroparesis) leading to prolonged acid clearance. |
| | • Overeating, particularly in a single session. |
| | • Decreased salivation, often drug-related (e.g., anti-cholinergic medications). |

## Figure 4: Causes and risk factors of PUD[25]




## Table 4: Causes and risk factors of Gastritis[26]

- Excessive alcohol intake
- Smoking
- Extreme stress. This can be from serious or life-threatening health problems.
- Long-term use of aspirin and over-the-counter pain and fever medicines
- Infections caused by bacteria and viruses.
- Major surgery
- Traumatic injury or burns.
- Autoimmune disorders.
- Chronic bile reflux.
- Pernicious anaemia

## Table 5: Causes and risk factors of Dyspepsia[19,20]

| Organic dyspepsia | Functional dyspepsia |
|---|---|
| • Peptic ulcer<br>• Gastroesophageal reflux disease<br>• Gastric or esophageal cancer<br>• Pancreatic or biliary disorders<br>• Intolerance to food or drugs<br>• Other infectious or systemic diseases | • Genetic predisposition<br>• Helicobacter pylori infection<br>• Inflammation<br>• Psychosocial factors.<br>• Delayed gastric emptying.<br>• Hypersensitivity to gastric distension<br>• Altered duodenal sensitivity to lipids or acids.<br>• Autonomic nervous system-central nervous system dysregulation.<br>• Dysbiosis and abnormal metabolites of the gastrointestinal microbiota (by disrupting biological barrier and disturbing immune function of intestinal mucosa, or causing dysregulation of the microbial-gut-brain axis) |

Acid pocket in GERD: The acid pocket was first reported in 2001 by Fletcher and colleagues in an article published in Gastroenterology. The authors observed pH 4 or 5 in the stomach, fell to approximately 2 in an area just below the sphincter of the esophagus, and then rose up to 6 or 7 in the esophagus. The region just below the esophageal sphincter, which was more acidic than the rest of the esophagus and stomach, seemed almost like a pocket of acid floating on top of the ingested meal. This pocket likely explained why the distal esophagus was sometimes more acidic than the stomach.[27]

Role of gut microbiome: Several studies have confirmed that dysbiosis and abnormal metabolites of the gastrointestinal microbiota may cause the occurrence and progression of functional dyspepsia by disrupting the biological barrier of the intestinal mucosa, by disturbing the immune function of the intestinal mucosa, or by causing dysregulation of the microbial-gut-brain axis.[28]

Gastric mucosal immunity: In accordance with the immune response of the human body, the gastric mucosal immunity also exerts through innate immunity and adaptive immunity synergistically. Pathogens damage the gastric mucosa by escaping immune responses. When the damage of the gastric mucosa cannot be repaired, the dynamic balance of gastric mucosa barrier will be broken, which further leads to gastric diseases. H. pylori-infective gastritis is a very remarkable clinical outcome of H. pylori infection, which is closely related to the gastric mucosal immunity.[29]

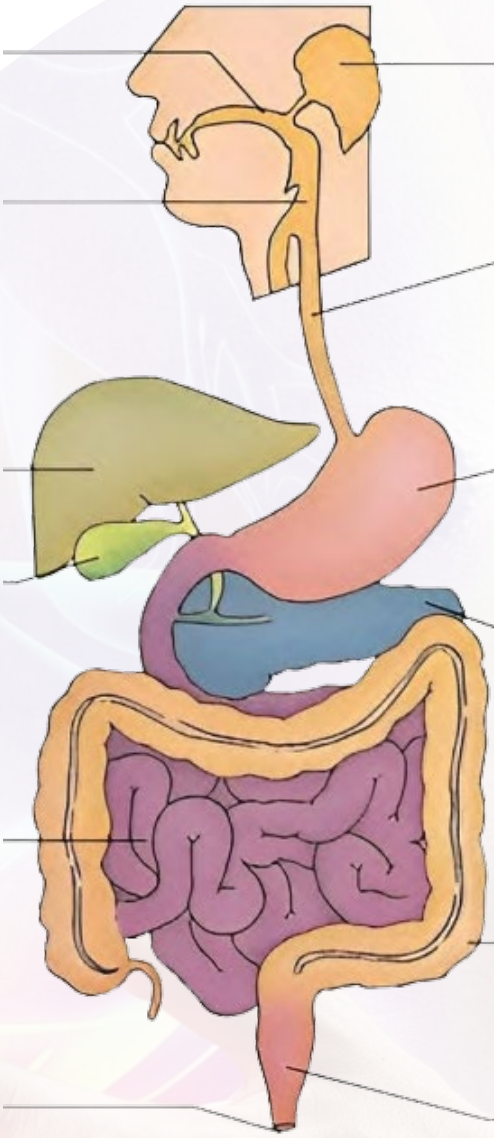
**Table 6: Causes and risk factors of gastroparesis**

| **Major causes** |
| --- |
| • Idiopathic<br>• Diabetes mellitus<br>• Postsurgical |
| **Less common causes** |
| • Connective tissue disease<br>• Ischemia<br>• Cancer<br>• Neurologic disease (including Parkinson's)<br>• Eating disorders<br>• Metabolic/endocrine conditions<br>• Medications (e.g. anticholinergics, calcium channel antagonists and opiates)<br>• Critical illness |

Source: Nat Gastoenterol Hepatol © 2011 Nature Publishing Group

## Anatomy of Digestive System:[30]

**Figure 5: Anatomy of Digestive System**



**Mouth**
- Breaks up food particles Assists in producing Spoken language

**Pharynx**
Swallows

**Liver**
- Breaks down and builds up many biological molecules
- Stores vitamins and iron
- Destroys old blood cells
- Destroys poisons
- Bile aids in digestion

**Gallbladder**
- Stores and concentrates bile

**Small intestine**
- Completes digestion
- Mucus protects gut wall
- Absorbs nutrients. most water
- Peptidase digests proteins
- Sucrases digest sugars
- Amylase digests polysachharides

**Anus**
- Opening for elimination of feces

**Salivary glands**
- Saliva moistens and lubricates food
- Amylase digests polysaccharides

**Esophagus**
- Transports food

**Stomach**
- Stores and churns food
- Pepsin digest protein
- HCL activates enzymes, breaks up food, kills germs
- Mucus protects stomach wall

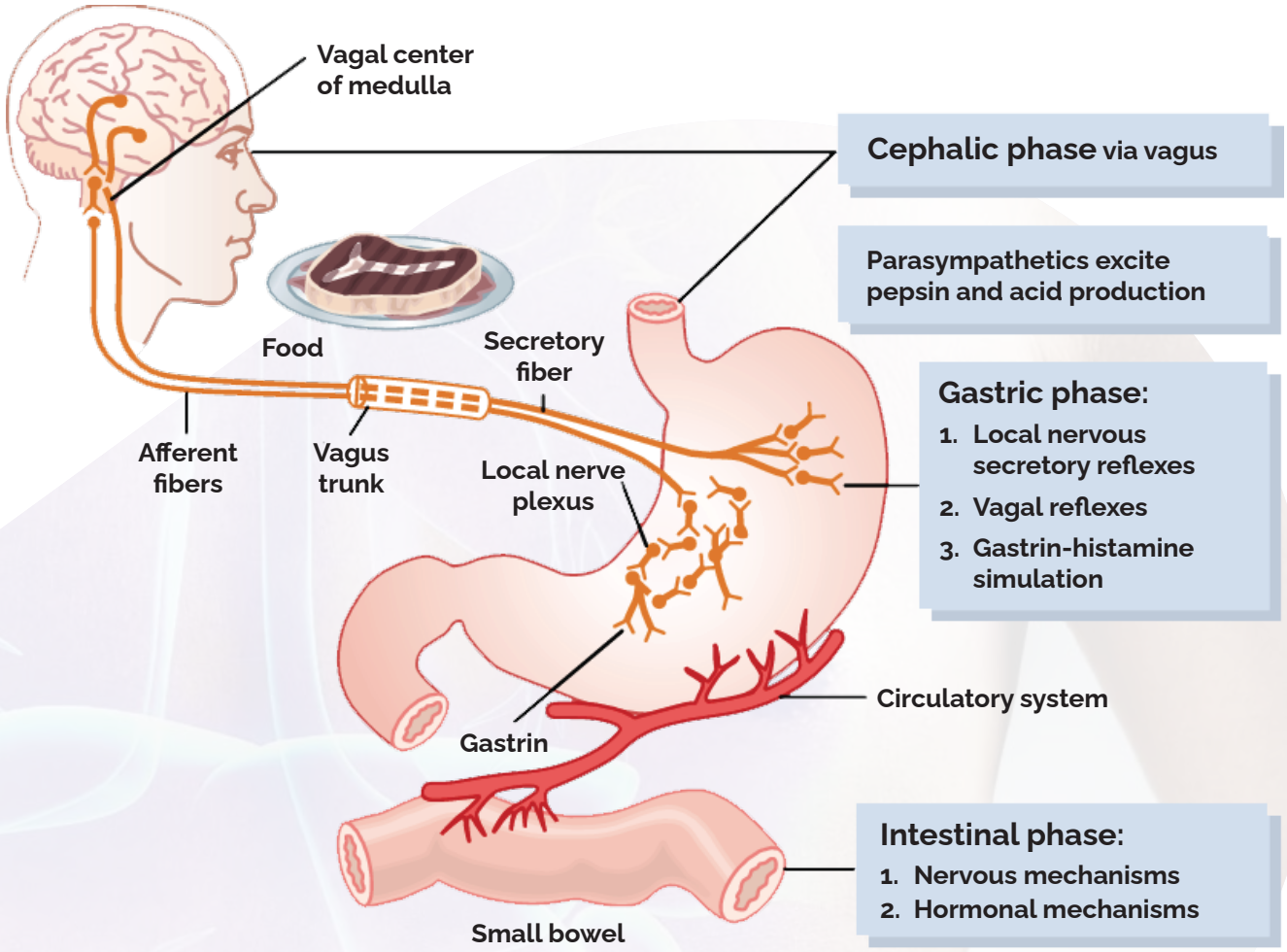
**Pancreas**
- Hormones regulate blood glucose levels
- Bicabonates neutralize stomach acid
- Trypsin and chymotrypsin digest proteins
- Amylase digest polysaccharides
- Lipase digests lipids

**Large intestine**
- Reabsorbs some water and ions
- Forms and stores faces

**Rectum**
- Stores and expels faces

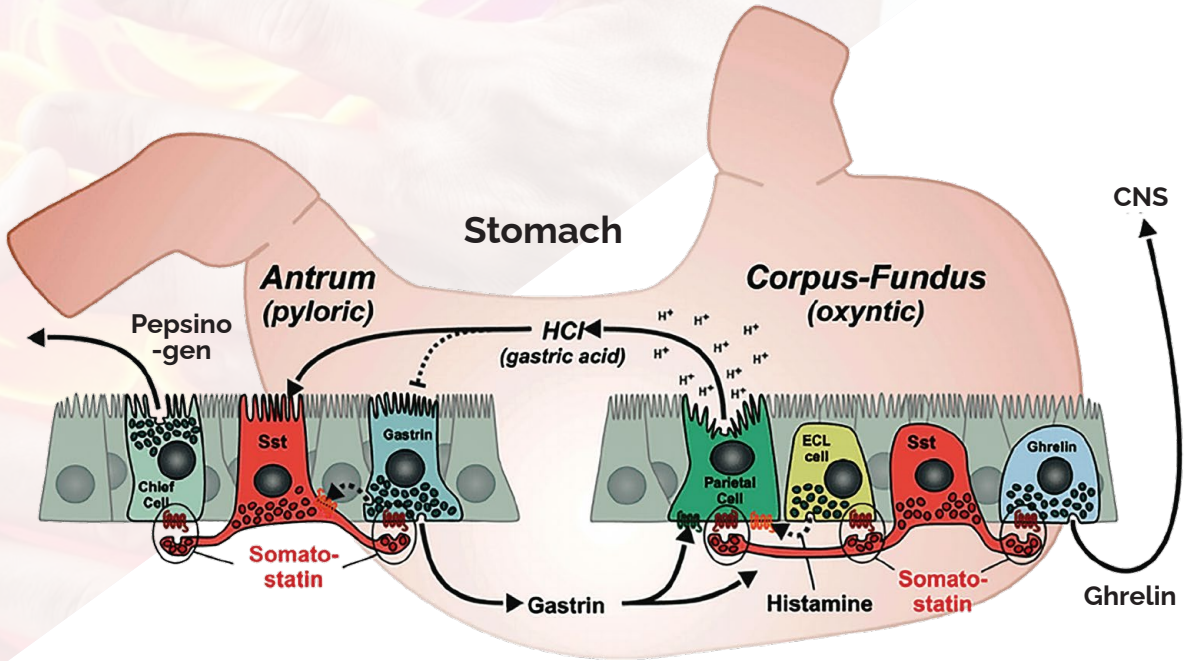
Gastric secretion occurs in three phases: cephalic, gastric, and intestinal. During each phase, the secretion of gastric juice can be stimulated or inhibited.[31]

Figure 6: Phases of gastric secretion




## Role of stomach acid and enzymes:[32, 33]

Figure 7: Role of stomach acid and enzymes



**Gastric juice Contains**

**HCl**
(kills bacteria and denatures protein)

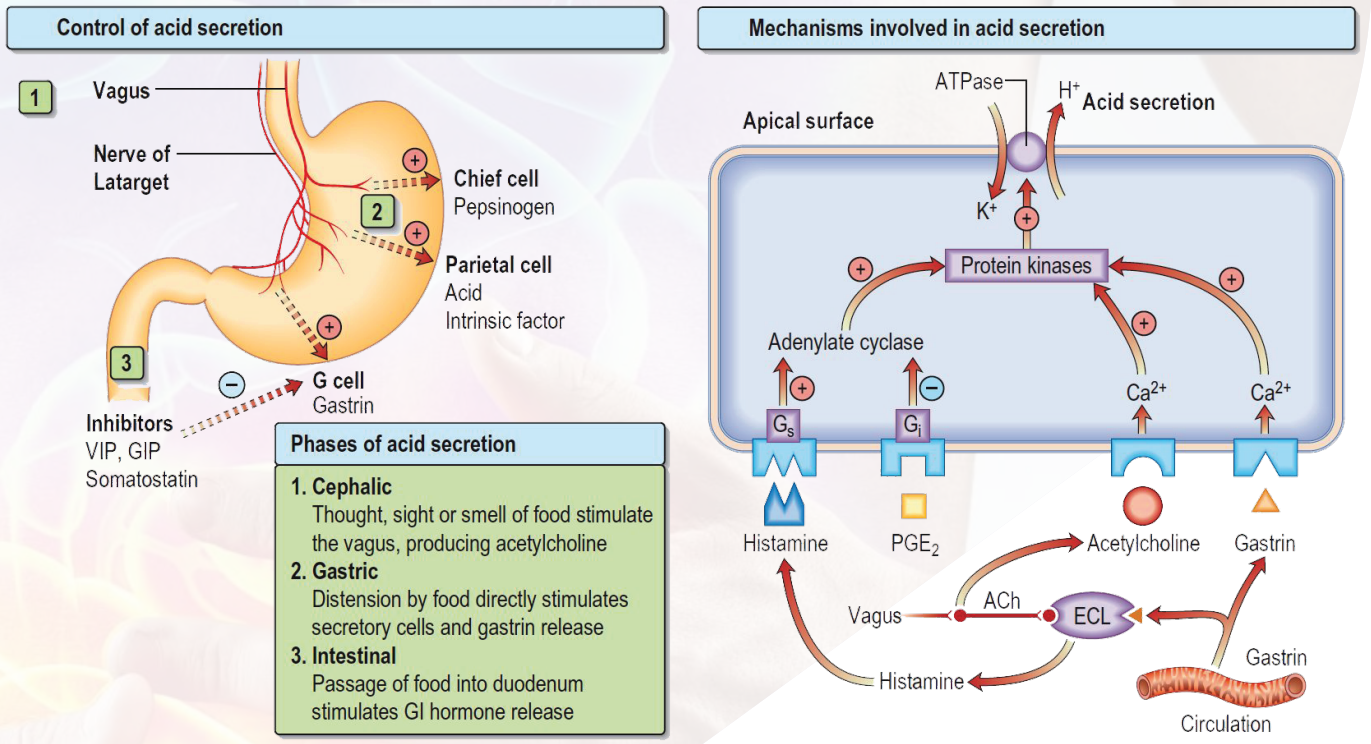
**Pepsin**
(Digestion of proteins)

**Intrinsic factor**
(Absorption of vitamin B12)

**Gastric lipase**
(Digestion of exogenous lipid)

## Acid Production and Regulation:[34, 35]

**Figure 8: Acid Production and Regulation**

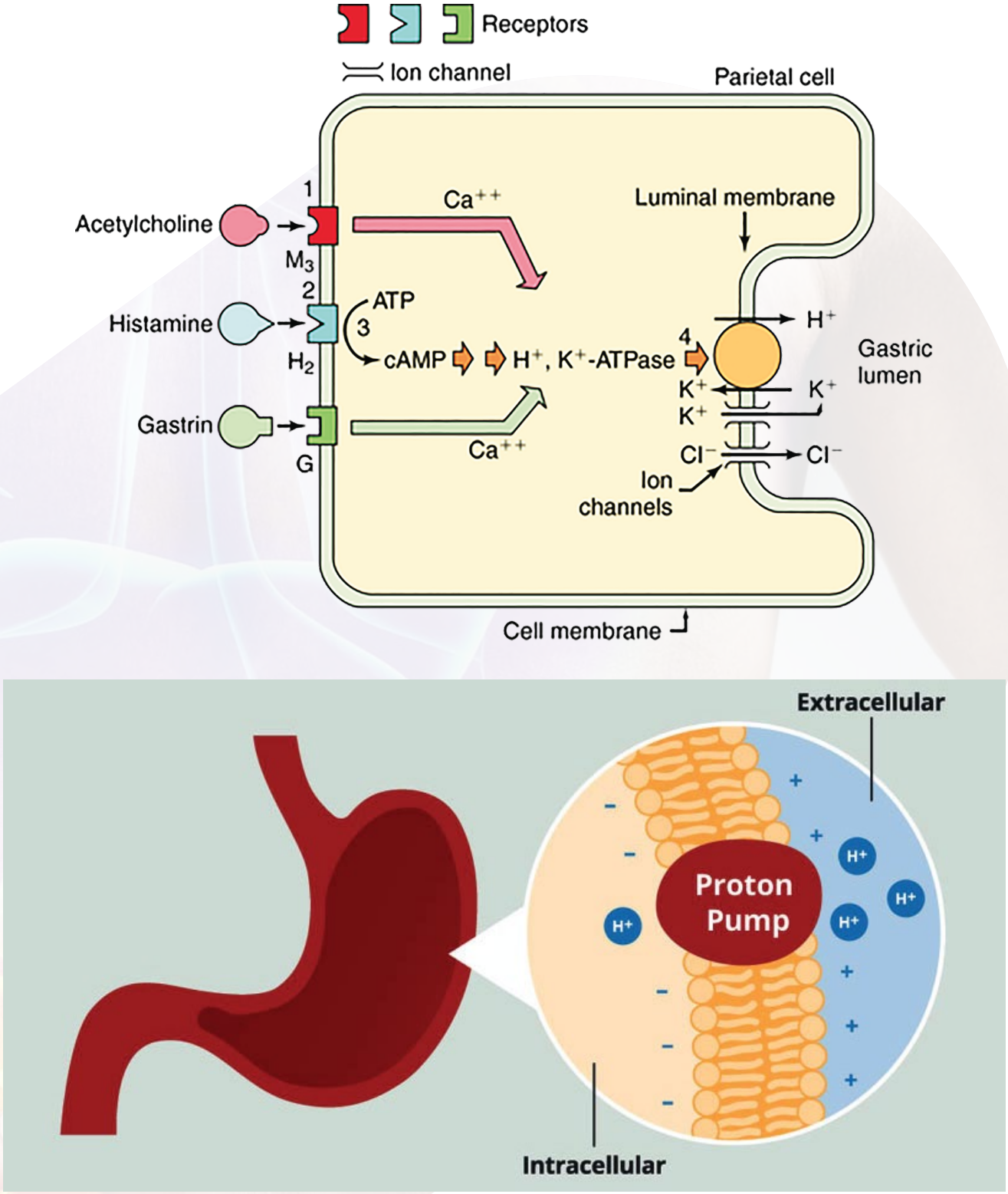



**Control of acid secretion.**

## Acid regulation by pareital cells: Proton pump

The parietal cells contain the H+/K+ ATPase or "proton pumps" located in the canaliculus of the parietal cell and responsible for the transport of acid (H+) into the stomach lumen. The main stimulants of acid secretion at the level of parietal cells are histamine, acetylcholine and to a lesser extent, gastrin.

Figure 9: Acid Production and Regulation



# Clinical presentation of APD

## GERD

GERD has a wide spectrum of clinical symptom-based and injury-based presentations, which may manifest either separately or in combination.[36]

**Table 7: Clinical symptoms of GERD**

| Typical symptoms | Atypical symptoms | Alarm symptoms |
|---|---|---|
| Heartburn<br>Regurgitation | Chronic cough<br>Hoarseness<br>Noncardiac chest pain<br>Globus<br>Throat irritation<br>Sleep disturbance | Dysphagia<br>Odynophagia<br>Weight loss<br>Melena<br>Hematemesis |

Extra GI manifestation of GERD - Bronchospasm, cough and arrhythmia

Patient with chief complaints of chest pain must be properly evaluated including looking at a differential diagnosis (biliary colic, pancreatitis, gastroparesis) before initial management. Taking a good clinical history is of prime importance.

**Table 8: Clinical presentation based on pathophysiologic mechanism of refractory GERD**

| Pathophysiologic Mechanism | Presenting Symptoms |
|---|---|
| Increased transient lower esophageal sphincter relaxation | Regurgitation, heartburn, chest pain |
| Hiatal hernia | Regurgitation, heartburn, chest pain |
| Hypotensive LES | Regurgitation, heartburn, chest pain |
| Reduced esophageal contractility | Dysphagia |
| Increased mucosal permeability | Heartburn |
| Persistent esophageal acid exposure on double dose PPI | Heartburn, chest pain |
| Delayed gastric emptying | Regurgitation, heartburn, chest pain |

## PUD

Signs and symptoms of peptic ulcer disease may vary depending upon the location of the disease and age. Gastric and duodenal ulcers can be differentiated from the timing of their symptoms in relation to meals. Nocturnal pain is common with duodenal ulcers. Those with gastric outlet obstruction commonly report a history of abdomen bloating and or fullness.[3]

Gastric ulcers are a break in the mucosa of the stomach lining that penetrates through the muscularis mucosa and extends more than 5 mm in diameter. When the stomach's defense mechanisms are compromised, alterations occur in the gastric mucosa, eventually leading to erosion and subsequent ulcer formation. Duodenal ulcers, on the other

hand, result from the corrosive impact of gastric secretions on the surface epithelium of the small intestine, particularly in areas that have previously experienced damage. Diagnosing and identifying the root cause of duodenal ulcers involves considering various underlying comorbidities. Among these, the two primary causal factors to address are H. pylori infection and NSAID usage. There are some commonly mistaken conditions that can also have similar presentations of PUD such as esophagitis, functional dyspepsia, gastritis, gastroenteritis, and GERD.

**Table 9: Clinical presentation of Gastric and duodenal ulcer**

| Gastric ulcer | Duodenal ulcer |
|---|---|
| • Epigastric pain (worse with eating)<br>• Epigastric tenderness<br>• Mild nausea and early satiety<br>• Upper GI bleeding<br>• Black tarry stools<br>• Hematemesis<br>• Coffee-ground emesis<br>• Bright red blood per rectum | • Dyspepsia<br>• GI bleeding<br>• Gastric outlet obstruction<br>• Perforation<br>• Fistula |

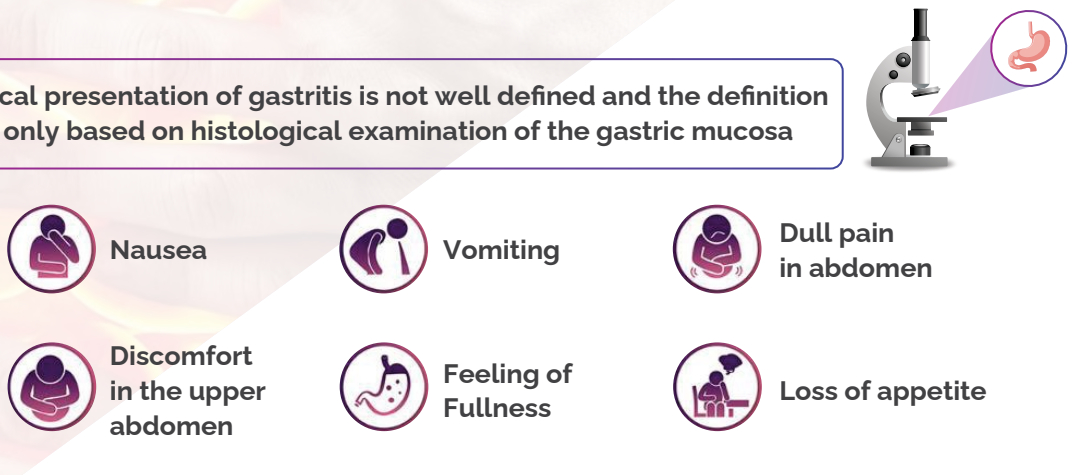
## Drug induced gastritis

Drug-induced gastritis is characterized by the diversity and the nonspecific nature of the presentation.

- Upper abdominal discomfort or pain.
- Loss of appetite
- Nausea, and vomiting
- Hematochezia
- Melena
- Hemorrhagic shock
- Gastric perforation

## Gastritis[37]

**Figure 10: Gastritis**



## Dyspepsia

Dyspepsia consists of various symptoms in the upper abdomen, such as fullness, discomfort, early satiation, bloating, heartburn, belching, nausea, vomiting, or pain.

## Functional dyspepsia

The Rome III criteria definition of functional dyspepsia includes at least one of the following: bothersome postprandial fullness, early satiation, epigastric pain, and epigastric burning; patients also must have no evidence of structural disease that would likely explain their symptoms, including upper endoscopic findings. The patient must meet the criteria for 3 months and must begin experiencing symptoms for at least 6 months before diagnosis.[38]

Symptom onset greater than 6 months prior to the diagnosis, with the following criteria fulfilled for the past 3 months:

- No structural disease by upper endoscopy to explain the symptoms.
- At least one of the following symptoms:
    a. Bothersome postprandial fullness
    b. Early satiation
    c. Epigastric pain
    d. Epigastric burning

**Postprandial Distress Syndrome**

At least one of the following:

- Bothersome postprandial fullness after ordinary sized meals occurring at least several times a week.
- Early satiation that prevents finishing a regular meal at least several times a week

**Epigastric Pain Syndrome**

Must include all the following:

- Epigastric pain or burning at least once a week.
- Intermittent pain
- Not generalized or localized to other abdominal or chest regions.
- Not relieved by defecation or passage of flatus
- Not related to gallbladder or sphincter of Oddi disorders

## Gastroparesis

- Indigestion
- Bloated stomach
- Feeling full very quickly and/or for a long time
- Upper abdominal pain
- Nausea and vomiting
- Regurgitating
- Loss of appetite
- Acid reflux and heartburn
- Blood sugar fluctuations
- Constipation

# Clinical investigation in APD

**Table 10: Clinical investigations in APD**

| GERD | PUD | Gastritis | Dyspepsia | Gastroparesis |
|---|---|---|---|---|
| • Empirical PPI therapy (PPI trial)<br>• Urea breath test or H. pylori stool antigen test<br>• Endoscopy (not 1st line)<br>• Esophageal biopsy<br>• Gastric biopsy Esophageal manometry<br>• pH or impedance pH monitoring<br>• Barium swallow<br>• PEP test<br>• GERD with FD overlap- volume reflux or delayed gastric emptying | • EGD<br>• Serum gastrin<br>• Computerized tomography | • Gastric mucosal biopsy<br>• Parietal cell antibody<br>• Intrinsic factor antibody H. pylori antibody (IgG)<br>• Urea breath test<br>• H pylori faecal antigen test | • EGD<br>• investigation for H. pylori abdominal USG<br>• C breath test<br>• Gastric emptying scintigraphy | • Wireless motility capsule testing<br>• Scintigraphic gastric emptying study<br>• Stable isotope (13C-spirulina) breath test (upper GI symptoms)<br>• Biopsy |

EGD: Esophagogastroduodenoscopy ; FD: functional dyspepsia

For more details on each diagnostic test, refer to the appendix.

## Clinician's perspective

| | |
|---|---|
| **Cases definitely requiring endoscopy** | • Middle aged patient with recurrent episodes<br>• Elderly patient (> 50 years) with symptoms<br>• Patient with moderate to severe disease<br>• To rule out Barrett's<br>• Patient with long-term GERD or has risk of complications<br>• Regurgitation or reflux during sleep<br>• Regurgitation coming out through the nose during daytime or sleep<br>• Patients with hiatus hernia (patients may need follow-up Barium meal study)<br>• 1 ≥ episode of coffee coloured vomitus (due to moderate-severe GERD with oesophageal ulceration)<br>• Dysphagia (patients may need follow-up oesophageal manometry or CT scan)<br>• Refractory symptoms<br>• Non-respondent to pharmacological management<br>• Before surgery |
| **Cases NOT requiring endoscopy** | • Young patient<br>• Short history<br>• First consultation |

# Management of Acid Peptic Disorders

Goals of therapy for APD include symptom relief, promoting mucosal healing, addressing underlying causes, and preventing complications.

Treatment strategies combine lifestyle modifications and medications.

**Table 11: Types of medications used and their importance in managing APD**

| Type of Medication | Importance |
|---|---|
| **Antacids** | Initial over-the-counter options. Offer temporary relief by neutralizing stomach acid. Suitable for mild symptoms. May not fully manage severe conditions or target underlying causes. |
| **Histamine H2-Receptor Blockers** | Examples: ranitidine, famotidine. Reduce stomach acid production. Provide symptom relief for mild to moderate cases. Might not sufficiently heal the mucosa or manage more severe conditions. |
| **Proton Pump Inhibitors (PPIs)** | Most significant class for acid peptic disease. Effectively suppress stomach acid production. Provide comprehensive symptom relief, promote mucosal healing, and address underlying causes. |
| **Combination Therapy for H. pylori Infection** | Most significant class for acid peptic disease. Effectively suppress stomach acid production. Provide comprehensive symptom relief, promote mucosal healing, and address underlying causes. |

## Medication for Acid peptic disorders[39]

**Table 12: Medication for Acid peptic disorders**

| | Category of Drugs | Role in Acid peptic Ulcer | Examples |
|---|---|---|---|
| 1 | Antacids and drugs given in combination | Neutralize stomach acid, providing immediate relief from ulcer-related pain and discomfort. can be used alone or in combination with other drugs | Non-systemic antacids (combining magnesium trisilicate, aluminium hydroxide, or calcium carbonate), systemic antacids (sodium bicarbonate, citric acid), antiflatulents (Simethicone), anaesthetics combined with antacids (Oxethazaine), Alginate, Alginate-antacids (Alginate with Sodium/Potassium bicarbonate), and almagate |
| 2 | Mucosal protective compounds | Provide a protective layer over the stomach lining, helping to prevent further damage and promoting healing of ulcers | Sucralfate and Rebamipide |

| | Category of Drugs | Role in Acid peptic Ulcer | Examples |
|---|---|---|---|
| 3 | H2-receptor antagonists (H2-Ras) | Reduce stomach acid production by blocking histamine receptors in the stomach, providing relief from ulcer symptoms | Cimetidine, Ranitidine, Nizatidine, Famotidine, and Lafutidine. |
| 4 | PPI | Reduce the production of stomach acid, thereby alleviating symptoms, promoting healing of the mucosa, and preventing complications associated with excessive acid production | Pantoprazole, Omeprazole, Esomeprazole, Rabeprazole, Lansoprazole. |
| 5 | Prokinetics<br><br>a) Dopamine receptor antagonists<br>b) Serotonin (5-HT4) receptor agonist | Improve gastrointestinal motility, facilitating the movement of food through the digestive tract. They can help reduce acid reflux and improve gastric emptying | Metoclopramide, Domperidone, Clebopride, Levosulpiride, Cinitapride, Mosapride, Cisapride, Itopride and Prucalopride |
| | c) AChE inhibitor | Acetylcholinesterase (AChE) inhibitors enhances the release of acetylcholine, improving gastric motility and reducing acid reflux | Acotiamide |
| 6 | Potassium competitive acid blockers (P-CABs) | Inhibit the acid-producing enzyme, potassium-competitive acid pump (proton pump), providing effective acid suppression | Vonoprazan, Tegoprazan, and Revaprazan. |
| 7 | Inhibitors of gastro-esophageal reflux | GABA-b receptor agonists, can help reduce the relaxation of the lower esophageal sphincter, reducing acid reflux | Baclofen |
| 8 | Parasympathomimetic | Parasympathomimetic drugs can stimulate the parasympathetic nervous system, enhancing gastric motility and reducing acid reflux | Bethanechol |
| 9 | Medical devices | Bio adhesive formulations, and esophageal sphincter devices can help improve symptoms and prevent acid reflux | Bio adhesive formulations: combinations of Hyaluronic acid and Chondroitin sulfate<br><br>Esophageal sphincter devices: bracelets or rings of magnets |

## Role of PPI in APD

PPI is the main stay of treatment for APD. The FDA approved indications for PPIs:

- Treatment of gastroesophageal reflux disease
- Treatment and prophylaxis for NSAID induced and drug induced ulcer
- Treatment of gastric and duodenal ulcers
- Treatment of H. pylori infection in combination with antibiotics
- Management of pathologic hypersecretory conditions including Zollinger-Ellison Syndrome
- Healing of erosive esophagitis
- Maintenance treatment for healed erosive esophagitis

**Figure 11: Mechanism of action of PPIs**

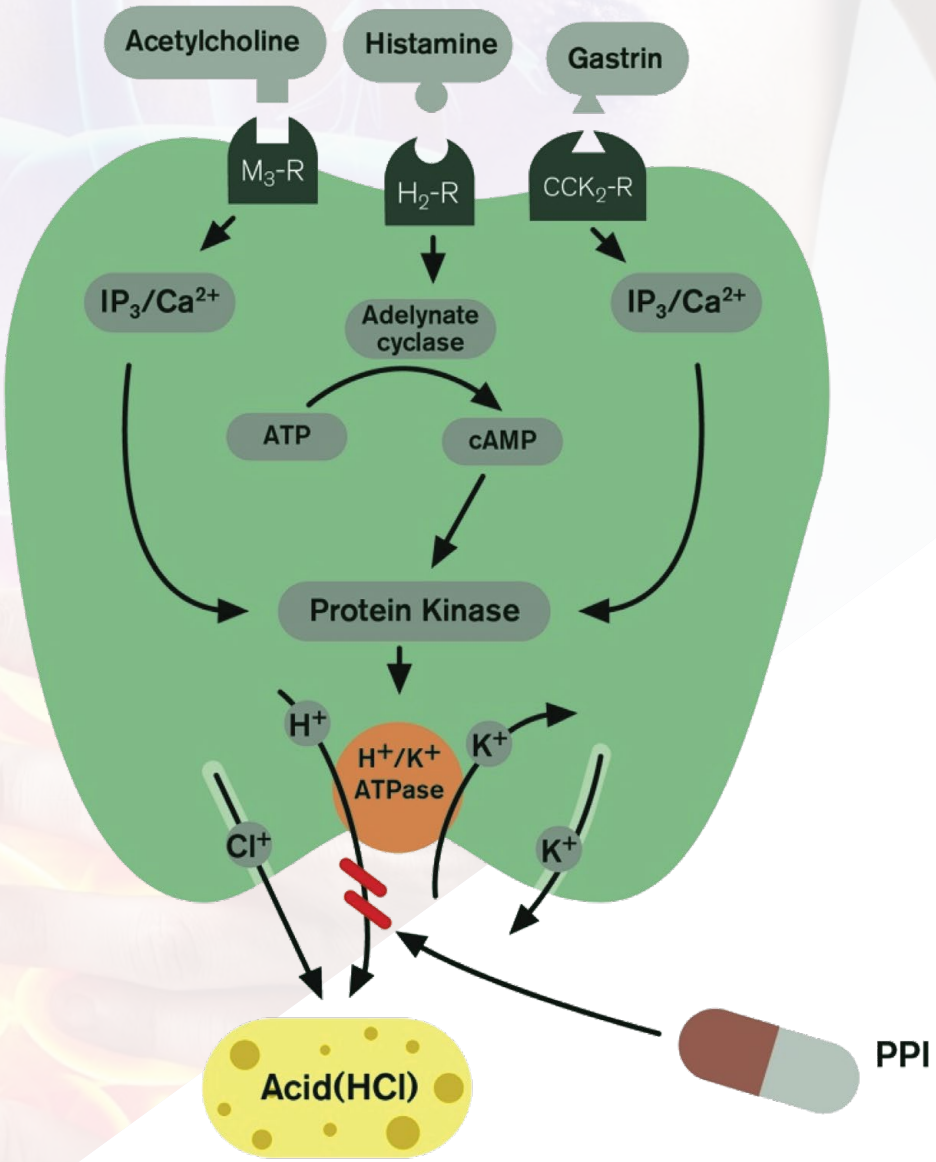
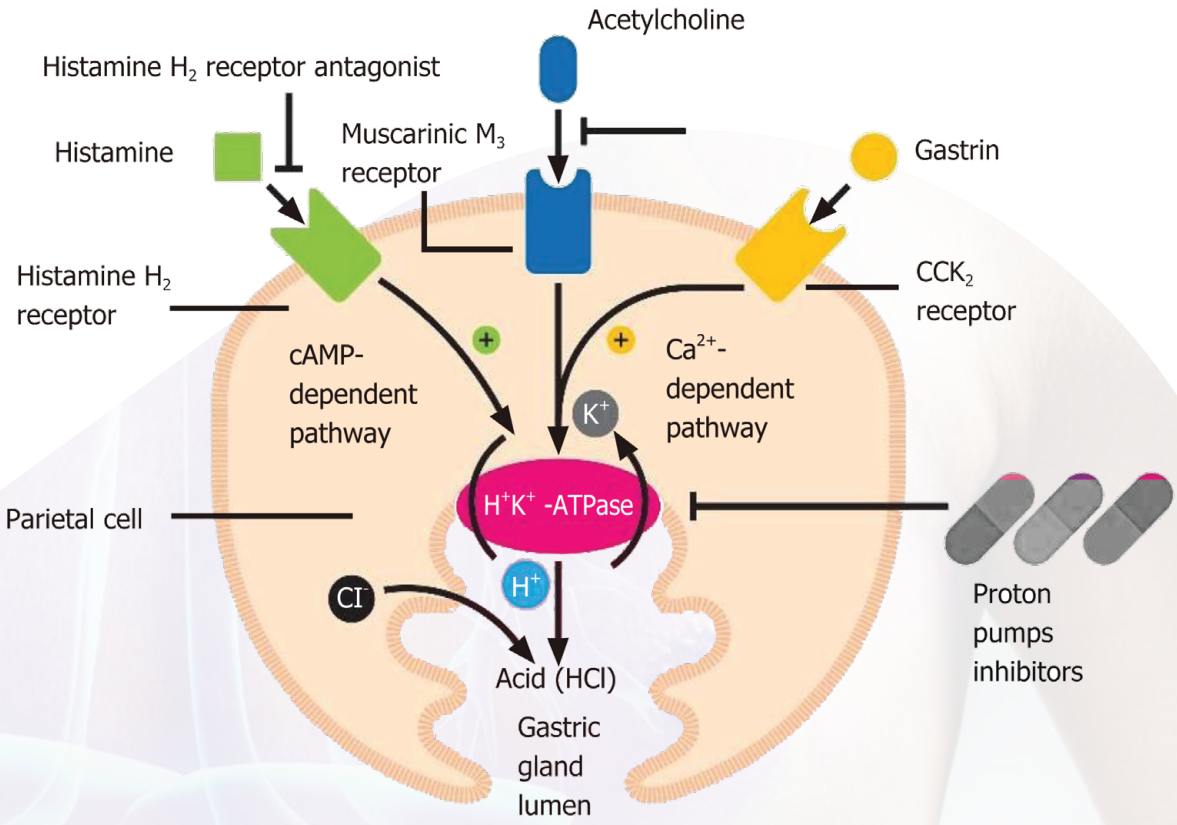


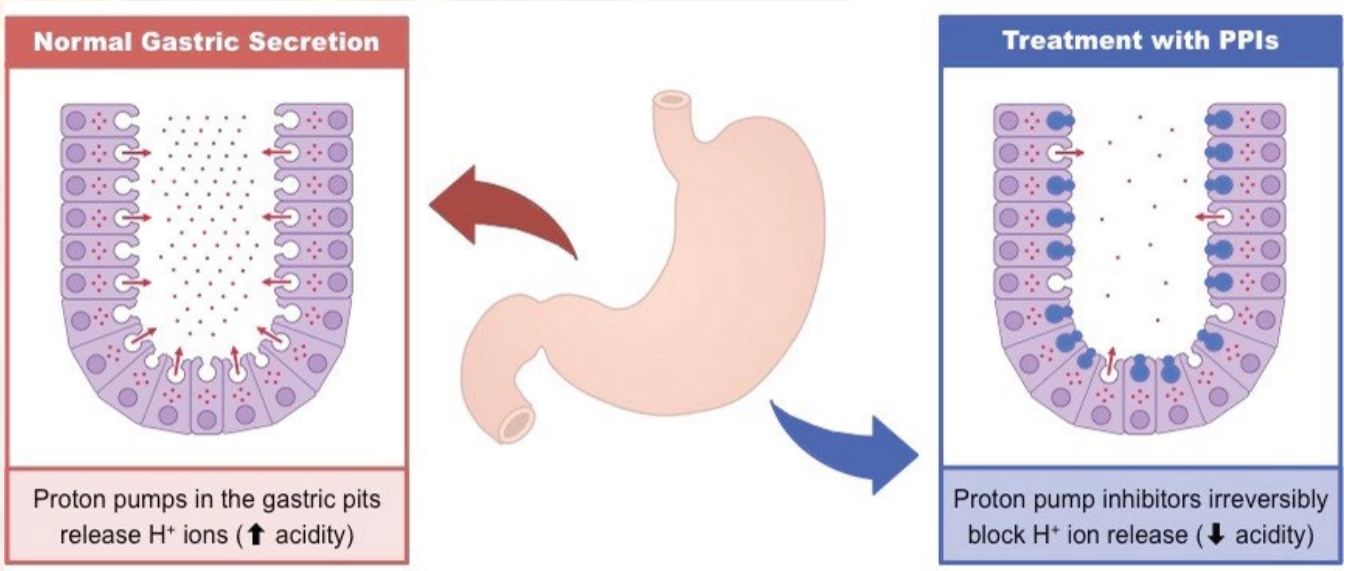
**Figure 12: Mechanism of action of PPIs**




These PPIs interact with the gastric H, K-ATPase or "proton pump", an α, β-heterodimeric enzyme located internally with respect to the cytoplasmic membrane of the resting parietal cells. When the parietal cell is activated, the H, K-ATPase enzyme moves from the cytoplasm to the apical portion of its membrane. Of the two subunits of the gastric H, K-ATPase, the α sub-unit has catalytic function, while the β sub-unit is fundamentally responsible for the proper functioning of this enzyme. It binds to the membrane, thereby preventing this enzyme from going back into the cytoplasm. The function of this protein is to exchange cytoplasmic hydronium with potassium present in the gastric lumen, which is associated with the secretion of chlorine leading to the formation of HCl. It is due to this activity that the PPIs come into play, irreversibly blocking the gastric H, K-ATPase and thus preventing acid secretion.

PPIs are most effective when the parietal cells are stimulated to secrete acid, as they are after a meal; as such, PPIs should be administered before a meal.[40]

**Figure 13: Acidity balance by PPIs**



## Effect of PPIs on acid pocket[27]

The parietal cells contain the H+/K+ ATPase or "proton pumps" located in the canaliculus of the parietal cell and responsible for the transport of acid (H+) into the stomach lumen. The main stimulants of acid secretion at the level of parietal cells are histamine, acetylcholine and to a lesser extent, gastrin.

PPIs cause the acid pocket to become a little smaller in volume and, more importantly, alter the composition of the pocket by increasing its pH (and, thus, decreasing its acidity). Normally, the acid pocket has a pH of approximately 2; after treatment with a proton pump inhibitor, the pocket's pH usually increases to 4 or 5. Thus, the pocket becomes less fortified and caustic.

Reasons for low response to PPIs in NERD:

In one study, patients with NERD had a 37% pooled symptomatic response rate to PPI OD at four weeks[41]. The potential reasons are:

- Weekly acidic reflux
- Hyper sensitivity of the oesophagus, psycho somatic factors, biliary reflux.
- Duodeno-gastro oesophageal reflux (PPI is not going to show any effect on bile and thus not be able to reduce the symptoms).
- Residual acid reflux from the acid
- Hiatus hernia

In GERD and NERD, patient-related factors like poor compliance in the dosing and timing of PPI lead to low response to PPIs.

**Table 13: Pharmacology of different PPI**

| Parameter | Rabeprazole | Omeprazole | Esomeprazole | Pantoprazole | Lansoprazole |
|---|---|---|---|---|---|
| Tmax | 2–5h | 0.5–3.5h | 1h | 2.5h | 1.7 |
| Clearance (mL/min) | 160–330 | 400–620 | 150–266 | 7.6-14.0 | 400-650 |
| $T_{1/2}$ | 1–2h | 0.5–1h | 1.3–1.6h | 1.1 h | 1.5 |
| Mechanism | Suppresses gastric acid secretion by inhibiting the gastric H+, K+ ATPase at the secretory surface of the gastric parietal cell | | | | |

## OMEPRAZOLE

**Table 14: Pharmacology and indications of Omeprazole are summarized below**

| Parameters | Omeprazole (OME) |
|---|---|
| Active Duodenal Ulcer | 20mg OD, 4 weeks |
| Helicobacter pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence | Dual or triple therapy: Omeprazole 20mg with Amoxicillin 1000mg/ clarithromycin 500mg for 14-18 days. |
| Symptomatic GERD | 20mg od upto 4 weeks |
| Treatment of EE due to Acid mediated GERD | 20mg od for 4-8 weeks |
| Pathological Hypersecretory conditions | Starting dose is 60 mg once daily. adjust to patient needs. Daily dosages of greater than 80 mg should be administered in divided doses. Dosages up to 120 mg three times daily have been administered. |

- Omeprazole is the first molecule in the PPI segment which has revolutionized APD management. Even at present it maintains its efficacy in symptom relief with the newer PPIs.
- Omeprazole is the most effective choice for drug induced hyperacidity because of excellent efficacy, safety and affordability.[42]
- Omeprazole has the shortest half-life and is the quickest to reach Tmax. This helps in quicker symptom relief compared to other PPIs.[42]
- In a recently conducted RWE, Omeprazole has been seen to be significantly better with more number of patients achieving relief in Epigastric pain, Regurgitation and Heartburn compared to a leading PPI present in the market both at 2 weeks & 4 weeks in patients suffering from GERD.[43]
- Improvement in heartburn at 2 & 4 weeks was 86% (O) vs 46% & 92% (O) vs 73%. Improvement in regurgitation at 2 & 4 weeks was 65% (O) vs 47% & 98% (O) vs 80%. Improvement in epigastric pain at 2 & 4 weeks was 79% (O) vs 58% & 90% (O) vs 76%. All of the values were statistically significant.[43]
- Omeprazole consistently achieves impressive healing rates for ulcers, with rates of 89% at 4 weeks and 95% at 8 weeks.[44]
- In the context of non-erosive reflux disease (NERD), Omeprazole excels in normalizing intra-esophageal acid exposure, particularly on days 2 and 3.[45]
- Comparably, it maintains a GERD healing rate of 94% at 8 weeks, rivaling newer generation PPIs.[46]
- Omeprazole demonstrates effectiveness in ulcer healing and H. pylori eradication, with notable rates of 96.4% for ulcer healing and 94% for eradication when administered at 40mg.[47]
- Omeprazole also surpasses other PPIs in acid control, as evidenced by higher daytime pH levels and intragastric pH >4 over 24 hours.[48]
- When managing specific conditions, Omeprazole consistently proves its clinical superiority in healing gastric and duodenal ulcers and maintaining remission in complicated GERD cases.[49, 50]

- In cases of acute duodenal ulceration, Omeprazole achieves healing rates on par with other PPIs, and it provides effective symptom relief, with more than 60% of endoscopy-negative reflux disease patients reporting heartburn resolution.[51]
- Omeprazole therapy was well tolerated and highly effective in resolving APD symptoms among T2DM patients receiving fixed oral hypoglycemic agents.[52]
- Omeprazole provides significant improvement in PAGI-SYM and TSQM questionnaires on day 14 and day 28. Patients reported the omeprazole-based therapy as effective, convenient, and satisfactory. Omeprazole therapy is safe and effective for the treatment of APD and shows good improvement in APD in patients suffering from duodenal ulcers, gastric ulcers, and reflux oesophagitis.[53]
- Omeprazole–domperidone combination was beneficial in providing symptomatic relief to patients with diabetes and APD. The combination therapy was well tolerated, with few reports of minor AEs.[54]
- Combination of Omeprazole and Domperidone has proved to be beneficial, in not only reducing the GERD symptoms but also improving the quality of life and treatment satisfaction of patients and the treatment was well tolerated.[55]
- A dissolution study of Omeprazole and Domperidone has found it to be the fastest and the longest in terms of its dissolution profile compared to any other PPI plus Domperidone combination present in the market.[56]
- RCTs found that Omeprazole use was not associated with the occurrence of adverse cardiovascular events and MACE. It also found that the risk of MI was insignificant with the use of Omeprazole.[57]
- When considering specific PPIs, the independent assessment of omeprazole's effects on cardiovascular health found it to be safe.[57]

## RABEPRAZOLE

**Table 15: Indications of Rabeprazole**

| Parameters | Rabeprazole (RPZ) |
|---|---|
| Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD) | 20 mg once daily, 4to8 weeks |
| Maintenance of Healing of Erosive or Ulcerative GERD | 20 mg OD |
| Symptomatic GERD in Adults | 20 mg OD, up to 4 weeks |
| Healing of Duodenal Ulcers | 20 mg OD after morning meal |
| Helicobacter pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence | 20 mg + Amoxicillin 1000mg +Clarithromycin 500mg BID for 7 days |
| Pathological Hypersecretory Conditions, Including Zollinger-Ellison Syndrome | Starting dose 60mg OD |
| Symptomatic GERD for 12 years and older | 20 mg OD up to 8 weeks. |

- Based on the mean 24-h gastric pH, Rabeprazole emerged as the most potent PPI, effectively suppressing gastric acid secretion.[58]
- It possesses the shortest half-life for conversion to its active sulphonamide form, indicating rapid action by swiftly inhibiting the H-K ATPase within just 5 minutes.[59]
- Rabeprazole exhibits unique properties related to pH control, with a notably high pKa value, enabling activation even in higher pH environments, thus showcasing its versatility as a therapeutic option.[60]
- PPIs are metabolised mainly by CYP2C19 and inhibition of this enzyme is heterogeneous within the class of PPIs. PPIs are classified based on their binding affinity for CYP2C19, including those with high and low CYP2C19-inhibitory potential. The hepatic metabolism of Rabeprazole involves both CYP-mediated and non-CYP-mediated metabolism, with the later taking the dominant role. Compared with the other PPIs, Rabeprazole is a weaker competitive inhibitor for CYP2C19 and has a minimal effect on the metabolic pathway of clopidogrel.[61]
- CYP2C19 inhibition by all proton pump inhibitors except Rabeprazole may reduce conversion to the active metabolite of clopidogrel, which may contribute to the lower efficacy of clopidogrel when co-administered with proton pump inhibitors.[62]
- Rabeprazole when co-administered with Clopidogrel, revealed negligible increases in the risk of major adverse cardiovascular events (MACE) and minimal interference with the metabolism of other drugs, as Rabeprazole gets metabolised predominantly via non enzymatic pathway. Odds ratio (individual PPI with clopidogrel leading to clinically significant MACE risk) was lowest with Rabeprazole compared to other PPIs which strengthens the concept that non-enzymatic pathway of Rabeprazole metabolism.[63]
- Rabeprazole is the only PPI with Mucin secretion enhancement. Rabeprazole's impact on mucin content and clinical efficacy in GERD patients with nocturnal heartburn was significant.[64] It excelled in maintaining intragastric pH levels during nighttime, effectively controlling nocturnal acidity.[65]
- It demonstrated superior pH management, sustained higher mean pH levels above 4.0 compared to other PPIs, effectively suppressing acid.[66]
- Rabeprazole exhibits better control over nocturnal acid breakthrough (NAB), rapid symptom relief, and impressive clinical effectiveness in mild to moderate erosive GERD patients.[67]

- Real-world assessments supported its effectiveness as a once-daily dose, ranking it highly for safety and tolerability, while highlighting the holistic patient experience, including medication adherence, symptom relief, convenience, cost-effectiveness, safety, and overall satisfaction.[68]
- ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease states that If one is considering a PPI switch, changing to a PPI that does not rely on CYP2C19 for primary metabolism (Rabeprazole) might be considered.[9]
- As per the one of the studies, approximately three-fourth of the respondents have reported their awareness on these co-prescription hazards, more than 80% have mentioned that anticoagulants may have higher chance of drug-to-drug interactions when given along with a PPI. Most respondents have ranked Rabeprazole in the top among PPIs in terms of safety and tolerability for acid peptic disease, reiterating the existing evidence, through this evidence from real world practice.[69]
- As per Power 1.0 study done by Sud R et al involving 3700 Dyspepsia patients across India, Patient satisfaction and convenience of therapy are higher with Rabeprazole compared to other PPIs. Rabeprazole was associated with the best rates of medication adherence, symptom relief, convenience of therapy, cost-effectiveness, and overall patient satisfaction compared to other PPIs.[68]
- As per the expert recommendations published in Cardiology and Therapy journal, A PPI with minimal drug-drug interactions should be preferred, especially in patients requiring clopidogrel or polypharmacy. Rabeprazole does not interact with clopidogrel to the same extent as other PPIs. No increased risk of MACE is observed when Rabeprazole is given in cardiac patients receiving DAPT (clopidogrel and aspirin). When concomitant use of a PPI and clopidogrel is warranted, Rabeprazole may be safer than other PPIs in terms of MACE risk.[70]
- In a ground breaking study, Rabeprazole shows a rapid and a sustained relief for GERD symptoms including sleep disturbances. Higher proportion of patients exhibited a complete treatment response with Rabeprazole vs other PPIs. Also, Rabeprazole demonstrated higher effectiveness vs other PPIs. 62.92% of patients on Rabeprazole showed complete relief from sleep disturbances by visit 1(day 1-7). >83% patients on Rabeprazole exhibited a complete treatment response as compared to 60% patients on other PPIs.[71]
- Most patients (94%) had excellent or good relief as assessed by their physician whilst 86% of patients rated treatment with Rabeprazole and domperidone as good or excellent. Rabeprazole and domperidone not only provided desired relief of symptoms of GERD but also is very well tolerated. This combination may also improve the quality of life of patients suffering from GERD.[72]
- Twelve weeks of treatment with combination of fixed dose combination of Rabeprazole (enteric-coated, EC) 20 mg + Domperidone (sustained release, SR) 30 mg capsule significantly improved reflux symptoms in patients with LPR. The combination was found to be safe and well tolerated.[73]
- As per one of the systematic reviews and meta-analysis of randomised controlled trials, the combination of a PPI and domperidone resulted in a significant reduction in global GERD symptoms. Adverse events associated with PPI plus domperidone treatment were similar to those associated with PPI monotherapy.[74]
- In diabetes patients with impaired GI motility, use of prokinetics like Itopride helps increase GI motility, thereby improving glycaemic control. Also, Itopride helps in significant improvement in HbA1c levels and gastric emptying time in diabetes patients with gastroparesis.[75]
- Itopride PPI combination shows significant improvement in Post prandial distress syndrome symptoms like post prandial fullness, early satiety and upper abdominal bloating.[76]
- As per the report of one of the efficacy studies done in Nigeria, the triple therapy regime, employing a combination of amoxicillin, clarithromycin and Rabeprazole, has shown great efficacy and safety in the eradication of H. pylori, demonstrating an average eradication rate of 87.2%. Vs 90% eradication rate recommended by World Gastroenterology Organisation guidelines.[77]
- Intravenous Rabeprazole is approved by DCGI since 2004 for or the treatment of gastritis & duodenal ulcer, gastroesophageal reflux disease (GERD) as an alternative to oral therapy in patients who are unable to take oral proton pump inhibitor.[78]

## ESOMEPRAZOLE

**Table 16: Pharmacology and indications of Esomeprazole are summarized below**

| Parameters | Esomeprazole (ESO) |
|---|---|
| Healing of EE | 20mg or 40mg OD, 4-8 weeks |
| Maintenance of healing of EE | 20mg OD |
| Treatment of symptomatic GERD | 20mg OD |
| Risk reduction of NSAID-associated gastric ulcer | 20 mg or 40 mg OD |
| H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence (Triple Therapy) | Amoxicillin 1000 mg twice daily, Clarithromycin 500 mg twice daily, Esomeprazole starting dosage 40 mg twice daily, then once daily; Duration of therapy: 7-14 days |
| Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome | Dosages of up to 240 mg/day have been administered |

- Pharmacokinetic studies have shown an increase in Esomeprazole's bioavailability over the first 5 days of therapy, potentially due to auto-inhibition of metabolism, distinguishing it from other PPIs with consistent bioavailability over time.[79]
- The full/standard doses (40 mg per day) of Esomeprazole should be recommended as first-line treatments for GERD in adults based on 4–8 weeks of short-term therapy for healing.[80]
- Studies have demonstrated that Esomeprazole 40 mg od is superior to all other PPIs at standard doses in terms of achieving higher 24-hour median intragastric pH thus making it truly the only PPI to offer 24 hours acid control.[81]
- Esomeprazole has demonstrated significant improvements in erosive esophagitis healing at 4 and 8 weeks, surpassing other PPIs. It also offers a higher probability of heartburn relief, making it a favorable choice for symptom management.[82]
- Esomeprazole exhibits superior efficacy by reporting significantly higher healing rates at week 8 compared to other PPIs, along with complete and sustained heartburn relief for the initial 4 weeks. It maintains a higher intragastric pH for a longer duration than other PPIs, demonstrating superior acid control capability.[83]
- Pharmacokinetic studies have shown an increase in Esomeprazole's bioavailability over the first 5 days of therapy, potentially due to auto-inhibition of metabolism, distinguishing it from other PPIs with consistent bioavailability over time.[79]
- Long-term use of Esomeprazole does not increase the risk of major adverse cardiovascular events, underlining its safety profile.[57]
- Co-prescription of PPIs like Esomeprazole and clopidogrel remained statistically non-significant for the risk of MI.[57]
- The overall results of this meta-analysis showed that long-term PPI (Esomeprazole) use was not associated with an increased risk of adverse cardiovascular events.[57]
- On day 5, intragastric pH was maintained above 4.0 for a mean of 14.0 h with Esomeprazole, highest amongst all other PPIs currently available.
- Esomeprazole also provided a significantly higher percentage of patients with an intragastric pH greater than 4.0 for more than 12 h relative to the other proton pump inhibitors ($p < 0.05$).[83]

## PANTOPRAZOLE

**Table 17: Pharmacology and indications of Pantoprazole are summarized below**

| Parameters | Pantoprazole |
|---|---|
| Short-Term Treatment of Erosive Esophagitis Associated With GERD | 40 mg OD for upto 8 weeks |
| Maintenance of healing of erosive esophagitis | 40mg OD |
| Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome | 40 mg bid |

- Pantoprazole has the ability to heal erosive esophagitis swiftly and reliably, with the 40 mg/day dosage group achieving an impressive 88% cumulative healing rate after 8 weeks.[84]
- Pantoprazole has high effectiveness and good tolerance in treating acute duodenal ulcers, achieving a remarkable 71% complete ulcer healing rate within just 2 weeks, while also establishing its equivalence to Omeprazole in ulcer healing and pain relief.[85]
- Research emphasized the dosing regimen, suggesting that a double daily dose of pantoprazole (40 mg) as part of a 7-day triple therapy was superior in eradicating H. pylori compared to a single 40 mg dose.[86]
- Insights into prophylaxis against gastrointestinal lesions revealed that pantoprazole 20 mg o.d., pantoprazole 40 mg o.d., and Omeprazole20 mg o.d. all offer equivalent, effective, and well-tolerated protection against GI lesions, including peptic ulcers.[87]
- Studies involving pediatric patients with GERD symptoms demonstrated the effectiveness of both 20 mg and 40 mg pantoprazole dosages, with noticeable improvements observed as early as 1 week.[88]

## LANSOPRAZOLE

**Table 18: Pharmacology, indications of Lansoprazole**

| Parameters | Lansoprazole |
|---|---|
| Duodenal ulcer Short term treatment<br>Maintenance of healed | 15 mg OD for 4 weeks<br>15 mg OD |
| H. pylori Eradication to Reduce Recurrence of Duodenal Ulcer | Triple therapy: 30mg bid for 10 or 14 days +Amoxicillin (1 g) + Clarithromycin (500mg)<br>Dual therapy: 30 mg tid + Amoxicillin (1 g) |
| Benign Gastric Ulcer | 30 mg OD upto 8 weeks |
| NSAID- associated gastric ulcer | 30 mg OD upto 8 weeks |
| GERD | 15 mg OD up to 8 weeks |
| EE | 30 mg OD upto 8 weeks |

- Lansoprazole, administered at a dose of 30 mg twice daily, demonstrated equal effectiveness and good tolerability compared to Omeprazole at a daily dose of 40 mg in controlling GERD symptoms.[89]
- Both 15 mg and 30 mg Lansoprazole effectively maintained healing in duodenal ulcer patients, with 85% of patients remaining ulcer-free.[90]
- Lansoprazole significantly extended the time to duodenal ulcer recurrence highlighting its importance as a maintenance therapy.[91]
- It effectively reduced symptoms of upper abdominal discomfort and heartburn, with a substantial number of patients achieving complete symptom resolution within 8 weeks.[92]

## Role of High dose of PPI in APD

The ACG guidelines suggest using high-dose intravenous PPI therapy (a combination of bolus and continuous infusion) for 72 hours following effective endoscopic treatment of high-risk peptic ulcers. Subsequently, a meta-analysis involving 22 randomized trials compared the effects of high-dose bolus PPI with continuous infusion to intermittent PPI therapy after evaluating peptic ulcer bleeding via endoscopy. The analysis found no significant discrepancies in outcomes such as mortality, risk of rebleeding, need for surgery, length of hospital stays, or blood transfusion requirement. Similarly, a systematic review from compared high-dose PPI therapy to intermittent PPI therapy after successful endoscopic treatment of high-risk peptic ulcers, indicated that intermittent PPI therapy was as effective as high-dose PPI with continuous infusion in terms of rebleeding within 7 or 30 days, mortality, and the need for blood transfusion.[9, 93]

As per the latest guideline of optimizing PPI published in Sept-Oct 2023, states **"In patients with severe erosive esophagitis or peptic stricture, initial treatment should be with double dose of PPIs for at least 8 weeks"**. Level of evidence - moderate; strong recommendation.[94]

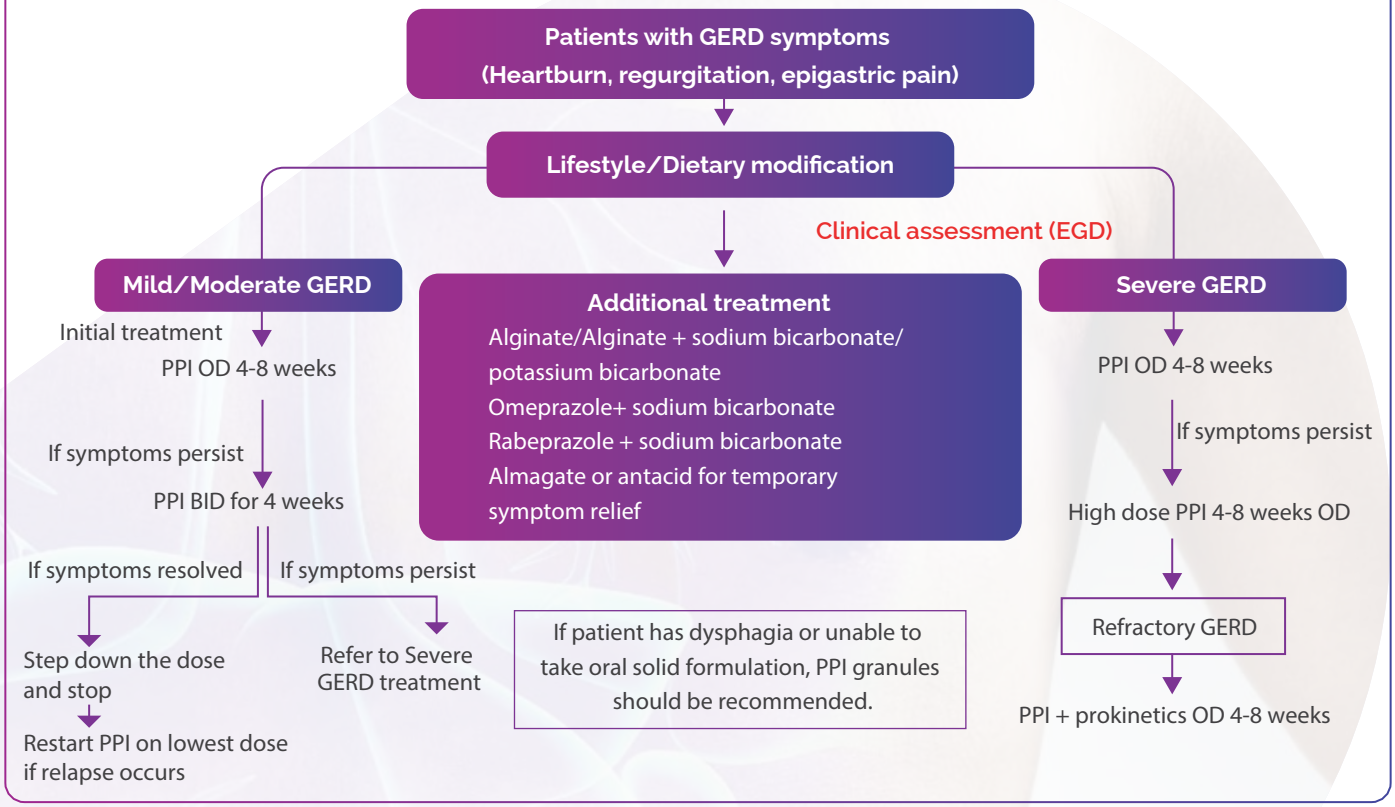
Endoscopic findings in the Rabeprazole 40 mg group showed an absolute improvement of 30% and relative improvement of 55% over another high dose PPI group. Rabeprazole (40 mg) was found to be better choice for mild-to-moderate GERD compared with other high dose PPI because of its better efficacy and safety profile.[95]

Most frequent regimens recommended for treatment of Helicobacter pylori infection in peptic ulcer disease.

| | Drug combinations | Regimen | Duration |
|---|---|---|---|
| Triple therapy | PPI plus amoxicillin* plus clarithromycin | Double doset of PPI every 12 h<br>1000 mg amoxicillin every 12 h<br>500 mg clarithromycin every 12 h | 14 Days |
| Quadruple non-bismuth-based c oncomitant therapy | PPI plus amoxicillin plus clarithromycin plus metronidazole | Standard dose of PPI every 12 h<br>1000 mg amoxicillin every 12 h 500 mg clarithromycin every 12 h 500 mg metronidazole every 12 h | 14 Days |
| Bismuth-based quadruple therapy | PPI plus bismuth subcitrate plus tetracycline plus metronidazole | Standard dose of PPI every 12 h<br>120 mg bismuth subcitrate every 6 h<br>500 mg tetracycline every 6 h<br>500 mg metronidazole every 8 h | 14 Days |
| Fluoroquinolone-based PPI plus amoxicillin plus triple therapy+ | PPI plus amoxicillin plus levofloxacin with or without bismuth | Standard dose of PPI every 12 h<br>1000 mg amoxicillin every 12 h<br>500 mg levofloxacin every 24 h<br>240 mg bismuth every 12 h | 14 Days |
| Rifabutin-based triple therapyS | PPI plus amoxicillin plus rifabutin | Standard dose of PPI every 12 h<br>1000 mg amoxicillin every 12 h<br>150 mg rifabutinevery 12 h | 10 Days |

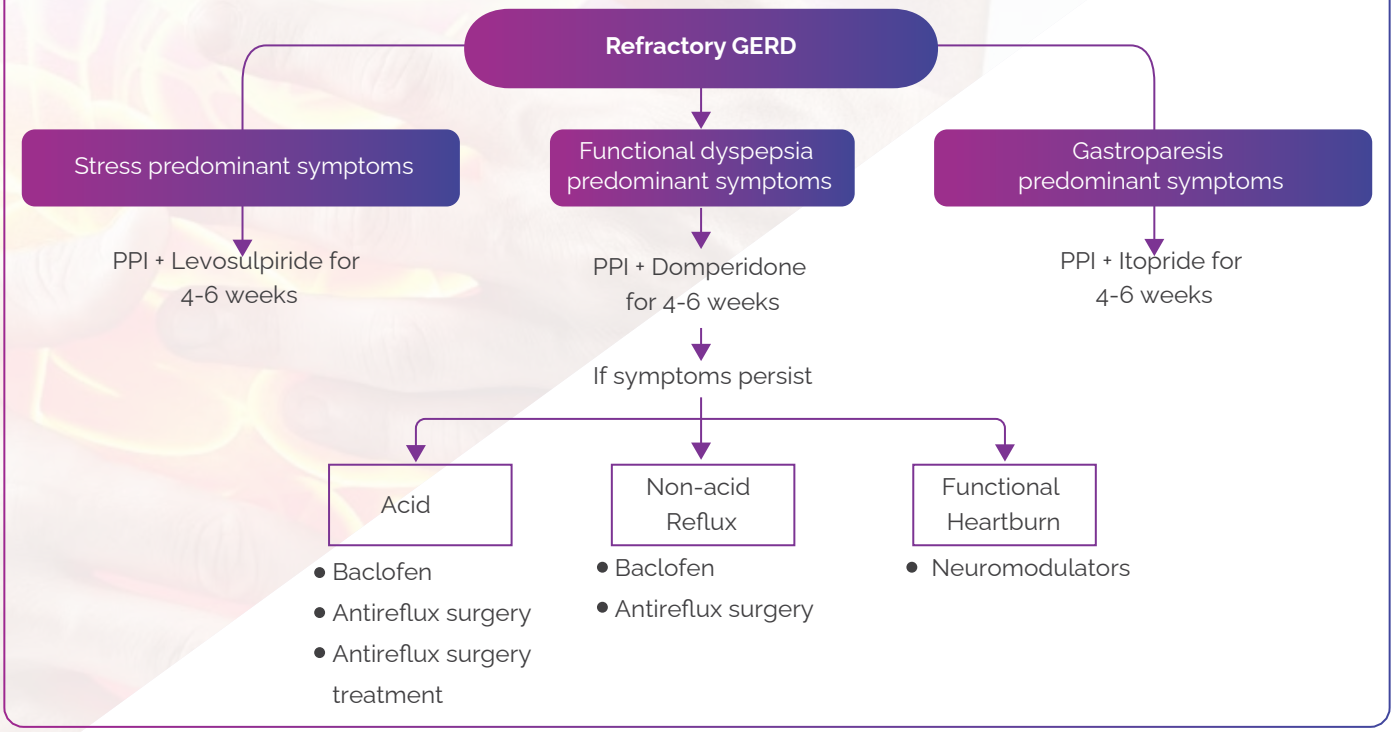
# Treatment for APD

**Figure 14: Algorithm for the treatment of GERD[96, 97]**

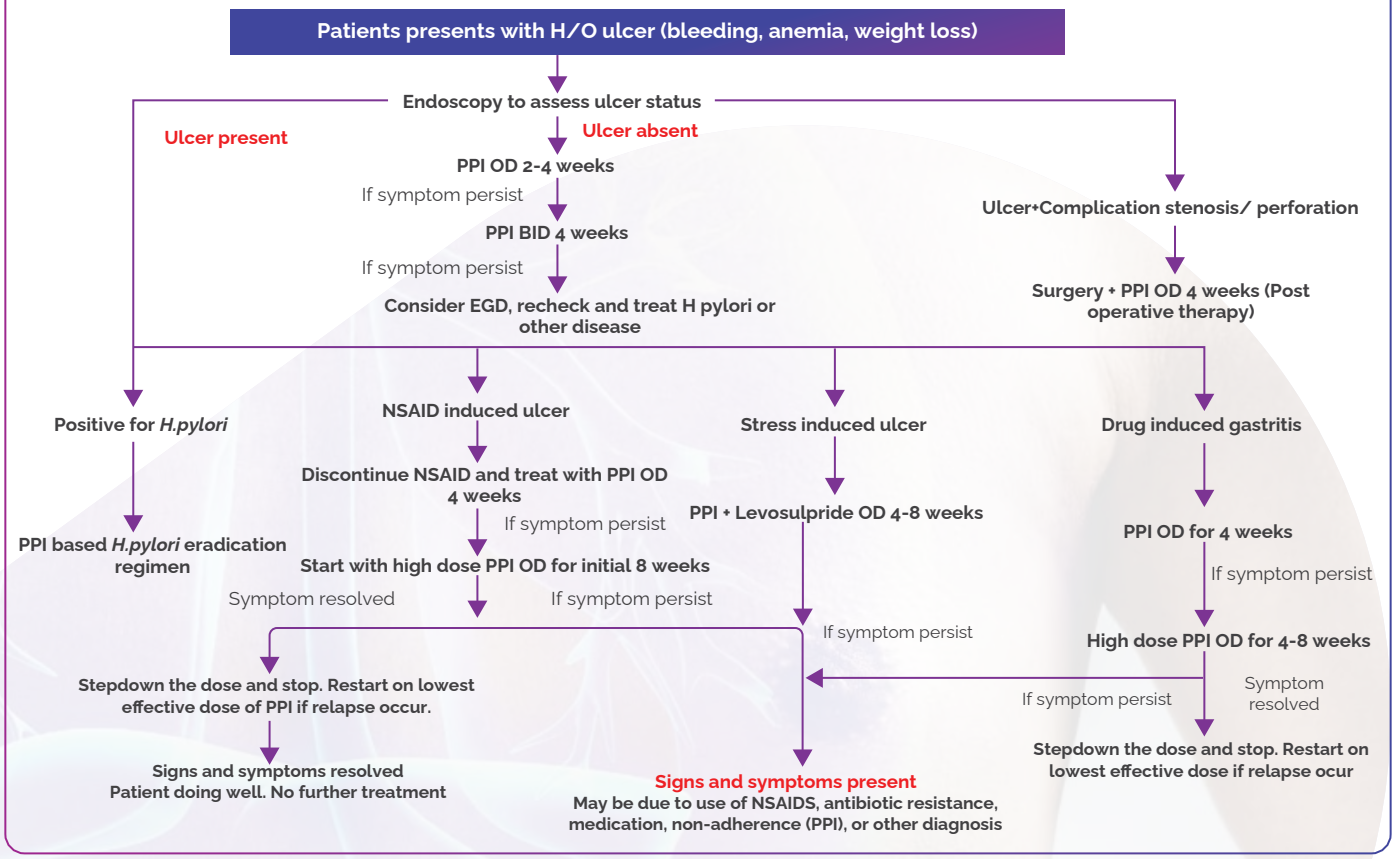



FDC of PPI + Prokinetics should be used judiciously in certain patients only.
Prokinetics such as Domperidone, Levosulpiride, Acotiamide, Itopride
PPI should be given for longer duration in patients with extra esophageal symptoms, since response to PPI is observed after 4-8 weeks in such cases.
PPI such as O: Omeprazole, E: Esomeprazole, R: Rabeprazole, P: Pantoprazole, L: Lansoprazole

**Figure 15: Algorithm for the treatment of refractory GERD**



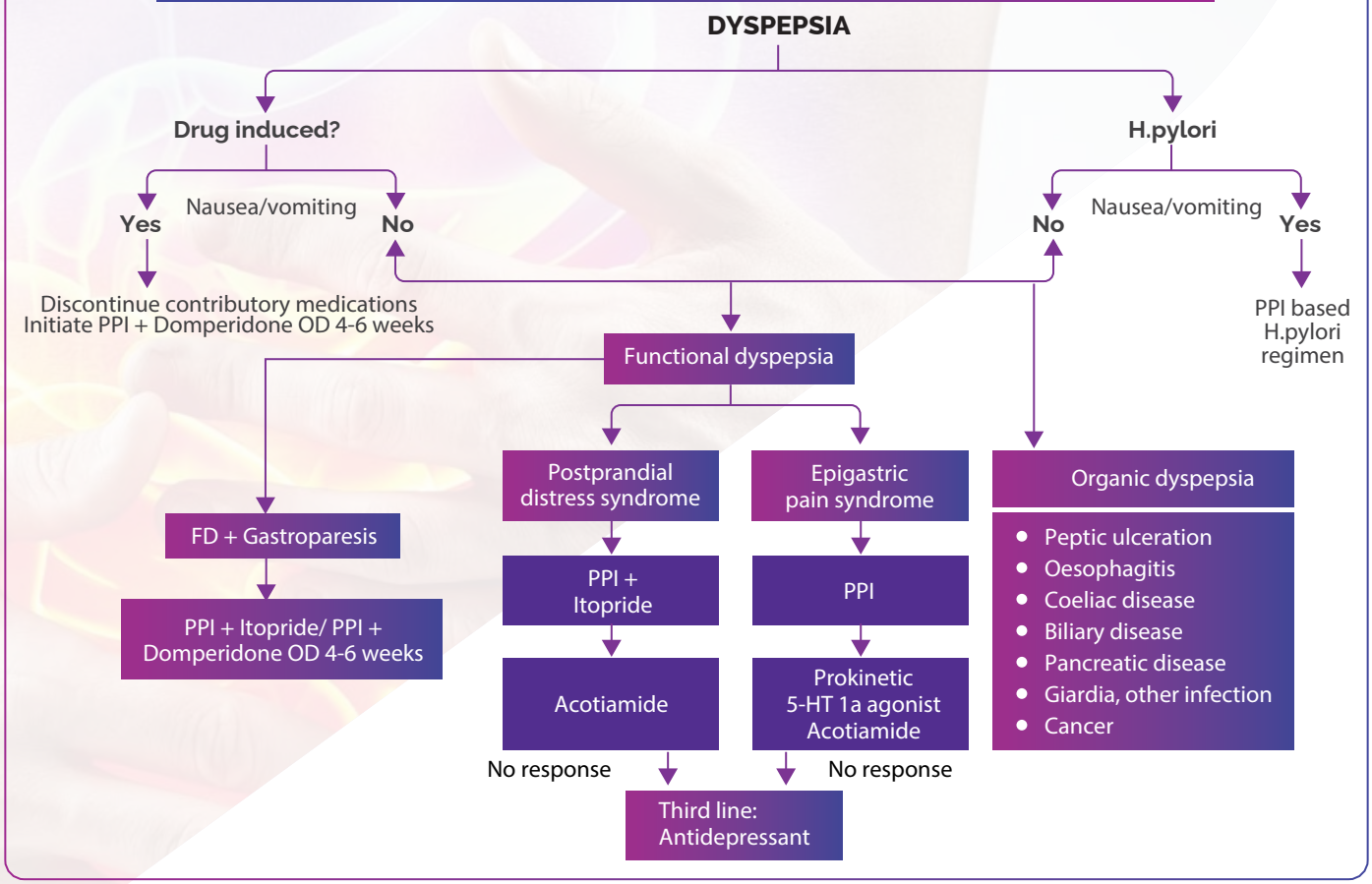
## Figure 16: Algorithm for the treatment of peptic ulcer disease[97]




Prokinetics such as Domperidone, Levosulpiride, Acotiamide, Itopride

PPI such as O: Omeprazole, E: Esomeprazole, R: Rabeprazole, P: Pantoprazole, L: Lansoprazole

## Figure 17: Algorithm for the treatment of dyspepsia[96-98]




FDC of PPI + Prokinetics should be used judiciously in certain patients only

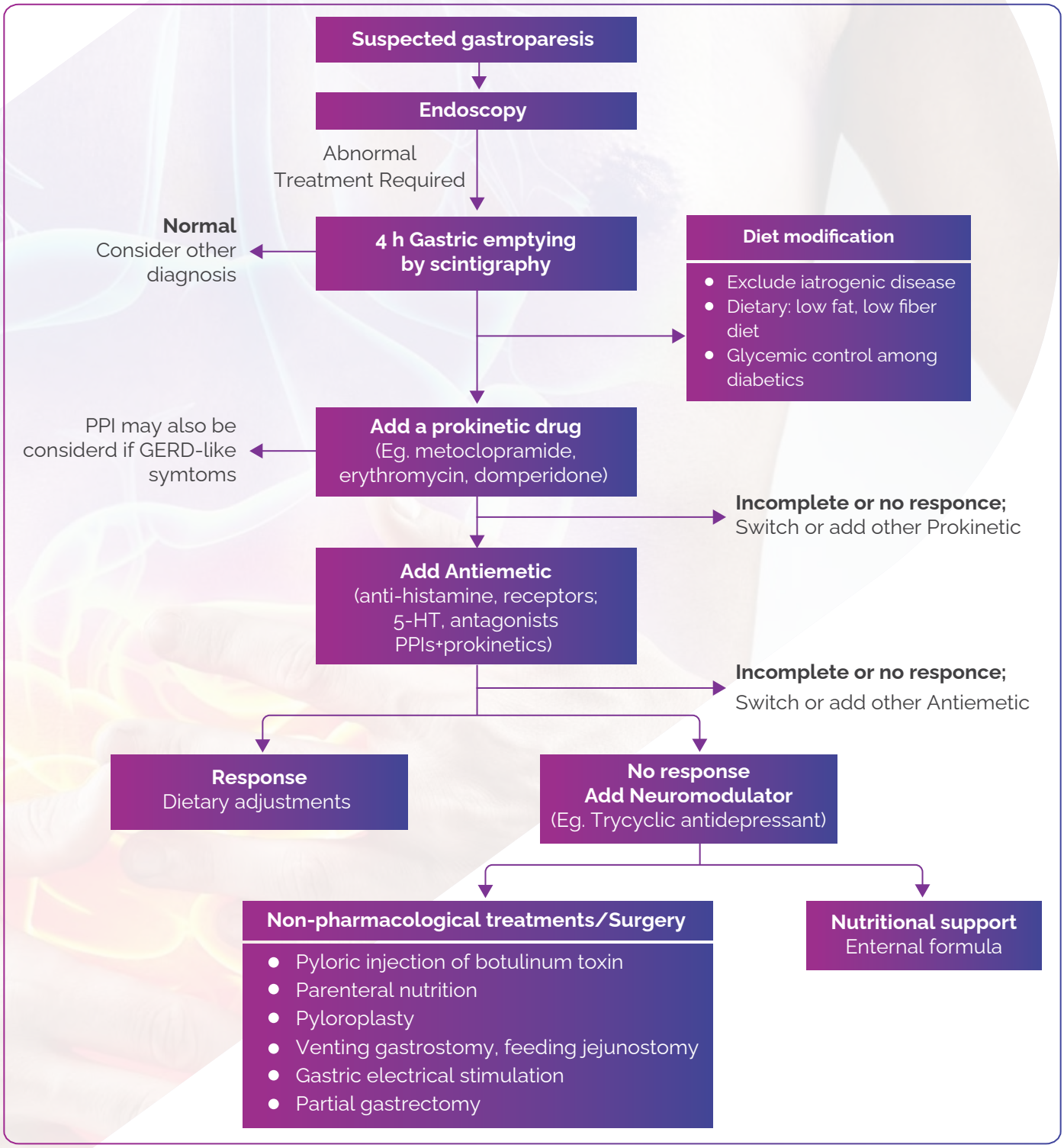
Prokinetics such as Domperidone, Levosulpiride, Acotiamide, Itopride

PPI such as O: Omeprazole, E: Esomeprazole, R: Rabeprazole, P: Pantoprazole, L: Lansoprazole

## Management for Gastritis[18]

- Treatment regimens differ from antibiotics (in H. pylori gastritis) to vitamin supplementation (in autoimmune metaplastic atrophic gastritis) to immunomodulatory therapy (in autoimmune enteropathy) to dietary modifications (in eosinophilic gastritis).
- Short term PPI reduces antral gastritis.
- H. pylori-associated gastritis: A triple-therapy of clarithromycin/proton-pump inhibitor/amoxicillin for 14 to 21 days is considered the first line of treatment. Clarithromycin is preferred over metronidazole because the recurrence rates with clarithromycin are far less compared to a triple-therapy using metronidazole. In case of clarithromycin resistance, metronidazole is the next choice. Quadruple bismuth containing therapy may be beneficial, particularly when using metronidazole.

## Management for gastroparesis[99]




Prokinetics have role in patients with viral gastroenteritis and should be given for 4-8 weeks

FDC of PPI + Prokinetics should be used judiciously in certain patients only

# When to refer to a specialist?

**Red flags in GERD[100]**

- Recurrent vomiting
- Dysphagia or odynophagia
- Weight loss
- Evidence of gastrointestinal blood loss e.g. haematemesis, iron deficiency or anaemia
- Duration of symptoms > 5 years or <6 months
- Epigastric mass
- Age >50 years

**Red flags in PUD for referral to a specialist[101]**

- Signs of acute bleeding
  - Melaena, self-reported or found on digital rectal examination
  - Blood in vomit (haematemesis)
  - Abnormally high pulse or low blood pressure
  - Severe anaemia
- Signs of perforation or penetration such as severe abdominal pain and peritonitis
- Symptoms suggestive of malignancy in patients over 50:
  - Dysphagia
  - Unexplained weight loss with upper abdominal pain or gastro-oesophageal reflux
  - Loss of appetite - Recurrent vomiting - Anaemia
- Second line eradication therapy fails
- Symptoms persist despite successful eradication
- Family history of gastric cancer

Red flags for dyspepsia:

- Dysphagia
- Unintentional weight loss
- Anemia
- Palpable epigastric mass
- Age> 55 yrs. with new onset dyspepsia,
- GI bleeding
- Persistent vomiting

**Table 19: Role of Nutraceuticals in APD management[14]**

| Entity | Action |
|---|---|
| Korean Red Ginseng | Notable for anti-inflammatory properties; inhibits 5-lipoxygenase (5-LOX) activity induced by H. pylori, leading to reduced gastric inflammation and oxidative DNA damage. |
| Allium Sativum (Garlic) | Displays antioxidant effects; suppresses H. pylori-induced gastric inflammation. Interaction with conventional drugs should be considered. |
| Curcuma Longa (Turmeric) | Anti-inflammatory and antioxidant qualities; associated with inhibition of H. pylori-induced 5-LOX activity. |
| Zingiber Officinalis (Ginger) | Offers anti-inflammatory and antioxidant benefits; inhibits PGE2 and parietal cell H+, K+-ATPase. Use may lead to side effects (nausea, vomiting) and interactions with certain drugs. |
| Zingiber Zerumbet | Demonstrates gastroprotective mechanisms; increases antioxidant GSH levels, reduces lipid peroxidation, yielding antioxidant, antiproliferative, anti-inflammatory, and antisecretory effects. Potential side effects and drug interactions. |
| Camellia Sinensis (Tea Plant) | Suppresses tumor necrosis factor-alpha (TNF-α) gene expression and urease inhibition. Shows antioxidant benefits; improves intestinal bacterial flora function. Possible interactions with drugs and side effects (dizziness, diarrhea, headaches, insomnia, heartbeat irregularities, potential iron deficiency). |

# Lifestyle modifications for APD management[102]

Lifestyle modifications play a crucial role in managing acid peptic disorders. Here are some key aspects to consider while patient counseling:

- Dietary Changes: Consuming smaller, frequent meals instead of large meals, avoiding spicy and fatty foods, reducing intake of caffeine, alcohol, and citrus fruits, and incorporating fiber-rich foods.
- Weight Management: regular exercise and a well-balanced diet.
- Stress Reduction Techniques: deep breathing exercises, meditation, yoga, and engaging in activities to promote relaxation and well-being.
- Avoidance of Triggering Factors: certain foods, beverages, smoking, or medications that can worsen acid production or irritate the stomach lining.
- Patient Education and Counseling: Patients should be informed about the causes, symptoms, and triggers of acid peptic disorders. This empowers patients to make informed decisions about their lifestyle choices and adhere to treatment plans.
- Prevent H. pylori Infection Prevention: Maintain good hygiene, avoiding contaminated food and water, and following appropriate antibiotic treatment, when necessary.

**Table 20: Lifestyle modifications for GERD management.**

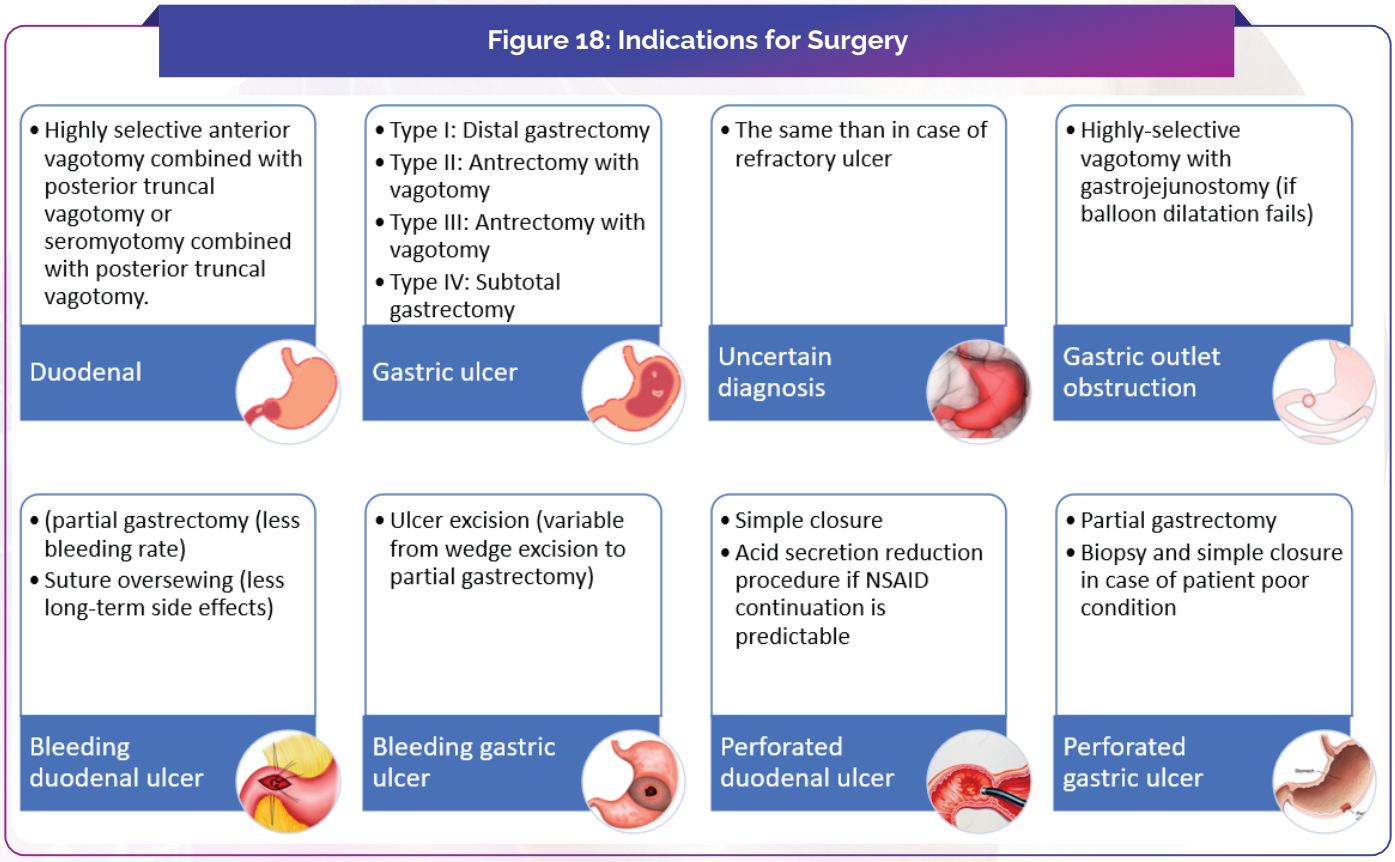
| Lifestyle modification | Strength of scientific evidence | Patho-physiologically conclusive? | Recommendable? |
|---|---|---|---|
| Avoid fatty meals | Equivocal | Equivocal | Yes |
| Avoid carbonated beverages | Moderate | Yes | Yes |
| Select decaffeinated beverages | Equivocal | Equivocal | Not generally |
| Avoid citrus | Weak | Yes | Yes, if citrus triggers symptoms |
| Eat smaller meals | Weak | Yes | Yes |
| Lose weight | Equivocal | Equivocal | Yes |
| Avoid alcoholic beverages | Weak | Mechanisms not understood; different alcoholic beverages have different effects | Yes |
| Stop smoking | Weak | Yes | Yes |
| Avoid excessive exercise | Weak | Yes | Yes |
| Sleep with head elevated | Equivocal | Equivocal | Yes |
| Sleep on the left side | Unequivocal | Yes | Yes |

# Surgical Interventions for Acid Peptic Disorders

Elective Surgery for Peptic Ulcer Disease has diminished significantly over the last 25 years.

## Indications for Surgery[103]

**Figure 18: Indications for Surgery**



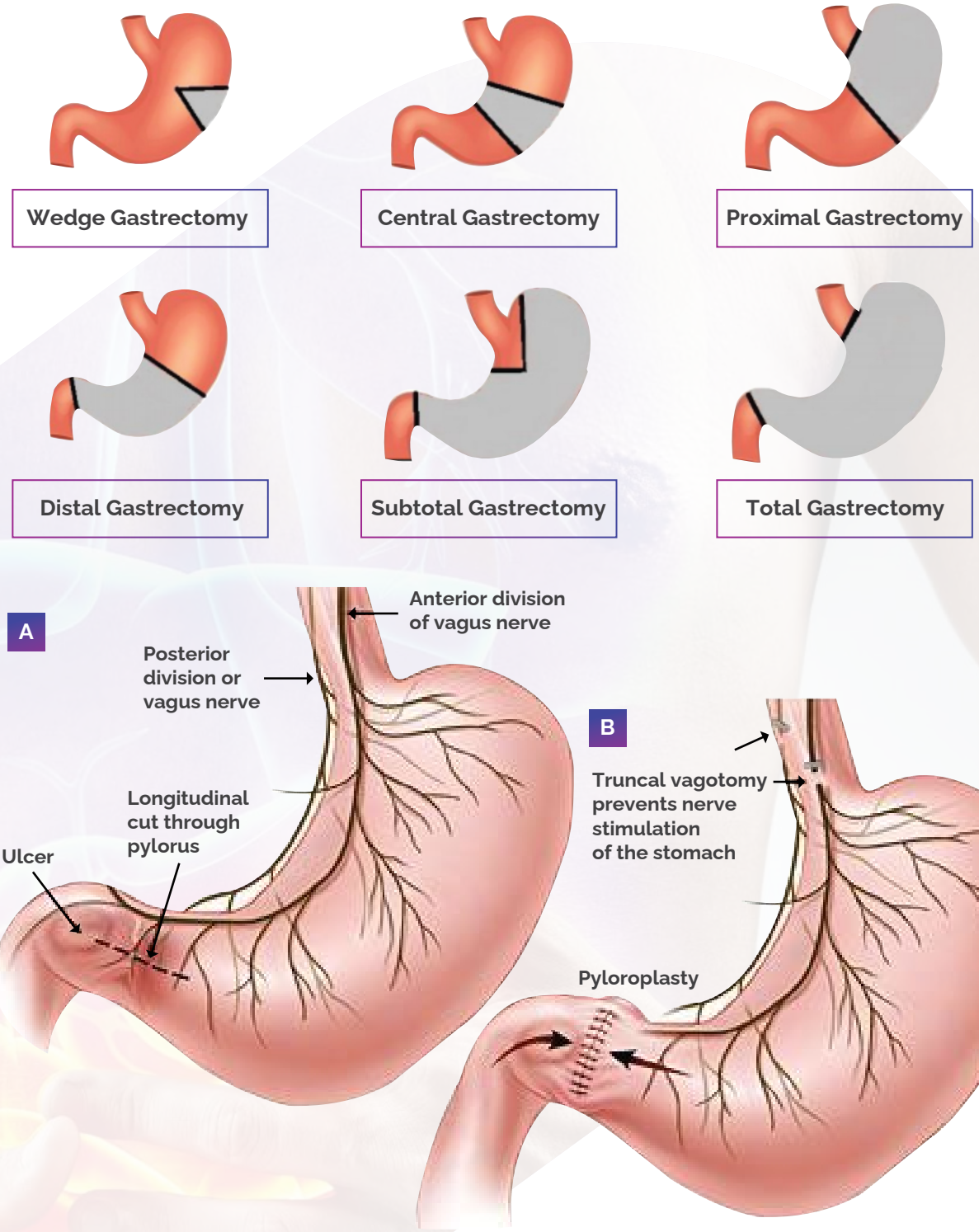

## Surgical Procedures

Surgical treatment for GERD has previously been limited to cases with chronic complicated reflux and severe symptomatology not responding to medication

Laparoscopic Nissen fundoplication is currently the 'gold-standard' for treating GERD in patients who don't respond completely to medications or can't take medications for another reason. Laparoscopic Nissen fundoplication is the most commonly performed antireflux procedure. The last few years novel endoscopic techniques have been introduced for the treatment of GERD. Endoluminal gastroplication (ELGP) was the first of the proposed endoscopic treatments for GERD. The endoluminal fundoplication (ELF) technique has been introduced to overcome some of the Plicator's disadvantages, such as the inability to reduce hiatal hernia and create a robust gastroesophageal valve.[104]

Below figure shows the different regions of the stomach which may be cut out during a gastrectomy surgery.[105]

**Figure 19: Various stomach regions that can be excised in a gastrectomy**




A vagotomy is conducted when acid production within the stomach can't be decreased by other means. The objective of the process is to disable the acid-producing capacity from the stomach. Vagotomy is indicated when there is blockage of digestive flow, bleeding, or perforation.[106]

**Table 21: Postoperative care and recovery steps**

| Step | Description |
|---|---|
| Diet and Nutrition | Initiate • Clear liquid diet • Soft diet • Regular diet. Nutritional supplements may be recommended for healing and to prevent malnutrition. |
| Early Mobilization | Encourage early sitting, standing, and walking to prevent deep vein thrombosis and pneumonia. Patient assistance is crucial, following the surgical team's safety guidelines. |
| Medication Management | Review and adjust drug dose and frequency. Emphasize medication adherence and stress the importance of follow-up appointments. |
| Follow-up Care | Establish a post-op follow-up plan, including scheduled clinic visits or consultations with the surgeon or gastroenterologist. |
| Patient Education | Educate patients on recognizing complications (infection, bleeding, bowel obstruction). Stress the importance of seeking immediate medical attention for any concerning symptoms. |

# Complications and Long-Term Outlook

## Potential Complications of Acid Peptic Disorders

APD if not diagnosed and treated promptly can lead to serious complications.

| Type of APD | Potential complications |
|---|---|
| PUD[3] | Upper gastrointestinal bleeding, gastric outlet obstruction, perforation, penetration, gastric cancer |
| GERD[107] | Esophagitis can vary widely in severity with severe cases resulting in extensive erosions, ulcerations, and narrowing of the esophagus. It may also lead to gastrointestinal bleeding. Chronic esophageal inflammation can lead to scarring resulting in complaints of dysphagia. Changes of Barrett's esophagus may extend proximally from the gastroesophageal junction (GEJ) and have the potential to progress to esophageal adenocarcinoma, making early detection very important in the prevention and management of malignant transformation |
| Gastritis[18] | Peptic ulcer, Chronic atrophic gastritis, Gastric metaplasia/dysplasia, Gastric cancer (adenocarcinoma), Iron-deficiency anemia, vitamin B12 deficiency, Gastric bleeding, Achlorhydria, Gastric perforation, Mucosa-associated lymphoid tissue (MALT) lymphoma, Neuroendocrine tumors (NET) |
| Dyspepsia[108] | Esophageal stricture, Pyloric stenosis, Barrett's esophagus |
| Gastroparesis[109] | Severe protein-calorie malnourishment, Bezoars, Mallory Weiss tears from retching and vomiting, Procedure-related complications |

## Long-Term Management and Follow-Up[110]

This involves a combination of lifestyle changes, medication therapy, and regular monitoring.

**Lifestyle modifications include:**

- Maintaining a healthy weight
- Avoiding triggering foods
- Eating smaller meals
- Avoiding lying down immediately after eating
- Smoking cessation

Medication therapy often includes the use of proton pump inhibitors (PPIs) or H2 blockers to reduce stomach acid production and promote healing. Antacids may provide short-term relief, and prokinetics can help improve stomach emptying and reduce acid reflux. Regular monitoring is essential and includes follow-up appointments, endoscopy to assess healing and detect complications, pH monitoring to evaluate acid suppression therapy effectiveness, and imaging tests like barium swallow or upper gastrointestinal series.

PPIs have proven to be very effective and safe in managing GERD, healing peptic ulcer disease, and reducing the incidence of nonsteroidal anti-inflammatory drug–associated gastropathy, becoming one of the most-prescribed medications by healthcare providers. PPIs are also the mainstay of treatment by physicians across due to their efficacy and low toxicity.

# Conclusion

## Future Directions in APD Management

The future of managing acid peptic disorders revolves around personalized treatments, targeted mechanisms, and non-pharmacological interventions. Some patients are refractory to PPI treatment, and alternative strategies, such as switching PPIs or adding H2RAs, may be eliminated with improved initial variable response to treatment. Alginates have a unique, non-systemic, physical, rather than pharmacological, mode of action. They aid in prevention of gastric reflux, inhibition of pepsin and bile acids and offer topical protection of the sensitive esophageal mucosa. Developing new compounds or other therapies based on physiological mechanisms may also be explored in the future.[1]

### Newer Prokinetics

Newer agents targeting diverse gastric (fundic, antral and pyloric) motor functions, including novel serotonergic 5-HT4 agonists, dopaminergic D2/D3 antagonists, neurokinin NK1 antagonists, and ghrelin agonist.[111] These are explained below:

**Table 22: Newer prokinetics targeting gastric functions**

| Name | Indication |
|---|---|
| Novel 5-HT4 Receptor Agonists | Prucalopride: FDA and EMA-approved for chronic constipation; effective in gastroparesis. Velusetrag: Efficacious in diabetic and idiopathic gastroparesis. Naronapride, Felcisetrag: Potential indications not specified |
| Dopaminergic D2/3 Antagonists | Trazpiroben: Increases volume to fullness during nutrient drink test in patients with functional dyspepsia |
| Neurokinin NK1 Antagonists | Tradipitant: Improves several symptoms of gastroparesis, including nausea, after 4 weeks of treatment |
| Ghrelin Agonists | Recombinant human ghrelin and synthetic pentapeptide ghrelin (Relamorelin): Being studied in patients with gastroparesis |
| Muco-protective Drugs[112] | Rebamipide: Effective in healing gastric ulcers. Polaprezinc and Nocloprost: Mucosal protective agents with potential, but efficacy in combination with antibiotics or NSAID prevention is unexplored |
| P-CABs (Potassium Competitive Acid Blockers)[113] | Inhibit H+, K+ ATPase via potassium-competitive reversible action. Have quick onset, act without proton pump activation, and acid reduction. Vonoprazan: Acid-stable, aids reflux esophagitis treatment. Linaprazan: GERD with esophagitis efficacy but lacks benefit for NERD patients. Revaprazan: First approved P-CAB, available in Korea and India. Tegoprazan: Approved for EE and NERD treatment in Korea |
| Other Drugs | GABA-B Receptor Agonists (Lesogaberan, Arbaclofen Placarbil): Being researched for the management of GERD. |

## Summary

- Diagnosis of acid peptic disorders are typically based on the patient's clinical presentation, including symptoms such as epigastric pain, abdominal discomfort, and dyspepsia.
- Confirmatory tests include endoscopy or, non-invasive tests like urea breath test or stool antigen test for detecting Helicobacter pylori infection.

- PPIs reduce stomach acid production, promote healing of the ulcer, and prevent recurrence. They are the mainstay of treatment for acid peptic ulcers.
- Helicobacter pylori Eradication: combination therapy involving PPIs and antibiotics is necessary to eradicate the bacteria. The choice of antibiotics may vary depending on local resistance patterns.
- The duration of PPI therapy for ulcer healing and prevention of recurrence varies but is typically around 4-8 weeks. H. pylori eradication therapy duration may differ but is often around 7-14 days.
- Lifestyle changes, such as avoiding smoking, alcohol, nonsteroidal anti-inflammatory drugs (NSAIDs), and trigger foods, can help promote ulcer healing and prevent complications.
- Regular follow-up visits with the healthcare provider are important to assess the response to treatment, monitor for complications, and adjust therapy as needed.
- In some cases, long-term maintenance therapy with a lower dose of PPI may be required to prevent ulcer recurrence, particularly for individuals at higher risk or with persistent H. pylori infection.

## Appendix

**Table 23: Diagnosis of GERD[9, 36]**

| Diagnostic tests | Significance |
|---|---|
| Empirical PPI therapy (PPI trial) | For extraoesophageal GERD, Classic symptoms, no alarm features. |
| Urea breath test or H. pylori stool antigen test | For uninvestigated dyspepsia or in population with high prevalence of H. pylori |
| Esophagogastroduodenoscopy (EGD) | For extraoesophageal GERD, Classic symptoms, no alarm features. |
| Esophageal biopsy | To exclude, non-GERD causes for symptoms – for example, EoE. |
| Gastric biopsy | For unknown H. pylori status in patients undergoing EGD for upper GI symptoms |
| Esophageal manometry | To diagnose motility disorders in endoscopy-negative patients unresponsive to PPI therapy. Preoperative evaluation for surgery Location of pH probe |
| pH or impedence pH monitoring | For atypical symptoms, PPI-refractory GERD symptoms Preoperatively, and non-erosive disease |
| Barium swallow | For evaluation of dysphagia and occasionally for characterization of hiatal hernia |
| PEP test | Non-invasive diagnostic test to help identify reflux. |

**Table 24: Diagnostic tests for PUD**

| Diagnostic tests | Significance |
|---|---|
| Esophagogastroduodenoscopy (EGD) | Indicated in patients with evidence of bleeding, weight loss, persistent vomiting; whose symptoms do not respond to medications; and older than 55 years. |
| Barium or diatrizoate meglumine and diatrizoate sodium (Gastrografin) contrast radiography (double-contrast hypotonic duodenography) | Indicated when endoscopy is not suitable or if complications such as gastric outlet obstruction suspected. These procedures are used less because it can miss small ulcers and does not allow direct treatment of an ulcer. |
| Serum gastrin | To suspect Zollinger Ellison syndrome |
| Computerized tomography | Helpful in the diagnosis of PUD's complications like perforation and gastric outlet obstruction. |

## Diagnostic tests for H pylori infections

The American College of Gastroenterology (ACG) recommends testing for H. pylori infection in patients with active PUD or history of PUD, dyspepsia symptoms, or gastric MALT lymphoma. The rationale for testing patients with a history of PUD who are currently asymptomatic is that detecting and treating H. pylori infection can reduce the risk of recurrence. The test-and-treat strategy for detecting H. pylori is appropriate in patients with dyspepsia and low risk of gastric cancer.[15]

| Diagnostic tests | Significance |
|---|---|
| Urea breath test | Used for initial diagnosis and test of cure |
| Histology | Detection of H pylori using microscopy of gastric mucosal biopsy |
| Rapid urease test | Biopsy from gastric mucosa |
| Culture and antimicrobial susceptibility tests | Detection of H pylori by culture from gastric biopsies. |
| Antibody tests | Detects IgG antibodies to H pylori in serum, sputum, or urine |
| Faecal antigen test (FAT) | Detects H pylori antigen in faeces using an immunoassay |

**Table 25: Diagnostic tests for drug induced gastritis**

| Diagnostic tests | Significance |
|---|---|
| Endoscopy | Confirms the diagnosis and remains the gold standard for the evaluation and management of drug-induced gastritis. It is usually necessary for patients who have either persistent symptoms after discontinuation of culprit medicine for one week or presentation |

**Table 26: Diagnostic test for gastritis[114]**

| Diagnostic tests | Significance |
|---|---|
| Gastric mucosal biopsy | For diagnosis of CG and indicates aetiology |
| Parietal cell antibody (serum) | Presence indicates chronic gastritis |
| Intrinsic factor antibody | Presence indicates pernicious anaemia which points toward bleeding gastric ulcer. |
| H. pylori antibody (IgG) | Indicates past H. pylori infection |
| Urea breath test | Confirms eradication of presence of H. Pylori |
| H. pylori faecal antigen test | Confirms eradication of presence of H. pylori |

## Table 27: Diagnostic test for dyspepsia[115]

| Diagnostic tests | Significance |
|---|---|
| Radiological method (Barium meal) | Gastroparesis can be diagnosed with barium meal |
| Ultrasonography | Does not involve ionizing radiation |
| Endoscopy | • Permits direct visualization of the oesophagus, gastric and duodenal mucosa<br>• First-line diagnostic procedure for patients with alarm features |
| Gastric emptying scintigraphy | Physiological meal used |
| C-13 Acetate breath test | Can be adapted for solid or liquid emptying (C-13 sodium acetate for liquid and C-13 octanoic acid for solids) |

## Table 28: Diagnostic test for Gastroparesis[40]

| Diagnostic tests | Significance |
|---|---|
| Gastric scintigraphy | Test provides a physiological, non-invasive, and quantitative measure of gastric emptying |
| 13-C-labeled octanoate breath test | Indirect means of measuring gastric emptying |
| MRI | MRI can differentiate gastric meal volume and total gastric volume, allowing gastric secretory rates to be calculated. |
| Wireless capsule system (SmartPill®) | Measures pH, pressure and temperature using miniaturized wireless sensor technology. This has been developed for ambulatory assessment of GI transit. |

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Medical initiative supported by:

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