PEPTIC ULCER DISEASE: ETIOPATHOGENESIS, COMPLICATIONS, AND MODERN TREATMENT APPROACHES

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Abstract

Background: Peptic ulcer disease (PUD) remains a common cause of upper gastrointestinal morbidity worldwide, arising when aggressive factors — chiefly Helicobacter pylori infection and nonsteroidal anti-inflammatory drug (NSAID) use — overwhelm the mucosal defenses that normally protect the gastric and duodenal epithelium from acid-peptic injury.

Methods: This narrative review synthesizes current evidence on the etiopathogenesis, complications, and treatment of PUD, drawing on the 2024 American College of Gastroenterology (ACG) clinical guideline for the treatment of Helicobacter pylori infection and contemporary reviews of NSAID-related and complicated peptic ulcer disease.

Results: H. pylori infection and NSAID use, alone or synergistically, account for the great majority of peptic ulcers, with acid-pepsin hypersecretion, smoking, and physiologic stress acting as additional aggressive factors against a mucosal defense system built on the mucus-bicarbonate barrier, prostaglandin-mediated cytoprotection, adequate mucosal blood flow, and epithelial renewal. Management now follows a test-and-treat paradigm in patients under 60 without alarm features, reserving endoscopy for older patients or those with alarm symptoms, and increasingly favors bismuth quadruple therapy or vonoprazan-based regimens over legacy clarithromycin-based triple therapy in regions with rising antibiotic resistance. Complications — bleeding, perforation, gastric outlet obstruction, penetration, and, for gastric ulcers, malignant transformation — carry distinct presentations and management pathways and remain the primary drivers of PUD-related mortality.

Conclusion: Because most peptic ulcers are now preventable and curable through correct identification and elimination of their causative aggressive factor, systematic H. pylori testing and eradication, judicious NSAID use with appropriate gastroprotection,

and prompt recognition of complications are central to modern PUD care, including in resource-limited settings such as Uzbekistan, where the test-and-treat strategy and basic endoscopy remain the most practical and impactful tools available.

Keywords

Peptic ulcer disease, Helicobacter pylori, NSAID-induced ulcer, bismuth quadruple therapy, vonoprazan, upper gastrointestinal bleeding, perforation, gastric outlet obstruction, test-and-treat.

Methods

This work was prepared as a narrative literature review. A literature search was conducted in September 2026 using PubMed and the publication database of the American College of Gastroenterology (ACG), with the search terms "peptic ulcer disease," "Helicobacter pylori eradication," "NSAID-induced ulcer," "bismuth quadruple therapy," "vonoprazan," and "peptic ulcer complications," combined with filters for publication in English between 2009 and 2026. Priority was given to the 2024 ACG clinical guideline for the treatment of Helicobacter pylori infection, the 2020 Japanese Society of Gastroenterology evidence-based guidelines for peptic ulcer disease, and contemporary comparative studies of eradication regimens and complication management; narrative summaries from established clinical reference sources were included for foundational background. Case reports and articles without accessible full text were excluded. A total of twelve sources meeting these criteria were selected and synthesized for this review.

Introduction

Peptic ulcer disease refers to mucosal defects of the stomach or duodenum that penetrate through the muscularis mucosae, arising from a disruption of the normal balance between acid-peptic injury and the mucosal defenses that protect the gastroduodenal epithelium. Although its incidence has declined substantially since the discovery of Helicobacter pylori and the widespread adoption of eradication therapy, PUD remains a frequent cause of dyspepsia, a leading cause of non-variceal upper gastrointestinal bleeding, and a condition whose complications continue to carry meaningful mortality when recognition or treatment is delayed.

Two causes — H. pylori infection and NSAID or aspirin use — together account for the great majority of peptic ulcers, and their relative contribution, combined with the growing challenge of antibiotic resistance in H. pylori eradication, has reshaped modern diagnostic and treatment algorithms over the past decade. At the same time, an idiopathic minority of ulcers, negative for both H. pylori and NSAID exposure, presents an increasingly recognized diagnostic challenge.

The aim of this review is to summarize the etiopathogenesis of peptic ulcer disease, describe its major complications and their management, and review current evidence-based treatment strategies, with attention to their relevance to gastroenterology and internal medicine practice in Uzbekistan.

Understanding and correctly managing peptic ulcer disease is relevant across several areas of clinical practice, including:

- Gastroenterology (endoscopic diagnosis, hemostasis, H. pylori eradication)
- Internal medicine and primary care (test-and-treat strategy, NSAID risk assessment)
- General and emergency surgery (management of perforation and refractory bleeding)
- Oncology (surveillance of non-healing gastric ulcers for malignancy)
- Cardiology and rheumatology (gastroprotection in patients requiring long-term aspirin or NSAID therapy)

Etiopathogenesis: The Acid-Mucosal Defense Balance

Peptic ulcer formation is best understood as the result of an imbalance between aggressive factors that injure the gastroduodenal mucosa and the protective mechanisms that normally defend against them, rather than as a disease of acid excess alone. H. pylori infection, present in a substantial proportion of the world's population, colonizes the gastric mucus layer and induces chronic inflammation, disrupts the mucus-bicarbonate barrier, and alters acid secretion patterns depending on the distribution of gastritis, thereby predisposing to both gastric and duodenal ulceration. NSAIDs and aspirin injure the mucosa through a complementary mechanism, inhibiting cyclo-oxygenase-1-dependent prostaglandin synthesis and thereby reducing mucosal blood flow, mucus and bicarbonate secretion, and epithelial repair capacity; when H. pylori infection and NSAID use coexist, their ulcerogenic and bleeding risk combine synergistically rather than merely additively.

Additional aggressive factors — including gastric acid and pepsin hypersecretion, cigarette smoking, and the severe physiologic stress of critical illness (stress ulceration) — act on the same defense system, which itself depends on an intact mucus-bicarbonate barrier, adequate mucosal prostaglandin synthesis, sufficient mucosal blood flow, and rapid epithelial renewal and repair. Ulceration occurs when aggressive factors overwhelm these defenses, and identifying which specific aggressive factor is responsible in a given patient directly determines the therapeutic approach, since treatment is aimed at removing or counteracting the causative factor rather than at symptom control alone. This conceptual balance is illustrated in Figure 1.

Figure 1. The Acid-Mucosal Defense Balance in Peptic Ulcer Disease

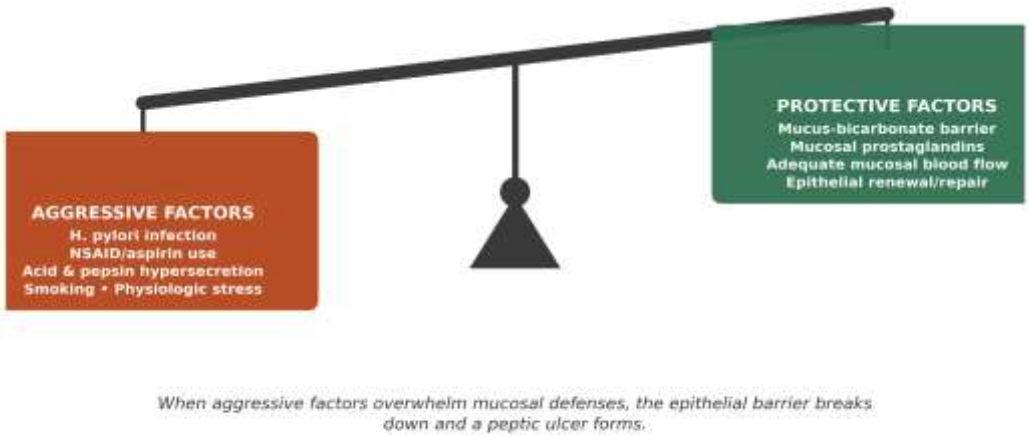

Figure 1. Peptic ulcer disease results from an imbalance between aggressive factors (H. pylori, NSAIDs, acid-pepsin, smoking, stress) and the mucosal defenses (mucus-bicarbonate barrier, prostaglandins, blood flow, epithelial renewal) that normally protect the gastroduodenal mucosa.

Modern Diagnostic and Treatment Strategy

Initial management of suspected PUD is increasingly governed by a test-and-treat paradigm: patients younger than 60 years with dyspepsia and no alarm symptoms (dysphagia, weight loss, gastrointestinal bleeding, anemia, or persistent vomiting) are tested non-invasively for H. pylori, using a urea breath test or stool antigen test, and treated if positive, without the need for upfront endoscopy. Upper endoscopy with biopsy is reserved for patients 60 years and older with new symptoms, for anyone with alarm features, and for confirmation and follow-up of complicated or gastric ulcers. Patients who test negative for H. pylori and are not using NSAIDs are managed empirically with a proton pump inhibitor and, if ulcers are confirmed endoscopically without an identifiable cause, are classified as having idiopathic peptic ulcer disease.

Treatment of H. pylori-associated PUD has shifted substantially in response to rising antibiotic resistance, particularly to clarithromycin: current ACG guidance favors 14-day optimized bismuth quadruple therapy or vonoprazan-based regimens as first-line empiric treatment over legacy clarithromycin-containing triple therapy in most regions. Vonoprazan, a potassium-competitive acid blocker, provides more rapid and sustained acid suppression than conventional PPIs and does not require meal-timed dosing, and clinical trials have shown it to be non-inferior to PPIs for both ulcer healing and prevention of recurrence. Mandatory confirmation of eradication with a test-of-cure — urea breath test or fecal antigen test performed at least four weeks after completing

antibiotics and at least two weeks after stopping PPI therapy — is now a standard component of care, since incomplete eradication predisposes to ulcer recurrence and ongoing complication risk. For NSAID-induced ulcers, the NSAID should be discontinued where possible and PPI therapy administered; when NSAID therapy cannot be stopped, maintenance PPI co-therapy, with or without a selective COX-2 inhibitor, and H. pylori eradication if present, are used to reduce recurrence, and all patients initiating long-term NSAID or daily low-dose aspirin therapy should be screened for H. pylori beforehand. This overall pathway, from initial presentation through eradication confirmation and complication surveillance, is summarized as a recurring clinical cycle in Figure 2.

Figure 2. The Modern PUD Diagnostic-Treatment Cycle

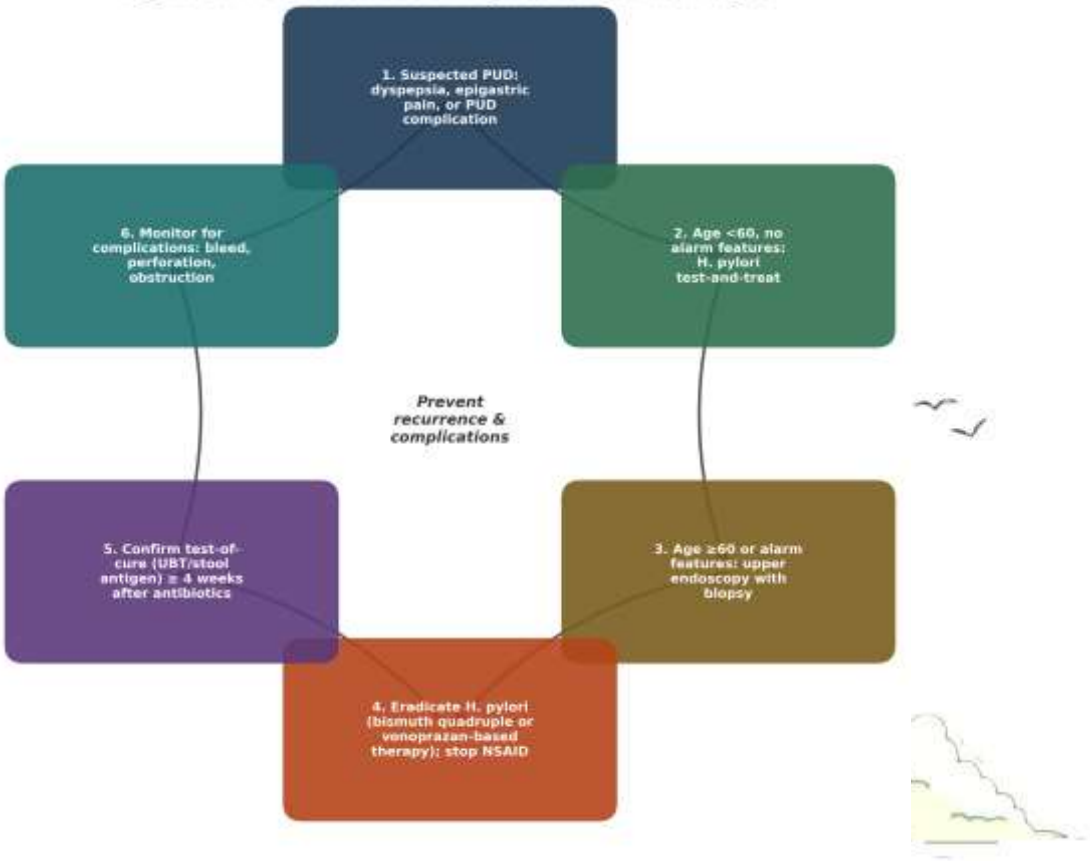

Figure 2. The recurring PUD diagnostic-treatment cycle: symptom-triggered test-and-treat or endoscopy based on age and alarm features, H. pylori eradication with NSAID discontinuation, mandatory confirmation of cure, and ongoing surveillance for complications.

Complications: Recognition and Initial Management

Although most peptic ulcers now heal readily with appropriate acid suppression and elimination of the causative aggressive factor, complications remain the principal source of PUD-related morbidity and mortality and require prompt recognition. Upper gastrointestinal bleeding is the most frequent and clinically urgent complication, presenting with hematemesis or melena and, in severe cases, hemodynamic instability; management requires fluid resuscitation, high-dose PPI therapy, and urgent endoscopy

with endoscopic hemostasis, typically within 24 hours of presentation. Perforation presents with sudden, severe abdominal pain and peritoneal signs, is confirmed by free intraperitoneal air on imaging, and constitutes a surgical emergency requiring prompt repair and broad-spectrum antibiotic coverage, since delayed intervention is associated with substantially increased mortality.

Gastric outlet obstruction, resulting from chronic scarring or acute edema of the pyloric channel or duodenum, presents with early satiety, non-bilious vomiting, and weight loss, and is managed with nasogastric decompression, acid suppression, and endoscopic balloon dilation, with surgery reserved for refractory cases. Penetration, most often of a posterior duodenal ulcer into the pancreas, produces persistent pain radiating to the back and is evaluated with cross-sectional imaging. For gastric ulcers specifically, malignant transformation is an important consideration that does not apply to duodenal ulcers, and repeat endoscopy with biopsy to confirm complete healing is mandatory for any gastric ulcer, since a non-healing ulcer despite adequate therapy should raise suspicion for underlying malignancy. These complications, their presentations, and their initial management are summarized in Table 1.

Table 1. Major Complications of Peptic Ulcer Disease

Complication	Clinical Presentation	Initial Management	Approx. Frequency*
Upper GI bleeding	Hematemesis, melena, or hematochezia if massive; hemodynamic instability in severe cases	Resuscitation, high-dose PPI, urgent endoscopy with hemostasis within 24 hours	Most common complication; ~15% lifetime risk in chronic PUD
Perforation	Sudden severe abdominal pain, peritonism, free air on imaging	Surgical consultation; emergency repair (often laparoscopic), broad-spectrum antibiotics	Uncommon (~2-3%) but high mortality if delayed
Gastric outlet obstruction	Early satiety, non-bilious vomiting, weight loss from chronic scarring/edema	NG decompression, PPI, endoscopic balloon dilation; surgery if refractory	Rare (~1-2%), usually from chronic pyloric channel/duodenal ulcers
Penetration	Persistent, boring pain radiating to the back (posterior duodenal ulcer into pancreas)	Cross-sectional imaging to define extent; PPI and H. pylori eradication;	Uncommon; most often posterior duodenal ulcers

Complication	Clinical Presentation	Initial Management	Approx. Frequency*
		surgery if uncontrolled	
Malignant transformation	Non-healing gastric ulcer despite adequate therapy; weight loss, anemia	Repeat endoscopy with biopsy to confirm healing; oncologic work-up if malignant	Relevant to gastric (not duodenal) ulcers; mandates healing confirmation

In healthcare systems with constrained access to advanced endoscopic therapy or newer agents such as vonoprazan — a relevant consideration for gastroenterology practice in Uzbekistan — the practical priority is to apply the test-and-treat strategy and bismuth quadruple or standard triple therapy rigorously, ensure NSAID use is critically reviewed in every patient with dyspepsia, and maintain a low threshold for urgent referral when alarm symptoms or signs of bleeding, perforation, or obstruction develop, since timely recognition remains the most important determinant of outcome even where the newest pharmacologic options are not always available.

Conclusion

Peptic ulcer disease arises from an imbalance between aggressive mucosal insults — principally H. pylori infection and NSAID use — and the mucosal defenses that normally protect the gastroduodenal epithelium, and modern management is built on correctly identifying and removing the causative factor rather than on acid suppression alone.

For clinical practice, this translates into two actionable priorities: applying the test-and-treat strategy and, where indicated, bismuth quadruple or vonoprazan-based eradication therapy with mandatory confirmation of cure, and maintaining vigilance for the major complications of PUD — bleeding, perforation, obstruction, penetration, and, for gastric ulcers, malignancy — so that they are recognized and managed promptly. Continued application of these principles, adapted to local resource constraints, holds substantial potential to reduce PUD-related morbidity and mortality, including within the healthcare system of Uzbekistan.

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