Peptic Ulcer Disease

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Definition

A **peptic ulcer** is a mucosal defect that has a diameter of at least 0.5 cm that penetrates the muscularis mucosae. Gastric and duodenal ulcers usually occur in an area of inflamed mucosa.

Peptic Ulcer Disease location

- Gastric ulcers are mainly located along the lesser curvature.
- Duodenal ulcers usually are located on the anterior or posterior wall of the duodenal bulb, occasionally at both sites (“kissing” ulcers).
- Anastomotic ulcer; ulceration at the gastroduodenal anastomosis.
- Other peptic ulcers can occur at sites of metaplastic or heterotopic gastric mucosa, for example, in Meckel's diverticulum, the rectum, or Barrett's esophagus.

Epidemiology

- The incidence of gastroduodenal ulcer is 1 - 2 per 1000.
- Two thirds of patients with ulcers are male.
- The disease is more common in smokers.
- PU is strongly related to ***H. pylori*** gastritis and duodenitis.
- Duodenal ulcers occur more frequently than gastric ulcers.
- The predominant age at which duodenal ulcers occur is between 20 and 50 years, whereas gastric ulcers most commonly occur in patients more than 40 years old.
- The epidemiology has shown secular variations.
- The risk of recurrent disease after initial healing is high.
- Removal of the underlying cause/causes of the ulcer can prevent nearly all ulcer recurrences.

Pathogenesis of Ulcers

Therapy is directed at enhancing host defense or eliminating aggressive factors; i.e., H. pylori.

Aggressive Factors

- Acid, pepsin
- Bile salts
- Drugs (NSAIDs)
- H. pylori

Defensive Factors

- Mucus, bicarbonate layer
- Blood flow, cell renewal
- Prostaglandins
- Phospholipid

Pathobiology

- **Helicobacter pylori**
- Most peptic ulcers are associated **with *H. pylori* colonization**
- The association between ***H. pylori*** colonization and ulcer disease is reported to be 85% of patients with gastric ulcer and 95% of patients with duodenal ulcer disease.
- Most persons who are ***H. pylori*** positive do not develop ulcer disease.
- The estimated risk for the development of ulcer disease during persistent ***H. pylori*** colonization is 5 to 15%, that is, 3-8 folds higher than the risk for patients who are ***H. pylori*** negative.

Pathobiology

- Helicobacter pylori cont
- The risk for development of an ulcer in the presence of ***H. pylori*** is determined by a combination of host and bacteria-related factors.
- Host factors include
  - Stress.
  - Smoking.
  - Immune response.
- Bacterial factors that increase the risk of ulcer include
  - Enhanced adherence.
  - High production of cytotoxin.
  - Other factors

Pathobiology

- **NSAIDs and Aspirin**
- NSAIDs are common causes of gastroduodenal ulcer disease.
- ***H. pylori*** and NSAID use account in most series for 80 to 95% of cases of gastritis and ulcer disease.
- The risk of developing an ulcer during NSAID use is higher in patients who are more than 60 years old, in patients who had a previous ulcer, in patients who use corticosteroids or high-dose NSAIDs, and in patients with major comorbid diseases.
- In patients who use anticoagulants, such as warfarin, or who have severe comorbid disease, an NSAID-induced ulcer is more likely to lead to life-threatening gastroduodenal hemorrhage.
- Selective COX2 inhibitors are associated with fewer gastroduodenal ulcers.

Pathobiology

- **Idiopathic Acid Peptic Disease**
- ***H. pylori*** and NSAID use account in most series for 80 to 95% of cases of gastritis and ulcer disease.
- The remainder is often referred to as ***idiopathic*** or ***H. pylori–negative, non-NSAID*** acid peptic disease.
- Some ulcers in ***H. pylori***–positive patients were not caused by ***H. pylori.***
- In patients with idiopathic ulcer disease, specific clues to the underlying cause are often provided by the medical history, including comorbidity and drug use, the endoscopic appearance of the ulcer, and the histologic features of the ulcer's margins and surroundings. In most cases, these initial data can direct further diagnostic studies (Table 141-1).

TABLE 141-1 -- DIFFERENTIAL DIAGNOSIS OF PEPTIC ULCER DISEASE

Origin	Condition	Frequency	Diagnostic Test	Findings
Microbes	*Helicobacter pylori*	Very common	*Helicobacter pylori* tests	Bacteria, enzymes, antigens, antibodies
			Histology	Gastritis
	Helicobacter heilmannii	Rare	Histology	Spiral bacteria, gastritis
	Treponema pallidum	Very rare	Serology	Antibodies
	Mycobacterial infection	Very rare	Histology, immune response testing, chest radiograph	Acid-fast bacteria, granuloma, immune response
	Cytomegalovirus, herpes simplex virus type 1	Rare	Histology, serology	Virus inclusions, antibodies
Drug use	Nonsteroidal anti-inflammatory drugs/aspirin	Very common	History, urine test	Nonsteroidal anti-inflammatory drug use
	Bisphosphonates	Rare	History	Bisphosphonate use
	Corticosteroids	Rare	History	Corticosteroid use, comorbidity
	Amphetamines/cocaine	Rare	History, drug testing	Drug use
Malignancy	Gastric cancer	Common	Histology	Malignancy
	Duodenal cancer	Rare	Histology	Malignancy
	Pancreatic cancer	Common	Histology, computed tomography	Malignancy
	Mucosa-associated lymphoid tissue lymphoma	Rare	Histology	Malignancy
	Metastatic cancer	Rare	Histology	Malignancy
Gastritis syndromes	Eosinophilic gastritis	Rare	Histology	Eosinophilic infiltration
	Lymphocytic gastritis	Rare	Histology, celiac disease screening	Lymphocytic infiltration, villous atrophy
Hyperacidic syndromes	Zollinger-Ellison syndrome	Rare	Serum gastrin, secretin test	Extreme hypergastrinemia, positive

TABLE 141-1 -- DIFFERENTIAL DIAGNOSIS OF PEPTIC ULCER DISEASE

Origin	Condition	Frequency	Diagnostic Test	Findings
	Antral G-cell hyperfunction	Very rare	Serum gastrin, secretin test	Moderate hypergastrinemia, negative secretin test
	Retained gastric antrum	Very rare	Medical history, gastrin	Billroth II resection, hypergastrinemia
	Systemic mastocytosis	Very rare	Histology of affected sites	Mast cell infiltration
	Chronic myelogenous leukemia	Very rare	Leukemia evaluation	Leukemia
Ischemia	Mesenteric vascular occlusion	Common	Angiography	Vascular disease
	Polycythemia vera	Rare	Blood counts	Polycythemia
Specific ulcer types	Cameron's ulcer	Common	Endoscopy	Ulcer in large hiatus hernia
	Marginal ulcer	Common	Endoscopy	Ulcer at anastomosis
Systemic inflammation	Crohn's disease	Common	Histology, ileocolonoscopy	Inflammation, granulomas
	Vasculitides	Rare	Histology, systemic evaluation	Vasculitis, signs of systemic disease
	Gastric amyloidosis	Very rare	Histology	Amyloid deposition
Other conditions	Stress ulcer	Fairly common in patients in intensive care units	Endoscopy	—
	Radiation therapy/chemotherapy	Rare	Endoscopy, history	—

Pathobiology

- **Other Drugs**
- Oral bisphosphonates is complicated by ulceration in 3 to 10% of treated patients.
- Although corticosteroid treatment also can be complicated by peptic ulcer disease, the relative risk is only slightly increased, except in;
  - Serious comorbid diseases.
  - long-term therapy or high-dose therapy.
  - Prior ulcers.
- Other patients who use corticosteroids are not at serious risk for ulcer disease and therefore do not require measures to prevent ulcers.
- Chemotherapy and Radiation therapy can be complicated by ulcer disease.

Clinical Manifestations

- The typical presentation of acid peptic disease is with recurrent episodes of pain.
- The pain is almost invariably located in the epigastrium and may radiate to the back or, less commonly, to the thorax or other regions of the abdomen.
- Some patients describe the pain as burning or piercing, whereas others describe it as an uncomfortable feeling of emptiness of the stomach, referred to as ***painful hunger.***
- Indeed, the pain may improve with ingestion of food, only to return in the postprandial period.
- The timing of the pain in relation to meals and the soothing effects of food, however, are quite nonspecific and may also occur in patients with functional dyspepsia without ulcer.
- Nocturnal epigastric pain that awakens patients several hours after a late meal is more likely to represent ulcer pain.

Clinical Manifestations

TABLE 142-1 -- KEY SYMPTOMS AND SIGNS OF PEPTIC ULCER

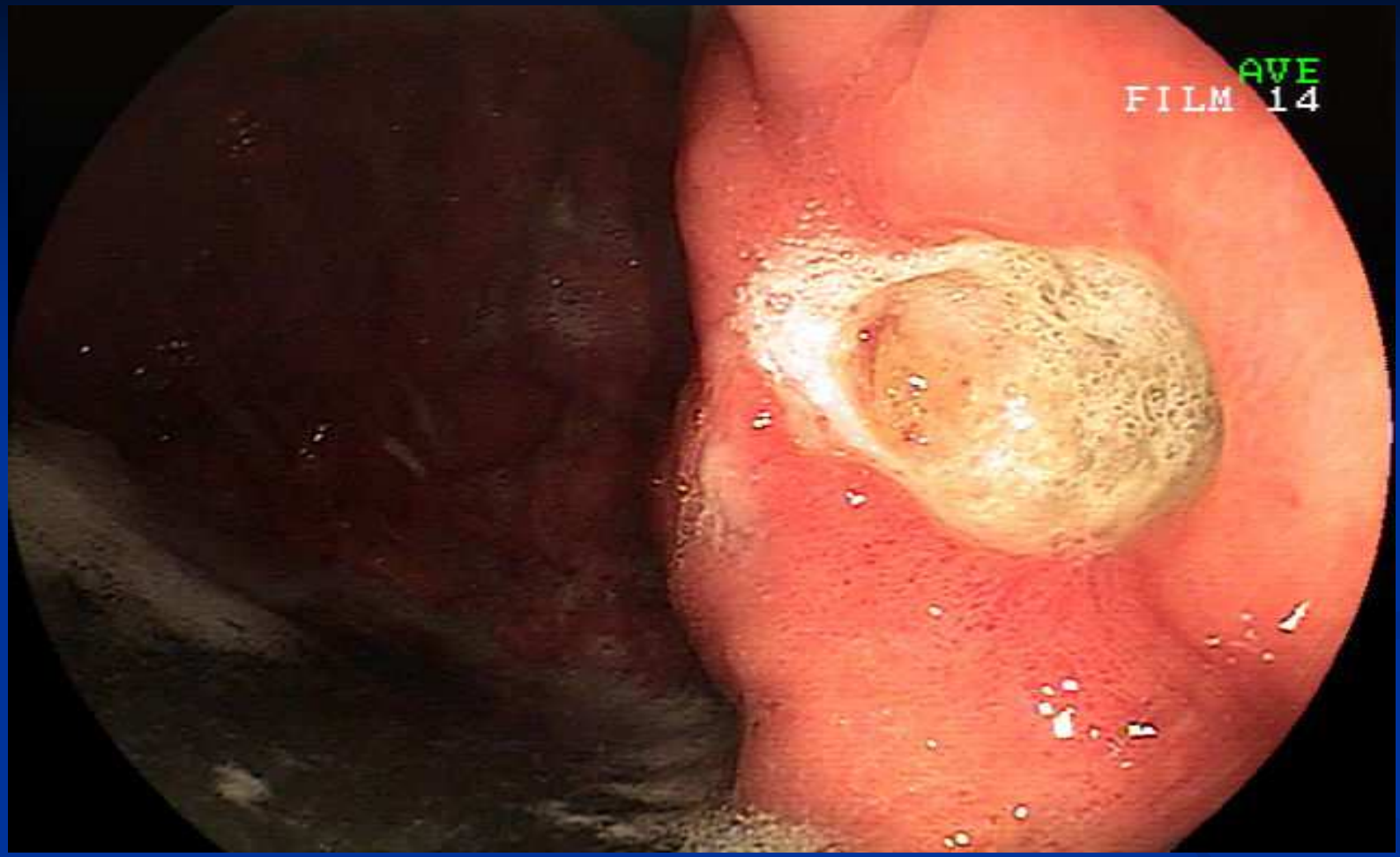
UNCOMPLICATED ULCER
No symptoms (“silent ulcer” up to 40%)
Epigastric pain
Pain may radiate to
Back
Thorax
Rest of abdomen (top most likely, bottom least likely)
Pain
Nocturnal
“Painful hunger”
Relieved by food
Continuous (top most specific, bottom least specific)
Nausea
Vomiting
Heartburn (mimics or associated with gastroesophageal reflex)

Clinical Manifestations

COMPLICATED ULCER
Acute perforation
Severe abdominal pain
Shock
Abdominal boardlike rigidity (and rebound and other signs of peritoneal irritation)
Free intraperitoneal air
Hemorrhea
Hematemesis and/or melena
Hemodynamic changes, anemia
Previous history of ulcer symptoms (80%)
Gastric outlet obstruction
Satiation, inability to ingest food, eructation
Nause, vomiting (and related disturbances)
Weight loss

Clinical Manifestations

- **Physical Examination**
- Physical examination is usually unrevealing.
- If significant bleeding has occurred, the patient may present with pallor or may even be hypovolemic.
- Ulcer-related bleeding may manifest not only very obviously in the form of hematemesis but also rather insidiously as melena.
- When a patient has acute perforation, severe epigastric and abdominal pain develop, the patient appears distressed. Characteristically, there is intense contracture of the abdominal muscles apparent on palpation, together with rebound and other signs of peritoneal irritation



EGD shows active gastric ulcer

Diagnosis

TABLE 142-2 -- DIAGNOSTIC PATHS AND TOOLS IN ULCER DISEASE

PATH 1	**MORPHOLOGIC DIAGNOSIS**
	Gastroduodenoscopy
	Barium contrast (inferior alternative)
	Endoscopic ultrasound (selected cases only)
	Computed tomography (useful in selected cases)
PATH 2	**ETIOLOGIC DIAGNOSIS**
	***HELICOBACTER PYLORI* TESTING**
	Histologic examination of gastric mucosa
	Stool antigen test
	Carbon-13–urea breath test
	Serum antibodies
	ULCER ASSOCIATED WITH NONSTEROIDAL ANTI-INFLAMMATORY DRUG USE
	History of drug ingestion
	Decreased platelet adherence
	Molecular identification (complex, expensive)
	ACID HYPERSECRETORY SYNDROMES
	Serum gastrin elevation
	Gastrin provocative tests (intravenous secretin, meal)
	Gastric analysis

Diagnosis

- **Differential Diagnosis**

  The differential diagnosis of ulcer-like symptoms includes many disorders of the upper abdominal organs, including;

- The differential diagnosis of upper abdominal symptoms includes liver and gallstone disease, and pancreatitis.
- Malignant diseases of the stomach , duodenum , pancreas , or bile ducts.
- "Nonulcer" or functional dyspepsia group,
- Gastro-esophageal reflux.
- GIT motility disorders.

Treatment

- **Helicobacter pylori Infection**
- ***H. pylori***–associated ulcers often heal spontaneously but frequently recur.
- Treatment for 14 days (Table 142-3) has about a 10% advantage over 7-day eradication therapy.
- After 4 weeks of acid suppressive therapy, more than 80% of ulcers will heal, and this number increases to more than 90% after 8 weeks of therapy.
- For patients in whom such therapy fails, a 4-to 10-day course of quadruple therapy is advised. This second-line regimen enables eradication of ***H. pylori*** in an additional 80 to 90% of patients.

Treatment

TABLE 142-3 -- OVERVIEW OF ANTIBIOTICS USED FOR *H. PYLORI* ERADICATION

Drug Class	Drug	Triple Therapy [*]	Quadruple Therapy [†]
Acid suppression	Proton pump inhibitor	20–40 mg bid [‡]	20–40 mg bid [‡]
Standard antimicrobials	Bismuth compound [§]	2 tablets bid	2 tablets bid
	Amoxicillin	1 g bid	—
	Metronidazole [ ]	500 mg bid	500 mg tid
	Clarithromycin	500 mg bid	—
	Tetracycline		500 mg qid
Salvage antimicrobials	Levofloxacin	300 mg bid	—
	Rifabutin	150 mg bid	—
	Furazolidone	100 mg bid	—

* Triple therapy consists of a proton pump inhibitor or bismuth compound, together with two of the listed antibiotics, usually given for 7 to 14 days.

† Quadruple therapy consists of a proton pump inhibitor plus a bismuth compound with two antibiotics as listed given for 4 to 10 days.

‡ Proton pump inhibitor dose equivalent to omeprazole 20 mg bid.

§ Bismuth subsalicylate or subcitrate.

Alternative = tinidazole, 500 mg bid. bid = twice daily; tid = three times daily.

Treatment

- **Disease Related to NSAID Use**
- The first step is to stop such therapy.
- Acid suppression with a PPI leads to healing of 85% of NSAID-induced gastric ulcers and more than 90% of duodenal ulcers within 8 weeks.
- Acid suppression with an H2-blocker, equivalent to ranitidine, 300 mg twice daily, heals 70% of ulcers within 7 weeks. The mucosal protective drug misoprostol has a similar effect.
- Patients need to continue the NSAID, a change to a COX2 inhibitor may be advantageous.
- Treatment must be continued for at least 8 weeks, and maintenance therapy is needed in patients who continue NSAID therapy.
- Gastric ulcers, larger lesions, and recurrent lesions heal more slowly.

Prognosis

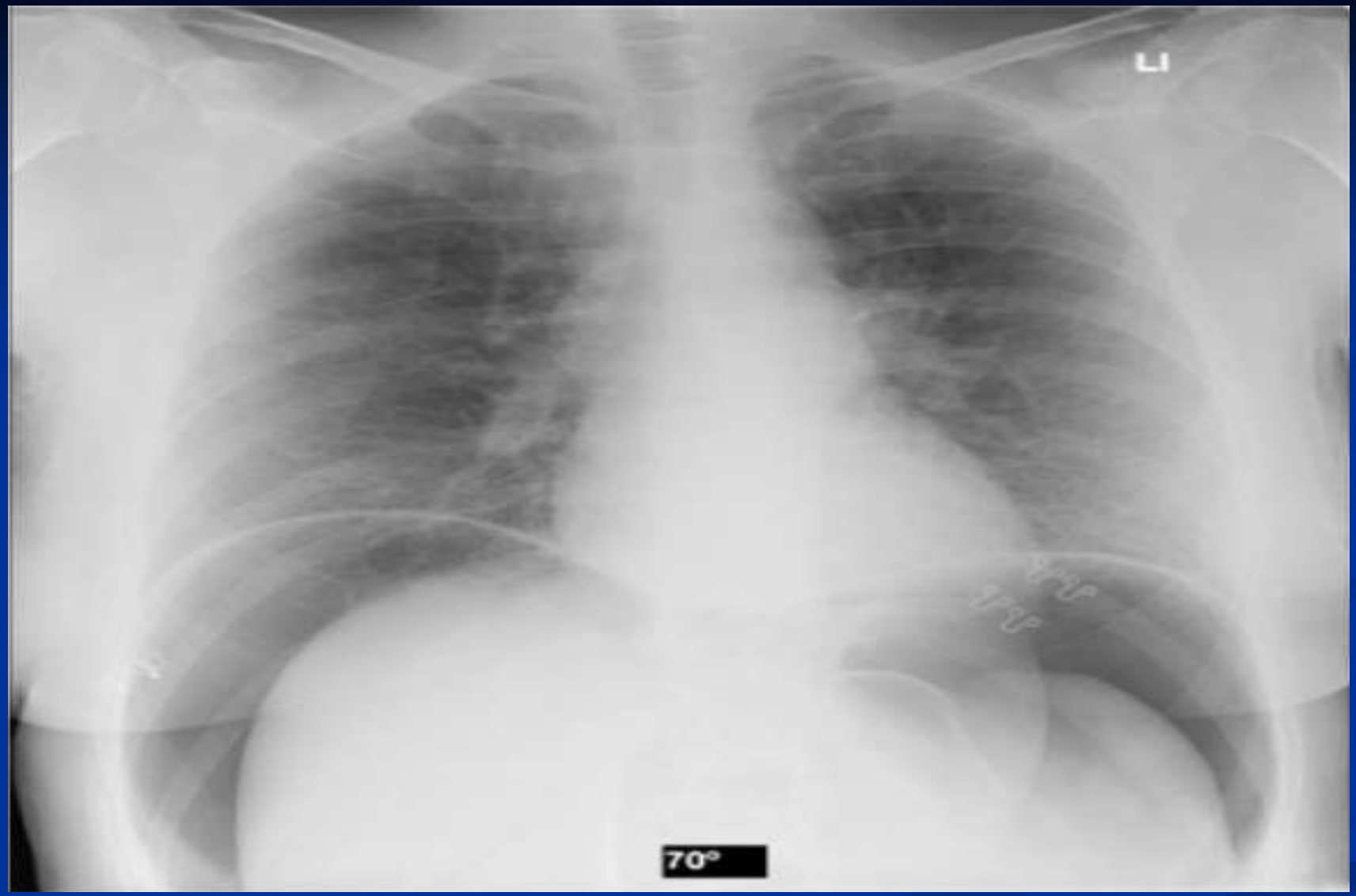
- Four major complications of ulcer disease are
  - Intractability.
  - Perforation.
  - Hemorrhage.
  - Stenosis.

Prognosis- *Intractability*

- ***Intractability*** is a term strictly applied to a patient with a persistent ulcer even after intensive and prolonged PPI therapy.
- These rare cases may result from poor compliance with recommended treatment, use of ulcerogenic drugs, or other diseases (e.g., Crohn's disease, ischemia, bacterial infection with a pathogen other than ***H. pylori,*** viral infections.
- **Other Causes of Acid Peptic Disease**
- Acid peptic disease related to alcohol or bisphosphonate should be addressed. Treatment of the Zollinger-Ellison syndrome requires high-dose PPIs and/or surgery. Crohn's disease, vasculitis sarcoidosis , polycythemia vera, amyloidosis and other rare causes of ulcer disease should be addressed by treating the underlying condition.

Complication-*Perforation*

- Acute perforation typically causes abrupt and severe abdominal pain, board like rigidity of the abdomen and other manifestations of peritoneal irritation. Hemodynamic shock is common.
- The clinical diagnosis can be confirmed in approximately 80% of patients by a plain abdominal radiograph. CT scan can be obtained if doubt persists. Leukocytosis develops rapidly.
- Treatment should begin by
  - Prophylactic antibiotics.
  - Nasogastric suction is helpful.
  - Correcting hemodynamic, fluid, and electrolyte imbalances.
- Emergency surgery is usually indicated.
- Due to longterm cure of ulcer disease through the eradication of ***H. pylori*** and the withdrawal of NSAIDs, suturing of the perforated ulcer may be adequate to avoid a more radical vagotomy with or without gastric resection.



Perforated peptic ulcer. Radiography shows free air under diaphragm

Complication- *Hemorrhage*

- Hemorrhage may manifest either as a serious acute event associated with hemodynamic shock and high mortality or as a slow or intermittent blood loss leading to chronic anemia.
- Rapid bleeding is usually apparent on the basis of clinical signs (pallor, systolic blood pressure <90 mm Hg, pulse >100/minute), and fluids and transfusions are indicated to prevent circulatory collapse.
- Intravenous PPIs in the acute phase is associated with reduced rebleeding, less need for blood transfusion and surgical intervention, and lower mortality rates.
- Once the patient is stabilized, EGD should be performed .
- Endoscopic techniques for hemostasis include
  - Thermal method –coagulation.
  - Injection sclerotherapy.
  - Mechanical compression with clips.

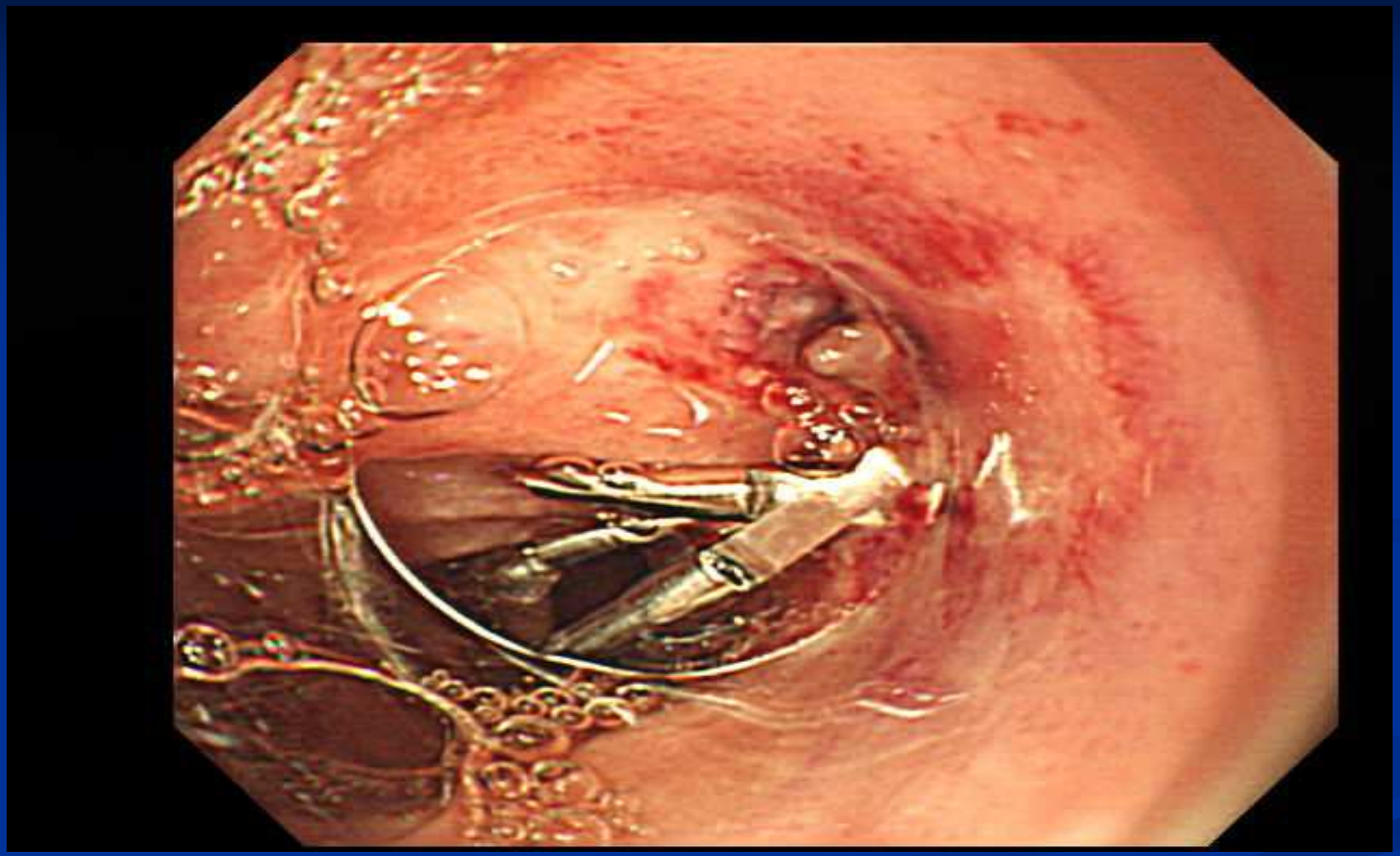
Complication- *Hemorrhage*

- If endoscopic therapy to stop bleeding is failed, surgical intervention should be considered.
- Management of patients who recover after a PU hemorrhage is similar to the treatment of patients with ordinary ulcers.

TABLE 142-4 -- ENDOSCOPY RESULTS IN PATIENTS WITH BLEEDING ULCERS [*]

Endoscopy Result	Ulcer Characteristics	Risk of Recurrent Bleeding (%)
Active bleeding	Arterial bleeding	80–90
	Oozing bleeding	10–30
Stigmata of recent bleeding	Nonbleeding visible vessel	50–60
	Adherent clot	25–35
	Flat pigmented spot	0–8
No signs of bleeding	Clean ulcer base	0–12

* The ulcer characteristics determine the risk of recurrent bleeding during follow-up.



Endoscopic hemostasis with clips for active duodenal ulcer complicated with bleeding

Complication- *Stenosis*

- ***Gastric outlet obstruction*** is now a rare complication.
- Most patients who develop clinically relevant gastric outlet obstruction have had an ulcer in the duodenal bulb and/or pyloric channel.
- Edema and inflammation play an important role, and occasionally a patient with active disease presents with symptoms of outlet obstruction as manifested by nausea, vomiting, and gastric stasis without a tight, chronic stenosis.
- Management therefore should involve three key steps:
  - **1.** Nasogastric tube aspiration and gastric lavage followed by early EGD.
  - **2.** Intense antisecretory therapy using intravenous PPIs.
  - **3.** Treatment of underlying ulcer disease.
- Tight, fibrous scarring may require endoscopic balloon dilation or surgical intervention.

Thank you