COX-2–specific inhibitors. According to available evidence, PPIs are superior to H_2 receptor antagonists in preventing gastroduodenal ulceration and improving dyspeptic symptoms during continued NSAID use. Similarly, PPIs provide protection against endoscopic NSAID ulcers at a rate at least comparable with that of misoprostol, with fewer associated GI symptoms. However, misoprostol, but not PPIs, has been shown in a prospective analysis to decrease the prevalence of ulcer complications.

COX-2–specific inhibitors (e.g., celecoxib, rofecoxib, valdecoxib) have suggested an improved GI safety profile with reduced incidence of ulcers and ulcer complications and at least similar effectiveness when compared with traditional NSAIDs. However, recent evidence suggesting an increased risk for cardiovascular events, specifically myocardial infarctions and strokes, associated with the use of selective COX-2 inhibitors, has led to significant public concern with subsequent market withdrawal of some of these agents and restricted use of others. These adverse effects are thought to be related, at least in part, to the inhibition of prostacyclin with the resultant unopposed *thrombogenic* effects of thromboxane A_2. Concern over this issue led to the withdrawal of rofecoxib and valdecoxib from the US market in 2005. Recommendations for the use of nonselective NSAID versus celecoxib and the use of either PPI or misoprostol involve risk stratification of the patient's cardiovascular risk and GI risk by the clinician.

More recent meta-analyses have suggested that concomitant *H. pylori* infection and NSAID use increase the risk for ulcer complications. Therefore, in patients who require chronic NSAID use, the current recommendation is to test for and eradicate *H. pylori*, given that it is a treatable risk factor.

Surgery

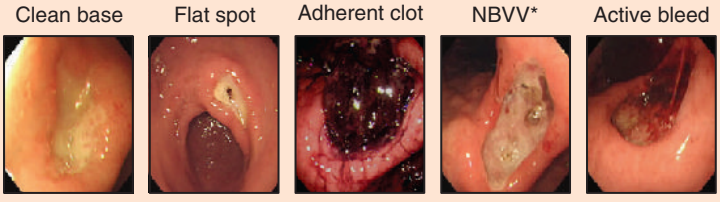
Because of the remarkable progress in pharmacologic acid suppression therapy and the recognition that ulcer disease can be cured by eliminating *H. pylori* infection and NSAIDs, surgery now plays a marginal role in treating uncomplicated PUD. Surgical intervention is now mostly reserved for managing the complications of peptic ulcers, especially gastric outlet obstruction and perforation. Some of the different surgical approaches are shown in Figure 36-7.

Complications of Peptic Ulcer Disease

Bleeding

PUD is the leading cause of upper GI bleeding, accounting for about 50% of cases and more than 150,000 hospital admissions annually in the United States. Although bleeding ceases spontaneously in 80% of patients, the mortality rate associated with bleeding ulcers is 5% to 10%. Patients with bleeding ulcers exhibit hematemesis, melena, or hematochezia, often without abdominal pain. The major risk factor for bleeding ulcers is NSAID use. Predictors for an adverse outcome include hemodynamic instability at presentation, bright red blood from the rectum or through the nasogastric tube, age older than 60 years, ongoing transfusion requirements, and an increasing number of underlying medical illnesses. All patients with upper GI bleeding should undergo early upper endoscopic examination, which allows for both therapeutic intervention and the determination of other predictors for rebleeding. Rebleeding rates are about 5% for clean-based ulcers, 10% for ulcers with flat spots, 22% for adherent clots, 43% for nonbleeding visible vessels, and 55% for active oozing or spurting from an ulcer (Fig. 36-8). Patients with large ulcers, greater than 1 to 2 cm in diameter, also have increased rebleeding and mortality rates. Endoscopic therapy with techniques such as multipolar or thermal coagulation, injection with epinephrine, or placement of hemostatic clips, clearly improves the outcome in patients with bleeding ulcers by decreasing mortality, length of hospital stay, number of blood transfusions, and need for emergency surgery.

Because most ulcer bleeding recurs within 3 days of initial presentation, patients with active bleeding or stigmata of hemorrhage, such as raised pigmented spots in an ulcer crater, can be discharged within 2 to 3 days if they are stable. Given the excellent prognosis for patients with clean-based ulcers, discharge within 24 hours of presentation or immediately after endoscopic examination appears to be safe. About 20% of patients rebleed after endoscopic therapy, and 50% of these can be successfully retreated. The remainder may be treated angiographically with either intra-arterial vasopressin or embolization techniques. Surgery is generally reserved for instances in which all other measures have failed. Although endoscopic therapy is the first treatment modality in the management of actively bleeding gastroduodenal ulcers, some evidence also suggests that adjuvant use of acid suppression therapy can reduce recurrent bleeding after initial endoscopic control. A continuous infusion of an intravenous PPI has been shown to reduce the incidence of recurrent ulcer hemorrhage following endoscopic therapy. Thus, patients with significant upper GI bleeding in whom a peptic ulcer is suggested should be treated with an intravenous PPI using a loading dose (80 mg of pantoprazole) followed by a continuous infusion (8 mg per hour of pantoprazole). If at the time of endoscopic



	Clean base	Flat spot	Adherent clot	NBVV*	Active bleed
Prevalence (%)	42	20	17	17	18
Rebleeding risk (%)	5	10	22	43	55

*Nonbleeding visible vessel

FIGURE 36-7 Operations for peptic ulcer disease.