ISSN: 313 9 -194 X (ONLINE)

Integrated Journal of Interdisciplinary Health Studies

Contents available at: *https://www.swamivivekanandauniversity.ac.in/ijihs/*

PEPTIC ULCER: PATHOPHYSIOLOGY, MECHANISM AND DIAGNOSIS

Rituparna Ghosh*[1], Ayan Sengupta[2]

[1]*Department of Medicine, Columbia Center for Translational Immunology, Columbia University Medical Center, NewYork-10032*

[2]*Department of Medical Laboratory Technology, School of Allied Health Sciences, Swami Vivekananda University, Telinipara, Barasat-BarrackporeRd, Bara Kanthalia, WestBengal-700121, India*

ARTICLEINFO

Received:15.07.2025
Revised:20.08.2025
Accepted:10.09.2025
Published:08.10.2025

Keywords: Peptic ulcer, NSAIDs, *Helicobacter pylori*, pathophysiology, diagnosis

Abstract

Indigestion symptoms might be a result of peptic ulcers. Most cases of peptic ulcer disease are seen in the proximal duodenum and stomach. It is a disorder that leads to the development of ulcers, or open sores, in the stomach lining. "Peptic" denotes connection to digestion. The primary digestive enzyme produced by our stomach, pepsin, is the source of the word. The muscularis mucosa is eroded by peptic ulcers, at least to the submucosa level. Nonsteroidal anti-inflammatory medications (NSAIDs) and Helicobacter pylori (H. pylori) infection are the most frequent causes of peptic ulcers. The mechanism encompasses the noteworthy function of the stomach and its corresponding enzymes in protecting the ulcers. Peptic ulcers are most frequently caused by uncommon or rare causes. The most typical indications and manifestations of stomach ulcers are gastritis, heartburn, bloating, and abdominal pain. Antibiotics to eradicate H. pylori or medications to lower stomach acids are possible forms of treatment. Numerous diagnostic and treatment approaches have been developed to advance our understanding of treating peptic ulcers, and this review article highlights the challenging scenarios that are covered.

1. Introduction

A peptic ulcer is a sore that appears on the mucous lining of the stomach, small intestine, or esophagus as a result of the mucous layer breaking down and exposing the underlying tissue to digestive enzymes and stomach acid. The major causes of this illness include prolonged nonsteroidal anti-inflammatory drug (NSAID) use, such as ibuprofen and aspirin, or Helicobacter pylori infection (Feldman et al., 2016). Peptic ulcer symptoms might include heartburn, nausea, bloating, burning in the stomach and in more severe cases, black, tarry stools or blood in the vomit. Antibiotics are often used in conjunction with drugs to treat stomach acid reflux, life style modifications to aid in healing and avoid recurrence, and other therapies to completely eradicate the bacterial infection (Sonnenberg and Everhart, 1996). Acid-induced lesions in the stomach and duodenum known as peptic ulcers are characterized by mucosa that has been completely destroyed, with the defect extending into the muscularis propria or submucosa (Ramakrishnan and Salinas, 2007). Because of pepsin or gastric acid secretion, it is characterized by discontinuity in the GI tract's inner lining. It penetrates the stomach epithelium's muscularis propria layer. Usually, it affects the proximal duodenum and stomach. The distal duodenum, jejunum, or lower esophagus may be affected (Narayanan et al., 2018). Peptic ulcers are mostly caused by *Helicobacter pylori* infection and long-term use of nonsteroidal

*Correspondence to: Dr. Rituparna Ghosh, Department of Medicine, Columbia Center for Translational Immunology, Columbia University Medical Center, New York-10032
E-mail:rg3652@cumc.columbia.edu

anti-inflammatory medicines (NSAIDs), such as aspirin, naproxen, and ibuprofen. The spiral-shaped bacterium *H. pylori* grow in the stomach's acidic environment. It induces inflammation and leaves the tissue vulnerable to acid injury by upsetting the mucous layer that shields the stomach lining. NSAIDs make the stomach's mucous membrane less protective by preventing prostaglandins from being produced, which makes the stomach more susceptible to damage from acid (Chey et al., 2007).

Excessive alcohol intake, smoking, stress, and a diet heavy in spicy or acidic foods are further contributing factors. Ulcer formation can also be influenced by genetic susceptibility and specific medical diseases, such as Zollinger-Ellison syndrome, which results in elevated production of acid (Crooks et al.,2013). The mismatch between the digestive activity of pepsin and acid and the preventive mechanisms that prevent mucosal digestion is a fundamental paradigm for ulcer development. It is still unclear which abnormalities are most significant despite the fact that ulcer patients have numerous disruptions in the normal physiology of the stomach and duodenum. Individual differences may exist in the essential defect or the final common denominator of ulceration may result from numerous flaws together (Talley et al., 2005). *H. pylori* colonize almost half of the world's population. Typically, the organism is picked up in childhood and doesn't go away without treatment. A lower socioeconomic status, unhygienic environment, and crowded living quarters are risk factors for contracting the infection. *H. pylori* are more widespread in underdeveloped nations and among particular ethnic groups. The prevalence of *H. pylori* in people of all ages has decreased in the previous five years in the United States. However, there are disparities according to ethnicity: the non-Hispanic white population has a 30%infection incidence, whereas Mexican Americans have over 60% (Grad et al., 2012).

2. PATHOPHYSIOLOGY AND EPIDEMIOLOGY

Peptic ulcers can be classified into three etiologic groups: ulcers caused by *Helicobacter pylori* infection, ulcers caused by nonsteroidal anti-inflammatory medicines (NSAIDs), and ulcers caused by severe acid peptic hypersecretion in Zollinger-Ellison syndrome (Laine and Jensen,2012). This article will focus on *H. pylori*-related ulcers, which make up the biggest and least known component of ulcer illness. Although the epidemiologic and pathophysiologic characteristics of gastric and duodenal ulcers are similar, they differ greatly. Patients with duodenal ulcers typically have higher parietal cell mass and acid secretion, and their ulcers usually begin at a younger age. IO Patients with gastric ulcers either secrete normal amounts of acid or less, which is frequently linked to a weakened mucosal barrier. Nonetheless, certain stomach ulcers have the elevated acid secretion typical of duodenal ulcer illness and are linked to duodenal ulcers. These ulcers are typically located in the pyloric or distal antrum (Stanley et al., 2011). Depending on how serious they are, peptic ulcers can be classified as either acute or chronic. An injury or perforation that pierces the lamina muscularis mucosa but only affects the submucosa is a hallmark of an acute peptic ulcer (Sood and Muthuraman, 2009).

In the mucosal layer, *H. pylori* induce an inflammatory response that results in damage and degeneration of epithelial cells as well as neutrophils, lymphocytes, plasma cells, and macrophages. In most cases, the antrum experiences more severe gastritis, while the corpus experiences little to no inflammation. *H. pylori* should be checked on every patient who has been diagnosed with peptic ulcers. Testing can be done in both invasive and noninvasive ways. Of the noninvasive ways, the stool antigen test and the urea breath test are the more practical and accurate than serologic testing (Wang et al.,2010).

3. Normal Gastric Physiology

The stomach lining is shielded by a thick layer of bicarbonate and mucus from the stomach's own acid and digesting enzymes. This defensive system is made up of several important parts: (Fock et al., 2013)

Mucous Layer: Secreted by epithelial cells, it creates a neutral milieu at the epithelial surface by acting as a physical barrier to retain bicarbonate ions.

Secretion of Bicarbonate: This neutralizes acid that seeps into the mucus.

Epithelial Cell Renewal: The mucosal barrier's integrity is preserved by the epithelial cells' quick turnover.

Prostaglandins: These substances stimulate the creation of mucus and bicarbonate, improve blood flow to the mucosa, and aid in the healing of epithelial cells.

4. Mechanism of Peptic Ulcer Formation

Helicobacter pylori Infection

The gram-negative, spiral-shaped bacteria *H. pylori* inhabit the stomach mucosa. It plays a part in the development of peptic ulcers by multiple mechanisms:

- *Production of Urease: H. pylori* are the source of urease, an enzyme that breaks down urea into ammonia and bicarbonate. Because of this response, the bacterium is able to survive in the stomach's acidic environment by neutralizing the gastric acid surrounding it (Cryer and Feldman,1992).
- *Adhesion and Colonization:* The bacteria use adhesins to cling to stomach epithelial cells, forming colonies underneath the mucous membrane.
- *Inflammatory reaction:* By triggering the immune system, *H. pylori* cause a persistent inflammatory reaction. As a result, inflammatory cytokines such TNF-α, IL-1, and IL-6 are produced, damaging epithelial cells and rupturing the mucosal barrier.

*Correspondence to: Dr. Rituparna Ghosh, Department of Medicine, Columbia Center for Translational Immunology, Columbia University Medical Center, New York-10032
E-mail:rg3652@cumc.columbia.edu

- *Virulence Factors:* The bacteria secrete virulence factors (like Cag A) and cytotoxins (like Vac A), which further harm and modify the function of epithelial cells and cause mucosal injury and ulceration.

NSAID-Induced Ulcers

NSAID scan lead to ulcers by both local and systemic means.

• *Systemic Effects:* Cyclooxygenase (COX) enzymes, especially COX-1, are inhibited by NSAIDs and are essential for prostaglandin synthesis. Decreased mucosal blood flow, poor epithelial cell repair, and decreased mucus and bicarbonate production are all caused by reduced prostaglandin levels (Szabo et al., 1985).

• *Local Effects:* The stomach mucosa may become immediately irritated by NSAIDs. Because they are acidic, they can become trapped in the epithelial cells, where they can directly damage cells and increase mucosal permeability to hydrogen ions, which can further injure tissue.

Imbalance between Aggressive and Defensive Factors

Peptic ulcer etiology is caused by an imbalance between protective and damaging elements for the gastric mucosa:

• *Aggressive Factors:* If stomach acid and pepsin levels are not appropriately controlled, they have the ability to break down the mucosal lining. The harmful effects of these drugs are exacerbated by *H. pylori* infection and NSAID use.

• *Defensive Factors:* The mucosal defense system is made up of the formation of mucus and bicarbonate, sufficient blood flow, quick turnover of epithelial cells, and prostaglandin synthesis. Ulcer formation may result from any interference with these defense mechanisms (e.g., caused by NSAIDs or *H. pylori*) (Malfertheiner et al., 2017).

5. Mechanism of NSAID

NSAIDs also injure mucosa by inhibiting cyclooxygenase-1 (COX-1), an enzyme that is essential for the creation of prostaglandins. To preserve the mucosal barrier, prostaglandins boost mucosal blood flow, secrete more bicarbonate and mucus, and stop cell division. Whereas NSAIDs inhibit cyclooxygenase reversibly in a concentration-dependent manner, aspirin acetylates the enzyme and inhibits it irreversibly. The main pathophysiologic reaction associated with NSAID-induced damage is believed to be a decrease in blood flow (Somasundaram et al., 2000). There are two different isoforms of COX: COX-1 is mostly in charge of prostaglandin synthesis in the gastrointestinal tract, while COX-2 is in charge of prostaglandin synthesis at sites of inflammation. NSAIDs are categorized as non-selective since they inhibit both COX-1 and COX-2. Examples of NSAIDs are ibuprofen, naproxen, aspirin, and indomethacin. NSAIDs that are specific to COX-2, such celecoxib or rofecoxib, inhibit COX-2 without also inhibiting COX-1, which may make them safer for use in the gastrointestinal tract. Approximately 3-5% fewer patients undergoing endoscopic investigations experienced ulceration than those using standard NSAIDs, which have a 20–40% incidence. These patients are receiving COX-2 inhibitors. However, many COX-2 selective NSAIDs have been removed off the market after it was demonstrated that they increased the risk of heart disease (Masclee et al., 2014). Patients having a history of peptic ulcers or hemorrhage, those using steroids or anticoagulants concurrently, those over 65, and those taking high dosages or combinations of several NSAIDs (even low dose aspirin) are the most vulnerable to NSAID-induced ulcers. To avoid ulcers, the patients should begin treatment as soon as possible if they require more than one drug. Moreover, the risk of bleeding increases when using drugs such anticoagulants, corticosteroids, aldosterone antagonists, or selective serotonin reuptake inhibitors. Patients who take NSAIDs and have H. pylori also have a different clinical course when they are older and have more comorbidities. The American College of Gastroenterology's current guidelines advocate testing and treating for H. pylori before starting long-term NSAIDs. Testing may also be recommended for individuals using long-term low-dose aspirin (Chey et al., 2017). The interaction between H. pylori and NSAIDs is contentious. The accuracy of this figure has been questioned because off also negative H. pylori tests and unintentional (or underreported) NSAID intake. Approximately 25% of PUD cases are unrelated to H. pylori, NSAIDs, or aspirin (Kanno et al., 2015).

Pathophysiological Changes

Pathophysiological Changes in Ulcer Formation: These changes include severe pain and stomach aches, as well as abrupt bursts in the upper abdomen, which will affect daily living.

• *Epithelial Injury:* When epithelial cells are initially damaged, less mucus and bicarbonate are produced, which permits acid to reach deeper layers.

• *Inflammation:* Prolonged inflammation brought on by *H. pylori* or NSAIDs exacerbates mucosal damage and prolongs the cycle of harm and slowed recovery.

• *Necrosis and Ulceration:* Prolonged exposure to pepsin and acid causes the mucosal tissue to necrotize, which in turn causes ulcers to form. Necrotic debris, inflammatory cells, and granulation tissue are commonly found at the base of ulcers (Kuipers, 1997).

Complications

Reversal medications such vitamin K, fresh frozen plasma(FFP), prothrombin complex concentrates (PCC), or recombinant factor VII a should be taken into consideration as part of the therapy plan for patients who have coagulopathy brought on by warfarin. Nevertheless, due to their potential side effects, these medicines must be used carefully. For example, excessive vitamin K dosages may lengthen the time it takes to

*Correspondence to: Dr. Rituparna Ghosh, Department of Medicine, Columbia Center for Translational Immunology, Columbia University Medical Center, New York-10032
E-mail:rg3652@cumc.columbia.edu

reach therapeutic warfarin levels once bleeding has stopped and therapeutic anticoagulation needs to be resumed (for example, in the context of mechanical heart valves). Recombinant factor VII a carries a higher risk of thrombosis and is more costly than FFP. It also carries the potential of creating volume overload. Vitamin K cannot be used to counteract the effects of novel oral anticoagulants (NOACs), which are being used more often. While apixaban does not appear to have an elevated risk of GI bleeding, the NOACs rivaroxaban and dabigatran do when compared to warfarin (Lanas-GimenoandLanas,2017). To treat a NOAC overdose, activated charcoal can be administered within four hours of consumption. If dabigatran-related bleeding becomes life-threatening, hemodialysis and idarucizumab may be utilized. After hemostasis has been reached, anticoagulant and antiplatelet drugs can be resumed; the exact timing will depend on how urgently anticoagulation needs to be restored. Due to the increased risk of in-stent thrombosis, patients receiving dual antiplatelet therapy following the implantation of drug-eluting stents should refrain from quitting both medications. After hemostasis is reached, individuals taking aspirin for cardiovascular disease should continue taking it as soon as possible—between one and three days, or within seven days. Low molecular weight heparin is advised for patients with a high risk of thrombosis (such as those with a mechanical mitral valve), and sub-therapeutic warfarin levels should be observed (Lanas and Chan, 2017).

• *Hemorrhage:* Hematemesis, or blood in the vomit, or melena, or black, tarry stools, are two symptoms of gastrointestinal bleeding that can result from erosion into a blood artery.

• *Perforation:* A full-thickness ulcer has the potential to rupture the duodenum or stomach wall, resulting in the potentially fatal illness peritonitis.

• *Penetration:* An ulcer may penetrate nearby organs, including the pancreatic.

• *Gastric Outlet Obstruction:* The pylorus can become obstructed by persistent ulceration-related scarring and edema, which can lead to vomiting and weight loss.

If not appropriately managed, peptic ulcers can result in a number of significant consequences. Bleeding is one of the most frequent side effects. Bleeding happens when the ulcer erodes into a blood artery, which can result in severe blood loss, anemia, and symptoms like hematemesis (blood vomiting) or melena (black, tarry stools). Another serious side effect is perforation, which occurs when an ulcer tears a hole in the stomach or intestinal wall. This can cause peritonitis, an infection of the abdominal cavity that is life-threatening and necessitates emergency surgery. Additionally, ulcers have the ability to penetrate into other organs, such the pancreas, causing excruciating pain and inflammation. Chronic ulceration and its repair can also leave scars and swelling in its wake. These can lead to gastric outlet obstruction, which prevents food from passing through the digestive tract and causes symptoms including severe vomiting, bloating in the abdomen, and weight loss. Prompt management of peptic ulcers is essential to prevent these potentially fatal sequelae (Mani Senthil Kumar et al., 2012).

6. DIAGNOSIS

Peptic ulcer diagnosis requires a thorough process that includes a thorough medical history, a physical examination, and a number of diagnostic procedures. A medical professional will first take a complete medical history, paying particular attention to symptoms like heartburn, nausea, bloating, and abdominal discomfort, as well as any relevant lifestyle choices or medication use, especially with regard to NSAIDs (Talley et al., 2005). The physician may palpate the abdomen as part of the physical examination to feel for any signs of discomfort or complications, such as rebound or guarding tenderness, which can be indicators of peritonitis from a perforated ulcer. Important diagnostic procedures are essential for both determining the underlying causes of peptic ulcers and establishing their existence. The gold standard for peptic ulcer diagnosis is an esophagogastroduodenoscopy (EGD), or upper gastrointestinal endoscopy. In order to detect ulcers and take tissue samples, this treatment entails passing a flexible tube equipped with a camera via the mouth and immediately visualizing the esophagus, stomach, and duodenum. Biopsies can be used to test for *Helicobacter pylori* infection, which is a prevalent cause of ulcers, and help rule out cancer (Sachar et al., 2014).

H. pylori non-invasive testing is also crucial. These include stool antigen tests, which look for *H. pylori* proteins in feces, and the urea breath test, which measures carbon dioxide in the breath following consumption of a urea solution broken down by *H. pylori*. Antibody tests against *H. pylori* can be performed on blood samples, but their specificity is reduced since they are unable to differentiate between chronic and current infections. Barium swallow X-rays can be used when endoscopy is not immediately possible or necessary. In order to enable X-ray imaging, which can identify ulcers as filling defects or abnormalities in the mucosal lining, this entails eating a barium solution that coats the lining of the upper gastrointestinal tract (Villanueva et al., 2013).

Further laboratory tests can be used to determine whether there is hidden gastrointestinal bleeding or anemia, such as the fecal occult blood test (FOBT) and complete blood count (CBC). Examining the levels of pancreatic and liver enzymes can assist in ruling out additional possible reasons of stomach discomfort. In conclusion, endoscopy is the gold standard for identifying peptic ulcers. Other diagnostic techniques include patient history, physical examination, and specialized testing. It is imperative to test for *H. pylori*, and non-invasive techniques provide useful substitutes. For successful therapy to be implemented and problems to be avoided, a prompt and correct diagnosis is necessary (Behrman, 2005).

CONCLUSION

A serious gastrointestinal ailment called peptic ulcers is defined by the erosion of the lining of the stomach or duodenum as a

*Correspondence to: Dr. Rituparna Ghosh, Department of Medicine, Columbia Center for Translational Immunology, Columbia University Medical Center, New York-10032
E-mail:rg3652@cumc.columbia.edu

result of an unbalanced defense system against aggravating elements including stomach acid and Helicobacter pylori infection. Timely diagnosis and efficient treatment are crucial for symptom management and the avoidance of serious consequences such bleeding, perforation, and obstruction of the stomach outlet. Extensive diagnostic techniques, including as endoscopy and *H. pylori* tests, enable precise identification and customized treatment. Acid-suppressing drugs, lifestyle changes, and antibiotics for *H. pylori* are usually part of an effective treatment plan. A comprehensive approach to diagnosing and treating peptic ulcers improves patient outcomes and quality of life. PUD is a condition with a declining clinical burden as a result of a decrease in *H. pylori* infections, easier access to anti-secretory medication, and more prudent NSAID use. However, because of its persistently high lifetime frequency and wide range of clinical presentations, PUD must be recognized and treated appropriately in order to prevent and minimize serious sequelae. Strategies to take into account while considering PUD include testing for and treating *H. pylori*, reducing mucosal injury caused by NSAIDs (by concomitant PPI prophylaxis or selecting COX-2 selective NSAIDs if available), and treating the infection. The most common complication in PUD bleeding management is resuscitation, anti-secretory therapy, endoscopy, and antithrombotic agent management. Thus, it's critical to research this vital subject and discover alternative, more effective treatments and preventions for peptic ulcer illness.

Acknowledgments

The authors are highly thankful to the Department of Medicine, Columbia Center for Translational Immunology, New York. The author also declares that no funds or grants were received during the preparation of this article.

Conflict of interest

All authors declare that there are no conflicts of interest.

Data availability statement

No data was used for the research described in the article.

Author's contribution

Rituparna Ghosh (RG) participated in the conception of the study. Ayan Sengupta (AS) participated in literature searches and extraction. AS wrote the manuscript and RG approved the final version for submission to this journal.

REFERENCES

Behrman S. W. (2005). Management of complicated peptic ulcer disease. Archives of surgery (Chicago, Ill. : 1960), 140(2), 201–208.

Chey, W. D., Leontia dis, G.I., Howden, C. W.,& Moss, S. F. (2017). ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. The American journal of gastroenterology, 112(2), 212–239.

Chey, W. D., Wong, B. C., & Practice Parameters Committee of the American College of Gastroenterology (2007). American College of Gastroenterology guideline on the management of Helicobacter pylori infection. The American journal of gastroenterology, 102(8), 1808–1825.

Crooks, C. J., West, J., & Card, T. R. (2013). Comorbidities affect risk of nonvariceal upper gastrointestinal bleeding. Gastroenterology, 144(7), 1384–e19.

Cryer, B., & Feldman, M. (1992). Effects of nonsteroidal anti-inflammatory drugs on endogenous gastrointestinal prostaglandins and therapeutic strategies for prevention and treatment of nonsteroidal anti-inflammatory drug-induced damage. Archives ofinternalmedicine,152(6),1145–1155.

Feldman, M., Friedman, L. S., & Brandt, L. J. Sleisenger and Fordtran's gastrointestinal and liver disease: pathophysiology/diagnosis/management. Tenth edition ed. 2 volumes. Philadelphia, PA: Saunders/Elsevier; 2016.p. xxxi.p.2369.p. 2389.

Fock, K. M., Graham, D. Y., & Malfertheiner, P. (2013). Helicobacter pylori research: historical insights and future directions. Nature reviews. Gastroenterology &hepatology, 10(8), 495–500.

Grad, Y. H., Lipsitch, M., & Aiello, A. E. (2012). Secular trends in Helicobacter pylori seroprevalence in adults in the United States: evidence for sustained race/ethnic disparities. American journal of epidemiology, 175(1), 54–59.

Kanno, T., Iijima, K., Koike, T., Abe, Y., Shimada, N., Hoshi, T., Sano, N., Ohyauchi, M., Ito, H., Atsumi, T., Konishi, H., Asonuma, S., & Shimosegawa, T. (2015). Accommodation in a refugee shelter as a risk factor for peptic ulcer bleeding after the Great East Japan Earthquake: a case-control studyof329 patients. Journal of gastroenterology, 50(1), 31–40.

Kuipers E. J. (1997). Helicobacter pylori and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer. Alimentary pharmacology & therapeutics, 11 Suppl 1, 71–88.

Laine, L., & Jensen, D. M. (2012). Management of patients with ulcer bleeding. The American journal of gastroenterology, 107(3), 345–361.

Lanas, A., & Chan, F. K. L. (2017). Peptic ulcer disease. Lancet (London, England), 390(10094), 613–624.

Lanas-Gimeno, A., & Lanas, A. (2017). Risk of gastrointestinal bleeding during anticoagulant treatment. Expert opinion on drug safety, 16(6), 673–685.

*Correspondence to: Dr. Rituparna Ghosh, Department of Medicine, Columbia Center for Translational Immunology, Columbia University Medical Center, New York-10032
E-mail:rg3652@cumc.columbia.edu

Malfertheiner, P.,Megraud, F., O'Morain, C. A., Gisbert, J. P., Kuipers, E. J., Axon, A. T., Bazzoli, F., Gasbarrini, A., Atherton, J., Graham, D. Y., Hunt, R., Moayyedi, P., Rokkas, T., Rugge, M., Selgrad, M., Suerbaum, S., Sugano, K., El-Omar, E. M., & European Helicobacter and Microbiota Study Group and Consensus panel (2017). Management of Helicobacter pylori infection-the Maastricht V/ FlorenceConsensusReport.Gut,66(1),6–30.

Mani Senthil Kumar, K. T., Puia, Z., Samanta, S. K., Barik, R., Dutta, A., Gorain, B., Roy, D. K., Adhikari, D., Karmakar, S., & Sen, T. (2012). The Gastroprotective Role of Acanthusilicifolius- A Study to Unravel the Underlying Mechanism of Anti-Ulcer Activity. Scientia pharmaceutica, 80(3), 701–717.

Masclee, G.M., Valkhoff, V.E., Coloma, P.M., deRidder, M., Romio, S., Schuemie, M. J., Herings, R., Gini, R., Mazzaglia, G., Picelli, G., Scotti,L., Pedersen,L., Kuipers, E. J., van der Lei, J., & Sturkenboom, M. C. (2014). Risk of upper gastrointestinal bleeding from different drug combinations. Gastroenterology, 147(4), 784–e14.

Narayanan, M., Reddy, K. M., & Marsicano, E. (2018). Peptic Ulcer Disease and Helicobacter pylori infection. Missouri medicine, 115(3), 219–224.

Ramakrishnan, K., & Salinas, R. C. (2007). Peptic ulcer disease. American family physician, 76(7), 1005–1012.

Sachar, H., Vaidya, K., & Laine, L. (2014). Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: a systematic review and meta-analysis. JAMA internal medicine, 174(11), 1755–1762.

Somasundaram, S., Sigthorsson, G., Simpson, R. J., Watts, J., Jacob, M., Tavares, I.A., Rafi, S., Roseth, A., Foster, R., Price, A. B., Wrigglesworth, J. M., & Bjarnason, I. (2000). Uncoupling of intestinal mitochondrial oxidative phosphorylation and inhibition of cyclooxygenase are required for the development of NSAID-enteropathy in the rat. Alimentary pharmacology & therapeutics, 14(5), 639– 650.

Sonnenberg, A., & Everhart, J. E. (1996). The prevalence of self-reported peptic ulcer in the United States. American journal of public health, 86(2), 200–205.

Sood, S., & Muthuraman, A. (2009). Activity oftacrolimus: an immunosuppressant, in pyloric ligation- induced peptic ulcer in the rat. Yakugaku zasshi : Journal of the Pharmaceutical Society of Japan, 129(12), 1523– 1528.

Stanley, A.J., Dalton, H.R., Blatchford, O., Ashley, D., Mowat, C., Cahill, A., Gaya, D. R., Thompson, E., Warshow, U., Hare, N., Groome, M., Benson, G.,& Murray, W.(2011). Multicentre comparison of the Glasgow Blatch ford and Rockall Scores in the prediction of clinical end-points after upper gastrointestinal haemorrhage. Alimentary pharmacology & therapeutics, 34(4), 470–475.

Szabo, S., Trier, J. S., Brown, A., & Schnoor, J. (1985). Early vascular injury and increased vascular permeability in gastric mucosal injury caused by ethanol in the rat. Gastroenterology, 88(1 Pt 2), 228–236.

Talley, N. J., Vakil, N. B., & Moayyedi, P. (2005). American gastroenterological association technical review on the evaluation of dyspepsia. Gastroenterology, 129(5), 1756–1780.

Villanueva, C., Colomo, A., Bosch, A., Concepción, M., Hernandez-Gea, V., Aracil, C., Graupera, I., Poca, M., Alvarez-Urturi, C., Gordillo, J., Guarner-Argente, C., Santaló, M., Muñiz, E., & Guarner, C. (2013). Transfusion strategies for acute upper gastrointestinal bleeding. The New England journal of medicine, 368(1), 11–21.

Wang, C.H., Ma, M. H., Chou, H.C., Yen, Z.S., Yang, C. W., Fang, C. C., & Chen, S. C. (2010). High-dose vs non-high-dose proton pump inhibitors after endoscopic treatment in patients with bleeding peptic ulcer: a systematic review and meta-analysis of randomized controlled trials. Archives of internal medicine, 170(9), 751–758.

*Correspondence to: Dr. Rituparna Ghosh, Department of Medicine, Columbia Center for Translational Immunology, Columbia University Medical Center, New York-10032
E-mail:rg3652@cumc.columbia.edu