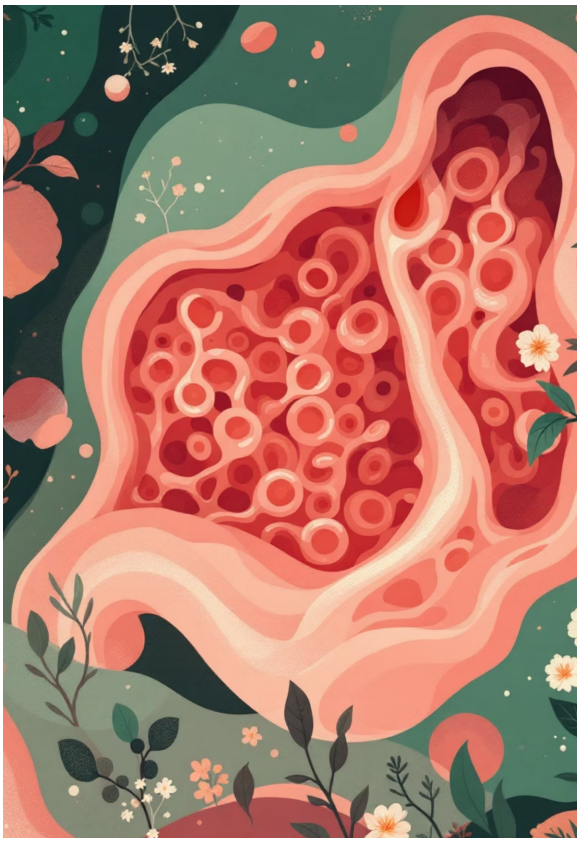

Management of Gastritis

Role of Vonoprazan

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Learning Objectives

01

Differentiate Gastritis from Gastropathy

Apply histological and endoscopic criteria to distinguish true inflammation from chemical mucosal injury.

02

Review Epidemiology, Classification & Pathophysiology

Understand the spectrum of gastritis subtypes and the mechanisms driving mucosal damage.

03

Apply a Structured Diagnostic Approach

Select appropriate testing modalities based on clinical presentation and risk stratification.

04

Select Evidence-Based Management

Match therapy to etiology, prioritizing cause-directed treatment over empiric acid suppression.

05

Compare PPIs with Vonoprazan

Evaluate the pharmacological advantages of potassium-competitive acid blockers in gastritis management.

06

Integrate Current Guideline Recommendations

Align clinical decisions with ACG, AGA, and international consensus statements.

Clinical Message: Treat the underlying cause rather than simply suppressing acid.

Gastritis versus Gastropathy

These entities differ in pathophysiology, histology, and management — yet they are frequently conflated in practice.

Gastritis

Definition: Histologically confirmed mucosal inflammation.

- Requires biopsy for definitive diagnosis
- Neutrophils and/or mononuclear infiltrate on histology
- Common causes: *H. pylori*, autoimmune, eosinophilic
- May progress to atrophy and metaplasia

Gastropathy

Definition: Mucosal injury with minimal or absent inflammation.

- Typically chemical or reactive in origin
- Epithelial damage, edema, vascular congestion
- Common causes: NSAIDs, alcohol, bile reflux
- Resolution follows removal of offending agent

Endoscopic erythema alone does **not** diagnose gastritis. Symptoms correlate poorly with histology.

Classification of Gastritis

A systematic classification improves diagnostic precision and directs targeted therapy. The preferred diagnosis should always identify the underlying etiology.

- **Non-atrophic:** Inflammation without gland loss; potentially reversible
- **Atrophic:** Gland loss; premalignant potential
- **Intestinal metaplasia:** Gastric epithelium replaced by intestinal-type cells
- **Dysplasia:** Neoplastic transformation; requires surveillance

By Etiology

- *H. pylori* (most common worldwide)
- Autoimmune (pernicious anemia)
- Drug-induced (NSAIDs, aspirin)
- Chemical / reactive (bile reflux)
- Infectious (CMV, HSV)
- Eosinophilic, granulomatous, radiation

Gastric Mucosal Defense Mechanisms

Gastritis develops when aggressive factors overwhelm the stomach's sophisticated protective systems. Understanding this balance is foundational to both prevention and treatment.

Defensive Factors

- **Mucus-bicarbonate barrier** — Neutralizes luminal acid at the epithelial surface
- n ions
- f injury
- **Rich mucosal blood flow** — Delivers oxygen and removes toxic metabolites
- **Prostaglandins (PGE_2)** — Stimulate mucus and bicarbonate secretion; maintain blood flow
- **Local immunity** — IgA, macrophages, and lymphocytes combat pathogens

Aggressive Factors

Hydrochloric acid & pepsin — Direct proteolytic and acid injury

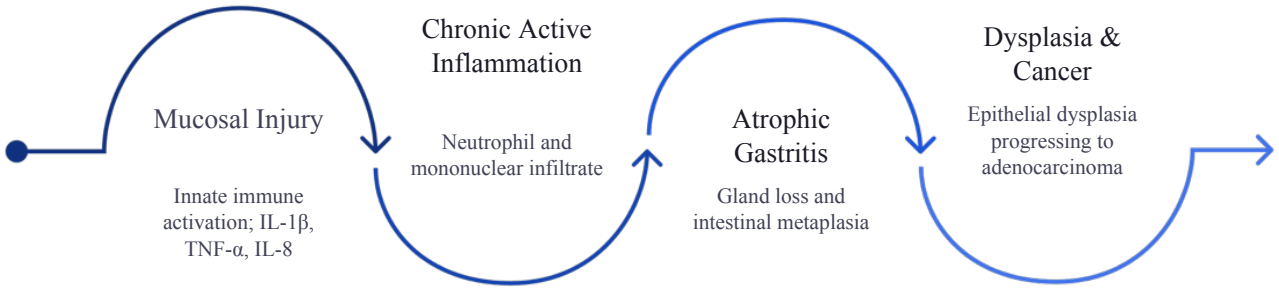
H. pylori — Disrupts tight junctions; triggers cytokine cascade

NSAIDs & aspirin — Inhibit COX-1, depleting protective prostaglandins

Alcohol & bile reflux — Direct epithelial toxicity and detergent effect

Pathophysiology: Cascade

Chronic *H. pylori* gastritis follows a well-characterized progression from inflammation to malignancy — the Correa cascade. Early intervention can interrupt this sequence.



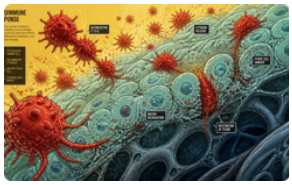
The sequential release of pro-inflammatory cytokines — particularly IL-1β, TNF-α, and IL-8 — drives progressive glandular destruction. Once atrophy and intestinal metaplasia develop, cancer risk rises substantially, underscoring the importance of early *H. pylori* eradication.

Etiology of Gastritis

Clinical clues should guide targeted investigations. A systematic approach to etiology ensures appropriate testing and avoids empiric therapy without a diagnosis.

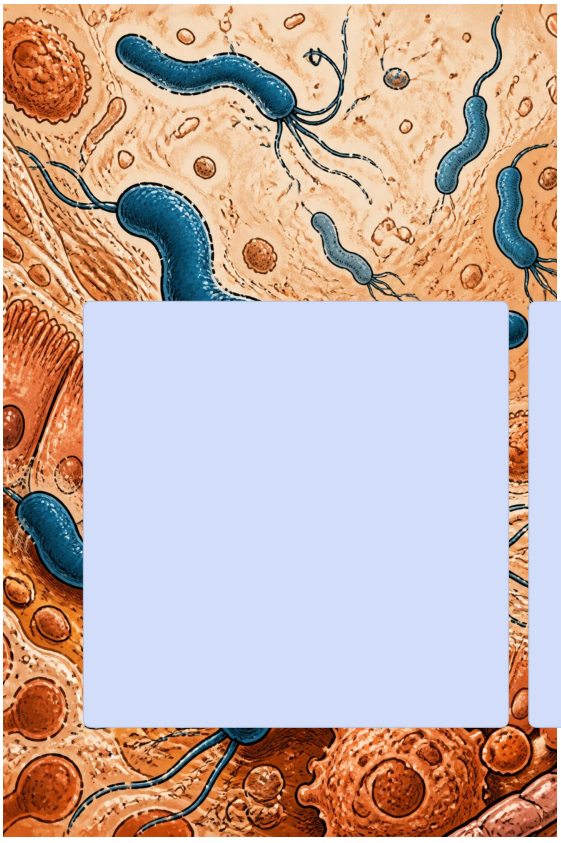
Common Causes

- ***H. pylori*** — Most prevalent cause worldwide; requires eradication
- **NSAIDs & aspirin** — COX inhibition; dose-dependent mucosal injury
- **Alcohol** — Direct epithelial toxicity; acute and chronic forms
- **Stress-related disease** — Critically ill patients; superficial erosions



Less Common Causes

- **Autoimmune** — Parietal cell antibodies; pernicious anemia; body-predominant
- **CMV / HSV** — Immunocompromised hosts; large ulcers
- **Crohn disease / sarcoidosis** — Granulomatous inflammation
- **Eosinophilic gastritis** — Allergic etiology; peripheral eosinophilia
- **Checkpoint inhibitors** — Immune-related adverse event; rising incidence



Helicobacter pylori Gastritis

H. pylori is a gram-negative, urease-producing bacterium that colonizes the gastric mucosa in approximately 50% of the world's population. It is the single most important modifiable risk factor for gastric cancer.

Chronic Active Gastritis

Universal consequence of colonization; neutrophilic and mononuclear infiltrate on histology

ılcers

Class I carcinogen (WHO); accounts for ~90% of non-cardia gastric cancers

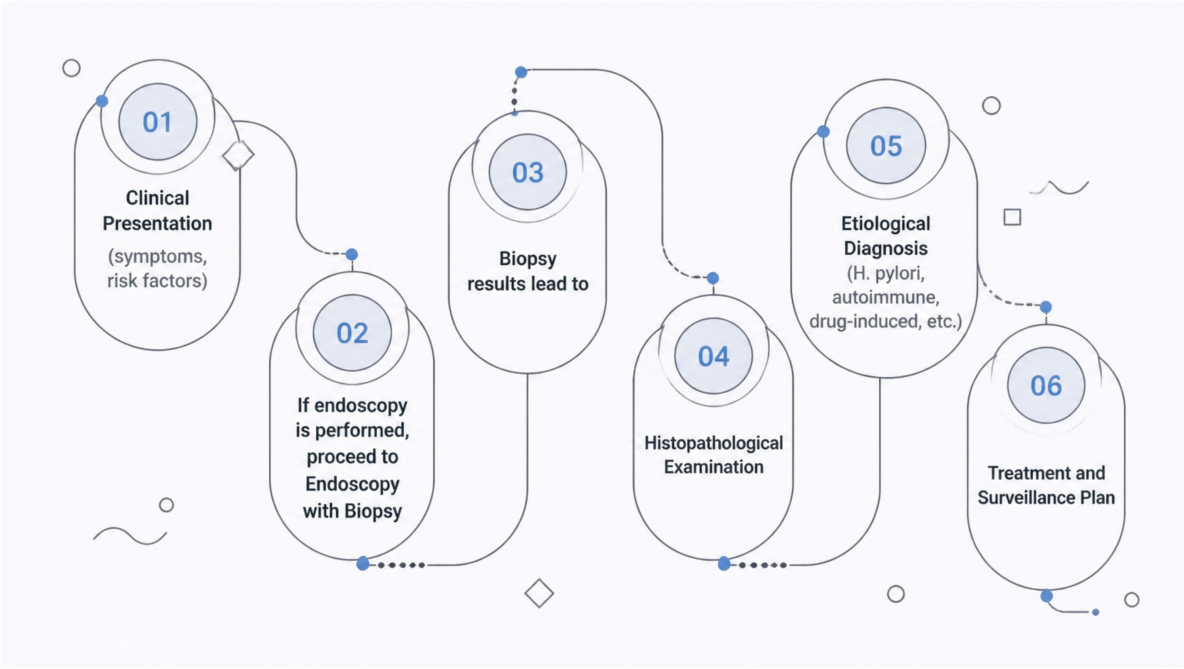
MALT Lymphoma

Mucosa-associated lymphoid tissue lymphoma; often regresses with eradication alone

Guideline Recommendation: All confirmed *H. pylori* infections should be treated. Eradication must be confirmed post-therapy using urea breath test or stool antigen (≥4 weeks after PPI cessation).

Diagnostic Approach

A thorough diagnostic workup is essential to identify the specific type and etiology of gastritis, guiding appropriate management and surveillance strategies.



Endoscopy with biopsy remains the gold standard for diagnosing gastritis and gastropathy, allowing for direct visualization of the mucosa and histological assessment. Serological tests, breath tests, and stool antigen tests are crucial for *H. pylori* detection, while specific antibody panels can identify autoimmune gastritis.

Management Principles

Effective management of gastritis focuses on addressing the underlying cause, eradicating pathogens, and mitigating aggressive factors, rather than merely suppressing symptoms.

Identify & Treat Etiology

Eradicate *H. pylori*, discontinue NSAIDs, manage autoimmune conditions, or remove other offending agents like alcohol or bile refluxants.

Acid Suppression

Utilize PPIs or H2RAs for symptomatic relief, ulcer healing, and to reduce further mucosal damage, especially in erosive gastritis.

Mucosal Protection

Consider sucralfate, bismuth, or prostaglandin analogs (e.g., misoprostol) in specific cases, particularly for NSAID-induced injury.

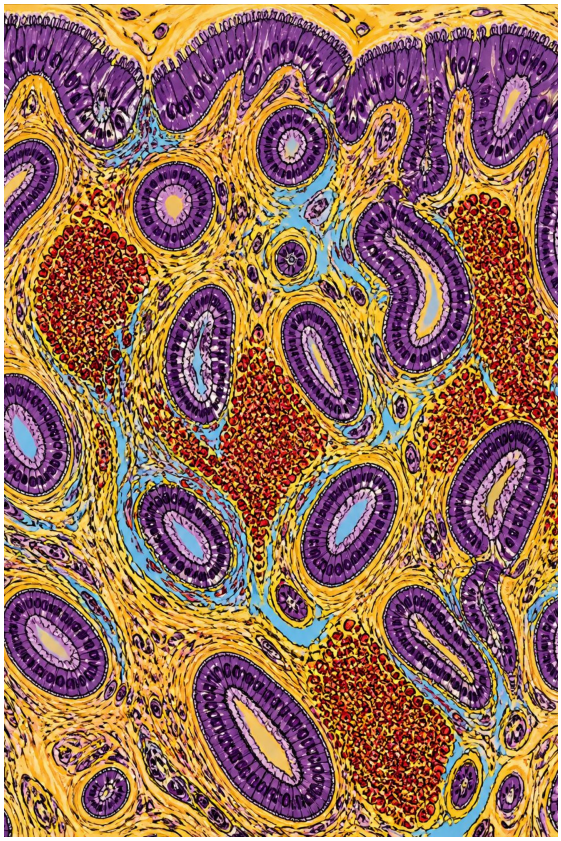
Surveillance

Regular endoscopic follow-up is essential for patients with atrophic gastritis, intestinal metaplasia, or dysplasia due to increased gastric cancer risk.

Tailored treatment regimens, guided by patient-specific factors and guideline recommendations, yield the best outcomes. Long-term PPI use should be regularly reviewed for necessity and minimal effective dose.

Autoimmune Gastritis

Autoimmune gastritis (AIG) is a chronic inflammatory condition driven by autoantibodies targeting parietal cells and intrinsic factor, resulting in progressive corpus- and fundus-predominant mucosal atrophy. Key consequences include vitamin B12 deficiency, iron deficiency, and hypergastrinemia. Patients carry an elevated risk of type I gastric neuroendocrine tumors and gastric adenocarcinoma. Management requires lifelong parenteral B12 replacement and endoscopic surveillance where indicated.



Drug-Induced Gastritis

Drug-induced gastritis is a common and often preventable cause of gastric mucosal injury. Direct mucosal irritation and disruption of prostaglandin-mediated cytoprotection are the primary mechanisms. Recognition of offending agents is essential for timely intervention.

Common Offending Agents

- NSAIDs and aspirin
- Potassium chloride and iron supplements
- Bisphosphonates
- Chemotherapy agents
- Immune checkpoint inhibitors

Management Strategy

- Discontinue the offending agent whenever feasible
- Initiate gastroprotection (PPI preferred) when indicated
- Test and treat *H. pylori* in high-risk patients to reduce cumulative mucosal injury

Clinical Presentation

ymptom severity does not reliably correlate with histological
ic patients.

- Nausea and vomiting
- Early satiety

Alarm-Associated Features

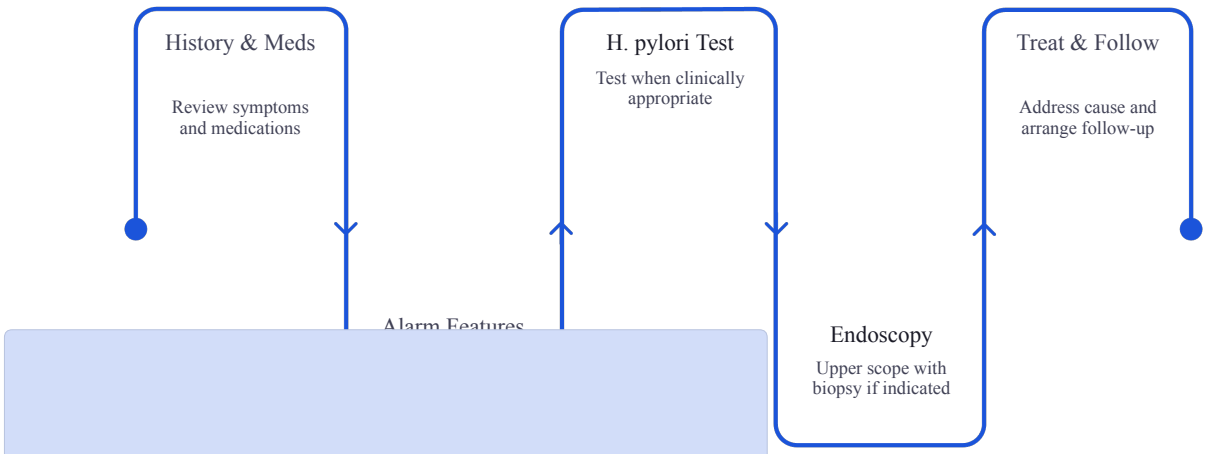
- GI bleeding (overt or occult)
- Iron deficiency anemia
- Unintentional weight loss

Histological Discordance

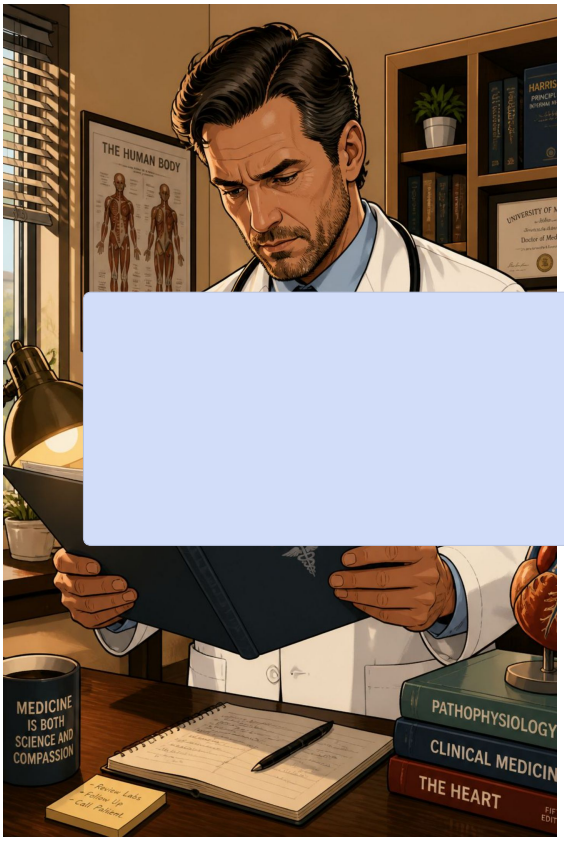
Symptoms alone cannot predict the degree of inflammation, atrophy, or intestinal metaplasia. Biopsy remains the gold standard for staging.

Diagnostic Approach

A systematic, stepwise approach ensures that underlying etiologies are identified, alarm features are not missed, and appropriate therapy is initiated. The sequence below guides clinicians from initial assessment through to definitive management.



Each step informs the next — a thorough medication review may identify drug-induced causes, while alarm features mandate expedited endoscopy regardless of initial test results.



Alarm Features

The presence of any alarm feature in a patient with dyspepsia or suspected gastritis warrants **prompt upper endoscopy** to exclude malignancy, significant ulceration, or other serious pathology. Age thresholds vary by guideline but typically range from 55–60 years for new-onset dyspepsia.

Demographic & Constitutional

shold with new dyspepsia

s, melena, or occult)

Physical & Laboratory

- Iron deficiency anemia
- Palpable abdominal mass

⚠ Any single alarm feature should trigger endoscopic evaluation without delay, regardless of symptom duration or response to empiric therapy.

Upper Endoscopy & Biopsy

Endoscopic Evaluation

Upper endoscopy allows direct visualization of the gastric mucosa to identify erosions, ulcers, atrophic changes, and suspicious lesions. High-definition white-light endoscopy with chromoendoscopy or virtual chromoendoscopy may enhance detection of premalignant changes.

Updated Sydney System Protocol

Standardized biopsy mapping ensures accurate histological staging and *H. pylori* detection:

- **Two biopsies** from the antrum (lesser and greater curvature)
- **One biopsy** from the incisura angularis
- **Two biopsies** from the corpus (lesser and greater curvature)

Histology assesses inflammation, activity, atrophy, intestinal metaplasia, and *H. pylori* density — each scored separately to guide surveillance intervals.

H. pylori Testing

Accurate detection of *Helicobacter pylori* is central to gastritis management. Test selection depends on clinical context, availability, and whether endoscopy is being performed. **PPIs should be discontinued for at least 2 weeks** prior to testing to minimize false-negative results.

Non-Invasive Testing

- **Urea breath test** — high sensitivity and specificity; preferred for initial diagnosis and post-treatment confirmation
- **Stool antigen test** — reliable alternative; useful

Invasive Testing (via Endoscopy)

- **Histology** — allows simultaneous assessment of gastritis grade and *H. pylori* density
- **Rapid urease test** — fast, cost-effective intra-procedural result
- **Culture / PCR** — reserved for suspected antibiotic resistance or treatment failure

General Management Principles

Effective management of gastritis requires a multifaceted approach that addresses the underlying etiology, mitigates ongoing mucosal injury, and monitors for long-term complications including premalignant transformation.

01

02

03

Avoid NSAIDs & Provide Acid Suppression

Minimize or eliminate NSAID use; prescribe PPIs for active inflammation, ulceration, or high-risk patients requiring continued NSAID therapy.

04

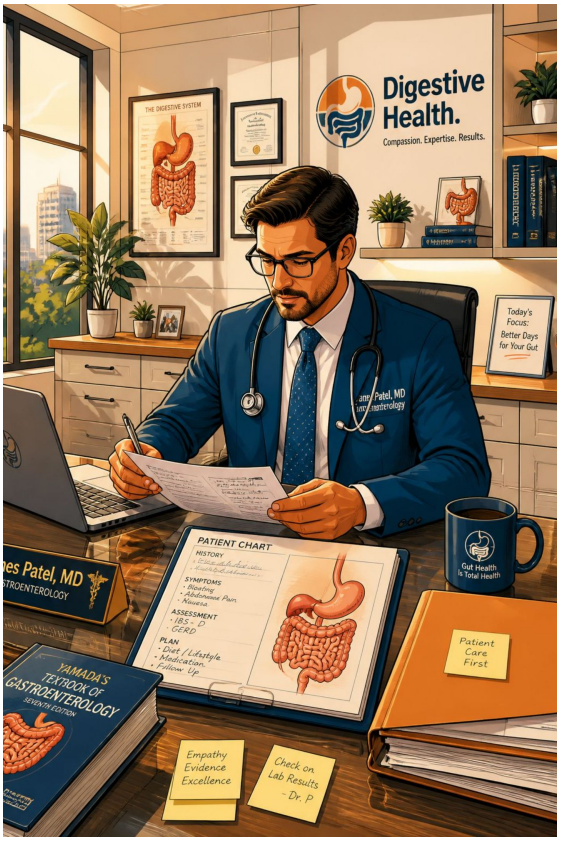
Correct Nutritional Deficiencies

Supplement vitamin B12 (parenteral for AIG), iron, and other micronutrients as indicated by laboratory findings.

05

Arrange Surveillance for Premalignant Conditions

Patients with advanced atrophy, intestinal metaplasia, or autoimmune gastritis require structured endoscopic surveillance per current guidelines.



General Principles of Management

Effective management of acid-peptic disease requires a systematic approach that addresses the underlying cause, promotes mucosal healing, and prevents long-term complications. Treatment must be individualized based on diagnosis, severity, and patient-specific risk factors.

Treatment Goals & Lifestyle Modification

Core Treatment Goals

- Identify and treat the underlying cause rather than symptoms alone

Lifestyle & Risk Factor Modification

- **Smoking cessation** — improves ulcer healing and reduces recurrence rates
- **ol** — avoid excessive intake; limit or abstain in active disease
- **Ds** — avoid unnecessary use; if essential, use the lowest effective with gastroprotection (PPI co-therapy)
- **y triggers** — no convincing evidence supports routine avoidance of , spicy food, or citrus in all patients; individualize advice based on om triggers

Clinical Pearl: Long-term acid suppression should only be continued when there is a clear, documented indication.

H. pylori Eradication Therapy

ajor risk factor for gastric malignancy. Eradication is a cornerstone of

Lowers Cancer Risk

Eliminates chronic active inflammation and reduces the long-term risk of gastric adenocarcinoma.

MALT Lymphoma Remission

Induces remission in early-stage gastric MALT lymphoma in a significant proportion of patients.

First-Line Regimen

14-day bismuth quadruple therapy is preferred in many regions. Always confirm eradication with a urea breath test or stool antigen test ≥4 weeks after completion.

Acid Suppression Therapy: Available Options

depends on diagnosis, severity, and indication.

H_2 Receptor Antagonists

ess
ith

Proton Pump Inhibitors

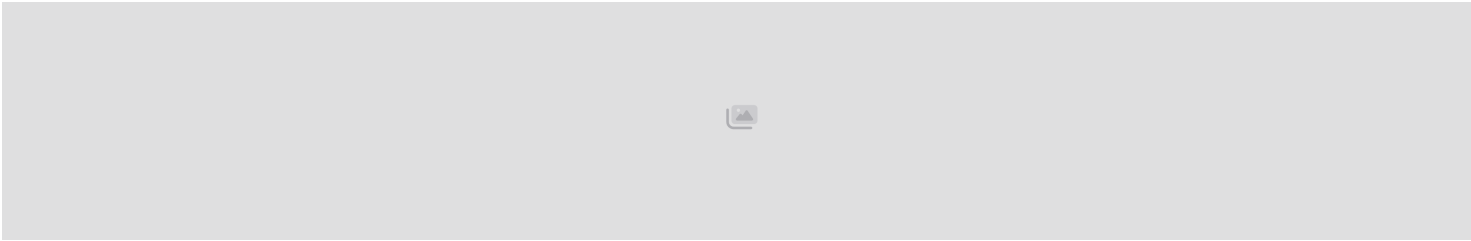
Standard first-line therapy. Irreversible H^+/K^+ ATPase inhibition with extensive evidence for ulcer healing and *H. pylori* eradication.

PCABs

Potassium-competitive acid blockers offer rapid, potent, meal-independent acid suppression. Vonoprazan is the most widely studied agent.

Sucralfate

Forms a protective barrier over ulcerated mucosa. Adjunctive role; limited systemic absorption.



Key References & Evidence Summa

Our management strategies are founded on robust scientific evidence and contemporary cl

Consensus Guidelines

Adherence to recommendations from leading gastroenterology societies (e.g., AGA, ACG, UEG) is central to our diagnostic and therapeutic approach.

Acid Suppression Efficacy

Extensive randomized controlled trials demonstrate the superior efficacy of PPIs for mucosal healing and symptom control in various acid-peptic conditions.

H. pylori Eradication

Lifestyle & Risk Factor Data

Evidence supports the critical impact of smoking cessation and judicious NSAID use on disease progression and recurrence, alongside individualized dietary adjustments.

Proton Pump Inhibitors (PPIs)

Mechanism of Action

PPIs are prodrugs that undergo acid-dependent activation and **irreversibly inhibit the H^+/K^+ ATPase** (proton pump), the final common pathway of acid secretion. Maximal effect requires several days of dosing as new pumps are synthesized.

Advantages

- Excellent ulcer healing rates across all grades of severity
- Extensive evidence base spanning decades of clinical use
- Cost-effective and widely available
- Well-established role in *H. pylori* eradication regimens

Limitations

- **Delayed onset** — maximal acid suppression may take 3–5 days
- **Meal-dependent dosing** — must be taken 30–60 minutes before meals

PPIs remain the global standard of care for most acid-related disorders.

Potassium-Competitive Acid Blockers (PCABs)

t and more consistent pH control than traditional PPIs.

PCABs **reversibly inhibit the potassium-binding site** of the H^+/K^+ ATPase. Unlike PPIs, they do not require acid activation and bind competitively in a potassium-dependent manner, achieving rapid and sustained pump blockade.

Key Advantages

- **Rapid onset** — first-dose effect with meaningful acid suppression on day 1
- **Meal-independent** — can be taken with or without food
- **Consistent acid suppression** — less influenced by CYP2C19 polymorphism
- **Superior nocturnal pH control** — addresses a key limitation of PPIs

Available Agents

Vonoprazan is the most widely available PCAB globally, approved in Japan, the United States, and multiple other regions. **Tegoprazan** is available in selected markets. Both agents share the core PCAB mechanism with subtle pharmacokinetic differences.

Case Studies: Clinical Application

To illustrate the practical application of these management principles, we will now review several clinical case studies. Each case highlights common scenarios and demonstrates how an individualized, evidence-based approach guides treatment decisions and optimizes patient outcomes.

Vonoprazan: A Next-Generation PCAB

Vonoprazan is the most extensively studied PCAB and is increasingly used as first-line therapy in selected indications, particularly *H. pylori* eradication and erosive esophagitis.

d 24-hour acid suppression
H control compared to

CYP2C19 Independent

Less influenced by CYP2C19 polymorphism, ensuring more predictable acid suppression across diverse patient populations.

H. pylori Eradication

Effective in eradication regimens, with several trials demonstrating higher eradication rates than PPI-based triple therapy.

Meal-Independent

Can be administered regardless of meal timing, improving adherence and convenience.

PPIs vs. Vonoprazan: Head-to-Head Comparison

Both drug classes are effective acid suppressants, but their pharmacological profiles differ in clinically meaningful ways.

Feature	PPIs	Vonoprazan (PCAB)
Mechanism	Irreversible H^+/K^+ ATPase inhibition	Reversible competitive K^+-binding inhibition
Onset of Action	Delayed (3–5 days to maximal effect)	Rapid (first-dose effect)
Dosing Relative to Meals	Must be taken 30–60 min before meals	Meal-independent
CYP2C19 Influence	Significant — affects efficacy	Minimal — more consistent suppression
Nocturnal Acid Control	May have breakthrough	Superior nocturnal pH control
H. pylori Eradication	Standard component of regimens	Higher eradication rates in several RCTs
Current Role	Global standard of care	Preferred in selected patients/indications

PPIs remain the standard therapy globally. Vonoprazan offers distinct pharmacological advantages in patients with CYP2C19 polymorphism, nocturnal symptoms, or difficult-to-treat *H. pylori*.

Cost-Effectiveness & Access Considerations

The choice between PPIs and vonoprazan often involves balancing clinical efficacy with real-world cost and patient access.

Proton Pump Inhibitors (PPIs)

- **Cost:** Generally low due to widespread generic availability, making them highly cost-effective.
- **Access:** Broadly accessible and integrated into most healthcare formularies worldwide.
- **Formulary Status:** Often preferred as first-line agents due to favorable cost-benefit ratio.

Vonoprazan (PCAB)

- **Cost:** Higher due to newer patent-protected status; potentially a significant out-of-pocket expense for patients.
- **Access:** Availability can be regional, with restricted formulary access in some markets.
- **Formulary Status:** May be reserved for specific indications or patients refractory to PPIs.

While vonoprazan offers distinct pharmacological advantages, the cost and access landscape currently favor PPIs as the initial broad-use therapy.

Clinical Evidence Supporting Vonoprazan

Multiple randomized controlled trials and meta-analyses have established the efficacy and safety of vonoprazan across key indications.

Faster Acid Suppression

RCTs consistently demonstrate superior day-1 intragastric pH control compared to PPIs, with faster achievement of target pH thresholds for mucosal healing.

High Healing Rates

Vonoprazan achieves high healing rates for erosive esophagitis and peptic ulcers, comparable or superior to standard-dose PPIs in head-to-head trials.

Superior H. pylori Eradication

The **PHALCON-HP** trial and other multicenter RCTs demonstrated significantly higher eradication rates with vonoprazan-based regimens versus PPI-based triple therapy, particularly in clarithromycin-resistant strains.

Comparable Short-Term Safety

Short-term adverse event profiles are comparable to PPIs. Most common events include diarrhea, constipation, headache, and nausea — generally mild and self-limiting.

Monitoring & Follow-Up Strategies

Effective management of acid-related disorders involves careful monitoring of treatment response, potential adverse effects, and long-term implications.

1

Efficacy Assessment

Evaluate for symptom resolution (e.g., heartburn, dyspepsia). For patients with erosive esophagitis or peptic ulcers, follow-up endoscopy may be necessary to confirm mucosal healing.

2

Safety & Adverse Effects

Monitor for common, generally mild short-term side effects. For chronic PPI users, consider potential long-term risks such as C. difficile infection, renal impairment, and bone fractures. PCABs have a distinct safety profile requiring continued vigilance.

3

H. pylori Eradication Confirmation

After treatment for *H. pylori*, a "test-of-cure" (e.g., urea breath test, stool antigen test) 4-8 weeks post-therapy is crucial to confirm successful eradication and prevent recurrence.

4

Long-Term Management

Regularly reassess the need for ongoing acid suppression. Explore opportunities for dose reduction or discontinuation, especially for patients on long-term therapy, balancing symptom control with minimizing risks.

Safety Profile & Summary

Adverse Effects of Vonoprazan

Common (short-term):

- Diarrhea
- Constipation
- Headache
- Nausea

Long-term considerations (class effect of acid suppression):

- Hypergastrinemia
- Increased risk of enteric infections
- Micronutrient deficiency (iron, B12, magnesium) with prolonged use

Current evidence supports a favorable safety profile for vonoprazan, comparable to PPIs in the short term.

Key Takeaways

- Treat the underlying cause — eradicate *H. pylori*, remove irritants
- PPIs remain the global standard; vonoprazan offers advantages in selected patients
- Vonoprazan provides rapid, potent, meal-independent acid suppression
- Superior *H. pylori* eradication rates demonstrated in RCTs (PHALCON-HP)
- Long-term acid suppression requires a clear indication and periodic review

Renal and Hepatic Impairment: Dosage Adjustments

Understanding the impact of organ dysfunction on vonoprazan pharmacokinetics is crucial exposure and potential adverse effects.

Renal Impairment

- **Mild-Moderate (eGFR ≥30 mL/min):** No dosage adjustment is generally required.
- **Severe (eGFR <30 mL/min):** Consider reducing the dose (e.g., 10 mg once daily) to avoid increased plasma concentrations. Close monitoring for adverse effects is recommended.
- **End-Stage Renal Disease (ESRD) on Dialysis:** Dosage reduction is often necessary, and careful monitoring of patients is advised.

Hepatic Impairment

- **Mild (Child-Pugh A):** No dosage adjustment is typically needed.
- **Moderate (Child-Pugh B):** A reduced dose (e.g., 10 mg once daily) is usually recommended due to significantly increased drug exposure.
- **Severe (Child-Pugh C):** Vonoprazan is generally not recommended or should be used with extreme caution at a substantially reduced dose (e.g., 5 mg once daily) with intensive clinical monitoring.

Always consult the official prescribing information for specific dosage recommendations and contraindications in renally or hepatically impaired patients.

Drug Interactions & Special Populations

Drug Interactions

Vonoprazan, as a PCAB, generally exhibits a favorable drug interaction profile compared to PPIs, primarily due to its distinct metabolic pathway.

- **pH-dependent Absorption:** Like PPIs, vonoprazan elevates gastric pH, potentially altering the absorption of medications requiring an acidic environment (e.g., azole antifungals, certain antiretrovirals like atazanavir, nelfinavir).
- **CYP Enzymes:** Metabolized mainly by CYP3A4, with minimal involvement of CYP2C19. This reduces the risk of interactions with drugs primarily metabolized by CYP2C19, which is common with many PPIs (e.g., clopidogrel).
- **Warfarin:** Clinical studies have shown no significant pharmacokinetic interaction with warfarin, indicating a lower risk compared to some PPIs.

Special Populations

- **Renal Impairment:** No dose adjustment is typically required for mild to moderate renal impairment. For severe impairment (eGFR < 30 mL/min/1.73m²), caution is advised, and dose reduction may be considered based on clinical judgment.
- **Hepatic Impairment:** Dosage adjustment may be necessary for patients with moderate to severe hepatic impairment due to reduced clearance. Specific recommendations vary by region; consult local guidelines.
- **Elderly:** No specific dose adjustment is generally needed for elderly patients, but careful monitoring is recommended given potential age-related physiological changes.
- **Pregnancy & Lactation:** Limited human data are available. Use during pregnancy or lactation should only occur if the potential benefit outweighs the potential risk. Animal studies have not indicated significant risks.

Thanks for Your attention